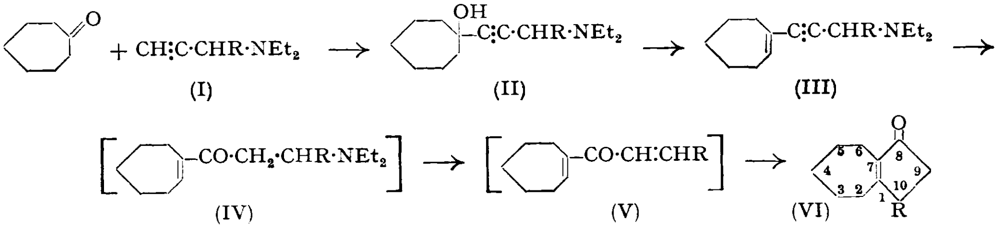
463. *A Convenient Synthesis of* bicyclo[5 : 3 : 0]*Dec*-1(7)-*en*-8-*one and Related Compounds.*

By A. M. Islam and R. A. Raphael.

Cyclisation of the readily prepared 1-(3-diethylaminoprop-1-ynyl)*cyclo*heptan-1-ol (II; R = H) by a hot mixture of phosphoric and formic acids containing mercuric acetate leads directly to *bicyclo*[5 : 3 : 0]dec-1(7)-en-8-one (VI; R = H). Application of the reaction to other allied bicyclic systems is described.

In recent years a series of memoirs by Nazarov and his co-workers (*inter al.*, *J. Gen. Chem. Russia*, 1950, **20**, 1431 *et seq.*, 2009, 2079, 2091, and earlier papers) has described the acid-induced cyclisation of a wide variety of allyl vinyl and divinyl ketones to substituted *cyclo*pentenones, the most general procedure involving treatment with a hot mixture of phosphoric and formic acids; the mechanism of the reaction has been discussed by Braude and Coles (*J.*, 1952, 1430). The wide applicability of the reaction suggested its extension to compounds of the *bicyclo*[5 : 3 : 0]decane system, the difficult accessibility of which has hampered the study of their dehydrogenation products, the azulenes. This approach has indeed already been envisaged by Braude and Forbes (*Nature*, 1951, **168**, 874) who developed a five-stage process for the conversion of *cyclo*heptanone into *bicyclo*[5 : 3 : 0]dec-1(7)-en-8-one. While presenting several novel features the route involved is rather lengthy and is not readily adaptable to large-scale working. A new approach to the problem was suggested by the recent availability of acetylenic amines of the general type (I) which are obtained from acetylene by the Mannich reaction (Copenhaver and Bigelow, " Acetylene and Carbon Monoxide Chemistry," Reinhold Publ. Corp., New York, 1949, p. 110). By their use a convenient two-stage conversion of *cyclo*heptanone into *bicyclo*[5 : 3 : 0]dec-1(7)-en-8-one (VI; R = H) has been achieved.

A condensation in liquid ammonia between *cyclo*heptanone and the lithium salt of 3-diethylaminoprop-1-yne (prepared *in situ* by treating 2-bromo-3-diethylaminoprop-1-ene with two mols. of lithamide) gave the corresponding acetylenic alcohol (II; R = H). Heating this compound with phosphoric–formic acid yielded mainly the dehydration product (III; R = H), but when the process was repeated in the presence of a small quantity of mercuric acetate conversion into the bicyclic ketone (VI; R = H) ensued. The identity of the material was confirmed by a mixed melting point of its semicarbazone with an authentic specimen (we are indebted to Professor J. W. Cook, F.R.S., for kindly providing a sample). The rationale of this cyclisation may be envisaged as follows. The initial formation of the dehydration product (III; R = H) is followed by hydration of the triple bond to form the unsaturated diethylamino-ketone (IV; R = H). The mode of addition leading to this vinyl ketone rather than to the isomeric allyl ketone may be confidently predicted from the results of Hamlet, Henbest, and Jones (*J.*, 1951, 2652) on the hydration of substituted vinylacetylenes; in this case the polarisation $\cdot\overset{\delta+}{C}\equiv\overset{\delta-}{C}\cdot CH_2\cdot\overset{+}{N}HEt_2$ would be further favoured by the juxtaposition of the strongly electron-attracting tertiary ammonium cation (for convenience the above flow sheet shows the compounds as free bases rather than salts). The position of the diethylamino-group in (IV) β to the carbonyl group favours the ready elimination of diethylamine (cf. the production of vinyl ketones from salts of Mannich bases; Mannich *et al.*, *Ber.*, 1941, **74**, 554; 1922, **55**, 356, 3504; *Arch. Pharm.*, 1927, **265**, 598) with the production of the divinyl ketone (V; R = H); Nazarov cyclisation of (V) then leads to the bicyclic product (VI). Although the conversion of *cyclo*heptanone into bicyclic ketone is small (26% allowing for recovered ketone; 15% overall) the method is rapid and simple and its attractiveness is enhanced by the ease of separation of the neutral product from any unchanged basic intermediates.



