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Some Reactions of *α-t*-Acetylenic-*t*-amines[1]

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The reactions of two *α-t*-acetylenic-*t*-amines, $(CH_3)_2C(NR_2)\text{—}C\equiv CH$, were studied in detail. These compounds, 3-dimethylamino-3-methyl-1-butyne and 3-pyrrolidino-3-methyl-1-butyne, were found to undergo the typical reactions of the triple bond and of the ethynyl hydrogen. From the two model compounds, twenty-six new substances of the following classes were prepared: acetylenic-1,4-amino alcohols, C-alkylated acetylenic amines, acetylenic-1,4-diamines, 2,7-diamino-3,5-diacetylenes, 2-amino-7-hydroxy-3,5-diacetylenes, 1,2-amino ketones, 1,2-amino alcohols, acetylenic amino acids, allylic amines, and saturated amines. These compounds were characterized by the formation of methiodide and hydrochloride salts.

A previous paper[3] described the synthesis of acetylenic secondary and tertiary amines through the interaction of acetylenic chlorides of the type $RR'C(Cl)\text{—}C\equiv CH$ with primary and secondary amines. Recently,[4] this method was studied in detail and shown to constitute a valuable new synthetic technique. Furthermore, it has been found[5] earlier that the acetylenic primary amines underwent alkylation, acylation, hydrogenation, and addition to carbonyl compounds in the expected manner. Since the properties of the tertiary amines had not been studied systematically and since these compounds constitute a new class of sterically hindered amines, an investigation of the reactions of *α-t*-acetylenic-*t*-amines for possible exploitation of the products as pharmaceutical agents[6] was considered to be of interest.

The transformations discussed below are shown in Fig. 1.

Each of the acetylenic-*t*-amines, 3-dimethylamino-3-methyl-1-butyne (II), and 3-pyrrolidino-3-methyl-1-butyne (III), gave with ammoniacal silver nitrate solution, curdy white precipitates typical of compounds possessing a terminal ethynyl group.

Treatment of II and III with ethylmagnesium bromide gave the Grignard but with somewhat surprising results. The rate of formation of the organometallic was much slower than anticipated and several hours of reflux were generally needed for complete reaction (stoichiometric evolution of ethane). It had been reported[7,8] that the addition of amines increased the rate of reaction between alkylacetylenes and ethylmagnesium bromide. The decreased basicity[9] of the amine function coupled with a decrease in the acidity of the ethynyl hydrogen may explain the pronounced decrease in rate exhibited by II and III.

Additions of carbonyl compounds (aldehyde or ketone) to an ethereal suspension of the Grignards of II and III, followed by hydrolysis, resulted, in several cases, in the formation of acetylenic-1,4-amino alcohols (IV, V, VI, VII). The Grignard reagents were sensitive to enolizable ketones and when cyclohexanone, desoxybenzoin, acetophenone or propiophenone was employed, no amino alcohol was isolated. When the lithium salt of III was condensed with acetophenone in liquid ammonia,[10] however, VIII could be obtained in low yield.

Esterification of IV with acetic anhydride or propionic anhydride and pyridine failed. This is in agreement with Huggil and Rose.[11]

The reaction between the sodium salts of II and III, in liquid ammonia, and ethyl and butyl bromides gave the C-alkylated derivatives,[12] IX, X, XI and XII.

By employing the Mannich reaction[13] with formaldehyde and diethylamine or pyrrolidine on II and III, the acetylenic 1,4-diamines XIII, XIV, XV and XVI were prepared in good to excellent yields.

Oxidative coupling of II and III to 2,7-bis(dimethylamino) - 2,7 - dimethyl - 3,5 - octadiyne (XVII) and 2,7-bis(pyrrolidino)-2,7-dimethyl-3,5-octadiyne (XVIII), respectively, was accomplished by two techniques. In one method the reaction mixture was heated at 50–55° at atmospheric pres-

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[1] Paper no. 74 on substituted acetylenes; previous paper, G. F. Hennion and A. P. Boisselle, *J. Org. Chem.*, **26**, 725 (1961).

[2] Eli Lilly Company Fellow, 1957–1959. Abstracted from the Ph.D. Dissertation of A. C. P., 1960.

[3] G. F. Hennion and K. W. Nelson, *J. Am. Chem. Soc.*, **79**, 2142 (1957).

[4] G. F. Hennion and R. S. Hanzel, *J. Am. Chem. Soc.*, **82**, 4908 (1960).

[5] G. F. Hennion and E. G. Teach, *J. Am. Chem. Soc.*, **75**, 4297 (1953).

[6] Pharmacological testing is in progress in the Lilly Research Laboratories, Indianapolis, Indiana.

[7] J. H. Wotiz, C. A. Hollingsworth, and R. Dessy, *J. Am. Chem. Soc.*, **77**, 103 (1955).

[8] J. H. Wotiz, C. A. Hollingsworth, and A. W. Simon, *J. Org. Chem.*, **24**, 1202 (1959).

