

2-NITRO-1,3-INDANDIONE
AND ITS USE AS A REAGENT FOR
THE IDENTIFICATION OF ORGANIC BASES

by

IRVEN WILFRED DAVIES JR.

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APPROVED:

Redacted for Privacy

Professor of Organic Chemistry

In Charge of Major

Redacted for Privacy

Chairman of Department of Chemistry

Redacted for Privacy

Chairman of School Graduate Committee

Redacted for Privacy

Dean of the Graduate School

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TABLE OF CONTENTS

General Discussion	1
Table 1. The yield of 2-nitro-1,3-indandione secured from 2 grams of 1,3-indandione under various conditions	4
Experimental	6
Table 2. The 2-nitro-1,3-indandionates of the aliphatic amines	8
Table 3. The 2-nitro-1,3-indandionates of the aromatic amines	10
Table 4. The 2-nitro-1,3-indandionates of the heterocyclic amines	13
Discussion of Results	15
Bibliography	17

2-NITRO-1,3-INDANDIONE AND ITS USE AS A REAGENT FOR THE IDENTIFICATION OF ORGANIC BASES

The most useful type derivative of primary and secondary amines are the amides, phenylthioureas, and sulfonamides; and of the tertiary amines, the picrates and the quaternary ammonia salts. Benzene sulfonyl chloride is probably the most frequently used reagent since it is employed in both the preparation of these derivatives and in the usual procedure (Hinsberg's method) for classifying amines. In 1936, G. Wanag (3,4) reported a new reagent, 2-nitro-1,3-indandione, which forms salts with both the inorganic and organic cations, such as the simple aliphatic, aromatic, and heterocyclic amines. He found these compounds to be crystalline, non-hygroscopic, sharp-melting salts that were very soluble in water. Later investigators at Wanag's suggestion used this strong acid to prepare certain derivatives of the alkaloids (2) and amino acids (1).

The fact that many of these salts hydrolyze to such an extent in water that a neutralization equivalent may be determined by standard procedures was not realized by Wanag. This property, coupled with its ease of salt formation, non-hygroscopic character, and sharp-melting point range makes it appear to be an unusually promising reagent for the identification of

organic bases. Although neutralization equivalents may also be obtained with the hydrochlorides of the bases, these salts are for the most part hygroscopic and therefore totally unsuitable for equivalent weight determination.

The salts were originally prepared by adding an aqueous solution of the acid to a dilute hydrochloric acid solution of the base. However, as 2-nitro-1,3-indandione itself is very insoluble in dilute hydrochloric acid, impure salts were obtained that had to be recrystallized several times. Since the precipitation procedures were not uniform, and products impure, a study of the salt formation in various solvents was undertaken. In the course of this work it was discovered that very pure salts of 2-nitro-1,3-indandione could be precipitated from acetone solution of the base or its hydrochloride.

2-Nitro-1,3-indandione was first prepared (3) by the direct nitration of 1,3-indandione with cold fuming nitric acid in glacial acetic acid. Wanag, reporting yields of 78%, found that the conditions for this reaction were very critical since the temperature at which nitration takes place and oxidation occurs is nearly the same. The critical conditions were confirmed in this laboratory; but the yields were uncertain and were never greater than 64%. Because of the uncertainties of this

reaction Wanag also attempted to prepare it by oxidizing 2-nitroso-1,3-indandione with concentrated nitric acid and by condensing sodium nitrite with 1,3-indandione at 80° - 90° C. (6) to give the sodium salt of 2-nitro-1,3-indandione. In each instance the yields were low.

