560. *Syntheses in the Morphine Series. Part II.* Substituted Hexahydrodiphenyls and Related Topics.*

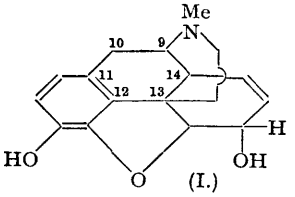
By J. A. Barltrop and J. S. Nicholson.

The Diels–Alder adducts derived from 2 : 3-dimethoxy-ω-nitrostyrene and butadiene or 2-ethoxybutadiene are transformed into 2-(2 : 3-dimethoxyphenyl)*cyclo*hexanone (VII) and 2-(2 : 3-dimethoxyphenyl)*cyclo*hexane-1 : 4-dione (XV) respectively. Preliminary experiments on the conversion of (VII) into substances more closely related to morphine are described.

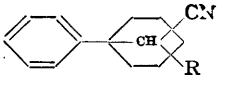
The reactions between arylmagnesium halides and α-cyano-α-*cyclo*hexylideneacetic ester and its derivatives are investigated.

This paper is largely concerned with the synthesis of intermediates containing a quaternary carbon atom substituted similarly to $C_{(13)}$ in morphine (I).

Birch and Robinson (*J.*, 1943, 502) discovered that aliphatic Grignard reagents react with ethyl α-cyano-α-*cyclo*hexylideneacetate by 1 : 4-addition, giving saturated compounds. Phenylmagnesium bromide has now been found to behave similarly, giving a 40% yield of ethyl α-cyano-α-1-phenyl*cyclo*hexylacetate (II; R = CO_2Et). The ester was hydrolysed with



(I.)



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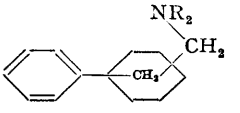
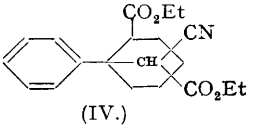


(III.)

sodium carbonate solution to the corresponding acid (II; R = CO_2H), which was readily decarboxylated to 1-cyanomethyl-1-phenyl*cyclo*hexane (II; R = H). Reduction of the nitrile afforded the base (III; R = H), which was converted into the dimethylamino-compound (III; R = Me) by formaldehyde and formic acid. Since the completion of this work, the preparation of compounds similar to those described above has been reported; Brown, Cook, and Heilbron (*J.*, 1949, S 113) obtained a low yield of 2-2′-diethylaminoethyl-2-phenyl*cyclo*hexanone by alkylating 2-phenyl*cyclo*hexanone with 2-diethylaminoethyl chloride, and Boekelheide (*J. Amer. Chem. Soc.*, 1947, **69**, 790) alkylated 2-phenyl*cyclo*hexanone in the 2-position with chloropropionitrile.



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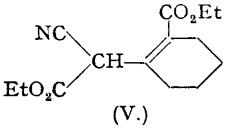

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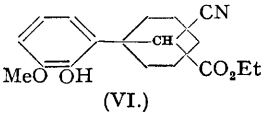


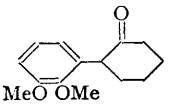
(VI.)

Attempts were made to extend the scope of the above synthesis to include molecules more closely related to morphine. First, in order to facilitate the construction of the phenanthrene 9 : 10-bridge, ethyl α-cyano-α-2-carbethoxy*cyclo*hexylideneacetate was condensed with phenylmagnesium bromide. The required product (IV) was, however, only obtained in very poor yield, presumably because the unsaturated ester tautomerised to (V). Secondly, in an attempt to introduce a more appropriately substituted benzene ring, the Grignard reagent derived from 3-iodoveratrole was added to α-cyano-α-*cyclo*hexylideneacetic ester, but there was obtained only a very small yield of a product believed to possess the structure (VI). The demethylation must have occurred during the actual preparation of the Grignard reagent, since carboxylation of the latter afforded guaiacolcarboxylic acid and not the expected 2 : 3-dimethoxybenzoic acid. A similar demethylation occurs when 2 : 3-dimethoxybenzonitrile reacts with methylmagnesium iodide (Amstutz, *J. Amer. Chem. Soc.*, 1949, **71**, 3836).

