[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, AMHERST COLLEGE]

The Wolff–Kishner Reduction. I. The Preparation and Properties of N-Alkyl- and N,N-Dialkylhydrazones

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The Wolff–Kishner reduction of a carbonyl group to a methylene group by decomposition of a hydrazone, azine or semicarbazone in the presence of an alkaline catalyst or platinum has recently been shown to be practicable for large-scale operations[1] and, in the absence of solvent, not to require the fairly high temperatures commonly employed.[2] It seems of interest to investigate the mechanism of the reaction with a view to widening its scope. As a first step, the effect of alkali on N-alkyl- and N,N-dialkylhydrazones was investigated.[3] In this paper the preparation of these substituted hydrazones is described.

Very few N-alkylated hydrazones are known. Of the compounds of this class reported in this paper only the methylhydrazone and diethylhydrazone of benzaldehyde, and the methylhydrazone of *p*-nitrobenzaldehyde are in the literature. A preparation of benzaldehyde methylhydrazone was claimed by Harries and Haga,[4] but their product was a high-melting solid whereas one would expect that the compound should be an oil of lower boiling point (because of less hydrogen bonding) than the liquid benzaldehyde hydrazone. In this paper the isolation of the methylhydrazone of the expected physical properties is described. The diethylhydrazones of benzaldehyde and *p*-nitrobenzaldehyde were prepared by Brady and McHugh.[5] Hurd and Spence[6] have reported the preparation of several oily diethylhydrazones without giving details or properties.

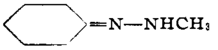
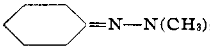
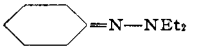
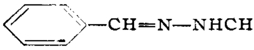
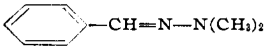
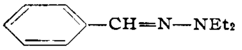
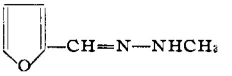
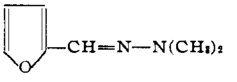
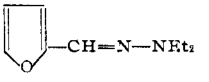
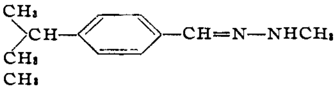
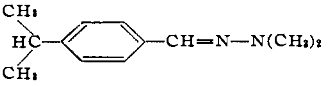
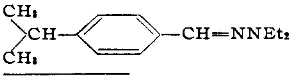
It was found that the hydrazones could be readily prepared by refluxing the appropriate carbonyl compound with an aqueous-alcoholic solution of the free alkylhydrazine. The latter was prepared by distilling to dryness an alkaline solution of a salt of the hydrazine. The hydrazones could also be prepared by refluxing an ether or benzene solution of the hydrazine with the carbonyl compound. In this case the hydrazine solution was prepared by solvent extraction of a cold basic solution of the hydrazine salt. The hydrazones were generally liquids, and almost all could be characterized as the picrate, styphnate, or N-nitroso derivative (in the case of monoalkylhydrazones). Furfural methylhydrazone was rapidly decomposed by picric acid in dry benzene, but the N-nitroso derivative was easily prepared. Cyclohexanone diethylhydrazone gave only a small yield of the styphnate in dry benzene while the picrate would not come out at all.

The ultraviolet absorption spectra of the hydrazone, methylhydrazone, dimethylhydrazone and diethylhydrazone of benzaldehyde are given in Fig. 1.

The molecular refractions of these materials were determined and found to show some remarkably high exaltations when the literature values for hydrazone nitrogen atomic refractivities were employed to calculate the molecular refractions.

It has been found[7] that for a series of four monoalkylhydrazones of aliphatic carbonyl compounds the calculated molecular refractions could be made to fit the observed values by assigning (1) to the C=N link the normal C=C bond refractivity of 1.733 units, (2) to the double-bonded nitrogen the normal secondary amine nitrogen value of 2.65 units, and (3) to the other nitrogen the normal primary amine nitrogen value of 2.45 units. These values were used to calculate the molecular refractions in Table I.

TABLE I

	$MR_{\text{obs.}}$	$MR_{\text{calcd.}}$	Exaltation
	39.12	39.16	−0.04
	43.70	43.78	− .08
	52.97	53.01	− .04
	44.86	42.38	2.48
	50.97	46.99	3.98
	60.68	56.23	4.45
	37.88	35.25	2.63
	43.67	39.87	3.80
	53.49	49.10	4.39
	59.86	56.23	3.63
	64.43	60.85	3.58
	73.70	70.08	3.62

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[1] Soffer, Soffer and Sherk, THIS JOURNAL, **67**, 1435 (1945); Herr, Whitmore and Schiessler, *ibid.*, **67**, 2061 (1945); Huang-Minlon, *ibid.*, **68**, 2487 (1946).

[2] Lock and Stach, *Ber.*, **76**, 1252 (1943); **77**, 293 (1944).

[3] See paper II of this series, THIS JOURNAL, **71**, 1356 (1949).

