315° dec. An analytical sample was obtained from water, m.p. 310–315° dec., (lit.[4,5] m.p. 304, 303–305, 305–306). The ninhydrin reaction was positive for the product as indicated by a purple color.

Anal. Calcd. for $C_4H_8N_2O_4$: C, 32.43; H, 5.45; N, 18.91· Found: C, 31.98; H, 5.80; N, 18.45.

RIDGEFIELD, N. J.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

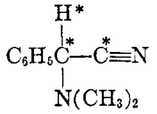
Reactions of α-Dimethylaminophenylacetonitrile and Its Ethylation Product with Basic or Nucleophilic Reagents[1]

GENE F. MORRIS AND CHARLES R. HAUSER

Received August 18, 1961

A study was made of the reactions of α-dimethylaminophenylacetonitrile (I) and its ethylation product (II) with basic or nucleophilic reagents including potassium amide, butyllithium, Grignard reagents, lithium aluminum hydride, and sodium. The reactions of I involved ionization of the α-hydrogen, addition to the nitrile carbon, and displacement of the nitrile group from the α-carbon; those of II occurred at the nitrile carbon and α-carbon. Some interesting comparisons are made between the reactions of phenylacetonitrile and aminonitrile I and between those of aminonitriles I and II.

α-Dimethylaminophenylacetonitrile (I) may be attacked by basic or nucleophilic reagents not only at the α-hydrogen or nitrile carbon as observed with phenylacetonitrile, but also at the α-carbon. Reactions involving each of these vulnerable positions, which are designated by asterisks in I, have been realized in the present investigation or previously as summarized in Table I.



$$C_6H_5\underset{N(CH_3)_2}{\overset{H^*}{\overset{*}{C}}}-\overset{*}{C}\equiv N$$

I

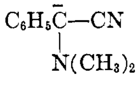
TABLE I

REACTIONS OF AMINONITRILE I WITH BASIC OR NUCLEOPHILIC REAGENTS[a]

Reagent	Position Attacked	Product Formed
KNH_2 (NH_3)[b]	α-Hydrogen	Carbanion I′
n-C_4H_9Li	α-Hydrogen Nitrile carbon	Carbanion I′ Amino ketone III
Prim. Alkyl-MgX[c] or C_6H_5MgBr[d]	α-Carbon	*t*-Amines IVa–e
t-C_4H_9MgCl	α-Carbon	Benzyldimethylamine
$LiAlH_4$	Nitrile carbon α-Hydrogen ?	Prim. amine VII Carbanion I′ ?
Na(NH_3)	α-Hydrogen α-Carbon or nitrile carbon	Carbanion I′ Benzyldimethylamine

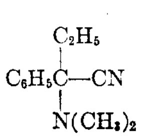
[a] Except where designated, the solvent was diethyl ether. [b] Ref. 3 and 4. [c] For result with benzylmagnesium chloride, see ref. 9. [d] Tetrahydrofuran.

Like phenylacetonitrile,[2] I is attacked exclusively at the α-hydrogen by potassium amide or sodium amide in liquid ammonia. This has recently been demonstrated by alkylation of the resulting carbanion I′ with benzyl[3] and alkyl[4] halides to form, for example, II.



$$C_6H_5\underset{N(CH_3)_2}{\bar{C}}-CN$$

I′



$$C_6H_5\underset{N(CH_3)_2}{\overset{C_2H_5}{C}}-CN$$

II

Ethylation to form II has now been employed to demonstrate ionization of the α-hydrogen of I by certain other reagents (see Table I), and II has served as the starting compound in the second phase of the present work (see Table III). Incidentally, carbanion I′ failed to condense with I under conditions similar to those used previously for the self-condensation of phenylacetonitrile.[5]

Also like phenylacetonitrile,[6] I is attacked partly at the α-hydrogen and partly at the nitrile carbon by *n*-butyllithium in ether. These two courses of reaction were demonstrated by ethylation of the reaction mixture, followed by hydrolysis with hot hydrochloric acid to form propiophenone and amino ketone III respectively (Equations 1a and 1b). Propiophenone has recently[4] been shown to be the product of acid catalyzed hydrolysis of aminonitrile II, which was formed as an intermediate in course 1a.

The yields of propiophenone and amino ketone III ranged from 21–42% and 34–39%, respectively. No other product was detected. The structure of amino ketone III was supported by its infrared

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(1) Supported by National Institutes of Health Grant CY-4455(C2).

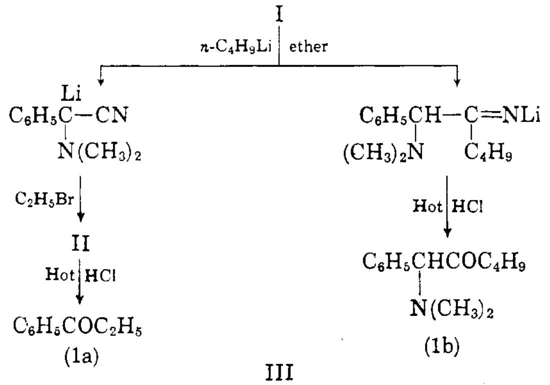
(2) C. R. Hauser and W. R. Brasen, *J. Am. Chem. Soc.*, **78**, 494 (1956).

(3) C. R. Hauser, H. M. Taylor, and T. G. Ledford, *J. Am. Chem. Soc.*, **82**, 1786 (1960).

(4) H. M. Taylor and C. R. Hauser, *J. Am. Chem. Soc.*, **82**, 1960 (1960).

(5) G. A. Reynolds, W. J. Humphlett, F. W. Swamer, and C. R. Hauser, *J. Org. Chem.*, **16**, 165 (1951).

