

TABLE I  
 $pK_a'$  VALUES OF ALKYLHYDRAZINES at 30°

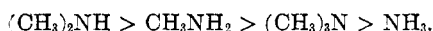
Hydrazine	Method of Preparation	$pK_a'^a$	$\Delta pK_a'^b$
NH <sub>2</sub> NH <sub>2</sub>	<sup>c</sup>	8.07 <sup>d</sup>	
CH <sub>3</sub> NHNH <sub>2</sub>	<sup>c</sup>	7.87	-0.20
(CH <sub>3</sub> ) <sub>2</sub> NNH <sub>2</sub>	<sup>c</sup>	7.21	-0.66
CH <sub>3</sub> NHNHCH <sub>3</sub>	<sup>e</sup>	7.52 <sup>f</sup>	-0.35
(CH <sub>3</sub> ) <sub>2</sub> NNHCH <sub>3</sub>	Ref. 5	6.56	-0.65
(CH <sub>3</sub> ) <sub>2</sub> NN(CH <sub>3</sub> ) <sub>2</sub>	Ref. 5	6.30 <sup>g</sup>	-0.26
C <sub>2</sub> H <sub>5</sub> NHNH <sub>2</sub>	<sup>h</sup>	7.99 <sup>f</sup>	-0.08
(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> NNH <sub>2</sub>	<sup>i</sup>	7.71	-0.28
C <sub>2</sub> H <sub>5</sub> NHNHCH <sub>2</sub> H <sub>5</sub>	<sup>i</sup>	7.78 <sup>f</sup>	-0.21

<sup>a</sup> Average deviation =  $\pm 0.05$ . <sup>b</sup> Difference of two adjacent members of the same series. <sup>c</sup> Purchased. <sup>d</sup> Reported value: 7.95 (at 25°) (ref. 4). <sup>e</sup> R. L. Hinman, *J. Am. Chem. Soc.*, **78**, 1645 (1956). <sup>f</sup> From titration of dihydrochloride. <sup>g</sup> This value taken from ref. 5. <sup>h</sup> G. Gever and K. Hayes, *J. Org. Chem.*, **14**, 813 (1949). <sup>i</sup> H. Zimmer, L. F. Audieth, M. Zimmer, and R. A. Rowe, *J. Am. Chem. Soc.*, **77**, 790 (1955). <sup>j</sup> R. Renaud and L. C. Leitch, *Can. J. Chem.*, **32**, 545 (1954).

#### DISCUSSION

The most striking fact about the results recorded in Table I is that substitution of an alkyl group for a hydrogen of the hydrazine molecule is accompanied by a decrease in base strength, and that further decreases accompany the introduction of additional alkyl groups. It is also apparent that each member of the ethylhydrazine series is more basic than its methyl homolog.

Although the latter effect parallels that in the amine series, the general base-weakening effect of alkyl groups in the hydrazine series is the opposite of what one would expect on the basis of the base strengths of the corresponding amines, or on the basis of the usual electron-donating character of alkyl groups. Thus, the methylamines fall in the following sequence<sup>8</sup> with respect to their base strengths:



The ethylamines fall in a similar order.<sup>8</sup>

The results reported in this note contradict the assumption occasionally found in the literature<sup>9,10</sup> that the alkylhydrazines are more basic than hydrazine itself, just as the methylamines are more basic than ammonia. The results are also pertinent to the theory which holds that successive alkylations of a hydrazine take place on the same nitrogen because the nitrogen which bears the more alkyl groups is always the more basic.<sup>10</sup> The term basic, as used in the reference cited, does not refer to the measured affinity of the nitrogen for a proton or other acid, but rather to an idealized elec-

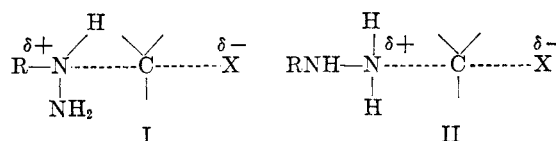
(8) H. C. Brown, H. Bartholomay, Jr., and M. D. Taylor, *J. Am. Chem. Soc.*, **66**, 435 (1944).