Extension of the synthesis to the homologous 3-diethylaminobut-1-yne (I; R = Me) gave the corresponding acetylenic alcohol (II; R = Me). The presence of the methyl group in this compound greatly facilitated its Nazarov cyclisation to (VI; R = Me), the conversion proceeding smoothly in the absence of mercuric salt. Application of the procedures to *cyclo*hexanone yielded 4 : 5 : 6 : 7-tetrahydroindanone and its 3-methyl homologue. The former product was also obtainable by the Nazarov cyclisation of 1-(3-hydroxyprop-1-ynyl)*cyclo*hexan-1-ol, prepared in low yield from *cyclo*hexanone and propargyl alcohol (Zeile and Meyer, *Ber.*, 1942, **75**, 356). Condensation of the lithium salt of 3-diethylaminoprop-1-yne with *cyclo*pentanone gave disappointing yields, much *cyclo*pentylidene*cyclo*pentanone being produced. However, the required material was obtained by subjecting 1-acetoxy-1-ethynyl*cyclo*pentane to the Mannich reaction with formaldehyde and diethylamine (Jones, Marszak, and Bader, *J.*, 1947, 1578). Nazarov cyclisation of the resulting 1-acetoxy-1-(3-diethylaminoprop-1-ynyl)*cyclo*pentane did furnish the expected *bicyclo*[3 : 3 : 0]oct-1(5)-en-2-one, but much tar was simultaneously produced and the yield was correspondingly low.

EXPERIMENTAL

In all experiments the concentration of formic acid was 90% and that of phosphoric acid 85%. All 2 : 4-dinitrophenylhydrazones were purified by chromatography (benzene–alumina) and crystallised from ethyl acetate–alcohol.

1-(3-*Diethylaminoprop*-1-*ynyl*)cyclo*heptan*-1-*ol* (II; R = H).—To a solution of lithamide (formed from lithium, 2·2 g., by the catalytic action of ferric nitrate) in liquid ammonia (400 c.c.) was added 2-bromo-3-diethylaminoprop-1-ene (30 g.) (Parcell and Pollard, *J. Amer. Chem. Soc.*, 1950, **72**, 2385), and the mixture stirred for 4 hr. A solution of *cyclo*heptanone (11·2 g.) in dry ether (15 c.c.) was then added dropwise during 30 min. and the stirring continued for a further 4 hr. After introduction of powdered ammonium chloride (10 g.) the ammonia was allowed to evaporate off and the residue treated with 2N-sulphuric acid and ether. The aqueous layer was then further extracted with ether; drying, evaporation, and distillation of the combined ethereal extracts gave unchanged *cyclo*heptanone (4·2 g.). Basification of the aqueous layer and isolation by means of ether gave 1-(3-*diethylaminoprop*-1-*ynyl*)cyclo*heptan*-1-*ol* (9·9 g., 72% based on reacted ketone) as a viscous oil, b. p. 102°/0·3 mm., n_{D}^{19} 1·4985 (Found: N, 6·4. $C_{14}H_{25}ON$ requires N, 6·3%).

bicyclo[5 : 3 : 0]*Dec*-1(7)-*en*-8-*one* (VI; R = H).—A mixture of the above acetylenic alcohol (4·4 g.), formic acid (12 g.), and phosphoric acid (3·5 g.) was boiled under gentle reflux for 6 hr. Water was then added and the precipitated oil extracted with ether. Washing (sodium carbonate solution), drying (Na_2SO_4), evaporation of the extract, and distillation of the residue gave the bicyclic ketone (VI; R = H) (0·25 g., 8%) b. p. 73°/0·2 mm., n_{D}^{18} 1·5241. The purified semicarbazone had m. p. 236° undepressed by an authentic sample (Cook, Philip, and Somerville, *J.*, 1948, 164, give b. p. 58—60°/0·1 mm., $n_{D}^{11\cdot 5}$ 1·5275, and semicarbazone m. p. 235—236°). The 2 : 4-*dinitrophenylhydrazone* crystallised as red needles, m. p. 230° (Found: C, 58·2; H, 5·2; N, 17·1. $C_{16}H_{18}O_4N_4$ requires C, 58·1; H, 5·4; N, 16·95%).

