[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STATE UNIVERSITY OF IOWA]

Some Observations on the Reductions of Acylhydrazines, Amides and Related Compounds with Lithium Aluminum Hydride[1]

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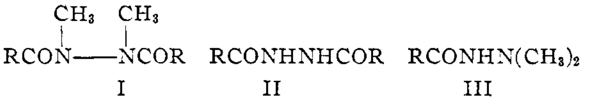
The slowness of the reductions of acylhydrazines containing the group –CONH– as opposed to the rapid reductions of acylhydrazines containing the group –CONR– is ascribed to the formation of an unreactive complex of the functional group with some form of the reducing agent, $-\overset{\overset{\ominus}{\text{OAlH}_3}}{\overset{|}{\text{C}}}{=}\text{N}-$, analogous to the formation of an aluminum enolate $-\overset{\overset{\ominus}{\text{OAlH}_3}}{\overset{|}{\text{C}}}{=}\text{C}<$, which resists attack by lithium aluminum hydride. Of four compounds studied, $C_6H_5CO\overset{\overset{CH_3}{|}}{N}NH_2$, $C_6H_5CO\overset{\overset{C_6H_5}{|}}{N}NH_2$, $C_6H_5CONHN(CH_3)_2$ and $C_6H_5CONHNH_2$, only the first two were reduced by the hydride to the corresponding hydrazines, thereby demonstrating that the replacement of an active hydrogen associated with the functional group is accompanied by deactivaton of the functional group toward lithium aluminum hydride. To determine the importance of the charge in the proposed intermediate, a related neutral compound, ethyl N-ethylbenzimidate, was treated with lithium aluminum hydride in refluxing tetrahydrofuran. Reduction was incomplete after 3 hr. From these and other results two related series of functional groups are arranged in order of decreasing reactivity toward lithium aluminum hydride.

From a comparison of the ease of reduction of mono- and diacylhydrazines of types I, II and III, by lithium aluminum hydride, it has been suggested that an acylhydrazine, which has a hydrogen on the



$$\underset{\text{I}}{\text{RCO}\overset{\overset{CH_3}{|}}{N}\text{——}\overset{\overset{CH_3}{|}}{N}\text{COR}}\qquad\underset{\text{II}}{\text{RCONHNHCOR}}\qquad\underset{\text{III}}{\text{RCONHN(CH}_3)_2}$$

acyl-substituted nitrogen ($-\overset{\overset{O}{\|}}{C}-\overset{\overset{H}{|}}{N}-$, types II and III) will be reduced more slowly by the hydride than will an acylhydrazine which lacks this structural feature (type I).[2] A similar, though less sharply defined, relationship between the structures of amides and their ease of reduction by lithium aluminum hydride has been reported.[3] In the latter investigation it was found that disubstituted amides ($RCONR_2$) are reduced more rapidly by the hydride in 30% excess than are monosubstituted amides in the presence of a 200–250% excess of the reducing agent. The authors attribute the slowness of the reductions of mono- and unsubstituted amides to the formation of slow-reacting complexes "by the action of (the hydride) on the hydrogen atoms attached to nitrogen." Since the previous investigations involved compounds containing the group –CONH– and others containing no active hydrogens, it was the purpose of the present work to determine whether the slowness of reduction in the presence of –CONH– is simply the result of complex formation which occurs on replacement of an active hydrogen, or whether some other affect is operating.

It is well-known that the rapid and usually quantitative replacement of an active hydrogen by reaction with lithium aluminum hydride is accompanied by the evolution of hydrogen gas and the formation of a complex between the substrate and some form of the reducing agent. The reduction of a functional group in the substrate may be hindered or entirely prevented by the precipitation of the complex.[4] The insolubility of the organic starting material may also contribute to long reaction times. At first sight the formation of a heterogeneous reaction mixture because of either of these factors would seem to explain the order of reactivity observed for acylhydrazines[2] and for amides.[3] Mono- and diacylhydrazines of types II and III as well as mono- and unsubstituted amides are usually less soluble in the customary solvents (ether, tetrahydrofuran, etc.). Since these types of compounds all have replaceable hydrogens, they are particularly prone to form complexes. That other factors are also involved, however, is suggested by the observations that some acylhydrazines (ethyl hydrazodicarboxylate and 1-benzoyl-2,2-dimethylhydrazine) react slowly or not at all in essentially homogeneous solution,[2,5] while others (*e.g.*, 1,2-diformyl-1,2-dimethylhydrazine[6]) are reduced rapidly in heterogeneous media.