(9) H. H. Sisler, G. M. Omietanski, and B. Rudner, *Chem. Revs.*, **57**, 1027 (1957).

(10) T. W. J. Taylor and W. Baker, *Sidgwick's Organic Chemistry of Nitrogen*, Clarendon Press, Oxford, 1937, pp. 378, 381.

tronic state of the nitrogen, predicted on the basis of the usual inductive or conjugative effects of the attached groups. In this sense, which is one frequently used today, the explanation is not incompatible with the present finding that the over-all basicity of the molecule decreases as alkyl groups are introduced.<sup>11</sup> When applied to phenylhydrazine, however, this theory predicts that alkylation should take place on the nitrogen which does not bear the phenyl group because of the greater predicted "basicity" of that nitrogen. Although it has been claimed that alkylation does in fact occur on the predicted nitrogen (Ref. 10, p. 382), the evidence in the literature shows that alkylation occurs mainly on the nitrogen which bears the phenyl group.<sup>12</sup>

A more refined and potentially useful explanation of the phenomenon of alkylation of hydrazines can probably be reached by application of the concept of nucleophilicity.<sup>13</sup> It should also be noted that the positive charge which develops in the transition state will be better stabilized on that nitrogen which bears the larger number of alkyl groups (I).



Similar considerations may explain the fact that the ease of alkylation increases as successive alkyl groups are introduced. Previous explanations have been based on the assumption that basicity in the alkylhydrazine series increases as the number of alkyl groups is increased.<sup>9,10</sup>

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 STATE UNIVERSITY OF IOWA  
 IOWA CITY, IOWA

(11) The measured base strength of an alkylhydrazine may actually be a measure of the average of the proton affinities of the two nitrogens.

(12) See for example: G. Minunni, *Gazz. chim. ital.*, **22**, II, 218 (1892); M. Busch and K. Lange, *J. prakt. chem.*, **144**, 291 (1935). Results confirming that alkylation of phenylhydrazine occurs on the phenyl-bearing nitrogen have been obtained by Mr. B. E. Hoogenboom in this laboratory. These results will be published in the near future.

(13) C. G. Swain and C. B. Scott, *J. Am. Chem. Soc.*, **75**, 141 (1953).

#### Formation of 1,3-Dimethyl-5,5-diphenylhydantoin and Related Reactions

ROY G. NEVILLE

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The reaction of benzil with urea in the presence of alkoxide ion gives a mixture of 5,5-diphenyl-

hydantoin (I) and 3a,6a-diphenyltetrahydroimidaz[d]imidazole-2,5-dione (II), the proportions of I and II depending upon the benzil to urea ratio.<sup>1,2</sup> Benzil and monoalkyl- or 1,3-dialkylureas condense in basic alcoholic solution to yield the monoalkyl- or 1,3-dialkyl-4,5-dihydroxy-4,5-diphenyl-2-imidazolidinone,<sup>3</sup> which on heating with acetic anhydride rearranges to the 3-monoalkyl- or 1,3-dialkyl-5,5-diphenylhydantoin.

As part of a study of alkyl and aryl ureas benzil was reacted with methylurea and 1,3-dimethylurea in 1:1 to 1:6 molar ratios, under basic conditions, in an attempt to prepare methyl derivatives of II. No evidence was found for the formation of these compounds, the sole products being the 4,5-dihydroxy-2-imidazolidinone derivatives.<sup>4</sup> Unlike the benzil-urea reaction, the dihydroxy derivatives yielded benzoic acid, not the hydantoin, on treatment with dilute base. On refluxing the dihydroxy compounds in a high-boiling hydrocarbon (*e.g.* *p*-cymene or dipentene), water was quantitatively eliminated and the corresponding hydantoin resulted.