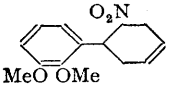
It has been realised for some time that 2-(2 : 3-dimethoxyphenyl)*cyclo*hexanone (VII) is potentially a useful intermediate for the synthesis of derivatives of morphine. It was first

* Part I, *J.*, 1947, 399.

prepared by Horning, Horning, and Platt (*J. Amer. Chem. Soc.*, 1947, **69**, 2929) by a tedious synthesis, proceeding in 5% overall yield, from *o*-veratraldehyde, and more recently by Bergmann, Pappo, and Ginsburg (*J.*, 1950, 1369). We have devised a new and shorter synthesis which gives 20% overall yield.



(VII.)



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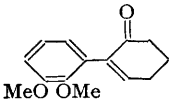
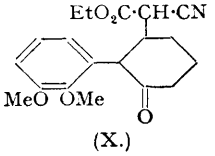
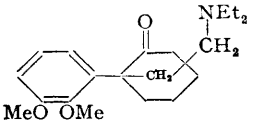


(IX.)

2 : 3-Dimethoxy-ω-nitrostyrene, prepared by condensing *o*-veratraldehyde with nitromethane, when heated with butadiene at 200°, gave a 70% yield of 4-(2 : 3-dimethoxyphenyl)-5-nitro*cyclo*hexene (VIII), which was readily hydrogenated to the corresponding nitro*cyclo*hexane. By the reaction described first by Nef (*Annalen*, 1894, **280**, 263), 1-(2 : 3-dimethoxyphenyl)-2-nitro*cyclo*hexane was converted into its sodium salt and rapidly acidified. 2-(2 : 3-Dimethoxyphenyl)*cyclo*hexanone (VII) was thus obtained in 35% yield. The unsaturated nitro-compound (VIII) behaved similarly in the Nef reaction and gave 6-(2 : 3-dimethoxyphenyl)*cyclo*hex-3- or -2-enone; the position occupied by the double bond could not be determined with certainty from the ultra-violet absorption spectrum.



(X.)



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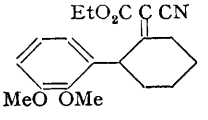
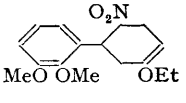


(XII.)

Bromination of (VII) gave 2-bromo-2-(2 : 3-dimethoxyphenyl)*cyclo*hexanone, which on dehydrobromination afforded the unsaturated ketone (IX), whence, by addition of cyanoacetic ester, we hoped to obtain the substance (X). The poor yields encountered in the preparation of (IX) (cf. Ginsburg and Pappo, *J.*, 1951, 516) prevented our accumulating sufficient material to investigate the Michael addition reaction. Nevertheless, a small quantity of a substance which may well possess the structure (X) was obtained by treating the bromodimethoxyphenyl-*cyclo*hexanone with sodiocyanoacetic ester.

The paper by Ginsburg and Pappo (*loc. cit.*) prompts us to report other attempts, as yet incomplete, to exploit the synthetical possibilities of dimethoxyphenyl*cyclo*hexanone. These have included alkylation with 2-diethylaminoethyl chloride to give 2-2′-diethylaminoethyl-2-(2 : 3-dimethoxyphenyl)*cyclo*hexanone (XI) and condensation with ethyl cyanoacetate. From the latter reaction the unsaturated ester (XII) was obtained in reasonable yield. Experiments on its conversion into a hydrophenanthrene are in progress.



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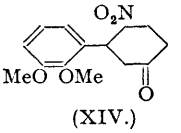

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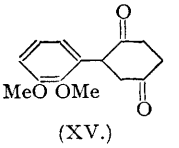
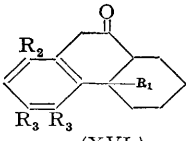


(XV.)

2-Ethoxybutadiene reacted smoothly with 2 : 3-dimethoxy-ω-nitrostyrene, giving 4-(2 : 3-dimethoxyphenyl)-2-ethoxy-5-nitro*cyclo*hexene (XIII). Theoretical considerations and Holmes and Mann's work (*J. Amer. Chem. Soc.*, 1947, **69**, 2000) make it certain that the product is the 2-ethoxy- rather than the 1-ethoxy-derivative. Hydrolysis with dilute acid afforded the nitro-ketone (XIV), from which, by the Nef reaction, 2-(2 : 3-dimethoxyphenyl)*cyclo*hexane-1 : 4-dione (XV) was obtained. This intermediate possesses a keto-group in a position equivalent to that of codeinone.