[4] Harries and Haga, *Ber.*, **31**, 62 (1898)

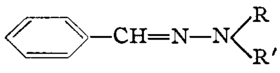
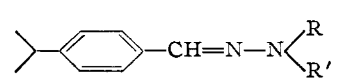
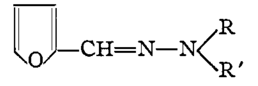
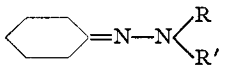
[5] Brady and McHugh, *J. Chem. Soc.*, 1648 (1922).

[6] Hurd and Spence, THIS JOURNAL, **49**, 266 (1927).

[7] Barrick, Drake and Lochte, *ibid.*, **58**, 160 (1936).

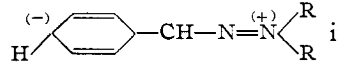
TABLE II

N-ALKYL- AND N,N-DIALKYLHYDRAZONES

		R	R′	Method	Yield	B. p., °C.	Mm.	n^t_D	d^t_4	t
1		CH_3	H	a and b	69 and 75	130–131	18	1.6053	1.0305	21.5
2		CH_3	CH_3	a and b	83 and 60	127–128	20	1.5920	0.9840	29
3		C_2H_5	C_2H_5	a	22	140–141	14	1.5754	.9604	24
4		CH_3	H[a]	a	58	148–152	7	1.5779	.9769	25
5		CH_3	CH_3[b]	a	59	147	10	1.5649	.9593	24
6		C_2H_5	C_2H_5	b	47	156–158.5	8	1.5548	.9506	23
7		CH_3	H[c]	a	80	113–116	15	1.5846	1.0978	25
8		CH_3	CH_3	a	73	98	9.5	1.5748	1.0423	24
9		C_2H_5	C_2H_5	b	50	113	7	1.5569	1.0003	25
10		CH_3	H	a	59	92–93	11	1.4990	0.9474	24
11		CH_3	CH_3	a	73	177–180	760	1.4697	0.9031	27
12		C_2H_5	C_2H_5	b	57	81–83	7	1.4646	0.8776	26

[a] M. p. (by immersion) is 10–12°. This compound is completely hydrolyzed by fifteen minutes contact with cold 5% HCl. [b] This material was not hydrolyzed after fifteen minutes contact with cold 5% HCl. [c] It is necessary to work up the reaction mixture immediately to avoid polymerization of the product. The compound is very sensitive to air oxidation. [d] Turns green on storage. [e] In ethanol this picrate is rapidly converted to the picrate of dimethylhydrazine, m. p. 140–142.5° dec. *Anal.* Calcd. for $C_8H_{11}N_5O_7$: C, 33.22; H, 3.83. Found: C, 33.06; H, 3.96.

It will be observed that in the cyclohexanone series no appreciable exaltation is found. In the benzaldehyde and furfural series the exaltations are not only unusually high but increase sharply with increased molecular weight.

The abnormalities in both the spectroscopic and refraction data are probably best explained by the existence of contributing resonance forms, typified by  in the case of the aromatic and furfural hydrazones. It would be expected that an increase in the number of alkyl groups on the terminal nitrogen of the hydrazones of aromatic carbonyl compounds would favor the increased participation of these resonance forms because of the electron-donating nature of the alkyl groups. It will be observed in Fig. 1 that the bathochromic shift of the maximum amounts to about 10 millimicrons as one passes from benzaldehyde methylhydrazone to the dimethylhydrazone. This is large in comparison with the almost negligible shift that occurs when such a change in structure does not alter the resonating character of the molecule.

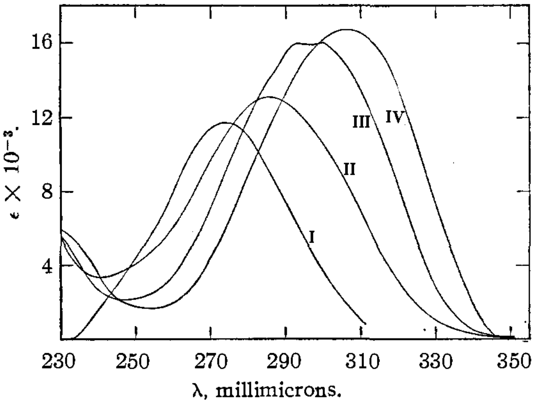


Fig. 1.—I, Benzaldehyde hydrazone; II, benzaldehyde methylhydrazone; III, benzaldehyde dimethylhydrazone; IV, benzaldehyde diethylhydrazone.

Similarly it is well known that the stabilization of resonance forms leads to abnormal exaltations of molecular refractivities.[8] It is not at all clear why the *p*-isopropylbenzaldehyde hydrazones should show identical exaltations; they would be expected to show the same changes as the benzaldehyde series, though the exaltations should be of a lower order of magnitude because of the resonance-damping effect of the isopropyl group.

Experimental

The two general methods for preparing the alkylhydrazones are described in detail for the preparation of benzaldehyde methylhydrazone. In Table II will be found the data on the preparation and properties of all the hydrazones prepared in this work.