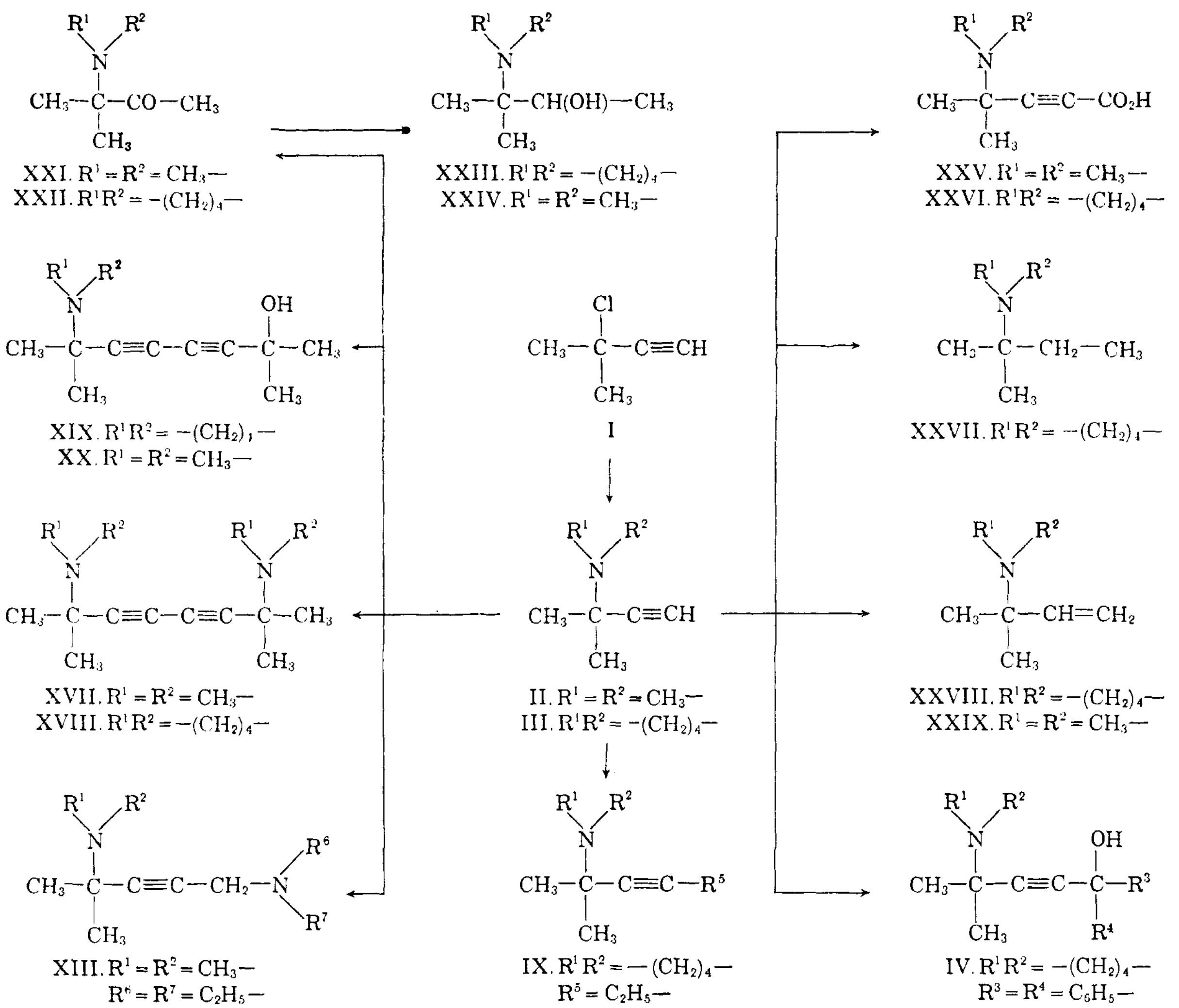
[9] K. N. Campbell, F. C. Fatora, and B. K. Campbell, *J. Org. Chem.*, **17**, 1141 (1952).

[10] G. F. Hennion and J. M. Campbell, *J. Org. Chem.*, **21**, 761 (1956).

[11] H. P. W. Huggil and J. D. Rose, *J. Chem. Soc.*, 335 (1950).

[12] R. F. Parcell and C. B. Pollard, *J. Am. Chem. Soc.*, **72**, 2385 (1950).

[13] J. D. Rose and B. C. L. Weedon, *J. Chem. Soc.*, 782 (1949).



XIII. $R^1 = R^2 = CH_3-$
$R^6 = R^7 = C_2H_5-$
XIV. $R^1 = R^2 = CH_3-$
$R^6R^7 = -(CH_2)_4-$
XV. $R^1R^2 = -(CH_2)_4-$
$R^6 = R^7 = C_2H_5-$
XVI. $R^1R^2 = -(CH_2)_4-$
$R^6R^7 = -(CH_2)_4-$

IX. $R^1R^2 = -(CH_2)_4-$
$R^5 = C_2H_5-$
X. $R^1R^2 = -(CH_2)_4-$
$R^5 = n\text{-}C_4H_9-$
XI. $R^1 = R^2 = CH_3-$
$R^5 = C_2H_5-$
XII. $R^1 = R^2 = CH_3-$
$R^5 = n\text{-}C_4H_9-$

IV. $R^1R^2 = -(CH_2)_4-$
$R^3 = R^4 = C_6H_5-$
V. $R^1R^2 = -(CH_2)_4-$
$R^3 = C_6H_5-$, $R^4 = H-$
VI. $R^1R^2 = -(CH_2)_4-$
$R^3 = C_6H_5-$
$R^4 =$ 4-pyridyl-
VII. $R^1 = R^2 = CH_3-$
$R^3 = C_6H_5-$
$R^4 = \text{cyclo-}C_6H_{11}-$
VIII. $R^1R^2 = -(CH_2)_4-$
$R^3 = C_6H_5-$
$R^4 = CH_3-$

Fig. 1. Reactions of α-*t*-acetylenic-*t*-amines

sure with passage of air.[13] The other method entailed the shaking of the reaction mixture under a slight oxygen pressure (2–4 *p.s.i.g.*). The latter method consistently gave the diamines in better yield and higher purity.

Treatment of II and III with 3-methyl-1-butyne-3-ol under oxidative coupling conditions produced moderate yields of the oxidative cross-coupled products XIX and XX, as well as the symmetrical diamines and diacetylenic glycol. This appears to be the first reported use of this technique with acetylenic amines.

Hydration of II and III in the presence of mercuric oxide and sulfuric acid afforded the amino ketones XXI and XXII. These ketones did not undergo the haloform reaction. By reduction with sodium borohydride in methanol[14] the corresponding 1,2-amino alcohols, XXIII and XXIV, were prepared.

Passage of dry carbon dioxide gas through a suspension of the sodium salts of II and III in ether[15] produced, after neutralization, the acetylenic

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[14] J. H. Biel and F. DiPierro, *J. Am. Chem. Soc.*, **80**, 4614 (1958).

amino acids, XXV and XXVI, respectively. As with many acetylenic acids, these compounds decarboxylated upon heating. The isolation and purification entailed the extraction and recrystallization of the amino acids from glacial acetic acid. 4 - Dimethylamino - 4 - methyl - 2 - pentynoic acid (XXV) was obtained as the amino acid in the zwitterion form. 4-Pyrrolidino-4-methyl-2-pentynoic acid (XXVI), on the other hand, could only be isolated containing one molecule of acetic acid per molecule of amino acid (elemental analysis and infrared spectrum). Attempts to prepare amides by the reaction of these acids with thionyl chloride or acetyl chloride, followed by addition of cold ammonium hydroxide, were unsuccessful.

Low pressure hydrogenation of III, employing either Raney nickel or 10% palladium on activated charcoal as catalysts, yielded 2-pyrrolidino-2-methylbutane (XXVII). With II under the same reaction conditions, extensive hydrogenolysis of the carbon-nitrogen bond was encountered. This is consistent with previous results.[5,16] If the hydrogenation of II and III was terminated after the absorption of one mole of hydrogen, the allylic amines, XXVIII and XXIX, were isolated in good yield. This indicated that the hydrogenolysis of the dimethylamine function upon attempted saturation of II occurred after the allylic compound was formed and can be attributed, at least in part, to the known fragility of such bonds.

Bromination of III gave somewhat unexpected results. Upon addition of bromine to a solution of III in carbon tetrachloride at 0°, a light yellow solid precipitated instantaneously. The infrared spectrum and physical properties indicated that this material was not a simple addition product. The only identifiable compound isolated was 3-pyrrolidino-3-methyl-1-butyne hydrobromide.

An attempt to prepare 1-bromo-3-pyrrolidino-3-methyl-1-butyne through the interaction of bromine and the Grignard reagent derived from III resulted in the coupled product, XVIII.