A different approach to the morphine system, which envisaged the preparation of systems of the type (XVI) by cyclising phenylacetyl*cyclo*hexenes (XVII), broke down because of the inaccessibility of these compounds. An attempted Darzens reaction between *cyclo*hexene and 2-bromo-4 : 5-dimethoxyphenylacetyl chloride was not successful. 2-Bromo-4 : 5-dimethoxyphenylacetylene, prepared by decarboxylation of the corresponding propiolic acid, proved to be most inert : it failed to react with sodium wire and, although it was converted into metallic

derivatives by treatment with ethylmagnesium bromide and with sodamide in liquid ammonia, these derivatives, on condensation with *cyclo*hexanone, gave only a 20% yield of 1-(2-bromo-4 : 5-dimethoxyphenylethynyl)*cyclo*hexanol (XVIII). This result agrees with findings by Fulton and Robinson (*J.*, 1933, 1463) who were unable to obtain any product from the Grignard



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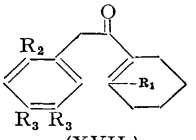
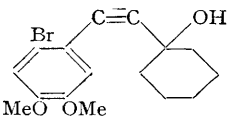


(XVII.)



(XVIII.)

derivative of 3 : 4-dimethoxyphenylacetylene and *cyclo*hexene oxide. An attempt to isomerise the ethynylcarbinol (XVIII) to (XVII; $R_1 = H$, $R_2 = Br$, $R_3 = OMe$) (cf. Fischer and Löwenberg, *Annalen*, 1929, **475**, 183; Hurd and Christ, *J. Amer. Chem. Soc.*, 1937, **59**, 118) by boiling formic acid gave only black, intractable products. Sodiophenylacetylene and 2-ethyl-*cyclo*hexanone gave 2-ethyl-1-phenylethynyl*cyclo*hexanol, but this compound also could not be rearranged to an unsaturated ketone.

Experimental.

*Ethyl α-Cyano-α-1-phenyl*cyclo*hexylacetate.*—A solution of phenylmagnesium bromide [from bromobenzene (4·9 g.), magnesium (0·75 g.), and ether (20 c.c.)] was slowly added, with stirring, to an ice-cold solution of ethyl α-cyano-α-*cyclo*hexylideneacetate (5·5 g.) in ether (20 c.c.). The mixture was set aside for 20 minutes and then refluxed for 30 minutes. The complex was decomposed with ice and dilute sulphuric acid and the product isolated with ether. The residual oil was shaken for 1 hour with an aqueous solution of potassium cyanide (4 g.), then isolated with ether and distilled. *Ethyl α-cyano-α-1-phenyl*cyclo*hexylacetate* (3·3 g.) was collected at 160—170° (bath)/0·2 mm. Redistillation gave the ester as a viscous oil, b. p. 158—163° (bath)/0·2 mm. (Found : C, 74·9; H, 7·6. $C_{17}H_{21}O_2N$ requires C, 75·3; H, 7·7%).

*α-Cyano-α-1-phenyl*cyclo*hexylacetic Acid.*—The above ester (6·7 g.) was boiled for 6 hours with 10% sodium carbonate solution (150 c.c.). After being washed with ether, the aqueous solution was acidified and the liberated oil isolated with ether. It crystallised on trituration with chloroform–light petroleum. The *acid* was crystallised twice from chloroform–light petroleum (b. p. 60—80°), from which it separated in small clusters of needles, m. p. 123—124° (Found : C, 74·0; H, 6·9; N, 6·1. $C_{15}H_{17}O_2N$ requires C, 74·1; H, 7·0; N, 5·7%).

*1-Cyanomethyl-1-phenyl*cyclo*hexane.*—The above acid (4·2 g.) was decarboxylated by heating it to 200° (oil-bath). The *cyanide* (3·1 g.) was obtained as a colourless oil, b. p. 175—185° (bath)/9 mm. (Found : C, 84·5; H, 8·8; N, 7·0. $C_{14}H_{17}N$ requires C, 84·4; H, 8·5; N, 7·0%).