Other examples can be cited to show that lithium aluminum hydride can be an effective reducing agent despite the insolubility of the substrate or the formation of an insoluble complex, although these factors may decrease its efficacy. Thus, powdered amino acids, though insoluble in tetrahydrofuran, are reduced in 1 to 3 hr. in that solvent to amino alcohols, which are obtained in 70–90% yields.[7] The three replaceable hydrogens in the amino acid provide ample opportunity for complex formation. Particularly pertinent to the present investigation are the reductions to the corresponding hydrazino alcohols of ethyl α-hydrazinopropionate and ethyl α-hydrazinocaproate,[8] each of which contains three active hydrogens. Ninety minutes of refluxing the caproate with lithium aluminum hydride in 50% excess, followed

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(1) Presented in part at the Minneapolis Meeting of the American Chemical Society, September 16, 1955.

(2) R. L. Hinman, THIS JOURNAL, **78**, 1645 (1956).

(3) V. M. Mićović and M. L. Mihailović, *J. Org. Chem.*, **18**, 1190 (1953).

(4) W. G. Brown in R. Adams' "Organic Reactions," Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951, p. 469.

(5) The small quantity of insoluble gray material from the unfiltered solution of lithium aluminum hydride is ignored in referring to the reaction mixture as "essentially homogeneous."

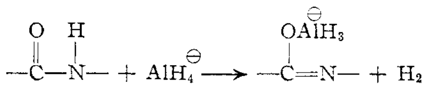
(6) J. B. Class, J. G. Aston and T. S. Oakwood, THIS JOURNAL, **75**, 2937 (1953).

(7) O. Vogl and M. Pöhm, *Monatsh.*, **84**, 1097 (1953).

(8) G. Gever, THIS JOURNAL, **76**, 1283 (1954).

by standing overnight at room temperature, gave 2-hydrazino-1-hexanol in 44% yield.

Since active hydrogens are replaced in all of these examples, the slow reductions of compounds containing the group –CONH– must be ascribed to inactivation of the functional group by a mechanism peculiar to compounds containing this group. Assuming that replacement of the active hydrogen is the first reaction which occurs, inactivation may come about as shown in the following equation

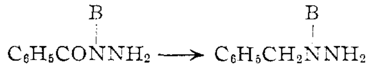


$$-\overset{\overset{\displaystyle O}{\|}}{C}-\overset{\overset{\displaystyle H}{|}}{N}- + AlH_4^{\ominus} \longrightarrow -\overset{\overset{\displaystyle OAlH_3^{\ominus}}{|}}{C}=N- + H_2$$

IV

The complex IV resembles that of an enolate ion $-\overset{\overset{\displaystyle OAlH_3}{|}}{C}\overset{\ominus}{=}C<$ which is reported to resist attack by lithium aluminum hydride.[4,9] If the complex IV also resists reduction, the addition of water at the end of the reaction would regenerate the original functional group. Only the enol-form of an enol-keto pair suffers replacement of the hydrogen by lithium aluminum hydride to yield the unreactive enolate ion. The relative percentages of the tautomers may therefore control the amount of reduction which will occur. Although the 1,2-diacylhydrazines of type II may exist partly in the lactim form,[10] the position of the hydrogen is unimportant, since it will react with the hydride whether it is attached to oxygen or to nitrogen.[9c] In either case the product can be represented by IV or as $-\overset{\overset{\displaystyle O^{(-)}}{\|}}{C}-\overset{(-)}{N}-$ to which IV is the principal contributing structure.

To gain additional evidence bearing on this hypothesis a series of benzoylhydrazines was prepared, containing active hydrogens on one or both of the two nitrogens. 1-Benzoyl-1-methylhydrazine (V) and 1-benzoyl-1-phenylhydrazine (VI) have replaceable hydrogens, but do not contain the –CONH– group and therefore cannot yield an intermediate of type IV. 1-Benzoyl-2,2-dimethylhydrazine (VII) contains this group but has no other active hydrogens. Benzhydrazide (VIII) has active hydrogens of both types. The results of their reactions with lithium aluminum hydride are compared in Table I. Only V and VI underwent reduction to a detectable extent.



$$C_6H_5CO\overset{\overset{\displaystyle B}{|}}{N}NH_2 \longrightarrow C_6H_5CH_2\overset{\overset{\displaystyle B}{|}}{N}NH_2$$

B = CH_3, or C_6H_5. IX

The products, 1-benzyl-1-methylhydrazine (IX, B = CH_3) and 1-benzyl-1-phenylhydrazine (IX, B = C_6H_5), respectively, were identified by conversion to hydrazones of aromatic aldehydes, thereby confirming the presence of an $-NH_2$ group in each hydrazine. The results are particularly striking in view of (1) the use of smaller excesses of the hydride with V and VI and (2) the formation of precipitates in both of these cases during the mixing of the reactants, but not with VII and VIII. That replacement of hydrogen occurred in each experiment was demonstrated by the evolution of hydrogen gas.

