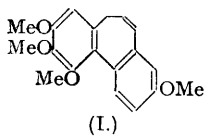
229. *Colchicine and Related Compounds. Part VII.*

By J. W. Cook, G. T. Dickson, Drummond Ellis, and J. D. Loudon.

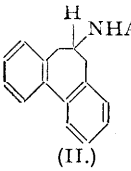
In connection with the interesting elimination of acetamide from *N*-acetylcolchinol methyl ether by means of phosphoric oxide, whereby the seven-membered ring compound deaminocolchinol methyl ether is obtained (Parts III and V), a study has been made of the action of phosphoric oxide on a series of acetylated amines having structural similarities to *N*-acetylcolchinol methyl ether. In most of these cases elimination of acetamide occurred, as with the colchicine derivative. The structure of *N*-acetylcolchinol methyl ether has not yet been completely established, and it may be that the conversion into deaminocolchinol methyl ether involves an enlargement of a six-membered ring. This possibility has been made much less probable by the synthesis of a *compound* having one of the structures (III) which has been under consideration for *N*-acetylcolchinol methyl ether. The synthetic compound (III), which has not

been resolved, was dehydrated by phosphoric oxide to give the *iso*quinoline derivative (VI). This behaviour is thus in sharp contrast to that of *N*-acetylcolchinol methyl ether.

It was shown in Parts III and V (Cook and Graham, *J.*, 1944, 322 : Barton, Cook, and Loudon, *J.*, 1945, 176) that *N*-acetylcolchinol methyl ether when heated with phosphoric oxide in xylene yields deaminocolchinol methyl ether (I) together with traces of the bond-isomeride, *iso*deaminocolchinol methyl ether. The process, which formally consists in the removal of acetamide, was subsequently used by Tarbell, Frank, and Fanta (*J. Amer. Chem. Soc.*, 1946, **68**, 502) for deaminating *N*-acetyliodocolchinol methyl ether, and by Cook, Dickson, and Loudon (Part VI, *J.*, 1947, 746; cf. Lettré, *Z. angew. Chem.*, 1947, **59**, 218) for converting (II) into the hydrocarbon corresponding to (I). Only in this last case is the structure of the parent amine definitely established, and further information on the deamination process has therefore been sought among suitable compounds of known structure. It was of particular interest to ascertain the behaviour of the acetylated amine (III) under the above treatment. The requisite material having been synthesised by an unambiguous route, the opportunity was taken to have the compound tested for the mitosis-arresting property, which characteristic of colchicine is retained in some degree by many degradation products of the alkaloid and appears to be adumbrated for amines of type (III) by the results reported in Part II (Cook and Engel, *J.*, 1940, 198).



(I.)



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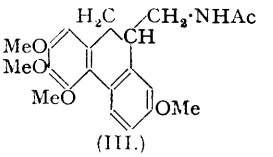
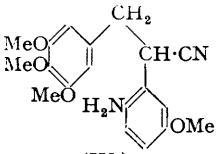


(III.)

For the synthesis of (III), 3 : 4 : 5-trimethoxybenzyl chloride was condensed with *2-nitro-5-methoxybenzyl cyanide*, and the resulting *2-nitro-5-methoxy-α-(3′ : 4′ : 5′-trimethoxybenzyl)-benzyl cyanide* was reduced to the amine (IV). In a mildly alkaline medium and depending on the conditions used, the diazotised amine reacted to give one or other of two *compounds*, $C_{19}H_{19}O_4N_3$, which are probably derivatives of dihydrocinnoline and indazole respectively : they were not examined further. In an acid environment, however, the diazonium salt in



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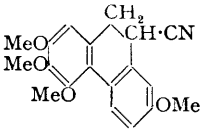

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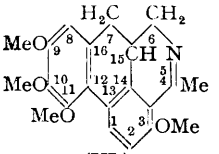

(VI.)

presence of copper underwent a Pschorr type of cyclisation, affording *9-cyano-2 : 3 : 4 : 7-tetramethoxy-9 : 10-dihydrophenanthrene* (V). The structure of (V) was confirmed by hydrolysis to the corresponding *acid* followed by dehydrogenation of the methyl ester to the known ester of 2 : 3 : 4 : 7-tetramethoxyphenanthrene-9-carboxylic acid (Part IV; Buchanan, Cook, and Loudon, *J.*, 1944, 325). Hydrogenation of (V), using a platinum catalyst, and acetylation of the resulting base gave *2 : 3 : 4 : 7-tetramethoxy-9-acetamidomethyl-9 : 10-dihydrophenanthrene* (III).