*1-2′-Aminoethyl-1-phenyl*cyclo*hexane.*—The above nitrile (2 g.), dissolved in boiling absolute ethanol, was treated with sodium (6·7 g.) added in small pieces during 15 minutes. The solution was acidified and steam-distilled. The residue was washed with ether and basified, and the liberated oil isolated with ether and distilled. The *amine* (1·6 g., 80%) was collected at 170—180° (bath)/9 mm. A portion of the base was converted into the *hydrochloride* by means of hydrogen chloride in ether. It separated from moderately concentrated hydrochloric acid in needles, m. p. 251—254° (Found : C, 69·6; H, 9·3; N, 5·9. $C_{14}H_{21}N,HCl$ requires C, 70·1; H, 9·2; N, 5·85%). The hydrochloride, on treatment with sodium picrate, afforded the *picrate*, which crystallised from 50% aqueous ethanol in plates, m. p. 178—180° (Found : C, 55·8; H, 5·6; N, 12·9. $C_{14}H_{21}N,C_6H_3O_7N_3$ requires C, 55·6; H, 5·6; N, 12·9%).

*1-2′-Dimethylaminoethyl-1-phenyl*cyclo*hexane.*—The above base (1·4 g.), dissolved in 90% formic acid (2·0 g.), was heated on the steam-bath for 6½ hours with 35% formaldehyde solution (1·8 c.c.). Hydrochloric acid (5 c.c.; 20%) was added and the whole evaporated to dryness under reduced pressure. The gummy hydrochloride was taken up in water, washed with ether, and basified, and the oil so obtained isolated with ether and distilled. The base (1 g.) was collected at 175—180° (bath)/9 mm. and converted into its *hydrochloride* with dry hydrogen chloride in ether. The salt separated from dry ethanol–ether in microscopic needles, m. p. 182—184° (Found : C, 71·7; H, 9·5; N, 4·8. $C_{16}H_{25}N,HCl$ requires C, 71·8; H, 9·7; N, 5·2%). The *picrate* crystallised from 90% ethanol in long blades, m. p. 169—171° (Found : C, 57·6; H, 6·0; N, 12·3. $C_{16}H_{25}N,C_6H_3O_7N_3$ requires C, 57·4; H, 6·1; N, 12·2%).

*Ethyl α-(2-Carbethoxy-1-phenyl*cyclo*hexyl)-α-cyanoacetate.*—A solution of phenylmagnesium bromide [from bromobenzene (2·64 g.), magnesium (0·4 g.), and ether (5 c.c.)] was added, with stirring, to a solution of ethyl α-2-carbethoxy*cyclo*hexylidene-α-cyanoacetate (4·0 g.) (Grewe and Mondon, *Ber.*, 1948, **81**, 279) in benzene (15 c.c.) at 0°. The mixture was refluxed for 4 hours, then decomposed with ice-cold dilute sulphuric acid, and the product isolated with ether. The oil so obtained was shaken with an excess of aqueous-alcoholic potassium cyanide to remove unchanged ester. The solution was then diluted with water and the product isolated with ether and distilled. The required *ester* (0·5 g.), a green viscous oil, was collected at 180—190° (bath/0·05 mm.) (Found : C, 69·5; H, 7·1. $C_{20}H_{25}O_4N$ requires C, 69·9; H, 7·3%).

*Ethyl α-Cyano-α-1-(2-hydroxy-3-methoxyphenyl)*cyclo*hexylacetate.*—A mixture of 2 : 3-dimethoxy-iodobenzene (1·1 g.) (Mauthner, *J. pr. Chem.*, 1937, **149**, 328), activated magnesium (0·2 g.), ether (0·3 c.c.), and anisole (2·5 c.c.) was heated to 130°. After 2—3 hours the reaction started and the

Grignard complex separated on the sides of the flask and on the magnesium. After a further hour's heating the mixture was cooled, stirred, treated with ethyl α-cyano-α-*cyclo*hexylideneacetate (1·2 g.) in benzene (10 c.c.), and boiled until homogeneous (1 hour). The complex was decomposed and submitted to treatment with potassium cyanide as above. Distillation of the product gave two fractions: (1) a colourless liquid, b. p. 135—140° (bath)/0·05 mm. (Found: C, 67·7; H, 8·2%), and (2) the *ester*, a gum, b. p. 240—250° (bath)/0·05 mm. (Found: C, 68·2; H, 7·2. $C_{18}H_{23}O_4N$ requires C, 68·2; H, 7·2%).