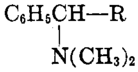
(6) See W. I. O'Sullivan, F. W. Swamer, W. J. Humphlett, and C. R. Hauser, *J. Org. Chem.*, **26**, 2306 (1961).



III

spectrum, which showed a strong band at 5.85 μ for the carbonyl group.[7]

However, unlike phenylacetonitrile, which is attacked at the α-hydrogen and nitrile carbon by Grignard reagents,[8] aminonitrile I is attacked by these reagents at the α-carbon to replace the nitrile group by the R group of the reagent. This type of reaction has been observed by Goodson and Christopher[9] with benzylmagnesium chloride to form tertiary amine IVa and by us with ethyl-, n-butyl-, phenyl-, and p-chlorobenzylmagnesium halides to give amines IVb–e, respectively. The yields were good to excellent. Several other α-dialkylaminophenylacetonitriles have been shown to react similarly with Grignard reagents.[10]



$\underset{N(CH_3)_2}{C_6H_5CH{-}R}$

IVa. R = $CH_2C_6H_5$
IVb. R = C_2H_5
IVc. R = n-C_4H_9
IVd. R = C_6H_5
IVe. R = $CH_2C_6H_4Cl$-p

In the earlier work[9,10] large excesses of the Grignard reagents were employed. We have found that, with only a 10% excess of analyzed ethylmagnesium iodide, I affords IVb in 85% yield, which appears to be about the maximum as none of I was recovered. The yield of IVb was approximately the same whether the reagent was added to I or I to the reagent. In Table II are summarized the yields of IVb and recovered I obtained with ethylmagnesium iodide on varying the proportions of reactants, the temperature, and the reaction period.

In this study with ethylmagnesium iodide, no detectable amount of ethane was evolved, showing that at least this Grignard reagent does not ionize the α-hydrogen of I. This may indicate that the α-hydrogen of I is less active than that of phenylacetonitrile, the α-hydrogen of which is ionized partly by such reagents.[8] The α-hydrogens of α-dimethylaminophenylacetic acid and the corresponding amide were suggested recently to be less active than those of phenylacetic acid and phenylacetamide, respectively.[11]

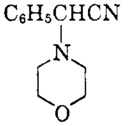
TABLE II

REACTION OF I WITH C_2H_5MgI TO FORM IVb

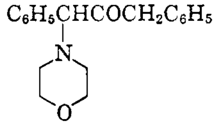
Mol. Eq., C_2H_5MgI	Temp.	Time, Hr.	Yield of IVb	Recovered I (%)
0.5	20	14	36	45
1.0	20	24	67	—[a]
1.0	35	2	48	—[a]
1.0	35	24	79	9
1.1	35	24	85	0

[a] Presumably some I remained as a distillation residue but it was not isolated.

Although Grignard reagents attack the α-carbon of I and probably also that of most other α-dialkylaminophenylacetonitriles,[9,10] benzylmagnesium chloride has been reported[9] to attack the nitrile carbon of certain of these types of compounds having oxygen in the dialkylamino portion of the molecule, for example, V, which affords VI. This was confirmed by us.



V



VI

In contrast to the primary Grignard reagents considered above, t-butylmagnesium chloride reacted with I to form benzyldimethylamine in 82% yield. This product presumably arose through the displacement of the cyanide ion of I by hydride ion to produce isobutylene as byproduct (Equation 2).

$$I \xrightarrow[\text{ether}]{t\text{-}C_4H_9MgCl} C_6H_5CH_2N(CH_3)_2 + CH_2{=}C(CH_3)_2 \quad (2)$$

This reaction was shown not to be accompanied by appreciable ionization of the α-hydrogen of I, as no propiophenone was obtained on treatment with ethyl bromide followed by acid (see Equation 1a). A little (5%) of I was recovered as benzaldehyde after the hydrolysis with acid.

Similar to phenylacetonitrile,[12] I was attacked partly at the nitrile carbon and apparently to some extent at the α-hydrogen by lithium aluminum hydride to give primary amine VII (45%) and hydrogen (26%). Other aminonitriles including the diethyl homolog of I have been reduced similarly.[13] Aminonitrile VIII, which has a less active α-hydrogen than I, has given the best reported yield (87%).[13b]

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(7) See L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, Wiley, New York, 1956, p. 249.

(8) C. R. Hauser and W. J. Humphlett, *J. Org. Chem.*, **15**, 359 (1950).

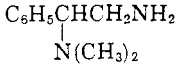
(9) L. H. Goodson and H. Christopher, *J. Am. Chem. Soc.*, **72**, 358 (1950).

(10) A. Christiaen, *Bull. soc. chim. Belg.*, **33**, 483 (1924); T. S. Stevens, J. M. Cowan, and J. MacKinnon, *J. Chem. Soc.*, 2568 (1931).

(11) G. F. Morris and C. R. Hauser, *J. Org. Chem.*, **26**, 4741 (1961).

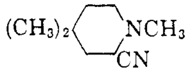
(12) L. M. Soffer and M. Katz, *J. Am. Chem. Soc.*, **78**, 1705 (1956).

(13) (a) Z. Welvart, *Compt. rend.*, **233**, 1121 (1951); **238**, 2536 (1954); **239**, 1299 (1954). (b) N. J. Leonard and F. Hauck, *J. Am. Chem. Soc.*, **79**, 5279 (1957).