In view of the poor or erratic results using fuming nitric acid and the promise of 2-nitro-1,3-indandione as an organic reagent a further study of the direct nitration of 1,3-indandione was made. Concentrated nitric acid was used as the nitrating agent in place of fuming nitric acid since initial work indicated a greater difference between the nitration and oxidation temperatures. Table 1 summarized the results obtained upon the nitration of two grams of 1,3-indandione under various conditions. Incomplete nitration takes place if the mixture is not heated to at least 45° C., or if the nitric acid concentration is diminished. If the mixture is heated over 50° C. but under 75° C. a large amount of a yellow by-product melting at 135° C. results. Complete oxidation to phthalic acid occurs if the nitration is allowed to proceed at temperatures above 80° C. Partial oxidation also occurs if the nitric acid content is increased. The light yellow precipitate of 2-nitro-1,3-indandione hydrate must be filtered rapidly and without agitation, as prolonged contact with the

Table 1

The yield of 2-nitro-1,3-indandione secured from two grams of 1,3-indandione under various conditions.

Temperature °C	Time cooling minutes	Acetic acid ml.	Nitric acid ml.	% yield
30	60	20	2	did not nitrate
40	60	20	2	76
48	60	20	2	84
56	60	20	2	70 some oxidation
64	60	20	2	25
80	60	20	2	traces
40	30	20	2	76
40	90	20	2	78
40	120	20	2	57
40	60	15	2	75
40	60	10	2	26
40	60	25	2	79
40	60	30	2	62
40	60	20	3	38

nitrating mixture causes a corresponding loss in yield. Neither can the precipitate be filtered too soon as sufficient time must be allowed for the precipitate to form. 1,3-indandione may also be nitrated with sodium nitrate in glacial acetic acid at 100°-105° C., or with nitrogen tetroxide in chloroform; but as the yields were poor these latter methods were abandoned.

2-Nitro-1,3-indandione can be readily brominated (3) or chlorinated (5) to form the 2-halo-2-nitro-1,3-indandione. However, it can be neither nitrated, nitrosated, benzoylated, or acetylated. It decomposed upon oxidation or upon the action of concentrated base or acid to form phthalic acid or phthalic anhydride.

Since the formula in Figure 1 cannot satisfactorily explain the acidic character of 2-nitro-1,3-indandione,

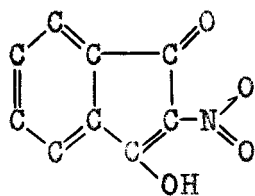


Figure 1
Enol-form

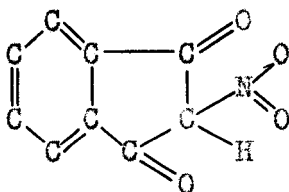


Figure 2
Keto-form

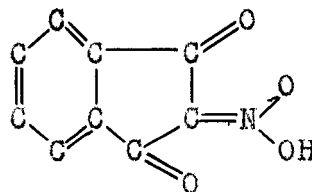


Figure 3
Keto-nitric acid form

two additional structures have been proposed (3). However there appears to be no direct evidence to substantiate either the enol-form (Figure 2) or the keto-nitric acid form (Figure 3).

EXPERIMENTAL

2-NITRO-1,3-INDANDIONE: Twenty grams of 1,3-indandione and 200 milliliters of glacial acetic acid are warmed in an Erlenmeyer flask on a water bath to about 48° C. To this is added in a single amount with constant agitation twenty milliliters of concentrated nitric acid (sp. g. 1.42). After about five seconds the reaction mixture, which darkens considerably, is cooled rapidly with running water or in an ice bath to 10° C. After one hour at this temperature the yellow precipitate of 2-nitro-1,3-indandione is removed by suction filtration and is washed with a little cold acetic acid. The yield after recrystallization from a little water is 22-24 grams (77-84%) of the yellow hydrate, containing one mole of water and melting at 113° C. Upon drying in a vacuum desiccator over sulfuric acid all the water of crystallization is lost, and the 2-nitro-1,3-indandione is transformed into an intense yellow, anhydrous powder, which cannot be recrystallized from an anhydrous solvent.

If the nitrating mixture is poured into water after removing the 2-nitro-1,3-indandione a yellow compound that melts at 135° C. and contains 5.19% nitrogen is secured. As the compound could not be kept in the crystalline state nothing further was done with it.

