

AN ABSTRACT OF THE THESIS OF

Larry Lee Hutchinson for the degree of DOCTOR OF PHILOSOPHY
in CHEMISTRY presented on September 21, 1976

Title: RADICAL ANIONS, RADICALS AND ANIONS. THE FORMA-
TION AND STEREOCHEMISTRY OF ALKYL LITHIUM
REAGENTS FROM LITHIUM 4, 4'-DI-TERT-BUTYLBIPHENYL
AND ALKYL HALIDES.

Abstract approved: Redacted for Privacy.
Peter K. Freeman

The reactions of alkyl halides with metals and radical anion solutions were investigated.

The reaction of exo- and endo-anti-3-chlorotricyclo[3.2.1.0^{2,4}]oct-6-ene with magnesium in THF followed by deuterolysis gave syn:anti deuteriation ratios of 2.2 and 0.42, respectively, with 85% monodeuterium incorporation. Analysis of the exo hydrocarbon involved epoxidation followed by a shift reagent study with Eu(fod)₃. Reaction of anti-3-chloro-exo-tricyclo[3.2.1.0^{2,4}]octane with lithium naphthalene dianion proceeded at -78° in THF with a rate constant of $5.5 \times 10^{-2} \text{ M}^{-1} \text{ min}^{-1}$, while under identical conditions lithium naphthalene exhibited a rate constant of $1.0 \text{ M}^{-1} \text{ min}^{-1}$. Deuterolysis of the dianion solution gave a syn to anti deuterium incorporation greater than 50. In contrast, 7-chloronorcarane in reacting with

lithium naphthalene in THF at -78° exhibited a rate constant of $0.035 \text{ M}^{-1} \text{ min}^{-1}$. Deuterolysis of the dianion solution gave a syn to anti deuterium incorporation greater than 50. In contrast, 7-chloro-norcaradiene in reacting with lithium naphthalene in THF at -78° exhibited a rate constant of $0.035 \text{ M}^{-1} \text{ min}^{-1}$ for the anti compound while the syn had a rate constant of 0.063. Upon deuterolysis, the deuterium incorporation was 75%, with an anti:syn ratio of 7.

Reaction of sodium or lithium naphthalene with MgBr_2 in THF gave a dark precipitate with properties expected for magnesium metal. Reaction of sodium anthracene with magnesium bromide in THF, or reaction of magnesium metals with anthracene in THF gave a yellow solution of the sparingly soluble magnesium anthracene dianion. Purification and crystallization gave an orange crystalline solid with a composition of $\text{MgA} \cdot 3\text{THF}$. Single crystal X-ray analysis indicated the unit cell to be triclinic with a volume of 4668 \AA^3 .

The reactions of a wide variety of alkyl halides with lithium naphthalene (N), biphenyl (B), di-tert-butylnaphthalene (DTBN) and 4,4'-di-tert-butylbiphenyl (DTBB) in THF were investigated. The reaction of LiDTBB with primary, secondary, tertiary and cyclopropyl halides in THF at -78° gave 90% or higher yields of the corresponding lithium reagent. LiDTBB was found to give less than 3% alkylation products with halides and reacted with CO_2 to give a 97%

recovery of DTBB, behaving in almost all respects as a solution of lithium metal in THF.

The stereochemistry of the product lithium reagents from the reaction of a number of alkyl halides in THF at -78° was investigated. The stereochemistry of the products from the reaction of cyclopropyl halides and LiDTBB was interpreted as being an exact copy of the radical stereochemistry. The reaction of syn- or anti-7-chloronorcarane gave an anti:syn lithium incorporation of 10, as determined by metal halogen exchange with 1,2-dibromoethane. Similarly, anti-3-chloro-exo-tricyclo[3, 3. 1. 0^{2, 4}] octane gave a ratio of syn-Li to anti-Li of 200. Reaction of anti-7-bromo-7-methylnorcarane with LiDTBB gave an anti-Li to syn-Li ratio of 3 as determined by gc.

The stereochemistry of the reaction of non-cyclopropyl secondary halides with LiDTBB was interpreted in terms of a mapping of the vibrational structure of the radicals upon the potential energy surface of the corresponding anion. For significantly pyramidal radicals this is the radical equilibrium. Reaction of syn-7-bromonorbornene gave an anti-Li:syn-Li of 3.8. The lithium reagents were shown to be configurationally stable at -78° in THF by preparation of the syn-Li compound by metal halogen exchange of the bromide with tert-butyllithium in THF at -50° , giving at least 95% retention. Lithium stereochemistry was determined by deuteriolysis followed by epoxidation and nmr shift reagent ($\text{Pr}(\text{fod})_3$) study.

Treatment of anti-7-chlorobenzonorbornadiene with LiDTBB was followed by deuterolysis. Analysis performed by hydroboration and $\text{Pr}(\text{fod})_3$ shift study indicated 99% deuterium incorporation with an anti:syn deuteration ratio of 1.33. Treatment of exo-2-chloronorbornane with LiDTBB followed by metal halogen exchange with 1,2-dibromoethane gave a 10:1 ratio of exo to endo bromine incorporation. Reaction of 4-chloro-tert-butylcyclohexane with LiDTBB followed by deuterolysis gave a 14:1 ratio of equatorial to axial deuterium incorporation as determined by ir.

Radical Anions, Radicals and Anions. The Formation and
Stereochemistry of Alkyl Lithium Reagents from Lithium
4, 4'-Di-tert-butylbiphenyl and Alkyl Halides.

by

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A THESIS

submitted to

Oregon State University

in partial fulfillment of
the requirements for the
degree of

Doctor of Philosophy

June 1977

APPROVED:

Redacted for Privacy

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Date thesis is presented _____ September 21, 1976

Typed by Clover Redfern for _____ Larry Lee Hutchinson

ACKNOWLEDGMENTS

I wish to sincerely thank Dr. Peter K. Freeman for his encouragement, guidance, patience and especially for the freedom he allowed on this research project.

Thanks are also due to Dr. Carroll W. DeKock for his assistance with the X-ray diffraction work and for the loan of the DeKock Soxhlet extractor. In addition I would like to thank my father for his moral and financial support and would like to acknowledge helpful discussions with Dr. Joseph W. Nibler, Karl E. Swenson and E. Philip Sietz.

Sincere appreciation is due to Kim Wise for the correction of my spelling and the typing of the rough draft.

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RADICAL ANIONS, RADICALS AND ANIONS. THE FORMATION
AND STEREOCHEMISTRY OF ALKYL LITHIUM REAGENTS
FROM LITHIUM 4, 4'-DI-TERT-BUTYLBIPHENYL AND
ALKYL HALIDES

HISTORICAL

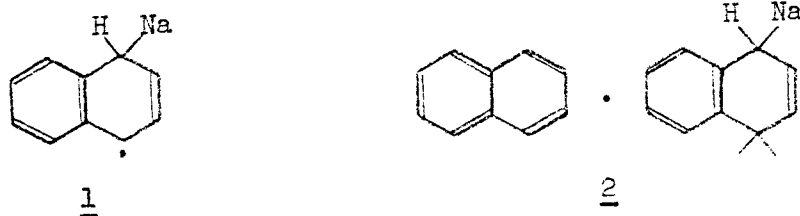
Physical Properties of Radical Anions

Radical anions are very simple species, consisting only of an aromatic hydrocarbon to which an electron has been added. The electron resides in the lowest previously unoccupied molecular orbital and is thus delocalized over the entire π framework of the molecule. It is a very simple matter to prepare radical anions--a rather different situation than exists with most of the commonly studied intermediates of organic chemistry; carbonium ions, carbenes, radicals, and anions. The addition of any alkali metal to any polycyclic aromatic hydrocarbon in an ether solvent of moderate cation solvating power under an inert atmosphere will result in rapid dissolution of the metal to form an intensely colored and usually paramagnetic solution.

The first reported formation of a radical anion may have appeared as long ago as 1867, when M. Berthelot (1) described the formation of a black addition product upon fusing potassium with naphthalene--with no solvent. The first true radical anion solutions, however, were prepared by Schlenk and Weikel in 1911 (2). The treatment of anthracene (among a variety of other organic compounds)

with sodium in diethyl ether gave rise to a blue solution. Naphthalene, however, gave no reaction. Twenty-five years later, Scott and co-workers (3) found that naphthalene and biphenyl would react rapidly with sodium if the solvent was either dimethyl ether or dimethoxyethane (DME) but only slowly in methyl ethyl ether. Either evaporation of the dimethyl ether or addition of large quantities of diethyl ether caused reversion to sodium and naphthalene.

The solutions were shown to conduct electrical current, but both this observation and the strong dependence upon the polarity of the solvent was lost upon the early workers, who continued to use such representations as (1) (Reference 4) and (2) (reference 5). The



radical nature of sodium naphthalene was demonstrated in 1953 by Weissman and co-workers by the observation of the esr spectrum of the ions in THF (6).

Since 1953, a wealth of information on the physical properties of aromatic radical anions and related species has been obtained via a variety of physical methods. Any attempt to cover all that is known about radical anions would fill many volumes. Consequently, in this

review only the properties of naphthalene, biphenyl, and anthracene radical anions and dianions which might be of use in the understanding of the reactions of such species with alkyl halides and radicals will be covered. Where data is available, additional emphasis will be placed on lithium as the counter ion, and the differences expected between sodium and lithium. For a recent review on the physical properties of radical anions and ketyls, see Reference 7.

The nature and kinetics of the reaction of radical anions depend greatly upon the identity of the aromatic hydrocarbon, the identity of the metal counter ion, the solvent, and the temperature. The effect of temperature is not necessarily 'the hotter, the faster'. Many instances exist where reactions proceed much more rapidly at lower temperatures than at higher temperatures.

The most important single property controlling the reactions of radical anions is the electron affinity of the parent hydrocarbon. Unfortunately, gas phase electron affinities tend to vary wildly from worker to worker and from method to method. For moderately recent compilations, see References 7, 8, 9, and 10. The most likely values for naphthalene and anthracene are 0.15 and 0.58 eV, respectively (8). More common and reliable means of determining affinities of aromatic hydrocarbons are polarography and potentiometric titration.

Potentiometric titration as developed by Hoijsink (11) and improved by Szwarc (12) involves addition of a standardized biphenyl

radical anion solution to a solution of the aromatic hydrocarbon under investigation while monitoring the voltage difference between the biphenyl solution and the hydrocarbon solution. Relative values obtained by the titration method parallel the values obtained from polarography even when the solvent chosen for the latter method is protic (13). This might have been expected, since the anions are large and diffuse and probably derive little stabilization from solvation.

The reduction potentials (relative solution electron affinities) for several aromatic hydrocarbons of interest in this thesis are presented in Table 1.

Table 1. Reduction potentials of selected aromatic hydrocarbons in DMF.

Compound	$E_{1/2}$ (volts) ^(a)	Reference
Naphthalene	-1.98	14
2, 6-Di- <u>tert</u> -butylnaphthalene	-2.07	14
2, 7-Di- <u>tert</u> -butylnaphthalene	-2.09	14
Biphenyl	-2.05	15
4, 4'-Di- <u>tert</u> -butylbiphenyl	-2.14 ^(b)	15
Anthracene	-1.46	

(a) Vs. Hg pool.

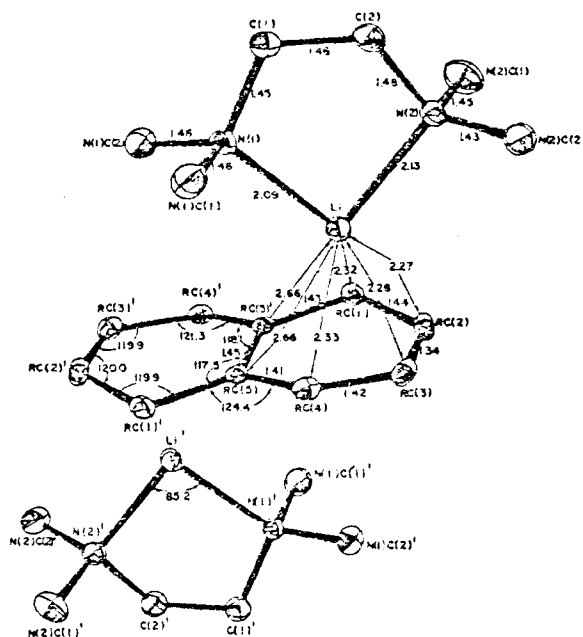
(b) Calculated from titration data for biphenyl vs. anthracene in HMPA (13).

Ion Pairing in Radical Anion Solvation

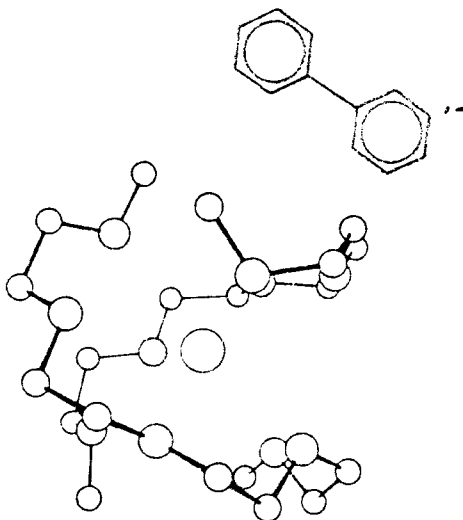
The effect of temperature and solvent on ion pairing and the effect of ion pairing on reaction rates and equilibria can cause some

very unusual results. As will be discussed, some reactions take place much faster at lower temperatures than at higher, and solutions can turn from green to purple to green again upon cooling. For recent reviews on ion pairing see References 16, 7, and 8.

For radical anions in ether solvents, there exists at least three thermodynamically distinct ionic species: contact, or tight ion pairs; solvent separated, or loose ion pairs; and free ions. Models of what contact ion pairs and loose ion pairs might look like have been recently provided by X-ray crystallography. The structure of the tetramethyl ethylenediamine (TMEDA) complex of lithium naphthalene dianion has been determined by Brooks, Rhine, and Stucky (17) and may serve as an example of a tight ion triple (or ion pair if one of the TMEDA-Li⁺ groups is ignored).



Recently, deBoer and co-workers have reported (18) the structure of a model solvent-separated ion pair --bis(tetraglyme) rubidium biphenyl. It is interesting that two tetraglyme molecules (tetra-ethylene glycol dimethyl ether) surround each rubidium with the ten oxygen atoms in a spherical shell (the large circle represents rubidium; the medium, oxygen; and the small, carbon).

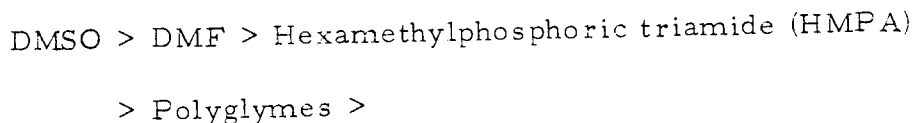


A solvent polarity order has been determined by Garst (19) from the spectral shifts of sodium benzophenone ketyl when measured in various solvents. The order is consistent with intuition and probably

Diglyme > DME > THF > MeTHF > Dioxane > Diethyl ether

represents accurately the cation solvating abilities of the solvents toward alkali metals, although dioxane and ether may occasionally be

reversed. To the above cation solvating order, one might include the following aprotic solvent order to the left side:



In THF and DME, the solvents most commonly used for radical anion reactions, the extent of ion pair dissociation to form free ions is very small (20, 21). Sodium radical anions in DME, and lithium radical anions in THF or DME exhibit a dissociation constant within a factor of three of 10^{-5} at all temperatures between $+25^{\circ}$ and -75° regardless of the nature of the aromatic hydrocarbon. The dissociation constants for sodium naphthalene, biphenyl, and anthracene in THF are all around 3×10^{-5} at -75° . At 25° , however, while anthracene had fallen by a factor of about 7, biphenyl had fallen by a factor of 35, and the dissociation constant of naphthalene had fallen by a factor of 260. This temperature dependence was interpreted in terms of naphthalene and biphenyl radical anions forming contact ion pairs in THF at the higher temperatures, but loose ion pairs at the lower temperatures. All others are solvent-separated (loose) under all conditions studied. It was also determined during these studies that the ionic sizes (including solvation sphere) of Li^{+} and Na^{+} are almost identical. The size of the ions in THF are larger than in DME and therefore loose ion pairs are tighter in DME than in THF even though

tight ion pairs have a greater tendency to form in THF than in DME. The ionic mobility data also show that, as expected, the anions are solvated only slightly.

In 1961, Atherton and Weissman (22) demonstrated that previously unexplained lines which had been observed in the esr spectrum of sodium naphthalene in THF arise from splitting due to the sodium nucleus. Two separate species were shown to exist--one which did not exhibit sodium splitting, and one which did. As the temperature was lowered to -70° , the species split by sodium disappeared, while in DME only the unsplit spectrum was seen at all temperatures. These workers postulated that the species giving rise to the esr spectrum which exhibited sodium splitting was an ion pair, while the other species was the free ion. The dissociation constants determined by this method were about ten times too large compared to the results from conductance measurements (21). Graceffa and Tuttle (23) have recently redetermined the dissociation constants by this method using rigorously purified sodium, and their values are compatible with the conductance-derived values. It was also assumed by Atherton and Weissman that the principal species in DME was the free ion. The conductance data, however, discounts this, leaving loose or solvent-separated ion pairs as the most probable species in solution.

In concordance with the esr work, Karasawa, Levin, and Szwarc (24) have determined the optical spectra of sodium biphenyl and

naphthalene over a wide temperature range. Their data indicates the presence of only contact ion pairs in tetrahydropyran (THP), only loose ion pairs in DME, and both forms in THF.

In 1972, Tuttle, Danner, and Graceffa (25) reported the results of a very interesting study involving the effect of added hydrocarbon solvents upon the esr spectrum of alkali metal-radical anion solutions. A rather large increase in the lithium hfc was observed when the mole fraction of THF in lithium naphthalene solutions was decreased by addition of pentane. A good fit between a proposed theory and experiment was obtained by assuming that only very little exchange of pentane for THF in the lithium solvent shell takes place over a wide range of bulk solvent composition--on the order of one-half molecule of THF out of perhaps 20 in the solvation sphere. From the temperature dependence of the lithium hfc, it is apparent that LiN exists mostly as solvent-separated ion pairs in THF at temperatures below 20°. Cesium and rubidium, on the other hand, apparently exist only as contact ion pairs, since their hfc's show little solvent or temperature dependence.

In a similar vein, Lee and co-workers (26) have detailed the results of studies involving the replacement of diethyl ether molecules with THF and the replacement of THP with DME by applying both spectrophotometric and esr techniques. The data indicate that, for sodium naphthalene in THP, the addition of DME to the contact ion

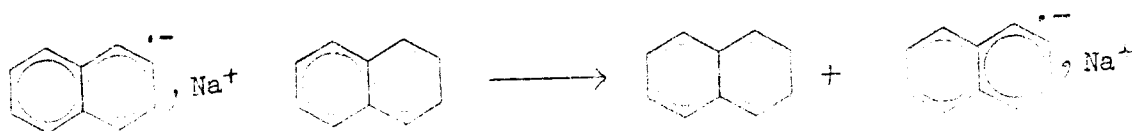
pairs (formed at all temperatures in THF) results in the replacement of only one THF molecule for each DME molecule. At the higher temperatures (room temperature), one or two THF molecules are displaced, but contact ion pairs are still the only form observed. At lower temperatures (-30°), solvent-separated ion pairs are formed with two DME molecules per sodium ion. Similar results were obtained with THF vs. diethyl ether, but with only contact ion pairs observed even at -90° unless a high concentration of THF is used (27). The addition of 0.1% tetraglyme to a dilute solution of sodium naphthalene in THF has been found to convert the contact ion pairs quantitatively into solvent-separated ones (28). From the esr data reported by Hirota (27), it is apparent that lithium naphthalene in diethyl ether exists only as contact ion pairs at all temperatures between -90° and $+20^{\circ}$. This, of course, is to be expected considering the low solvating ability of diethyl ether.

Takeshita and Hirota (29) have reported the results of their investigation of the alkali metal nmr of naphthalene radical anion solutions in a variety of solvents and over a wide temperature range. While the hyperfine splitting constants are about 0.2 gauss lower than the esr values, the overall conclusion in terms of ion pairing is the same. Sodium naphthalene in THF exists as contact ion pairs at room temperature, shifting to solvent-separated pairs at lower temperatures (ca. -40°). Lithium naphthalene in THF and sodium naphthalene in

DME exist as solvent-separated ion pairs at temperatures below 20°. Similar results were obtained by other workers (30). Alkali metal nmr studies on biphenyl radical anions obtained by Canters and deBoer (31) provided conclusions parallel to the naphthalene case.

The concordance between nmr techniques on the one hand and esr, optical spectra, and conductance measurements on the other is a very important finding, because the latter methods are only useful with concentrations on the order of 10^{-4} molar or less, while the nmr experiments involve approximately 0.5 molar solutions. Thus it seems that concentration has little effect on ion pairing equilibria. This in turn indicates that aggregates higher than ion pairs may not play a significant role in the chemistry of aromatic radical anions -- at least for naphthalene or biphenyl.

The exchange reaction between aromatic hydrocarbons and their radical anions has been studied extensively, especially by the research groups of Szwarc, Hirota, and Weissman. In the case of free ions, the reaction involves nothing more than the transfer of an electron with minor solvent reorganization and is thus expected to be quite fast. In the case of ion pairs, the metal ion must also be



transferred, and such transfers would be expected to be much slower. The rate constants for these reactions have been measured by means of esr line broadening techniques. In 1962, Zandstra and Weissman (32) noted that, while the rate constant for ion pairs or free ions in tetrahydropyran (THP) or in 2-methyltetrahydrofuran (MeTHF) decrease with decreasing temperature, the rate constant for ion pairs exhibited 'bizarre behavior'. The rate constant at first decreased as the temperature was lowered from 80° to 21°, and then started increasing as the temperature was lowered toward -35°. At -35°, the ion pair exchanged ten times as fast as at 21°. These workers were somewhat at a loss to explain these results, although one of the theories proposed would have been correct if they had considered two ion pairs rather than two 'vibrational states'. It is now well-known that the strongly curved Arrhenius plots which result from any electron transfer reaction of sodium naphthalene in THF are due to equilibria between two ion pairs (8). Contact ion pairs, which are present at higher temperatures, exchange much more slowly than the solvent-separated ion pairs prevalent at lower temperatures. This is expected, of course, since much more solvent reorganization would be required in the exchange of a contact ion than a loose one. The loose ion pairs are favored at low temperatures because dissociation of a contact ion pair to a solvent-separated pair allows for much more cation solvation and is therefore expected to be exothermic. Opposing

this at the higher temperatures is the large and negative entropy change caused by immobilizing additional solvent molecules. In addition to the well documented dichotomy between contact and solvent-separated ion pairs, Hirota has obtained evidence for two types of contact ion pairs (27), while Hofelmann and co-workers (28) have postulated two types of solvent-separated ion pairs. The rate of interconversion between tight and contact ion pairs of sodium naphthalene in THF is on the order of 10^8 at -70° (33). The esr spectra of sodium di-tert-butylnaphthalene (DTBN) in THF exhibits the same temperature and solvent effects upon the sodium hfc's as observed for sodium naphthalene but with a much larger value in the case of DTBN (34). This has been explained, not in terms of tighter ion pairs in the case of DTBN, but simply that the tert-butyl groups prevent the sodium ion from undergoing as large of vibrational excursions to the sides and thus keeping it closer to a region of maximum coupling (35). The esr spectrum of potassium 4, 4'-di-tert-butylbiphenyl (DTBB) has been reported (15), as have spectra for a number of tert-butylnaphthalenes (36).

The rates of the exchange reaction just described for a few naphthalene radical anion systems is presented in Table 2. For a more extensive compilation, see Reference 8. It can be concluded that the rate of exchange of naphthalene radical anion is essentially diffusion controlled for free ions and for solvent-separated ion pairs, but is

two to three orders of magnitude slower for contact ion pairs. In addition, Shimada and Szwarc (37) have obtained results which indicate free ions can transfer electrons over considerable distances. ESR studies of **3** indicate that the rate of transfer from one naphthyl group to the other is $9 \times 10^6 \text{ sec}^{-1}$ at 15° in HMPA. The smallest separation of the two naphthyl moieties as was estimated from a model is 9 \AA . The rate of electron transfer in the ion paired species would be of great interest but has not yet been reported, although it is likely to be too slow to allow the use of ESR techniques.

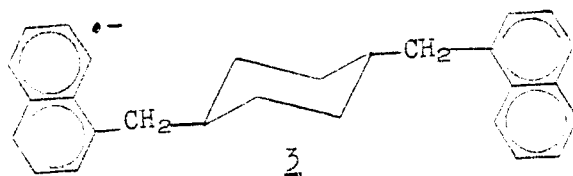


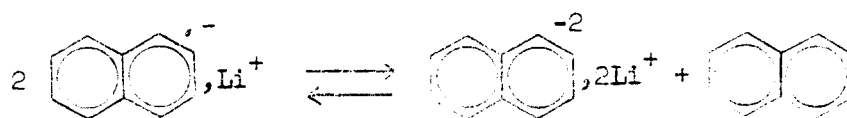
Table 2. Rate constants for electron exchange of naphthalene radical anions at room temperature.

Ion Pair	Metal	Solvent	Rate Constant $\times 10^{-7}$	Reference
			($\text{M}^{-1} \text{ sec}^{-1}$)	
Solvent-separated	Li^+	THF	100	33
Contact	Na^+	THF	0.2	28
"	Na^+	MeTHF	0.5	32
"	Na^+	THF	1.3	33
Solvent-separated	Na^+	THF	170	33
"	Na^+	DME	134	33
"	Na^+	THF/DME	130	33
Free ions	Na^+	THF/DME	120	33
Glymated, tight	Na^+	THF	45	28
Glymated, loose	Na^+	THF	250	28
Free ions	Na^+	HMPA	50	8

Dianion Formation and Properties

With the possible exception of benzene, all known aromatic hydrocarbons which have been studied will accept two electrons to form diamagnetic dianions. In the case of those hydrocarbons with a relatively high electron affinity such as anthracene, dianion formation is quite facile. On the other hand, in order to form the naphthalene dianion, the correct conditions must be met (metal, solvent, and temperature).

Under certain conditions, radical anions can undergo disproportionation to form the dianion and free hydrocarbon, as exemplified here by lithium naphthalene.



Some radical anions disproportionate so readily that it is difficult to prepare the simple monoanion. The most intensely studied material of this type is tetraphenylethylene (38).

Lithium naphthalene dianion was first reported in 1964 by Shatenshtein, Petrov, and Belouseva (39) almost simultaneously with Buschow and Hoijtink (40), and a year later by Smid (41). Shatenshtein observed formation of the dianion in diethyl ether due to disproportionation of the radical anion, while Smid simply stirred an excess of Li with naphthalene in THF until the green color of the radical anion

turned to the purple color of the dianion. Buschow and Hoijsink observed the dianion in 2-methyltetrahydrofuran (MeTHF) at -80° , but it is not clear whether this was due to disproportionation or to an excess of lithium. In 1967, Hsieh (42), apparently unaware of the results of Shatenshtein, reported the formation of lithium naphthalene dianion prepared from excess lithium in ether. ESR studies of the radical anion in ether over a temperature range of -100° to $+26^{\circ}$ were performed with the result that the lithium hfc decreased only very slightly from 0.50 gauss at 26° to 0.30 gauss at -100° , in concert with the results of Hirota discussed earlier. In addition, Hsieh estimated from the intensity of the ESR signal that less than 2% of the lithium naphthalene was in the form of the radical anion, with the remainder being the dianion as indicated by the purple color observed for the solutions. Upon quenching the reaction mixture with water, mostly dihydronaphthalene was formed, with only about 6% naphthalene. Also reported was the formation of naphthalene dianion in THF from excess Li similar to the work by Smid.

The effect of temperature upon lithium naphthalene in MeTHF is most interesting (43). This substance exists as the green radical anion at -120° as shown by both ESR and optical spectra. As the temperature is warmed to -70° , the ESR signal disappears and the optical spectrum becomes identical with that reported for the dianion in MeTHF at -80° by Buschow and Hoijsink as just discussed. As the

temperature is increased toward room temperature, the purple dianion changes back into the green radical anion. Szwarc has been partly successful in explaining these results (38) and the theory presented here is an elaboration (especially concerning the higher temperature results) of that of Szwarc. Since MeTHF is of low solvating ability, it is to be expected that the monoanion would have to exist as tight ion pairs at the higher temperatures. Since formation of solvent-separated ion pairs from contact pairs should be exothermic (16), and since this change results in a loss of entropy due to formation of a tighter solvent shell, it can easily be seen that solvent-separated ion pairs will be favored at the lower temperature where $T\Delta S$ is less negative. We have already observed this effect for sodium naphthalene ion pairs in THF. Since dianions naturally have a much higher cation affinity than monoanions, one would expect their formation by disproportionation to increase as one goes to poorer solvents. This is caused by lessened stability of the monoanion due to formation of contact ion pairs while very little change would occur in the energy of the dianion, which is expected to exist as contact ion pairs under all conditions. The formation of lithium naphthalene dianion in ether as reported by Shatenshtein serves as an example of this effect. Why then does lithium naphthalene in MeTHF disproportionate only at moderately low temperatures and not at $+20^\circ$ or -120° ? The fact that the equilibrium favors the radical anion at sufficiently

low temperatures is not surprising. Under these conditions, $T\Delta S$ is quite small and the exothermicity of lithium cation solvation is dominant. The formation of the dianion at somewhat higher temperatures is also easy to explain. The $T\Delta S$ term has become more negative and the formation of the contact ion pairs of the dianion increases the entropy of the system by releasing solvent molecules. What is surprising is the formation of monoanions again at room temperature. The equilibrium we have to consider is that between the dianion contact pairs and radical anion pairs. We must also keep in mind the extensive disproportionation of lithium naphthalene to form the dianion in ether at room temperature (39). Since it is expected that the energy of interaction of a dianion and two cations is more than twice the interaction of a monoanion and a cation (38), it would be expected that disproportionation would occur even when both mono- and dianions form contact ions as is observed in ether. Thus it would seem that we are at a loss to explain both results simultaneously. The best we can do is to point out that MeTHF is a better solvent than ether, and that the greater energy of solvation of the looser contact ion pairs of the monoanion, as compared to the tighter contact ions of the dianion, is perhaps sufficient to outweigh the decreased entropy due to the slightly greater solvation relative to the dianion in MeTHF but not in diethyl ether.

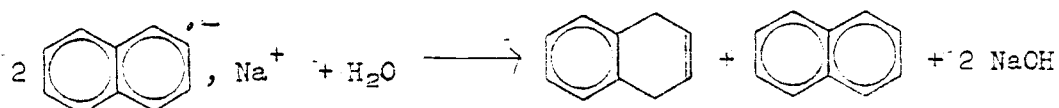
Summary of the Physical Properties of Selected Radical Anions

Dissociation to free ions in THF and DME is very slight at useful concentrations and is relatively independent of the nature of the anion or the cation for solvent-separated ion pairs. Formation of contact ion pairs relative to solvent-separated pairs is favored (a) in solvents of lower solvating power, (b) for sodium over lithium, and (c) at higher temperatures. Very low concentrations of tetraglyme or crown ethers can convert contact ion pairs into solvent-separated ones. Lithium naphthalene or biphenyl exists as solvent-separated ion pairs in THF and DME at or below room temperature. Sodium naphthalene exists as solvent-separated ion pairs in DME at temperatures below 20° and in THF at low temperatures, while existing as contact ion pairs in THF near room temperature.

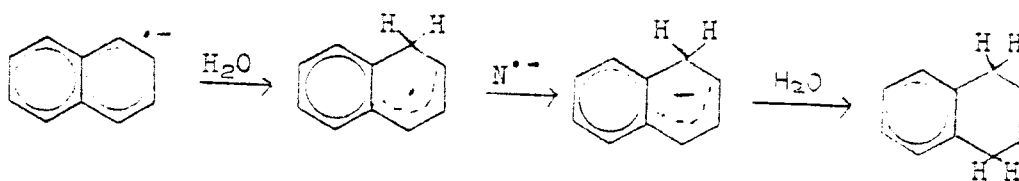
Electron transfer in exchange reactions occurs two to three orders of magnitude faster for free ions and solvent-separated ion pairs relative to contact ion pairs due to the necessity of more extensive solvent reorganization with the latter species. Disproportionation of radical anions into dianions is expected to occur most readily in solvents of low solvating ability. Dianions are expected to have a much greater tendency to exist as contact forms than are the corresponding radical anions.

Reaction of Naphthalene and Anthracene Radical
Anions with Water

The reaction of sodium naphthalene with water gives approximately an equal mixture of naphthalene and dihydronaphthalenes. A



mechanism for this reaction was proposed in 1956 by Paul, Lipkin, and Weissman (44) and is illustrated here by naphthalene.



In 1965, Bank and Closson obtained evidence against two alternative mechanisms by means of a labeling experiment (45). In 1971, Bank and Bockrath (46) reported on the kinetics of the reaction of sodium naphthalene in THF with water, using the stopped flow technique. The rate constant was found to be first order in both naphthalene and water, with a numerical value of $1.01 \times 10^4 \text{ M}^{-1} \text{ sec}^{-1}$ at 20° . By temperature variation in THF, solvent variation between THF and DME, and the addition of tetraglyme, it was concluded that contact ion pairs react much more rapidly than solvent-separated ions in contrast to the electron transfer reactions previously discussed. That disproportionation is not first occurring to give the naphthalene

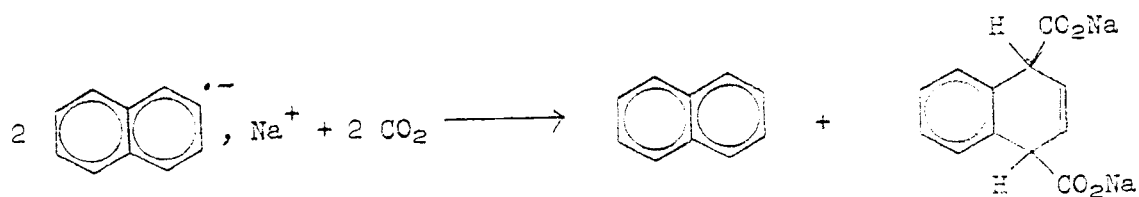
dianion which might then react with water, was shown by a strict first order rate dependence on naphthalene radical anion. Evidence was also obtained from the kinetic data that hydronaphthalene anion intermediate reacts much more rapidly than the parent radical anion.

Almost simultaneously, the research groups of Bank (47), Szwarc (48), and Dye (49) reported on the kinetics of sodium anthracene-water reactions by the stopped flow method. Sodium anthracene is much less reactive toward water than is sodium naphthalene. Bank and Bockrath (47) found a first order dependence on both anthracene and water in agreement with the Paul, Lipkin, and Weissman mechanism. In THF, the rate constant is $664 \text{ M}^{-1} \text{ sec}^{-1}$. These workers concluded from a solvent study that contact ions are much more reactive than solvent-separated pairs in harmony with the sodium naphthalene-water reaction. Rainis, Tung, and Szwarc (48) also found first order dependence on anthracene radical anion but observed mixed first and second order in proton donor (alcohols were used in addition to water). When the proton donor was t-butyl alcohol, slow disproportionation of anthracene radical anion to the dianion which appeared to react at a diffusion controlled rate was found. Minnich, Long, Ceraso, and Dye found a second order dependence on anthracene radical anion, and between one and one-third order in alcohol (THF solvent). Solvent was found to be very important. The reaction of potassium anthracene in ethylene diamine with 0.19 molar

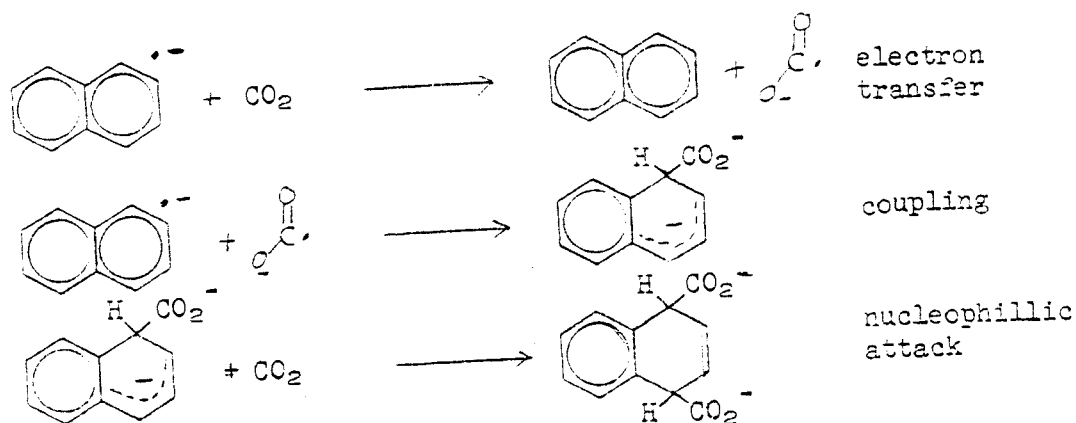
water is too slow to be observed over a period of 5-10 minutes. This is consistent with other work done in DMF (50). The different results obtained by different research groups is testimony to the complexity of the reaction. The mechanism appears to be dependent upon concentration, solvent, identity of the proton donor and its concentration, and the metal ion concentration.

For references to pulse-radiolysis and electrolytic studies of hydration, see Reference 49. For references to the use of radical anions as bases in condensation reactions, as initiators for polymerization, and reaction with a variety of miscellaneous substances, see Reference 9.