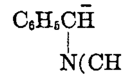
$C_6H_5\underset{N(CH_3)_2}{\underset{|}{C}}HCH_2NH_2$

VII



VIII

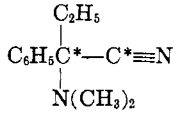
Also similar to phenylacetonitrile which has been reported[14] to be converted by sodium in liquid ammonia to its carbanion and toluene, I reacted with this reagent to give carbanion I′ and benzyldimethylamine (52–62%). The presence of I′ was established by ethylation to form II (27%). The benzyldimethylamine appears to have arisen through the intermediate formation of carbanion IX, which acquired a proton from the medium. This carbanion might have been formed through attack of the reagent on either the α-carbon or nitrile carbon of I. In the former course, the radical produced by displacement of cyanide ion would acquire an electron from sodium, and in the latter the resulting radical-ion or dianion would undergo β-elimination to form IX. The formation of carbanion I′ might have involved attack at the α-hydrogen of I by the reagent, by carbanion IX, or by amide ion generated in the reaction mixture.



$C_6H_5\underset{N(CH_3)_2}{\underset{|}{C}}\bar{H}$

IX

Next, a study was made of the action of the same group of nucleophilic reagents on aminonitrile II, which is a typical alkylation product of I. As II has no α-hydrogen, it can be attacked by such reagents at only the α-carbon or nitrile carbon. Reactions involving each of these vulnerable positions, which are designated by asterisks in II (see below), have been realized in the present investigation or previously as summarized in Table III.



$C_6H_5\overset{C_2H_5}{\overset{|}{\underset{N(CH_3)_2}{\underset{|}{C^*}}}}—C^*\equiv N$

II

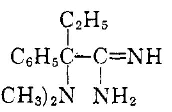
TABLE III

REACTIONS OF AMINONITRILE II WITH NUCLEOPHILIC REAGENTS[a]

Reagent	Position Attacked	Product Formed
KNH_2 (NH_3)	Nitrile carbon	Amidine X
n-C_4H_9Li or C_6H_5Li	Nitrile carbon	Imines XIIa–b
Prim. Alkyl-MgX[b]	α-Carbon	t-Amine XIV
t-C_4H_9MgCl[b]	α-Carbon	t-Amine IVb
$LiAlH_4$	α-Carbon or nitrile carbon	t-Amine IVb
Na (NH_3)	α-Carbon or nitrile carbon	t-Amine IVb

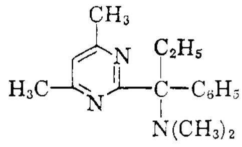
[a] Except where designated, the solvent was diethyl ether. [b] Ref. 4.

Whereas aminonitrile I was attacked exclusively at the α-hydrogen by potassium amide in liquid ammonia, aminonitrile II was attacked at the nitrile carbon by this reagent to form amidine X in 55% yield. This product was cyclized with acetylacetone to form pyrimidine XI in 30% yield, a type of reaction known to be characteristic of amidines.[15]



$C_6H_5\overset{C_2H_5}{\overset{|}{\underset{(CH_3)_2N}{\underset{|}{C}}}}—\underset{NH_2}{\underset{|}{C}}=NH$

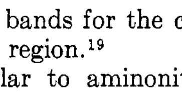
X



XI

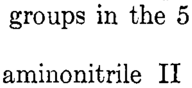
The amidine structure X was further supported by its infrared spectrum which showed a strong band at 2.9 μ for the N—H group[16] and at 6.13 μ for the C═N group.[17]

While aminonitrile I was attacked partly at the α-hydrogen and partly at the nitrile carbon by butyllithium, aminonitrile II was attacked at the latter position by this reagent and also by phenyllithium to form amino-imines XIIa and XIIb in yields of 55 and 70%, respectively. The imine groups of these products were hydrolyzed in good yields to give the amino ketones XIIIa and XIIIb, respectively.



$C_6H_5\overset{C_2H_5}{\overset{|}{\underset{(CH_3)_2N}{\underset{|}{C}}}}—\underset{R}{\underset{|}{C}}=NH$

XIIa. R = C_4H_9-n
XIIb. R = C_6H_5



$C_6H_5\overset{C_2H_5}{\overset{|}{\underset{(CH_3)_2N}{\underset{|}{C}}}}—\underset{R}{\underset{|}{C}}=O$

XIIIa. R = C_4H_9-n
XIIIb. R = C_6H_5

The structures XIIa–b were further supported by their infrared spectra, which showed strong bands for the N—H group in the 2.95–3.1 μ region[18] and for the C═N group at 6.1 μ.[17] The infrared spectra of the amino ketones XIIIa–b showed the expected strong bands for the carbonyl groups in the 5.86–5.95 μ region.[19]

Similar to aminonitrile I, aminonitrile II has recently[4] been shown to react with primary Grignard reagents to form tertiary amines of type XIV and with t-butylmagnesium chloride to give the hydride ion reduction product which would be tertiary amine IVb. In certain of the latter types of reaction, the olefinic by-product was also isolated.[4]

However, unlike aminonitrile I, which was re-

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(14) See L. H. Baldinger and J. A. Niewland, *J. Am. Chem. Soc.*, 55, 2851 (1933).

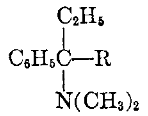
(15) See A. A. Morton, *The Chemistry of Heterocyclic Compounds*, McGraw-Hill, New York and London, 1946, p. 484.

(16) Ref. 7, p. 205.

(17) Ref. 7, p. 269. As no values are listed specifically for amidines, comparisons were made with amides (N—H) and (C═N).

(18) Ref. 7, p. 252.