2-*Hydroxy*-3-*methoxybenzoic Acid*.—2 : 3-Dimethoxyiodobenzene (0·5 g.) was converted into the Grignard derivative as described above and treated with solid carbon dioxide. The complex was decomposed with ice and dilute sulphuric acid and extracted with ether, and the ethereal solution extracted with sodium carbonate solution. Acidification of the extract gave guaiacolcarboxylic acid (40 mg.), m. p. and mixed m. p. 142—146°.

2 : 3-*Dimethoxy*-ω-*nitrostyrene*.—2 : 3-Dimethoxybenzaldehyde (33·2 g.) in ethanol (250 c.c.) and nitromethane (12·3 g.) was cooled in ice and treated with a solution of sodium hydroxide (8·2 g.) in water (10 c.c.), slowly and with stirring. After 30 minutes, the mixture was poured into an excess of 17% hydrochloric acid. The precipitated *nitro-styrene* was collected and crystallised from ethanol. It formed massive yellow needles (32 g., 77%), m. p. 86° (Found: C, 57·2; H, 5·1; N, 6·3. $C_{10}H_{11}O_4N$ requires C, 57·4; H, 5·3; N, 6·7%).

4-(2 : 3-*Dimethoxyphenyl*)-5-*nitro*cyclo*hexene*.—The above nitro-styrene (10·4 g.) and butadiene (12 c.c.), dissolved in pure dry xylene, were heated in a sealed tube at 200° for 14 hours. Evaporation of the solvent left a black mass, which separated from ethanol in crystals (9·2 g., 70%), m. p. 80—82°. The *adduct* crystallised from light petroleum (b. p. 60—80°) in long colourless rods, m. p. 81—83° (Found: C, 64·0; H, 6·3; N, 5·2. $C_{14}H_{17}O_4N$ requires C, 63·9; H, 6·5; N, 5·3%).

1-(2 : 3-*Dimethoxyphenyl*)-2-*nitro*cyclo*hexane*.—The above nitro-compound (0·5 g.) in acetic acid (5 c.c.) was hydrogenated over platinum oxide (20 mg.). The theoretical quantity of hydrogen was rapidly absorbed. The solution, filtered from catalyst, on dilution with water gave 1-(2 : 3-*dimethoxyphenyl*)-2-*nitro*cyclo*hexane* (0·45 g.), which separated from light petroleum (b. p. 60—80°) in colourless blades, m. p. 81—82·5° (Found: C, 63·5; H, 7·5; N, 5·6. $C_{14}H_{19}O_4N$ requires C, 63·4; H, 7·2;

Ethyl α-Cyano-α-2-(2 : 3-dimethoxyphenyl)cyclohexylideneacetate.—2-(2 : 3-Dimethoxyphenyl)*cyclo*hexanone (0·7 g.) was boiled under reflux with ethyl cyanoacetate (0·3 g.), acetic acid (0·4 c.c.), ammonium acetate (0·2 g.), and benzene (5 c.c.) for 7 hours at 160° (oil-bath) and the water formed was continuously separated. The mixture was diluted with ether, washed with concentrated sodium carbonate solution and with water, and distilled. *Ethyl α-cyano-α-2-(2 : 3-dimethoxyphenyl)*cyclo*hexylideneacetate* (0·5 g.), a colourless oil, was collected at 190—195° (bath)/0·01 mm. (Found : C, 68·9; H, 7·3; N, 4·6. $C_{19}H_{23}O_4N$ requires C, 69·3; H, 7·0; N, 4·25%).

*2-2′-Diethylaminoethyl-2-(2 : 3-dimethoxyphenyl)*cyclo*hexanone.*—Dimethoxyphenyl*cyclo*hexanone (0·7 g.) in toluene (10 c.c.) was added to a solution of sodamide, prepared by dissolving sodium (0·1 g.) in liquid ammonia (10 c.c.), and the mixture was set aside for 2 hours to allow the ammonia to evaporate. The mixture was stirred and treated with 2-diethylaminoethyl chloride (0·7 g.) in toluene (10 c.c.). The temperature was raised to 85° during 1 hour and kept at that point for 5 hours with stirring. After the mixture had been finally boiled for 1 hour, the bases were extracted with dilute hydrochloric acid. The aqueous extract was washed with ether, then basified, and the liberated bases were isolated with ether and distilled. Two fractionations gave the *amino-ketone* as an oil (0·3 g.), b. p. 185—195° (bath)/0·01 mm. (Found : N, 4·35. $C_{20}H_{31}O_3N$ requires N, 4·25%). The base gave no crystalline derivatives except an extremely hygroscopic methiodide.