SALTS OF 2-NITRO-1,3-INDANDIONE: To a solution of the organic nitrogen base or base hydrochloride in acetone is added a slight excess of a saturated solution of 2-nitro-1,3-indandione. (The solution is prepared by adding five grams of the acid to 150 ml. of acetone. The solubility of 2-nitro-1,3-indandione in acetone is 0.025 g./ml. at 18° C.; and 0.032 g./ml. at 24° C.) If the precipitate does not form immediately the solution is evaporated at room temperature to about one-half of its original volume. The salts are recrystallized from 95% ethyl alcohol, water, or a combination of both. The salts thus prepared are very pure and melt within a range of one degree.

A list of the salts prepared with their corrected melting points, analysis, and solubility in various solvents is to be found in Tables 2, 3, and 4. The salts formed from bases which were so strong as not to permit the determination of neutralization equivalents are marked N.T. (not titratable) in the table. The values which are reported agree within 2% of the theory.

The 2-nitro-1,3-indandionates of the aliphatic amines.

the 2-nitro-1,3-indandionate of	m.p.		% N		soluble in			
	°C.	N.E.	calc.	found	water	ethanol	acetone	ether
Simple:								
Methyl amine (4)	205	N.T.	12.64	12.84	*	*		
Ethyl amine (4)	203		11.89	11.40	*	*		
n-Propyl amine (4)	185		11.22	11.20	*	*		
iso-Propyl amine	205	N.T.	11.22	11.30	*	*		
n-Butyl amine	147	N.T.	10.62	10.64	*	*	*	*
iso-Butyl amine (4)	178		10.62	10.54	*	*		
n-Amyl amine	158	N.T.	10.07	9.73	*	*	*	*
iso-Amyl amine	162	N.T.	10.07	10.24	*	*	*	*
iso-Hexyl amine	155	N.T.	9.59	9.23	*	*	*	*
n-Heptyl amine (4)	150		9.17	9.28	*	*	*	*
n-Heptyldecyl amine (4)	119		6.29	6.20	*	*	*	*
Allyl amine (4)	181		11.32	11.00	*	*		
Cyclohexyl amine (4)	213		10.00	9.68	*			
Camphyl amine (4)	169		8.43	8.22	*	*	*	*
Bornyl amine (4)	211		8.14	7.60	*	*	*	
Methylenediamine	229	N.T.	13.08	13.06	*			
Ethylenediamine (4)	205		12.67	12.80	*	*		
Propylenediamine	208	N.T.	12.28	12.03	*			
Putrescine (1)	-		11.92	12.03				
Cadaverine (1)	-		11.57	11.20				
Di-methyl amine (4)	210		11.86	11.20	*	*		
Di-ethyl amine (4)	181		10.61	10.83	*	*	*	*
Di-propyl amine (4)	210		9.59	9.85	*	*	*	*
Di-isopropyl amine	237	N.T.	9.59	9.61	*	*	*	
Di-n-butyl amine	204	N.T.	8.75	8.79	*	*	*	*
Di-iso-butyl amine (4)	231		8.75	9.10	*	*	*	*
Di-sec.-butyl amine	234	N.T.	8.75	8.81	*	*	*	
Di-n-Amyl amine	137	N.T.	8.05	8.00	*	*	*	*
Di-isoamyl amine (4)	190		8.05	8.05	*	*	*	*
Di-n-hexyl amine	117	N.T.	7.45	7.40	*	*	*	*
Di-iso-hexyl amine	133	N.T.	7.45	7.52	*	*	*	
Di-cyclohexyl amine	235	N.T.	7.45	7.48	*	*	*	
Di-n-heptyl amine	107	N.T.	6.92	7.01	*	*	*	
Di-n-octyl amine	91	N.T.	6.50	6.61	*	*	*	
Di-R-ethyl-hexyl amine	144	N.T.	6.50	6.44	*	*		
Di-n-nonyl amine	88	N.T.	6.09	6.11	*	*	*	
Di-n-decyl amine	58	N.T.	5.73	5.81	*	*	*	
Tri-methyl amine (4)	162		11.20	11.40	*	*	*	*
Tri-ethyl amine (4)	oil		8.91	8.95	*	*	*	*
Tri-isobutyl amine (4)	111		7.45	7.81	*	*	*	*