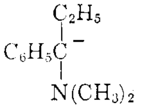
(19) Ref. 7, p. 132.



$$\mathrm{C_6H_5}\overset{\mathrm{C_2H_5}}{\underset{\mathrm{N(CH_3)_2}}{\mathrm{C}}}\mathrm{—R}$$

XIV

duced by lithium aluminium hydride, aminonitrile II was cleaved by this reagent to form amine IVb in 90% yield. This product might have arisen not only from the attack of hydride ion of the reagent on the α-carbon of I, but also through attack of hydride ion on the nitrile carbon followed by β-elimination to form carbanion XV, which acquired a proton in some manner. Aminonitrile XVI has previously been observed to undergo the analogous cleavage.[13b]



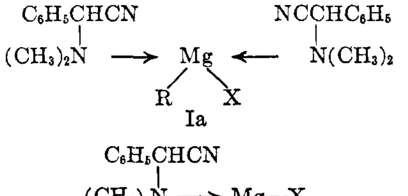
$$\mathrm{C_6H_5}\overset{\mathrm{C_2H_5}}{\underset{\mathrm{N(CH_3)_2}}{\mathrm{C}}}{}^{-}$$

XV

XVI

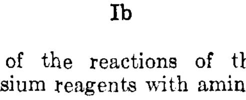
Finally, whereas only part of aminonitrile I was cleaved by sodium in liquid ammonia, essentially all of aminonitrile II was cleaved by this reagent to form amine IVb in 89% yield. This product appears to have arisen through the intermediate formation of carbanion XV, which acquired a proton from the medium. As with I (see above) this cleavage might have involved attack of the reagent on either the α-carbon or nitrile carbon. The higher yield of cleavage product from II than from I may be ascribed to the absence of an α-hydrogen in II.

Influence of metallic cation. The fact that butyllithium and the corresponding Grignard reagent react differently with the aminonitrile I or II indicates that the metallic cation of the reagent plays an important role in the course of the reaction.[20] Although both reagents might coordinate through their metallic cations with the amino nitrogen of I or II, only the Grignard reagent undergoes the rather unusual type of displacement of the nitrile group (see Tables I, II, and III). This appears to involve complexes Ia and/or Ib, the intermediate formation of which may be indicated by the immediate precipitation observed on mixing the reactants.



$$\begin{array}{ccccc} \mathrm{C_6H_5CHCN} & & & & \mathrm{NCCHC_6H_5} \\ | & & & & | \\ \mathrm{(CH_3)_2N} & \longrightarrow & \mathrm{Mg} & \longleftarrow & \mathrm{N(CH_3)_2} \\ & & \mathrm{R}\ \ \ \mathrm{X} & & \end{array}$$

Ia



$$\begin{array}{ccc} \mathrm{C_6H_5CHCN} & & \\ | & & \\ \mathrm{(CH_3)_2N} & \longrightarrow & \mathrm{Mg—X} \\ & & | \\ & & \mathrm{R} \end{array}$$

Ib

Recently[21] the analogous reactions of α-*N*,*N*-dimethylaminobenzyl *n*-butyl ether with Grignard reagents to give amines of type IV was suggested to involve the intermediate formation of the corresponding coordination complexes, that corresponding to Ib being assumed as the reactive intermediate. While Ib might be the reactive intermediate in the present reactions,[22] we have observed that conditions that should favor the formation of complex Ia still permit the reaction to proceed. Thus, addition of analyzed ethylmagnesium iodide to aminonitrile I in the ratio of 1:2 afforded amine IVb in about half the yield as that obtained when the ratio was 1:1 (see Table II).

EXPERIMENTAL[23]

α-Dimethylaminophenylacetonitrile (I). This compound, b.p. 76–78° at 0.8 mm, n_{D}^{25} 1.5116, was prepared in 94% yield from benzaldehyde and the appropriate reagents by the sodium bisulfite method as described recently.[11]

Reactions of I *with nucleophilic reagents.* A. *With potassium amide.* Aminonitrile I was converted to its carbanion I′ by potassium amide in liquid ammonia, and this carbanion was ethylated with ethyl bromide employing 0.8 mole each of the reactants in 800 ml. of liquid ammonia essentially as described recently[4] (0.2 mole scale, yield of II, 86%). There was obtained 137–140 g. (92–94%) of 2-*N*,*N*-dimethylamino-2-phenylbutyronitrile (II), b.p. 70–72° at 0.5 mm., n_{D}^{25} 1.5113. The infrared spectrum of this compound failed to show absorption in the 4.5 μ region for the nitrile group.[24]

In an attempt to effect self-condensation of I, a mixture of 0.10 mole of this compound and 0.05 mole of potassium amide in 400 ml. of liquid ammonia was stirred for 8 hr., and the ammonia then replaced by 250 ml. of anhydrous ether. After stirring at 25–30° for 14 hrs., 4 ml. of glacial acetic acid was added followed by water. On working up the ether layer, there was recovered 76% of I, b.p. 61–62° at 0.4 mm., n_{D}^{23} 1.5129, having an infrared spectrum identical to the original I.

B. *With butyllithium.* Butyllithium was prepared in ether and standardized as described previously.[25] This reagent (100 ml. 1.23 moles) was added from an addition funnel to a stirred solution of 16.7 g. (0.106 mole) of I in 250 ml. of ether[26] cooled in an ice bath and protected under dry nitrogen. After 6 hr., 13 g. (0.12 mole) of ethyl bromide was added to alkylate carbanion I′, and the ice bath was removed. After 1 hr. at room temperature, 250 ml. of about 1.5*N* hydrochloric acid was added, and the mixture was refluxed overnight. The two layers were separated and the aqueous acid layer was extracted with ether. The combined ethereal solution was dried over anhydrous magnesium sulfate, the solvent removed, and the residue distilled to give 6.0 g. (42%) of propiophenone, b.p. 77–78° at 4.2 mm.,

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(20) A study of the reactions of the corresponding sodium and potassium reagents with aminonitriles I and II is planned.

(21) A. T. Stewart, Jr., and C. R. Hauser, *J. Am. Chem. Soc.*, **77**, 1098 (1955).

(22) The possible elucidation of the mechanism of the reaction employing optically active I is being investigated.

