312. *Researches on Acetylenic Compounds. Part XI. The Mannich Reaction with Monosubstituted Acetylenic Compounds.*

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The scope of the Mannich reaction with mono-substituted acetylenic compounds, previously only applied to activated substances such as phenyl- and vinyl-acetylenes, has been extended to include alkylacetylenes and several types of acetylenic alcohols. Excellent yields are obtainable except with the α-ethynylcarbinols [containing the grouping $>C(OH)\cdot C{\equiv}CH$], but their acetates react normally. No suggestions for this anomalous behaviour can as yet be offered.

The application of the well-known Mannich reaction (for summary see Blicke, "Organic Reactions," 1942, I, p. 303) in the acetylenic series has hitherto been restricted to compounds containing an activated ethynyl group, *e.g.*, phenyl- and substituted phenyl-acetylenes (Mannich and Chang, *Ber.*, 1933, **66**, 418) and vinylacetylene (Coffman, *J. Amer. Chem. Soc.*, 1935, **57**, 1978; Carothers and du Pont, U.S.P. 2,110,199). With acetylene itself the reaction has to be effected under pressure in the presence of a copper acetylide catalyst, under which conditions propargylamines ($HC{\equiv}C\cdot CH_2\cdot NR_2$) and the corresponding diamines are formed, the former preponderating (I.G. Farb., B.P. 510,904; U.S.P. 2,273,141).

$$Ph\cdot C{\equiv}CH + H\cdot CHO + HNR_2 \longrightarrow Ph\cdot C{\equiv}C\cdot CH_2\cdot NR_2$$

The present study was undertaken with a view to extending the scope of the Mannich reaction to various types of acetylenic compounds. During the progress of this work information became available that some similar studies had been made in Germany (B.I.O.S. Final Report No. 266; item No. 22) and although no experimental details are available, it seems that copper catalysts were invariably employed.

In all the reactions described in this paper the appropriate reagents were heated in dioxan solution at about 80° in nitrogen. 1-Hexyne, the only hydrocarbon examined, gave a 75% yield of 1-*diethylaminohept*-2-*yne* (I). α-Ethynylcarbinols of type (II), invariably gave exceedingly poor yields of the expected amines, but their acetates on the other hand behaved normally and yields of *amines* (III) ranging from 50 to 90% were obtained with the acetates of representative primary, secondary, and tertiary carbinols. The inhibiting effect of the hydroxyl group is apparently restricted to the α-position since the β-ethynylcarbinol [$CH_3\cdot CH(OH)\cdot CH_2\cdot C{\equiv}CH$] gave a 60% yield of amine. With conjugated ethynyl-ethylenic carbinols such as (IV) no inhibiting effect of the hydroxyl groups was observed, 80—85% yields of the expected amines being achieved both with the carbinols themselves and with their acetates. The products in these cases all exhibited similar light absorption properties in the ultra-violet, arising from the presence of the conjugated ethylenic-acetylenic chromophore.

(I.) $C_4H_9\cdot C{\equiv}C\cdot CH_2\cdot NEt_2$ $RR_1C(OH)\cdot C{\equiv}CH$ (II.)

(III.) $RR_1C(OAc)\cdot C{\equiv}C\cdot CH_2\cdot NEt_2$ $CH_3\cdot CH(OH)\cdot CH{=}CH\cdot C{\equiv}CH$ (IV.)

The partial and complete hydrogenation and also other reactions of the acetylenic amino-alcohols described in this paper are being studied and will be reported on in a subsequent communication.

Experimental.

Light-absorption data were determined in alcoholic solutions.

1-*Diethylaminohept*-2-*yne* (I).—To a warm solution of diethylamine (16 g.) and trioxymethylene (7·2 g.) in dioxan (20 c.c.), a solution of 1-hexyne (16·4 g.) in dioxan (10 c.c.) was added and the mixture was heated on a steam-bath for 15 hours in an atmosphere of nitrogen. Ether was added, and the basic product was isolated by washing with 2N-hydrochloric acid and then liberated with sodium hydroxide (10%). After ether extraction, drying (Na_2SO_4), and evaporation, distillation gave 1-*diethylaminohept-2-yne* (25·7 g.; 77%), b. p. 100°/20 mm., $n_D^{12^\circ}$ 1·4513 (Found : C, 78·95; H, 12·5. $C_{11}H_{21}N$ requires C, 78·95; H, 12·6%). The *picrate*, prepared in methanol, crystallised from this solvent as long prisms, m. p. 75° (Found : C, 51·8; H, 6·2. $C_{17}H_{24}O_7N_4$ requires C, 51·5; H, 6·1%).

1-*Dimethylamino-4-acetoxyprop-2-yne.*—A mixture of dimethylamine (6 g.), trioxymethylene (4·7 g.), and propargyl acetate (12 g.) in dioxan (25 c.c.) was heated for 34 hours on a steam-bath. The *amine* (8·8 g.) had b. p. 65°/0·7 mm., $n_D^{23^\circ}$ 1·4531 (Found : C, 61·55; H, 8·85. $C_8H_{13}O_2N$ requires C, 61·9; H, 8·45%). The *methiodide* crystallised from methanol–ether in prisms, m. p. 140° (Found : C, 36·75; H, 5·55. $C_9H_{16}O_2NI$ requires C, 36·35; H, 5·45%).