Benzaldehyde Methylhydrazone: Method (a).—Twenty-one and six-tenths grams (0.15 mole) of methylhydrazine sulfate was dissolved in 25 ml. of warm water and dropped slowly from a separatory funnel into excess aqueous sodium hydroxide. The free hydrazine was distilled off, and several more portions of water added to the damp salt cake and distilled off. To the distillate was added about 25 ml. of ethanol and 15.9 g. (0.15 mole) of benzaldehyde, and the mixture heated on the steam-bath for three hours. The ethanol was removed *in vacuo*, the residual solution extracted with ether, the ether solution washed and dried, and the ether removed. The residual oil was distilled at 20 mm. After a small forerun had been removed the product came over at 129–133° as a pale yellow oil of characteristic camphoraceous-basic odor.

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[8] Palermiti and Curran, THIS JOURNAL, 70, 3526 (1948).

TABLE II (*Continued*)

				Analyses, %					
		Neut. eq.		Carbon		Hydrogen		Nitrogen	
Derivative	M. p., °C.	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
Picrate	133.0–133.5	363	358	46.28	46.46	3.61	3.60		
N-nitroso cpd.	73.0–73.5							25.75	25.36
Picrate	142.5–143.5	377	377	47.74	47.90	4.01	3.94		
Chloroplatinate	180–188 dec.	353	357						
Picrate	166–168 dec.	405	400	50.37	49.98	4.72	4.95		
Picrate	138–140 dec.	405	412	50.37	50.63	4.72	4.55		
Picrate	157–166 dec.	419	425	51.55	51.21	5.04	4.63		
Picrate	122–123 dec.	447	455	53.68	53.69	5.63	5.39		
Styphnate	117.5–120 dec.	231.6	236						
N-nitroso cpd.	108–109.5							27.44	26.72
Picrate[d]	124–125 dec.	367	367	42.51	42.15	3.57	3.65		
Picrate[d]	140–145 dec.	395	402						
Styphnate	135–136 dec.	205.6	207.5	43.80	43.63	4.17	3.74		
Picrate[e]	124–125 dec.			45.53	45.21	5.19	5.06		
Styphnate	137–140 dec.	192.5	193						
Styphnate	135–138 dec.	206.5	211.5	46.48	46.78	5.62	5.10		

The yield was 13.85 g. (69%). (If the alcohol–water solution of the product is allowed to stand at room temperature for several days the yield is far lower and a large amount of non-distillable polymer is formed.)

Method (b).—To 20 ml. of cold 50% sodium hydroxide in an ice-bath was added 14.4 g. (0.10 mole) of finely powdered methylhydrazine sulfate. The mixture was well stirred until the pale yellow hydrazine salt had dissolved; a heavy white precipitate of sodium sulfate came down during this period. The suspension was extracted twice with 50-ml. portions of ether, and the ether solution dried over potassium hydroxide pellets for an hour. To the filtered ether solution was added 10.6 g. (0.10 mole) of benzaldehyde; a mildly exothermic reaction set in immediately. The solution was refluxed one half hour, washed twice with 40% sodium bisulfite, with water, and dried over sodium hydroxide. After removal of the ether the product was distilled at 18 mm.; b. p. is 130–131°: yield is 10.03 g. (75%). The material was redistilled *in vacuo* for purification. The boiling point is 133° at 20 mm. (130–131° at 18 mm., 118–119° at 8 mm.); $n^{21.5}\text{D}$ 1.6053; $d^{21.5}{}_4$ 1.0305; MR_{obs} 44.86; $MR_{\text{calcd.}}$. 42.38. (This material was found to be quite stable to cold 5% hydrochloric acid for half an hour or so at least. This fact was made use of several times to separate the hydrazone from unchanged benzaldehyde.)

Picrate.—To a solution of 2.29 g. of picric acid in warm benzene was added a benzene solution of 1.34 g. of benzaldehyde methylhydrazone. The yellow precipitate that formed was filtered and recrystallized from benzene; m. p. 133–133.5° (dec.).

Harries and Haga reported that benzaldehyde methylhydrazone was a colorless crystalline solid, m. p. 179°.

The **N-nitroso derivative** was prepared by refluxing a mixture of 5.36 g. of freshly-distilled benzaldehyde methylhydrazone with 9.36 g. of isoamyl nitrite in 50 ml. of hexane for two hours. The solution was cooled to −20° and two crops of pale yellow crystals totalling 2.25 g. (35% yield) were obtained. Two recrystallizations of this material from ethanol–water gave massive pale yellow prisms, m. p. 73.0–73.5°. This material gives a strong Liebermann nitroso test.

An attempt was made to prepare the N-acetate by the method employed by Brady and McHugh[4] to prepare the N-acetate of *p*-nitrobenzaldehyde methylhydrazone. Only unreacted starting material was recovered from the reaction mixture.

Summary

The preparation and physical properties of the methyl-, dimethyl- and diethylhydrazones of benzaldehyde, *p*-isopropylbenzaldehyde, furfural and cyclohexanone are reported.

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