(23) Melting points and boiling points are uncorrected. Infrared spectra were obtained using a Perkin-Elmer Infracord. Analyses were by Galbraith Microanalytical Laboratories, Knoxville, Tenn., and Spang Microanalytical Laboratories, Ann Arbor, Mich.

(24) Ref. 7, p. 263.

(25) R. G. Jones and H. Gilman, *Org. Reactions*, **VI**, 352–353 (1951).

(26) Dried and distilled from lithium aluminum hydride.

n_D^{25} 1.5232 (2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 194–195°). The aqueous acid layer of the reaction mixture was made alkaline and extracted with ether. The ether extract was dried over magnesium sulfate, the solvent removed, and the residue distilled to give 8.9 g. (38%) of 1-*N*,*N*-dimethylamino-1-phenyl-2-pentanone (III), b.p. 95–98° at 0.3 mm., n_D^{27} 1.5038.

Anal. Calcd. for $C_{14}H_{21}NO$: C, 76.68; H, 9.65; N, 6.39. Found: C, 76.18; H, 9.25; N, 6.21.

The infrared spectrum of this product showed a strong band at 5.85 μ for the carbonyl group as well as other bands at 3.4–3.6, 6.9, 8.8, 9.6–9.8, 13.2, 14.2 μ.

Similar results were obtained in other experiments in which the temperature was varied from −80° to 35°. The addition was carried out directly and inversely with no apparent difference. However, the ratio of propiophenone to amino ketone III varied considerably. In none of the experiments was the possible tertiary amine IVc detected.

C. With Grignard reagents. Certain of these reagents in ether[26] were placed in a graduated dropping funnel and standardized.[27]

Ethylmagnesium iodide (139 ml. of 0.793*N* solution, 0.11 mole of reagent)[27] was added to a stirred solution of 16.0 g. (0.10 mole) of I in 100 ml. of anhydrous ether[26] to produce a precipitate. The reaction mixture was stirred at room temperature for 24 hr., during which time no evolution of ethane was detected (gas burette). Excess 2*N* hydrochloric acid was added, and the two layers were separated. The ether layer was evaporated to leave only a trace of residue. The aqueous acid layer was made basic to litmus with concentrated ammonium hydroxide solution, and the resulting mixture was extracted with ether. The ether extract was dried over anhydrous magnesium sulfate, and the solvent removed. The residue was distilled to yield 13.8 g. (85%) of 1-dimethylamino-1-phenylpropane (IVb), b.p. 41–42° at 0.3 mm., n_D^{24} 1.5012 (reported, b.p. 105–106° at 25 mm., n_D^{25} 1.5002[28] and 77.5–79° at 7.3 mm., n_D^{25} 1.5016).[4] The picrate, recrystallized from ethanol, melted at 167.5–169°, which was not depressed on admixture with an authentic sample.[4]

This reaction was carried out under several sets of conditions as summarized in Table II. The recovered I from certain of the reactions was isolated by distillation, and was characterized by acid catalyzed hydrolysis to benzaldehyde; 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 242–243°.

n-Butylmagnesium bromide (175 ml. of 0.677*N* solution, 0.118 mole of reagent)[27] was added to a stirred solution of 17.25 g. (0.108 mole) of I in 250 ml. of anhydrous ether[26] at 0° (ice bath). After 48 hr., the reaction mixture was worked up (see reaction with ethylmagnesium iodide) to give 16.85 g. (82%) of 1-dimethylamino-1-phenylpentane (IVc), b.p. 77–78° at 0.95 mm., n_D^{18} 1.5002 (reported b.p. 71–74° at 1.2 mm., n_D^{25} 1.4966).[4] The picrate, recrystallized from ethanol, melted at 159–160°, which was not depressed on admixture with an authentic sample.[4]

Phenylmagnesium bromide was prepared from 0.2 mole each of bromobenzene and magnesium in 200 ml. of tetrahydrofuran (THF).[26] To this stirred solution was added 0.1 mole of I in 100 ml. of THF.[26] After refluxing for 5 hrs., the reaction mixture was decomposed with 350 cc. of 1.5*N* hydrochloric acid, and most of the THF was removed by distillation. Cooling the solution caused precipitation of 22.0 g. (89%) of benzohydryldimethylamine hydrochloride (hydrochloride of IVd), m.p. 217–222°. A sample of this hydrochloride was neutralized with sodium hydroxide solution to liberate the free amine (m.p. 68–70°) (IVd) (reported,[29] m.p. 69–70°), which was treated with methyl iodide in acetonitrile to give the methiodide, m.p. 172–174° (recrystallized from absolute ethanol). This m.p. was not depressed on admixture with an authentic sample of the methiodide.[29]

p-Chlorobenzylmagnesium chloride, prepared from *p*-chlorobenzyl chloride (Eastman Kodak Co., practical grade) and magnesium in ether, was treated with I to give, in good yield, 1-dimethylamino-1-phenyl-2-(4-chlorophenyl)ethane (IVe), b.p. 129–130° at 0.57 mm., $n_D^{25.5}$ 1.5644.

Anal. Calcd. for $C_{16}H_{18}ClN$: C, 73.97; H, 6.98; Cl, 13.65; N, 5.39. Found: C, 73.84; H, 7.21; Cl, 13.63; N, 5.21.

The picrate, recrystallized from ethanol, melted at 134–135.5°.