TABLE I

REDUCTION OF ACYLHYDRAZINES BY LITHIUM ALUMINUM HYDRIDE IN TETRAHYDROFURAN

	Reaction time, hr.	Yield of alkylhydrazine, %	Excess LiAlH₄, %	Solubility[a]	Homogeneity[b]	Starting material recovered, %
$C_6H_5CO\overset{\overset{\displaystyle CH_3}{|}}{N}NH_2$(V)	3	55	38	S	P	[c]
$C_6H_5CO\overset{\overset{\displaystyle C_6H_5}{|}}{N}NH_2$(VI)	3	45	43	S	P	[c]
$C_6H_5CONHN(CH_3)_2$ (VII)	4	0	100	S	H	70
$C_6H_5CONHNH_2$ (VIII)	3	0	100	S	H	80

[a] S = acylhydrazine soluble in tetrahydrofuran. [b] P = precipitate formed as reactants were mixed. H = homogeneous reaction mixture. [c] A small quantity of unidentified material was isolated, but no starting material was found.

These results provide convincing evidence for the formation of an unreactive product of the aluminum enolate type in the reactions of lithium aluminum hydride with acylhydrazines containing the group –CONH–. This concept can be extended to explain the sluggishness of mono- and unsubstituted amides as compared with disubstituted amides.[3] While the inactivation of the functional group is an important factor in retarding reduction, the affects of heterogeneity of the reaction mixture cannot be ignored. The latter will frequently hinder reduction also. In the reductions of V and VI, for example, it is likely that the yields would have been higher had the reaction mixtures remained homogeneous.

Since IV contains a carbon–nitrogen double bond, which is known to undergo reduction by lithium aluminum hydride in such compounds as azines,[11] hydrazones[6] and Schiff bases,[12] it was of interest to determine whether the slowness of reduction is characteristic of a group which bears an oxygen on the carbon of the carbon–nitrogen double bond, or whether the negative charge is primarily responsible for retarding the rate. To this end a representative imido ester, ethyl N-ethylbenzimidate (X), was prepared and treated with lithium aluminum hydride in refluxing tetrahydrofuran. After 3 hr. benzylethylamine (XI) was isolated in 49% yield, and about 10% of the starting material was recovered. (The hydride was used in 20% excess of that required for conversion of the imido ester to the amine.)

It seems likely that the reaction proceeds by an initial reduction of the carbon–nitrogen double bond giving an intermediate from which the ethoxy group is then cleaved by the reducing agent as

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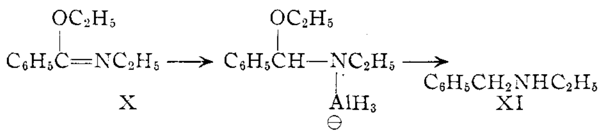
[9] (a) W. G. Dauben and J. F. Eastham, THIS JOURNAL, **75**, 1718 (1953); (b) A. S. Dreiding and J. A. Hartman, *ibid.*, **75**, 939 (1953); (c) F. A. Hochstein, *ibid.*, **71**, 305 (1949).

[10] (a) H. T. Hayes and L. Hunter, *J. Chem. Soc.*, 332 (1940); (b) F. Arndt, L. Loewe and L. Ergener, *Rev. Faculté Sci. de l'Université d' Istanbul*, **XIII**, 103 (1948).

[11] R. Renaud and L. C. Leitch, *Can. J. Chem.*, **32**, 545 (1954).

[12] R. N. Castle, D. L. Aldous and M. Hall, *J. Am. Pharm. Assoc.*, **42**, 435 (1953).



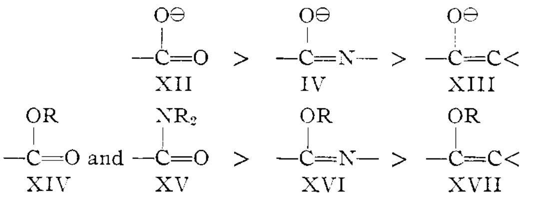
$$\underset{\text{X}}{C_6H_5\overset{\overset{OC_2H_5}{|}}{C}{=}NC_2H_5} \longrightarrow C_6H_5\overset{\overset{OC_2H_5}{|}}{C}H-\underset{\underset{\underset{\ominus}{AlH_3}}{|}}{N}C_2H_5 \longrightarrow \underset{\text{XI}}{C_6H_5CH_2NHC_2H_5}$$