*2-Ethoxy-4-(2 : 3-dimethoxyphenyl)-5-nitro*cyclo*hexene.*—2 : 3-Dimethoxy-ω-nitrostyrene (2 g.) in dry xylene (5 c.c.) was heated at 200° for 15 hours with 2-ethoxybutadiene (1·3 g.) (Holmes and Mann, *J. Amer. Chem. Soc.*, 1947, **69**, 2000) and quinol (30 mg.). Distillation afforded a viscous, yellow oil, b. p. 190—210° (bath)/0·1 mm., which on redistillation gave the enol *ether* (2·3 g.), b. p. 195—205° (bath)/0·1 mm. (Found : C, 63·0; H, 6·9; N, 4·9. $C_{16}H_{21}O_5N$ requires C, 62·5; H, 6·8; N, 4·6%). The substance could not be hydrogenated over platinum oxide at 40° and atmospheric pressure.

*3-(2 : 3-Dimethoxyphenyl)-4-nitro*cyclo*hexanone.*—A solution of the above ether (0·5 g.) in methanol (50 c.c.) was kept for 1·5 hours with 6N-sulphuric acid (2 c.c.) and water (3 c.c.). The mixture was copiously diluted with water, and the *ketone* isolated with ether. The gum so obtained crystallised when warmed with ether. Recrystallisation from ether gave long, colourless prisms (0·3 g.), m. p. 94·5—96·5° (Found : C, 60·1; H, 6·1; N, 4·4. $C_{14}H_{17}O_5N$ requires C, 60·2; H, 6·1; N, 5·0%). In alcoholic solution, the ketone gave an amorphous 2 : 4-*dinitrophenylhydrazone*, which became crystalline in boiling benzene. Crystallisation from acetic acid and then from xylene gave orange-yellow prisms, m. p. 212° (decomp.) (Found : C, 52·5; H, 4·7. $C_{20}H_{21}O_8N_5$ requires C, 52·3; H, 4·6%).

*2-(2 : 3-Dimethoxyphenyl)*cyclo*hexane-1 : 4-dione.*—The above nitro-ketone (0·4 g.), dissolved in ethanol (5 c.c.), was treated with sodium hydroxide (0·5 g.) in ethanol, and the resulting yellow solution added dropwise to ice-cold 2N-sulphuric acid (50 c.c.). After a short time, the solution was warmed to 60°, then cooled, and the dark solution extracted with ether. Distillation of the dried ethereal extract gave a colourless oil, b. p. 185—195° (bath)/0·06 mm., which crystallised on trituration with ether. The *diketone* (60 mg.) separated from ether in stout prisms, m. p. 96—98° (Found : C, 67·4; H, 6·5. $C_{14}H_{16}O_4$ requires C, 67·8; H, 6·5%).

2-Bromo-4 : 5-dimethoxyphenylpropiolic Acid.—(*A*) Ethyl 3 : 4-dimethoxycinnamate (30 g.) in chloroform (150 c.c.) was slowly treated with bromine (40·7 g.) in chloroform (50 c.c.) and left overnight. Evaporation of the chloroform under reduced pressure gave a gum, which was boiled under reflux for 7 hours with a solution of potassium hydroxide (35 g.) in ethanol (300 c.c.). The ethanol was distilled, water was added, and the solution filtered. On acidification, a brown oil separated, which crystallised on storage. Three recrystallisations from aqueous methanol gave the *propiolic acid* as colourless plates, m. p. 178° (decomp.) (Found : C, 43·9; H, 3·6. $C_{11}H_9O_4Br,H_2O$ requires C, 43·6; H, 3·6%).

(*B*) Ethyl 2-bromo-4 : 5-dimethoxycinnamate (19·6 g.) was converted into the dibromide as above and refluxed with a solution of potassium hydroxide (27·3 g.) in ethanol (150 c.c.) for 7 hours. Similar working up gave the propiolic acid (11 g.), m. p. 178° (decomp.) alone or when mixed with the specimen prepared as above.