Refluxing benzil with methylurea or 1,3-dimethylurea in dipentene, or fusion of these reactants, similarly yielded 3-methyl-5,5-diphenylhydantoin (III), or 1,3-dimethyl-5,5-diphenylhydantoin (IV). The formation of 3-substituted, or 1,3-disubstituted, hydantoins by refluxing in a high-boiling inert solvent, in entire absence of base, constitutes an alternative synthetic approach to these compounds.

To establish that the products of reaction of benzil with dimethylurea under basic and neutral conditions were, in fact, different, their ultraviolet absorption spectra were determined, I being employed as a reference compound. The results obtained are shown in Table I.

On refluxing 1:1 to 1:3 molar ratios of benzil and 1,3-diphenylurea in alcoholic solution in presence of isopropoxide, or hydroxide,<sup>5</sup> ion no reaction occurred and diphenylurea was quantitatively recovered. Similarly, heating in dipentene, or fusion, of 1:1 to 1:3 molar ratios of these compounds failed to cause reaction. The reaction in neutral solution was also unsuccessful using phenyl-

TABLE I  
ULTRAVIOLET ABSORPTION SPECTRA OF COMPOUNDS I, IV,  
AND V

Compound	$M\mu$	$\epsilon$
I	251.5 <sup>a</sup>	989
	258.3	712
	264.8	455
	268.5 <sup>a</sup>	240
IV	258.5	782
	262.5 <sup>a</sup>	546
	264.5 <sup>a</sup>	514
	269.3	337
V	252.3	303
	258.3	387
	261.7	318
	264.2	308
	268.0	209

<sup>a</sup> Shoulder value.

urea, 1,3-diphenylthiourea, and 1,3-diphenylguanidine.

Proof that the product of reaction of benzil and methylurea under basic conditions rearranged to give the 3-methyl-, and not the 1-methyl-, hydantoin, was obtained by independent synthesis of the 3-methyl compound.

#### EXPERIMENTAL

*1,3-Dimethyl-4,5-dihydroxy-4,5-diphenyl-2-imidazolidinone*, V. This compound was prepared by a modification of the method of Linsker and Evans.<sup>6</sup> Metallic sodium (4.6 g., 0.2 g.-atom) was dissolved in refluxing isopropyl alcohol (150 ml.), followed by 1,3-dimethylurea (17.6 g., 0.2 mole), then benzil (21.0 g., 0.1 mole). The "permanganate" colored solution was heated at reflux for 30 min. then poured while hot into a solution of sodium acetate (40 g.) in water (2 l.). After standing overnight in the refrigerator the crystalline white precipitate was filtered, washed with cold water, then with isopropyl alcohol, and dried in an air oven at 110°. Yield, 28.4 g. (95%), m.p. 201°. Three recrystallizations raised the m.p. to 202°.

*Anal.* Calcd. for  $C_{17}H_{18}N_2O_3$ : C, 68.44; H, 6.08; N, 9.39. Found: C, 68.41; H, 6.03; N, 9.24.

Using 1:1 to 1:6 molar ratios of benzil to dimethylurea, yields of 20 to 25 g. of V were obtained. No evidence was obtained for the formation of the tetramethyl derivative of II.

Employing an identical procedure to that used for the preparation of V, benzil (2.10 g., 0.01 mole), methylurea (0.74 g., 0.01 mole), and sodium (0.46 g., 0.02 g.-atom) yielded 2.4 g. (85%) of 1-methyl-4,5-dihydroxy-4,5-diphenyl-2-imidazolidinone (VI), m.p. 216°.

*1,3-Dimethyl-5,5-diphenylhydantoin*, IV. Employing the method of Biltz, benzil (7.0 g., 0.03 mole) and 1,3-dimethylurea (3.5 g., 0.03 mole) were fused and gradually heated to 205°. The mixture was maintained at this temperature for 10 min. The yield of cooled melt was 8.9 g. (95.5%). Recrystallization from isopropyl alcohol gave 8 g. of IV as colorless, stubby needles, m.p. 197°. No evidence was obtained for the tetramethyl analog of II on fusion of 1:2 to 1:6 molar ratios of benzil and dimethylurea, and working up the product.