The compounds listed in Fig. 1 were characterized by the formation of methiodide and/or hydrochloride salts.

EXPERIMENTAL[17]

3-Chloro-3-methyl-1-butyne (I) was prepared as previously described.[18]

3-Dimethylamino-3-methyl-1-butyne (II) was prepared by a modification of the earlier procedure.[3] 3-Chloro-3-methyl-1-butyne (255 g., 2.5 moles) at 0–5°, was added to 710 g. (6.3 moles) of a 40% aqueous solution of dimethylamine at 0–5°, in a 2-l., round bottom flask fitted with a mechanical stirrer. The reaction mixture was stirred for 4 days while the temperature was maintained near 15°. The dark orange precipitate was collected, washed with cold water and dissolved in cold 3*N* hydrochloric acid. The acidic solution was extracted with two 150-ml. portions of ether (discarded) and treated three times with decolorizing charcoal. The resulting light yellow solution was cooled and made strongly alkaline with cold concentrated ammonium hydroxide solution. The white precipitate was collected, washed with cold concentrated ammonium hydroxide solution and finally with water. After dissolving the wet solid in ether, the ether layer was separated, dried overnight with anhydrous potassium carbonate and then for five additional hours over potassium hydroxide pellets. The ether was removed by distillation through a 25-cm. helix-packed column to yield 148.3 g. (53%) of white solid, m.p. 99–101° (lit. (3), m.p. 99–102°).

3-Pyrrolidino-3-methyl-1-butyne (III) was prepared in a similar manner from 300 g. (2.92 moles) of 3-chloro-3-methyl-1-butyne, 639 g. (9.0 moles) of pyrrolidine and 240 ml. of water. The reaction mixture was allowed to stand at 15° for 3 days and then worked up as described above. A 55% yield of white solid with m.p. 74–76° was obtained.

1,1-Diphenyl-4-pyrrolidino-4-methyl-2-pentyne-1-ol (IV). Magnesium turnings (1.6 g., 0.066 g.-atom), covered with 75 ml. of anhydrous ether, were converted to ethylmagnesium bromide in the usual way with 7.4 g. (0.068 mole) of ethyl bromide diluted with 100 ml. of anhydrous ether in a 1-l., three-necked, round bottom flask fitted with a water-cooled Allihn condenser, mercury sealed stirrer and dropping funnel. Drying tubes containing calcium chloride were attached to the condenser and dropping funnel. 3-Pyrrolidino-3-methyl-1-butyne (6.85 g., 0.05 mole) in 100 ml. of anhydrous ether was added dropwise with stirring. After 4 hr. of reflux a curdy white precipitate appeared and the reaction mixture was refluxed for an additional 4 hr., during which time precipitation was complete. Benzophenone (9.4 g., 0.05 mole) in 100 ml. of anhydrous ether was added dropwise with stirring (10 min.) and the reaction mixture was stirred overnight and then boiled for 4 hr. Hydrolysis was effected with ammonium chloride solution and the ether layer was separated, washed with two 200-ml. portions of cold water and dried over anhydrous potassium carbonate. Distillation of the ether left a light yellow solid. The product was washed with cold petroleum ether (b.p. 35–60°) and crystallized twice from benzene-petroleum ether to yield colorless crystals, weight 8.6 g. (54%), m.p. 138–139°.

The infrared spectrum revealed bands at 2.8, 8.5 and 4.5 μ assigned[19] to —OH, tertiary —C—O and —C≡C—, respectively.

Anal. Calcd. for $C_{22}H_{25}NO$: C, 82.72; H, 7.89; N, 4.39. Found: C, 81.84; H, 7.85; N, 4.17.

The *hydrochloride* was prepared by addition of ethereal hydrogen chloride to a cooled solution of the amino alcohol (10.0 g., 0.031 mole) in 150 ml. of anhydrous ether. The precipitate was collected and crystallized from absolute ethanol; yield 9.0 g. (81%); m.p. 200–205° dec.

Anal. Calcd. for $C_{22}H_{26}ClNO$: C, 74.24; H, 7.36; N, 3.94. Found: C, 73.57; H, 7.33; N, 3.71.

The other hydrochlorides named below were prepared by a similar procedure unless otherwise stated.

The *methiodide* was prepared from 7.3 g. (0.023 mole) of amino alcohol and 5 g. (0.035 mole) of methyl iodide in 100 ml. of benzene. After standing for 48 hr., the precipitate was collected and crystallized from absolute ethanol; yield 9.5 g. (91%); m.p. 203–204° dec.

Anal. Calcd. for $C_{23}H_{28}INO$: N, 3.04. Found: N, 2.81. The other methiodides described were prepared by the same procedure unless otherwise stated.

1-Phenyl-4-pyrrolidino-4-methyl-2-pentyne-1-ol (V) was prepared in the same way from 1.6 g. (0.066 g.-atom) of magnesium turnings, 7.4 g. (0.068 mole) of ethyl bromide, 6.85 g. (0.05 mole) of 3-pyrrolidino-3-methyl-1-butyne and

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[15] M. Olomucki and I. Marszak, *Compt. rend.*, 242, 1338 (1956).

[16] E. R. H. Jones, R. N. Lacey, and P. Smith, *J. Chem. Soc.*, 940 (1946).

[17] All melting and boiling points are uncorrected.

[18] G. F. Hennion, J. J. Sheehan, and D. E. Maloney, *J. Am. Chem. Soc.*, 72, 3542 (1950).

[19] L. H. Bellamy, *The Infrared Spectra of Complex Molecules*, Wiley, Inc., New York, 1954.

5.3 g. (0.05 mole) of freshly distilled benzaldehyde. The product was crystallized from benzene-petroleum ether; yield 8.3 g. (68%), m.p. 102–105°.

Anal. Calcd. for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76. Found: C, 78.69; H, 8.71; N, 5.85.

The *hydrochloride* had m.p. 180–183°.

Anal. Calcd. for $C_{16}H_{22}ClNO$: C, 68.68; H, 7.93; N, 5.01. Found: C, 68.58; H, 7.95; N, 4.92.

1-Phenyl-1-(4-pyridyl)-4-pyrrolidino-4-methyl-2-pentyne-1-ol (VI) was prepared by the same procedure from 1.6 g. (0.066 g.-atom) of magnesium turnings, 7.4 g. (0.068 mole) of ethyl bromide, 6.85 g. (0.05 mole) of 3-pyrrolidino-3-methyl-1-butyne and 10.0 g. (0.055 mole) of 4-benzoylpyridine. The yellow solid was crystallized from ethyl acetate-petroleum ether and then from ethanol-water; yield 5.2 g. (32%), m.p. 136–137°.

Anal. Calcd. for $C_{21}H_{24}N_2O$: C, 78.71; H, 7.55; N, 8.74. Found: C, 77.11; H, 7.56; N, 8.14.