Naphthalene (51, 5), biphenyl (52 for LiB), and anthracene (53) radical anions react with carbon dioxide to give diacids as exampli-

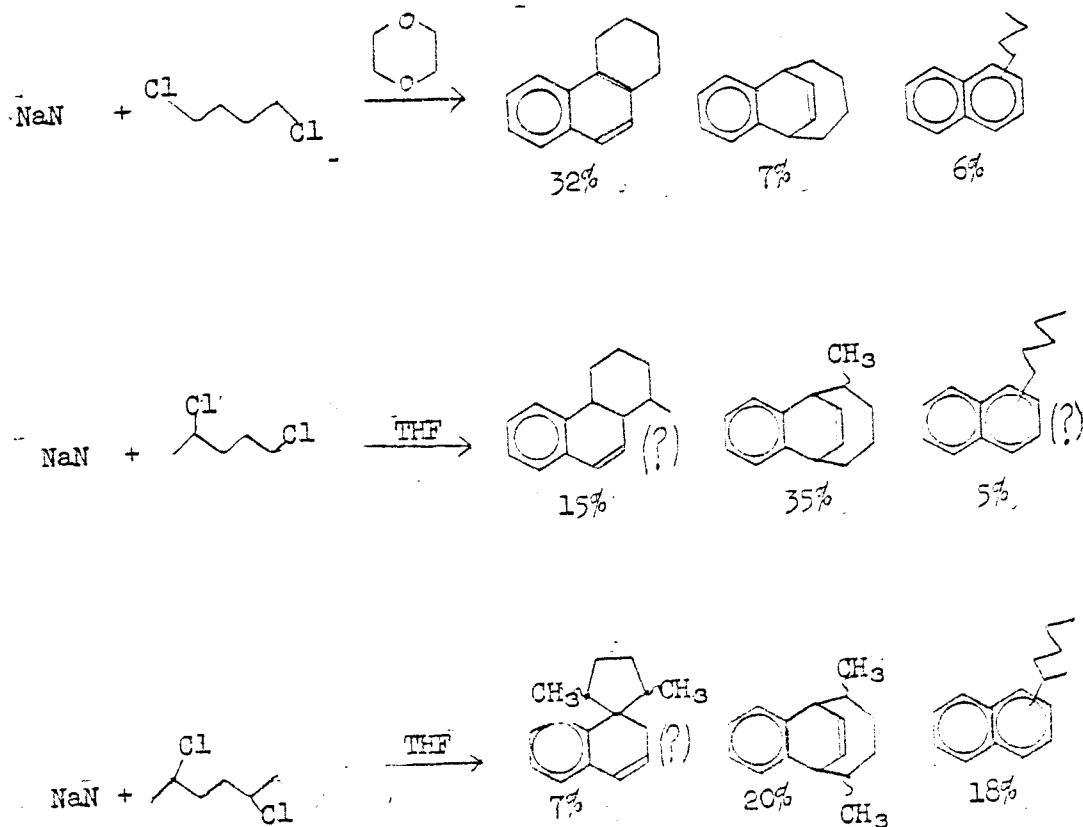


fied by sodium naphthalene. When one considers the large number of recent publications concerning the mechanism for the hydration of radical anions, it is surprising that no interest has been expressed in the corresponding reaction with carbon dioxide. Although no mechanism has yet been proposed for this reaction, the following scheme should suffice as a working hypothesis.



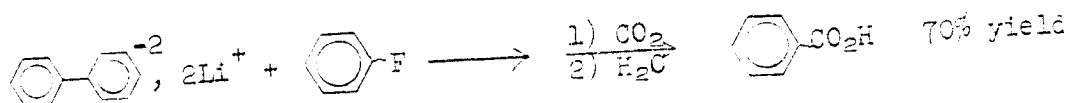
The Reaction of Alkyl Halides with Radical Anions

Concomitant with the discovery that sodium naphthalene could be easily formed in DME, Scott (3) recognized that the reactions of this substance could be divided into two classes. Sodium naphthalene can act simply as a solubilized form of sodium with the naphthalene acting as an inert carrier. Alternately, sodium naphthalene can undergo reactions to give products containing the naphthalene moiety. For example, with alkyl halides, products typical of the classic Wurtz reaction such as hydrocarbons, dimer and olefin are obtained along with a variety of mono- and dialkylated naphthalenes. Of greatest interest to the early workers were the alkylated naphthalenes. Perhaps the most interesting study was that of Lipkin, Galiano, and Jordan (54) who revealed that the products of dihalides with sodium naphthalene in dioxane and THF include interesting polycyclic



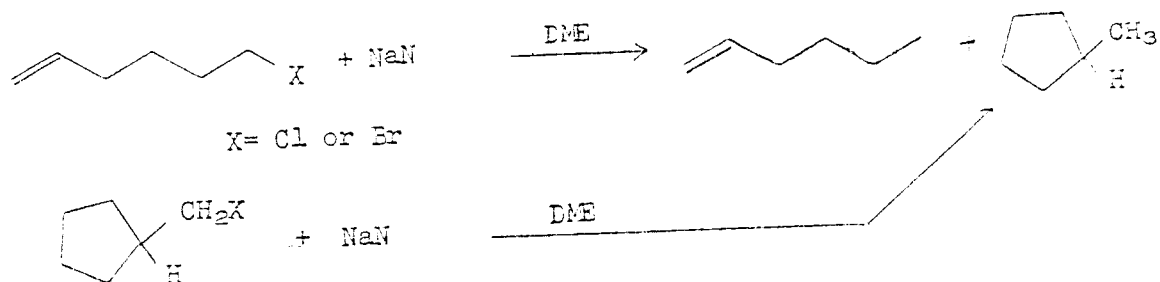
compounds which were obtained in moderate yields. The yields shown are based on naphthalene used. A (?) was placed by those structures which, when viewed from today's perspectives, seem incorrectly assigned.

The same year of Lipkin's publication, Eisch (55) reported on the cleavage of a number of types of compounds by lithium biphenyl dianion. Among these was the reaction of fluorobenzene. Also reported was the cleavage of THF to give butanol.



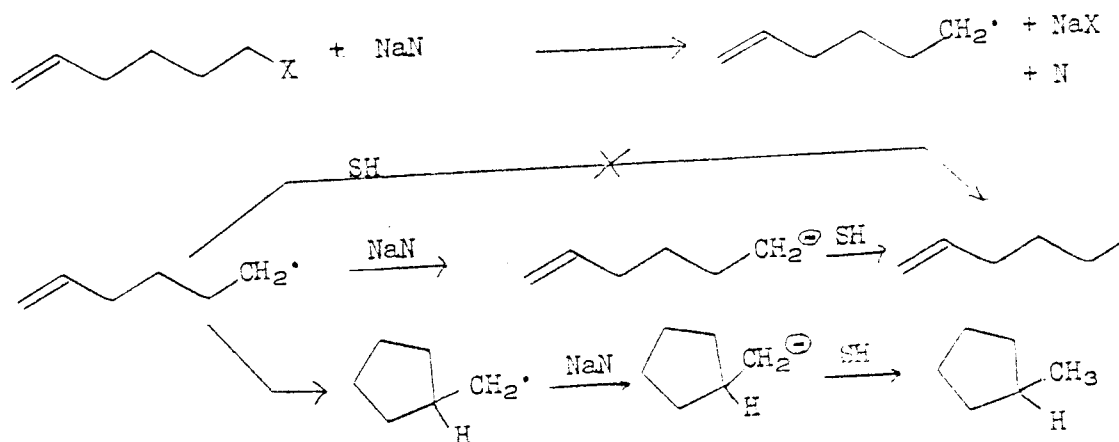
Early work by Warhurst on the rates of reaction of halides with a great diversity of radical anions and ketyls can be found in Reference 126 and earlier papers. The products of these reactions were not investigated.

Mechanistic studies got off to a good start in 1966 when two very important papers appeared simultaneously, followed in short order by a third. Garst, Ayers, and Lamb (56) found that 5-hexenyl and cyclopentylmethyl chlorides and bromides react essentially instantaneously with sodium naphthalene in DME to give around 50% yields of the corresponding hydrocarbons. The reaction with 5-hexenyl halides gives both 1-hexene and methylcyclopentane, while cyclopentylmethyl halides give only methylcyclopentane. Variation of the concentration



and method of mixing in the 5-hexenyl case gave larger ratios of uncyclized to cyclized product when the effective concentration of the sodium naphthalene was the highest. The most likely mechanism was

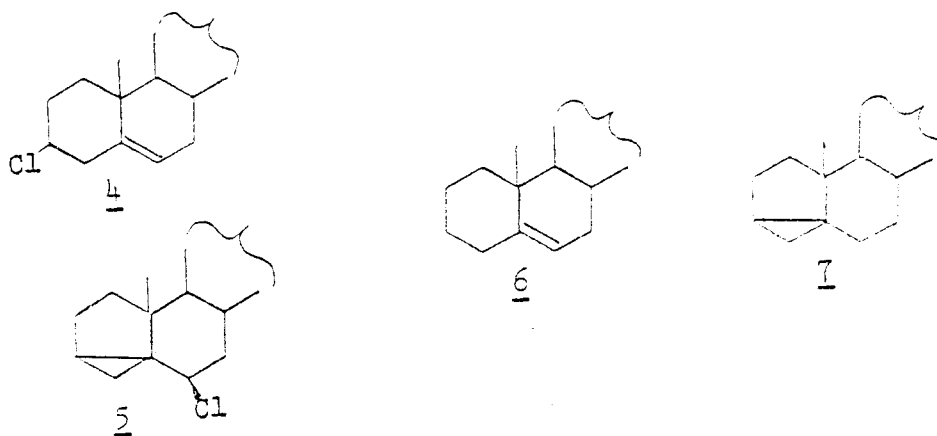
interpreted as shown below. Control experiments with 6-heptenoyl



peroxide proved that the 5-hexenyl radical completely cyclizes to cyclopentylmethyl radical before reacting with DME. Cyclization of the 5-hexenyl anion could not have been occurring since the yield of methylcyclopentane dropped to near zero when high concentrations of sodium naphthalene were used. Since the rate constant for cyclization of 5-hexenyl radical was known to be near 10^5 sec^{-1} , it was concluded that the rate of reaction between the radical and naphthalene radical anion is near or at the diffusion controlled limit. Attempts at trapping the anions were unsuccessful due to the expected rapid reaction with solvent. Alkyl sodiums attack all solvents except aliphatic hydrocarbons.

In a companion communication (57), Cristol and Barbour arrived at substantially identical conclusions by means of a study of the reactions of cholesteryl chloride (4) and 3-cyclocholestanyl chloride (5)

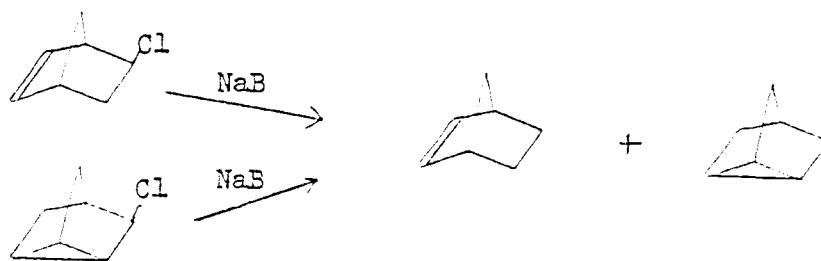
with sodium biphenyl in DME. When starting from 4, only 6 is



formed, while both 6 and 7 are formed from 5. The 7:6 ratio was larger for the more concentrated solutions of sodium biphenyl. From these results it was concluded that the rearrangements must be due to radical intermediates and not the anions from which the final products were shown to arise. A common nonclassical radical (or carbanion) intermediate was shown not to exist in this system. Attempted carbonation gave no acids.

Due to the rapidity of the reactions, the actual concentrations under which the reactions took place are difficult to ascertain. Since 0.4 molar halide was added to excess 1.0 molar sodium biphenyl, it might be assumed that the effective concentration is between 1.0 and 0.1 molar. As can be seen from Table 3, sodium biphenyl is a better trapping agent for this radical rearrangement than is the excellent (59) hydrogen donor triphenyltin hydride. In a similar study, Cristol and

Gleason (60) investigated the reactions of exo-5-chloronorbornene and nortricycyl chloride with sodium biphenyl. Starting from either chloride, the same mixture of hydrocarbons was obtained at either



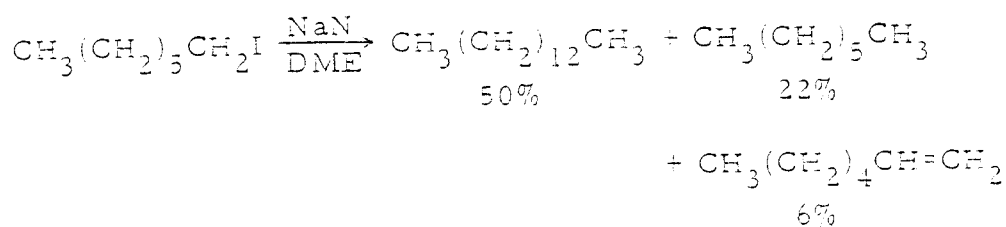
high or low concentrations of sodium biphenyl when the reaction was run at room temperature. When the reaction was run at -58° , however, more olefin was obtained from the olefinic chloride than from the nortricycyl chloride. From the data given, it can be calculated that sodium biphenyl was approximately 50% effective in trapping the radicals before rearrangement at -58° , but was too slow to do any trapping at 25° . Considering the very close similarity of the cholesteryl and norbornyl systems, the great difference in temperature sensitivity exhibited by the two systems is surprising.

These workers also claimed to have trapped the alkyl anions by combining streams of equimolar quantities of sodium biphenyl and the alkyl halides in a capillary and passing the mixture onto Dry Ice. The yield of acid was quite low.

Table 3. Comparison of the reaction of triphenyltin hydride and sodium biphenyl with 3,5-cyclocholestan-6-yl chloride. Data obtained from Reference 58.

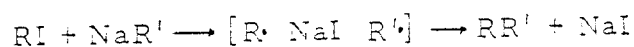
Reagent	Concentration	Temperature	% Unrearranged Hydrocarbon
Ph ₃ SnH	0.08	15°	0
Ph ₃ SnH	0.40	15°	4
Ph ₃ SnH	0.08	-20°	18
Ph ₃ SnH	1.0	-15°	30
NaB	1.0-0.1	25°	20
NaB	1.0-0.1	-20°	41
NaB	1.0-0.1	-70°	60

Sargent, Cron, and Bank (61) reported that the reactions of sodium naphthalene with primary and secondary iodides give large yields of dimer products. Chlorides and bromides, on the other



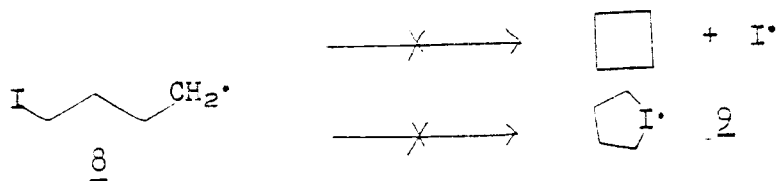
hand, gave zero and 5% yields of dimer, respectively. The authors proposed that the high yields of dimers in the case of iodides resulted from the high rate of the iodide reaction, generating a high enough concentration of radicals that dimerization can compete with reduction to anions. The fact that mixtures of 1- and 2-iodopropane gave rise to statistical amounts of dimers was used as evidence against dimer

formation for nucleophilic attack of anions upon iodide. Two years later, Garst and Barbas (62) pointed out that the statistical distribution of products, while ruling out S_N2 reactions, were consistent with geminate radical pair formation from the reaction of an alkyl iodide molecule with an alkyl sodium in analogy to the proposed mechanism for coupling of the corresponding lithium reagents (63, 64). To test



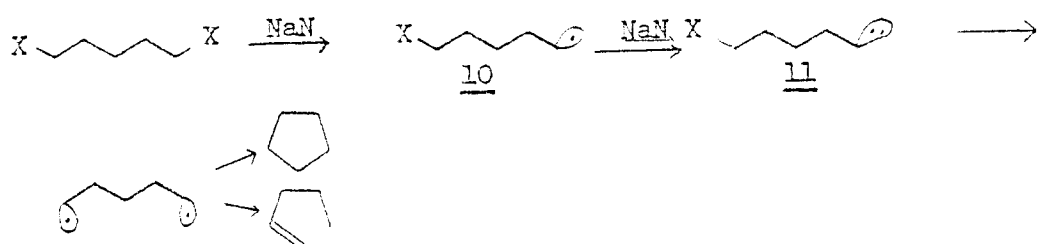
this mechanism, these workers treated sodium naphthalene with 1, 4-diiodobutane under normal, inverse, and evaporative addition with the same result in each case: 50% yield of cyclobutane and no dimers. With monoiodides, about 50% dimer formation is observed for the first two methods but only 10% for evaporative additions. The complete lack of dimers is strong evidence against Bank's radical combination mechanism since 4-iodo radicals should couple as well as ordinary primary radicals. It was argued (65) that the 4-iodobutyl radicals do not unimolecularly decompose to cyclobutane and iodide atoms nor form a cyclic complex (9) on the basis that the degree of naphthalene alkylation for 1, 4-diiodobutane is identical with that of ordinary primary halides. The first process would cause the yield of hydrocarbon to be larger than is observed for primary radicals. The second process would give a radical (9) with very different electronic properties than a normal primary radical. The extent of coupling was

known to be sensitive to electronic effects.



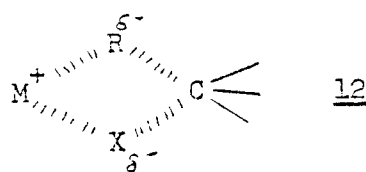
Kaplan (66) has criticized this proof of the nonexistence of 9 on the premise that 9 might be the principal constituent of an equilibrium with 8, while 3 might react with sodium naphthalene to the exclusion of 9. In view of the fact that sodium naphthalene reacts with primary radicals at diffusion controlled rates, such selectivity in reacting with 8 but not 9, while not completely impossible, would seem to stretch credibility to an excessive extent.

The reactions of 1, 4-dihalobutanes and of 1, 5-dihalopentanes with sodium naphthalene give a mixture of the corresponding cycloalkane and olefin (67). The formation of both products was explained as arising from either combination or disproportionation of an intermediate diradical. It was found, however, that the ratio of cyclopentane to 1-pentene was dependent on the nature of the halogen vary-



ing from 2.8 for the iodide to >100 for the chloride. Various explanations were proposed such as memory of initial halogen dependent

diradical conformations, partial reduction of 10 directly to the diradical, reduction of 11 to the radical anion, followed by loss of a sodium atom and front side S_N2 displacement induced by the low dielectric constant of the medium. This last mechanism would involve a transition state such as 12 competing with E2 elimination or perhaps

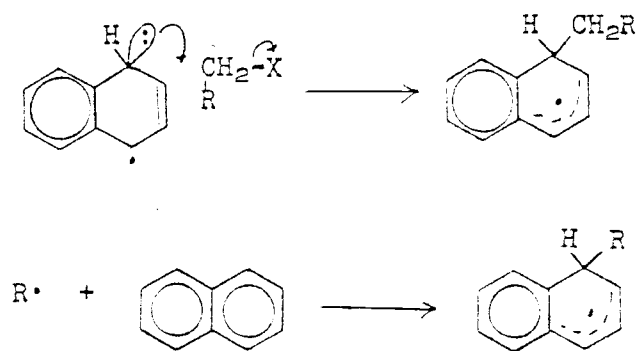


diradical formation. The other proposed mechanisms were either rejected on experimental grounds or simply did not seem likely.

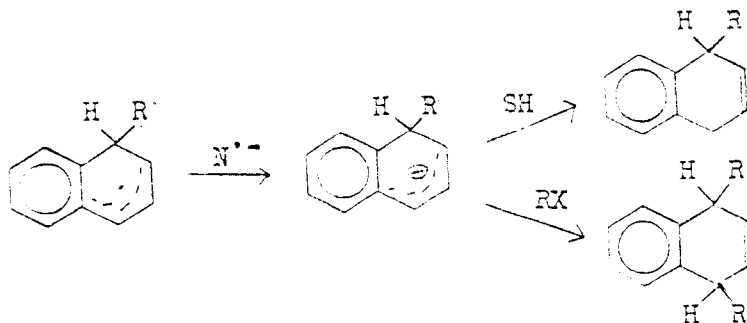
The reactions of 1,6-dihalohehexanes with naphthalene radical anion were also studied. Double reduction, resulting in the formation of hexane, was found in this case. In fact, by using lithium naphthalene with the dichloride, the hexane was formed in 40% yield, while the reaction with sodium naphthalene gave only 10% yield. This is to be expected since alkyl sodiums should be far more reactive than alkyl lithiums, while at the same time lithium naphthalene is known to react 100 times as fast as sodium naphthalene with primary fluorides.

A fair amount of work has been reported on the reactions of vicinal dihalides with radical anions both from synthetic and mechanistic points of view. For references, see Holy (9), and Garst and co-workers (63).

The mechanism for the formation of alkylated naphthalenes was proposed by Lipkin, Divis, and Jordan in 1968 (69) to involve S_N2 displacement of halide by the radical anion. In 1963, Hoijtink (70) had proposed the mechanism to be radical attack upon naphthalene. In



both mechanisms, the delocalized radical would pick up another electron to give the anion which might give either mono- or dialkylated products.



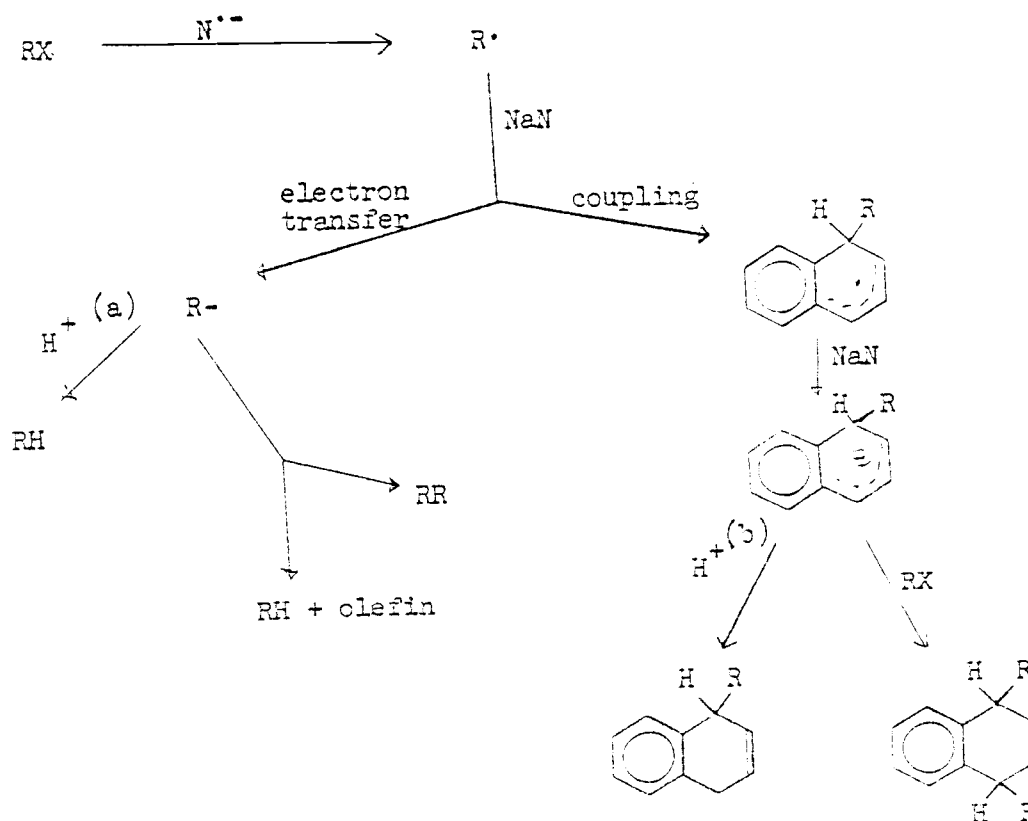
In 1968, the research groups of Garst and Sargent simultaneously arrived at an alkylation mechanism involving coupling between the radical anion and the radical. Garst, Barbas, and Barton (71) found the ratio of alkylation to reduction (RH) to be independent of the

identity of the halide. This is incompatible with the S_N2 mechanism, since a large effect should have been seen upon going from chloride to iodide. Sargent and Lux (72) also showed that the S_N2 mechanism was inoperative and were also able to provide evidence against radical addition to naphthalene. The latter was achieved by the observation that the yield of products was not affected by inclusion of an excess of naphthalene. A possible addition of the alkyl anion to naphthalene was also eliminated. To examine the alkylation mechanism, Sargent and Lux treated a variety of iodides with sodium naphthalene in DME and carefully examined the yields of the various products. For primary, secondary, and tertiary iodides, the alkylation to reduction ratio increased upon going from primary to tertiary--a result clearly incompatible with an S_N2 mechanism but easily compatible with radical-radical anion coupling. Tertiary radicals couple to a greater extent than primary since the (presumably) higher reduction potentials for tertiary radicals slow down the electron transfer process more than the increase in bulkiness slows down the coupling. The data of Sargent and Lux was used to calculate the entries in Table 4, with the electron transfer to coupling ratio being effectively defined in the general mechanism of Scheme 1.

The large value of the electron transfer to coupling ratio exhibited by neopentyl iodide reflects the sensitivity of the coupling process to steric effects. While coupling must involve fairly short

distances, electron transfer presumably can take place over much larger distances and would have little if any steric requirements. The effect of halide structure on the dialkylations yields is in the direction expected for a conventional S_N2 reaction.

Scheme 1. The general scheme for the reaction of radical anions with halides as illustrated by naphthalene radical anions.



(a) From solvent except with Li. See discussion section.

(b) Probably on workup.

Table 4. Electron transfer vs. coupling and extent of dialkylation in the reaction of pentyl iodides with sodium naphthalene in THF.

	ET ^(a) Coupling	Dialkylation Monoalkylation
$(\text{CH}_3)_3\text{CCH}_2\text{I}$	4.8	0
$\text{CH}_3(\text{CH}_2)_4\text{I}$	1.7	2.5
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CHICH}_3$	0.74	0.72
$\text{CH}_3\text{CH}_2(\text{CH}_3)_2\text{CI}$	0.39	0

(a) ET-electron transfer. See Figure 1 for definition. Calculated from yield data given in Reference 72 by the following formula:

$$\text{ET/coupling} = \frac{\text{Yield of RH} + 1/2 \text{ yield of RR}}{\text{Yield of monoalkylated} + 1/2 \text{ yield of dialkylated naphthalenes}}$$

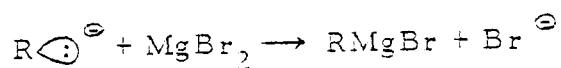
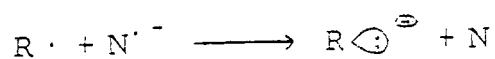
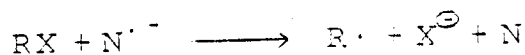
where yields were based on RX.

In 1971, Cheng, Headley, and Halsal (73) reported that halo-benzenes react with sodium naphthalene to give 85% benzene, 7% biphenyl, 1-2% terphenyl, and 1-2% phenylated naphthalenes. Treatment of the reaction mixture with D_2O at -60° gave no deuterium incorporation in the benzene. This led Cheng to postulate the absence of anions requiring that the products are derived by radical attack on neutral hydrocarbons. Since this mechanism was completely at odds with the accepted view of the reaction of alkyl halides with sodium naphthalene, less than two months later Sargent (74) argued that the results obtained by Cheng *et al* were in full accord with Scheme 1. The lack of deuterium incorporation in the benzene is fully expected,

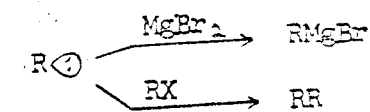
since phenyl sodium would attack THF rapidly even at -60° . The biphenyl probably arises from nucleophilic substitution on the halide.

Recently, Asirvatham and Hawley (75) have presented evidence that formation of dimer from the electrochemical reduction of p-fluorobenzonitrile takes place by combination of two p-fluorobenzonitrile radical anions. This mechanism conceivably might be operative for sodium naphthalene reductions of fluoro aryls but not for chloro, bromo, or iodo aryls since it depends upon the halo radical anion to have appreciable stability. However, the dimer formation reported by Cheng for fluorobenzene is only double that of bromo, chloro, and iodo benzene.

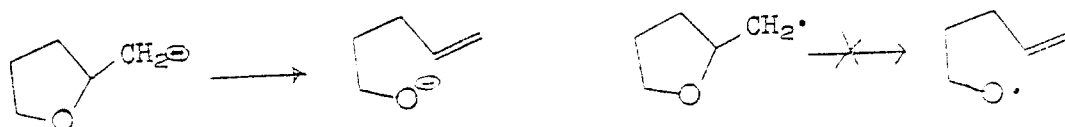
Direct evidence for the existence of alkyl anions (Scheme 1) may have been produced by Bank and Bank (76) in 1969. Injection of sodium naphthalene into a mixture of magnesium bromide and hexyl chloride, bromide, or iodide followed by the addition of deuterium oxide gave rise to 36% yields of hexane which was 85% deuterated. It should be noted, however, that the deuteration was determined by using as a standard deuterated hexane obtained from a Grignard reaction. Grignard reactions are well known to give sizeable yields of hydrocarbon as a side reaction to the Grignard reagent (77). The deuteration was taken as evidence of Grignard formation which, in turn, was taken to arise from metal exchange with the alkyl sodium (anion). The extent of coupling as compared to electron transfer was



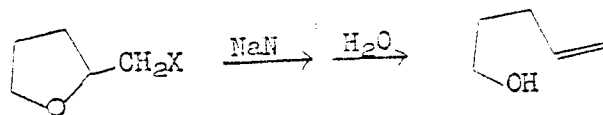
not affected by the inclusion of magnesium bromide. The yield of dimer in the case of the iodide was, however, cut in half. This was taken to indicate that dimer formation arises from anion-halide reactions which are intercepted by the magnesium bromide. The residual coupling was taken to indicate part of the dimer did arise from radical coupling. It should be pointed out, however, that the residual dimer could be simply a reflection of competition between the magnesium bromide and the alkyl iodide for the anion.



Convincing evidence for the existence of the postulated anion intermediates was reported by Garst (44, 78, 79). Tetrahydrofurfuryl anions are known to open while the corresponding radical does not.



The reaction of either tetrahydrofurfuryl bromide or iodide with sodium naphthalene gives 83% yields of 4-penten-1-ol. Reaction of

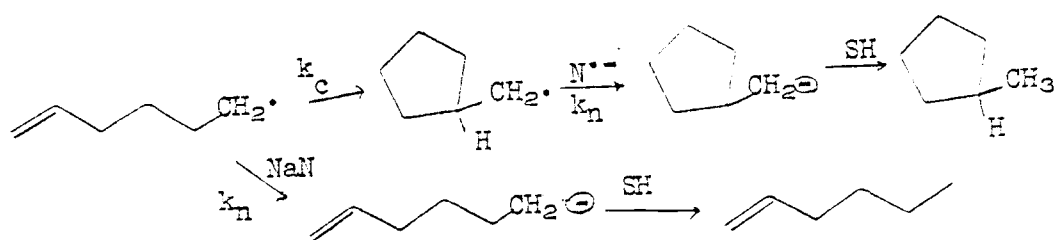


the radical with solvent would have given 2-methyltetrahydrofuran, which is not observed. The reaction of the iodide does not give rise to any dimer products. This provides additional evidence against formation of dimer from radicals. The fact that an 83% yield of reduction product was obtained for these primary halides while normal primary halides give around 50% reduction has been explained (67) as due to the inductive effect of the oxygen increasing the electron affinity of the radical. That it cannot be due to increased steric effects is seen from the observation that cyclopentylmethyl chloride gives 50% reduction and 50% alkylation (80). The solvent derived intermediate which results from proton abstraction by the alkyl anions has been captured before decomposition by Smith and Ho (81).

While the reactions of chlorides, bromides, and iodides with sodium naphthalene appear to be instantaneous and complete before either temperature or concentration equilibration can be achieved, Garst and Barton (80) reported that primary fluorides react with sodium naphthalene at convenient rates. This allowed a more precise calculation of the rate of reaction of radicals with sodium naphthalene through use of the 5-hexenyl system. The extent of cyclization which one expects from the above process is described by the equation

$$rx_0 + 1 = e^{rx_0/(1+s)}$$

where $r = k_N/k_C$, x_0 = initial concentration of sodium naphthalene, and s = extent of precyclization electron transfer (1-hexene/methylcyclopentane). This equation (82,80) holds when the fluoride is in



excess. As x_0 was varied over a range from 0.00028 to 0.0046 molar, s varied from 2.0 to 15.2. The value of r calculated from this data is 1.6×10^4 for sodium naphthalene and 1.0×10^4 for sodium biphenyl with the standard deviation being around 20%. A value of 1×10^5 for k_C had been obtained by Carlsson and Ingold (59) from a study with tributyltin hydride. Although this rate was not determined in DME, it would not be expected to be solvent dependent. Thus the rate for reaction of sodium naphthalene in DME with primary radicals is on the order of $1.6 \times 10^9 \text{ M}^{-1} \text{ sec}^{-1}$. The corresponding value for sodium biphenyl is $1.0 \times 10^9 \text{ M}^{-1} \text{ sec}^{-1}$. The calculated upper limit for a diffusion controlled reaction is $1.2 \times 10^{10} \text{ M}^{-1} \text{ sec}^{-1}$ (80) but since only one-fourth of the encounters between radicals and

radical anions will be singlets (83) the maximum rate would be $3 \times 10^9 \text{ M}^{-1} \text{ sec}^{-1}$. Thus it can be seen that the reaction is very close to the diffusion controlled limit and may in fact actually be diffusion controlled. However, it should be noted that sodium biphenyl reacts only 60% as fast as sodium naphthalene and that this difference seems to be somewhat outside the range of error. It would be quite surprising if sodium biphenyl does react slower than sodium naphthalene since biphenyl has a lower solution electron affinity than does naphthalene.

Unfortunately at the present time there exist no reports on the effect of changing the solvent or of adding complexing agents upon the rate constant k_N . If there is no change in going from, say, methyl-tetrahydrofuran (tight ion pairs) to DME + crown ether (very loose ion pairs) one could safely say that the reaction is diffusion controlled since it would be very unlikely that the transition state would have the same cation affinity as starting materials. Since the reaction is so fast one would expect the charge to be more delocalized in the transition state relative to starting material (see discussion of rates below). In this case the transition state would have a lower cation affinity than the reactants and tight ion pairs should react more slowly than loose ones. The effect on k_N of changing the metal counter ion would give additional information although it would be more difficult to interpret. The only metal effect reported thus far gives anomolous results.

Lithium naphthalene gives erratic and rather small s values (much cyclization). The range of s was from 0.05 to 4, and appeared to give more cyclization with higher lithium naphthalene concentrations -- the inverse of what is expected (76). It appears that 5-hexenyl lithium does not cyclize since the s value does not change upon standing (84). Although no explanation was provided, it would seem that the reason might lie in the fact that the lithium reagent produced from the radical anion reaction is not of the common garden variety. In solvents such as THF and DME, lithium agents are known to exist at least as dimers and more commonly as tetramers (85). By necessity, the lithium reagent produced from an alkyl halide and lithium naphthalene is the monomer form. It would not seem unreasonable to assume that the monomer is far more reactive towards cyclization than the tetramer. The reduced cyclization at higher concentrations is thus readily explained since cyclization, which is first order, must compete with polymerization, which is second order. It might be predicted, then, that addition of butyllithium or lithium bromide to the reaction mixture might lower the extent of cyclization by rapid complex formation with the monomer.

While there exists little information concerning metal ion, solvent, and temperature effects on the second electron transfer (Scheme 1), the situation is reversed in the case of the first electron transfer. In a study of the rate of reaction of primary alkyl fluorides

with alkali metal naphthalenes, Garst and Barton (86) found that changing the metal ion from cesium to lithium results in at least a 5×10^4 increase in the rate of reaction with sodium and potassium intermediate. Actually no reaction at all was observed with cesium. The authors postulate that the transition state is of greater cation affinity (charge localization) than the reactants. The interaction of the anion with metal cation lowers the transition state energy relative to the reactants to a greater extent in the case of the smaller lithium cation than the larger cesium cation, giving rise to the observed rate changes as a function of the cation identity. These considerations are effectively gas phase arguments, as they ignore the effect of solvation. The authors calculated the gas phase exothermicities for alkali naphthalene ion pairs reacting with ethyl fluoride to give naphthalene, ethyl radical and M^+ , F^- ion pairs. The exothermicities in Kcal/mole are: Li^+ , 32; Na^+ , 18; K^+ , 6; Cs^+ , 0; and free ions, -30. The reaction rates of 5-hexenyl fluoride with lithium, sodium, and potassium naphthalene radical anions, when plotted against the just-mentioned exothermicities, give a straight line indicating, perhaps, that solvation effects do not outweigh the gas phase aspects of the reaction when DME is the solvent. One might expect, however, that the addition of tetraglyme or crown ether might decrease the magnitude of the metal ion effect and that even the direction of effect might

possibly change if one were to go to a very powerful solvent such as hexamethylphosphoramide.

While the rate of reaction of primary fluorides is quite slow and amenable to study by conventional techniques, the rate of reaction of sodium naphthalene with chlorides, bromides, and iodides is much faster, requiring the use of special techniques. Bockrath and Dorfman have determined the rates of reaction of butyl iodide and bromide with naphthalene and biphenyl radical anions using the pulse radiolysis method (87). This technique, while limited to very fast reactions, is especially powerful since ion pairs or free ions can be studied at will simply by including or not including a salt of the cation in the solution. The results obtained by this method are compiled in Table 5. From the table it can be seen that the rate of reaction of sodium naphthalene with alkyl halides spans a range of twelve orders of magnitude. It can also be seen that free ions are one to two orders of magnitude faster than ion pairs in reaction with bromides and iodides. This was taken to indicate that the cation affinity of the transition state is less than that of the reactants (charge dispersal in the transition state). Ion pairing would stabilize the reactants more than the transition state. The reaction rates of sodium biphenyl or naphthalene with butyl iodide in THF gives Arrhenius plots with great curvature. The rate in the case of sodium biphenyl is the same at $+60^\circ$ as at -65° with intermediate temperatures giving faster rates.