When (III) was heated with phosphoric oxide in xylene, water was eliminated and the nitrogenous product is assigned the structure (VI). Accordingly it appears that the deamination reaction is here superseded by the usual Bischler–Napieralski synthesis of a dihydro*iso*quinoline from an acylated 2-phenylethylamine. The contrast thereby presented to the production of (I) from *N*-acetylcolchinol methyl ether strongly suggests that the latter compound cannot have a structure analogous to (III) and hence, by excluding the possibility of ring-enlargement during deamination, tends to confirm the view (Part V) that the 7-membered ring of (I) is already present in the amine, *viz.* colchinol methyl ether, itself. We are greatly indebted to Professor H. Lettré who has kindly examined the (±) compound (III) and reports that it shows a definite inhibitory effect on mitosis in chicken-heart fibroblasts, although it is considerably less potent than *N*-acetylcolchinol methyl ether.

The fact that (II) undergoes deamination rather than the Bischler–Napieralski reaction is probably due in part to the unfavourable steric conditions for the latter process, and, accordingly, in extending our inquiry to derivatives of diphenyl-ethylamine (VII) and -propylamine (VIII), search was made for basic products of the dihydro*iso*quinoline type. The requisite amines

(VII.) $CH_2Ph{\cdot}CH(NHR)Ph$ (VIII.) $CH_2Ph{\cdot}CH(NHR){\cdot}CH_2Ph$
(IX.) $CH_2Ph{\cdot}CH_2{\cdot}CH(NHAc)Ph$ (X.) p-$MeO{\cdot}C_6H_4{\cdot}CH_2{\cdot}CH_2{\cdot}CH(NHAc)Ph$
(XI.) p-$MeO{\cdot}C_6H_4{\cdot}CH_2{\cdot}CH{:}CHPh$ (XII.) p-$MeO{\cdot}C_6H_4{\cdot}CH{:}CH{\cdot}CH_2Ph$

were prepared by Leuckart's method (cf. Ingersoll *et al.*, *J. Amer. Chem. Soc.*, 1936, **58**, 1808) from the appropriate ketones in reaction with formamide. The acetyl and benzoyl derivatives of 1 : 2-diphenylethylamine (VII; R = Ac or Bz) distilled unchanged, preferably under reduced pressure, although some stilbene was produced when the former was heated under reflux conditions (>300°). Both acyl derivatives readily afforded stilbene when heated with phosphoric oxide in xylene, and the absence of basic products showed that cyclodehydration to derivatives of 3 : 4-dihydro*iso*quinoline had not occurred. Even under the milder conditions used for the latter type of reaction by Gulland and Haworth (*J.*, 1928, 582), *viz.*, treatment with phosphorus pentachloride in cold chloroform, the benzoyl derivative gave some stilbene but no basic product. The *toluene*-p-*sulphonyl* derivative (VII; R = p-$Me{\cdot}C_6H_4{\cdot}SO_2$) could not be distilled without decomposition to stilbene, and it also afforded stilbene when heated with phosphoric oxide in xylene. In contrast to this behaviour the *toluene*-p-*sulphonyl* derivative (VIII; R = p-$Me{\cdot}C_6H_4{\cdot}SO_2$) of diphenyl*iso*propylamine was stable to distillation under reduced pressure and was recovered unchanged after being heated with phosphoric oxide in xylene. Diphenyl*iso*propylamine itself (VIII; R = H) was also unaffected by being heated with phosphoric oxide in xylene, but its *acetyl* derivative (VIII; R = Ac) afforded a mixture of 1 : 3-diphenylpropene and 3-*benzyl*-1-*methyl*-3 : 4-*dihydro*iso*quinoline* which was isolated as its *picrate*. 1-*Acetamido*-1 : 3-*diphenylpropane* (IX), similarly treated, yielded 1 : 3-diphenylpropene as the sole product isolated.