1-Phenyl-1-cyclohexyl-4-dimethylamino-4-methyl-2-pentyne-1-ol (VII) was similarly prepared from 4.37 g. (0.18 g.-atom) of magnesium turnings, 22.2 g. (0.24 mole) of ethyl bromide, 16.7 g. (0.15 mole) of 3-dimethylamino-3-methyl-1-butyne and 29.0 g. (0.15 mole) of phenyl cyclohexyl ketone. The yellow, semi-solid material was washed with pentane and crystallized from petroleum ether; yield 10.0 g. (22%), m.p. 139.5–140°.

Anal. Calcd. for $C_{20}H_{29}NO$: C, 80.22, H, 9.76; N, 4.68. Found: C, 80.74; H, 10.02; N, 4.53.

The *hydrochloride* had m.p. 192–193° dec.

Anal. Calcd. for $C_{20}H_{30}ClNO$: C, 71.51; H, 9.00; N, 4.17. Found: C, 71.51; H, 9.18; N, 4.03.

2-Phenyl-5-pyrrolidino-5-methyl-3-hexyne-2-ol (VIII). Lithiumamide (0.12 mole) was prepared from 0.84 g. (0.12 g.-atom) of lithium metal, 300 ml. of liquid ammonia and 0.10 g. of ferric nitrate nonahydrate in a 1-l., three-necked, round bottom flask fitted with a Dry Ice condenser, mercury sealed stirrer, and dropping funnel. 3-Pyrrolidino-3-methyl-1-butyne (13.7 g., 0.10 mole) in 100 ml. of anhydrous ether was added dropwise with stirring (20 min.) and the mixture was stirred for an additional 90 min. Twelve grams (0.10 mole) of freshly distilled acetophenone in 100 ml. of anhydrous ether was added dropwise. The mixture was then stirred for 6 hr. and allowed to stand overnight (ammonia evaporated). Ether (100 ml.) was added and hydrolysis was effected with 5 ml. of methanol followed by 50 g. of crushed ice and 150 ml. of water. The ether layer was separated, washed with two 150-ml. portions of water and dried over anhydrous potassium carbonate. The ether was removed by distillation and the residue allowed to stand for 1 week in an evaporating dish. The yellow solid was then dissolved in anhydrous ether and the hydrochloride precipitated by addition of ethereal hydrogen chloride. The precipitate was crystallized twice from absolute ethanol-anhydrous ether; yield 1.5 g. (5.0%), m.p. 188–189°.

Anal. Calcd. for $C_{17}H_{24}ClNO$: C, 69.49; H, 8.23; N, 4.77. Found: C, 69.62; H, 8.23; N, 4.85.

This *hydrochloride* (0.15 g.) was dissolved in water and the solution was filtered and made strongly alkaline with concd. ammonium hydroxide solution. The precipitate was washed with water and recrystallized from ethanol-water; m.p. 127–129°.

2-Pyrrolidino-2-methyl-3-hexyne (IX). Sodium amide was prepared in the usual manner[20] from sodium metal (6.0 g., 0.26 g.-atom) and 350 ml. of liquid ammonia in a 1-l., three-necked, round bottom flask fitted with a Dry Ice condenser, mercury sealed stirrer and dropping funnel. 3-Pyrrolidino-3-methyl-1-butyne (27.4 g., 0.20 mole) in 200 ml. of anhydrous ether was added dropwise with stirring (30 min.) and the reaction mixture was stirred an additional 90 min. Thirty-three grams (0.31 mole) of ethyl bromide in 100 ml. of anhydrous ether was added dropwise (30 min.). The reaction mixture was then stirred for 4 hr. and allowed to stand overnight for evaporation of the ammonia. One hundred milliliters of ether was added, followed by 5 ml. of methanol and 250 ml. of crushed ice and water. The ether layer was separated, washed with 150 ml. of water and dried over anhydrous potassium carbonate. Distillation through a modified Claisen flask with a 25-cm. Vigreux section gave 27.8 g. (84% yield) of fractions boiling between 88–90° (19 mm.) and 91–92° (21 mm.), n_{D}^{25} 1.4632–1.4641. Redistillation gave a colorless liquid, b.p. 92° at 21 mm., n_{D}^{25} 1.4645.

The infrared spectrum exhibited a band at 4.5 μ, characteristic of an unsymmetrically disubstituted acetylene.

Anal. Calcd. for $C_{11}H_{19}N$: C, 79.94; H, 11.59. Found: C, 79.98; H, 11.04.

The hydrochloride, recrystallized from absolute ethanol-anhydrous ether, had m.p. 176–178°.

Anal. Calcd. for $C_{11}H_{20}ClN$: N, 6.94. Found: N, 6.98. The methiodide, recrystallized from absolute ethanol-ethyl acetate, melted at 140–141°.

Anal. Calcd. for $C_{12}H_{22}NI$: N, 4.56. Found: N, 4.51.

2-Pyrrolidino-2-methyl-3-octyne (X) was prepared in the same way from 3.0 g. (0.13 g.-atom) of sodium, 13.7 g. (0.10 mole) of 3-pyrrolidino-3-methyl-1-butyne and 17.8 g. (0.13 mole) of *n*-butyl bromide. The product distilled at 120° (18 mm.), n_{D}^{25} 1.4638, weight 15.3 g. (78% yield). Redistillation gave a colorless liquid, b.p. 75° at 1 mm., n_{D}^{25} 1.4640.

Anal. Calcd. for $C_{13}H_{23}N$: C, 80.76; H, 11.99; N, 7.25. Found: C, 81.12; H, 12.03; N, 7.47.

The *hydrochloride* had m.p. 127–129°.

Anal. Calcd. for $C_{13}H_{24}ClN$: N, 6.10. Found: N, 6.16.

The *methiodide* melted at 159–160°.

Anal. Calcd. for $C_{14}H_{26}NI$: N, 4.18. Found: N, 4.12.

2-Dimethylamino-2-methyl-3-hexyne (XI) was prepared in the same way from 6.0 g. (0.26 g.-atom) of sodium, 22.2 g. (0.20 mole) of 3-dimethylamino-3-methyl-1-butyne and 32.7 g. (0.30 mole) of ethyl bromide. The fractions boiling between 70–71° (36 mm.), n_{D}^{25} 1.4378–1.4380, were collected; weight 23.7 g. (85% yield).

Anal. Calcd. for $C_9H_{17}N$: C, 77.63; H, 12.31; N, 10.06. Found: C, 77.54; H, 11.91; N, 9.93.

The *hydrochloride* had m.p. 224–225° dec.

Anal. Calcd. for $C_9H_{18}ClN$: N, 7.97. Found: N, 8.07.

The *methiodide* melted at 187–188° dec.

Anal. Calcd. for $C_{10}H_{20}NI$: N, 4.98; Found: N, 4.99.