This is simply an expression of the facts that contact ion pairs react more slowly than solvent-separated ion pairs and that lowering the temperature converts contact ion pairs to solvent-separated ones. The authors found that the concentration of naphthalene or biphenyl had no effect on the rate of recombination, implying that the lifetime of $n\text{-BuBr}^{\cdot-}$ or $n\text{-BuI}^{\cdot-}$ is very short. As Sargent has pointed out (91), the cross-section for the reaction of sodium atoms with alkyl halides and even with vinyl chloride is on the order of 0.1 to 1 \AA^2 . If the radical anion ($\text{RCI}^{\cdot-}$) was capable of existence, the cross-section should be on the order of 10^2 to 10^4 \AA^2 (118). One would expect that halo-radical anions would be viable species only in those cases where relatively low-lying antibonding orbitals are available and where the carbon-halogen bond is strong. Undoubtedly fluoronaphthalene, probably fluorobenzene, and possibly chlorobenzene would be such species.

While the reaction of primary bromides with contact paired sodium naphthalene is too slow to measure using the pulse radiolysis method, it is not too fast for stopped flow techniques. Bank and Juckett (88) have used this technique to study the rate of reaction of sodium naphthalene and anthracene with n -hexyl bromide and chloride. The results are compiled in Table 5. Comparison of entries #10 with #11 and #12 would indicate that for primary chlorides, solvent-separated ion pairs react about five times faster than contact pairs. However, while the predominant species is the contact ion pair,

Table 5. Rates of electron transfer reactions of radical anions with halides at 20-25°.

Entry #	Radical Anion ^(a)	Ion Pair Type	Solvent	Halide	Rate Const. (M ⁻¹ sec ⁻¹)	Method ^(b) and Ref.
1	S, B	Free	THF	<u>n</u> -BuI	9.6 x 10 ⁹	PR, 87
2	S, N	Free	THF	<u>n</u> -BuI	7.4 x 10 ⁹	PR, 87
3	S, B	Free	THF	<u>n</u> -BuBr	3.4 x 10 ⁷	PR, 87
4	S, N	Free	THF	<u>n</u> -BuBr	3.3 x 10 ⁷	PR, 87
5	Na, B	Contact	THF	<u>n</u> -BuI	4.3 x 10 ⁸	PR, 87
6	Na, N	Contact	THF	<u>n</u> -BuI	9.3 x 10 ⁷	PR, 87
7	Na, B	Contact	THF	<u>n</u> -BuBr	1.3 x 10 ⁶	PR, 87
8	Na, N	Contact	THF	<u>n</u> -BuBr	< 4 x 10 ⁵	PR, 87
9	Na, N	Contact	THF	<u>n</u> -C ₆ H ₁₃ Br	7.2 x 10 ⁴	SF, 88
10	Na, N	Contact	THF	<u>n</u> -C ₆ H ₁₃ Cl	2.0 x 10 ²	SF, 88
11	Na, N	Loose	DME	<u>n</u> -C ₆ H ₁₃ Cl	1.1 x 10 ³	SF, 88
12	Na, N	Glymated ^(c)	THF	<u>n</u> -C ₆ H ₁₃ Cl	1.2 x 10 ³	SF, 88
13	Na, A	Loose	DME	<u>n</u> -C ₆ H ₁₃ Cl	6.6 x 10 ⁻²	SF, 88
14	Na, A	Loose	THF	<u>n</u> -C ₆ H ₁₃ Br	3.3 x 10 ²	SF, 88
15	Na, A	Loose	DME	<u>n</u> -C ₆ H ₁₃ Br	3.3 x 10 ²	SF, 88
16	Na, A	Loose	THF	<u>n</u> -C ₆ H ₁₃ I	2.2 x 10 ⁴	SF, 88
17	Na, N	Contact	MeTHF	<u>n</u> -C ₆ H ₁₃ F	3.4 x 10 ⁻⁴	SF, 88

Table 5. Continued.

Entry #	Radical Anion ^(a)	Ion Pair Type	Solvent	Halide	Rate Const. (M ⁻¹ sec ⁻¹)	Method ^(b) and Ref.
18	Na, N	Contact	THF	<u>n</u> -C ₆ H ₁₃ F	1.9 x 10 ⁻⁴	C, 90
19	Na, N	Loose	DME	<u>n</u> -C ₆ H ₁₃ F	2.5 x 10 ⁻⁴	C, 90
20	Na, N	Glymated ^(c)	THF	<u>n</u> -C ₆ H ₁₃ F	1.2 x 10 ⁻⁴	C, 90
21	Na, N	Crown ^(d)	DME	<u>n</u> -C ₆ H ₁₃ F	4.5 x 10 ⁻⁵	C, 90
22	Li, N	Loose	DME	5-hexenyl fluoride	2.7 x 10 ⁻²	C, 86
23	Na, N	Loose	DME	5-hexenyl fluoride	2.8 x 10 ⁻⁴	C, 86
24	K, N	Contact	DME	5-hexenyl fluoride	2.0 x 10 ⁻⁶	C, 86
25	Cs, N	Contact	DME	5-hexenyl fluoride	< 5 x 10 ⁻⁷	C, 86

+

(a) A = anthracene, B = biphenyl, N = naphthalene, S⁺ = solvent derived cation.

(b) PR = pulse radiolysis, SF = stopped flow, C = conventional spectrophotometric.

(c) Tetragylme.

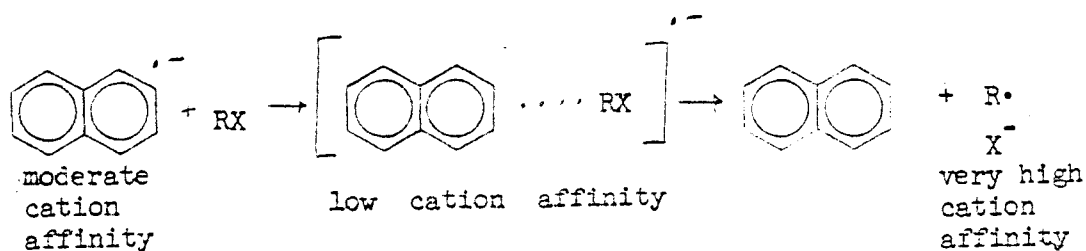
(d) 18-crown-6.

approximately 7% of the sodium naphthalene exists as solvent-separated ion pairs. These could be giving rise to a fraction of the reaction in this solvent, in which case the reactivity difference between tight and loose pairs would be somewhat greater than five. As in the case of the Bockrath and Dorfman work described above, Bank and Juckett found a wildly curved Arrhenius plot in the reaction of sodium naphthalene with 1-chlorohexane in THF, the plot changing from a positive to a negative slope at approximately 5°.

The hexyldihydronaphthyl anion was found to be quite stable in THF with no decay in 140 hours. This anion, which reacts with water much faster than the parent radical anion, was found to react very slowly with hexyl chloride. This difference in reactivities is hardly surprising in view of the totally different types of reaction being compared. The hexyldihydronaphthyl anion reacts with halides by the relatively slow S_N2 process because its oxidation potential at 23 kcal/mole is too high to allow electron transfer (89).

Garst, Roberts, and Abels have investigated the solvent effects for the rate of reaction of sodium naphthalene with hexyl fluoride (90). The solvent effects on the corresponding reactions with primary iodides, bromides, and chlorides as discussed above indicate that there is greater charge delocalization in the transition state relative to the reactants since solvent-separated ion pairs were found to react faster than contact ion pairs. Since the metal ion effect on the

reaction of naphthalene radical anion with 5-hexenyl fluoride (86) had indicated that the transition state for the fluoride reaction had greater charge localization than the reactants, it was postulated that solvents of greater cation solvating ability would slow the reaction. This effect was found although the magnitude was disappointingly low. In going from the very tight pairs found in MeTHF to the crown ether complex in DME caused a decrease by a factor of only one-seventh. In fact, in going from THF to DME the rate actually increases. On a curve of cation affinity vs. reaction coordinate, the authors placed the iodides, bromides, and chlorides in a region where the charge is delocalized between the radical anion and the halide in the transition state. Application of Hammond's postulate would suggest that the



degree of bond breaking in the transition state should increase in the order $\text{RI} < \text{RBr} < \text{RCl} < \text{RF}$. The cation affinity of the transition state might be expected to reach a minimum somewhere in the series (approximately at bromide) and then start to rise as the transition state moves toward the product side. It was postulated, then, that

primary fluorides might have a transition state which has a slightly higher cation affinity than the reactants. It might be concluded that the degree of bond breaking (or extent of formation of alkyl halide radical anion) in the transition state is not very great even for fluorides. This conclusion is based on the expected very much greater cation affinity of a fluoride anion compared to that of naphthalene radical anion and the apparent lack of significant difference in transition state vs. reactant cation affinities.

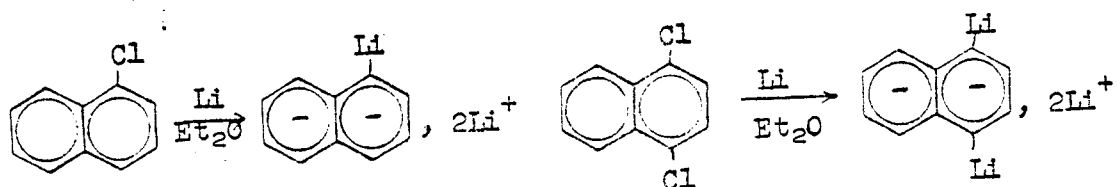
The previously discussed metal ion effects, which span a range of about five powers of ten, would seem to present an enigma considering the extremely small solvent effects observed. Metal ion effects are complex since there is a competition between the anion in question and solvent molecules for the cation and the entropy change in going from contact to solvent-separated ion pairs is in opposition to ΔH .

A compilation of electron transfer:coupling ratios (see Scheme 1) for a number of systems is presented in Table 6. From the values shown for entries 9-14, it can be seen that contact ion pairs (Na in MeTHF and THF, Cs) tend to couple somewhat more than the corresponding solvent-separated ion pairs (Na in DME, Li). It is interesting to note that, with primary radicals, anthracene undergoes almost no electron transfer, while biphenyl undergoes almost no coupling.

Table 6. Partitioning between electron transfer and coupling for selected halides and radical anions. See also Table 4.

Entry #	Halide	Radical Anion ^(a)	Metal	Solvent	ET Coupling	Ref.
1		A ^{•-}	Na	DME	0.01	67
2		A ^{•-}	Na	DME	0.015	67
3		A ^{•-}	Na	DME	1.13	67
4		N ^{•-}	Na	DME	4.88	67
5		N ^{•-}	Na	THF	1.9	67
6		N ^{•-}	Na	DME	1.0	80
7		N ^{•-}	Na	DME	0.85	67
8		N ^{•-}	Li	DME	1.44	67
9	"	N ^{•-}	Na	DME	1.27	67
10	"	N ^{•-}	Cs	DME	0.72	67
11	"	N ^{•-}	Li	THF	1.17	67
12	"	N ^{•-}	Na	THF	0.67	67
13	"	N ^{•-}	Cs	THF	0.72	67
14		N ^{•-}	Na	MeTHF	0.47	67
15		N ^{•-}	Na	THF or DME	> 50	91
16		B ^{•-}	Na	DME	> 50?	80

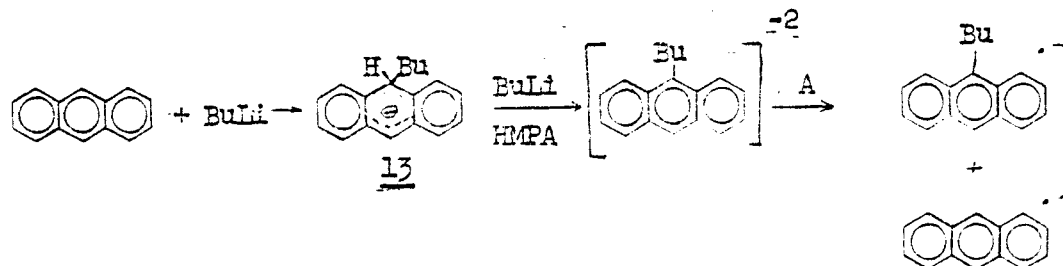
(a) A = anthracene, N = naphthalene, B = biphenyl.



The reactions of radical anions with alkyl halides give rise to the CIDNP phenomena when the reactions are carried out in low fields but not in high. Garst has recently reviewed his work on this subject (93). For very recent work, see References 94 and 68.

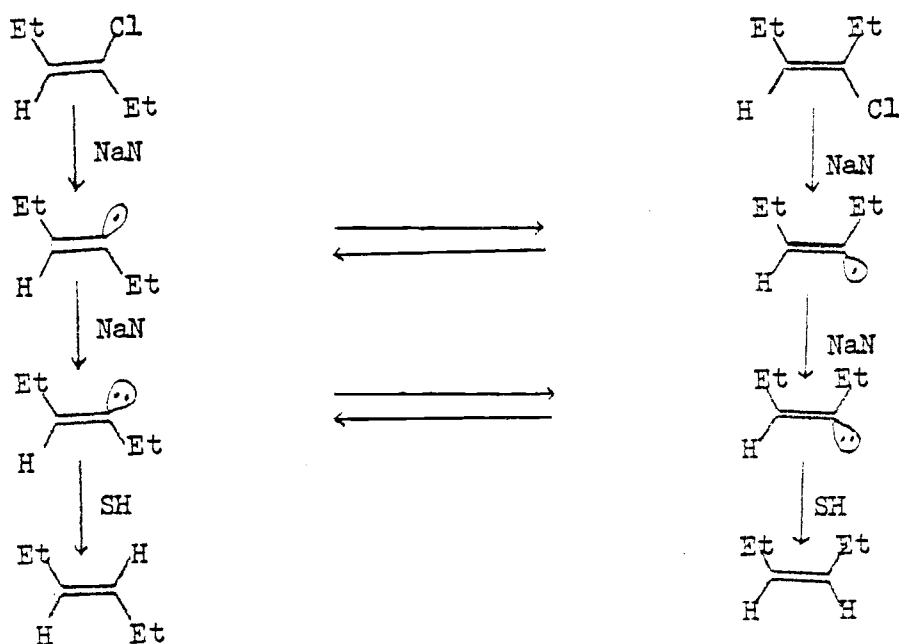
Panek has reported in a recent communication (95) that a large excess of *n*-butyllithium reacts with 10^{-4} molar biphenyl in THF solutions containing hexamethylphosphoramide (HMPA) to give the radical anion. To a radical anion chemist, this is a most peculiar finding, seeming to be almost the inverse of the alkyl halide-radical anion reaction. A variety of organometallic compounds were reported to undergo such reactions with a variety of aromatic hydrocarbons. No mechanism was given, although the term 'one-electron reduction' was used to describe the process. The fate of the butyl group was not discussed. With anthracene in THF in the absence of HMPA a 99% yield of the alkylate 13 was obtained resulting from the formal addition of butyllithium across the 9, 10 positions. When the HMPA concentration was increased to 5.2 molar, the alkylate yield dropped to 7%, while the radical anion was obtained in 93% yield (yields determined

by spectrophotometric methods). A mechanism which might explain Panek's results is shown below. The reaction of compounds similar



to 13 with butyllithium in highly polar solvents to form the dianion is known (96). The two radical anions would probably not be distinguishable by their uv spectra.

Not long after it has become known that sodium naphthalene reacts with primary radicals at nearly diffusion controlled rates, this fact was put to good use. Sargent and Browne (91) reported the first successful attempt to trap the cis and trans isomers of a vinyl radical before complete equilibration could occur. E- and Z-3-chloro-3-hexenes were treated with sodium naphthalene in DME or THF at 27° and at 0° . A mixture of cis- and trans-3-hexene was formed in at least 98% yield. The mechanism presented for this reaction is the usual one. The trans:cis product ratios for reaction in THF are shown in Table 7. It can be calculated from the data given that the equilibrium trans:cis ratio would be around 4.7. This calculation is based on the assumption that the average trapping time of the radical derived from the E and Z chlorides is the same. As can be seen, the



product distribution depends on the configuration of the starting chloride and indicates a trapping efficiency in the order of 50%. Interconversion of the anions was known not to occur. Vinyl radical hydrogen abstraction from hydrogen donors gives the thermodynamically less stable alkene and, of course, could not compete with reaction with sodium naphthalene anyway. One important point which the authors make is that transfer of an electron to either radical should take place with equal ease, whereas hydrogen abstraction could be quite sensitive to steric effects.

Another 'first' made possible by the speed of the electron transfer from sodium naphthalene to radicals was reported by Jacobus and Pensak (97) in 1969. These authors were able to trap an optically

active tertiary cyclopropyl radical before complete equilibration could occur in the absence of cage effects. Starting from (+)-(S)-1-bromo-1-methyl-2,2-diphenyl cyclopropane (12), 29% optically pure hydrocarbon was formed with partial retention. As in the vinyl case, the anions were known not to equilibrate.

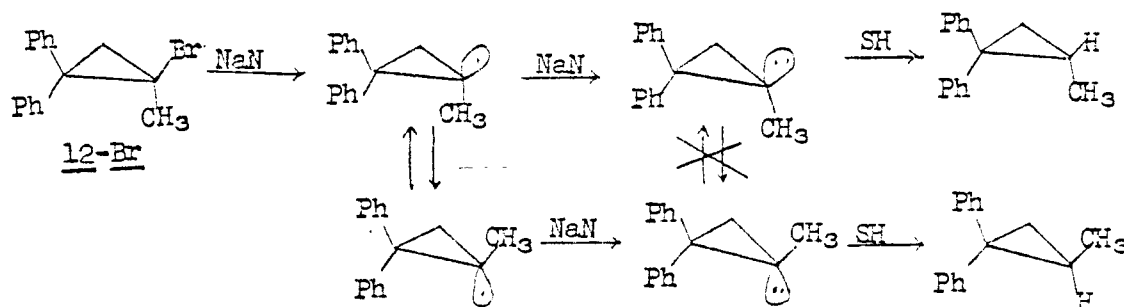
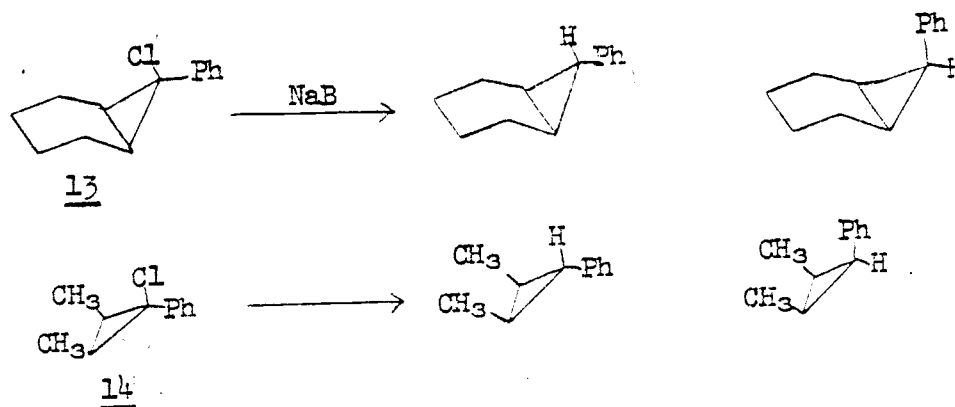


Table 7. Vinyl radical trapping with sodium naphthalene in THF.

Reactant	<u>Trans:cis</u> at 0°	<u>Trans:cis</u> at 27°
	2.23	2.85
	5.67	5.67

The only other work which has been reported concerning the stereochemistry of the products of radical anion reactions with halides concerns the reactions of 13 and 14 with sodium biphenyl (98). In this case the intermediate anions, because of the a phenyl group,

are interconvertible. The fact that mostly trans products were



obtained has no bearing on the radical stereochemistry or perhaps even on the anion stereochemistry if the energy of activation for proton abstraction from solvent is higher than the interconversion barrier. Solvent and concentration effects were observed, but were not explained satisfactorily.

The Structure and Equilibria of Radicals

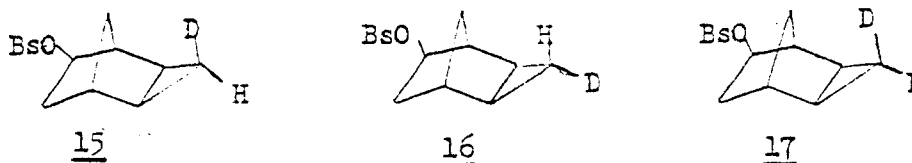
Since radicals are intermediate between carbonium ions and anions, they tend to show properties that are also intermediate. Among the radicals with firmly established structures are methyl, trifluoromethyl, cyclopropyl and vinyl. Methyl has been long established as nearly planar but with a very broad minima and thus undergoes wide ranging vibrations (umbrella mode) whereas trifluoromethyl is pyramidal (99, 100). Cyclopropyl is pyramidal with a low barrier to inversion. Vinyl is bent and with perhaps twice the inversion

barrier of cyclopropyl (101, 91, 102). Alpha-fluorocyclopropyl has a substantial barrier to inversion and can be completely trapped before inversion by triphenyltin hydride (103). Chlorocyclopropyl can only be partially trapped and fluorocyclobutyl can not be trapped at all with triphenyltin hydride (104). ESR studies indicate cyclobutyl and cyclohexyl to be planar (105). tert-Butyl radicals have alternately been considered to be planar and nonplanar. At the time of this writing nonplanarity is in vogue with a barrier to inversion of approximately 500 calories and essentially tetrahedral geometry (106, 107). Pauling's theory that electronegative substituents increase the pyramidal character of radicals has been displaced theoretically (108) and disproven experimentally (99). The new theory explains the nonplanarity of both trifluoromethyl and tert-butyl as being due to π -conjugative destabilization of the planar form.

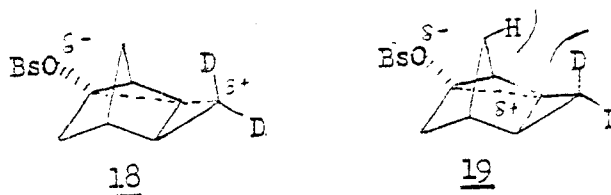
RESULTS AND DISCUSSION

Introduction

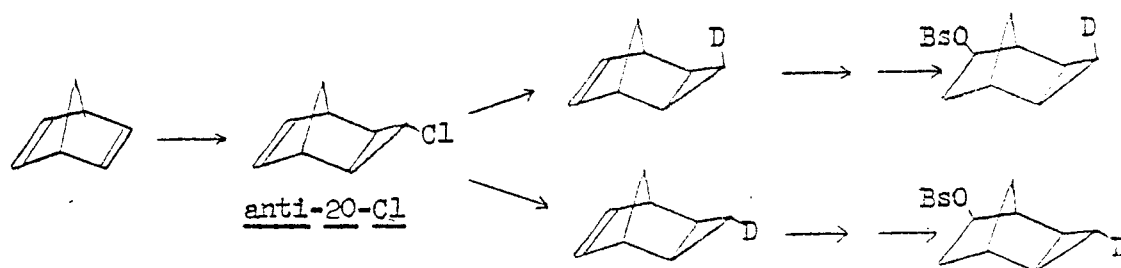
The research described in this section obtained its impetus from some very interesting results obtained during an effort to find a synthetic scheme to compounds 15 and 16. These brosylates were, in turn, required for a deuterium isotope study which was sparked by



the result of a solvolysis study on 17 by Freeman and Blazeovich (109). The deuterium isotope effect upon the rate of solvolysis of 17 was found to be 1.20--a tremendous effect considering the distance of the deuterium atoms from the leaving group. This isotope effect might arise from either delocalization of charge unto the C3 position (18), or perhaps relief of non-bonded compressional strain due to delocalization along the 2, 4 bond as in 19. The obvious way of distinguishing

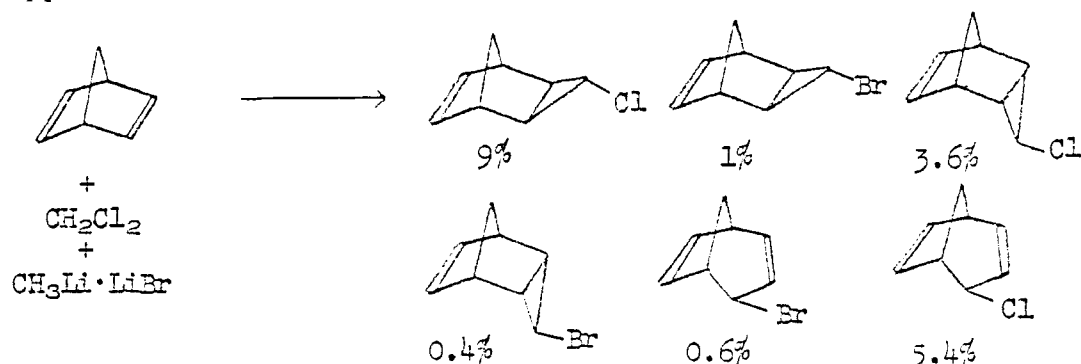


among these two possibilities would be to examine the deuterium isotope effect upon the solvolysis of 15 and 16. If 18 is the more accurate representation of the transition state, then both 15 and 16 should exhibit essentially the same isotope effect of around 1.1 each. If, on the other hand, 19 represents the transition state, then 15 would give rise to a deuterium isotope effect of 1.2, while 16 would be expected to give rise to an isotope effect of 1.0. The scheme picked to synthesize 15 and 16 is shown below. The key step in this sequence



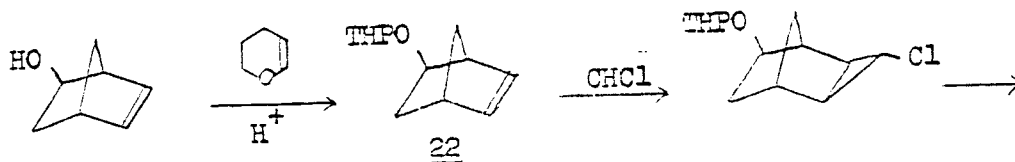
is the stereoselective replacement of chlorine by deuterium in such a way as to give either syn-20-D or anti-20D depending upon reagent.

The synthesis of anti-20-Cl gives a variety of products (110) in approximately 20% total yield. The allylic halides could be easily



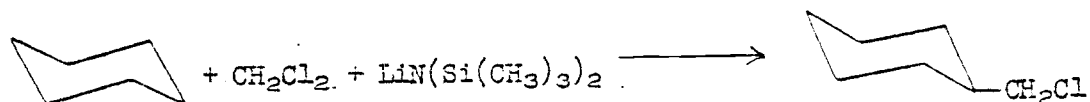
removed by treatment with aqueous silver nitrate, but separation of the exo and endo ring systems was much more difficult. Not only was it found impossible to separate anti-20-Cl from anti-21-Cl by distillation, but it was not even possible to separate these two compounds by gas chromatography with a least ten columns tried. The same was true of the hydrocarbons. It was eventually found that both the chlorides and corresponding hydrocarbons could be separated by chromatography on a column of silver nitrate-impregnated Silicar.

Another synthetic route which was attractive because the tedious silver nitrate chromatography would be unnecessary, would have involved the following sequence. The addition of the elements of



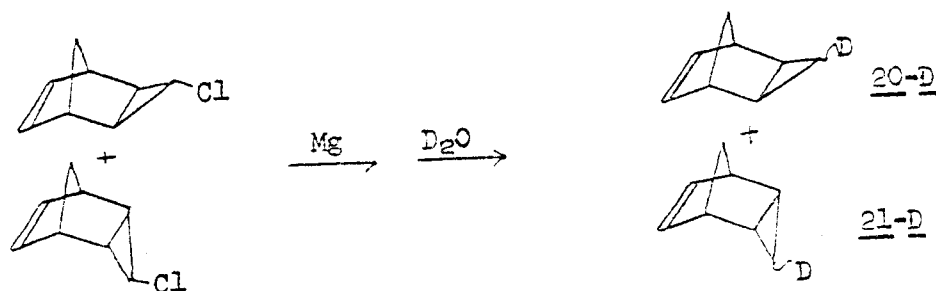
monochlorocarbene to norbornene gives only products of exo addition with none of the troublesome endo products (111), and it was assumed that 22 would act in a like manner. However, experiments using norbornene as a model indicated that under conditions where norbornene is the limiting reagent, the yields did not exceed 6%, rendering this synthetic pathway untenable. Various other bases were tried as a replacement for methyllithium, but in no case did the yield exceed 6%. Lithium tetramethylpiperidide and lithium hexamethyldisilazane were among those tried. The reaction of methyllithium

with dichloromethane is commonly assumed to go via a carbenoid species such as CHCl_2Li without actual formation of the carbene. However, it was found, when attempting to react norbornene with dichloromethane and lithium hexamethyldisilazane in refluxing cyclohexane solvent, that in addition to a 6% yield of the expected adduct, a new product appeared. Upon analysis, this compound was discovered to be cyclohexylchloromethane. Such a product must come about by formation of free monochlorocarbene, since carbenoids are unreactive to insertion into CH bonds.



It would appear that two theories might be put forth to explain the unexpected formation of the free carbene. The reaction of lithium hexamethyldisilazane with dichloromethane might give the free carbene directly, unlike the reaction using methyllithium, perhaps as a result of differing extents of types of association. Methyllithium is known to exist as a tetramer. The alternate hypothesis would have the carbenoid being formed, but then decomposing to give the free carbene in competition with reaction with the olefin. Since norbornene is apparently a poor olefin for such addition reactions, and since the olefin was present in rather low concentrations, the last mechanism would seem as likely as the first.

To the end of finding a suitable means of converting anti-20-Cl to the corresponding deuterated hydrocarbons, the Grignard reaction was examined. It was found to be repeatedly impossible to induce reaction of a purified mixture of anti-20-Cl and anti-21-Cl with magnesium in spite of adding methyl iodide, dibromoethane, and even slow addition of butyl bromide. All the additives underwent reaction, but no conversion of the cyclopropyl chlorides was observed. On the other hand, reaction of the crude mixture from the methyllithium-methylene chloride synthesis proceeded quite rapidly. Perhaps this was due to the presence of the bromides. Quenching the Grignard reaction mixture with D_2O followed by chromatography using silver nitrate on Silicar gave the pure deuterated hydrocarbons. The products from the allylic halides were not investigated. It is not possible

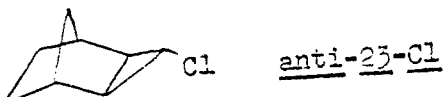


to analyze 20-D directly by nmr due to coincidence of a number of adsorptions. Epoxidation with peracetic acid followed by addition of europium shift reagent ($Eu(fod)_3$) allowed both the syn- and anti-C3 proton absorptions to be separated from the other resonances.

Examination of the nmr spectrum so obtained indicated 20 was $89 \pm 5\%$

monodeuterated with an excess of syn over anti deuterium incorporation in a ratio of 2.2 ± 0.3 to 1. Direct examination of 21 revealed $85 \pm 5\%$ deuterium incorporation, with an excess of anti over syn deuterium incorporation in a ratio of 2.4 ± 0.5 to 1. Similarly, reduction of a mixture of 20-Cl and 21-Cl with sodium in tert-butyl alcohol-0-d-THF followed by the same analysis procedure just described indicated the exo hydrocarbon (20-D) to be $98 \pm 5\%$ deuterated with the syn:anti ratio being 1.16 ± 0.2 , while the endo hydrocarbon (21-D) was $93 \pm 5\%$ deuterated with the anti deuteration predominating over the syn in a $2.7 \pm 0.3:1$ ratio. It is striking that the exo and endo isomers give such different syn to anti ratios, being essentially reversed in the case of the Grignard reaction.

To find a means of effecting the stereospecific replacement of the chlorine in anti-20-Cl, a more convenient system was required as a model. It was found that the saturated halide anti-3-chlorotricyclo-[3.2.1.0^{2,4}]-octane (anti-23-Cl) was an excellent substitute, since



the stereochemical environment of the reactive center is essentially identical. Its synthesis from norbornene and methylene chloride-methylolithium as before, although giving low yields, does not give rise to any of the troublesome endo adducts (111). The corresponding hydrocarbon can be analyzed for syn and anti deuterium incorporation

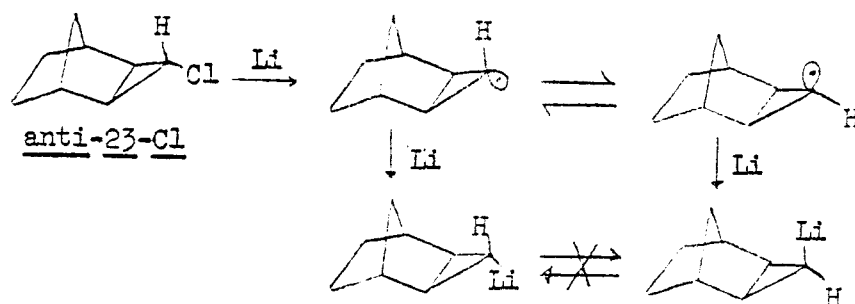
directly by nmr since the two protons are out in the open with only minor overlap of the syn-C3 proton and the C2, C4 protons marring integration accuracy. Thus anti-23-Cl was used in all further study. The results of treatment of anti-23-Cl with potassium, sodium, and lithium in tert-butyl alcohol-0-d-THF and with lithium in ether followed by deuterolysis are compiled in Table 8 along with the results just discussed. Deuterium incorporations were above 95%.

Table 8. The stereochemistry of reduction of selected cyclopropyl halides with metals.

Halide		<u>Syn-D:Anti-D</u>
<u>anti-20-Cl</u>	(1)Mg, THF (2)D ₂ O	2.2 ± 0.3 ^(a)
<u>anti-20-Cl</u>	Na/ <u>t</u> -BuOD-THF, reflux	1.16 ± 0.2
<u>anti-21-Cl</u>	(1)Mg, THF (2)D ₂ O	0.86 ± 0.15
<u>anti-21-Cl</u>	Na/ <u>t</u> -BuOD-THF, reflux	0.42 ± 0.09
<u>anti-23-Cl</u>	(1)Li, Et ₂ O, 0° (2)D ₂ O	2.1 ± 0.3
<u>anti-23-Cl</u>	Li/ <u>t</u> -BuOD-THF, reflux	1.70 ± 0.05
<u>anti-23-Cl</u>	Na/ <u>t</u> -BuOD-THF, reflux	2.11 ± 0.05
<u>anti-23-Cl</u>	K/ <u>t</u> -BuOD-THF, reflux	1.25 ± 0.05

^(a)Standard deviations from nmr integration data.

The mechanism (112, 77, 113, 114) commonly put forth for reactions such as these is essentially identical with the well-known radical anion-alkyl halide reaction discussed in the introduction. This mechanism is illustrated here by the reaction of anti-23-Cl with lithium in ether. The classic esr experiments of Fessenden and Schuler (115) in

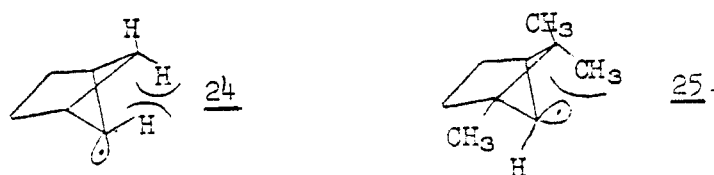


1963 indicated that secondary cyclopropyl radicals have a pyramidal configuration but interconvert with a rate constant of 10^8 to 10^{10} sec^{-1} . Thus it is apparent that only very fast reactions could trap even a fraction of the initially formed radical before equilibration. It would not seem unreasonable, however, to propose that a metal surface might be capable of donating an electron rapidly enough. After all, the radical is formed on or very near the surface and has to diffuse only a short distance (if any at all) to pick up another electron. It is apparent from the high deuterium incorporations that few radicals escape from the surface.

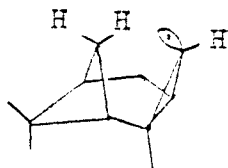
The syn to anti ratios observed from anti-20-Cl and anti-23-Cl were postulated to result from competition between inversion of the initially formed radical and its trapping by reaction on the surface to form the metal alkyl. It was thought that the syn radical might be more stable than the anti due to the compressional effect of the syn- C_8 proton.



A similar argument has been presented recently in a communication concerning an esr study of the bicyclo[2.1.1]hex-5-yl radical (160). From analysis of splitting constants, it was concluded that radicals 24 and 25 have the configurations shown. The switching of



the stable configuration between 24 and 25 was attributed to destabilization of the configuration exhibited by 24 in 25 by the compressional effect of the methyl group on the α -hydrogen. It should be pointed out, however, that the simplicity of the esr data analysis may make the conclusions rather speculative. Hatem and Wagell (116) have used similar arguments to explain syn stereospecificity in the reactions of the α -halocyclopropyl radical shown.

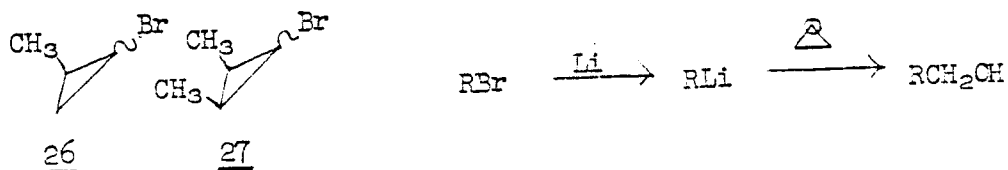


Cyclopropyl lithium and Grignard reagents have been shown to be configurationally stable (117, 113). The sodium and potassium

reagents are another matter, however. If one assumes that the metal alkyl is initially formed in the least stable syn configuration and are able to isomerize to the anti configuration at a rate competitive with reacting with tert-butyl alcohol-0-d, it would be expected that varying the alcohol concentration from high to low values should increase the proportion of the anti product. However, no change was observed upon changing the ratio of THF to alcohol from zero to thirty in the reduction with potassium.