2-Bromo-4 : 5-dimethoxyphenylacetylene.—The above propiolic acid (4 g.) in diethylaniline (15 c.c.) was kept at 180° until evolution of carbon dioxide ceased (*ca.* 30 minutes). The mixture was poured into dilute sulphuric acid, and the precipitated solid taken up in ether and washed with dilute sulphuric acid, sodium carbonate solution, and water. Distillation of the ether gave a brown solid, which when steam-distilled afforded *2-bromo-4 : 5-dimethoxyphenylacetylene* (2·4 g.) in the distillate. The compound crystallised from light petroleum (b. p. 80—100°) in rhombs, m. p. 101—102° (Found : C, 50·2; H, 3·7. $C_{10}H_9O_2Br$ requires C, 49·8; H, 3·7%).

*1-(2-Bromo-4 : 5-dimethoxyphenylethynyl)*cyclo*hexanol.*—The above acetylene (1·2 g.) in ether (15 c.c.) was added to a solution of ethylmagnesium bromide [from ethyl bromide (0·8 g.), magnesium (0·12 g.), and ether (3 c.c.)]. A brown solid separated. The whole was refluxed for 30 minutes and treated with *cyclo*hexanone (5 g.) in benzene (10 c.c.). After being boiled for 1 hour and kept overnight, the solution was decomposed with ammonium chloride solution and extracted with ether. Steam-distillation of the residue from the ethereal extract gave unchanged acetylene (0·4 g.) in the distillate. The residual non-volatile material was isolated with ether, dissolved in chloroform–light petroleum (4 : 1), and passed down an alumina column. The eluted *alcohol* (0·2 g.) crystallised from light petroleum (b. p. 80—100°) in fine needles, m. p. 116—117° (Found : C, 56·9; H, 5·4. $C_{16}H_{19}O_3Br$ requires C, 56·6; H, 5·6%). The same yield of product was obtained by performing the condensation in the presence of sodamide in liquid ammonia.

Attempted Preparation of 2-Bromo-4 : 5-dimethoxyphenzyl cyclo*Hex-1-enyl Ketone.*—(*A*) The above alcohol (0·2 g.) was refluxed for 45 minutes with 90% formic acid (2 c.c.). The black solution was poured into dilute sodium hydroxide solution and extracted with ether. Evaporation of the ether left an intractable gum, which would form no satisfactory ketonic derivatives.

(*B*) Stannic chloride (1·7 g.) was added to a solution of 2-bromo-4 : 5-dimethoxyphenylacetyl chloride (1·9 g.) in carbon disulphide (30 c.c.), cooled to −10°, and treated slowly with a solution of *cyclo*hexene (0·55 g.) in carbon disulphide (10 c.c.). Next morning, the carbon disulphide was decanted and the residual black mass treated with ice-cold hydrochloric acid and ether. The ethereal extract was washed with dilute hydrochloric acid, sodium carbonate, and water, dried, and evaporated. The residual oil was boiled for 2 hours with diethylaniline and poured into dilute hydrochloric acid. Ether-extraction yielded a gummy material which resisted all methods of purification, including chromatography.

2-*Ethyl*-1-*phenylethynyl*cyclo*hexanol*.—Phenylacetylene (2 g.) was converted into its sodium salt with sodium wire (0·46 g.) in ether (10 c.c.). 2-Ethyl*cyclo*hexanone (2·5 g.) (King, Barltrop, and Walley, *J.*, 1945, 277) in ether (10 c.c.) was slowly added to the suspension of the sodium salt and the whole refluxed for one hour. The homogeneous solution was treated with dilute hydrochloric acid and extracted with ether. The ether yielded an oil which was steam-distilled to remove starting materials. The residue was isolated with ether and distilled. 2-*Ethyl*-1-*phenylethynyl*cyclo*hexanol* (2·1 g.) was collected at 200—205° (bath)/13 mm. as a colourless oil, n_D^{25} 1·5585 (Found : C, 84·3; H, 9·1. $C_{16}H_{20}O$ requires C, 84·2; H, 8·8%).

Attempted Preparation of Benzyl 2-*Ethyl*cyclo*hex*-1-*enyl Ketone*.—The above ethynyl alcohol (0·5 g.) was boiled for 30 minutes with 90% formic acid (10 c.c.), and poured into dilute sodium hydroxide solution, and extracted with ether. Distillation of the ether gave an oil which contained some ketonic material, but no pure substance could be isolated.

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