2-Dimethylamino-2-methyl-3-octyne (XII) was prepared in the same way from 6.0 g. (0.26 g.-atom) of sodium, 22.2 g. (0.20 mole) of 3-dimethylamino-3-methyl-1-butyne and 35.5 g. (0.26 mole) of *n*-butyl bromide. Fractions boiling between 87–88° (21 mm.), n_{D}^{25} 1.4418–1.4428, were collected; weight 25.5 g. (76% yield). Redistillation gave a colorless liquid, b.p. 84° at 16 mm., n_{D}^{25} 1.4425.

Anal. Calcd. for $C_{11}H_{21}N$: C, 78.97; H, 12.65. Found: C, 79.10; H, 12.57.

The *hydrochloride* had m.p. 146–148°.

Anal. Calcd. for $C_{11}H_{22}ClN$: N, 6.87. Found: N, 6.97.

The *methiodide* melted at 184–186°.

Anal. Calcd. for $C_{12}H_{24}NI$: N, 4.53. Found: N, 4.87.

1-Diethylamino-4-methyl-4-dimethylamino-2-pentyne (XIII). To a solution of 8.0 g. (0.11 mole) of diethylamine and 30 ml. of purified dioxane in a 100-ml., round bottom flask fitted with a water-cooled condenser was added 11.1 g. (0.10 mole) of 3-dimethylamino-3-methyl-1-butyne and 6.0 g. (0.20 mole) of paraformaldehyde. The reaction mixture was heated at reflux for 13 hr. and then distilled through a modified Claisen flask with a 25-cm. Vigreux column. Fractions boiling at 75–76.5° (1.5 mm.) weighed 18.1 g. (93% yield), n_{D}^{25} 1.4536–1.4539. Redistillation gave a colorless liquid, b.p. 53° (0.2 mm.), n_{D}^{25} 1.4540.

Anal. Calcd. for $C_{12}H_{24}N_2$: N, 14.27. Found: N, 14.50.

The *dihydrochloride*, recrystallized from absolute ethanol-ethyl acetate, had m.p. 203–206°.

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[20] T. H. Vaughn, R. R. Vogt, and J. A. Nieuwland, *J. Am. Chem. Soc.*, **56**, 2120 (1934).

Anal. Calcd. for $C_{12}H_{26}Cl_2N_2$: C, 53.52; H, 9.73; N, 10.41. Found: C, 53.68; H, 9.87; N, 10.22.

The *dimethiodide* melted at 213° dec.

Anal. Calcd. for $C_{14}H_{30}N_2I_2$: C, 35.01; H, 6.30; N, 5.83. Found: C, 35.07; H, 6.36; N, 5.86.

1-Pyrrolidino-4-methyl-4-dimethylamino-2-pentyne (XIV) was prepared from 11.0 g. (0.10 mole) of 3-dimethylamino-3-methyl-1-butyne, 7.81 g. (0.11 mole) of pyrrolidine and 6.0 g. (0.20 mole) of paraformaldehyde. The reaction mixture was refluxed for 24 hr. Distillation gave 15.9 g. (82% yield) of material collected in three fractions boiling at 79–80° (0.6 mm.), n_D^{25} 1.4749–1.4750. Redistillation gave b.p. 74° at 0.4 mm., n_D^{25} 1.4748.

Anal. Calcd. for $C_{12}H_{22}N_2$: N, 14.42. Found: N, 14.60.

The *dihydrochloride* had m.p. 133–137°.

Anal. Calcd. for $C_{12}H_{24}Cl_2N_2$: C, 53.93; H, 9.05; N, 10.48. Found: C, 53.89; H, 8.94; N, 10.49.

The *dimethiodide* was prepared as follows. Seventeen grams (0.12 mole) of methyl iodide was added to 8.0 g. (0.04 mole) of the diamine in 50 ml. of absolute ethanol and the reaction mixture was allowed to stand at room temperature for 8 hr. A yellow solid was collected and dissolved in a minimum quantity of water. Addition of acetone effected the formation of a colorless oil. The aqueous layer was decanted and acetone was then added to the oil which subsequently solidified upon cooling. This solid was dissolved in a solution of anhydrous methanol and 5.7 g. (0.04 mole) of methyl iodide. After 1 hr., the salt was precipitated by the addition of anhydrous ether. Recrystallization from absolute ethanol-anhydrous methanol gave 14.9 g. (76% yield) of crystals; m.p. 222–223° dec.

Anal. Calcd. for $C_{14}H_{28}I_2N_2$: N, 5.86. Found: N, 5.87.

1-Diethylamino-4-methyl-4-pyrrolidino-2-pentyne (XV) was prepared from 13.7 g. (0.10 mole) of 3-pyrrolidino-3-methyl-1-butyne, 8.0 g. (0.11 mole) of diethylamine and 6.0 g. (0.20 mole) of paraformaldehyde. The reaction mixture was refluxed for 48 hr. Distillation gave 14.4 g. (65% yield) collected in three fractions boiling at 135–136° (20 mm.), n_D^{25} 1.4710–1.4713. Redistillation gave a colorless liquid, b.p. 76.5° (0.4 mm.), n_D^{25} 1.4710.

Anal. Calcd. for $C_{14}H_{26}N_2$: N, 12.60. Found: N, 12.64.

The *dihydrochloride* had m.p. 185–188°.

Anal. Calcd. for $C_{14}H_{28}Cl_2N_2$: C, 56.94; H, 9.56; N, 9.49. Found: C, 57.00; H, 9.65; N, 9.48.

The *dimethiodide* was prepared by adding methyl iodide to a solution of the diamine in absolute ethanol. After 6 hr. at room temperature, the salt was precipitated with ether; m.p. 192–194° dec.

Anal. Calcd. for $C_{16}H_{32}N_2I_2$: C, 37.96; H, 6.37; N, 5.53. Found: C, 38.14; H, 6.54; N, 5.61.

1,4-Bis(pyrrolidino)-4-methyl-2-pentyne (XVI) was prepared from 13.7 g. (0.10 mole) of 3-pyrrolidino-3-methyl-1-butyne, 7.81 g. (0.11 mole) of pyrrolidine and 6.0 g. (0.20 mole) of paraformaldehyde. Distillation gave 18.2 g. (83% yield) collected in three fractions boiling at 94–95° (0.3 mm.), n_D^{25} 1.4910–1.4915. Redistillation gave a colorless liquid, b.p. 140° at 0.8 mm., n_D^{25} 1.4915.

Anal. Calcd. for $C_{14}H_{24}N_2$: N, 12.71. Found: N, 12.87.

The *dihydrochloride* had m.p. 221–222° dec.

Anal. Calcd. for $C_{14}H_{26}Cl_2N_2$: C, 57.33; H, 8.94; N, 9.55. Found: C, 57.27; H, 9.04; N, 9.61.

The *dimethiodide* melted at 200–202° dec.

Anal. Calcd. for $C_{16}H_{30}I_2N_2$: C, 38.11; H, 6.27; N, 5.56. Found: C, 38.04; H, 6.27; N, 5.52.