Walborsky and Young (77) have observed formation of optically active Grignard reagent from (+)-(S)-1-bromo-1-methyl-2,2-diphenylcyclopropane (12-Br) and magnesium. Walborsky and Aronoff (113) obtained corresponding results from 12-Br and lithium. Both the Grignard and lithium reagents were shown to be configurationally quite stable. The reduction of 12-I with sodium in ether gave hydrocarbon with optical purity equal to that formed as a by-product of the reaction with lithium (ca. 60% purity). Walborsky felt that the formation of optically active lithium reagent indicated some other process in addition to that shown above must be operative since it had been shown that the radical in question was incapable of retaining its optical purity. This conclusion is not valid. Jacobus and Pensak had, in fact, shown that this radical was capable of retaining its configuration to a modest degree, even under conditions where the rate of trapping is rather less than what would be expected at a metal surface.

Dewar and Harris (114) found that even secondary cyclopropyl halides give significant retention of configuration. The results obtained from the reaction of cis and trans 26 and 27 with lithium in ether followed by reaction with ethylene oxide are shown in Table 9.



The authors interpreted these results in terms of partial trapping of the initially formed radical by the lithium surface before equilibration could occur.

Table 9. Stereochemistry of lithium reagent formation from 26 and 27.

Compound	<u>cis:trans</u> Alcohol	
<u>cis-26</u>	1.38	(0.83 calculated equilibrium value)
<u>trans-26</u>	0.54	
<u>cis-27</u>	1.17	(0.67 calculated equilibrium value)
<u>trans-27</u>	0.45	

One somewhat unsettling observation which may cast some doubt upon the validity of the above mechanism is the fact that the degree of trapping observed in the case of the secondary radical is essentially the same as that found in the case of the tertiary radical (around 60%). It would be expected that secondary radicals should invert much more rapidly than tertiary radicals since they can do so by proton tunneling

(114). Perhaps a combination of steric effects on the metal surface caused by the bulky phenyl groups of the tertiary radical, and the decreased electron affinity caused by the electron donating methyl group may slow down the rate of the second electron transfer. The complex nature of any metal-liquid interface makes mechanistic interpretation difficult.

Low Temperature Potassium Reduction of anti-23-Cl

Since none of the reductions gave the desired stereochemical purity, a low-temperature potassium/tert-butyl alcohol-0-d reduction of anti-23-Cl was undertaken. It was expected that, if the product ratio observed is the result of a competition between inversion of the radical and its diffusion back to the metal surface where it is then trapped as the stable lithium reagent, then changing the temperature should induce a rather large change in the product ratio. The rate of diffusion of a molecule is directly proportional to the temperature and inversely proportional to viscosity (118). On the other hand, the rate of inversion of the radical should be exponentially related to temperature and one might well expect that this would outweigh the effect of temperature on diffusion. Thus it was expected that markedly lowering the temperature would greatly increase the degree of retention. Since lowering the temperature of the reaction also decreases its rate, experimentally it was necessary to produce a

colloidal form of potassium to increase the surface area, and thus the rate of reaction. This was accomplished by evaporating metallic potassium onto a frozen surface of THF under high vacuum conditions. It was found that upon warming, a black, very finely divided suspension of potassium results. This suspension was not stable at temperatures of -40° or above, as it conglomerated under such conditions. The experiment was performed by depositing layers of tert-butyl alcohol- O - d , THF, potassium metal vapor, THF, tert-butyl alcohol- O - d and finally anti-23-Cl. The frozen layers were then melted by warming to -95° in a slush bath and then stirred for 30 minutes. The mixture was then stirred at -78° for 1.5 hours. At this temperature, a visible reaction occurred resulting in a lightening of the color of the precipitate. Upon workup, it was found that the deuterium incorporation in the hydrocarbon was excellent at 95%, but surprisingly enough, the syn to anti incorporation ratio was 1.28-- almost exactly the same as that obtained in refluxing THF. This result seemed to be inconsistent with the proposed mechanism. However, it will now be shown that this result can be accommodated by the theory if the experimental activation energy is taken to be 1.7 Kcal.

Carvajal and co-workers (119) have reported the viscosity of THF over the temperature range of $+25$ to -70° . Although the temperatures involved in this study were outside this range, it was found

by non-linear least squares methods that Carvajal's data can be represented very well by the equation

$$\eta_{\text{THF}} = 2.80 + (1.63 \times 10^3) \text{EXP}((-0.02279) \cdot T),$$

where T is the temperature in $^{\circ}\text{K}$ and η is in millipoises. A standard deviation of 0.9% was obtained and is testimony to the excellent fit obtained. Using this equation to extrapolate the viscosity data to -80° and $+65^{\circ}$, we can calculate the theoretical ratio of diffusion rate constants:

$$\frac{k_{\text{diffusion}, -80^{\circ}}}{k_{\text{diffusion}, +65^{\circ}}} = \frac{193^{\circ}\text{K}/23 \times 10^{-3} \text{ poise}}{338^{\circ}\text{K}/3.5 \times 10^{-3} \text{ poise}} = 0.087.$$

It will be shown below that the most stable configuration of the radical, 23-yl, is the syn configuration. If we now assume that the rate of anti-23-yl inverting to syn-23-yl is given by the equation (120):

$$k = \frac{ekT}{h} e^{\Delta S^{\ddagger}/R} e^{-\Delta E^{\ddagger}/RT},$$

and if we assume ΔS^{\ddagger} to be zero, then we can calculate the ΔE^{\ddagger} , which gives the same ratio of rate constants as did the diffusion calculation above:

$$0.087 = \frac{k_{\text{inversion}, -80^{\circ}}}{k_{\text{inversion}, +65^{\circ}}} = \frac{193^{\circ}\text{K} \cdot e^{-\Delta E^{\ddagger}/(1.98)(338)}}{338^{\circ}\text{K} \cdot e^{-\Delta E^{\ddagger}/(1.98)(338)}};$$

$$\Delta E^{\ddagger} = 1.7 \text{ Kcal.}$$

This is a perfectly reasonable value for the heat of activation for a cyclopropyl radical. Ab initio MO-SCF calculations performed recently by Ellinger and co-workers (101) place the inversion barrier for the cyclopropyl radical itself at 3.8 Kcal. It must be emphasized that the value of 1.7 Kcal obtained above does not constitute a 'value' for the inversion barrier since proton tunneling was not taken into consideration, and since the mechanism is undoubtedly much more complex than that assumed. It simply demonstrates that it is not yet necessary to discard the proposed mechanism because of the lack of temperature dependence observed.

Reaction of anti-23-Cl with Lithium Naphthalene

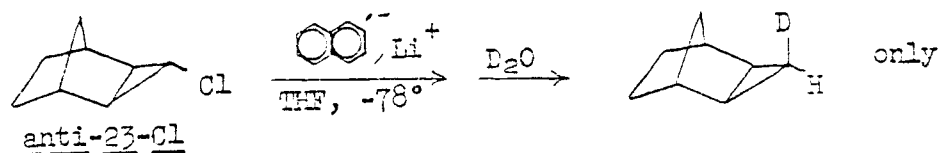
As was discussed in the historical section, the well-studied sodium naphthalene reduction of alkyl halides produces alkyl anions, but the potentially useful anion is immediately destroyed by reaction with solvent. Attempts at carbonation and deuteration have met with little success. As previously discussed, the inclusion of magnesium bromide in the reaction, followed by deuterium oxide, was reported to give only 80-85% deuterium incorporation and probably gives much less.

It would seem obvious that utilizing lithium naphthalene rather than sodium naphthalene and running the reaction at low temperatures, should allow the anion to be trapped as the very useful lithium reagent.

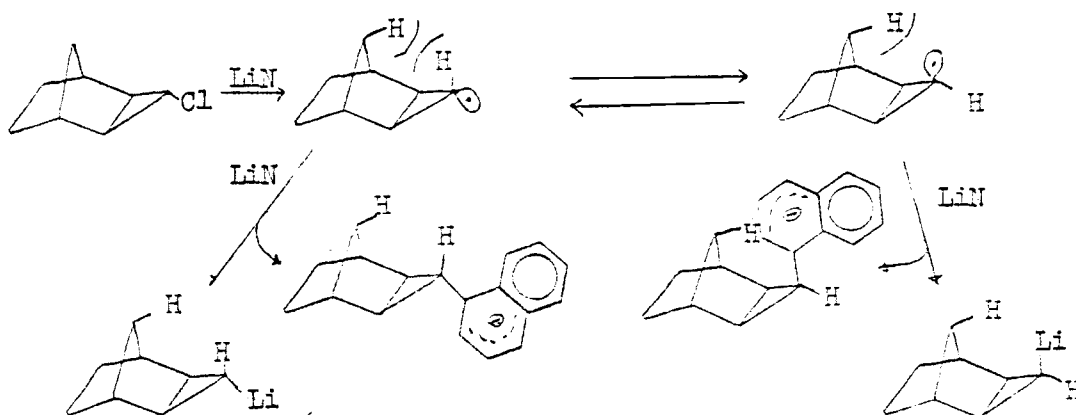
Surprisingly enough, there existed very little in the literature concerning such a system. The closest thing to a complete study of lithium naphthalene reactions with halides was reported by Screttas (82). The only alkyl halides studied were cyclohexyl chloride and butyl chloride, bromide and iodide which gave rather low lithium reagent yields of 70, 45, 37 and 16% respectively. The reactions of phenyl halides under the same conditions (-50° , THF) gave much higher yields of around 90%.

Eisch, in 1962, reported that phenyl fluoride gives a 70% yield of lithium reagent when reacted with lithium biphenyl dianion (55). Garst (121) has quoted unpublished results concerning the reduction of 5-hexenyl chloride with lithium naphthalene in DME. The addition of deuterium oxide resulted in the formation of 1-hexene and methylcyclopentane with only 35% deuteration.

Fortunately we were unaware of the above rather discouraging results. The reaction of anti-23-Cl with lithium naphthalene in THF at -78° followed by deuterolysis gave astounding results: 96% deuterium incorporation and a syn:anti ratio of at least 100:1 -- complete inversion!

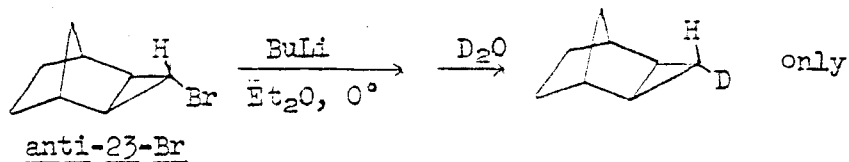


One might imagine several reasons for the extremely high stereospecificity observed. As was discussed in the historical section, primary, secondary and tertiary halides give large amounts of coupling products in the reaction with sodium naphthalene. The two radicals, anti-23-yl and syn-23-yl might differ markedly in their ability to form bonds with the bulky naphthalene radical anion. Thus the possibility existed that the high stereospecificity resulted from



exclusive coupling in the case of the unhindered anti radical and exclusive electron transfer in the case of the highly hindered syn radical. To test this possibility, the alkylated naphthalenes were searched for by gas chromatography, but none were found. Another theory easily disposed of would have the anti lithium reagent isomerizing to the syn. This would seem highly unlikely on energetic grounds and there is little reason to believe that the lithium reagents in question should not be stereochemically stable at -78° , when similar compounds are known to be stable at room temperature (114, 113).

However in order to prove the contention that the lithium reagents are stable, metal-halogen exchange of anti-23-Br with butyl lithium at 0°, followed by deuterolysis was performed. Only the anti deuterated material was obtained.



Testimony to the fact that cyclopropyl lithium reagents are configurationally very stable was obtained from an experiment in which anti-23-Cl was treated with lithium naphthalene at -78°, followed by slow warming to 0° over a period of six hours, and then quenched with deuterium oxide. Although the lithium reagent had apparently attacked solvent, since it was only 82% deuterated, no isomerization had occurred in spite of the very high strain of the syn lithium reagent.

The theory which seems to be most likely is essentially identical to that discussed for the metal reduction of anti-23-Cl. In that case, it was postulated that the radicals are formed almost in contact with the metal surface which can then quickly donate another electron--fast enough to trap some of the first-formed radical. In the present case, the first-formed radical would have to have a diffusive encounter with another lithium naphthalene ion pair, and this can be estimated to require approximately 10^{-8} seconds in 0.1 molar lithium

naphthalene at -80° by using the equation:

$$k_{\text{diffusion control}} = \frac{2RT}{3000\eta} [2 + r_a/r_b + r_b/r_a] \text{ l/mole-sec.}$$

(Reference 118)

$$= 1.9 \times 10^9 \text{ l/mole-sec at } -80^{\circ} \text{ in THF.}$$

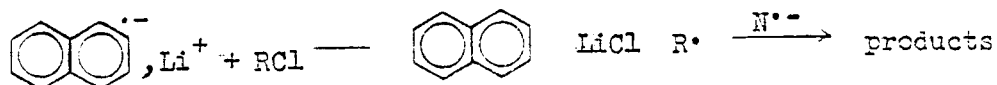
The particle sizes r_a and r_b were assumed to be equal, and η was taken as 0.023 Poise as above. It was also assumed that only one-quarter of the encounters would be singlets and capable of reaction (83). This rate of trapping is undoubtedly several orders of magnitude slower than that on the surface of a metal.

Since the rate at which radicals are scavenged by lithium naphthalene is likely to be very close to diffusion controlled, it is highly unlikely that any selectivity in reacting with one configuration faster than another could be exhibited by the radical anion. Even if the rate is not diffusion controlled, it would be expected that there would exist no selectivity to the steric requirements of a radical. This conclusion is based on the fact that electron transfer can occur over rather large distances (see Historical Section). The only case where electron transfer from a radical anion to a radical might show discrimination would be where coupling products are formed, since this is competitive with electron transfer. Since coupling products are not observed, we are left with the conclusion that the radical, syn-23-yl is much more stable than anti-23-yl. This experiment

constitutes the first determination of the configuration of a secondary radical using a radical anion as a non-discriminating radical trap and only the second determination of the configuration of any radical by such a method. (The first was a by-product of the vinyl radical experiment of Sargent and Browne described in the Historical Section.)

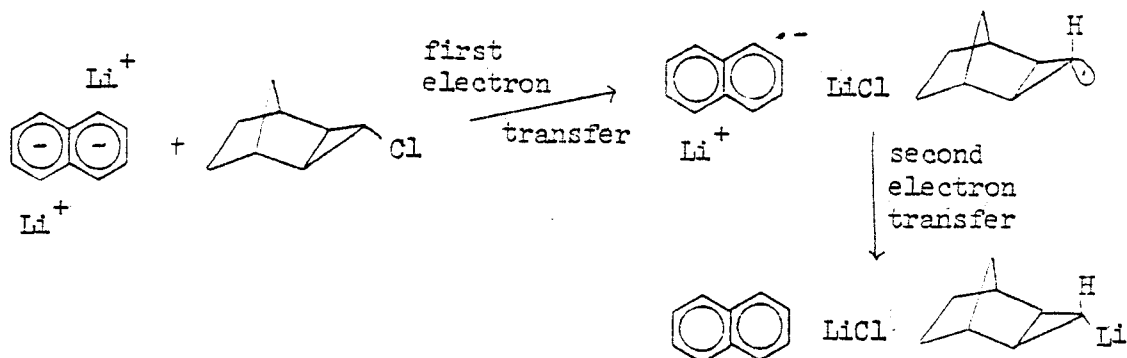
Reaction of anti-23-Cl with Lithium Naphthalene Dianion

The reaction of a lithium naphthalene ion pair with a halide produces an alkyl radical with an inert naphthalene molecule in juxtaposition. The radical must then diffuse to another radical anion with the proper spin state to produce the final product, requiring on the order of 10^{-8} seconds.



It was reasoned that the corresponding reaction of the dianion would result, after the first electron transfer, with the radical in juxtaposition not with a 'dead' naphthalene molecule, but rather with a very much 'alive' radical anion and in the proper spin state. The second electron, then, might be transferred within the solvent shell soon enough to capture the first-formed configuration of the radical before inversion has time to take place. In the case of anti-23-Cl, this

would give the desired anti-23-Li.



The first attempts to form the dianion by reacting naphthalene and excess lithium chips were unsuccessful. The rate at which the lithium dissolved was apparently too slow relative to the rate of attack upon THF by the dianion. A purplish-black solution was prepared from lithium dispersion, but the syn to anti ratio of deuterium incorporation from the reaction with anti-23-Cl was only 6.8, and even this may have been caused by some of the halide reacting with the excess lithium metal.

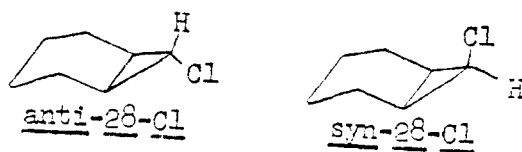
Finally, a pure, deep purple solution of the dianion, free from excess lithium metal, was successfully made by high vacuum lithium vaporization techniques. (See the experimental section for details.) Reaction of anti-23-Cl with this solution at -78° followed by deuterolysis gave only the syn deuterated hydrocarbon--thus the hope of trapping the anti radical had not been realized.

Was it possible that the dianion might be so unreactive that the small amount of monoanion present might be reacting to the exclusion

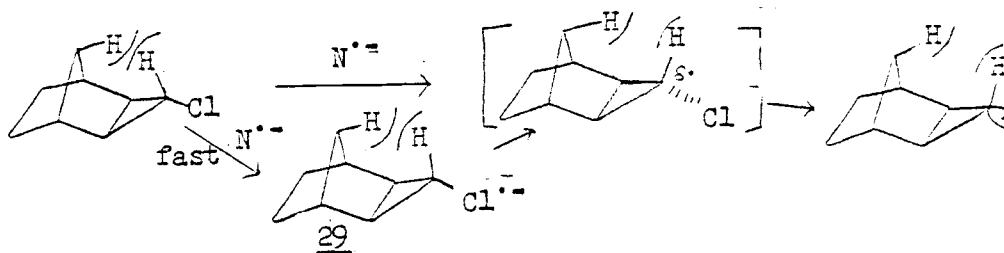
of the dianion? To provide an answer for this question, it was necessary to determine the rate of reaction of the monoanion with anti-23-Cl in the same apparatus and under the same conditions as those used for the dianion experiment. The value so obtained for the second-order rate constant for the reaction between lithium naphthalene and anti-23-Cl is $1.0 \text{ M}^{-1} \text{ min}^{-1}$. From knowledge of the dianion and radical anion concentrations during the dianion experiment, it could be calculated that the dianion was, in fact, undergoing most of the reaction. If one were to assume that only the monoanion in the dianion solution were reacting, the second order rate constant for the monoanion must be greater than $4.5 \text{ M}^{-1} \text{ min}^{-1}$ --almost five times faster than the actual measured rate constant for the monoanion. The rate constant for the reaction of lithium naphthalene dianion in THF with anti-23-Cl would then be calculated to be $0.055 \text{ M}^{-1} \text{ min}^{-1}$. This value is only one-eighteenth of the rate constant for the monoanion. Why, then, does the dianion, which is less stable than the monoanion, react so slowly, and why did the hoped-for trapping not occur? The answer to both questions may be the same. It was stated in the Historical Section that dianions are expected to be very tight contact ion triples in ether solvents, while lithium naphthalene radical anion consists of loose ion pairs in THF. It was also shown in at least two types of electron transfer reactions--electron exchange and dissociative electron attachment to alkyl iodides, bromides and chlorides--

that tight ion pairs react between one and two orders of magnitude slower than free ions or loose ion pairs. Thus, although the dianion is a higher energy species than the monoanion, it reacts more slowly because of the great influence of ion pairing upon the rate of reaction. Similarly, it would be reasonable to postulate that the rate of reaction of a tight ion pair with a radical might be slower than the diffusion controlled rate of the solvent-separated ion pairs studied by Garst. If this is the case, the anti-23-yl radical as formed in reaction with the dianion is in juxtaposition, not with a highly active loose ion pair, but with a, perhaps, half-dead contact ion pair. The radical might then simply diffuse away and convert to the more stable syn configuration before picking up its second electron.

Since the configurational preference of the 23-yl radical was found to lie heavily upon the syn side due to the compressional strain caused by the syn-C8 hydrogen, it was of interest to examine 7-chloronorcarane (28-Cl) where the norbornane CH_2 bridge is missing. Reaction of a syn and anti mixture of 28-Cl with 0.1 molar lithium naphthalene in THF at -78° revealed that anti-28-Cl reacts with a second-order rate constant of $0.035 \pm 0.005 \text{ M}^{-1} \text{ min}^{-1}$, with

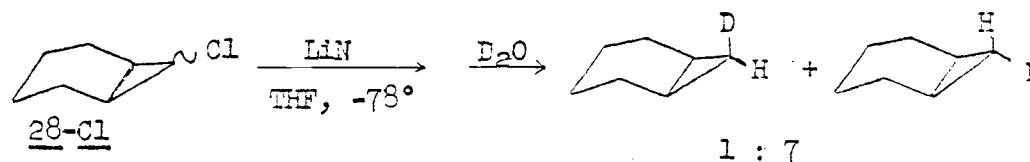


the syn reacting almost twice as fast ($k_{\text{syn}}/k_{\text{anti}} = 1.85$). Thus, the rate constant for anti-23-Cl is thirty times greater than that of anti-28-Cl. Conceivably, this substantial difference between the two otherwise very similar systems may arise from a relief of compressional strain in the transition state in the case of anti-23-Cl. This would



imply a fair degree of bond breaking in the transition state. This might be reasonable, since the reaction is rather slow compared to other radical anion-alkyl halide reactions. It would be more difficult to reconcile this rate difference if halo-radical anion 29 shown above was an intermediate.

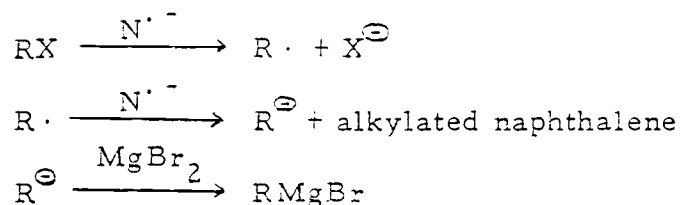
In another run, deuterium oxide was added and the norcarane isolated. The deuterium incorporation was 71%, with an anti:syn ratio of 7 ± 2 . This is the opposite direction shown by 23. As will be seen later, lithium naphthalene does not couple with cyclopropyl radicals. The above ratio, according to the arguments made above, can be



taken to represent the conformational equilibrium of the corresponding radicals.

Reaction of Magnesium Bromide with Sodium Naphthalene

As was discussed in the Historical Section, the first successful trapping of the alkyl anion produced by the reaction of sodium naphthalene with primary halides was reported in 1969 by Bank and Bank (76). The experimental procedure used by the authors involved injecting a solution of sodium naphthalene into an equimolar solution of the halide and magnesium bromide. When the resultant solutions were subjected to deuterolysis, an 85% deuterium incorporation was claimed. The reaction scheme proposed by the authors envisions the following sequence. One of the requirements Bank and Bank set forth

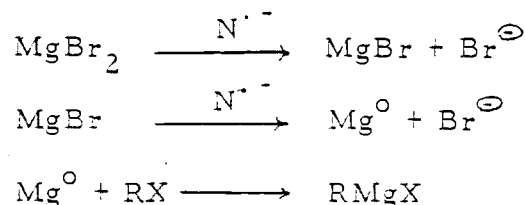


for an anion trapping agent was that it not react with sodium naphthalene. We have observed, however, that when magnesium bromide in THF is added to a sodium naphthalene solution in THF, the green color of the radical anion changes to blackish-grey and upon standing, a blackish-grey precipitate settles out. When magnesium bromide was

added to a lithium naphthalene solution, again a precipitate was formed, but this time it was more finely divided and was jet-black rather than grey in color. In addition, a metallic mirror formed on the sides of the flask. Addition of water to either of these two suspensions resulted in partial reaction and the evolution of gas. Addition of dilute hydrochloric acid caused the remaining precipitate to rapidly dissolve, with the further formation of gas. It would seem quite reasonable to postulate that the black precipitate from the lithium naphthalene reaction is metallic magnesium, while the grey precipitate from the sodium naphthalene reaction is simply a co-precipitate of magnesium metal and sodium bromide. A black insoluble magnesium naphthalene precipitate would not be expected to give off gas upon reacting with water, and most certainly would not require the addition of dilute hydrochloric acid for complete reaction. It has been reported (96) that anthracene dianion will reduce cadmium(II) chloride and nickel(II) acetylacetonate to the metals.

Further evidence that the grey precipitate was magnesium was obtained by its reaction with a mixture of syn- and anti-28-Cl followed by deuterolysis. The reaction, which required 15 minutes for completion at room temperature, gave an 84% yield of norcarane which was 73% deuterated. The anti to syn deuterium incorporation ratio was 0.78 ± 0.08 , in contrast to reaction with lithium naphthalene, which gave an anti:syn ratio of 7. The reaction of

7-bromonorcarane with magnesium turnings gave an anti:syn ratio of 0.95 ± 0.3 . This is within the limits of error of being the same as with the precipitate from the sodium naphthalene-magnesium bromide reaction. From the above findings, it is apparent that some reactions run using the magnesium bromide trapping technique may proceed by the following sequence of reactions, rather than or in addition to the mechanism proposed by Bank and Bank. Thus caution must

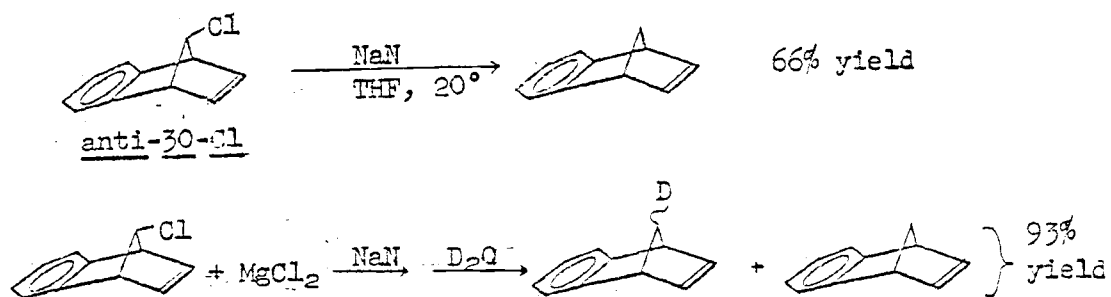


be exercised when using the magnesium bromide reaction for mechanistic purposes since the above sequence is an ever-present possibility. When the reaction is done under the conditions described by Bank and Bank, the magnesium which reacts with the halide to give the Grignard reagent might be in any form, from atoms to large conglomerates. Simply showing that the stereochemistry from the bulk magnesium Grignard is different from that obtained by the Bank and Bank magnesium bromide reaction would have no bearing on which mechanism is operative.

It would appear that for the specific primary halides reported by Bank and Bank, the anion trapping mechanism was operative

because the percent yields of hydrocarbons with and without the magnesium bromide are the same (35%). This implies that radical-radical anion coupling is still taking place. If the magnesium atom mechanism was producing much product, the yields of hydrocarbon would be expected to be much higher than observed.

One system which shows symptoms of the metal atom reduction mechanism has appeared in the literature recently. Buske and Ford have reported the preparation of anti-7-benzonorbornadienyl Grignard reagents by a variety of methods (122, 123). Among the techniques used was the sodium naphthalene-magnesium chloride method. The reaction of anti-30-Cl with sodium naphthalene in the absence of added magnesium chloride gave a 66% yield of hydrocarbon. This is rather higher than the yield from a simple secondary halide (40%), but is



reasonable considering the effects of both steric requirements and an increased electron affinity caused by angle strain. If the anion trapping mechanism were operating in this case, the yield with magnesium chloride should be no greater than that without it. Instead, the yield is 93%--clearly incompatible with the mechanism of Bank.

The anion trapping mechanism might be expected to operate under those conditions where sodium naphthalene reacts faster with the alkyl halide than with the magnesium salt. The magnesium atom mechanism will be operative when the converse is true. Whether magnesium chloride (Buske and Ford) or magnesium bromide (Bank and Bank) is used might also have an effect in determining which scheme operates.

Magnesium Anthracene Dianion

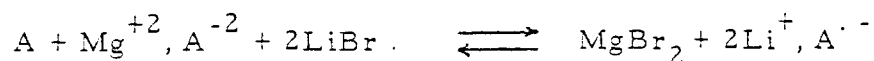
In contrast to the black precipitate which forms when magnesium bromide reacts with sodium naphthalene, the corresponding reaction with sodium anthracene (deep blue) gives a white precipitate and a green-yellow solution. With lithium anthracene there is no visible reaction. It was also discovered that reacting metallic magnesium with anthracene in the presence of excess magnesium bromide gives rise to a green-yellow solution identical in color to that obtained from sodium anthracene. This solution has the curious property of reversably changing color as the temperature is varied. At approximately $+40^{\circ}$ the solution is bright yellow, at 20° it is green-yellow and as the temperature is lowered to -40° , the color smoothly changes to deep blue. Upon continued stirring of the reaction mixture at room temperature, an orange-yellow flocculent precipitate slowly formed. As no reports have yet appeared in the literature concerning the

structure or physical properties of aromatic radical anions or dianions which contain other than Group I metals in ether solvents, and since the magnesium-anthracene complex was a solid, it was hoped that it could be crystallized for chemical and perhaps X-ray structure analysis. It quickly became obvious that the complex is only sparingly soluble in THF, and attempts to prepare the complex in DME or diethyl ether were unsuccessful. Conventional techniques of crystallization could not be used due to the low solubility and extreme air sensitivity of the complex. Extraction of the orange-yellow precipitate over a period of two months in the DeKock-Streitwieser Soxhlet extractor (see Figure 4) with THF gave large clear orange needles in a yellow solution. The material left on the frit of the extractor was a yellow-green solid, apparently insoluble in THF. This material was not examined further. The composition of the orange pyrophoric crystals was determined to be $\text{MgA} \cdot 3\text{THF}$, where A stands for anthracene. The analysis was achieved by EDTA titration for magnesium and gas chromatographic analysis for anthracene with THF determined by weight difference. Since the value of three for the number of THFs of solvation is rather odd, the ratio of THF to anthracene was also determined by the relative integrations of THF and anthracene in the nmr of a carbon tetrachloride solution of a sample of the solid which had been treated with oxygen gas. As expected for an anthracene dianion, hydrolysis with water gave,

9, 10-dihydroanthracene with only 2% anthracene. The small amount of anthracene was probably formed from adventitious oxygen.

X-ray single crystal work on the $\text{MgA} \cdot 3\text{THF}$ crystals proved to be quite difficult both from the standpoint of obtaining a suitable crystal free of twinning and analyzing the data. The method by which an untwinned crystal was finally obtained is described in the experimental section. It was determined that the unit cell was triclinic with a volume of 4668 \AA^3 . The calculated density, assuming eight $\text{MgA} \cdot 3\text{THF}$ units per unit cell, of 1.19 g/cm^3 is in excellent agreement with the experimental density of 1.18 g/cm^3 . Because of the very large size and lack of symmetry of the unit cell, plans for a structure determination were abandoned.

Returning to the interesting color changes described earlier, it would seem that a ready explanation is now available. This is illustrated below, where the first equilibrium lies on the right at low temperatures and on the left at higher temperatures. Starting from



purified $\text{MgA} \cdot 3\text{THF}$ crystals, it was found that both excess anthracene and magnesium bromide must be present for the blue or green color to form. Addition of lithium bromide to a solution of magnesium

anthracene dianion containing excess anthracene gave a deep blue color, indicating that the bottom equilibrium lies to the right. Thus the reason why sodium anthracene reacts with magnesium bromide while lithium anthracene does not is simply due to the fact that sodium bromide is insoluble in THF, while lithium bromide is quite soluble.

The fact that magnesium anthracene dianion is yellow in solution seems significant. The alkali metal anthracene dianion solutions are reported to be purple (96). Thus the structural difference between the alkali metal dianion and the magnesium dianion must be quite great to cause such an extreme shift in spectra.

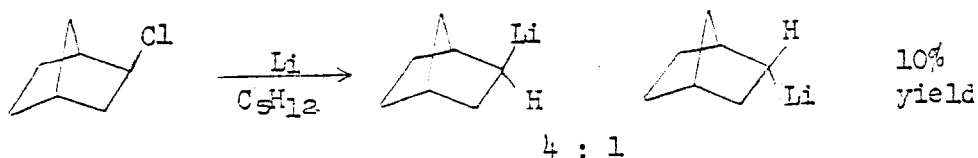
Attempts to obtain an nmr spectrum of the magnesium anthracene dianion were fruitless except for one low-intensity sharp singlet at approximately $\delta 6$. The solubility in THF may be too low but more likely the absorptions are shifted upfield into the THF peaks. The chemical shifts of the 1, 2, and 9 positions of the alkyl metal anthracene dianion are reported to be at $\delta 3.36$, 4.25 , and 1.89 , respectively (9). None of these regions could be observed due to THF absorptions.

Alkyl Lithium Reagents from Alkyl Halides and Lithium Radical Anions

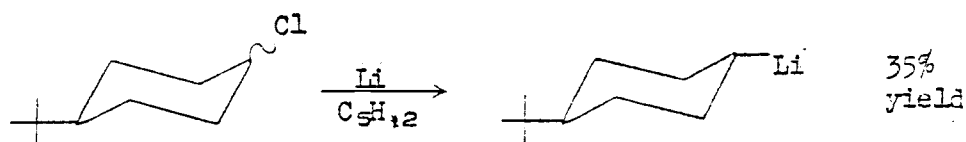
Alkyl lithium reagents are potentially very valuable synthetic reagents for organic synthesis. Often the yields of products from

addition reactions with ketones and nitriles exceed those of the more common Grignard reagents (85). Some reactions, such as formation of lithium dialkyl cuprates (124), are specific for lithium reagents. However, lithium reagents, other than those commercially available, have not achieved as wide-spread use as one might expect in view of their superior properties. This can be ascribed to the fact that their preparation from the halide and lithium metal often gives rather low yields or requires considerable 'magic' in order to attain high yields. An example is provided in a paper by Smith (127) of Foot Mineral Company concerning the optimization of the yield of tert-butyllithium from tert-butyl chloride. The optimum yield of 70-80% was obtained when pentane was used as the solvent, when the lithium contained 1% sodium, and, amazingly enough, when 0.5% of tert-butyl alcohol was included in the mixture. Changing any of these conditions resulted in a reduction or elimination of yield. Vinyl lithium formation (128) was found to be optimized at 70-80% when THF was the solvent, when high-speed stirring was used, and the reaction temperature was -33° .

Applequist and Chmurny have reported (129) that exo-2-norbornyl chloride and lithium metal in refluxing pentane give yields of the lithium reagent as high as 33% but averaging about 10%.



Alexandrov reported that a variety of attempts to prepare 4-tert-butylcyclohexyllithium from the bromide were unsuccessful (130). Glaze and Selman later were successful to the extent of 35% yield by utilizing the chloride with lithium containing 1% sodium (131). This illustrates another difficulty of the conventional procedure--bromides



give much poorer yields than chlorides. This is undoubtedly due to the greater tendency of bromides to undergo side reactions (coupling) with lithium reagents.

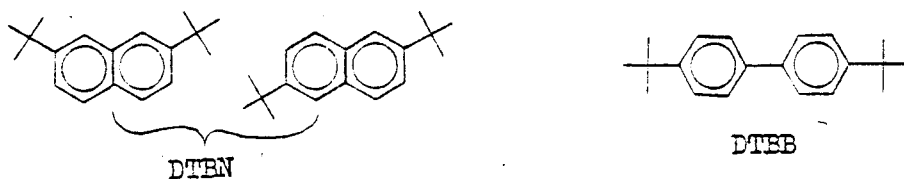
Quite obviously, a synthetic organic chemist who has just spent a year making a few milligrams of a key intermediate would not attempt to convert it to a lithium reagent by the usual method. Under such conditions a synthetic procedure which works the very first time to generate lithium reagents in high yield would be needed. We are pleased to report that such a procedure has, in fact, been developed, based upon research in the virtually virgin field of lithium radical anion-alkyl halide reactions. It is important to note that this valuable new synthetic procedure was developed as a 'spin-off' of basic research which, having no immediate or practical goal, was of the type not in vogue by funding agencies. Our interest in the reactions of alkyl halides with lithium radical anions was derived, then, not

from a desire to develop a new synthetic technique, but rather to develop a new method for the determination of configurational equilibria involving radicals. This will be discussed later. Suffice it to say that for both synthetic and mechanistic purposes, the yield of lithium reagent must be high.

The coupling reaction between alkyl radicals and naphthalene radical anion greatly reduces the maximum yield of reduction products which one can attain using naphthalene radical anion. Since coupling requires that bond-forming distances be attained in the transition state while electron transfer could presumably take place over fairly large separations, it was reasoned that increasing the steric bulk of the radical anion might inhibit coupling. Placing methyl groups on naphthalene would not be acceptable since the protons of the methyl groups would be benzylic and would destroy the lithium reagent. tert-Butyl groups, on the other hand, have no acidic protons and are quite bulky.

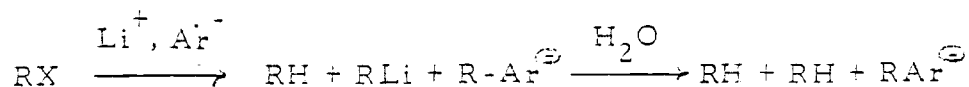
A study of the reactions of lithium naphthalene (N), biphenyl (B), di-tert-butyl naphthalene (DTBN), and di-tert-butyl biphenyl (DTBB) with a spectrum of alkyl halides was thus initiated. The tert-butylated hydrocarbons were obtained quite easily by the Friedel-Crafts reaction of tert-butyl chloride with naphthalene (132) or biphenyl (15). The reaction with naphthalene gives an approximately equal mixture of 2,6- and 2,7-di-tert-butylnaphthalene. It is very

difficult to separate these isomers by crystallization, and thus the mixture was used in all reactions.

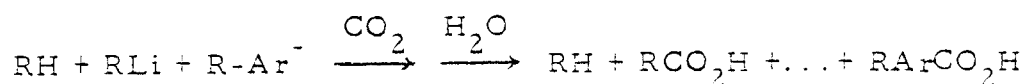


The information sought in this study was (1) the yield of reduction products (RH and RLi), and (2) the degree of lithium incorporation (anion trapping). From knowledge of the yield of reduction products, the extent of coupling (alkylation) can be obtained in the case of chlorides by subtraction from 100% since dimerization does not occur. Bromides, however, form around 5% dimers.