The results obtained with the acetylated diphenylpropylamines (VIII; R = Ac) and (IX) sufficiently indicate that the relevant derivatives of 1 : 3-diarylpropane may undergo the deamination reaction irrespective of whether the 1-(3) or 2-centre carries the amino-residue. In consequence, the fact of deamination is no guide to a more precise orientation of the amino-residue in *N*-acetylcolchinol methyl ether. Using the *compound* (X), an attempt was made to discover whether prototropic change to (XII) accompanied normal deamination to (XI) [cf. the simultaneous production of (I) with traces of its bond-isomeride], but, although (XI) was the only product identified, because of practical difficulties the possible formation of (XII) could not be definitely excluded and the point remains unsettled. The field of inquiry here covered is too restricted to permit of conclusions regarding the generality of the deamination process, and the results of a few experiments imply the need for caution. For instance, aceto*cyclo*hexylamide was smoothly converted into *cyclo*hexene and methyl cyanide, but neither acetoethylamide nor acetopropylamide yielded detectable quantities of the corresponding olefins.

Experimental.

2-*Nitro*-5-*methoxytoluene*.—This is conveniently prepared by the following method (cf. Buchanan, Loudon, and Robertson, *J.*, 1943, 168). Concentrated sulphuric acid (30 g.) was slowly added to 3-methoxytoluene (15 g.) at 30—40°, the solution being kept at that temperature until a test-portion gave no turbidity with water. Water (15 c.c.) was added, and then, with the temperature kept below 20°, nitric acid (15 c.c., d 1·42) was added with stirring. After 30 minutes the container was loosely covered (a vigorous reaction ensues) and was set aside for 12 hours without temperature control. The resulting mixture was diluted with water, and the solid product was collected, washed, dried, and purified by crystallisation or distillation; m. p. 55°, yield 60%.

2-*Nitro*-5-*methoxybenzyl Cyanide*.—2-Nitro-5-methoxyphenylpyruvic acid (37 g.) prepared as described by Blaikie and Perkin (*J.*, 1924, **125**, 296) but using potassium instead of sodium ethoxide, was dissolved in the minimum amount of warm ethanol, cooled rapidly, and poured into a cold solution of hydroxylamine in water (from 16·2 g. of hydroxylamine hydrochloride, 8·7 g. of sodium hydroxide, and 100 c.c. of water). The *oxime*, which separated on standing, had m. p. 170° (decomp.) from acetic acid (Found: C, 47·8; H, 3·8. $C_{10}H_{10}O_6N_2$ requires C, 47·25; H, 3·9%). It was dried and added portionwise to a fourfold weight of acetic anhydride at 100°. 2-*Nitro*-5-*methoxybenzyl cyanide* was obtained by concentrating the solution under reduced pressure, and had m. p. 84° from benzene (yield 80%) (Found: C, 56·2; H, 4·3. $C_9H_8O_3N_2$ requires C, 56·2; H, 4·2%).

2-*Nitro*-5-*methoxy*-α-(3′ : 4′ : 5′-*trimethoxybenzyl*)*benzyl Cyanide*.—A solution of sodium ethoxide, made from sodium (0·66 g.) and ethanol (18 c.c.), was added to 2-nitro-5-methoxybenzyl cyanide (5 g.) dissolved in warm lime-dried ethanol (65 c.c.), and the resulting purple solution was treated with 3 : 4 : 5-trimethoxybenzyl chloride (5·56 g.) (Part III, *loc. cit.*), also in warm ethanol (40 c.c.). The whole, protected from moisture, was left at room temperature for 48 hours; the required product was then obtained as straw-coloured crystals, m. p. 163—164° from ethanol; yield 80% (Found: C, 61·4; H, 5·5; N, 7·5. $C_{19}H_{20}O_6N_2$ requires C, 61·3; H, 5·4; N, 7·5%).