Anal. Calcd. for $C_{23}H_{21}ClN_4O_7$: Cl, 6.92; N, 10.93. Found: Cl, 7.09; N, 11.16.

t-Butylmagnesium chloride[30] (195 ml. of 0.662 *N* solution, 0.129 mole of reagent)[27] was diluted to 300 ml. with ether,[26] and 16.0 g. (0.10 mole) of I in 50 ml. of ether[26] was added to produce a white precipitate. After 10 min., 11 g. (0.1 mole) of ethyl bromide was added slowly. After stirring for one hour, 100 ml. of 2*N* hydrochloric acid was added, and the layers were separated. The aqueous acid layer was heated on the steam bath for 16 hr. to hydrolyze any unchanged I and ethylation product II. After cooling, the resulting mixture was extracted with ether, and the ether extract combined with the original ether layer. The ether solution was dried and the solvent removed to leave about 1 g. of an oil, which afforded 1.36 g. (5%) of benzaldehyde 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 240–242°. No propiophenone was detected. The aqueous acid solution was made alkaline to litmus, and extracted with ether. The ether solution was dried, and the solvent removed. The residue was distilled to give 11.1 g. (82%) of benzyldimethylamine, b.p. 66–67° at 15 mm., n_D^{26} 1.4987; picrate m.p. and mixed m.p. 93–94°.

D. With lithium aluminum hydride. To a stirred slurry of 7.6 g. (0.2 mole) of lithium aluminum hydride in 200 ml. of ether was added, at such a rate as to maintain reflux, a solution of 32.0 g. (0.2 mole) of I in 100 ml. of ether.[26] Hydrogen (1260 ml., 26%) was evolved. After refluxing for 24 hr., 50 ml. of water was added cautiously producing a pasty mass, from which the ether solution was decanted and combined with several ether extracts of the pasty mass. The ether solution was dried over anhydrous magnesium sulfate, and the solvent removed. The residue was distilled to give 17.2 g. of material boiling up to 80° at 0.6 mm. leaving a residue that was not investigated. The distillate was warmed with a mixture of 3*N* hydrochloric acid and ether for 24 hr., and the two layers were separated. The aqueous acid layer was made strongly alkaline with sodium hydroxide solution, and sodium chloride was added. The resulting mixture was extracted several times with ether, and the combined ether solution was dried. The solvent was removed, and the residue was distilled to give 14.9 g. (45%) of 2-dimethylamino-2-phenylethylamine (VII), b.p. 65° at 0.5 mm., n_D^{28} 1.5235.

Anal. Calcd. for $C_{10}H_{16}N_2$: C, 73.12; H, 9.82; N, 17.08. Found: C, 73.03; H, 9.74; N, 16.98.

This product was soluble in water. Its infrared spectrum showed a band at 2.97 μ for the N—H group; other bands were at 3.4, 3.6, 6.9, 9.7, 13.0, 13.2, and 14.2 μ.

E. With sodium. To a stirred blue solution of 4.6 g. (0.2 g.-atom) of sodium in 300 ml. of liquid ammonia (distilled from sodium) was added 16.0 g. (0.1 mole) of I. After 10 min. (when the color had changed to greenish yellow), 16.0 g. (0.1 mole) of ethyl iodide in 100 ml. of dry ether was added. After 1 hr., excess ammonium chloride was added, and the ammonia allowed to evaporate as more

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[27] See H. Gilman, E. A. Zoellner, and J. B. Dickey, *J. Am. Chem. Soc.*, **51**, 1576 (1929).

[28] J. F. Bunnett, J. L. Marks, and H. Moe, *J. Am. Chem. Soc.*, **75**, 985 (1953).

[29] S. W. Kantor and C. R. Hauser, *J. Am. Chem. Soc.*, **73**, 4127 (1951).

[30] See S. V. Puntambeker and E. A. Zoellner, *Org. Syntheses*, **Coll. Vol. I**, 2nd ed., 524 (1948).

ether was added. The resulting ether suspension was shaken with sodium bicarbonate solution to neutralize the excess ammonium chloride, and the two layers were separated. The ether solution was dried over Drierite, and the solvent removed. The residue was distilled to give 7.1 g. (53%) of benzyldimethylamine, b.p. 56–58° at 5 mm., and 5.05 g. (27%) of II, b.p. 70–72° at 0.4 mm., n_D^{25} 1.5114. The benzyldimethylamine was identified as its picrate (m.p. and mixed m.p. 93–94°) and the aminonitrile II by acid catalyzed hydrolysis to propiophenone (2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 194–195°).

In another experiment in which no ethyl iodide was added, there was obtained benzyldimethylamine, b.p. 47–48° at 2.8 mm., n_D^{24} 1.4996, in 62% yield (picrate, m.p. and mixed m.p. 93–94°).

Reaction of aminonitrile V *with benzylmagnesium chloride to form amino ketone* VI. In the earlier procedure,[9] VI was isolated as its hydrochloride salt, for which only a chloride ion analysis was reported. In the present procedure, the free amino ketone VI was isolated.

To the Grignard reagent, prepared from 0.3 mole each of benzyl chloride and magnesium, was added a solution of 0.1 mole of V in ether. After stirring for 16 hr., the reaction mixture was decomposed with hydrochloric acid, and the two layers were separated. The acid aqueous layer was refluxed for several hours, cooled, and neutralized with sodium hydroxide solution. The liberated oil was taken up in ether, and the ether solution was dried. The solvent was removed to leave an oil that soon solidified. Recrystallization from ligroin (b.p. 60–90°) afforded 20 g. (68%) of 1-morpholino-1,3-diphenyl-2-propanone (VI) m.p. 55–60°, and further recrystallization gave 15.7 g. (53%) of this compound, m.p. 62–64°.

Anal. Calcd. for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17; N, 4.74. Found: C, 77.51; H, 7.16; N, 4.81.

The infrared spectrum of this compound showed a strong band at 5.90 μ for the carbonyl group.

Saturation of an ether solution of a sample of VI with anhydrous hydrogen chloride precipitated the hydrochloride, m.p. 204–206°; reported[9] m.p. 204–206°.