This compound was also obtained by refluxing benzil and dimethylurea (in the above proportions) in 100 ml. of *p*-

(1) H. Biltz, *Ber.*, **40**, 4799, 4806 (1907); **41**, 167, 1379 (1908); *Ann.*, **368**, 156, 243 (1909); E. Ware, *Chem. Revs.*, **46**, 403 (1950); K. Hofmann, *Imidazole and Its Derivatives, Part I*, Interscience Publishers, Inc., New York, N. Y., 1953, pp. 66, 74, and 230; R. C. Elderfield, *Heterocyclic Compounds*, John Wiley & Sons, Inc., New York, 1957, volume 5, p. 261.

(2) W. R. Dunnivant and F. L. James, *J. Am. Chem. Soc.*, **78**, 2740 (1956).

(3) H. Biltz, *Ber.*, **41**, 167, 171 (1908); *Ann.*, **368**, 156, 201 (1909).

(4) In the condensation of benzil with urea in presence of alkoxide ion 4,5-dihydroxy-4,5-diphenyl-2-imidazolidinone is never isolated.

(5) F. L. James, private communication.

(6) F. Linsker and R. L. Evans, *J. Am. Chem. Soc.*, **68**, 947 (1946).

cymene or dipentene. The mixture was heated for 10 hr. and the evolved water (0.6 ml., 100%) was collected in a Dean-Stark trap. Dimethylurea was soluble in the boiling solution and, on cooling, white crystals separated. The yield was 8.5 g. (91%). After three recrystallizations from alcohol the m.p. remained at 197°. The mixed melting point of a 1:1 mixture of the products by both methods was undepressed.

*Anal.* Calcd. for  $C_{17}H_{18}N_2O_2$ : C, 72.84; H, 5.75; N, 10.00. Found: C, 73.21; H, 6.08; N, 9.94.

On refluxing VI (1.42 g., 0.005 mole) for 8 hr. in dipentene (35 ml.), water (0.09 ml., 100%) distilled and was collected in a Dean-Stark trap. On cooling and recrystallizing from alcohol 1.31 g. (98%) of white needles of III, m.p. 215°, was obtained. The hydantoin, III, could also be obtained directly by refluxing for 1.5 hr. a mixture of benzil (2.10 g.), methylurea (0.74 g.), and dipentene (75 ml.)<sup>7</sup> until no more water distilled. The methyl group of III was shown to be in the 3-position by preparing III from I by the methylation procedure of Klosa.<sup>8</sup> The mixed melting point of III prepared by both methods was undepressed.

*Formation of IV from V.* Compound V (9.93 g., 0.03 mole) was refluxed in dipentene (200 ml.) and, after 30 min., the theoretical volume of water (0.6 ml.) had collected in the water trap. Further heating for 60 min. yielded no more water. After cooling to 0° the crystalline solid was filtered, washed with alcohol, and dried in air. The yield was 9.2 g. (98.5%). Three recrystallizations from alcohol gave IV, m.p. 197°. The mixed-melting point of this compound with that prepared by the method of Biltz was undepressed.

*Attempt to form IV from V by the action of base.* One g. of V, sodium hydroxide (0.5 g.), and isopropyl alcohol (50 ml.) were refluxed for 30 min., then poured into water (200 ml.). Addition of concentrated hydrochloric acid to pH 4 produced a flocculent white precipitate which was filtered and recrystallized from dilute alcohol to yield 0.6 g., m.p. 150°, corresponding with benzoic acid. The mixed melting point with authentic benzoic acid was undepressed.

*Attempts to react benzil with phenylurea, etc.* In place of dimethylurea in the procedure for the preparation of V the following compounds were employed: phenylurea, 1,3-diphenylurea, 1,3-diphenylthiourea, and 1,3-diphenylguanidine. In each case no evidence of any reaction was obtained and the original compounds were quantitatively recovered. Fusion of benzil with diphenylurea, in 1:1 molar ratio at 205°, as in the preparation of IV, yielded a yellow product which after recrystallization from alcohol melted at 95° (benzil). Similar results were obtained using diphenylthiourea and diphenylguanidine.