shown in the equation. This is in accord with the observation that lithium aluminum hydride cleaves the $-\overset{|}{N}-\underset{|}{\overset{|}{C}}-O-$ group at the carbon–oxygen bond.[13] That reduction of the carbon–nitrogen double bond is the slower step was revealed by an experiment in which X (which requires two equivalents of hydride for reduction to the amine) was treated with 1.3 equivalents of hydride. Very little hydride remained at the end of the 3-hour reaction period, and only X (26%) and XI (37%) were isolated. No material with the properties of $C_6H_5CH(OC_2H_5)NHC_2H_5$ was found, although the products were heated with dilute acid and then examined for benzaldehyde. In addition, it has been reported that when N-(α-ethoxybenzyl)-acetanilide stands in an ethereal solution of the hydride for 1 hr. at room temperature, N-benzyl-N-ethylaniline is formed in 88% yield.[14]

That the carbon–nitrogen double bond of X is reduced more slowly than the carbon–oxygen double bond of an ester[15] or disubstituted amide[3] of comparable structure, may be due to the lower electronegativity of nitrogen and to the accession of electrons from the oxygen to the carbon–nitrogen double bond. The nitrogen of the double bond can also partly satisfy its demands for electrons by obtaining the latter from the attached alkyl group. These factors would all decrease the polarity of the double bond, making it less susceptible to attack by $AlH_4^{\ominus}$. The reductions of Grignard reagent–nitrile adducts and of N-(1-phenylpropyl)-1-phenylpropylideneimine (which is apparently formed in the reduction of the propionitrile–phenylmagnesium bromide adduct) are also slow.[16] In these cases, too, nitrogen can draw electrons from the bond to magnesium or to the alkyl group.

The tendency of the carbon–nitrogen double bond to resist attack by nucleophilic agents is also revealed in the stability of Schiff bases in aqueous alkali.[17] Similarly, compound X was recovered unchanged after 7 hr. of refluxing with 25% sodium hydroxide. From 4 hr. of refluxing with potassium hydroxide in 69% ethanol, 21% of X was obtained, together with N-ethylbenzamide (25% yield). Compound X also failed to react under the conditions of the hydroxamic acid test for esters,[18] in which hydroxylamine or $\overset{\ominus}{N}HOH$[19] is the nucleophilic agent.

From these studies the relative reactivities toward lithium aluminum hydride of two series of functional groups can be organized. The first series is that of anions of type IV, which resemble enolate ions XIII, but also resemble carboxylate ions XII. From the experiments previously described[2-4] the indicated relationship is derived. This is the same order that would be predicted solely on the basis of the polarity of the carbon of the functional group.



$$\underset{\text{XII}}{-\overset{\overset{O^{\ominus}}{|}}{C}{=}O} > \underset{\text{IV}}{-\overset{\overset{O^{\ominus}}{|}}{C}{=}N-} > \underset{\text{XIII}}{-\overset{\overset{O^{\ominus}}{|}}{C}{=}C<}$$

$$\underset{\text{XIV}}{-\overset{\overset{OR}{|}}{C}{=}O} \text{ and } \underset{\text{XV}}{-\overset{\overset{NR_2}{|}}{C}{=}O} > \underset{\text{XVI}}{-\overset{\overset{OR}{|}}{C}{=}N-} > \underset{\text{XVII}}{-\overset{\overset{OR}{|}}{C}{=}C<}$$

Closely related to the anions XII, IV and XIII, are carboxylic esters XIV, imido esters XVI and enol ethers XVII, respectively. Another related group is that of the disubstituted amides XV. The experimental evidence[3,4,20] reveals the order shown.[21]

It should be noted also that the first two members of the series of anions are frequently less reactive than are their neutral counterparts in the second series. This is supported by the many observations that carboxylic acids are reduced less readily than esters[22] and by a comparison of the ease of reduction of mono- and unsubstituted amides with that of ethyl N-ethylbenzimidate. Although this order of reactivity (for acids and esters) has been ascribed to the use of heterogeneous media in reduction,[22] in at least one instance, the reduction of methyl phthalate, preferential reduction of the ester group occurred *only* when *no* precipitate formed.[23] It is likely that careful examination of reaction conditions will reveal many other reactions in which free acids are reduced more slowly than esters in homogeneous media, although the effect of operating in a heterogeneous medium cannot be ignored. The slowness of reduction may be the result of repulsion of $\overset{\ominus}{AlH_4}$ by the anion to be reduced or it may be that the hybrid character of the anions stabilizes them relative to the esters.[24] The orders of reactivity are also supported by the

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(13) N. G. Gaylord, *Experientia*, **10**, 351 (1954).