Table 3

The 2-nitro-1,3-indandionates of the aromatic amines.

the 2-nitro-1,3-indan- dionate of	m.p. °C.	N.B.	% N		soluble in				
			calc.	found	water	ethanol	acetone	ether	
Simple:									
Aniline (3)	209	284	9.86	9.94	*	*			
o-Toluidine (3)	198		9.40	9.47	*	*			
m-Toluidine (3)	194		9.40	9.57	*	*			
p-Toluidine (3)	193		9.40	9.71	*	*			
Xylidine 1,3,4 (4)	192		8.98	9.39	*	*			
Xylidine 1,3,2 (4)	185		8.98	9.10	*	*			
Xylidine 1,4,2 (4)	198		8.98	9.46	*	*			
Xylidine 1,3,5 (4)	218		8.98	9.41	*	*			
Benzyl amine (4)	180		6.39	6.65	*	*			
a-Phenyl ethyl amine(4)	207		8.97	8.97	*	*			
b-Phenyl ethyl amine(4)	169		8.97	8.47	*	*			
Benzedrine	193	326	8.59	8.64	*				
Benzhydryl amine (4)	205		7.52	7.53	*	*			
o-Ethyl aniline (4)	183		8.98	9.33	*	*			
p-Ethyl aniline (4)	181		8.98	9.16	*	*			
o-Aminobiphenyl (4)	183		7.78	7.60	*	*			
m-Aminobiphenyl (4)	198		7.78	8.10	*	*			
p-Aminobiphenyl (3)	190		7.78	7.71	*	*			
a-Naphthylamine (4)	210		8.39	8.55	*	*			
b-Naphthylamine (4)	193		8.39	8.81	*	*			
Tetrahydro-a-naphthyl amine-ar (4)	204		8.28	8.01	*	*			
Tetrahydro-b-naphthyl amine-ac (4)	233		8.28	8.52	*	*			
o-Phenylenediamine (4)	174		14.05	14.20	*				
m-Phenylenediamine (4)	200		11.43	10.87	*				
p-Phenylenediamine (4)	263		11.43	11.20	*				
Toluylenediamine-1,2,4 (4)	183		11.13	11.33	*				
2-Amino fluorene (4)	195		7.56	7.72	*				
2,7-Diamino fluorene(4)	240		9.89	9.79					
Benzidine (4)	213		9.90	10.30					
o-Tolidine (4)	216		9.44	9.27	*				
Dibenzylamine (4)	203		7.22	7.60	*	*	*		
N-Isobutyl benzyl amine	220	N. F.	7.91	7.88	*	*	*		
N-methyl aniline (3)	186		9.40	9.27	*	*	*		

Table 3 continued

The 2-nitro-1,3-indandionates of the aromatic amines.