2,7-Bis(dimethylamino)-2,7-dimethyl-3,5-octadiyne (XVII). Ten grams (0.11 mole) of cuprous chloride, 7.5 g. of ammonium chloride and 9 ml. of water were added to a solution of 11.1 g. (0.10 mole) of 3-dimethylamino-3-methyl-1-butyne and 50 ml. of 2*N* hydrochloric acid in a 150 ml. flask fitted with a mechanical stirrer and gas dispersion tube. The reaction mixture was heated at 50–55° with stirring and passage of air for 10 hr. The resulting mixture was then cooled and made strongly alkaline with cold concd. ammonium hydroxide. A solid precipitated and the suspension was extracted with three 200-ml. and two 150-ml. portions of ether The ether extracts were combined and dried over anhydrous potassium carbonate. The ether was then distilled and the solid residue allowed to stand overnight to remove volatile impurities. Crystallization from ethanol-water gave 6.5 g. (59% yield), m.p. 181–184°.

Anal. Calcd. for $C_{14}H_{24}N_2$: C, 76.31; H, 10.98; N, 12.71. Found: C, 76.40; H, 10.90; N, 12.85.

The *dihydrochloride*, recrystallized from ethanol-water, had m.p. 240–241°.

Anal. Calcd. for $C_{14}H_{26}Cl_2N_2$: C, 57.33; H, 8.94; N, 9.55. Found: C, 56.96; H, 9.06; N, 9.47.

The *dimethiodide* melted at 210° dec.

Anal. Calcd. for $C_{16}H_{30}I_2N_2$: C, 38.11; H, 6.00; N, 5.55. Found: C, 38.66; H, 6.19; N, 5.95.

2,7-Bis(pyrrolidino)-2,7-dimethyl-3,5-octadiyne (XVIII). Thirteen grams (0.13 mole) of cuprous chloride, 7.5 g. of ammonium chloride and 15 ml. of water were added to a solution of 13.7 g. (0.10 mole) of 3-pyrrolidino-3-methyl-1-butyne and 50 ml. of 2*N* hydrochloric acid in a thick-walled bottle. The resulting mixture was shaken under an oxygen pressure of 2–4 *p.s.i.g.* The reaction mixture became warm and after 2 hr. 15 ml. of water was added and shaking with oxygen was continued for an additional 2 hr. Addition of cold concd. ammonium hydroxide effected the precipitation of a solid and the resulting slurry was extracted with a 300-ml., a 200-ml. and two 100-ml. portions of ether. The ether extracts were combined and dried over anhydrous potassium carbonate. Distillation of the ether gave a solid residue which was crystallized from ethanol-water; yield 11.0 g. (80%); m.p. 142–144°.

When the procedure described above for the preparation of XVII was employed, a 52% yield was obtained.

Anal. Calcd. for $C_{18}H_{28}N_2$: C, 79.36; H, 10.36; N, 10.28. Found: C, 79.15; H, 9.94; N, 10.31.

The *dihydrochloride* had m.p. 195–208° dec.

Anal. Calcd. for $C_{18}H_{30}Cl_2N_2$: N, 8.11; Found: N, 7.99.

7-Pyrrolidino-2,7-dimethyl-3,5-octadiyne-2-ol (XIX). A mixture of 6.85 g. (0.05 mole) of 3-pyrrolidino-3-methyl-1-butyne, 25 ml. of 2*N* hydrochloric acid, 25 g. (0.25 mole) of 3-methyl-1-butyne-3-ol, 7.5 g. of ammonium chloride, 12.0 g. (0.12 mole) of cuprous chloride and 75 ml. of water in a thick-walled bottle was shaken under an oxygen pressure of 1–2 *p.s.i.g.* The resulting mixture became warm and a solid precipitated. After 3 hr., an additional 3 g. of cuprous chloride and 25 ml. of water were added and shaking with oxygen was continued for 1 hr. After addition of cold concd. ammonium hydroxide solution (until the mixture was strongly alkaline) a brown precipitate was collected, washed with cold dilute ammonium hydroxide and finally with water. This solid was extracted with a 50-ml. and a 25-ml. portion of 2*N* hydrochloric acid. The acidic solution was decolorized with charcoal, cooled and made strongly alkaline with cold concd. ammonium hydroxide. A yellow, oily layer formed which subsequently solidified upon standing at room temperature. Crystallization from ethanol-water and then from petroleum ether (b.p. 35–60°) yielded 5.7 g. (52%) of white needles, m.p. 125–127°.

The infrared spectrum exhibited the expected bands at 2.8 and 4.5 μ.

Anal. Calcd. for $C_{14}H_{21}NO$: C, 76.66; H, 9.65; N, 6.39. Found: C, 76.66; H, 9.71; N, 6.42.

The *hydrochloride* had m.p. 193–195°.

Anal. Calcd. for $C_{14}H_{22}ClNO$: C, 64.05; H, 9.10; N, 5.75. Found: C, 63.99; H, 8.66; N, 5.85.

7-Dimethylamino-2,7-dimethyl-3,5-octadiyne-2-ol (XX) was prepared similarly from 5.6 g. (0.05 mole) of 3-dimethylamino-3-methyl-1-butyne, 27 ml. of 2*N* hydrochloric acid, 25 g. (0.25 mole) of 3-methyl-1-butyne-3-ol, 12.0 g. (0.12 mole) of cuprous chloride, 7.5 g. of ammonium chloride and 75 ml. of water. After shaking with oxygen maintained at 1–2 *p.s.i.g.* for 3 hr., an additional 6 g. of cuprous chloride and 25 ml. of water were added and the reaction mixture was shaken with oxygen for 1 hr. The amino alcohol was recrystallized twice from benzene-petroleum ether and then from ethanol-water; yield 3.0 g. (31%) of white plates, m.p. 149.5–152.5°.

Anal. Calcd. for $C_{12}H_{19}NO$: C, 74.57; H, 9.91; N, 7.25. Found: C, 74.81; H, 10.03; N, 7.12.

The *hydrochloride* had m.p. 242–243° dec.

Anal. Calcd. for $C_{12}H_{20}ClNO$: C, 62.73; H, 8.77; N, 6.10. Found: C, 62.63; H, 8.54; N, 5.92.

3-Dimethylamino-3-methyl-2-butanone (XXI). Mercuric oxide (1.5 g.) was added to a solution of 18.2 g. of 96% sulfuric acid, 35 g. of water, 11.1 g. (0.10 mole) of 3-dimethylamino-3-methyl-1-butyne and 15 ml. of methanol. The reaction mixture was heated at 80–90° for 3 hr., cooled and made strongly alkaline by dropwise addition of cold concd. sodium hydroxide solution. After extraction of the oil with two 75-ml. portions of ether, the ether extracts were combined and dried over anhydrous potassium carbonate. Removal of the ether at atmospheric pressure and distillation of the residue through a semi-micro Vigreux column gave 6.9 g. (54% yield) of a fraction with b.p. 78° (68 mm.), n_D^{20} 1.4278. Redistillation gave a colorless liquid, b.p. 72° at 52 mm., n_D^{20} 1.4280.