Neutralisation of the aqueous layer with ammonia and isolation by means of ether gave 1-(3-*diethylaminoprop*-1-*ynyl*)cyclo*hept*-1-*ene* (III; R = H) (3·2 g., 80%) as a colourless mobile oil, b. p. 88°/0·2 mm., n_{D}^{17} 1·5088 (Found: N, 6·7. $C_{14}H_{23}N$ requires 6·8%).

When mercuric acetate (0·5 g.) was added after the above reflux period and the heating continued for a further 4 hr. isolation as above gave a greatly enhanced yield (35%) of the bicyclic ketone. Subjection of (III; R = H) to this procedure gave a similar yield of the ketone.

1-(3-*Diethylaminobut*-1-*ynyl*)cyclo*heptan*-1-*ol* (II; R = Me).—To a solution of lithamide (from lithium, 1·7 g.) in liquid ammonia (400 c.c.) was added 3-diethylaminobut-1-yne (I; R = Me) (28 g.), and the mixture stirred for 1 hr. *cyclo*Heptanone (20 g.) in an equal volume of dry ether was then added and the stirring was continued for a further 4 hr. After addition of ammonium chloride (10 g.) and evaporation of the ammonia, the residue was treated with excess of 2N-sulphuric acid, and the non-basic constituents were extracted with ether; from this extract unchanged *cyclo*heptanone (11·5 g.) was recovered. The aqueous layer was basified with concentrated aqueous ammonia, and the precipitated oil isolated by ether; distillation gave 1-(3-*diethylaminobut*-1-*ynyl*)cyclo*heptan*-1-*ol* (13·5 g., 80% based on ketone which reacted), b. p. 104°/0·5 mm., n_{D}^{15} 1·4962 (Found: N, 6·1. $C_{15}H_{27}ON$ requires N, 5·9%). Employment of the Grignard derivative of the acetylenic amine in this condensation gave a much lower yield (35%) of the required product and very little *cyclo*heptanone was recovered.

10-*Methyl*bicyclo[5 : 3 : 0]*dec*-1(7)-*en*-8-*one* (VI; R = Me).—The above acetylenic alcohol (II; R = Me) (5 g.) was heated under reflux with formic acid (10 g.) and phosphoric acid (3·5 g.) for 4 hr. Working up as in the above cognate preparation gave 10-methyl*bicyclo*-[5 : 3 : 0]dec-1(7)-en-8-one (1·2 g., 35%), b. p. 140°/15 mm., n_{D}^{20} 1·5138; the 2 : 4-dinitrophenylhydrazone formed red needles, m. p. 236°, undepressed on admixture with an authentic sample (Braude and Forbes, *loc. cit.*, give n_{D}^{23} 1·5118 and 2 : 4-dinitrophenylhydrazone, m. p. 236°).

4 : 5 : 6 : 7-*Tetrahydroindan*-1-*one*.—(*a*) Treatment as in the above cognate preparation of lithamide (from lithium, 2·2 g.) in liquid ammonia (400 c.c.) with 2-bromo-3-diethylaminoprop-1-ene (30 g.), followed by addition of *cyclo*hexanone (14 g.), gave 1-(3-*diethylaminoprop*-1-*ynyl*)-cyclo*hexan*-1-*ol* (13 g.) as a viscous oil, b. p. 84°/0·2 mm., n_{D}^{19} 1·4959 (Found: N, 7·0. $C_{13}H_{23}ON$ requires N, 6·7%). This product (4 g.) was heated under reflux for 4 hr. with formic acid (10 g.) and phosphoric acid (3 g.); mercuric acetate (0·5 g.) was then added and the heating continued for a further 4 hr. Working up in the usual manner gave 4 : 5 : 6 : 7-tetrahydroindanone (1 g., 52%), b. p. 154°/16 mm., n_{D}^{16} 1·5022 [2 : 4-dinitrophenylhydrazone, m. p. 238° undepressed by an authentic specimen (Mathieson, *J.*, 1951, 177 gives m. p. 238°)]. If the mercuric acetate

treatment was omitted only a trace of ketonic material was formed, the product (90% yield) consisting of 1-(3-*diethylaminoprop*-1-*ynyl*)cyclo*hex*-1-*ene*, b. p. 78°/0·2 mm., n_D^{18} 1·5001; light absorption in EtOH: $\lambda_{max.}$ 2300 Å (ε = 9500) (Found: N, 6·9. $C_{13}H_{21}N$ requires N, 7·3%). Application of the mercuric acetate treatment to this converted it into tetrahydroindanone (48%). (*b*) When 1-(3-hydroxyprop-1-ynyl)*cyclo*hexan-1-ol (5 g.) prepared by the procedure of Zeile and Meyer (*loc. cit.*) was heated for 4 hr. with formic acid (10 g.) and phosphoric acid (2 g.) there was isolated the same tetrahydroindanone (2·2 g., 50%).