The technique used in the survey will now be described. To a solution of the radical anion cooled to -78° , was added an accurately measured quantity of the gc internal standard (nonane or decane), followed by the halide. In most cases, a large excess of the radical anion was used. After sufficient time had elapsed for completion of the reaction, an aliquot was taken and immediately quenched in water. Gc analysis using a digital integrator gave the total yield of hydrocarbon and lithium reagent (RH + RLi). It is of interest to note at this point that it was necessary to determine the gas chromatography



response factors by running through the same sequence of steps used in a real reaction, only with the product being injected rather than the halide. Determination of gc response factors in the normal manner gave up to 10% lower results. After the first aliquot was taken, carbon dioxide was bubbled in until the intense color of the radical anion disappeared, and then a few minutes more. This treatment destroys the lithium reagent by generating acids, ketones, and other materials. An aliquot of this mixture was then taken and treated as



before. The percent reduction on the yield of hydrocarbon (RH) is taken to be the percent efficiency in trapping the anion as the lithium reagent. The term 'anion trapping' is derived from literature usage. It is very rare to see the metal ion represented in the electron transfers, implying that the anion generated is free, even though this may not have been intended in all cases. Considering the high cation affinity of an alkyl anion, the low dielectric constant for the solvents used, and the fact that the radical anions exist as ion pairs, it is not likely that free anions play a significant role in the mechanistic scheme. In this section 'anion trapping' implies only the phenomenological outcome of an experiment designed to determine the fraction of reduction products which contain a carbon-lithium bond.

Results selected from Tables 12-18 are presented in Table 10.

The % yield of lithium reagent is the product of '% RH Yield' and '% Anion Trapping'.

Table 10. Survey of lithium radical anion-alkyl halide reactions.

Halide	LiN		LiDTBN		LiDTBB	
	%RH ^(a) Yield	% Anion ^(b) Trapping	%RH Yield	% Anion Trapping	%RH Yield	% Anion Trapping
1-Chlorooctane	92(2)	45(8) ^(c)	96	49	100(1)	94(1) ^(d)
1-Bromooctane	79	47	--	--	96	91
2-Chlorooctane	63(0)	24(5) ^(d)	96	21 ^(e)	101	87
2-Bromooctane	57	25 ^(e)	--	--	99(2)	83(4) ^(d)
3-Chloro-3-methylheptane	39(1)	74(5) ^(d)	89	81	97	88 ^(e)
7-Chloronorcarane	99	65 ^(f)	99	89	99	95 ^(e)

(a) $\pm 4\%$ Estimated error. Numbers in parentheses are standard deviations (SD).

(b) % Reduction in RH yield upon carbonation.

(c) Average and SD of 8 runs.

(d) Average and SD of 3 runs.

(e) Average of 2 runs.

(f) Warmed to -5° to speed up reaction.

It is apparent from Table 10 that lithium di-tert-butylbiphenyl (LiDTBB) gives excellent yields of lithium reagents. The maximum extent of coupling is a few percent and is probably much less, while the % anion trapping is typically around 90%. LiDTBB closely approaches the ideal of a homogeneous solution of lithium metal in

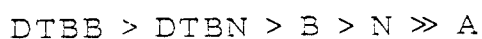
THF, with the DTBB moiety functioning only as an inert carrier of an electron, at least in reactions with alkyl halides and radicals.

It is interesting to note that lithium naphthalene or lithium biphenyl, when reacting with CO_2 , gives a mixture of the hydrocarbon and the dihydrocarboxylic acids. In contrast, LiDTBB gives a 97% isolated recovery of pure DTBB. It is not known what the inorganic products are. No experiments with DTBN have been done specifically on the reaction with water or carbon dioxide. However, it was noticed during the experiments with alkyl halides that while LiDTBB produced only a slight cloudiness with carbon dioxide, lithium naphthalene and LiDTBN both produced very thick milky suspensions. It is probable that DTBN reacts normally.

Another abnormality of DTBB is seen in the fact that while the hydrocarbon reacts quite readily in THF with both lithium and potassium, no reaction with sodium beyond a very slight coloration of the surface could be induced. Various conditions include temperature variation between 20° and -78° while the metal was being sliced in situ to expose fresh surface.

In addition to the steric effect of the tert-butyl groups, another factor which may reduce coupling in the case of DTBB is the 0.16 V higher reduction potential relative to naphthalene (see Table 2). Biphenyl radical anion undergoes relatively more electron transfer than naphthalene. It has been reported (30) that sodium biphenyl

reacting with 5-hexenyl fluoride gives virtually quantitative yields of reduction products. Unfortunately, lithium biphenyl precipitates out of solution under the conditions used in this study (-78°). Nevertheless, one run was made using the tertiary chloride 3-chloro-3-methylheptane (see Table 16). The extent of electron transfer is 56%, rather larger than naphthalene radical anion, which gives only 39% electron transfer. It is likely that for primary and perhaps secondary halides, lithium biphenyl would give almost as high yields of lithium reagents as DTBB. However, its inhomogeneous nature at -78° would seem to complicate the interpretation in mechanistic studies. Combining these results with the literature observation (67) that sodium anthracene undergoes only 1% electron transfer with even primary substances, the following order of electron transfer vs. coupling can be constructed.



It is seen from Table 2 that this is also the order of reduction potentials.

The reaction of lithium naphthalene dianion in diethyl ether with 2-bromooctane gives only 9% electron transfer vs. 57% for lithium naphthalene in THF. Similarly, lithium di-tert-butyl naphthalene (as the dianion) gives only 34% electron transfer in diethyl ether vs. 96% in THF (as the radical anion) when reacting with 2-bromooctane.

These observations combined with a perusal of Table 6 strongly indicate that loose ion pairs give relatively more electron transfer than contact ion pairs which, in turn, give much more electron transfer than the very tight ion triples of the dianions. Thus, if one is attempting to synthesize alkylated dihydronaphthalenes, the highest yields would be obtained in the least polar solvent. Unfortunately, the extensive coupling exhibited even by DTBN in ether virtually rules out the possibility of synthesizing alkyl lithiums in the less acidic diethyl ether solvent rather than THF.

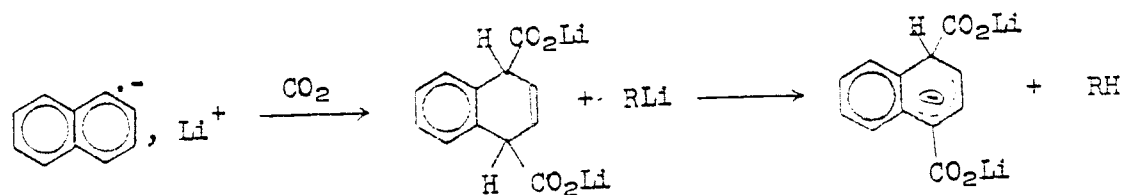
Looking now at the extent of anion trapping as indicated by the carbon dioxide quench method (Table 10), it is seen that LiDTBB gives vastly different results than either lithium naphthalene or LiDTBN. LiDTBB gives anion trapping values consistently near 90%, while the values for lithium naphthalene and LiDTBN vary from 21% to 81%. One is also struck by the close tracking between lithium naphthalene and LiDTBN. How is it possible for LiDTBB to give 87% anion trapping, while under identical conditions lithium naphthalene and LiDTBN give less than 25%? If for some reason LiDTBB gives the lithium reagent directly while lithium naphthalene and LiDTBN give the free anion which would presumably react very rapidly with solvent, then addition of a large excess of lithium bromide should increase the extent of anion trapping. The addition of sufficient lithium bromide to make the solution 0.4 molar failed to affect the

anion trapping (entries 8 and 9, Table 15). Increasing either the naphthalene or lithium quantities also did not affect the % anion trapping. This shows that disproportionation to the dianion was not causing the low yields (Runs 7 and 8, Table 12). Running the reaction of lithium naphthalene at -63° rather than -78° did not much affect the anion trapping, although increasing the reaction temperature to 0° did cut it in about half (Runs 9 and 10, Table 12). Entry 17, Table 12 was run to test the hypothesis that adventitious water was destroying the lithium reagent. The addition of bromobutane in large excess before adding 1-chlorooctane would create enough butyllithium to protect the octyllithium from destruction by small quantities of a proton source. Again, very little effect was observed.

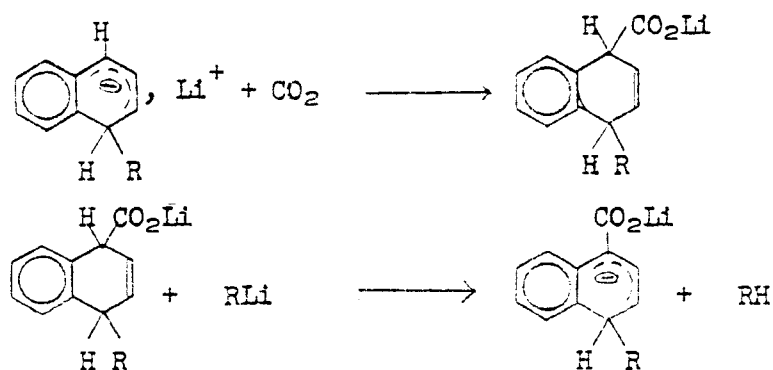
Another possible reason for the low yields of anion trapping which came to mind is that the very reactive first-formed alkyl lithium monomer might be metalating the naphthalene. Such metalizations are known to occur much more rapidly with TMEDA complexes of alkyl lithiums (85) and much more rapidly with alkyl dimers than with normal tetramers and hexamers (153). To test this hypothesis, the conditions were changed such that, rather than using a large excess of radical anion, the reaction was run on a completely stoichiometric scale. If metalization of naphthalene were taking place, then one should be able to observe a reduction in the % recovery of naphthalene upon carbonation. When this experiment was

run, two things were apparent. Firstly, there was less than a 1% reduction in the recovery yield of naphthalene, where a 10% reduction was expected on the basis of the untrapped anion product observed. Secondly, the extent of anion trapping as revealed by the carbon dioxide quench method jumped from 47% to 93% for 1-bromooctane (Runs 1 and 2, Table 13). The effect on anion trapping of going from the usual stoichiometry (ca. 13%) to 100% for 2-bromooctane was also quite sizeable (25% to 52%; Runs 2 and 3, Table 14), but no effect was observed for 3-chloro-3-methylheptane (74% to 70%; Runs 1, 2, and 3, Table 16). When the reaction of lithium naphthalene with 1-bromooctane was run at medium degrees of stoichiometry, the % anion trapping was also intermediate (Runs 8 and 9, Table 13). From these results it can be deduced that the anion is probably completely trapped as the lithium reagent, but that upon carbonation the lithium reagent is somehow converted into the hydrocarbon when excess radical anion is present.

All of the above data can be accommodated by the theory that in all cases the % anion trapping is high, but that the following reaction is competitive with reaction of the alkyl lithium



with carbon dioxide. This easily explains why LiDTBB gives high anion trapping by the carbon dioxide quench method, while lithium naphthalene and LiDTBN do not. Unlike lithium naphthalene and LiDTBN, which give dicarboxylic acid salts upon reaction with carbon dioxide, LiDTBB gives back DTBB unchanged. This also explains why going from those conditions where a large excess of radical anion is present to where no excess is present induces a large jump in the degree of anion trapping for 1-bromooctane, but not for 3-chloro-3-methylheptane. In the former case, little or no coupling is observed, while in the latter case, a large amount of coupling does take place. Thus even when excess radical anion is not present, the tertiary lithium reagent can abstract a proton as shown below.



Quite obviously, the above theory is open to experimental confirmation or rejection. Treatment of a lithium naphthalene solution with 0.24 equivalents of 1-chlorooctane followed by the usual procedure gave the result of 53% anion trapping. Repeating this experiment with a lithium naphthalene solution made from naphthalene- d_3 gave

69% anion trapping. The octane produced after carbonation was isolated and subjected to low-voltage mass spectral analysis. The octane produced was found to be 90.8 ± 0.5 monodeuterated. This experiment proves that the hydrocarbon found after the carbon dioxide quench was formed by abstraction of a proton from naphthalene. It has previously been shown that metalation does not take place. Additional evidence that the anion is nearly completely trapped as the lithium reagent was obtained by addition of deuterium oxide to a reaction run exactly as just described but without the carbon dioxide quench. The octane was found to be $96.0 \pm 0.9\%$ monodeuterated. This is slightly greater than the % anion trapping as indicated by the carbon dioxide quench in the case of the 1-chlorooctane and LiDTBB. It is probable that the lithium incorporation produced in all the other substrates by lithium naphthalene and LiDTBN are just as high, or slightly higher, than those indicated by the carbon dioxide quench in the case of LiDTBB. Even with LiDTBB, the % anion trapping figures are probably just lower limits.

General Considerations on the Use of LiDTBB for Lithium

Reagent Synthesis. For at least some substrates it is important that the reaction be run at -78° or colder. From Entries 9 and 10 of Table 14, we see that the yield of anion trapping drops from 83% to 70% when the reaction with 2-bromooctane is run at -60° , even though secondary lithium reagents are stable in THF below about -50° .

Inverse addition of LiDTBB to 2-bromooctane, although synthetically desirable, also gives poor results (Entry 11, Table 14). This is undoubtedly due to the fact that the lithium reagent and unreacted bromide are in contact for perhaps 0.5 hours by this method, but less than a fraction of a second by the normal addition. Lithium DTBB has advantages over lithium naphthalene in reactions with secondary cyclopropyl chlorides because this reaction is excessively slow with lithium naphthalene, but is over within 5 minutes with LiDTBB. Other than nonvolatility, LiDTBB has no advantage over lithium naphthalene for primary halides, or over lithium biphenyl for both primary and probably secondary halides in synthetic procedures. For mechanistic studies, lithium biphenyl is unsuitable in modest concentrations at -78° due to apparent inhomogeneity. The use of LiDTBN or LiDTBB is necessary to achieve good yields with tertiary substrates.

Since LiDTBB gives essentially 100% electron transfer, it would seem that it ought to be possible to use DTBB in a catalytic fashion. This would require the use of lithium dispersion to allow fast enough formation of the radical anion at -78° . It might be possible to use less than 10% of the theoretical amount of DTBB, thus making separation of products from the DTBB easier.

The Stereochemistry of LiDTBB-Cyclopropyl Halide Reactions

The stereochemistry of the lithium reagents which result from the newly developed lithium di-tert-butylbiphenyl (LiDTBB)-alkyl halide reaction is of interest for two reasons. Firstly, stereochemistry is of paramount importance to the synthetic chemist. From the examples to be discussed in this section and the next, it should be possible to get a feel for the stereochemical outcome of a given LiDTBB reaction. Secondly, the stereochemistry observed may give important information about the configurational equilibria of radicals and anions, obtainable more easily and with fewer ambiguities than with any other chemical method.

It has been previously argued that the stereochemical outcome of the reaction between lithium naphthalene and the cyclopropyl halides, anti-23-Cl and 28-Cl, represents the population of the corresponding radicals. The arguments will be expanded and summarized here.

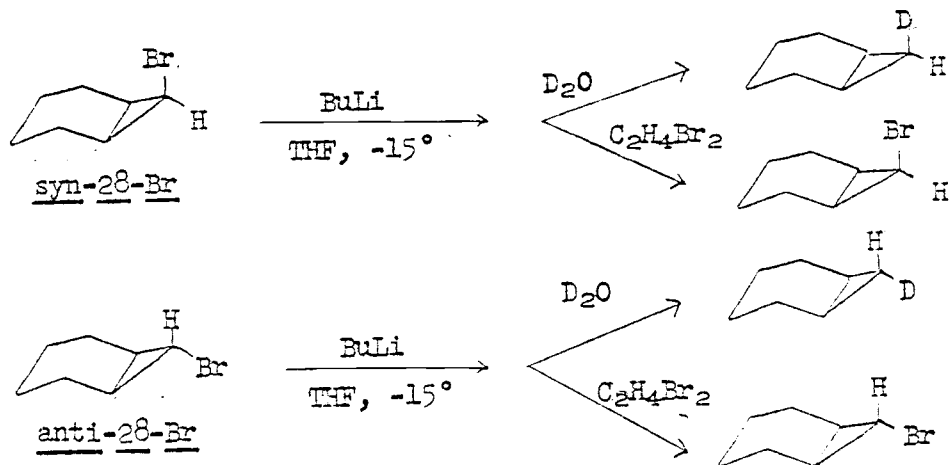
Cyclopropyl radicals are highly pyramidal and hold their configuration for on the order of 10^{-8} to 10^{-10} sec⁻¹. This is far slower than the time of a single collision between molecules in solution, and is even slower than the time of an encounter. (An encounter is thought to consist of a number of collisions and lasts around 10^{-11} seconds (133).) Thus it is clear that any reaction which is diffusion

controlled and reacts with retention of configuration to give stable products would be capable of accurately giving the equilibrium population of radicals. The argument that LiDTBB reacts with cyclopropyl radicals at diffusion controlled rates is very good. It is generally accepted that cyclopropyl radicals are highly unstable (reactive) while cyclopropyl anions are relatively stable, in comparison to primary systems. It would be expected, then, that the electron affinity of a cyclopropyl radical is higher than of a primary radical. The electron affinity of DTBB is 0.16 volt lower than that of naphthalene. Since the rate of electron transfer is expected to be dependent upon the difference of electron affinities, it is clear that cyclopropyl radicals can be expected to react with LiDTBB faster than primary radicals react with lithium naphthalene and the latter reaction is known to be diffusion controlled.

The stability of the products is also definite. It was demonstrated that cyclopropyl lithium reagents are thoroughly stable even under adverse conditions. Even the free cyclopropyl anion would be expected to be stable at -78° (134). It should be noted that all of the arguments given above apply with even greater force to vinyl radicals.

The 7-Norcaranyl System (28). The reaction of a mixture of syn- and anti-7-chloronorcarane (syn:anti = 1.5) with LiDTBB in THF at -78° followed by quenching with deuterium oxide gave 28-D. Nmr analysis indicated the anti:syn ratio to be 5:1. However, the analysis

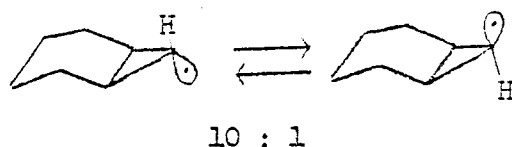
of this compound by nmr was plagued by the presence of unknown impurities. The ratio of anti to syn deuteration is very sensitive to the presence of even very small amounts of impurities whenever the anti to syn ratio is very large or very small. For this reason, the deuteration experiment only gives the direction and approximate magnitude of the configuration of the lithium reagents. Due to the unsatisfactory nmr analysis, a better method of determining the lithium reagent populations was required. It appears well-established that metal halogen exchange between alkyl lithium reagents and ethylene dibromide goes with retention of configuration (35). To show that ethylene dibromide could be used as a suitable quench of the lithium reagents, syn- and anti-23-Li were prepared separately by metal-halogen exchange of syn- and anti-28-Br and the resultant lithium reagents were quenched both with deuterium oxide and with ethylene dibromide. Retention was observed in all cases. This demonstration of retention of configuration is not sufficient in itself to allow



ethylene dibromide to be used to determine lithium reagent ratios. It must also be shown that the yields from the two forms are the same. To this end, a mixture of 7-bromonorcaranes (anti:syn = 1.33) was treated in the same manner just described but with the inclusion of an internal standard. The overall yield for the anti-bromide was 92%, with the syn bromide giving an 84% yield (final anti:syn = 1.45). Repetition of this procedure using deuterium oxide as the quench gave an anti to syn deuteration ratio of 1.39. Thus, either deuterium oxide or ethylene dibromide should be suitable to determine the population of 28-Li.

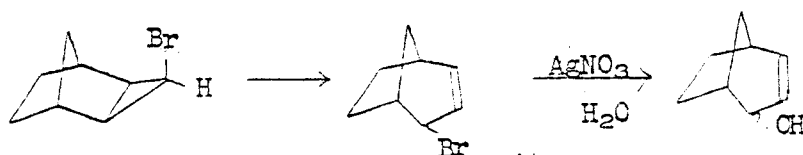
From a reinvestigation of the reaction of LiDTBB with the 1.5:1 mixture of anti- and syn-28-Cl using ethylene dibromide as the quench, it was found that the anti to syn ratio of bromides was 10 ± 2 (estimated error). As described in the Historical Section, optically active 2,2-diphenyl-1-methyl-1-bromocyclopropane gives a slight amount of retention when reacting with 1 molar sodium naphthalene at 20°. Proton tunneling of the radicals derived from 28-Cl would be expected to cause interconversion to occur much too rapidly to allow the first-formed configuration to be trapped by 0.15 molar LiDTBB, even at -78°. This is, in fact, the case. Purified syn- and anti-28-Cl were separately subjected to the above procedure with the result that the anti to syn ratio of bromides was 11:1 in each case. These results indicate that the anti radical is more stable than the syn as

indicated below.



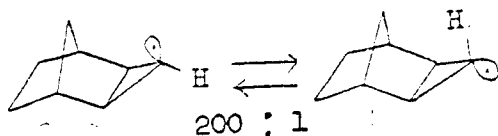
The exo-Tricyclo 3.2.1.0^{2,4}octyl System (23). The stereochemistry of the reaction of anti-23-Cl with lithium naphthalene followed by deuterium oxide to give at least a 100:1 syn:anti deuteration ratio was described previously. Repetition of this reaction with LiDTBB gave identical results.

To get a better number for the syn to anti ratio, the reaction with LiDTBB was repeated, but using ethylene dibromide as the quench. The syn bromide is known to spontaneously decompose (57) as shown. Treatment of the reaction mixture with aqueous silver



nitrate removed the allylic bromide. Gc analysis showed only one peak other than solvent and internal standard. This peak had the correct retention time for anti-23-Br. From the integration of this peak relative to the internal standard, it was concluded that the anti bromide was formed in less than 0.5% yield. Similar results were obtained by gc analysis of the crude reaction mixture before silver

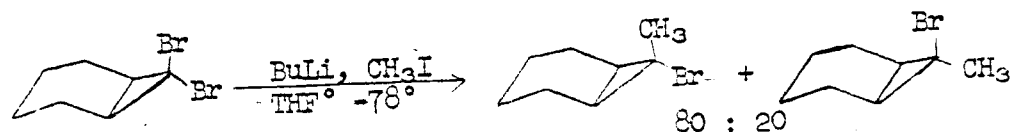
treatment. However, decomposition products of the allylic bromide interfered with analysis. Since the yield of lithium reagents in the LiDTBB reaction was determined to be at least 90% (Table 18), the syn radical concentration was at least 200 times that of the anti.



It is interesting to note that the syn lithium reagent reacts with ethylene dibromide with at least 99.5% retention. This is in the face of not inconsiderable compressional strain.

The 7-Methylnorcaranyl System (31). This system is of interest not only to determine the position of the radical equilibrium, but also since it might be possible to trap the radical before complete equilibration can occur. This was considered to be a possibility in this case since the fast proton tunneling expected with the norcaranyl radical is absent in this system. It was also hoped that running the reaction at a low temperature would lower the rate of inversion and result in more trapping than Jacobus and Pensak observed with the 2,2-diphenyl-1-methylcyclopropyl radical at 20°.

The synthesis of anti-7-bromo-7-methylnorcarane (anti-31-Br) followed the literature method. The anti bromide could be obtained pure by distillation, but the syn bromide was contaminated with other



materials and was not investigated. Reduction of anti-3,1-Br with sodium in tert-butyl alcohol gave the two hydrocarbons, syn- and anti-3,1-H as identified by the chemical shift of the C7 proton in analogy to other 7-norcaranyl systems. This assignment was supported by the following experiment. Reaction of LiDTBB with anti-3,1-Br at -78° in THF was followed by quenching a sample of the mixture in water. Gc analysis indicated the two hydrocarbons to be present in a ratio of 2.75, with the hydrocarbon assigned the syn-hydrogen structure predominating. The remainder of the reaction mixture was then quenched with ethylene dibromide. Gc analysis showed two compounds in the bromide region in a ratio of 1.5, with the minor component having the correct retention time for the starting bromide. Gc collection and nmr analysis confirmed this assignment. The major bromide exhibited an nmr spectrum in accord with that described in Reference 135 for syn-7-bromo-anti-7-methylnorcarane. Since in all cases known, ethylene dibromide reacts with lithium reagents with retention of configuration, and since the major bromide was the syn-bromo compound, the major component of the

hydrocarbon mixture is, again, indicated to be the syn-hydrogen isomer.

The stereochemistry of the products from the reaction of anti-31-Br with radical anions under a variety of conditions is presented in Table 11. The method of carbon dioxide quenching was used to determine the extent of lithium incorporation as it should be valid for LiDTBB reactions. It had been hoped that relatively more of the anti-hydrogen compound (retention) would be found at higher concentrations, due to the radical being trapped before equilibration. As can be seen from the first four entries of Table 11, the opposite trend (if any) is observed. A possible reason for this may lie in a change in viscosity with a change in the concentration of the radical anion. It was noticed that the 0.30 molar LiDTBB solution was very thick--even to the point of making stirring difficult. Since the rate of a diffusion controlled reaction is inversely related to viscosity, it may be that doubling the concentration of LiDTBB actually decreases the rate of trapping by more than doubling the viscosity.

Although the maximum range for the first four determinations is only 20%, it is far outside the range of error routinely achieved in gc analysis (4%). However it is not unreasonable as an error of workup. This is especially true in the case of the fourth entry in Table 11, where when an aliquot was taken and quenched in water, no organic phase was produced because insufficient nonpolar organic molecules

were present in the THF to prevent it from being completely miscible with water. For future workers, it is recommended that the mole fraction of nonpolar solutes in the THF be kept constant by the addition of pentane where necessary.

Table 11. The reaction of anti-31-Br with electron donors in THF.

Addition Mode	Conc. ^(a) (Molar)	Temp. °C	Electron Donor	<u>Retention</u> ^(b) Inversion	% Anion ^(c) Trapping
Normal	0.17	-78	LiDTBB	0.356	95
"	0.029	"	"	0.377	94
Evaporative	0.30	"	"	0.398	--
Inverse	0.01	"	"	0.426	95
Normal	0.17	+20	"	0.510	--
Inverse	0.01	-60	"	0.414	93
"	0.01	-40	"	0.414	97
Normal	0.17	+20	KDTBB	0.571	--
"	0.15	-78	Li ₂ DTBN ^(c)	0.235	86

(a) Concentration of pot solution - electron donor in all but inverse addition.

(b) anti-31-H:syn-31-H.

(c) By CO₂ quench method.

(d) Dianion in ether.

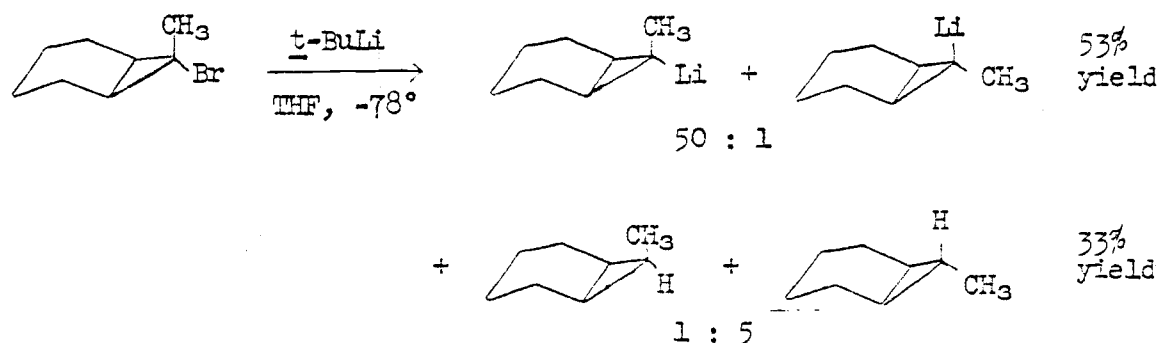
The very low retention to inversion ratio observed for lithium di-tert-butylnaphthalene dianion in diethyl ether may be due to selective electron transfer. As previously mentioned, the dianion is expected to be very tightly ion paired and might undergo electron transfer relatively sluggishly, thus giving rise to the possibility of selectivity.

Since the results obtained from the attempts to observe trapping were the inverse of what was expected, another chemical test of the identities of the two hydrocarbons was made. Walborsky reported that 12-Br readily underwent metal-halogen exchange with butyllithium in THF at -8° (117). In this, as in all cases of metal-halogen exchange, retention of configuration was observed. Attempts to induce metal-halogen exchange with anti-31-Br and butyllithium in

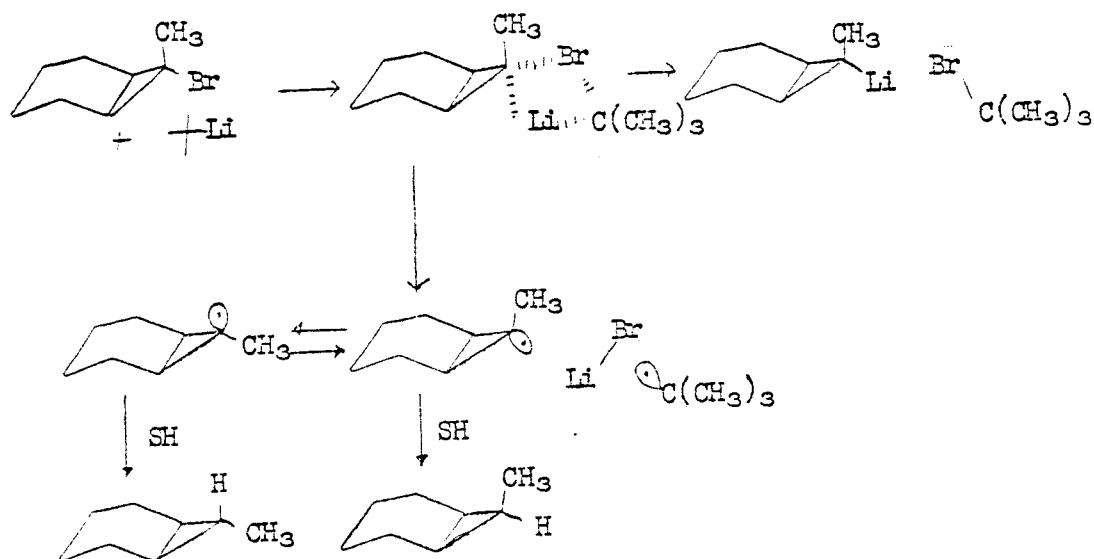


THF, even at 20° , were not successful, giving only a little hydrocarbon and no lithium reagent. The butyllithium seems to react with solvent faster than with the bromide. Even the reaction with sec-butyllithium in THF at -40° to -20° was unsuccessful. Some hydrocarbons were slowly produced as revealed by aliquots quenched in water, but were not derived from the lithium reagent since quenching with dimethyl carbonate did not reduce the size of the peaks on the gc. Finally, exchange with tert-butyllithium at -78° for 5 minutes in THF was successful. Even here, however, peculiar results were obtained. Analysis by gc of an aliquot quenched in water, and of the remainder after treatment with carbon dioxide revealed that, while a 53% yield of lithium reagent was obtained, a 33% yield of hydrocarbons was simultaneously produced. The lithium reagent was produced with

retention of configuration--again confirming the identification of the two hydrocarbons. The hydrocarbon side products of the exchange



reaction were of essentially inverted configuration, with the major hydrocarbon having the configuration of the most stable radical as determined from the LiDTBB experiments. Upon re-examination of Walborsky's data it was seen that, although the formation of the lithium reagent took place with 100% retention as determined by carbonation, a fair amount of racemic hydrocarbon must have been formed since the optical purity of the hydrocarbon obtained by protonation of the reaction mixture was only 60-85%. A mechanism which accounts for both retention in metal-halogen exchange and racemization in the hydrocarbon side products is shown below. The four-center intermediate shown is often postulated as a transition state in metal-halogen exchange reactions (85).



The Reaction of Planar and Rapidly Inverting Cyclic Radicals
with LiDTBB - - Theoretical Considerations

If the product stereochemistry resulting from the reaction of a cyclopropyl radical with lithium 4, 4'-di-tert-butylbiphenyl (LiDTBB) represents the radical configuration of a one-to-one basis, then what meaning can be ascribed to the product configuration resulting from a non-cyclopropyl cyclic secondary radical? Such radicals run the gamut from essentially planar to fairly pyramidal, and in all cases are undoubtedly undergoing wide-ranging vibrational motions. Because of this, any theory of the reaction of LiDTBB with such radicals is on shaky grounds in comparison to the corresponding case with cyclopropyl radicals. Nevertheless, an attempt will now be made to describe the detailed process and to at least define those

considerations necessary for a more complete theory.

Is the transfer of an electron fast or slow? A scenario for a slow transfer would have the charge density on the radical start to increase as soon as the radical diffuses to a favorable position. As the negative charge builds up on the radical, the cation moves in, solvent molecules reorganize, and the alkyl lithium is generated without intervention of the free anion. At the opposite extreme, the electron may be transferred to the radical in a time fast compared with molecular motions and perhaps even vibrational motions (e. g., a vertical process). An alternative process would have the radical diffusing to the cation followed by electron transfer from the remote radical anion. Since the solvent molecules around the cation are held quite tightly it is not likely that any could be displaced by the radical rapidly enough to account for the known diffusion controlled rate. Whether the electron transfer is fast or slow would appear to be dependent upon the relative electron affinities of the radical and donor hydrocarbon. Unfortunately, accurate or even approximate electron affinities for radicals are not available at the present time. In the discussions which follow, the implicit assumption will be that electron transfer from di-tert-butylbiphenyl radical anion to cyclic secondary radicals is irreversible and fast with respect to vibrational motion. This assumption is made to simplify mechanistic considerations to a manageable level, and can be considered as a first approximation

upon which the more likely 'slow transfer' theory might be based. It will be seen, however, that the experimental results to be described in this thesis can be readily explained in terms of this assumption.

How severe are the stereochemical constraints on electron transfer? It has been previously mentioned that electron transfer between naphthalene moieties can take place at a separation of 9 \AA with a rate constant of 10^7 for the free ions. It will be remembered, however, that primary radicals reacting with sodium naphthalene at room temperature not only undergo electron transfer, but also couple to generate alkylated naphthalenes. This process presumably requires bond-forming distances to be attained, albeit quite long ones since it is, in essence, a radical-radical combination with a low or non-existent activation barrier. It has previously been pointed out that the competition between electron transfer and coupling appears to depend strongly upon the electron affinity of the aromatic hydrocarbon, as well as the electron affinity of the radical. This would seem to imply that the transition state for electron transfer becomes more and more remote from the radical anion as the electron affinity of the aromatic hydrocarbon decreases and as the electron affinity of the alkyl radical increases. DTBB has one of the lowest electron affinities of any hydrocarbon known from which radical anions can be conveniently made. Its electron affinity is 0.16 Volt below that of naphthalene. Since even naphthalene radical anion reacts with primary

radicals at diffusion controlled rates, it would not seem unreasonable to postulate that the reaction of LiDTBB with radicals takes place with equal ease with all possible conformations of a radical, irrespective of the steric environment around the radical center.

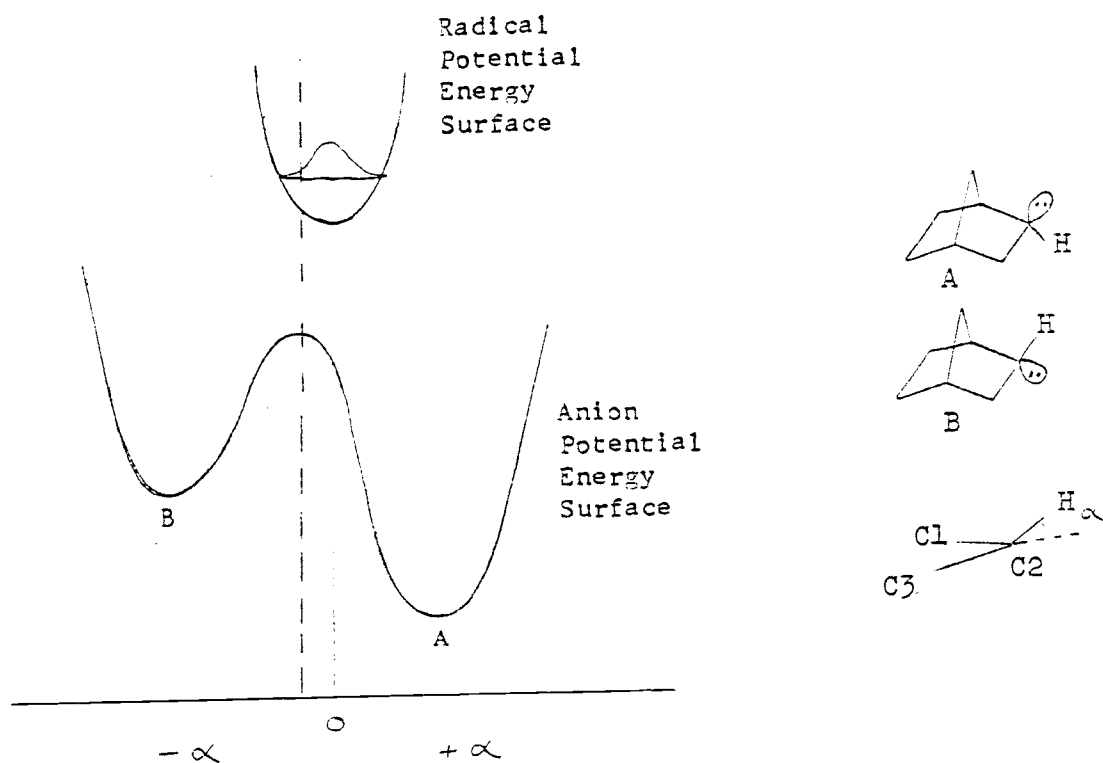
If electron transfer to the radical gives the free anion, is it possible that the anion undergoes equilibration before combining with a cation? Experimental inversion rates for anions are not available. Molecular orbital calculations which are, in general, quite good at predicting the inversion barrier for amines (134, 136) predict (137) that the inversion barrier for carbanions should be quite similar to that of amines. The experimental rate of inversion of dimethylamine is $1.6 \times 10^9 \text{ sec}^{-1}$ (138). While a rate of inversion of 10^9 may seem rather rapid, it is actually much too slow to affect the stereochemical outcome of the reaction of a radical with LiDTBB. The collapse of the hypothetical alkyl anion-lithium cation ion pair is expected to be very much faster than if the anion were, for example, generated unpaired in a 0.1 molar solution. Yet even in the latter case, since the rate constant for diffusive encounters between oppositely charged species in THF solution is greater than $10^{11} \text{ M}^{-1} \text{ sec}^{-1}$ at 25° (118), the rate of capture of the anion by a lithium cation would be at least ten times the rate of inversion of dimethylamine. All of the systems investigated in this work are cyclic, and most have a fair amount of ring strain. This would be expected to greatly increase the barrier

to inversion. The effect of ring strain is seen by the fact that the rate of inversion of the cyclopropyl anion analog, aziridine, is 1.6 sec^{-1} at 20° (extrapolated from data given in Reference 134). Thus it can be concluded that anion equilibration is probably not a factor in determining the product stereochemistry arising from the reaction of a radical and LiDTBB.