A strong band at 5.89 μ in the infrared spectrum clearly indicated the presence of a carbonyl function.

Anal. Calcd. for $C_7H_{15}NO$: C, 65.07; H, 11.70; N, 10.84. Found: C, 64.87; H, 12.06; N, 10.70.

The *hydrochloride* had m.p. 145–149°.

Anal. Calcd. for $C_7H_{16}ClNO$: C, 50.75; H, 9.74; N, 8.46. Found: C, 50.14; H, 10.28; N, 8.07.

The *methiodide* melted at 213–214° dec.

Anal. Calcd. for $C_8H_{18}INO$: C, 35.43; H, 6.69; N, 5.17. Found: C, 35.72; H, 6.80; N, 5.37.

3-Pyrrolidino-3-methyl-2-butanone (XXII) was prepared by a similar procedure with 2.5 g. of mercuric oxide, 13.7 g. (0.10 mole) of 3-pyrrolidino-3-methyl-1-butyne, 18.2 g. of 96% sulfuric acid, 20 ml. of methanol and 20 ml. of water. The reaction mixture was heated at 75–80° on a steam bath for 3 hr. Distillation of the product gave a fraction with b.p. 90° (18 mm.), n_D^{21} 1.4581, weight 8.0 g. (52% yield). Redistillation gave b.p. 87.5–88° at 16 mm., n_D^{20} 1.4588.

Anal. Calcd. for $C_9H_{17}NO$: C, 69.63; H, 11.04; N, 9.02. Found: C, 69.61; H, 10.77; N, 8.89.

The *methiodide* melted at 169–187° dec.

Anal. Calcd. for $C_{10}H_{20}INO$: C, 40.41; H, 6.78; N, 4.71. Found: C, 40.62; H, 6.92; N, 4.68.

3-Pyrrolidino-3-methyl-2-butanol (XXIII). To 7.2 g. (0.047 mole) of 3-pyrrolidino-3-methyl-2-butanone in 50 ml. of methanol was added, in small portions, 9.0 g. (0.24 mole) of sodium borohydride. The ensuing reaction was quite exothermic. After addition was complete, the mixture was heated on a steam bath for 2 hr., cooled, added to 60 g. of ice and then acidified by dropwise addition of 60 ml. of cold 5*N* hydrochloric acid. The mixture was concentrated to near dryness at room temperature and the residue diluted with water to a total volume of 100 ml. Potassium hydroxide pellets (30 g.) were added in small portions to the cooled mixture. An oil separated and was extracted with four 50-ml. portions of ether. Sodium chloride (10 g.) was added to the aqueous layer followed by further extraction with two 50-ml. portions of ether. The ethereal extracts were combined, dried superficially with anhydrous potassium carbonate and finally with anhydrous magnesium sulfate. The ether was removed by distillation and the residue distilled through a semi-micro Vigreux column; yield 6.0 g. (81%) of fractions with b.p. 99–100° (17 mm.), $n_D^{20.4}$ 1.4670–1.4674. Redistillation of the product gave b.p. 99° at 18 mm., n_D^{25} 1.4653.

The infrared spectrum showed the expected —OH band at 2.95 μ.

Anal. Calcd. for $C_9H_{19}NO$: C, 68.74; H, 12.18; N, 8.91. Found: C, 68.88; H, 11.93; N, 9.04.

The *methiodide* melted at 188–189°.

Anal. Calcd. for $C_{10}H_{22}INO$: C, 40.14; H, 7.41; N, 4.68. Found: C, 40.18; H, 7.49; N, 4.70.

3-Dimethylamino-3-methyl-2-butanol (XXIV) was prepared in a similar manner from 8.0 g. (0.62 mole) of 3-dimethylamino-3-methyl-2-butanone and 11.3 g. (0.31 mole) of sodium borohydride. The yield was 6.6 g. (88%) of fractions boiling at 90° (60 mm.), n_D^{25} 1.4375–1.4400. Redistillation gave b.p. 90° at 60 mm., n_D^{25} 1.4400.

Anal. Calcd. for $C_7H_{17}NO$: C, 64.07; H, 13.06; N, 10.68. Found: C, 64.02; H, 13.36; N, 10.55.

The *methiodide* decrepitated at 166–169° and melted with decomposition at 248–252° (preheated block).

Anal. Calcd. for $C_8H_{20}INO$: N, 5.13; Found: N, 5.00.

4-Dimethylamino-4-methyl-2-pentynoic acid (XXV). Sodium metal (3.0 g., 0.13 g.-atom) was converted to the amide in the usual manner[20] with 300 ml. of liquid ammonia in a 1-l., three-necked, round bottom flask fitted with a mercury sealed stirrer, gas outlet tube and dropping funnel. 3-Dimethylamino-3-methyl-1-butyne (11.1 g., 0.10 mole) dissolved in 100 ml. of anhydrous ether was added dropwise with stirring (20 min.). After evaporation of the ammonia at room temperature the gas outlet tube was replaced with an Allihn condenser and attached drying tube (soda lime) and a gas inlet tube replaced the dropping funnel. The mixture was then boiled on a steam bath for 6 hr. to remove remaining ammonia. During this period, 200 ml. of anhydrous ether was added. The reaction mixture was cooled to room temperature and diluted with ether to a total volume of 500 ml. Dry carbon dioxide gas was then bubbled through the mixture for eleven hours. Cold water (200 ml.) was added and the mixture was shaken until there were two clear layers. The aqueous layer was separated, extracted with 100 ml. of ether (discarded), filtered and acidified to *p*H 3 with 50% sulfuric acid. Evaporation of this solution to dryness at room temperature gave 23.0 g. of a solid residue. This solid was extracted with two 75-ml. portions (A and B, respectively) of warm (75°) glacial acetic acid. On cooling to room temperature, a solid crystallized from A; weight 6.1 g. Upon addition of ether, 4.2 g. of solid precipitated from B. These fractions were combined, dissolved in warm (80°) glacial acetic acid and the solution allowed to cool to room temperature. The product was collected and washed with ether. The yield was 8.0 g. (52%) of colorless crystals which decarboxylated cleanly to 3-dimethylamino-3-methyl-1-butyne on heating.

The infrared spectrum revealed a band at 6.2 μ (assigned to $—CO_2—$) and the absence of any band assigned to O—H stretching vibrations. This is consistent with the zwitterion form of the amino acid. In contrast, the spectrum of 4-pyrrolidino-4-methyl-2-pentynoic acid (XXVI) contained not only the band at 6.3 μ but also a band at 5.85 μ (assigned to C═O stretching vibration of $—CO_2H$) and at 2.9 μ (stretching vibration of bonded OH). This is to be expected if XXVI is an acetic acid salt or is solvated by one molecule of acetic acid per molecule of amino acid.

Anal. Calcd. for $C_8H_{13}NO_2$: C, 61.91; H, 8.44; N, 9.03. Found: C, 62.16; H, 8.63; N, 8.94.