(14) A. W. Burgstahler, THIS JOURNAL, **73**, 3021 (1951).

(15) Ref. 4, p. 477.

(16) A. Pohland and H. R. Sullivan, THIS JOURNAL, **75**, 5898 (1953).

(17) N. V. Sidgwick, "The Organic Chemistry of Nitrogen," 2nd Ed., The Clarendon Press, Oxford, England, 1937, p. 65.

(18) R. E. Buckles and J. C. Thelen, *Anal. Chem.*, **22**, 676 (1950).

(19) E. R. Alexander, "Principles of Ionic Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 165.

(20) Enol ethers have been used to protect carbonyl groups from reduction, as have thio-enol ethers. For the former see C. Meystre and K. Miescher, *Helv. Chim. Acta*, **32**, 1758 (1949), and C. Meystre and A. Wettstein, *ibid.*, **32**, 1978 (1949). For thio-enol ethers see G. Rosenkranz, St. Kaufmann and J. Romo, THIS JOURNAL, **71**, 3689 (1949).

(21) It is assumed that the steric and electronic environment of molecules under consideration will be comparable. Should either or both of these factors be markedly different in two molecules, the order of reactivity may be different from that stated above. Thus, reduction of an isocyanate, which is complete in 0.5–2 hours (A. E. Finholt, C. D. Anderson and C. L. Agre, *J. Org. Chem.*, **18**, 1338 (1953)), probably proceeds through an intermediate similar to IV: $C_6H_5N{=}C{=}O \rightarrow C_6H_5N{=}\overset{\ominus}{CHOAlH_3}$. However, the absence of hindering groups about the double bond probably facilitates further reaction. Another example is the rapid reduction of benzoxazole to *o*-methylaminophenol (N. G. Gaylord, Abstracts of Papers, 128th Meeting of the American Chemical Society, Minneapolis, Minn., September, 1955, p. 71-O).

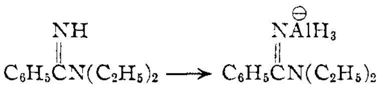
(22) Ref. 4, p. 478.

(23) E. L. Eliel, A. W. Burgstahler, D. E. Rivard and L. Haefele, THIS JOURNAL, **77**, 5092 (1955).

(24) These arguments also apply to enols and their ethers, although no differences in reactivity have been reported. It is likely that they are both so unreactive that gross differences of the type discussed here will not be observed.

observation that an ester is reduced more rapidly than is a monosubstituted amide (*i.e.*, XIV > IV) in the same compound, as in the selective reduction of the methyl ester of dibenzoylhistidine to monobenzoylhistidinol.[25]

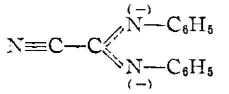
Another class of closely related compounds is that of the amidines. On the basis of the polarity of the carbon of the functional group, an amidine would be expected to undergo reduction somewhat less rapidly than an imido ester of similar structure. The behavior of N,N-diethylbenzamidine (XVIII) has been reported.[26] After 20 hr. of refluxing in ether, benzylamine was isolated in 15% yield, and 75% of the amidine was recovered. Although at first sight this seems to support the view that a carbon–nitrogen double bond is reduced more slowly than a carbon–oxygen double bond, the presence of a replaceable hydrogen in the functional group must again be taken into account. Undoubtedly replacement of the hydrogen will be the first reaction, yielding XIX which is the substance actually undergoing reduction. For this reason XVIII is not an entirely suitable example for comparison with the other types of compounds which are neutral. For the same reason the comparison of the reduction of XVIII to the reduction of N,N-diethylbenzamide[26] is of doubtful validity.



$$C_6H_5\overset{\overset{\displaystyle NH}{\|}}{C}N(C_2H_5)_2 \longrightarrow C_6H_5\overset{\overset{\displaystyle \overset{\ominus}{N}AlH_3}{\|}}{C}N(C_2H_5)_2$$

XVIII XIX

The reaction of a large excess of lithium aluminum hydride with N,N′-diphenyl-α-cyanoformamidine resulted in the reduction of the cyano group while the amidine function was essentially unaffected.[27] Here again, the substance actually undergoing reduction must be the anion XX resulting from the rapid replacement of the active hydrogen.



XX

Such a fragment would be highly stabilized toward attack by the reducing agent for the reasons discussed above.