1-*Diethylamino-4-acetoxyhept-2-yne* (III; R = H; R_1 = *n*-Pr).—The standard method (20 hours' heating) employed with diethylamine (8 g.), trioxymethylene (3·9 g.), and 3-acetoxyhex-1-yne (14 g.; Bowden, Heilbron, Jones, and Weedon, *J.*, 1946, 45) in dioxan (15 c.c.) gave the *amine* (20 g.), b. p. 81°/0·1 mm., $n_D^{19^\circ}$ 1·4546 (Found : C, 69·2; H, 10·4. $C_{13}H_{23}O_2N$ requires C, 69·25; H, 10·3%). The same base was obtained, but in poorer yield, by carrying out the reaction at 20°. The *oxalate* crystallised from ethanol–ether as fine prisms, m. p. 90·5° (Found : C, 57·2; H, 7·65. $C_{15}H_{25}O_6N$ requires C, 57·1; H, 8·0%).

1-*Diethylamino*-1'-*acetoxy*-3-cyclo*hexylprop-2-yne* (III; RR' = C_5H_{10}).—Diethylamine (12 g.), trioxymethylene (5·4 g.), and ethynyl*cyclo*hexanyl acetate (24·9 g.) in dioxan (25 c.c.) after being heated for 30 hours gave the *amine* (29·7 g.), b. p. 111°/0·6 mm., $n_D^{13^\circ}$ 1·4806 (Found : C, 71·95; H, 10·25. $C_{15}H_{25}O_2N$ requires C, 71·65; H, 10·05%). The *picrate* crystallised from methanol in plates, m. p. 114° (Found : C, 52·5; H, 5·9. $C_{21}H_{28}O_9N_4$ requires C, 52·45; H, 5·9%).

1-*Diethylaminohex-2-yn-5-ol.*—After a mixture of diethylamine (12·4 g.), trioxymethylene (6·75 g.), and pent-1-yn-4-ol (12·6 g.; Haynes and Jones, *J.*, 1946, 956) had been heated on a steam-bath for 30 hours, the *amine* (15 g.) was isolated with b. p. 73°/0·1 mm., $n_D^{15^\circ}$ 1·4740 (Found : C, 71·0; H, 11·45. $C_{10}H_{19}ON$ requires C, 70·95; H, 11·3%). The *picrate* crystallised from benzene in prisms, m. p. 78° (Found : C, 48·4; H, 5·65. $C_{16}H_{22}O_8N_4$ requires C, 48·2; H, 5·55%).

1-*Diethylaminohex-4-en-2-yn-6-ol.*—A mixture of diethylamine (16 g.), trioxymethylene (7·2 g.), and pent-2-en-4-yn-1-ol (16·4 g., Haynes, Heilbron, Jones, and Sondheimer, Part XIII, this vol., p.1583) in dioxan (25 c.c.) on being heated for 25 hours on a steam-bath gave the *amine* (25·4 g.), b. p. 135°/1 mm., $n_D^{20^\circ}$ 1·5102 (Found : C, 72·1; H, 10·25. $C_{10}H_{17}ON$ requires C, 71·8; H, 10·25%). Light absorption : Maximum, 2270 A.; ε = 15,500. Inflexion, 2370 A., ε = 12,500. The *a-naphthylurethane* crystallised from petroleum (b. p. 80—100°) in plates, m. p. 79° (Found : C, 75·05; H, 7·4. $C_{21}H_{24}O_2N_2$ requires C, 74·95; H, 7·2%).

1-*Diethylaminohept-4-en-2-yn-6-ol.*—The standard method (36 hours' heating) employed with diethylamine (12·4 g.), trioxymethylene (6 g.), and hex-3-en-5-yn-2-ol (13·8 g.; Heilbron, Jones, and Weedon, *J.*, 1945, 81) in dioxan (20 c.c.) gave the *amine* (21 g.), b. p. 85°/0·1 mm., $n_D^{15^\circ}$ 1·5003 (Found : C, 73·1; H, 10·75. $C_{11}H_{19}ON$ requires C, 72·85; H, 10·55%). Light absorption : Maximum, 2270 A.; ε = 15,000. Inflexion, 2350 A.; ε = 13,000. The *picrate*, prepared in methanol, crystallised from benzene in plates, m. p. 118° (Found : C, 49·95; H, 5·55. $C_{17}H_{22}O_8N_4$ requires C, 49·75; H, 5·4%).

1-*Dimethylamino-6-acetoxyhept-4-en-2-yne.*—A mixture of dimethylamine (5 g.), trioxymethylene (3·6 g.), and 2-acetoxyhex-3-en-5-yne (13·8 g.; Jones and McCombie, *J.*, 1943, 261) in dioxan (30 c.c.) after being heated for 24 hours on a steam-bath gave the *amine* (16·2 g.), b. p. 72°/0·5 mm., $n_D^{17^\circ}$ 1·4808 (Found : C, 68·15; H, 8·7. $C_{11}H_{17}O_2N$ requires C, 67·65; H, 8·8%). The *methoperchlorate* crystallised from methanol–ether in plates, m. p. 112·5° (Found : C, 46·75; H, 6·35. $C_{12}H_{20}O_6NCl$ requires C, 46·5; H, 6·5%).

1-*Diethylamino-6-acetoxyhept-4-en-2-yne.*—Prepared as above using diethylamine (8 g.) instead of dimethylamine, the *amine* (19·1 g.) had b. p. 108—110°/1 mm., $n_D^{19^\circ}$ 1·4800 (Found : C, 69·5; H, 9·4. $C_{13}H_{21}O_2N$ requires C, 69·9; H, 9·5%).

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