2-*Amino*-5-*methoxy*-α-(3′ : 4′ : 5′-*trimethoxybenzyl*)*benzyl Cyanide*.—The above nitro-compound (8 g.), dissolved by gentle warming in sodium-dried dioxan (300 c.c.), was hydrogenated at ordinary temperature and pressure in presence of 2% palladised strontium carbonate (8 g.). Absorption was complete in

2 to 3 hours. The filtered catalyst was washed with warm dioxan, the combined filtrates were concentrated in a vacuum, and the residue was separated from some colloidal palladium by extraction with ether (charcoal). The recovered gummy amine was characterised as the *acetyl* derivative, m. p. 171—172° from ethanol (Found: C, 65·4; H, 6·4; N, 7·3. $C_{21}H_{24}O_5N_2$ requires C, 65·6; H, 6·25; N, 7·3%), but the crude amine was used for diazotisation.

9-*Cyano*-2 : 3 : 4 : 7-*tetramethoxy*-9 : 10-*dihydrophenanthrene* (V).—A solution of the above amine in dioxan (25 c.c.) was slowly poured into 3N-hydrochloric acid (72 c.c.) cooled in ice, and the resulting suspension was diazotised at −8° with sodium nitrite (1·28 g.) in water (20 c.c.), added during 15 minutes. After 1 hour's stirring, copper bronze (8 g.) was added (effervescence), and stirring was continued first (15 mins.) at −8° and then at room temperature (30 mins.). The product, which had begun to separate, was extracted with a little ether, and the two-layered mixture was left at 0° overnight. The copper was filtered off and extracted with warm ether, and the combined ether extracts were washed with brine and dilute sodium hydroxide and dried (K_2CO_3). The product, recovered from the ether, had m. p. 135—136° from methanol (Found: C, 70·3; H, 5·8; N, 4·5. $C_{19}H_{19}O_4N$ requires C, 70·15; H, 5·8; N, 4·3%), and the yield, based on the nitro-compound, was 45%.

Products $C_{19}H_{19}O_4N_3$.—(*a*) After diazotisation as before, the solution was made alkaline by addition of a slight excess of sodium carbonate, and was warmed gradually on the water-bath. After standing (at room temperature) overnight, the separated solid was collected, washed, dried, and crystallised several times from ethanol and finally from ligroin, forming almost colourless crystals, m. p. 122° (Found: C, 64·7; H, 5·55, N, 12·4. $C_{19}H_{19}O_4N_3$ requires C, 64·6; H, 5·4; N, 11·9%).

(*b*) The acid diazo-solution was poured into 10% sodium acetate solution, warmed to 50° and containing suspended copper bronze. After being heated to 70° the solution was left at room temperature overnight. An ether extract of the resulting solid was washed with dilute hydrochloric acid and then with water, and evaporated. The residue formed colourless crystals, m. p. 142° from ethanol (charcoal) (Found: C, 64·5; H, 5·2; N, 12·0%). A mixed m. p. of the products of (*a*) and (*b*) showed a marked depression.

2 : 3 : 4 : 7-*Tetramethoxy*-9 : 10-*dihydrophenanthrene*-9-*carboxylic Acid*.—The cyanide (V; 0·3 g.) was heated under reflux with potassium hydroxide (1 g.) in methanol (8 c.c.) for 48 hours. After concentration, addition of water, and extraction with ether, the aqueous layer was acidified; the precipitated *acid* had m. p. 190—192° from methanol (Found: C, 65·9; H, 5·7. $C_{19}H_{20}O_6$ requires C, 66·3; H, 5·8%).

The acid (35 mg.) was esterified by the action of dry hydrogen chloride on a solution in methanol. After evaporation of the solvent over potassium hydroxide in a vacuum, the methyl ester, m. p. 121°, was recovered in ether and was dehydrogenated by heating it (20 mg.) with palladium black (10 mg.) at 200—230° for several hours in a slow stream of carbon dioxide. The apparatus was arranged so that any starting material which distilled unchanged was condensed on a further quantity of catalyst (10 mg.) and could then receive a second heat treatment. The product was distilled directly from the catalyst (245°/0·2 mm.), the condensate being identified by (micro) m. p. and mixed m. p. 99—102° (from methanol) as methyl 2 : 3 : 4 : 7-tetramethoxyphenanthrene-9-carboxylate.