Reactions of aminonitrile II *with nucleophilic reagents.* A. *With potassium amide.* To a stirred solution of 0.2 mole of potassium amide[31] in 500 ml. of anhydrous liquid ammonia was added 37.6 g. (0.2 mole) of II. After 4 hrs., the heavy white suspension was treated with 10.6 g. (0.2 mole) of solid ammonium chloride, and the ammonia evaporated (steam bath) as an equal volume of ether was added. The resulting ether suspension was filtered. The ether filtrate was evaporated to leave 5.9 g. of 2-dimethylamino-2-phenylbutyramidine (X), m.p. 125–128°. The solid on the funnel was taken up in hot benzene and, after filtering, the solvent was removed to leave 19.7 g. of X, m.p. 124–127°; total yield 25.6 g. (62%). Recrystallization from benzene-hexane afforded 22.6 g. (55%) of X, m.p. 125–128° and at 126–127° after another crystallization from benzene-hexane.

Anal. Calcd. for $C_{12}H_{19}N_3$: C, 70.20; H, 9.33; N, 20.47; mol. wt., 205. Found: C, 69.96; H, 9.72; N, 20.30; mol. wt., 205, 208 (Rast).

Its infrared spectrum (KBr) showed bands at 2.92 (N—H), 6.13, 7.0, 8.7, 13.1, and 14.1 μ.

Cyclization was effected by adding 3.0 g. (0.03 mole) of acetylacetone and 1 g. of anhydrous potassium carbonate to a solution of 6.1 g. (0.03 mole) of X in 50 ml. of hot ethanol, and refluxing the mixture for 16 hr. The reaction mixture was poured into 400 ml. of water, the resulting white precipitate was collected, washed with water, and dried to give 2.4 g. (30%) of pyrimidine XI, m.p. 216–225°. A sample, recrystallized from methanol, melted at 223–225°.

Anal. Calcd. for $C_{17}H_{23}N_3$: C, 75.80; H, 8.61; N, 15.60. Found: C, 75.62; H, 8.44; N, 15.80.

Its infrared spectrum contained peaks at 3.4 (C—H), 6.1, 8.0, 10.2, 11.6, 13.2, and 14.2 μ.

When aminonitrile II was treated with lithium amide as described above for potassium amide, no amidine X was isolated, and 91% of II was recovered.

B. *With butyllithium.* To a stirred ethereal solution of butyllithium (125 ml. of 1.54 *N* solution; 0.192 mole)[25] was added dropwise (gentle refluxing) 36.2 g. (0.192 mole) of II in 150 ml. of ether.[26] The resulting dark red solution was allowed to stand overnight. After cooling in an ice bath, 35 ml. of water was added with stirring, followed by 12.6 ml. of glacial acetic acid to produce a yellow solution. The layers were separated and the ether layer, with which was combined two ether extracts of the aqueous layer, was dried over anhydrous magnesium sulfate, and the solvent removed. The residue was distilled to give a forerun, b.p. 40–102° (mainly 40–43°) at 0.27 mm., and a fraction, b.p. 102–123° at 0.27 mm., which was redistilled through a 30 cm. Vigreux column to yield 26.0 g. (55%) of 3-phenyl-3-dimethylamino-4-octane ketimine (XIIa) as a light yellow oil, b.p. 114° at 0.27 mm., n_D^{24} 1.5218.

Anal. Calcd. for $C_{16}H_{26}N_2$: C, 77.99; H, 10.64; N, 11.37. Found: C, 77.94; H, 10.54; N, 11.49.

The infrared spectrum of XIIa (taken as a thin film) showed the following bands for an imine; N—H at 3.09 μ and C=N at 6.08 μ.

A 5.2-g. sample of XIIa was heated with 5% hydrochloric acid at 50° for 20 hr. After cooling, the solution was made alkaline to the phenolphthalein end-point, and the resulting mixture was extracted with ether. The ether solution was dried and distilled to give 4.4 g. (85%) of 3-phenyl-3-dimethylamino-4-octanone (XIIIa), b.p. 104–105° at 0.3 mm., n_D^{22} 1.5132.

Anal. Calcd. for $C_{16}H_{25}NO$: C, 77.68; H, 10.19; N, 5.66. Found: C, 77.51; H, 10.26; N, 5.58.

The infrared spectrum of XIIIa had bands at 3.4–3.6 μ (C—H), 5.85 μ (C=O), and 6.88, 8.88, 9.6, 10.1, 13.2, and 14.3 μ.

C. *With phenyllithium.* To a stirred etheral solution of phenyllithium (500 ml. of 0.48 *N*, 0.24 mole)[25] was added a solution of 45 g. (0.24 mole) of II in 100 ml. of ether.[26] After refluxing for 3 hr. and standing overnight, the reddish-brown solution was decomposed with water and acetic acid (see preceding experiment) to give 44.8 g. (70%) of 2-dimethylamino-1,2-diphenyl-1-butane ketimine (XIIb), b.p. 134–140° at 0.3 mm., m.p. 73–76°, and at 76.5–78° after crystallization from hexane.

Anal. Calcd. for $C_{18}H_{22}N_2$: C, 81.16; H, 8.33; N, 10.52. Found: C, 81.29; H, 8.19; N, 10.40.

The infrared spectrum of XIIb showed bands at 2.95 μ (N—H), 3.2–3.4 (C—H), 6.13 μ (C=N).

A 10.0-g. sample of imine XIIb was hydrolyzed with 5% hydrochloric acid (16 hr.) (see preceding experiment) to give 9.3 g. (93%) of 2-dimethylamino-1,2-diphenyl-1-butanone (XIIIb), b.p. 143–144° at 0.25 mm., n_D^{26} 1.5784.

Anal. Calcd. for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found: C, 80.79; H, 8.11; N, 5.30.

Its infrared spectrum (KBr) showed bands at 3.3–3.6, 6.0 (C=O), 6.9, 8.2, 11.8, 13.0–13.4, and 14.0–14.4 μ.