*Ultraviolet absorption spectra of I, IV, and V.* Spectral determinations were carried out in the standard manner using a Beckman spectrophotometer, Model DU, and matched 1-cm. quartz cells. Spectral measurements were made from 220 to 300  $\mu$ . Comparison of the spectrum of I showed it to be very similar to that of IV, and quite different from that of V.

*Acknowledgment.* The author thanks Mr. R. E. Wilde<sup>9</sup> for the preparation of compound I and for the spectral determinations.

RESEARCH LABORATORIES  
FINE CHEMICALS INC.  
10336 BOTHELL WAY  
SEATTLE 55, WASH.

(7) Using xylene a 10-hr. reflux time was required.

(8) J. Klosa, *Arch. Pharm.*, **285**, 274 (1952).

(9) Present address: Department of Chemistry, University of Washington, Seattle, Wash.

## Cleavage of Tetrahydrofuran by 2,3-Dichloro-*p*-dioxane and 2,3-Dichlorotetrahydrofuran Using Zinc Chloride as a Catalyst

N. B. LORETTE

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Reported in the literature are many examples of tetrahydrofuran ring cleavage with a number of different compounds. Those containing an active halogen break the furan ring and bring about the formation of 4-halobutoxy derivatives. Some that have been used are the hydrogen halides,<sup>1-3</sup> acid chlorides<sup>4,5</sup> and methyl iodide.<sup>6</sup> Reppe and Kroper<sup>7</sup> claim that during the chlorination of tetrahydrofuran to 2,3-dichlorotetrahydrofuran a small amount of 2-(4'-chlorobutoxy)-3-chlorotetrahydrofuran is formed. They report that this comes from the reaction between 2,3-dichlorotetrahydrofuran and 4-chlorobutanol-1 which is formed during the chlorination of tetrahydrofuran by the action of HCl on tetrahydrofuran. No references were found where an alpha halo ether was used to cleave tetrahydrofuran.

Tetrahydrofuran was opened with 2,3-dichloro-*p*-dioxane to give 2,3-di(4'-chlorobutoxy)-*p*-dioxane in 40 to 43% yields. It was also opened with 2,3-dichlorotetrahydrofuran to give 2-(4'-chlorobutoxy)-3-chlorotetrahydrofuran in 53% yield. These reactions were carried out in anhydrous systems in which there appeared to be no HCl present to cleave the tetrahydrofuran. The amount of catalyst (zinc chloride) was varied from 5 to 20 g. per mole of alpha chloroether. The only effect noted was a slightly higher reaction rate at the higher catalyst concentration. There was no reaction when no catalyst was used.

The 2,3-di(4'-chlorobutoxy)-*p*-dioxane prepared by a more conventional method<sup>8</sup> using 4-chlorobutanol had the same physical properties and infrared spectrum as when prepared using tetrahydrofuran.

(1) D. Starr and R. M. Hixon, *Org. Syntheses, Coll. Vol. II*, 571 (1943).

(2) N. D. Scott, U. S. Patent 2,491,834; *Chem. Abstr.*, **44**, 2542h (1950).

(3) F. Codignola and M. Piacenze, Italian Patent 424,590; *Chem. Abstr.*, **43**, 4284b (1949).

(4) M. E. Synerholm, *Org. Syntheses, Coll. Vol. III*, 187 (1955).

(5) S. B. McFarlane and J. Lomartire, U. S. Patent 2,513,504; *Chem. Abstr.*, **44**, 8944a (1950).

(6) A. Muller, E. Funder-Fritzsche, A. Müller, E. Funder-Fritzsche, W. Konar, and E. Rintersbacker-Wlasak, *Monatsh.*, **84**, 1206 (1953).

(7) W. Reppe and H. Kroper, German Patent 703,956; *Chem. Abstr.*, **36**, 10506 (1942).

(8) C. L. Butler and L. H. Cretcher, *J. Am. Chem. Soc.*, **54**, 2987 (1932).