Experimental[28]

Preparation of Acylhydrazines.—The acylhydrazines were prepared by known methods. Benzhydrazide was obtained from the reaction of ethyl benzoate and 85% hydrazine hydrate in ethanol solution.[29] 1-Benzoyl-2,2-dimethylhydrazine was prepared by the method described in the previous paper in this series.[2] 1-Benzoyl-1-methylhydrazine was prepared by a modification of the method of Michaelis and Hadanck.[30] The product was obtained as a pale yellow oil, soluble in water, boiling ether and cold benzene. From the treatment of a small portion with benzaldehyde and a trace of glacial acetic acid white needles were obtained, m.p. 84–85° after crystallization from pet. ether (b.p. 60–70°); (reported m.p. of 1-methyl-1-benzoyl-2-benzylidenehydrazine, 82°).[30]

Variations in the method of Michaelis, such as the use of dimethylformamide as a solvent for benzoic anhydride or the addition of sodium hydroxide or sodium carbonate prior to or during the addition of benzoic anhydride, resulted in the formation of a white solid, m.p. 138–142° (crude), which was probably 1,2-dibenzoyl-1-methylhydrazine (lit.[30] m.p. 145°). From a melt of equimolar quantities of methylhydrazine sulfate and benzamide[31] the same product was obtained in low yield. This result is readily explained, since 1-benzoyl-1-methylhydrazine is converted to methylhydrazine and 1,2-dibenzoyl-1-methylhydrazine on attempted distillation.[30]

1-Benzoyl-1-phenylhydrazine.—Prepared by the method of Lockemann,[32] it could not be induced to crystallize. Conversion of the impure oil to the sulfate which was washed once with cold ethanol and four times with ether and recrystallized from water gave white needles, m.p. 193–194° dec. (lit.[33] 191° dec.). Warming the pure salt with a saturated solution of sodium carbonate yielded the free base, which crystallized when the solution was cooled. Two recrystallizations from 30% ethanol yielded white needles of 1-benzoyl-1-phenylhydrazine, m.p. 65–67° (lit.[32] 69–70°). 1-Benzoyl-1-phenyl-2-benzylidenehydrazine, prepared from the product above, melted at 114–115° after one recrystallization from 95% ethanol (lit.[34] 114°).

Reactions with Lithium Aluminum Hydride.—The acylhydrazines in solution in tetrahydrofuran were added to a solution of lithium aluminum hydride in the same solvent; the general procedure and work-up were similar to that described previously.[2] 1-Benzoyl-2,2-dimethylhydrazine, which was recovered unchanged, was identified by the undepressed mixed m.p. with an authentic sample. Benzhydrazide, which was also recovered unchanged, was identified as 1-benzoyl-4-phenylthiosemicarbazide, m.p. and mixed m.p. with an authentic specimen 163–165° (lit.[35] 166–167°). The disposition of the products from the reductions of V and VI is described in more detail.

1-Benzyl-1-methylhydrazine.—Hydride: 4.0 g. (0.11 mole) in 100 ml. of solvent; 1-benzoyl-1-methylhydrazine: 11.5 g. (0.08 mole) in 75 ml. of solvent. Distillation of the crude product under reduced pressure gave 5.7 g. (55%) of colorless liquid, b.p. 119–122° (34–36 mm.). Since the residual oil was insoluble in water, it was not starting material. For identification a portion of the distillate was converted to the 1-benzoyl-1-methylhydrazone of *p*-nitrobenzaldehyde. The orange crystals melted at 103–105° after two crystallizations from absolute ethanol, one from a 4:1 mixture of pet. ether (b.p. 60–70°), and benzene, and a final crystallization from absolute ethanol.

Anal. Calcd. for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.62; N, 15.61. Found: C, 66.89; H, 5.36, N, 15.49.

1-Benzyl-1-methyl-4-phenylthiosemicarbazide was also prepared, m.p. 145–146.5° after one crystallization from 95% ethanol and two from a mixture of benzene and cyclohexane (4:1).

Anal. Calcd. for $C_{15}H_{17}N_3S$: C, 66.37; H, 6.32; N, 15.49. Found: C, 66.05; H, 6.09; N, 15.89.

1-Benzyl-1-phenylhydrazine.—Hydride: 1.2 g. (0.03 mole) in 50 ml. of solvent; 1-benzoyl-1-phenylhydrazine (VI): 4.5 g. (0.021 mole) in 50 ml. of solvent. Distillation of the crude product gave 1.9 g. (45%) of pale yellow liquid, b.p. 124–127° (0.55 mm.).