the 2-nitro-1,3-indandionate of	m.p. °C.	N.E.	% N		soluble in				
			calc.	found	water	ethanol	acetone	ether	
Simple:									
N-ethyl aniline (4)	183		8.98	9.61	*	*	*		
N-propyl aniline (4)	191		8.59	8.82	*	*	*		
N-butyl aniline (4)	209		8.24	8.54	*	*	*		
N-isobutyl aniline (4)	207		8.24	8.29	*	*	*		
N-methyl-o-toluidine (4)	190		8.98	9.00	*	*	*		
N-ethyl-o-toluidine (4)	192		8.59	8.62	*	*	*		
N-ethyl-p-toluidine (4)	164		8.59	8.84	*	*	*	*	
N-methyl-a-naphthyl amine	199	N.T. N.F.	8.05	7.93	*				
N-methyl-b-naphthyl amine	177	N.T.	8.05	8.32	*	*			
Dimethyl aniline (3)	133	N.T.	8.98	9.07	*	*	*	*	
o-Dimethyl toluidine (4)	150		8.59	8.43	*	*	*	*	
p-Diethyl toluidine (4)	149		7.91	8.21	*	*	*	*	
a-Dimethyl naphthyl amine (4)	153		7.73	7.65	*	*	*	*	
Phenol:									
o-Aminophenol	205	300			*				
m-Aminophenol	210	300			*	*			
p-Aminophenol	-	300			*	*			
2,4-Diaminophenol	200	315							
1-amino 2-naphthol	-	350			*	*	*		
Ether:									
o-Phenetidine	206	328			*	*			
m-Phenetidine	210	328			*	*	*		
p-Phenetidine	190	328			*	*			
o-Anisidine	198	314			*	*	*		
m-Anisidine	205	314			*	*			
p-Anisidine	203	314			*	*			
o-Dianisidine	226	313			*				
Halogen:									
o-Chloroaniline	182	318			*	*	*	*	
m-Chloroaniline	192	318			*	*	*	*	
p-Chloroaniline	188	318			*	*	*	*	
5-Iodo 2-toluidine	192	424			*	*	*	*	

Table 3 continued

The 2-nitro-1,3-indandionates of the aromatic

amines.

the 2-nitro-1,3-indan- dionate of	m.p. °C.	N.E.	% N		soluable in				
			calc.	found	water	ethanol	acetone	ether	
Nitro:									
o-Nitroaniline	162	329			*	*	*	*	
m-Nitroaniline	182	329			*	*	*		
p-Nitroaniline	175	329			*	*	*	*	
3-Nitro-4-aminotoluene	156	343			*	*	*	*	
Ketone:									
2-Aminoacetophenone	184	326			*				
4-Aminoacetophenone	199	326			*				
p-Dimethylaminobenzal- dehyde	oil								
p,p'-Tetramethyldiamino- benzophenone	oil								
Acid and acid derivative:									
m-Aminobenzoic acid	212	164			*	*			
o-Aminobenzoid acid	189	164			*	*			
p-Aminobenzoic acid	213	164			*	*			
Ethyl anthranilate	197	356			*	*	*		
Methyl anthranilate	167	342			*	*	*		
p-Amino acetanilide(4)	212			11.77	12.15	*			
Benzamide (4)	195			13.51	13.52	*	*		
Sulfanilamide	214	363		7.71	7.84	*			
o-Toluidine-5-sulfonic acid	-	395		7.09	7.11	*			
Anthranilamide	208	326		8.59	8.36	*			
Azo and azine:									
Benzalazine	145d	295		9.49	9.56	*	*		
Hydrazobenzene	-	375		11.20	11.01	*	*		
Dimethylaminoazobenzene	188			13.46	13.41	*			
Diazoaminobenzene	191	269		12.09	12.31	*			

Table 4

The 2-nitro-1,3-indandionates of the heterocyclic amines.