4-Pyrrolidino-4-methyl-2-pentynoic acid (XXVI) was prepared in a similar manner from 3.0 g. (0.13 g.-atom) of metallic sodium, 300 ml. of liquid ammonia and 13.7 g. (0.10 mole) of 3-pyrrolidino-3-methyl-1-butyne dissolved in 100 ml. of anhydrous ether. The solid residue obtained from evaporation of the acidified aqueous solution was extracted with two 60-ml. portions of glacial acetic acid at 80°, and the solutions allowed to cool at room temperature. The solid was collected and recrystallized from glacial acetic acid as described above. The yield was 9.6 g. (40%) of material which decarboxylated on heating.

Anal. Calcd. for $C_{12}H_{19}NO_4$ ($C_{10}H_{15}NO_2 \cdot CH_3CO_2H$): C, 59.73; H, 7.94; N, 5.81. Found: C, 59.65; H, 7.85; N, 5.90.

2-Pyrrolidino-2-methylbutane (XXVII). 3-Pyrrolidino-3-methyl-1-butyne (13.7 g., 0.10 mole) was dissolved in 75 ml. of absolute ethanol in a thick-walled bottle and 2–3 g. of Raney nickel (wet with alcohol) was added. The mixture was shaken with hydrogen at an initial pressure of 50 *p.s.i.g.* until the pressure drop indicated absorption of 0.2 mole of hydrogen (5 hr.). The catalyst was filtered off, the ethanol removed at atmospheric pressure and the residue distilled through a modified Claisen flask with a 25-cm. Vigreux column. The fractions boiling at 80–81° (39 mm.), n_D^{25} 1.4479, weighed 9.0 g. (64% yield). Redistillation yielded 8.2 g. of a colorless liquid, b.p. 80° (38 mm.), n_D^{25} 1.4482.

The infrared spectrum exhibited no absorption bands usually assigned to carbon-carbon unsaturation.

When the preparation was repeated using 1.0 g. of 10% palladium on activated charcoal as the catalyst, a 50% yield was realized.

Anal. Calcd. for $C_9H_{19}N$: C, 76.52; H, 13.56; N, 9.92. Found: C, 76.94; H, 13.59; N, 9.63.

The *hydrochloride* had m.p. 137–142°.

Anal. Calcd. for $C_9H_{20}ClN$: C, 60.82; H, 11.34; N, 7.88. Found: C, 60.20; H, 11.03; N, 7.90.

3-Pyrrolidino-3-methyl-1-butene (XXVIII). To 13.7 g. (0.10 mole) of 3-pyrrolidino-3-methyl-1-butyne and 60 ml. of petroleum ether in a thick-walled bottle was added 0.07 g. of 10% palladium on activated charcoal. The mixture was shaken with hydrogen at an initial pressure of 50 *p.s.i.g.* until the pressure drop indicated absorption of 0.1 mole of hydrogen (1 hr.). The catalyst was filtered off, the petroleum ether removed by distillation at atmospheric pressure and the residue distilled through a modified Claisen with a 25-cm. Vigreux column. The fractions boiling between 74–74.5° (36 mm.), n_D^{25} 1.4560–1.4571 were collected; weight 12.8 g. Redistillation gave b.p. 56° at 16 mm., n_D^{25} 1.4571, weight 12.0 g. (86% yield).

The infrared spectrum showed bands at 3.28, 6.14, 7.07, 9.98, 10.99 and 14.55 μ.

Anal. Calcd. for $C_9H_{17}N$: C, 77.63; H, 12.31. Found: C, 76.99; H, 12.52.

The *methiodide* had m.p. 152–158° dec.

Anal. Calcd. for $C_{10}H_{20}NI$: N, 4.98. Found: N, 5.00.

3-Dimethylamino-3-methyl-1-butene (XXIX) was prepared by the same procedure with 11.1 g. (0.10 mole) of dimethylamino-3-methyl-1-butyne, 0.065 g. of 10% palladium on activated charcoal and 60 ml. of petroleum ether. The hydrogenation time was 10.5 hr. The fractions boiling between 110–114°, n_D^{25} 1.4225–1.4230 were collected; weight 7.3 g. (63% yield). Redistillation gave material with b.p. 113°, n_D^{25} 1.4231.

Anal. Calcd. for $C_7H_{15}N$: C, 74.27; H, 13.36. Found: C, 74.78; H, 13.06.

The *methiodide* had m.p. 155–158° dec.

Anal. Calcd. for $C_8H_{18}N$: N, 5.49. Found: N, 5.75.

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NOTRE DAME, IND.

[CONTRIBUTION FROM THE RESEARCH AND DEVELOPMENT DEPARTMENT, ORGANIC CHEMICALS DIVISION, AMERICAN CYANAMID CO.]

The Chlorination of *N*,*N*-Dimethylaniline

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The chlorination of *N*,*N*-dimethylaniline with molecular chlorine gives 2-chloro- and 2,4-dichloro-*N*,*N*-dimethylaniline as the chief products. The chlorination with *N*-chlorosuccinimide, however, yields 39% 4-chloro- and 43% 2-chloro-*N*,*N*-dimethylaniline. This 4-chloro derivative has been found more reactive than the 2-chloro isomer in a competitive reaction with chlorine at about 40°, but the two have been found to react at about the same rate with *N*-chlorosuccinimide in the kinetic studies made.

Chlorination of *N*,*N*-dimethylaniline was reported by Krell[1] in 1872 to give an undefined mixture of monochlorodimethylanilines as well as 2,4-dichloro- and 2,4,6-trichloro-*N*,*N*-dimethylaniline. The nature of the mixture of the monosubstituted products was elucidated by Tishchenko[2] who reported that equal quantities of 2- and 4-chloro-*N*,*N*-dimethylanilines were formed on treatment of a suspension of *N*,*N*-dimethylaniline in aqueous sodium carbonate with chlorine. More recently Danilov and Koz'mina[3] have stated that chlorination with *N*-chloroacetanilide gave rise to both 2- and 4-chloro derivatives while Carpmael[4] found that the use of chlorine gave only 2-chloro-*N*,*N*-dimethylaniline as the monosubstituted product. These results are in marked contrast with the bromination and nitrosation of *N*,*N*-dimethylaniline which give principally the 4-substituted product. The present work was undertaken to investigate the apparent anomaly of this chlorination reaction.

It was found that chlorination of *N*,*N*-dimethylaniline with chlorine in various solvents, sulfuryl chloride in chlorobenzene, dichlorine oxide in carbon tetrachloride, and sodium hypochlorite in acid and basic solutions all gave 2-chloro- and 2,4 dichloro-*N*,*N*-dimethylaniline. The 4-chloro-*N*,*N*-dimethylaniline was found only in small or trace quantities. Chlorination with *N*-chloro reagents such as *N*-chlorosuccinimide, 1,3-dichloro-5,5-di-

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