Treatment of the product with benzaldehyde gave a hydrazone, m.p. and mixed m.p. with an authentic sample 108–109° (lit.[36] 111°). A mixture of this hydrazone and 1-benzoyl-1-phenyl-2-benzylidenehydrazine (the benzaldehyde derivative of the starting material) melted from 83–95°.

1-Benzoyl-1-phenyl-2-(*o*-nitrobenzylidene)-hydrazine was also prepared, m.p. and mixed m.p. with an authentic specimen 106–107° (lit.[37] 105–106°).

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[25] P. Karrer, M. Suter and P. Waser, *Helv. Chim. Acta*, **32**, 1936 (1949).

[26] R. T. Gilsdorf and F. F. Nord, THIS JOURNAL, **74**, 1885 (1952).

[27] G. Ehrensvard and R. Stjernholm, *Acta Chem. Scand.*, **3**, 971 (1949).

[28] M.p.'s and b.p.'s are uncorrected.

[29] R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," Ed. III, John Wiley and Sons, Inc., New York, N. Y., 1948, p. 186.

[30] A. Michaelis and E. Hadanck, *Ber.*, **41**, 3285 (1908).

[31] A. Galat, THIS JOURNAL, **65**, 1566 (1943).

[32] G. Lockemann, *Ber.*, **43**, 2226 (1910).

[33] A. Michaelis and F. Schmidt, *ibid.*, **20**, 1713 (1887).

[34] R. Walther, *J. prakt. Chem.*, [2] **53**, 463 (1896).

[35] M. Busch, E. Opfermann and H. Walther, *Ber.*, **37**, 2330 (1904).

[36] A. Michaelis and B. Philips, *Ann.*, **252**, 289 (1889).

[37] L. Vecchiotti, *Gazz. chim. ital.*, **43**, [II] 637 (1913).

The authentic sample of 1-benzyl-1-phenylhydrazine was obtained from the reaction of benzyl chloride and phenylhydrazine.[38]

N-Ethylbenzimido Chloride.—This substance was obtained in 80% yield by the method of von Braun and Pinkernelle.[39]

Ethyl N-Ethylbenzimidate.—The product, obtained in 71% yield by the method of Landers,[40] was a colorless liquid, b.p. 101–102° (12 mm.), n^{24}_{D} 1.5020, d^{20}_{4} 0.960 (b.p. lit.[40] 105° (11 mm.)).

Hydroxamic Acid Test.—When the test was carried out as described by Buckles and Thelen[18] for esters (Test B in their paper), a pale yellow solution was obtained, as is customary in a negative result.

When X was heated with 20% hydrochloric acid for a few seconds, the mixture became homogeneous, then separated again into layers with an accompanying wintergreen-like odor of ethyl benzoate. Subjection of the new organic layer to Test B of Buckles and Thelen resulted in a strong wine color, a positive test for the presence of an ester. Since imido esters are readily converted to esters of carboxylic acids by the action of mineral acids,[40] these observations confirmed the structure of X.

When X was heated with hydroxylamine hydrochloride for a few seconds, the odor of ethyl benzoate was detected and a positive result was observed on application of Test B.

In a hydroxamic acid test employing the higher-boiling propylene glycol as the solvent,[41] X gave a positive result.

Reaction of Ethyl N-Ethylbenzimidate (X) with Lithium Aluminum Hydride.—The procedure was similar to that previously described.[2] Hydride: 2.3 g. (0.06 mole) in 100 ml. of dry tetrahydrofuran; X: 17.7 g. (0.1 mole) in 75 ml. of tetrahydrofuran. At the boiling point the initially colorless solution assumed a yellow-green hue, which disappeared on cooling the reaction mixture at the end of the 3-hr. reflux period. From distillation of the crude material through a short Vigreux column two products were obtained. The lower boiling material, b.p. 82–85° (11 mm.), had the properties of N-benzyl-N-ethylamine (XI) (lit.[42] b.p. 82–83° (15 mm.)). The yield was 6.6 g. (49%).

Treatment of a sample in pet. ether (b.p. 60–70°), with phenyl isothiocyanate, yielded white crystals. After one crystallization from a mixture of benzene and pet. ether (b.p. 60–70°) and three crystallizations from alcohol-water mixtures, the white needles melted at 94–95° and had the composition of N-benzyl-N-ethyl-N′-phenylthiourea.

Anal. Calcd. for $C_{16}H_{17}N_2S$: C, 71.06; H, 6.71; N, 10.37. Found: C, 71.22; H, 6.42; N, 10.36.

The higher boiling product, b.p. 97–99° (10 mm.), n^{24}_{D} 1.5020, was starting material X.