It will be demonstrated that cyclic secondary lithium reagents are configurationally stable under the reaction conditions used in this study (THF at -78°). Lithium reagents, however, are known to exist as tetramers or at least as dimers in ether solutions while the first-formed lithium reagent is, by necessity, the monomer. Although no absolute assurances can be given that the monomers do not undergo equilibration before association to higher aggregates, it will be assumed that they do not. They surely must have higher inversion barriers than free anions, and one would expect that they also have a very short lifetime.

If the above postulates and arguments are accepted, then it is claimed that the stereochemistry which is obtained from the reaction of a radical with LiDTBB can be considered to result from a mapping of the radical probability distribution upon the potential energy curve of the corresponding anion. For purposes of discussion, the 2-norbornyl radical and anion will be used. It will be assumed that the exo anion (A) is more stable than the endo anion (B). An assumed

potential energy surface for these anions as a function of the out-of-plane angle, α , is sketched along with the surface for a hypothetical, strictly planar radical. It must be stressed that a transition from the upper curve (the radical) to the lower curve (the anion) represents a chemical reaction, and not an electronic transition. The solid vertical line represents planarity ($\alpha = 0$), while the dashed line repre-



sents the division between A and B. If it is assumed that a radical on the B side of the dashed line picks up an electron it will form anion B and vice versa. Then it can be seen that even in the case of strict planarity of the radical, the more stable anion will be formed

in greater abundance than the least stable anion. In fact, the more constrained the radical is, the larger the A:B ratio that results. In reality it would be expected that the same forces which cause A to be more stable than B would also operate on the radical, but to a lesser degree. This would tend to move the potential energy curve for the radical in the direction of A, and thus give rise to an even greater preponderance of A.

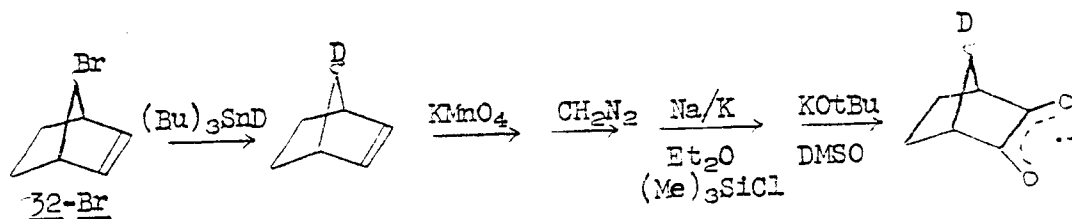
If the radical were pyramidal rather than planar, the probability distribution of radicals would correspond to an equilibrium between radical configurations. If the radical were highly pyramidal with the a probability distribution of each configuration not approaching the top of the inversion barrier between A and B, then the product distribution would mirror the radical distribution and be unaffected by the relative stabilities of A and B. It is likely, however, that the relative stabilities of the two radical forms will mimic the relative stabilities of the anions. It is difficult to imagine a case where this would not be true although an anion, being charged, would respond to an electric field where a radical would not.

It can be concluded that the products which result from the reaction of LiDTBB with planar radicals give direction and perhaps magnitude information on the relative stabilities of the anions. On the other hand, with 'significantly' pyramidal radicals, information on the direction and magnitude of the radicals is obtained.

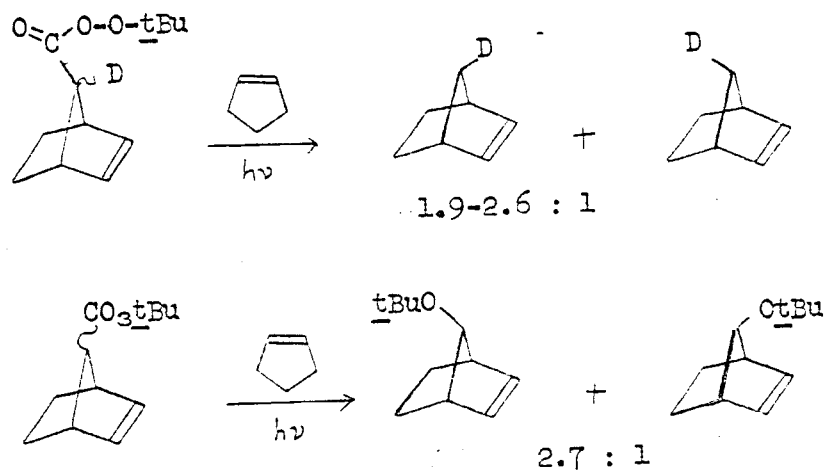
Intermediate radical geometries will of course give intermediate results, but in all cases it is expected that radicals and anions will respond in the same way to molecular forces.

The Reaction of Planar and Rapidly Inverting Cyclic Radicals
with LiDTBB--Four Systems

The 7-Norbornenyl System (32). The 7-norbornenyl radical has recently been a center of controversy. Since the 7-norbornenyl cation is well-known to be strongly non-classical, it was expected by some workers that the 7-norbornenyl radical would also be non-classical. Warkentin and Sanford (139) reported that the reduction of syn- or anti-7-bromonorbornene (32-Br) with tributyl tin hydride gave only anti deuterium incorporation and claimed that the radical was non-classical. Their analysis, however, was based upon very noisy nmr spectra of the hydrocarbons. The syn- and anti-C7 protons are badly overlapped and generally buried in the nmr of this compound. Cristol and Noreen (140), in examining the spectra published by Warkentin, estimated that both anti and syn deuterium compounds were present in a ratio of 70:30. Simultaneously, Russell and Holland (141) reported their reinvestigation of Warkentin's work. The norbornene was converted in a series of reactions to the semidione as shown. The esr spectrum of this species indicated an anti:syn ratio of 4.9 ± 0.1 .



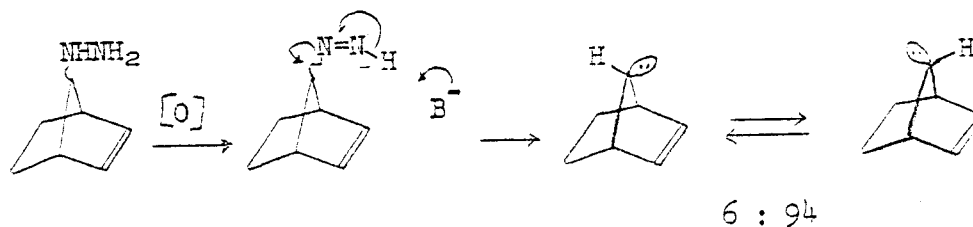
Kochi, Bakuzis, and Krusic have recently performed chemical and esr studies on the 7-norbornenyl radical (142). Photolysis of the syn or anti deuterated peresters gave the same mixture of deuterated norbornenes. Photolysis of the non-deuterated peresters gave the same mixture of ethers regardless of the stereochemistry of the starting peresters. The esr results indicate that the radical is pyramidal, but with a very low barrier to inversion (a few hundred



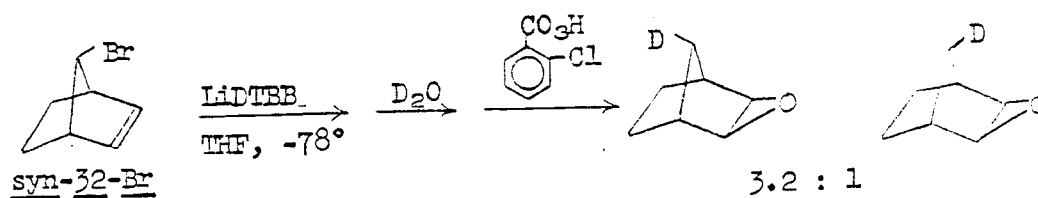
calories?). It was not specifically stated that the anti radical predominates, but rather that the esr results are not inconsistent with this.

It is seen that all of the reactions tend to favor the anti position. However, only the last reaction can be regarded as anything approaching the true configurational preference for the radical. While the last process involves radical-radical recombination with approximately zero activation energy, the others have quite substantial activation energies and have been shown in the case of other much more pyramidal systems to involve steric effects (143, 144). From the similarity of the results obtained from the three reactions, it is apparent that the two faces of the 7-norbornenyl radicals present essentially identical steric requirements to an incoming reactant.

Stille and Sannes (145) have determined that the 7-norbornenyl anion prefers the anti configuration by a factor of 94:6 at 60°. The anion was produced by basic oxidation of the corresponding hydrazene derivatives (syn and anti) in both deuterium oxide and in tert-butyl alcohol-O-d. The preference for the anti position was explained in terms of an antibonding bishomocyclopropenyl interaction with the double bond in the syn form. Similar considerations apply to the radical.

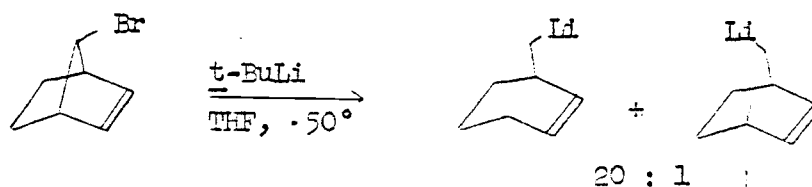


It was of great interest, then, to apply the LiDTBB reaction to this very well-studied system. Reaction of syn-32-Br with LiDTBB in THF at -78° , followed by deuterolysis, led to 32-D. To determine the anti to syn ratio, the norbornene was treated with m-chloropero-benzoic acid, and the resulting epoxide was analyzed by nmr with the aid of the shift reagent, $\text{Pr}(\text{fod})_3$. Using this technique, the syn- and anti-C7 protons could be separated completely from each other and from all other signals. The results indicate that the anti:syn deuterium ratio was $3.8 \pm 0.2:1$.



Although chloropropyl lithium reagents are well-known to hold their configuration, nothing was known about simple secondary lithium reagents in THF. Since the lithium reagents had to hold their configuration for only 30 seconds before deuterolysis was performed, and since the temperature was quite low (-78°), it seems reasonable to assume the deuteration ratio observed is the same as the stereochemistry of the first-formed lithium reagents. To prove that the lithium reagents are capable of holding their configurations, syn-32-Li was prepared by metal-halogen exchange with tert-butyllithium in

THF at -50° . After only 4 minutes, almost all of the bromide had reacted, and after 30 minutes at -50° , the reaction mixture was quenched with deuterium oxide. The norbornene was isolated and analyzed as above. Deuterium incorporation was 90%, with a syn:anti ratio of at least 20:1, confirming that the reagents are stable at -78° and probably at -50° . This represents the first reported metal-halogen exchange on a simple secondary bromide. Other attempts

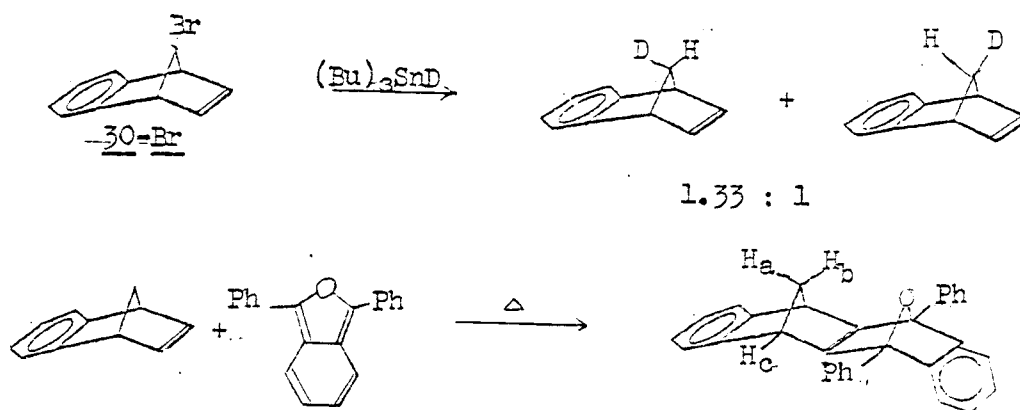


have met with failure, leading one author to conclude that halogen-metal exchange occurs only between alkyllithiums and alkyl iodides and does not occur with bromides (146).

It can be readily seen that the lithium reagent ratio obtained in the LiDTBB reaction was not due to equilibration of the free anions. If the anti to syn ratio for the free anion equilibrium as determined by Stille is 15 at $+60^{\circ}$, then it should be on the order of 100 at -78° . Thus, it can be concluded that if the 7-norbornenyl radical is significantly pyramidal, then the ratio of anti to syn radicals is 3.8 at -78° . At the temperature of Kochi's perester decomposition (32°) the anti:syn ratio would be 2.4. This is remarkably similar to the 2.7

ratio obtained for the tert-butyl ether products as mentioned above.

The 7-Benzonorbornadienyl System (30). Recently, interest has been shown in this system by a number of workers. Cristol and Noreen (140) reported that the reduction of either syn- or anti-30-Br with tributyltin deuteride gave the same ratio of syn to anti deuterium incorporation of 1.33. Due to severe overlap of nmr signals from the hydrocarbon, analysis was performed by conversion to the Diels-Alder adduct as shown. Although H_A is in the clear, H_B is partially overlapped with H_C . This method of analysis was also used by



Buske and Ford (122) in their work on the Grignard reaction of 30-Br and 30-Cl as was previously discussed. The reaction of syn- and anti-30-Cl with sodium naphthalene and magnesium chloride followed by deuterolysis gave mostly anti deuteration. However, the ratio of syn to anti was dependent upon the configuration of the starting halide. This is additional evidence that the anion trapping mechanism of Bank and Bank (76) is not operating in this system. Thus, it is not clear

what meaning can be ascribed to the syn to anti ratios which were obtained.

The lone pair orientation of 7-azabenzonorbornadiene has been determined recently (147). An approximately equal mixture of syn and anti was indicated, with perhaps a slight excess of the anti form. Unfortunately, the method of determination involved the use of shift reagents which are likely to exhibit discrimination of one form over the other due to steric differences.

The esr spectrum of the 7-benzonorbornadienyl radical at -116° has been reported recently (148). The α -proton coupling constant (8.3 Gauss) indicated that this radical is somewhat more pyramidal than 7-norbornenyl ($a(H_7) = 10.9$ Gauss). The radical was assigned to the anti configuration on the basis of coupling constants alone and with no mention of how much of the syn radical could be in rapid equilibrium with the anti. This assignment is very difficult to accept in light of the similar environment on both sides of C-7.

The reaction of anti-30-Cl with LiDTBB in THF was carried out at -78° , followed thirty seconds later by deuterolysis. The hydrocarbon was hydroborated and the alcohol analyzed by nmr with the aid of $Pr(fod)_3$. The shifted spectrum is shown in Figure 1. As can be seen, this procedure results in completely unambiguous integrations for both the syn and the anti protons. The nmr indicates $99 \pm 3\%$ deuterium incorporation with an anti:syn ratio of 1.33 ± 0.02 . The

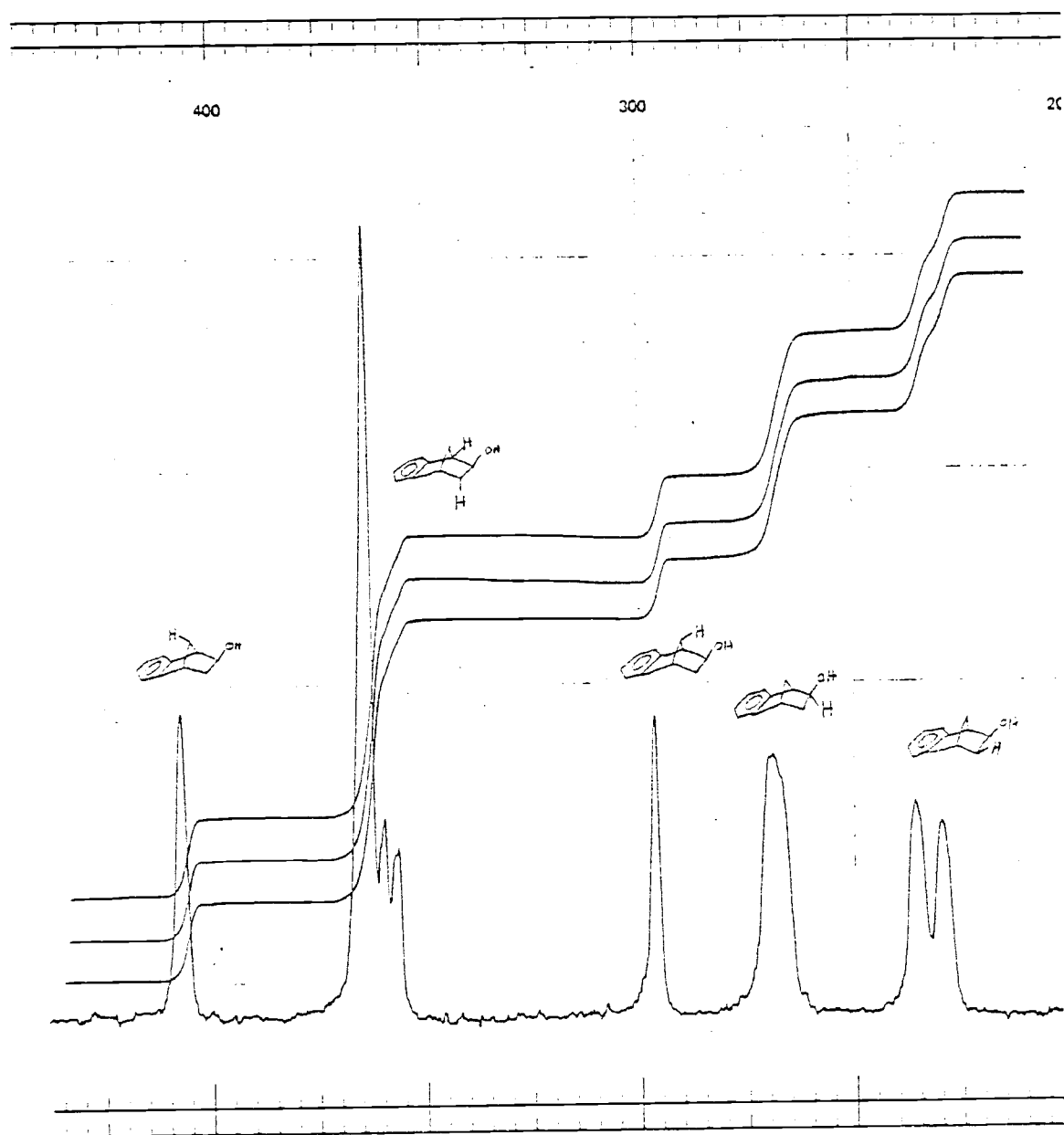
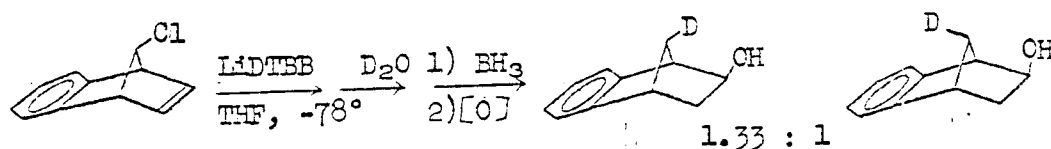


Figure 1. Nmr spectrum of 7-deuteriobenzonorboren-2-ol with added Pr(fod)_3 .

deuteration ratio is curiously the same as reported by Cristol and Noreen, but in the opposite direction. If the 7-benzonorbornadienyl radical can be considered significantly pyramidal, then the ratio of anti to syn radical configurations at the temperature of the esr study discussed above is probably no greater than about 1.5.

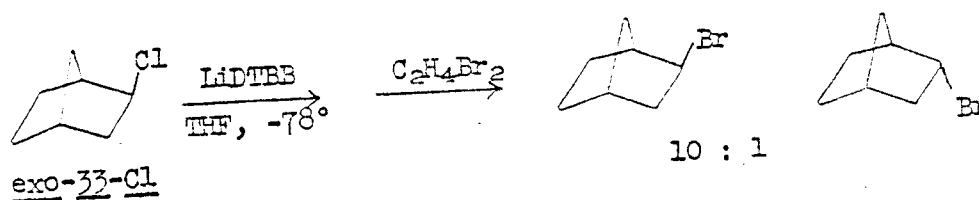


The 2-Norbornyl System (33). While the α -proton esr coupling constant for the two previous systems indicated a pyramidal geometry, the 2-norbornyl radical would appear to be only slightly pyramidal if at all. The α coupling constant is around 21 Gauss (149) and, although it was claimed that the radical is pyramidal, the large coupling constant indicates that it is probably insignificantly pyramidal.

The 2-norbornyl radical has a propensity for exo attack. This has been reviewed from the standpoint of stereochemical control of attack upon a planar radical (150). For example, either the exo- or endo-tert-butyl peresters gave an exo to endo ratio of tert-butyl ethers of 1.65. Either exo- or endo-2-chloronorbornane in reaction with tributyltin deuteride gave a ratio of exo to endo deuteration of 5.3 (151).

The 2-norbornyl anion has been studied by Stille, Feld, and Freeburger (152) by the same technique described for the 7-norbornenyl anion. At 67°, the exo to endo equilibrium value for the anion is at least 30, although the analysis was not as straightforward as in the previous case.

The treatment of exo-2-chloronorbornane with LiDTBB was performed as usual in THF at -78° and followed by deuterolysis. Analysis by ir indicated mostly exo deuteration, but was difficult to quantitate. Repetition of the reaction, but with a quench of ethylene dibromide, followed by nmr analysis of the gc-collected bromide peak indicated both exo- and endo-2-bromonorbornanes to be present in a ratio of 10:1.



The 4-tert-Butylcyclohexyl System (34). The cyclohexyl radical is generally regarded as being essentially planar, with an α -proton esr coupling constant of 21.3 Gauss (105). Treatment of 4-chloro-tert-butylcyclohexane with LiDTBB in THF at -78° followed by deuterolysis gave a mixture of cis- and trans-34-D. Ir analysis in the C-D stretching region (see Experimental Section) indicated an equatorial to axial ratio of 14:1. This is in agreement with the



14 : 1

A summary of the lithium reagent configurations obtained for the systems in this section and the preceding one is shown in Figure 2.

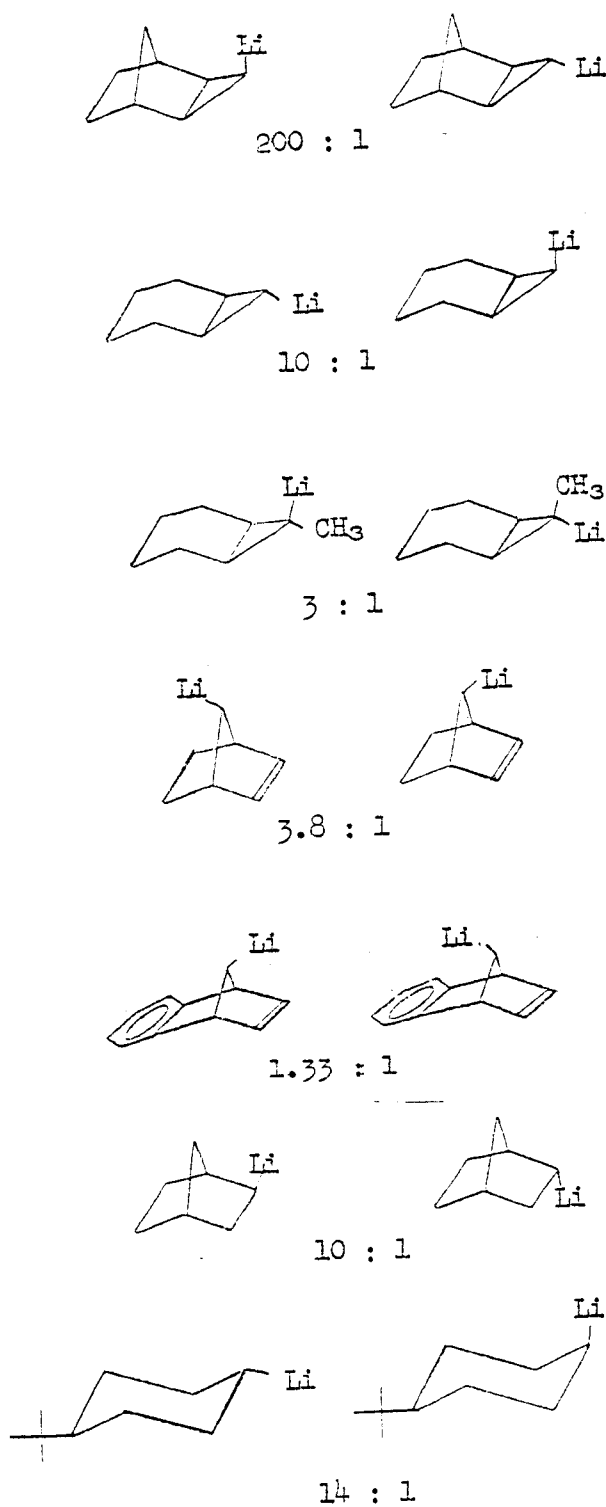


Figure 2. Lithium reagent configurations from the reaction of radicals with LiDTBB in THF at -78° .

EXPERIMENTAL

General Laboratory Procedures and Conditions

All temperatures are uncorrected. Nmr spectra were obtained on a Varian HA-100 Spectrometer (100 MHz). Ir spectra were obtained on a Perkin-Elmer 621 infrared spectrophotometer. Mass spectra were obtained using an Atlas CH7 mass spectrometer. Gc analyses were carried out with a Varian Aerograph A90-P2. Unless otherwise noted, the detector and injector temperatures were set at 230°. The flow rate for 1/4" columns was generally set at 60 ml/min, with ca. 20 ml/min for 1/8" columns. The columns used will be referred to by the letter designation as defined below:

Column A 4' x 1/4" 5% CW20M on 30-60 Chromosorb W

Column B 10' x 1/4" 10% SE30 on Anakrom 110-120 AS

Column C 10' x 1/4" 10% Ucon--water soluble with 1% KOH
on 60-40 Chromosorb W

Column D 8' x 1/4" 10% CW20M on 30-60 Chromosorb W

Column E 20' x 1/8" 8% Apiezon-N on 80-100 Chromosorb
WAS

Column F 15' x 1/4" 5% OV-17 on 60-80 Chromosorb G

Ether solvents were distilled from sodium benzophenone dianion and stored over 4A molecular sieves under nitrogen. Errors are standard deviations on multiple integrations (gc or nmr) unless

otherwise noted. The term high vacuum as used in this thesis means 10^{-5} torr or less.

Preparation of *exo*- and *endo-anti*-3-Chlorotricyclo[3.2.1.0^{2,4}]oct-6-ene. The title chloride was prepared by the procedure of Magid and Wilson (110). To a rapidly stirred mixture of 92 g (1 mol) of norbornadiene and 43 g (0.5 mol) of methylene chloride cooled in an ice bath, was added dropwise over a period of 2 h, 160 ml of 1.9 M MeLi · LiBr in ether (Alfa). Workup in the normal manner was followed by distillation through a short-path distillation apparatus. Material collected between 43° and 60° at 4.5 torr weighed 10 g (23% yield based on MeLi). The distilled material consisted of a mixture of the two title chlorides along with the corresponding bromides (ca. 10% of the chlorides) and the cyclopropane ring-opened halides. This mixture was used in the Grignard described below. The ring-opened halides could be removed by treatment with a solution of 6 g of AgNO₃ dissolved in 100 ml of acetone and 10 ml of water for a few minutes. The standard workup followed by a quick chromatography on alumina and then short-path distillation provided a pure mixture of *exo*- and *endo-anti*-chlorides in a ratio of 2:1 by nmr.

The two epimers could be separated by chromatography on a 10% AgNO₃ on Silicar column (see below) with a loading of 1 g on a 2.5 x 22 cm column. Ether (10%) in pentane was used as the eluant

with progress being followed by TLC (see below).

Grignard reaction of *exo*- and *endo-anti*-3-Chlorotricyclo
[3.2.1.0^{2,4}]oct-6-ene. To 4.8 g of Mg turnings and 50 ml of THF in a nitrogen filled 250 ml flask, was added 2 ml of CH₃I. The solution rapidly turned milky-grey and after 5 min, 18 g of the mixture of chlorides described immediately above was added in one lot. After 5 min, the solution began frothing with sufficient vigor to bring the material close to the top of the reflux condenser. When the reaction quieted down, a clear brown solution resulted, which was heated at reflux for an additional 12 h. Addition of 5 g of D₂O was followed two h later with sufficient HCl to dissolve the inorganic solids. Workup with pentane followed by distillation at 60-70° at 100 torr resulted in 5.5 g of crude hydrocarbon mixture (0.5 g forerun discarded). Nmr showed the presence of the expected bicyclic and *exo*- and *endo*-tricyclic hydrocarbons, which were then purified as described below. In spite of many attempts, it was repeatedly impossible to induce reaction in a purified chloride mixture using the normal Grignard techniques. This includes liberal use of C₂H₄Br₂, CH₃I, and slow addition of butyl bromide. All of the additives reacted with the Mg, but only very little conversion of the cyclopropyl chlorides could be induced. The presence of approximately 10% bromides in the crude mixture appears to be necessary for the Grignard reaction to proceed.

A portion (3.7 g) of the above hydrocarbon mixture was chromatographed on 140 g of 10% AgNO_3 on Silicar using 10% ether in pentane with the eluate being collected in six-inch test tubes. Tubes 11-16 contained 0.8 g of endo, tubes 17-19 contained 0.5 g of a mixture of endo and exo, and tubes 20-30 contained 1.9 g of exo. The remainder was eluted with 30% ether in pentane into a single flask and consisted of a mixture of exo and diene.

Nmr of the endo material indicates $85 \pm 5\%$ D incorporation and an anti:syn ratio of 2.4 ± 0.5 . In the deuterated material, the syn proton absorbs at 60.33 (t, $J=3$ Hz), while the anti proton absorbs at 60.53 (t, $J=7$ Hz). Similar direct analysis of the exo isomer was not possible due to coincidence of a number of absorptions. The analysis was accomplished by both epoxidation and hydroboration followed by shift reagent nmr analysis.

Epoxidation and Analysis of 3-Deuterio-exo-Tricyclo[3.2.1.0^{2,4}]

oct-6-ene from the Grignard Reaction. The purified exo alkene (100 μl) was treated with 200 μl of 40% $\text{CH}_3\text{CO}_3\text{H}$, 30 mg of $\text{NaOAc} \cdot 2\text{H}_2\text{O}$ and 50 μl of chloroform at 0° for 1 h. Dilution with 200 μl of pentane, extraction with 3 x 1 ml of 50% NaOH followed by gc collection from column A at 100° (inj. = det. = 150° , flow rate = 220 ml/min) gave 20 mg of pure epoxide. $\text{Eu}(\text{fod})_3$ shift analysis indicated $90 \pm 10\%$ D incorporation with a syn:anti ratio of 2.5 ± 0.5 . Integration of the syn proton was excellent, but the anti proton was difficult

to integrate due to trailing from the fod protons. A separate run of epoxidation and shift analysis indicated $89 \pm 5\%$ D incorporation with a syn:anti ratio of 2.2 ± 0.3 .

Hydroboration and Analysis of 3-Deuterio-*exo*-Tricyclo[3.2.1.0^{2,4}]oct-6-ene from the Grignard Reaction. To 62 mg of gc-collected *exo* alkene and 46 mg of NaBH_4 dissolved in 10 ml of anhydrous 1,2-dimethoxyethane (DME) cooled to 0° , was added with stirring 61 mg of H_2SO_4 dissolved in 10 ml of DME. The resultant solution was allowed to stir for 30 min at 0° , and then 30 h at 20° . To this mixture was then added, cautiously at first, 5.5 ml of 3N NaOH followed by 5.5 ml of 30% H_2O_2 . The mixture was then warmed to $40\text{--}50^\circ$ for 30 min. The usual workup followed by gc collection gave 20 mg of alcohol. A shift study ($\text{Eu}(\text{fod})_3$) indicated $70 \pm 10\%$ monodeuterium incorporation with a syn:anti ratio of 2.0 ± 0.5 . Integration of the syn proton was marred by overlap with the cyclopropyl bridgehead protons, and the results of this study are considered less reliable than with the epoxide.

Reduction of *exo*- and *endo*-anti-3-Chlorotricyclo[3.2.1.0^{2,4}]oct-6-ene with Sodium in *tert*-Butyl Alcohol-O-d. To 0.5 g (3.5 mmol) of a mixture of *exo* and *endo* chlorides dissolved in 1 ml of *t*-BuOD and 1 ml of THF, was added 230 mg (10 mmol) of Na in small pieces. The mixture was heated at reflux for three h, at which time no starting chlorides were observed by gc. The flask was extracted

with pentane and the usual workup was followed by gc collection (column B, 115°) which yielded 284 mg of hydrocarbon (76% yield). This mixture was subjected to AgNO_3 on Silicar chromatography followed by gc collection to yield 65 mg of the exo hydrocarbon and 13 mg of the endo material. Nmr analysis of the endo isomer indicated a $93 \pm 5\%$ D incorporation with the anti:syn ratio being 2.7 ± 0.3 . The exo isomer was converted to its epoxide by reaction with 60 mg of meta-chloroperbenzoic acid (85%, Aldrich) in 200 μl of methylene chloride at 0° for 2 h. Workup with 3 N sodium hydroxide and pentane was followed by gc collection from column C, with the collector and detector at 100° to prevent the facile decomposition. Nmr $\text{Eu}(\text{fod})_3$ shift analysis shows $98 \pm 5\%$ D incorporation with the syn:anti ratio being 1.16 ± 0.2 (error is estimate based on the degree of overlap between the anti and syn proton resonances).

Preparation of a Silver Nitrate on Silicar Chromatography

Column. To 23 g of Silicar contained in a 500 ml 24/40 flask, was added a solution of 2.3 g of AgNO_3 dissolved in 20 ml of water and 50 ml of acetone. The flask was placed on a rotary evaporator and the acetone and water were removed with the aid of a heat lamp. The resultant dry powder was dried further in an oven at 70° for 4 h.

A slurry of the 10% AgNO_3 on Silicar powder in pentane was then added in ca. twenty portions to a chromatography column filled with pentane. The column was rotated at a constant rate of one

rotation in 4 sec while gently but rapidly tapping the side of the column with the rubber handle of a screwdriver. A layer of Ottawa sand 1/2" deep was added to the top.

Preparation of Silver Nitrate-impregnated TLC Plates. To 15 g of AgNO_3 dissolved in 100 ml of water, was added 30 g of TLC grade PF254 silica gel. Glass microscope slides were dipped into the resultant slurry and air dried. Development was with 10% ether in pentane with the endo isomers of both hydrocarbons and chlorides described above moving faster than the corresponding exo isomers. Visualization was accomplished by spraying the plates with dilute KMnO_4 in acetone.

Formation of Carbene Insertion Product from the Reaction of Lithium Hexamethyldisilazane (HMDS) with Methylene Chloride. In an attempt to find a suitable synthesis of anti-3-chloro-exo-tricyclo[3.2.1.0^{2,4}]octane, a modification of the general procedure of Martel and Hiriart (155) was tried. A solution of LiHMDS (0.95 M, 11 ml) in cyclohexane prepared from HMDS (Aldrich) and n-BuLi (1 mmol each) was added via a syringe at a constant rate over a period of five h to a refluxing solution of 1 g (1 mmol) of norbornene, 5 g of methylene chloride, and 20 ml of cyclohexane. The tip of the syringe needle was below the surface of the liquid. Workup in the usual way but including extraction with 6 M HCl was followed by gc analysis. The yield of the hoped-for tricyclic chloride was estimated to be 3%. In

addition, however, a large peak with ca. half the retention time of the chloride was observed. Gc collection followed by nmr and ir analysis showed the product to be cyclohexylchloromethane, formed in ca. 12% yield. Ir: 2920(s), 2850(s), 1450(s), 1305(m), 1265(m), 961(m), and 725 cm^{-1} (s); nmr: δ 3.31 (2H, d, J=5.6 Hz) [Lit. (N10): δ 3.31, d, J=5.6 Hz], δ 2 to 0.9 (11H, complex).

Preparation of anti-3-Chloro-exo-tricyclo[3.2.1.0^{2,4}]octane (anti-23-Cl). The title halide was prepared from the reaction of norbornene with methylene chloride and methyl lithium-lithium bromide followed by treatment with AgNO_3 as before using a slight modification of the method of Jefford and Medary (111). Other attempts at preparation using a variety of bases including lithium 2,2,6,6-tetramethylpiperidide failed to give better yields.

Analysis of 3-Deuterio-exo-tricyclo[3.2.1.0^{2,4}]octane. In the nmr of the deuterated hydrocarbon, the anti proton absorbs at δ -0.23 (t, J=7.26 Hz), while the syn proton absorbs at δ +0.15 (t, J=3 Hz). The syn and anti deuterio compounds have their C-D stretching frequencies too close together to permit analysis by ir in this region.