the 2-nitro-1,3-indandionate of	m.p. °C.	N.E.	% N		soluble in				
			calc.	found	water	ethanol	acetone	ether	
Simple:									
Pyridine (4)	168	270	10.37	10.60	*	*			
a-Picoline (4)	161		9.85	9.77	*	*			
b-Picoline	146	284	9.85	9.96	*	*			
g-Picoline	175	284	9.85	9.71	*	*			
Quinoline (4)	155		8.75	8.68	*	*		*	
2-Methyl quinoline (4)	157		8.38	8.32	*	*	*	*	
4-Methyl quinoline	198	334	8.38	8.46	*	*			
6-Methyl quinoline	161	334	8.38	8.39	*	*			
7-Methyl quinoline	182	334	8.38	8.17	*	*	*	*	
8-Methyl quinoline (4)	160		8.38	8.11	*	*	*	*	
Acridine (4)	163		7.57	7.60	*	*	*	*	
Isoquinoline	187	320	8.75	8.94	*	*			
2-Phenyl,4,6-dimethyl-pyrimidine	142	375			*	*	*		
Piperidine (4)	182		10.15	10.20	*	*	*	*	
Pyrrolidine	215	N.F.	10.68	10.89	*	*	*	*	
Morpholine	d.	N.F.	10.07	10.22	*	*			
Acid and acid derivative:									
Nicotinic acid	171	157			*				
Nicotinamide	196	313			*	*			
Ethyl nicotine	143	342			*	*			
Creatinine (1)	-								
Halogen:									
4,7-Dichloroquinoline	167	389			*	*	*	*	
5-Bromo-8-nitro-quinoline	151	444			*	*	*	*	
Nitro:									
5-Nitroquinoline	182	365			*	*			
8-Nitroquinoline	185	365			*	*			
5-Methyl-8-nitroquinoline	159	379			*	*			
7-Methyl-8-nitroquinoline	136	379			*	*	*		
5-Methoxy-8-nitroquinoline	179	395			*	*			

Table 4 continued

The 2-nitro-1,3-indandionates of the heterocyclic amines.								
the 2-nitro-1,3-indandionate of	m.p. °C.	N.E.	% N		soluble in			
			calc.	found	water	ethanol	acetone	ether
Amine:								
2-Amino pyridine (4)	197		14.67	14.60	*	*		
2,6-Diaminopyridine	235	245			*			
2-Amino-4-methyl-pyrimidine	177	300			*			
2,4-Dihydroxy-6-amino-pyrimidine	-	318			*			
5-Amino uracil	-	318			*			
2-Amino thiazol	208	291			*	*		
4(2',3'-Dihydroxypropyl-amine)-6-chloroquinazoline	207	455			*	*	*	*
4(w'-hydroxyhexylamine)-6-chloroquinazoline	188	480			*	*	*	*
4(2'-hydroxyethylamine)-quinazoline	243	389			*	*	*	
Alkaloid:								
Quinine (4)	186		8.14	7.94	*	*		
Strychnin (4)	226		8.00	7.42	*	*		
Brucine (4)	185		7.18	6.92	*	*		
Alypine (2)								
Berberine (2)								
Brucine (2)								
p-Phetonine (2)								
Eucaïne A (2)								
Piperazine (2)								
Theobromine (2)								
Theophylline (2)								
Nicotine		oil						

DISCUSSION OF RESULTS

2-Nitro-1,3-indandione forms crystalline, sharp melting salts in acetone solution with both the simple and substituted amines, such as the amino acids, proteins, hydroxylamines, amides, halo-, azo-, and nitroamines. Accurate neutralization equivalents may be determined for the salts of the weak and moderately weak bases such as aniline and quinoline but not for the weak bases as the mono-, di-, and trialkyl amines, morpholine, and piperidine. The base may be regenerated by the addition of alkali to the salt.

The solubility of the salts of the aliphatic primary and secondary amines decreases in the polar solvents and increases in the non-polar solvents with increasing molecular weight. The melting points of the salts of the iso-amines are higher than the normal amines. The salts of the aromatic and heterocyclic amines are even less soluble in the non-polar solvents than are the aliphatic amines. Substitution of a methyl, Hydroxy, or amino group decreases both the melting point and the solubility. The substitution of a halogen, nitro, or carboxyl groups increases the solubility.

The keto active compounds, hydrazine, phenylhydrazine, hydroxylamine, semicarbazide, give yellow salts

which, on slightly warming, split out water to form colored precipitates. Usually a mixture is formed consisting of salt, -azone, and -azone salt that is impossible to separate.

The salts are either white or a light yellow, with the exception of the golden-brown dimethylaminoazobenzene.

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