D. *With lithium aluminum hydride.* To a stirred slurry of 5.9 g. (0.15 mole) of lithium aluminum hydride in 200 ml. of ether was added dropwise (gentle refluxing) a solution of 28.2 g. (0.15 mole) of II in 75 ml. of anhydrous ether. After stirring at room temperature for 7 hr., the reaction mixture was worked up (see lithium aluminum hydride reduction of I) to give 22.0 g. (90%) of 1-dimethylamino-1-phenylpropane (XV), b.p. 43–44° at 0.7 mm., $n_D^{23.5}$ 1.5010; picrate, m.p. and mixed m.p. 167.5–169°.

E. *With sodium.* To a stirred blue solution of 9.2 g. (0.4 g.-atom) of sodium in 500 ml. of liquid ammonia (distilled from sodium amide) was added 27.6 g. (0.2 mole) of II. The resulting solution (grey) was treated with *t*-butyl alcohol (100 ml.) to destroy sodium amide, and the am-

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(31) See C. R. Hauser and T. M. Harris, *J. Am. Chem. Soc.*, **80**, 6360 (1958).

monia was evaporated. The residue was treated with 100 ml. of water and 110 ml. of concentrated hydrochloric acid, and most of the *t*-butyl alcohol was distilled. After cooling, the acid solution was made alkaline with sodium hydroxide solution, and the resulting mixture was extracted with ether. The ether extract was dried, and the solvent removed. The residue was distilled to give 28.9 g. (89%) of 1-dimethylamino-1-phenylpropane (IVb), b.p. 58–58.5° at 2.5 mm., n_D^{25} 1.5016. The picrate, m.p. and mixed m.p 167–168°, was recrystallized from ethanol.

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[CONTRIBUTION FROM THE ROHM & HAAS COMPANY]

Vinylation of Pentaerythritol

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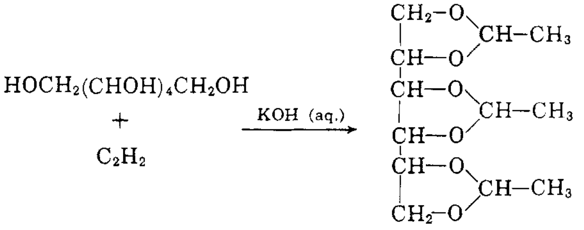
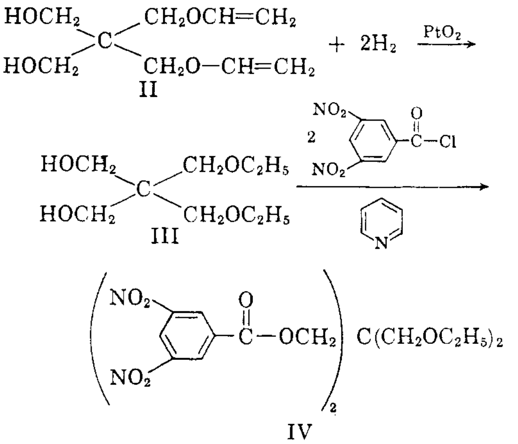
The catalytic vinylation of pentaerythritol in aqueous base afforded a mixture of products from which the pure divinyl ether II was isolated in 22% yield. The total mixture of compounds obtained from the aqueous vinylation was treated further with acetylene under non-aqueous basic conditions to give a mixture of the tetravinyl ether of pentaerythritol (V) (60–70%) and 5,5-di(vinyloxymethyl)-2-methyl-1,3-dioxane (VII) (30–40%). There appears to be a relationship between the acidity of an alcohol and its tendency to undergo vinylation in an aqueous solution. Simple monohydric aliphatic alcohols do not undergo base-catalyzed vinylation in water, whereas, polyhydroxy compounds capable of forming intramolecular hydrogen bonds react with acetylene in aqueous base to give products of vinylation.

It is well known that phenols[1,2] and mercaptans[3] undergo vinylation smoothly in aqueous base to give aryl vinyl ethers and vinyl sulfides, respectively; indeed, these reactions proceed even in the presence of weakly basic catalysts (sodium carbonate, potassium carbonate, amines, etc.). With one exception,[4] previously reported vinylations of aliphatic polyhydroxy compounds appear to have been conducted exclusively under non-aqueous conditions.[5] Shtishevskii and Obolonskaya[4] treated mannitol with acetylene in aqueous potassium hydroxide and obtained mannitol triacetal (I) along with a complex mixture of products which could not be separated.



I

The base-catalyzed vinylation of pentaerythritol has not heretofore been reported. Owing to the high melting point of pentaerythritol and its low solubility in most organic solvents, an aqueous medium was employed for the reaction. The treatment of an aqueous solution of pentaerythritol with acetylene under 10–30 atm. pressure in the presence of a catalytic quantity of potassium hydroxide at 145–175° afforded a distillable liquid mixture of products in 50–70% yield. From the mixture which contained hydroxyl, vinyl ether, and acetal functionality, only the divinyl ether II (yield 22%) was isolated. The structure of the colorless crystalline ether II was established by analytical and spectroscopic data, as well as by quantitative hydrogenation to the diethyl ether of pentaerythritol (III), from which the crystalline di-3,5-dinitrobenzoate ester (IV) was prepared.



IV

Acetylene was absorbed slowly by the basic aqueous solution of pentaerythritol even after 14 hours of reaction. A comparison of the data for two experiments (Table I, Exp. No. 3 and 4) conducted under identical conditions except for the time of reaction shows that although twice as

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[1] M. Ban, T. Tamamoto, and S. Otsuka, *Nippon Kagaku Zasshi*, **77**, 176 (1956); *Chem. Abstr.*, **52**, 300 (1958).

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