Alkali Metal-tert-Butyl Alcohol-O-d in Tetrahydrofuran Reduction of anti-3-Chloro-exo-tricyclo[3.2.1.0^{2,4}]octane(anti-23-Cl). To a solution of the title chloride (50 mg, 0.35 mmol) in a mixture of 1 ml of t-BuOD (98% d_1) and 2 ml of anhydrous THF, heated at reflux, was added 5 mmol of the alkali metal. Heating at reflux was continued

until aliquotes indicated the absence of starting chloride. Reaction time, yield, and syn:anti deuterio ratio are given in the table.

Deuterium incorporations were above 95% as determined by nmr.

Metal	Time	Yield	<u>syn:anti</u>
Na	1.5 h	70%	2.11
K	0.5 h	50%	1.25
Li	1.0 h	16%	1.70

The Effect of Solvent Composition on the Reduction of anti-3-Chloro-exo-tricyclo[3.2.1.0^{2,4}]octane with Potassium/t-BuOD. To a refluxing mixture of 1.0 ml of t-BuOD and the indicated amount of THF, was added 150 mg of potassium metal followed 30 sec later by 20 μ l of the title chloride. The syn:anti deuteration ratio is presented in the table. The deuteration in all cases was above 90%. Syn to anti deuteration was determined by analysis of the nmr spectrum of the gc collected material.

THF Added (ml)	<u>syn:anti</u> Deuterium	Reflux Time (hr)	Isolated Yield (%)
0	1.27 \pm 0.13	0.5	50
2	1.25 \pm 0.10	0.5	50
6	1.22 \pm 0.13	1.0	57
30	1.20 \pm 0.06	3.0	53

Reaction of anti-3-Chloro-exo-tricyclo[3.2.1.0^{2,4}]octane with Lithium in Ether. A suspension of Li was prepared by leaching 200 mg of a 20% Li (1% Na:99% Li) dispersion in paraffin with two 3 ml portions of pentane followed by the addition of 3 ml of anhydrous ether. To this mixture was added 50 mg of the title chloride, and,

after 1 min at room temperature, the flask was cooled to 0°. After 5 min the reaction was 75% complete, and after 15 min all chloride was absent. D₂O (0.5 ml) was then added and followed by the usual workup and gc collection; 40% yield, 87% deuterium incorporation, syn:anti = 2.1 ± 0.3.

Reaction of anti-3-Bromo-exo-tricyclo[3.2.1.0^{2,4}]octane(anti-23-Br)-n-BuLi. To 1 ml of 1 M n-BuLi in hexane (Ventron) and 3 ml of anhydrous ether, was added 55 mg of the title bromide. After 10 min at 0°, reaction was complete. D₂O (1 ml) was added after 45 min, and workup as above gave 20 mg (85% yield) of hydrocarbon. Nmr analysis indicated greater than 95% deuterium incorporation with syn:anti less than 0.06:1.

Low Temperature Reaction of anti-3-Chloro-exo-tricyclo[3.2.1.0^{2,4}]octane(anti-23-Cl) with Potassium and t-BuOD. A 500 ml three neck flask was connected to the high vacuum line via the center neck. Into one neck was inserted a viewing window consisting of a piece of glass cut from a microscope slide and attached to a sawed off 24/40 inner joint with Torr-Seal epoxy. An assembly consisting of two 1.6 mm diameter copper wires spaced 1 cm apart projecting through a 24/40 inner joint and sealed with Torr-Seal epoxy was placed in the other neck. The flask side of each wire was tipped with an alligator clip to hold a nichrome coil. The coil was formed from 3 strands of #30 nichrome wire wound together with an electric drill

and then formed around the sharpened end of a pencil. The cone shaped coil was 2 cm long, and had 4 cm of lead wire which, when attached to the alligator clips, and inserted into the side arm, suspended the coil approximately in the center of the flask. Power was applied to the coil by a Variac (voltage usually 10 V or so) connected to the projecting copper wires.

The flask was dried by a high vacuum combined with flaming of the exterior of the vessel. After the flask was considered dry (ca. 3 h), nitrogen was admitted and, with a strong flow, the coil assembly was pulled out until the coil was accessible but still in the neck of the flask. A 200 mg piece of potassium metal, which had been cleaned with a knife under mineral oil, was washed with toluene and immediately placed in the coil. The assembly was seated in its joint and the flask was immediately re-evacuated. After 1 h at room temperature under a high vacuum, the flask was immersed in liquid nitrogen and 1 ml of previously degassed t-BuOD was deposited on the walls of the flask, followed by about 20 ml of THF. The coil was then heated at about one-half the voltage required to produce a red glow. The potassium deposited over a period of 30 min with the filament being constantly monitored through the window. The very dark blue-black coating was then covered with 15 ml of THF, 1.0 ml of t-BuOD, and finally, 40 μ l of the title chloride. All depositions were done slowly so as to minimize local melting. The flask was warmed to -90° with

a toluene slush bath, and the black mixture was stirred for 30 min at this temperature. The mixture was then allowed to warm to -78° and was stirred for an additional 1.5 h. The blue-black suspension underwent visible reaction and slowly lightened to grey after 45 min. The mixture was allowed to warm to -10° over a period of 2 h, at which time the mixture consisted of a milky white suspension. Careful addition of water resulted in burning particles being shot out of the neck of the flask. Workup in the usual way and nmr analysis indicated at least 95% D incorporation and a syn:anti ratio of 1.28.

Reaction of anti-3-Chloro-exo-tricyclo[3.2.1.0^{2,4}]octane(anti-23-Cl) with Lithium Naphthalene. A solution of lithium naphthalene was prepared by stirring 2 g (15.6 mmol) of naphthalene, 0.10 g of Li (14 mmol) in small pieces, and 20 ml of THF at room temperature for 3 h. The dark green solution was cooled to -78° , and 50 mg of the title chloride dissolved in 3 ml of THF was added dropwise. After stirring for 8 min, 1 ml of D₂O in THF (3 ml) was slowly added. The usual workup was followed by a two stage gc collection from column B. Coupling products were searched for by analyzing the crude reaction mixture on a short (3') 5% SE30 column under conditions where hydrocarbons of similar molecular weight came off in 5 min (Ph₃CH, 250°). No peaks were observed in this region, and thus the maximum extent of coupling was estimated to be 0.1%.

Nmr analysis indicated greater than 96% deuterium incorporation. The ratio of anti-C3 proton nmr integration to syn integration was 28:1, with the splitting pattern of the residual syn proton indicating that at least 75% of this signal originated from the undeuterated species. The syn:anti deuteration ratio corrected for the presence of undeuterated hydrocarbon is, therefore, at least 100:1.

Preparation of Lithium Naphthalene Dianion using High Vacuum Line Techniques. Two 500 ml three neck round-bottom flasks, each with a glass covered stir bar, were attached in adjacent positions on the high vacuum line by their center necks. The right-hand flask was used for vaporization of Li and formation of the dianion, while the left-hand flask was used for the reaction of the dianion with the chloride to be described below.

A liquid transfer assembly was constructed out of 4 mm pyrex tubing and two 24/40 inner joints. When in place, one end of the tubing was near the bottom of the generation flask, with the tubing passing up through one joint, across the space between the two flasks and terminating just inside the reaction flask. Between the two flasks the tubing was formed into a strain relief coil of 4 turns 4 in in diameter and 4 in long. The open end in the generation flask was plugged with a tuft of glass wool to filter out Li particles. The remaining neck of the generation flask was used to hold the nichrome vaporization coil described above in the low temperature potassium experiment.

The apparatus was dried under a high vacuum for several h with intensive flaming, especially of the coil. Using argon gas rather than nitrogen, a 200 mg cube of lithium was placed in the vaporization coil as described in the previous experiment. After the apparatus had been under high vacuum for approximately one h, the vaporization of lithium was commenced. Difficulty is often encountered at this point for two reasons; one, the oxide film on the molten lithium is very tough and tenacious, requiring that the entire apparatus be vibrated vigorously to break through the film, and two, when the lithium does wet the nichrome it lowers the resistance of that portion of the filament which becomes covered with lithium, causing a greatly increased flow of current which often burns out that portion not wet with lithium. At the same time, the walls of the flask become blackened by the vaporized lithium, making it difficult or impossible to judge the temperature of the filament. For these reasons it is suggested that, if at all possible, tungsten be substituted for nichrome in any such apparatus.

After lithium vaporization was complete (15 min) the apparatus was pressurized with argon, the vaporization assembly removed, and 100 ml of THF was vacuum transferred into the formation flask. Early experiments were confounded by rapid decomposition of the dianion solution and formation of a fine precipitate which clogged the glass wool filter plug. These problems were alleviated by the

removal of the vaporization assembly before dianion formation. Apparently, the decomposition of the dianion is catalyzed by metal contamination from the filament in analogy to the well known catalysis of the sodium and ammonia reaction by traces of iron.

A solution of 1 g of naphthalene in 10 ml of THF was formed by the usual high vacuum line techniques and transferred under argon flow to the generation flask with a dry argon-purged syringe. The mixture was stirred at 0-10° until gc analysis of aliquots quenched in water showed a naphthalene to dihydronaphthalene ratio of less than 0.01. Column D was used in this and subsequent analyses. The dianion solution was then transferred to the reaction flask through the transfer tube and glass wool filter plug by partially evacuating the reaction flask while keeping the generation flask pressurized. The reaction flask is cooled in a thick slurry of Dry-Ice and isopropanol during and after the transfer. The color of the dianion solution is a deep purple almost indistinguishable from the color of grape juice.

Reaction of anti-3-Chloro-exo-tricyclo[3.2.1.0^{2,4}]octane(anti-23-Cl) with Lithium Naphthalene Dianion Produced by High Vacuum Line Techniques. After the dianion solution described immediately above had stirred for 15 min at -78°, an aliquot was taken and quenched in water. Gc analysis as before showed that the conversion of naphthalene to its dianion was 99.4% complete, corresponding to the solution being ca. 0.00047 M in radical anion and 0.078 M in

dianion. A mixture of 40 μ l (45 mg) of the title chloride and 40 μ l of tridecane as internal standard was then injected. Aliquots were withdrawn at intervals with a dry nitrogen filled pipette and as rapidly as possible injected into 1 ml of water in a 2 dram vial. The stopper to the reaction flask was removed only far enough to allow insertion of the pipette and a brisk stream of Ar exiting through the neck was used to minimize introduction of air.

The aliquots were analyzed by injecting about 50 μ l of the organic phase in column D with the column temperature initially at 120°, and then increased to 150° after the title chloride had eluted. Due to the low concentrations involved, gc analysis of the aliquots are shown in the table:

Aliquot Number	Time (min)	Chloride:C ₁₃	Naphthalene:C ₁₃
1	10	1.27	0.76
2	20	1.04	1.11
3	30	1.04	1.16
4	55	1.04	1.16
5	80	0.709	1.12
6	109	0.643	1.43
7	175	0.592	--
8	199	0.386	1.73

The mixture was then quenched with D₂O (2 ml) and workup in the normal fashion was followed by gc collection of the deuterated hydrocarbon from column D at 100°. Nmr indicated at least 97% D incorporation with the syn:anti ratio being at least 50:1.

A plot of $\ln(\text{chloride:C}_{13})$ vs. time is shown in Figure 3. Least squares fitting of this data gives a pseudo first order rate constant of $5.4 \pm 0.7 \times 10^{-3} \text{ min}^{-1}$. If the halide were reacting exclusively with the dianion, the second order rate constant at -78° is $k_{N-2} = 6.8 \pm 2.0 \times 10^{-2} \text{ M}^{-1} \text{ min}^{-1}$. The data given above indicates the concentration of the radical anion as determined by the relative proportion of naphthalene to internal standard upon hydrolysis increased by a factor of 2.3 from 10 min into the reaction to 200 min. If the halide was reacting exclusively with the radical anion, the graph of Figure 3 should be curved downward. While the graph does not appear to be curved, the extensive scatter in the data does not allow for definite conclusions to be made. Since the concentration of the radical anion was determined to be $4.7 \times 10^{-4} \text{ M}$ before addition of the halide, it is likely that the concentration is ca. $1.2 \times 10^{-3} \text{ M}$ at point #8. If one (conservatively) uses this to determine the second order rate constant assuming reaction with the radical anion rather than with the dianion, the value of $4.5 \text{ M}^{-1} \text{ min}^{-1}$ is obtained. This is ca. five times as large as the actual rate constant determined for the radical anion below. Thus it would seem that most of the halide does in fact react with the dianion.

Kinetics of the Reaction of *syn*-3-Chloro-*exo*-tricyclo

$[3.2.1.0^{2,4}]$ octane(*anti*-23-Cl) with Lithium Naphthalene. This study was carried out exactly as in the case of the dianion, except that only

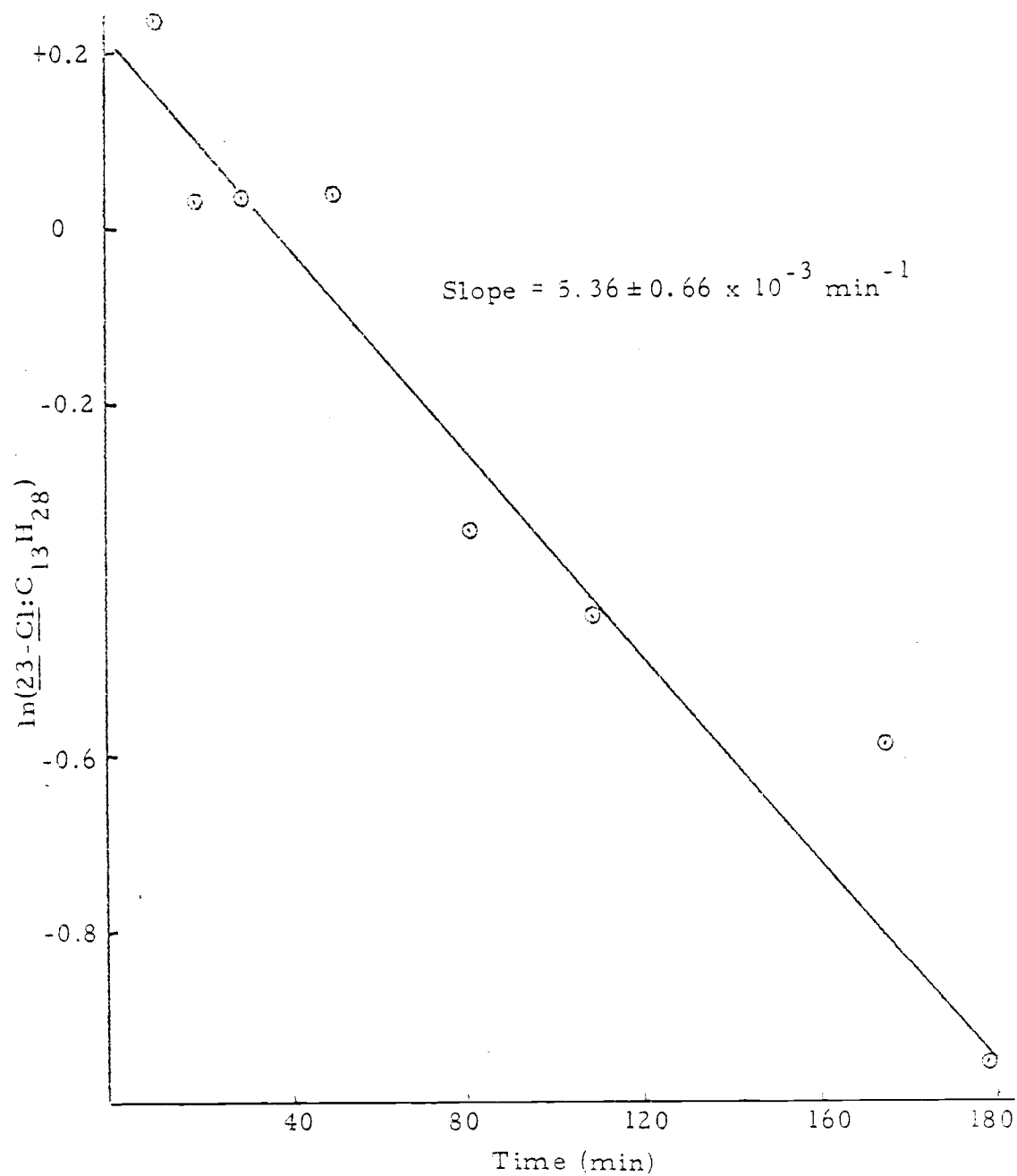


Figure 3. Graph of $\ln(23\text{-Cl:C}_{13}\text{H}_{28})$ vs. time for the reaction of 23-Cl with lithium naphthalene dianion.

50 mg of Li was used, gc separations were done isothermally at 150°, and the sum of naphthalene (Nap) and dihydronaphthalene (Nap-H₂) was used as the gc internal standard. The data from this study are shown in the table:

Aliquot Number	Time (min)	Chloride	Nap-H ₂	Nap	Chloride/(Nap+Nap-H ₂)
1	8	4290	44790	67990	0.0380
2	23	2537	64260	83430	0.0172
3	35	721	39630	63670	0.00698

Taking the average value for the three aliquots of $2 \cdot \text{Nap-H}_2 / (\text{Nap-H}_2 + \text{Nap})$ to be the fraction of the naphthalene converted to the radical anion, we arrive at a concentration of 0.063 M for the radical anion. The concentration can be considered to be constant since the reduction due to reaction with chloride is only 10%. Least squares fitting in $\ln(\text{RCl}/(\text{Nap-H}_2 + \text{Nap}))$ vs. time gives a pseudo first order rate constant of $6.24 \times 10^{-2} \text{ min}^{-1}$ and thus a second order rate constant of $1.0 \text{ M}^{-1} \text{ min}^{-1}$, about 15 times faster than the dianion reaction.

Stability Study of *syn*-3-Lithio-*exo*-tricyclo[3.2.1.0^{2,4}]octane (*syn*-23-Li). After the above kinetic analysis was complete, the reaction mixture was allowed to warm from -78° to 0° over a period of 6 h before being quenched with D₂O. The deuterium incorporation was only 82%, and the *syn:anti* ratio could not be determined directly from the integration of the nmr signals. As in previous cases, an

analysis of the intensities of the splitting of the syn-C₃-H signal was required. The corrected syn:anti ratio is at least 30:1.

Preparation of 7-Chloronorcarane (28-Cl). To a solution of 20 ml of cyclohexene and 3.5 g of hexamethyldisilazane (Aldrich), was added 10 ml of 2.1 M n-BuLi (hexane, Ventron) followed by 7 g of CH₂Cl₂. After 5 h of reflux, gc analysis of an aliquot of the mixture indicated a syn:anti ratio of 1.272 ± 0.004 . Workup as usual and distillation at 50° and 10 torr gave 2 g (35% yield) of pure chloride mixture with syn:anti = 1.53 ± 0.02 . Identity of the halides was established by gc collection and nmr analysis. The proton α to Cl in the anti compound is a triplet at $\delta 2.56$, $J=3.1$ Hz. A similar mixture of syn- and anti-7-chloronorcaranes could be obtained by lithium aluminum hydride reduction of 7,7-dichloronorcarane in refluxing diglyme (see also Reference 156).

Kinetics and Products of the Reaction of 7-Chloronorcarane with LiN. A solution of LiN was prepared under conditions B and cooled to -78°. Internal standard (nonane) and a mixture of syn- and anti-7-chloronorcarane (0.48 mmol, syn:anti = 1.65) was injected. Aliquots were taken at intervals and analyzed by gc as described in the general conditions section. The integrations are listed in the table:

Time (min)	Nonane	<u>anti-28-Cl</u>	<u>syn-28-Cl</u>
0	42620	15370	27520
7	20350	11030	19530
29	37400	12200	20550
60	30570	9450	14980
97	41220	11310	15540
173	39590	8010	9001

Linear least squares fitting of $\ln(\text{integration of chloride/integration of nonane})$ vs. time gives pseudo first order rate constants of $3.3 \pm 0.2 \times 10^{-3} \text{ min}^{-1}$ for the anti chloride, and $6.0 \pm 0.3 \times 10^{-3} \text{ min}^{-1}$ for the syn chloride. Assuming the concentration of LiN to be 0.095 M (the LiN drops from 0.11 to 0.08), the second order rate constants are $0.035 \pm 0.005 \text{ M}^{-1} \text{ min}^{-1}$ for the anti chloride, and $0.063 \pm 0.009 \text{ M}^{-1} \text{ min}^{-1}$ for the syn chloride. The ratio of the syn to anti rate constants is 1.85.

In another run, D_2O was added and the product analyzed by nmr: 71% deuterium incorporation, anti:syn = 7 ± 2 .

Reaction of 7-Chloronorcarane (28-Cl) with the Product of Sodium Naphthalene and Magnesium Bromide. A solution of sodium naphthalene was prepared from 1.28 g (1.0 mmol) of naphthalene and 23 mg (1.0 mmol) of sodium in 50 ml of THF. To this solution was added an approximately 0.25 M MgBr_2 solution in THF until the green color was absent. Nonane (45.5 mg) and 7-chloronorcarane (55.4 mg, syn:anti = 1.65) were then added at room temperature. An aliquot taken after 10 min indicated ca. 80% reaction. The mixture was

allowed to stir for 2 h, and was then quenched with D_2O . Gas evolution was noticed when the D_2O was added. Gc analysis indicated a yield of 84%. Nmr analysis indicated a D incorporation of $73 \pm 4\%$ with the anti:syn ratio being 0.78 ± 0.08 .

Reaction of 7-Bromonorcarane with Magnesium Turnings. To 0.2 g of Mg turnings (Grignard grade) in 15 ml of THF, was added 50 μ l of ethylene dibromide followed by 20 μ l of methyl iodide. The solution was heated at reflux until the initial reaction appeared to be over. The title bromide (syn:anti = 1.2, 66.7 mg) was then injected, and the solution was heated at reflux for 2 h. Nonane (18.9 mg) and D_2O (2 ml) were then added and workup as usual followed by gc analysis indicated a 77% yield. Nmr analysis indicated $39 \pm 10\%$ D incorporation with an anti:syn ratio of 0.95 ± 0.3 .

Preparation of Crystalline Magnesium Anthracene Dianion in THF. To 1 g of magnesium turnings (Grignard grade) contained in a 100 ml flask equipped with a glass covered magnetic stirring bar and attached to the high vacuum line, was transferred 3 to 4 ml of THF from sodium benzophenone dianion. The flask was repressurized, 40 μ l of ethylene dibromide was added, and the solution was heated to 40° for 1 h to activate the Mg surface. A sidearm containing 2 g of anthracene (recrystallized 5X from ethanol) was attached and the assembly was immediately evacuated. High vacuum was maintained for 15 min to dry the sidearm and to remove any excess ethylene

dibromide. THF (40 ml) was then transferred in and the sidearm rotated to allow the anthracene to drop into the THF solution. After stirring for 1 h at room temperature, the solution was a clear green color. Heating the solution to ca. 40° caused the color to shift to a bright yellow, while cooling to the vicinity of -40° or so gave rise to a deep blue color. The color changes are continuous and reversible. After 24 h at room temperature, the mixture consisted of an orange-yellow flocculent solid in a green-yellow solution. The mixture was then heated to $30-40^{\circ}$ with stirring for 1 week. At this time the orange precipitate was quite thick.

Purification and Growth of Magnesium Anthracene Dianion

Crystals. The above suspension of magnesium anthracene was syringed into the extraction chamber of a DeKock soxhlet extractor (see Figure 4) which had been dried on the high vacuum line for 3 h and then filled with nitrogen. The extractor was then carefully evacuated and held at a high vacuum for an hour. THF (50 ml) was then transferred in and the apparatus removed from the line. The orange solid was washed 4X by distilling THF from the bulbs up to the extraction chamber with the washings being poured into the side-arm bulb. The THF was then distilled into the lefthand bulb (Figure 4) and the apparatus was placed in a constant temperature box. Both bulbs were immersed in an oil bath such that the THF level was 1-2 cm above the oil level. The constant temperature box was heated to

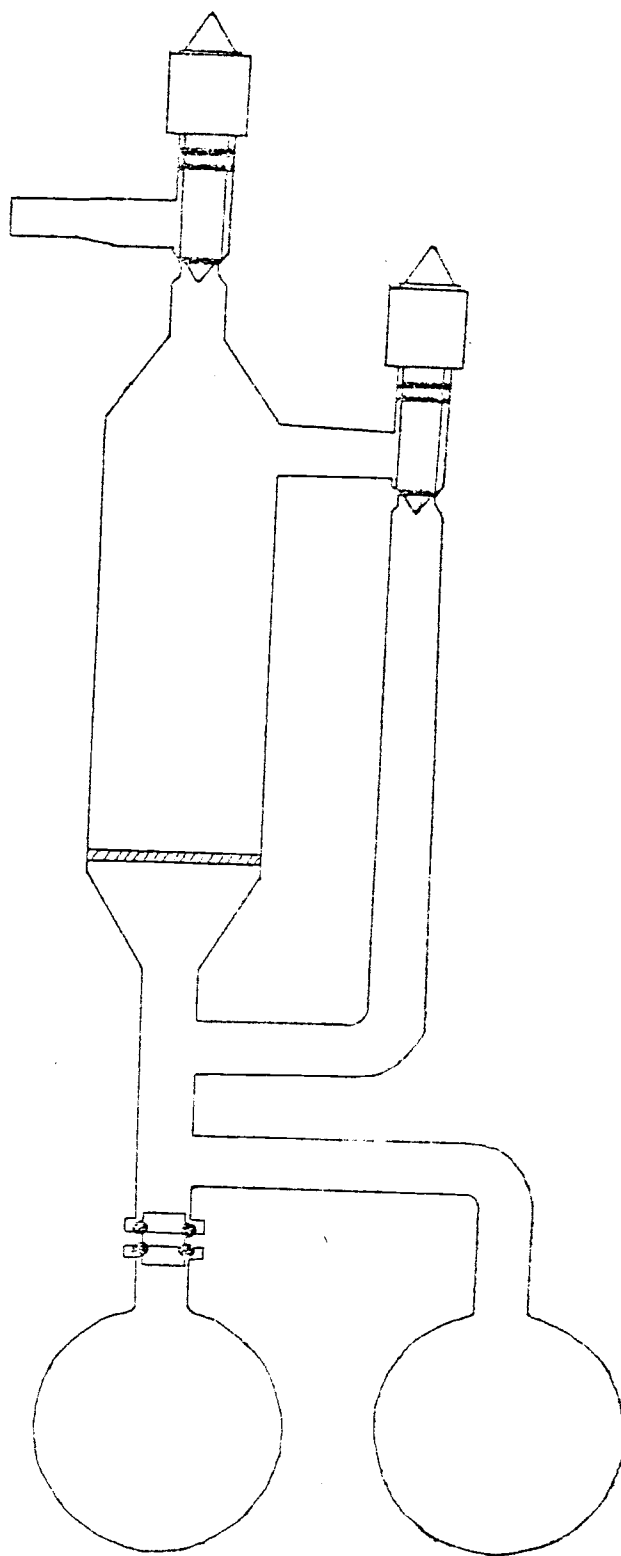


Figure 4. A schematic drawing of the DeKock soxhlet extractor.

40° and the oil bath was heated by means of a nichrome coil to such a power level that the extraction proceeded at a slow rate. The proper power level was determined by trial and error over a period of one week, while the extraction took place over a period of 2 months.

The magnesium anthracene dianion grew as clear orange needles up to 4 cm in length and 3-4 mm in width. A yellow-green solid of undetermined composition was left on the frit of the extractor. After the completion of the crystallization, the THF was poured into the sidearm bulb and then removed on the high vacuum line. The crystals were then transferred to storage tubes in a dry box.

Analysis of the Magnesium Anthracene Dianion Crystals. A

portion of the purified material was transferred to a tared flask in the dry box and the weight determined to be 0.6565 g. The flask was then connected to the high vacuum line, evacuated and 1-2 ml of degassed water was transferred in. The mixture was allowed to stand for 1 h. Standardized nitric acid (10.00 ml, 3.94 mmol) and benzene (20 ml) were then added, and the mixture was stirred for 1 h. The aqueous phase was separated and back-titrated with 0.200 M NaOH, requiring 4.09 ml. Thus, 3.12 meq of base was formed in the treatment of the orange solid with water, equivalent to 1.56 mmol of Mg. The neutralized solution was then diluted to 100.0 ml. Titration of a portion with AgNO_3 showed the absence of bromide ion. Titration of the remainder on 25.00 ml lots with 1.022×10^{-2} M disodium EDTA

using erichrome black-T indicator and pH 10 buffer required an average of 39.0 ml, equivalent to 1.60 mmol of Mg.

Gc analysis of the organic phase showed the ratio of anthracene to 9,10-dihydroanthracene to be 0.0246 ± 0.0009 (10 injections). To the benzene solution was then added 0.3270 g of anthracene as internal standard, and the ratio of dihydroanthracene to anthracene was determined to be 0.372 ± 0.014 . The response factor for dihydroanthracene vs. anthracene was determined to be 1.015 ± 0.014 . Thus, present in the benzene layer was 0.2957 g of dihydroanthracene and 0.0073 g of anthracene, or 1.68 mmol of anthracene, in the original sample. If the quantity of both anthracene and magnesium in the original sample are taken to be 1.60 mmol (the EDTA titration is expected to be more accurate than the gc analysis), and the remainder by weight taken to be THF, the empirical formula is $\text{MgA} \cdot 2.88\text{THF}$, or $\text{MgA} \cdot 3\text{THF}$ when rounded off.

Confirmation that the ratio of THF to anthracene is 3 was obtained by nmr. In the dry box, a portion of the crystals was placed in a vacuum-dried nmr tube. Exposure of the crystals to O_2 gas was followed by the addition of CCl_4 . Nmr integration of the anthracene protons relative to the THF protons indicates a 3.1 ± 0.4 mole ratio of THF to anthracene.

Preliminary X-ray Single Crystal Analysis of Magnesium

Anthracene Dianion. A single crystal suitable for structure analysis

was obtained in the following manner: In the inert atmosphere box, a small pile of crystals was placed on a smear of Apiezon-N grease on a microscope slide and quickly mixed. The slide was placed in a miniature inert atmosphere container composed of a piece of Pyrex tubing with large rubber balloons capping the ends. The crystals were manipulated by means of short pieces of tungsten or stainless steel wire epoxied to the ends of a glass rod. The crystals were observed through a dissecting microscope during the manipulations. The crystals were cleaved in a small pool of mineral oil in hopes of cleaving single crystals from twined ones. Selected crystals were set off to one side and later loaded into 0.3 and 0.5 mm X-ray capillaries in the inert atmosphere box.

The chosen crystal was mounted on a Syntex P_1 computer-controlled four circle diffractometer equipped with a graphite-monochromatized Mo-K α X-ray source. A one h rotation photograph of the 0.6 x 0.3 x 0.1 mm crystal followed by the Syntex auto-centering procedure, accurately located eleven reflections from a variety of positions. Examination of the output from the Syntex auto-indexing routine indicated that the crystal was triclinic and with a rather large unit cell. Execution of the Syntex least-squares refinement program using three selected axes from the autoindexing routine resulted in the following unit cell parameters (standard deviations):

$$a = 19.193(.029), b = 8.127(.009), c = 30.503(.409) \text{ \AA}, \alpha = 97.14(.11),$$

$\beta = 98.54(.13)$, and $\gamma = 89.92(.11)$ deg. The unit cell volume is $4668(12)\text{\AA}^3$ and assuming eight $\text{MgA} \cdot 3\text{THF}$ units per unit cell gives a calculated density of 1.19 g/cm^3 in good agreement with the experimental density of 1.18 g/cm^3 obtained by flotation in benzene-bromobenzene mixture.

That the crystal is single is shown from examination of partial rotation photographs taken about each of the three chosen axes. No reflections off the layer lines were observed. In addition, ω -scans of several reflections gave sharp symmetrical peaks with no evidence of twinning.

General Conditions for the Preparation of Radical Anion

Solutions. A 100 ml three neck 14/20 morton flask containing a 2.5 cm glass covered magnetic stir bar was simultaneously dried and filled with argon by passing a steady stream of the gas in through the right hand neck of the flask with alternately one and then the other of the two stoppers floating in the exiting argon stream, while heating the flask with a high-temperature heat gun. After the flask had cooled to about 35° , the weighed amount of aromatic hydrocarbon was added through a briskly exiting stream of argon via a 14/20 funnel. The required amount of solvent was then added by carefully pouring from the storage container while passing a rapid stream of argon through the flask. The space above the liquid in the storage container was blown out with nitrogen as soon as possible (within 10 sec) after the

addition. The required amount of alkali metal was weighed out on an analytical balance to within 1-2 mg of the target weight. An oversize piece was first weighed and then trimmed to the proper weight with a knife, cleaning off any oxide crust in the process. Lithium was handled with tweezers in the open air as only a very slight amount of oxidation occurred during the short time the metal was exposed to the atmosphere. Potassium and sodium, however, had to be coated at all times with mineral oil to prevent excessive oxidation and reaction with atmospheric moisture. The piece of metal was then placed in the center neck of the flask and, with a rapid flow of argon, portions of the metal were flattened with curved surgical scissors so as to maximize the clean surface area, and cut into the solution. A 35 mg piece of lithium typically was cut into at most three pieces. This procedure was found to result in more rapid formation of the radical anion than cutting many small pieces of lithium into the solution.

The color of the radical anion pervaded the solution within 10-20 sec after the first piece was dropped in. The solution was cooled to 0° in the case of lithium radical anions to prevent excessive decomposition during the formation. The solution was stirred rapidly until no unreacted metal could be discerned in the dark solution. This required typically 3-4 h for LiDTBB formation in THF.

Standard Conditions A: THF, 30 ml, aromatic hydrocarbon, 6 mmol and alkali metal, 5 mmol, were treated as in the general

conditions above. This results in a solution 0.17 M in radical anion.

Standard Conditions B: As in A above but with the addition of 20 μ l (1.56 meq) of Br_2 . This results in a solution 0.11 M in radical anion and 0.05 M in LiBr.

General Conditions for Quantitative Radical Anion-Alkyl Halide

Reactions. To the radical anion solution as prepared above and cooled to -78° by a Dry Ice-isopropanol bath, was added 60 μ l of the internal standard via a Hamilton 100 μ l syringe followed by 60 μ l of the halide. For most halides this amount represents 13% of the stoichiometrically required halide. Whenever a sample was added to or withdrawn from the reaction flask, a brisk flow of argon was used to prevent introduction of atmospheric gases. The stoppers were removed only to the extent required for the insertion of the syringe or pipette. In all cases the halide was ejected from the syringe as rapidly as possible (less than 0.5 sec) with the very fine spray sweeping across the radical anion solution. The stirring rate (glass covered magnetic stir bar) was set as high as possible. The reactions of secondary and tertiary chlorides and bromides, as well as primary and cyclopropyl bromides with lithium naphthalene (LiN) or lithium di-tert-butylbiphenyl (LiDTBB), are complete in less than a few seconds. Primary chlorides require 30 sec with LiDTBB, while secondary cyclopropyl chlorides require as much as 5 min. LiN requires about thirty times as long as LiDTBB.

Aliquots were taken with a dried disposable pipette with a shortened tip. The pipette was filled with nitrogen and the liquid was expelled by introduction of nitrogen from a rubber balloon attached to the inlet of the pipette bulb. When a sample was taken, the liquid was sucked up and then ejected directly into 2 ml of water in a 2 dram vial as rapidly as possible--total time for the solution to be in contact with the pipette was typically less than 3 sec. To the THF layer was then added 0.5 ml of pentane, and then water was added until the vial was full. The cap was then replaced and the vial inverted and agitated to extract as much THF into the water as possible. The water was then removed, fresh water added, the vial again agitated and then stored with the cap down. The pentane layer is effectively sealed by the glass on the top and sides and by the water on the bottom. Vials allowed to stand upright lost the pentane in short order and the relative composition of product to internal standard was not stable. Vials stored in the upside down manner were stable indefinitely.

After the aliquot was taken, CO_2 was bubbled in until the solution went colorless and for 1 min longer. The CO_2 was generated from Dry Ice in a 50 ml flask and dried by passing through Drierite. Commercial 'Bone Dry' CO_2 (Matheson) gave identical results. The CO_2 quench was worked up in a manner identical to the previous aliquot.

The water and CO₂ quench aliquots were analyzed on column E at 100° with the aid of a Hewlett-Packard 3373B integrator. Integration ratios were consistent to within 1%. The % reduction of yield of hydrocarbon after the CO₂ quench is taken to be the indicated RLi yield (see Tables 12-18).

Response Factors. Response factors were obtained by running through the full procedure (except the CO₂ quench) given above, but using the product in place of starting material. The response factors so obtained were as much as 10% different than those obtained by simply analyzing a known solution of internal standard and product. The weight-weight response factors determined by this procedure are: for octane vs. nonane, 1.056 ± 0.02 ; for tricyclo[3.2.1.0^{2,4}]octane (23-H) vs. decane, 1.24 ± 0.02 ; for 4-t-butylcyclohexene vs. nonane, 1.29 ± 0.03 ; for norcarane vs. nonane, 1.164 ± 0.007 . 3-Methylheptane is assumed to have the same response factor as octane, and t-butylcyclohexane is assumed to be the same as 4-t-butylcyclohexene.

Special Conditions

Evaporative Additions: A solution of LiDTBB was made in the usual way under conditions A and, after the lithium had dissolved, the flask was attached to the high vacuum line and degassed. A previously degassed sample of the halide was then allowed to evaporate into the -78° solution over a period of 30 min. The top half of the reaction

flask was heated periodically with a heat gun to prevent the halide from condensing and running in as a liquid. Aliquots were taken as usual. Due to the necessity of heating the top of the flask while cooling the bottom, the actual temperature of the solution may be somewhat higher than -78° .

Stoichiometric Reactions: Full stoichiometry (100%) experiments were run as usual except that 6 mmol of both aromatic hydrocarbon and lithium were used to make the radical anion solution and the halide was added dropwise until the color of the radical anion just disappeared, leaving an intense red color. Lower ratios of halide to radical anion were run under conditions A with the calculated amount of halide added as usual.