Anal. Calcd. for $C_{11}H_{15}NO$: N, 7.91. Found: N, 8.22.

It gave a negative result with the hydroxamic acid test, but on warming a sample with dilute hydrochloric acid the odor of ethyl benzoate appeared, and after being made basic, the mixture gave a positive test for the presence of an ester. Although 1.2 g. (7%) of pure material was isolated in the last fraction of the distillation, the presence of X in each of the intermediate fractions was revealed by the odor of ethyl benzoate detected when a sample of each fraction was warmed with dilute hydrochloric acid. From the refractive indexes it is estimated that at least 3% of X was present. The hold-up from the distillation also yielded the odor of wintergreen on treatment with acid and probably consisted mainly of X. Thus the total quantity of unreacted X is at least 10% of that used in the reaction.

The Behavior of Ethyl N-Ethylbenzimidate (X) in Base. (a) Aqueous Sodium Hydroxide.—A heterogeneous mixture of 40 ml. of 25% sodium hydroxide solution and 5 ml. (4.8 g.) of X was refluxed for 7 hr., cooled and extracted thrice with 25-ml. portions of ether. No precipitate formed when the aqueous solution was acidified with 20% hydrochloric acid. The combined, dried ether extracts were distilled, yielding 3.0 g. of X (63% recovery). The hold-up also contained X.

(b) Potassium Hydroxide in Aqueous Ethanol.—X (4.8 g.) was dissolved in a solution of 8 g. of potassium hydroxide in 55 ml. of 69% ethanol and boiled under reflux for 4 hr. The cooled solution was poured into 100 ml. of water and then extracted thrice with 25-ml. portions of ether. No precipitate was obtained when the aqueous solution was acidified. Distillation of the combined, dried extracts yielded 1.0 g. (21%) of X and 1.0 g. (25%) of colorless liquid, b.p. 159–161° (11 mm.). The latter crystallized on standing and melted at 68–69°. Its mixture with N-ethylbenzamide (m.p. 69–71°) melted at 69–71°.

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[38] G. Minunni, *ibid.*, **22** [II], 217 (1892).

[39] J. v. Braun and W. Pinkernelle, *Ber.*, **67B**, 1218 (1934).

[40] G. D. Landers, *J. Chem. Soc.*, **83**, 320 (1903).

[41] S. Soloway and A. Lipschitz, *Anal. Chem.*, **25**, 898 (1952).

[42] W. Schlenk and E. Bergmann, *Ann.*, **463**, 281 (1928).

[CONTRIBUTION FROM THE UNIVERSITY OF CALIFORNIA, RADIATION LABORATORY, LIVERMORE SITE]

Some Methylhydrazonium Salts; An Improved Synthesis of Tetramethylhydrazine[1]

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1,1-Dimethyl-2-formylhydrazine, 1-formyl-1,2,2-trimethylhydrazine, pentamethylhydrazonium iodide and bromide, 1-formyl-2,2,2-trimethylhydrazonium iodide and 1-formyl-1,2,2,2-tetramethylhydrazonium iodide have been synthesized. A new synthesis of trimethylhydrazine and tetramethylhydrazine is reported.

Although tri-[2] and tetra-[3] methylhydrazonium salts have been known for some time, the preparation of the pentamethyl salts has not been reported due, no doubt, to the inability of earlier workers to prepare the necessary precursor, tetramethylhydrazine, the synthesis of which has only recently been reported.[4] Various attempts to prepare pentamethylhydrazonium salts from other precursors have been unsuccessful. Direct alkylation of hydrazine with methyl halides, methyl *p*-toluenesulfonate, trimethyl phosphate or trimethyl phosphite produced only trimethylhydrazonium salts.[2,5] Likewise alkylation of *sym*-dimethylhydrazine produced tetramethylhydrazonium salts.[3] Attempted alkylation of trimethylhydrazonium iodide with methyl iodide resulted in cleavage of the N–N bond to produce tetramethylammonium iodide.[2]

The work of Class, Aston and Oakwood[4] has now made available the necessary tetramethylhydrazine, but their method is erratic and affords

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[1] This work was performed under the auspices of the Atomic Energy Commission, Contract W-7405-eng-48.

[2] C. Harries and T. Haga, *Ber.*, **31**, 56 (1898).

[3] H. Wieland and E. Schlamberg, *ibid.*, **53B**, 1329 (1920).

[4] J. B. Class, J. G. Aston and T. S. Oakwood, THIS JOURNAL, **75**, 2937 (1953).

[5] F. Klages, G. Nober, K. Kircher and M. Bock, *Ann.*, **547**, 1 (1941).