3-*Methyl*-4 : 5 : 6 : 7-*tetrahydroindan*-1-*one*.—By interaction of lithamide (from lithium, 1·5 g.), 3-diethylaminobut-1-yne (25 g.), and *cyclo*hexanone (20 g.) as in the above cognate preparation, there was obtained 1-(3-*diethylaminobut*-1-*ynyl*)cyclo*hexan*-1-*ol* (25 g.) as a viscous oil, b. p. 100°/0·6 mm., n_D^{21} 1·4910 (Found: N, 5·85. $C_{14}H_{25}ON$ requires N, 6·2%). Heating a mixture of this (4 g.), formic acid (10 g.), and phosphoric acid (3·5 g.) for 6 hr. furnished 3-methyl-4 : 5 : 6 : 7-tetrahydroindan-1-one (1·4 g., 51%), b. p. 135°/16 mm., n_D^{19} 1·5116; the 2 : 4-dinitrophenylhydrazone formed red needles, m. p. 242° undepressed by an authentic sample (Hamlet, Henbest, and Jones, *loc. cit.*, give n_D^{15} 1·5135, and 2 : 4-dinitrophenylhydrazone, m. p. 246°).

bicyclo[3 : 3 : 0]*Oct*-1(5)-*en*-2-*one*.—On being heated with four times its volume of acetic anhydride for 2 hr. 1-ethynyl*cyclo*pentan-1-ol was converted into its *acetate* (86% yield), b. p. 68°/15 mm., n_D^{16} 1·4595 (Found: C, 70·75; H, 7·2. $C_9H_{12}O_2$ requires C, 71·0; H, 7·8%). The acetate (8·5 g.), diethylamine (4 g.), paraformaldehyde (2·2 g.), and dioxan (10 c.c.) were heated by steam for 3 hr., then set aside overnight. Dilute hydrochloric acid was added and the neutral constituents were extracted with ether. Basification of the aqueous layer with sodium hydroxide solution followed by isolation by means of ether gave 1-*acetoxy*-1-(3-*diethylaminoprop*-1-*ynyl*)cyclo*pentane* (11 g., 83%), b. p. 76°/0·2 mm., n_D^{18} 1·4722 (Found: N, 5·75. $C_{14}H_{23}O_2N$ requires N, 5·9%). This product (8 g.) was heated under reflux for 5 hr. with formic acid (15 g.) and phosphoric acid (3 g.); the mixture rapidly darkened. Working up as in the cognate experiments gave *bicyclo*[3 : 3 : 0]oct-1(5)-en-2-one (0·3 g., 7%), b. p. 122°/15 mm., n_D^{21} 1·5226 (Cope and Schmitz, *J. Amer. Chem. Soc.*, 1950, **72**, 15 give n_D^{25} 1·5202). The semicarbazone of this product melted unsharply at *ca.* 205° (Cope and Schmitz, *loc. cit.*, give m. p. 230—232·2°) even after repeated crystallisation; this suggests contamination of the product with the uncyclised divinyl ketone. The 2 : 4-*dinitrophenylhydrazone* was readily purified, however, and crystallised in red needles, m. p. 196°; light absorption in EtOH: $\lambda_{max.}$ 3800 (ε = 27,500) and 2550 Å (ε = 16,500) (Found: N, 18·75. $C_{14}H_{14}O_4N_4$ requires N, 18·5%). Neutralisation of the acid aqueous layer gave 1-(3-*diethylaminoprop*-1-*ynyl*)cyclo*pent*-1-*ene* (5 g., 87%) b. p. 57°/0·2 mm., n_D^{16} 1·4995 (Found: N, 7·95. $C_{12}H_{19}N$ requires N, 7·9%). Cyclisation of this enyne by the mercuric acetate technique gave a similar yield (6%) of *bicyclo*[3 : 3 : 0]octenone.

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