Inverse Addition: A 100 ml flask, equipped with a glass covered stir bar was dried under a high vacuum for 1-2 h, and 30 ml of THF was transferred in from THF which had been dried over sodium benzophenone dianion. The flask was pressurized with nitrogen, and one of the stoppers was replaced with a septum stopper. The THF was cooled to the appropriate temperature and the internal standard was added, followed by the halide. A solution of LiDTBB made under conditions A was then added dropwise at such a rate that 30-45 min was required for completion. The solution slowly took on a red color until the last drop, which caused the solution to turn green to blue-green. The quench with H_2O did not result in the usual

formation of an organic phase, presumably due to the lessened amount of organic solute present. Thus the ratio of product to internal standard may be in considerable error (see internal standard section above).

Reaction of Lithium Naphthalene Dianion and Di-*t*-butylnaphthalene Dianion with Alkyl Halides in Ether. The title dianions were prepared by treatment of 4.8 mmol of the corresponding hydrocarbon with 4.5 mmol of Li in 30 ml of diethyl ether as described for the radical anions. The temperature of the ether solution was maintained below -20° to prevent decomposition. Li seems to react more readily with DTBN than with naphthalene itself. After all the lithium had dissolved, the deep purple solution was cooled to the appropriate temperature, and the internal standard and halide were added. Aliquots were then taken as previously described except that no pentane was added.

Reaction of Lithium Naphthalene- d_8 with 1-Chlorooctane. A lithium naphthalene solution was made from 0.340 g of naphthalene- d_8 , 17 mg of Li, and 15 ml of THF (approximately half normal scale). To this solution cooled to -78° , was added 50.0 μ l of nonane, followed by 50.0 μ l (43.3 mg) of 1-chlorooctane. The reaction was then treated as described above under general conditions. After the CO_2 quench aliquot had been taken, H_2O was added and the reaction worked up in the usual way. Gc collection of the octane from column F at 75° was

followed by low voltage mass spectral analysis: $90.8 \pm 0.5\%$ d_1 , $0.2 \pm 0.3\%$ d_2 . From gc analysis of the aliquots, the % yield of octane was 91% with an indicated RLi yield of 69%.

Repetition of the above sequence with undeuterated naphthalene but not including the collection and analysis of the octane indicated an 89% yield of octane with an indicated RLi yield of 53%. Assuming a competition between reaction of RLi with CO_2 or with the dihydronaphthalenedicarboxylate (see discussion), the deuterium isotope effect can be calculated as being 2.0.

Reaction of Lithium Naphthalene with 1-Chlorooctane Followed by Deuterolysis. A solution of LiN was made under the same conditions as immediately above. Reaction with 50 μ l (43.3 mg) of 1-chlorooctane was followed 15 min later by the addition of 0.75 ml of D_2O . Workup as usual was followed by gc collection from column F at 75° . Low voltage mass spectral analysis revealed the octane to be $96.0 \pm 0.9\%$ d_1 , and $0.3 \pm 0.3\%$ d_2 .

Preparation of *syn*- and *anti*-7-Lithionorcarane (28-Li) and Reaction with D_2O . A mixture of *syn*- and *anti*-7-bromonorcarane prepared by the method of Martel and Hiriart (155) was subjected to gc separation (180° , column F). Nmr of the *syn* bromide displayed a triplet at 63.24 ($J=8.0$ Hz) while the corresponding triplet for the *anti* bromide is at 62.53 ($J=3.4$ Hz). Each bromide, ca. 50 μ l, was treated separately with 1 ml of 2.3 M *n*-BuLi (hexane, Ventron) and

Table 12. Reaction of 1-chlorooctane with lithium radical anions.

Entry #	Conditions	Radical Anion	Hydrocarbon Yield (%)	Indicated RLi Yield (% of HC)
1	A	N ^{•-}	93	53
2	B	N ^{•-}	92	39
3	B	N ^{•-}	88	40
4	B	N ^{•-}	92	37
5	B	N ^{•-}	91	35
6	B	N ^{•-}	94	60
7	B (xs of N)	N ^{•-}	91	48
8	B (xs of Li)	N ^{•-}	90	45
9	B (-63°)	N ^{•-}	91	35
10	B (0°)	N ^{•-}	79	25
11	B (in DME) ^(a)	N ^{•-}	78	53
12	A (sodium, rt)	N ^{•-}	44	--
13	A	DTBB ^{•-}	101	94
14	B	DTBB ^{•-}	100	95
15	B	DTBB ^{•-}	99	94
16	B	DTBN ^{•-}	96	49
17	A, scavanged ^(b)	N ^{•-}	96	56

(a) Not homogeneous.

(b) Bromobutane added before 1-ClC₈ (1-BrC₄:1-ClC₈ = 2.5).

Table 13. Reaction of 1-bromooctane with lithium radical anions.

Entry #	Conditions	Radical Anion	Hydrocarbon Yield (%)	Indicated RLi Yield (% of HC)
1	A	N ^{•-}	79	47
2	100% stoich	N ^{•-}	76?	93
3	A	DTBB ^{•-}	96	94
4	B	DTBB ^{•-}	96	91
5	A (potassium)	N ^{•-}	25 ^(a)	--
6	A	N ^{•-}	80	41
7	A	N ^{•-}	80	44
8	A, 87% stoich	N ^{•-}	78	83
9	A, 45%	N ^{•-}	79	56

(a) An approximately 70% yield of dimer was detected by gc.

Table 14. Reaction of 2-bromooctane with lithium radical anions.

Entry #	Conditions	Radical Anion	Hydrocarbon Yield (%)	Indicated RLi Yield (% of HC)
1	A	N ^{•-}	57	29
2	B	N ^{•-}	57	21
3	100% stoich	N ^{•-}	51?	52
4	dianion	N ⁻²	9	49
5	"	DTBN ⁻²	34	42
6	A	DTBB ^{•-}	100	87
7	B	DTBB ^{•-}	101	79
8	B	DTBB ^{•-}	97	82
9	A, -60°	DTBB ^{•-}	94	70
10	A, -50°	DTBB ^{•-}	94	72
11	inverse	DTBB ^{•-}	82 ^(a)	46
12	A, potassium	DTBB ^{•-}	64 ^(b)	--

(a) Including ca. 20% olefin.

(b) Including ca. 20% olefin. Did not check for dimer.

Table 15. Reaction of 2-chlorooctane with lithium radical anions.

Entry #	Conditions	Radical Anion	Hydrocarbon Yield (%)	Indicated RLi Yield (% of HC)
1	A	N ^{•-}	63	30
2	B	N ^{•-}	63	21
3	B	N ^{•-}	63	22
4	A	DTBB ^{•-}	104	87
5	B	DTBB ^{•-}	101	87
6	B	DTBB ^{•-}	101	81 ^(a)
7	100% stoich	DTBB ^{•-}	95	86
8	A (+ 1 g LiBr)	DTBN ^{•-}	97	21
9	B	DTBN ^{•-}	95	21

(a) Failed to grease joints of reaction flask.

Table 16. Reaction of 3-chloro-3-methylheptane with lithium radical anions.

Entry #	Conditions	Radical Anion	Hydrocarbon Yield (%)	Indicated RLi Yield (% of HC)
1	A	N ^{•-}	39	78
2	B	N ^{•-}	38	69
3	100% stoich	N ^{•-}	35	70
4	B	N ^{•-}	40	76
5	B ^(a)	B ^{•-}	56	79
6	A	DTBB ^{•-}	95	87
7	B	DTBN ^{•-}	89	81
8	B	DTBB ^{•-}	98	90

(a) LiB seemed to precipitate.

Table 17. Reaction of 7-chloronorcarane with lithium radical anions.

Entry #	Conditions	Radical Anion	Hydrocarbon Yield (%)	Indicated RLi Yield (% of HC)
1	A	DTBB ^{•-}	99	95
2	B	DTBB ^{•-}	99	94
3	A (+ 1 g LiBr)	DTBN ^{•-}	99	88
4	B (warm to -5°)	N ^{•-}	99	65

Table 18. Reaction of some selected halides with lithium di-tert-butylbiphenyl.

Entry #	Halide	Conditions	Radical Anion	Hydrocarbon Yield (%)	Indicated RLi Yield (% of HC)
1	4- <u>tert</u> -butylchloro-cyclohexane	B	DTBB ^{•-}	99	88
2	4- <u>tert</u> -butyl-1-chloro-cyclohexene	B ^(a)	DTBB ^{•-}	104	76
3	<u>anti</u> -23-Cl	B	DTBB ^{•-}	99	89

(a) Too slow at -78°, warmed to -20°.

5 ml of THF at -15° . After 10 min, 1 ml of D_2O was added. Workup and gc collection was followed by nmr analysis (CCl_4); from the syn bromide, δ 0.51 (triplet, $J=8.75$ Hz); from the anti bromide, δ 0.02 ($J=5.5$ Hz). Deuteration is above 95% (only one of the two possible C7 protons was observed in each case).

Treatment of a mixture of anti and syn bromides in a ratio of 1.33 ± 0.02 with n-BuLi followed by D_2O as above gave 80% D incorporation in a ratio of 1.39 ± 0.15 , anti to syn.

Stereochemistry of the Reaction of 7-Lithionorcarane (28-Li) with Ethylene Dibromide. A solution of syn-7-lithionorcarane was prepared by adding 25 μ l of pure gc-collected syn-7-bromonorcarane to a solution of 1 ml of n-BuLi (2.5 M, Ventron) and 25 ml of THF at -78° , followed by warming to 0° for 5 min. An aliquot showed no bromide to be present. The solution was cooled down to -78° , and an excess of ethylene dibromide (220 μ l) was then syringed in. An aliquot showed only syn-7-bromonorcarane with less than 1% anti.

The same procedure was repeated for the anti bromide with the result that only the anti bromide was observed for the sequence.

A mixture of syn and anti bromides with an anti:syn ratio of 1.33 ± 0.02 was subjected to the above procedure. Gc analysis on column F at 140° using dodecane as internal standard indicated an overall yield of 92% for the anti bromide and 84% for the syn with the final anti:syn ratio being 1.45 ± 0.02 .

Stereochemistry of the Reaction of 7-Chloronorcarane (28-Cl)

with LiDTBB. To a solution of LiDTBB made under conditions A and cooled to -78° , was added $2 \times 100 \mu\text{l}$ of 7-chloronorcarane (syn:anti = 1.5). The solution was allowed to stir for 15 min at which time D_2O (2 ml) was added and the solution was allowed to warm to 0° . The reaction was worked up in the normal way and separation of the product from DTBB was accomplished by bulb to bulb distillation at 1 atm and 160° . Gc collection of the distillate using column F at 90° followed by nmr analysis indicated greater than 100% deuterium incorporation. This is symptomatic of impurities in the sample. If the deuterium incorporation is assumed to be 95% (the lithium reagent yield from the carbonation experiments) the anti:syn ratio is 5:1. A similar run but with 1 g of LiBr added indicated 87% D incorporation and an anti:syn ratio of 5.6.

Stereochemistry of the Reaction of anti-3-Chloro-exo-tricyclo

[3.2.1.0^{2,4}]octane (anti-23-Cl) with LiDTBB. To a solution of LiDTBB in THF at -78° made under conditions B, was added internal standard (dodecane, 22.3 mg) followed by the title chloride (48.6 mg). After 15 min, 220 μl of 1,2-dibromoethane was added in one injection. The mixture was warmed to 0° and an aliquot was treated with excess AgNO_3 in H_2O for 5 min, followed by the usual extraction procedure. Other than solvent and internal standard, the gc (column F at 140°) showed only a small peak at the retention time of the anti bromide.

Assuming 90% yield of the lithium compounds (see Table 18) the ratio of syn to anti lithium is at least 200:1.

Repetition of the above reaction but with D_2O as the quench, followed by nmr analysis of the deuterated hydrocarbon, gave results identical to the LiN experiment (e.g., 100:1 syn:anti deuteration).

Preparation of anti-7-Bromo-7-methylnorcarane (anti-31-Br).

The title compound was prepared by a modification of the procedure of Kitatani, Hiyama, and Nozaki (155). To a mixture of 40 ml of THF, 10 ml of TMEDA (Aldrich), and 10 g of 7,7-dibromonorcarane, which was cooled to -78° , was added 4 g of CH_3I over a period of 1 min. To this mixture was then added dropwise, 16 ml of 2.5 M n-BuLi (hexane, Ventron) over a period of 15 min. After warming to 0° , the reaction was worked up as usual and subjected to vacuum distillation through a 38 cm 14/20 vigreux column. The material boiling between 66.4° and 66.5° at 5.2 torr weighed 5 g and was about 99% pure by gc (column F at 160° , inj. = 170°); nmr (CCl_4): δ 1.69 (singlet, CH_3), complex series of absorptions from δ 1.1 to 2.0.

Reduction of anti-7-Bromo-7-methylnorcarane (anti-31-Br) with Sodium in tert-Butyl Alcohol. To ca. 1 g of the title bromide dissolved in 5 ml of THF and 2 ml of t-BuOH, was added 0.2 g of Na slices. The mixture was stirred at room temperature for 3 h, at which point no starting bromide was present. Analysis on column E at 100° indicated the presence of two products on a ratio of 3:1, with

the material of shorter retention time predominating. Gc collection using column F at 100° and nmr analysis indicated the larger peak to be anti-7-methylnorcarane; nmr (CCl₄): δ 1.73 (4H, broad), δ 1.19 (4H, broad), δ 1.01 (3H, doublet, J=5.5 Hz, CH₃), δ 0.52 (2H, broad), δ 0.33 (1H, complex). The minor peak is assigned the structure syn-7-methylnorcarane; nmr (CCl₄): δ 1.83 (2H, broad), δ 1.26 (6H, complex), δ 0.98 (3H, doublet, J=5.5 Hz, CH₃), δ 0.76 (3H, broad); ir (CCl₄): 940, 960, 1080, 1180, 1390, 1455, 1465, 3005 cm⁻¹, usual stretching frequencies.

Reaction of anti-7-Bromo-7-methylnorcarane (anti-31-Br) with LiDTBB with Dibromoethane Quench. To a solution of LiDTBB in THF at -78° made under conditions A, was added 400 mg of the title bromide. An aliquot was taken in the usual way, and gc analysis on column F at 100° showed two peaks in a ratio of 2.75 with the anti methyl compound predominating. Treatment of the remainder of the reaction mixture with 450 mg of dibromoethane was followed by gc analysis, which showed two peaks in the bromide region with a ratio of 1.5. Gc collection and nmr analysis showed the minor component to be identical with the starting material, while the major component's nmr was compatible with the structure syn-7-bromo-7-methylnorcarane; nmr (CCl₄): δ 1.76 (singlet), complex pattern from δ 1.9 to 1.0 and a highly split absorption centered at δ 0.84.

Metal-halogen Exchange of anti-7-Bromo-7-methylnorcarane

(anti-31-Br). To a mixture of 1 ml of 2.3 M t-BuLi in pentane (Ventron) and 10 ml of THF maintained at -78° , was added 50 μ l of nonane followed by 90 μ l of the title bromide. After 5 min had elapsed, an aliquot was taken and quenched in water, and the remainder of the reaction mixture was treated with CO_2 as with the radical anion reactions. Assuming a unity response factor, syn-7-methylnorcarane was formed in 58% yield, while the anti compound was formed in 28% yield. The CO_2 quench revealed that 90% of the syn compound was lithiated vs. less than 4% of the anti. The identity of the hydrocarbon products was indicated by gc retention times on both column E and F at 100° . The anti compound was gc collected and its ir spectrum shown to be identical to the corresponding product from the Na/t-BuOH reduction.

Metal-halogen Exchange Between syn-7-Bromonorbornene (syn-32-Br) and t-Butyllithium in THF. A solution of t-butyllithium in THF was prepared by injecting 1 ml of 2.3 M t-butyllithium in pentane (Ventron, caution--very pyrophoric) into 10 ml of THF maintained at $50 \pm 5^{\circ}$. After 5 min, 80 μ l of the title bromide was injected all at once. After 4 min, most of the starting bromide was absent and after 22 min, none was observed. After 30 min, 1 ml of D_2O was added and the mixture worked up as usual. Gc collection from column E at 55° gave 29 mg of a low-melting solid whose nmr is consistent with

7-deuterionorbornene contaminated with a material giving rise to a sharp singlet at 60.8--probably 2,2,3,3-tetramethyl butane.

The olefin was epoxidized by treatment with 70 mg of m-chloroperbenzoic acid (Aldrich, 85%) in 1 ml of CH_2Cl_2 at 10° . After standing at 20° for 15 min, the solution was extracted with 5 x 5 ml of 3 M NaOH and then worked up in the usual manner. Gc collection was accomplished using column C at 110° with the detector and injector both at 100° . Temperatures above 150° were found to cause decomposition of the epoxide. The white crystals (16 mg) were dissolved in CCl_4 and $\text{Pr}(\text{fod})_3$ was added until the 2,3 protons were at 140 Hz upfield of TMS. At this point in the addition, the syn-C7 proton was 188 Hz, the anti-C7 proton was 84 Hz, and the endo 5,6 protons were 14 Hz upfield of TMS, with the exo 5,6 protons at 47 Hz and the bridgehead protons 55 Hz downfield of TMS. The integrations of the syn- and anti-7 protons relative to the 2,3 protons indicated a 90% D incorporation with at least a 20:1 syn:anti deuterium ratio.

Stereochemistry of the Reaction of syn-7-Bromonorbornene (syn-32-Br) with LiDTBB. To a solution of LiDTBB in THF made under conditions A and cooled to -78° , was added 2 x 100 μl of the title bromide. After 30 sec, 2 ml of D_2O was added and the mixture was worked up as usual. Separation of the olefin from the DTBB was accomplished by bulb to bulb distillation at 150° for 45 min. The crude distilled product was epoxidized as in the case of the metal

halogen exchange reaction described immediately above and was analyzed by nmr as before: 90% D incorporation and an anti:syn ratio of 3.8 ± 0.2 .

Reaction of anti-7-Chlorobenzonorbornadiene (anti-30-Cl) with LiDTBB. To a LiDTBB solution made up according to conditions A and cooled to -78° , was added dropwise over a period of 45 sec a solution of 0.30 g (1.7 mmol) of the title chloride dissolved in 1.0 ml of THF. Within 30 sec, 2 ml of D_2O was added. The product was worked up in the usual way, and the deuterated hydrocarbon was separated from DTBB by bulb to bulb distillation using an Aldrich Kugelrohr apparatus at 140° and 10 torr for ca. 20 min. A portion of the olefin was hydroborated and the alcohol gc collected from column F at 200° . $Pr(fod)_3$ was added to the alcohol in CCl_4 until the 2-endo proton (α to OH) was 558 Hz upfield of TMS. At this point, the 1-bridgehead proton was 334 Hz, the 3-endo proton is 320 Hz, the 3-exo proton is 610 Hz, the 7-syn proton is 472 Hz, and the 7-anti proton is 208 Hz upfield of TMS. Integration of the 7-syn and 7-anti proton signals relative to the other 4 protons indicates $99 \pm 3\%$ D incorporation and anti:syn deuterium ratio of 1.33 ± 0.02 (syn or anti is relative to the benzo ring).

Stereochemistry of the Reaction of exo-2-Chloronorbornane with LiDTBB. To a solution of LiDTBB made under conditions A and cooled to -78° , was added $2 \times 100 \mu l$ of exo-2-chloronorbornene

prepared from norbornene and HCl by the method of Schmerling (157). After 30 sec, 1 ml of D₂O was added and the clear solution warmed to 0° and worked up in the usual manner followed by gc collection from column F at 70°. Ir analysis at 858 for exo and 836 cm⁻¹ for endo as recommended by Nickon and Hammons (157) indicates a 5:1 exo to endo ratio assuming equal molar extinction coefficients. The analysis is less than fully satisfactory, however, due to severe overlap of absorptions in this region.

In like fashion, reaction of the title chloride (320 mg, 5% excess) with LiDTBB solution (from which 2 ml had been removed for other purposes) was followed by quenching within 30 sec with excess ethylene dibromide. The solution was warmed to 0° and worked up in the usual way. Gc analysis showed only one peak in the bromide region. Gc collection and nmr analysis of this peak indicates it to be a mixture of 91% exo and 9% endo bromides. The ratio was determined by nmr integrations of the proton α to bromine which for the exo bromide falls at δ 3.9--cleanly separated from the α proton of the endo bromide which falls at δ 4.2 (Reference 128).

Stereochemistry of the Reaction of 4-Chloro-*t*-butylcyclohexane with LiDTBB. To a THF solution of LiDTBB at -78° made under conditions B, was added ca. 220 mg of the title chloride prepared by the method of Glaze, et al. (159) (cis/trans = 4). After 5 min, D₂O (2 ml) was added, followed by the usual workup. The product was

separated from the DTBB by bulb to bulb distillation using an Aldrich Kugelrohr at 210° for 10 min. Gc collection (column F at 120°) was followed by ir analysis in the C-D stretching region. The spectrum was calibrated with an indene external standard using the 2305, 2173, and 2050 cm^{-1} bands. The ratio of equatorial to axial deuteration is at least 14:1 using the frequencies given by Glaze et al. for the axial and equatorial compounds and the assumption that the molar extinction coefficients for the two compounds are approximately the same.

BIBLIOGRAPHY

1. M. Berthelot, Justus Liebigs Ann. Chem., 143, 97 (1867).
2. W. Schlenk and T. Weikel, Ber., 44, 1182 (1911).
3. N.D. Scott, J.F. Walker, and V.L. Hansley, J. Am. Chem. Soc., 58, 2442 (1936).
4. C.B. Wooster, Chem. Rev., 11, 11 (1932).
5. J.F. Walker and N.D. Scott, J. Am. Chem. Soc., 60, 951 (1938).
6. S.I. Weissman, J. Townsend, D.E. Paul, and G.E. Pake, J. Chem. Phys., 21, 2227 (1953).
7. M. Szwarc, Ed., "Ions and Ion Pairs in Organic Reactions, Vol 1", John Wiley and Sons, New York, 1972.
8. M. Szwarc, Ed., "Ions and Ion Pairs in Organic Reactions, Vol 2", John Wiley and Sons, New York, 1974.
9. N.L. Holy, Chem. Rev., 74, 243 (1974).
10. K.W. Egger and A.T. Cocks, Helvetica Chimica Acta, 56, 1516 (1973).
11. G.J. Hoijsink, E. deBoer, P.H. Van derMeij, and W.P. Weijland, Rec. Trav. Chim., 73, 487 (1956).
12. J. Jagur-Grodzinski and M. Szwarc, J. Phys. Chem., 69, 628 (1965).
13. Reference 8, p. 38.
14. A.G. Evans, B. Jerome, and N.H. Rees, Perkin II, 447 (1973).
15. M.D. Curtis and A.L. Allred, J. Am. Chem. Soc., 87, 2554 (1965).
16. J.F. Garst, "Solute-Solvent Interactions", J.F. Coetzee and C.D. Ritchie, Eds., Marcel Dekker, New York, 1969, Chapter 8.

17. J.J. Brooks, W. Rhine, and G.D. Stucky, J. Am. Chem. Soc., 94, 7346 (1972).
18. J.J. Mooij, A.A.K. Klaasen, E. deBoer, H.M.L. Degens, Th.E.M. van der Hark, and J.H. Noordik, J. Am. Chem. Soc., 98, 680 (1976).
19. Reference 16, p. 554.
20. D. Nicholls, C. Sutphen, and M. Szwarc, J. Phys. Chem., 72, 1021 (1968).
21. P. Chang, R.V. Slates, and M. Szwarc, J. Phys. Chem., 70, 3180 (1966).
22. N.M. Atherton and S.I. Weissman, J. Am. Chem. Soc., 83, 1330 (1961).
23. P. Graceffa and T.R. Tuttle, J. Phys. Chem., 77, 1566 (1973).
24. Y. Karasawa, G. Levin, and M. Szwarc, Proc. Roy. Soc., Ser. A, 326, 53 (1971).
25. T.R. Tuttle, Jr., J.C. Danner, and P. Graceffa, J. Phys. Chem., 76, 2866 (1972).
26. L. Lee, et al., J. Am. Chem. Soc., 93, 4149 (1971).
27. N. Hirota, J. Am. Chem. Soc., 90, 3603 (1968).
28. K. Hofelmann, J. Jagur-Grodzinski, and M. Szwarc, J. Am. Chem. Soc., 91, 4645 (1969).
29. T. Takeshita and N. Hirota, J. Chem. Phys., 58, 3745 (1973).
30. B.M.P. Hendriks and G.W. Canters, Mol. Phys., 20, 193 (1971).
31. G.W. Canters and E. deBoer, Mol. Phys., 26, 1311 (1973).
32. P.J. Zandstra and S.I. Weissman, J. Am. Chem. Soc., 84, 4408 (1962).
33. N. Hirota, R. Carraway, and W. Schook, J. Am. Chem. Soc., 90, 3611 (1968).

34. A Crowley, N. Hirota, R. Kreilick, J. Chem. Phys., 46, 4815, (1967).
35. I. B. Goldberg and J. R. Bolton, J. Phys. Chem., 74, 1965 (1970).
36. A. G. Evans, B. Gerome, and N. H. Rees, Perkin II, 2091 (1973).
37. K. Shimada and M. Szwarc, Chem. Phys. Lett., 28, 540 (1974).
38. Reference 8, p. 99.
39. A. I. Shatenshtein, E. S. Petrov, and M. I. Belouseva, Org. Reactivity (USSR), 1, 191 (1964).
40. K. H. J. Buschow and G. J. Holjtkink, J. Chem. Phys., 40, 2501 (1964).
41. J. Smid, J. Am. Chem. Soc., 87, 655 (1965).
42. H. L. Hsieh, J. Organomet. Chem., 7, 1 (1967).
43. Unpublished results by deBoer quoted in Reference 8, p. 92.
44. D. G. Paul, D. Lipkin, and S. I. Weissman, J. Am. Chem. Soc., 78, 116 (1956).
45. S. Bank and W. D. Closson, Tetrahedron Let., 1349 (1965).
46. S. Bank and B. Bockrath, J. Am. Chem. Soc., 93, 430 (1971).
47. S. Bank and B. Bockrath, J. Am. Chem. Soc., 94, 6076 (1972).
48. A. Rainis, R. Tung, and M. Szwarc, J. Am. Chem. Soc., 95, 659 (1973).
49. E. R. Minnich, L. D. Long, J. M. Ceraso, and J. L. Dye, J. Am. Chem. Soc., 95, 1061 (1973).
50. S. Hayano and M. Fujihira, Bull. Chem. Soc. Jap., 44, 2046 (1971).
51. W. Schlenk and E. Bergmann, Justus Liebigs Ann. Chem., 463, 91 (1928).

52. G.P. Kaplan, Z.F. Kazakova, and A.D. Petrov, Izv. Akad. Nauk. SSR, Ser. Khim., 1440 (1966).
53. W. Schlenk and E. Bergmann, Justus Liebigs Ann. Chem., 463, 83 (1928).
54. D. Lipkin, F.R. Galiano, and R.W. Jordan, Chem. Ind. (Britain), 1657 (1963).
55. J.J. Eisch, J. Org. Chem., 28, 707 (1963).
56. J.F. Garst, P.W. Ayers, and R.C. Lamb, J. Am. Chem. Soc., 88, 4260 (1966).
57. S.J. Cristol and R.V. Barbour, J. Am. Chem. Soc., 88, 4262 (1966).
58. S.J. Cristol and R.V. Barbour, J. Am. Chem. Soc., 90, 2832 (1968).
59. D.J. Carlsson and K.V. Ingold, J. Am. Chem. Soc., 90, 7047 (1968).
60. S.J. Cristol and R.W. Gleason, J. Org. Chem., 34, 1762 (1969).
61. G.D. Sargent, J.N. Cron, and S. Bank, J. Am. Chem. Soc., 88, 5363 (1966).
62. J.F. Garst and J.T. Barbas, Tetrahedron Let., 3125 (1969).
63. A.R. Lepley and G.L. Closs, Eds., "Chemically Induced Magnetic Polarization", John Wiley and Sons, New York, 1973.
64. H.E. Zieger, I. Anger, and L. Maresca, J. Am. Chem. Soc., 95, 8201 (1973).
65. J.F. Garst and J.T. Barbas, J. Am. Chem. Soc., 91, 3385 (1969).
66. L. Kaplan, "Bridged Free Radicals", Marcel Dekker, New York, N.Y., 1972, p. 302.
67. J.F. Garst and J.T. Barbas, J. Am. Chem. Soc., 96, 3239 (1974).

68. J.F. Garst, et al., J. Am. Chem. Soc., 97, 5242 (1975).
69. D. Lipkin, G.J. Divis, and R.W. Jordan, Am. Chem. Soc., Div. Petrol. Chem., Preprints, 13, D65 (1968).
70. G.J. Hoijsink, Chem. Ing. Tech., 35, 333 (1963).
71. J.F. Garst, J.T. Barbas, and F.E. Barton, II, J. Am. Chem. Soc., 90, 7159 (1968).
72. G.D. Sargent and G.A. Lux, J. Am. Chem. Soc., 90, 7160 (1968).
73. T.C. Cheng, L. Headley, and A.F. Halasa, J. Am. Chem. Soc., 93, 1502, (1971).
74. G.D. Sargent, Tetrahedron Let., 3279 (1971).
75. M.R. Asirvatham and M.D. Hawley, J. Am. Chem. Soc., 97, 5024 (1975).
76. S. Bank and J.F. Bank, Tetrahedron Let., 4533 (1969).
77. H.M. Walborsky and A.E. Young, J. Am. Chem. Soc., 86, 3288 (1964).
78. J.F. Garst, Am. Chem. Soc., Div. Petrol. Chem., Symposium Preprints, 13, D65, (1968).
79. J.F. Garst, Unpublished results quoted in Reference 63, p. 261.
80. J.F. Garst and F.E. Barton, II, Tetrahedron Let., 587, (1969).
81. J.G. Smith and I. Ho, J. Org. Chem., 37, 4260 (1972).
82. C.G. Screttas, Chem. Commun., 752 (1972).
83. J.K. Kochi, Ed., "Free Radicals, Vol 1", John Wiley and Sons, New York, 1973, p. 40.
84. J.F. Garst and C.D. Smith, J. Am. Chem. Soc., 98, 1526 (1976) Footnote 14.
85. B.J. Wakefield, "The Chemistry of Organolithium Compounds", Pergamon Press, New York, 1974.

86. J.F. Garst and F.E. Barton, II, J. Am. Chem. Soc., 96, 523 (1974).
87. B. Bockrath and L.M. Dorfman, J. Phys. Chem., 77, 2618 (1973).
88. S. Bank and D.A. Juckett, J. Am. Chem. Soc., 97, 567 (1965).
89. Reference 83, p. 542.
90. J.F. Garst, R.D. Roberts, and B.N. Abels, J. Am. Chem. Soc., 97, 4925 (1975).
91. G.D. Sargent and M.W. Browne, J. Am. Chem. Soc., 89, 2788 (1967).
92. G.D. Sargent, C.M. Tatum, Jr., and S.M. Kastner, J. Am. Chem. Soc., 94, 7174 (1972).
93. J.F. Garst in Reference 63.
94. J.F. Garst and J.A. Pacifici, J. Am. Chem. Soc., 97, 1802 (1975).
95. E.J. Panek, J. Am. Chem. Soc., 93, 8460 (1973).
96. R.G. Harvey, L. Nazareno, and H. Cho, J. Am. Chem. Soc., 95, 2376 (1973).
97. J. Jacobus and D. Pensak, J. Chem. Soc., D, 400 (1969).
98. D.B. Ledlie, R.L. Thorne, and G. Weiss, J. Org. Chem., 35, 2186 (1971).
99. P.J. Krusic and R.C. Bingham, J. Am. Chem. Soc., 98, 230 (1976).
100. J.K. Kochi, Ed., "Free Radicals, Vol 2", John Wiley and Sons, New York, 1973, p. 363.
101. Y. Ellinger, et al., J. Chem. Phys., 62, 10 (1973).
102. G.M. Whitesides, C.P. Casey, and J.K. Krieger, J. Am. Chem. Soc., 93, 1379 (1971).

103. T. Ando, et al., J. Org. Chem., 35, 33 (1970).
104. L.J. Altman and R.C. Baldwin, Tetrahedron Let., 2531 (1971).
105. Reference 100, p. 479.
106. J.B. Lisle, L.F. Williams, and D.E. Wood, J. Am. Chem. Soc., 98, 227 (1976).
107. P.J. Krusic and P. Meakin, J. Am. Chem Soc., 98, 228 (1976).
108. R.C. Bingham and M.J.S. Dewar, J. Am. Chem. Soc., 95, 7182 (1973).
109. P.K. Freeman and J.N. Blazeovich, Unpublished results.
110. R.M. Magid and S.E. Wilson, J. Org. Chem., 36, 1775 (1971).
111. C.W. Jefford and R.T. Medary, Tetrahedron Let., 23, 4123 (1967).
112. H.W.H.J. Bodewitz, C. Blomberg, and F. Bickelhaupt, Tetrahedron Let., 281 (1972).
113. H.M. Walborsky and M.S. Arnoff, J. Organomet. Chem., 51, 55 (1973).
114. M.J.S. Dewar and J.M. Harris, J. Am. Chem. Soc., 91, 3652 (1969).
115. R.W. Fressenden and R.H. Schuler, J. Chem. Phys., 39, 2147 (1963).
116. P.J. Hatem and B. Waegell, Tetrahedron Let., 2019 (1973).
117. H.M. Walborsky, F.J. Impastato, and A.E. Young, J. Am. Chem. Soc., 86, 3283 (1964).
118. D.N. Hague, "Fast Reactions", Wiley-Interscience, New York, 1971.
119. C. Carvajal, et al., J. Am. Chem. Soc., 87, 5548 (1965).
120. K.J. Laidler, "Chemical Kinetics", McGraw-Hill, New York, 1965.

121. J.F. Garst, Accounts Chem. Res., 4, 400 (1970).
122. G.R. Buske and W.T. Ford, J. Org. Chem., 41, 1998 (1976).
123. W.T. Ford and G. Buske, J. Am. Chem. Soc., 96, 621 (1974).
124. E.J. Corey and D.J. Beames, J. Am. Chem. Soc., 94, 7210 (1972).
125. F.R. Jensen and K.L. Nakamaye, J. Am. Chem. Soc., 88, 3437 (1966).
126. A. Mathias and G. Warhurst, Trans. Faraday Soc., 56, 348 (1960).
127. W.N. Smith, Jr., J. Organomet. Chem., 82, 1 (1974).
128. W.N. Smith, Jr., J. Organomet. Chem., 82, 7 (1974).
129. D.E. Applequist and G.N. Chmurny, J. Am. Chem. Soc., 89, 875 (1967).
130. N.E. Alexandrov, J. Organomet. Chem., 5, 301 (1966).
131. W.H. Glaze and C.M. Selman, J. Organomet. Chem., 11, P3 (1968).
132. H.M. Crawford and M.C. Glessman, J. Am. Chem. Soc., 76, 1108 (1954).
133. F.J. Adrian, J. Chem. Phys., 53, 3374 (1970).
134. R.E. Carter, T. Drakenberg, and N.A. Bergman, J. Am. Chem. Soc., 97, 6990 (1975).
135. K. Kitatani, T. Hiyama, and H. Nozaki, J. Am. Chem. Soc., 97, 949 (1975).
136. S. Skaarup, L.L. Griffin, and J.E. Boggs, J. Am. Chem. Soc., 98, 3140 (1976).
137. A. Rauk, et al., J. Am. Chem. Soc., 93, 6507 (1971).
138. M.D. Harmony, Chem. Phys. Lett., 10, 337 (1971).

139. J. Warkentin and E. Sanford, J. Am. Chem. Soc., 90, 1667
140. S.J. Cristol and A.L. Noreen, J. Am. Chem. Soc., 91, 3870 (1969).
141. G.A. Russell and G.W. Holland, J. Am. Chem. Soc., 91, 3969 (1969).
142. J.K. Kochi and P. Bakuzis, J. Am. Chem. Soc., 95, 1516 (1973).
143. L.A. Singer and N.P. Kong, J. Am. Chem. Soc., 88, 5213 (1966).
144. L.A. Singer and J. Chen, Tetrahedron Let., 939 (1971).
145. J.K. Stille and K.N. Sannes, J. Am. Chem. Soc., 94, 8489 (1972).
146. Reference 63, p. 292.
147. K. Yoshikawa, et al., J. Am. Chem. Soc., 98, 3272 (1976).
148. T. Kawamura, et al., J. Am. Chem. Soc., 97, 1628 (1975).
149. T. Kawamura, T. Koyama, and T. Yonezawa, J. Am. Chem. Soc., 95, 3220 (1973).
150. P.D. Bartlett, G.N. Fickes, F.C. Haupt, and R. Helgeson, Accounts Chem. Res., 3, 177 (1970).
151. G.M. Whitesides and J.S. Filippo, J. Am. Chem. Soc., 92, 6611 (1970).
152. J.K. Stille, W.A. Feld, and M.E. Freeburger, J. Am. Chem. Soc., 94, 8485 (1972).
153. W.H. Glaze and C.H. Freeman, J. Am. Chem. Soc., 91, 7198 (1969).
154. I. Morishima, K. Yoshikawa, and K. Okada, J. Am. Chem. Soc., 98, 3787 (1976).
155. B. Martel and J.M. Hiriart, Synthesis, 201 (1972).

156. J. T. Groves and K. W. Ma, J. Am. Chem. Soc., 96, 6527 (1974).
157. L. Schmerling, J. Am. Chem. Soc., 68, 195 (1946).
158. A. Nickon and J. Hammonds, J. Am. Chem. Soc., 86, 3323 (1964).
159. W. H. Glaze, C. M. Selman, A. L. Ball Jr., and L. E. Bray, J. Org. Chem., 34, 641 (1969).
160. M. Matsunaga and T. Kawamura, J. Am. Chem. Soc., 97, 3519 (1975).