2 : 3 : 4 : 7-*Tetramethoxy*-9-*acetamidomethyl*-9 : 10-*dihydrophenanthrene* (III).—The cyanide (V; 0·7 g.), dissolved in a mixture of acetic (30 c.c.) and sulphuric (1·2 c.c.) acids, was hydrogenated at ordinary pressure in presence of active Adams's catalyst (0·07 g.). Absorption was complete in several hours. The filtered solution was diluted with ether (250 c.c.) and then extracted with water (200 c.c. in all). The cooled aqueous extract was treated with a moderate excess of 15% aqueous sodium hydroxide and was then shaken with acetic anhydride (15 c.c.). The *acetamido*-compound separated on standing and formed micro-needles, m. p. 150° from ether; yield 66% (Found: C, 68·2; H, 6·6; N, 3·9. $C_{21}H_{25}O_5N$ requires C, 67·9; H, 6·7; N, 3·8%).

The amine *hydrochloride*, m. p. 226—228° (Found: C, 61·9; H, 6·6. $C_{19}H_{23}O_4N$,HCl requires C, 62·4; H, 6·6%), was similarly prepared by hydrogenating the cyanide (0·15 g.) in methanol (18 c.c.) to which had been added methanol (2 c.c.) saturated with hydrogen chloride. It was found advantageous to warm the flask occasionally during hydrogenation. The product was precipitated by adding ether to the concentrated filtrate.

Action of Phosphoric Oxide on (III).—The compound (III; 0·12 g.) was heated under reflux with phosphoric oxide (0·3 g.) in xylene (5·5 c.c.) for 30 minutes. The phosphoric residue, washed by decantation free of the solution which contained some unchanged (III), was treated with dilute sodium hydroxide. 3 : 9 : 10 : 11-*Tetramethoxy*-4-*methyl*-6 : 15-*dihydro*-5-*azabenzanthrene* (VI), recovered in ether, formed yellow crystals, m. p. 156—157°, from ether (Found: C, 71·7; H, 6·5. $C_{21}H_{23}O_4N$ requires C, 71·4; H, 6·5%). It dissolved in hot dilute hydrochloric acid to a golden yellow solution from which, on cooling, slender orange needles of the hydrochloride crystallised, m. p. 218° (decomp.).

Amines of the diphenyl-ethylamine and -propylamine types were prepared by Leuckart's reaction from the appropriate ketone and formamide; the resulting formyl derivative was hydrolysed by heating it with hydrochloric acid, whereby the hydrochloride either crystallised or was isolated by passing dry hydrogen chloride through a dried solution of the base in ether.

Aceto-1 : 2-diphenylethylamide, m. p. 151° from ethanol (Leuckart and Janssen, *Ber.*, 1889, **22**, 1469, give m. p. 148°), distilled unchanged at 200° (air bath)/12 mm. or at 260—280° (air bath)/760 mm., but, after 30 minutes' heating at 325—340°, distillation of the residue gave stilbene, m. p. and mixed m. p. 121°, while the smell of acetamide was discernible. The amide (0·5 g.), phosphoric oxide (2 g.,) and xylene (35 c.c.) were heated under reflux for 20 minutes; the hot xylene solution was decanted, the phosphoric residue was washed with fresh hot solvent, and the combined solutions were fractionally distilled, affording stilbene (70%), b. p. 180—200° (air bath)/10 mm., m. p. and mixed m. p. 122°.

Benzo-1 : 2-diphenylethylamide, m. p. 176°, distilled unchanged at 310—325° (air bath)/755 mm. or 210—215°/10 mm., and gave a 60% yield of stilbene when treated as above with phosphoric oxide in xylene. The amide (1 g.) and phosphorus pentachloride (1·2 g.) in chloroform (7·5 c.c.) were kept for 3 days at room temperature. Aqueous extracts gave no basic material, but concentration of the dried chloroform solution afforded a semi-solid residue from which unchanged material, m. p. and mixed

m. p. 173—174°, was recovered by adding ligroin, while fractional distillation of the filtrate yielded stilbene, m. p. and mixed m. p. 120—122°.

Toluene-p-*sulphon*-1 : 2-*diphenylethylamide*, m. p. 104° from ethanol (Found : C, 72·1; H, 6·0, $C_{21}H_{21}O_2NS$ requires C, 71·8; H, 6·0%), when heated under distillation conditions yielded only stilbene, which was also obtained by concentrating the decanted solution after heating the sulphonamide with phosphoric oxide in xylene.

2-Amino-1 : 3-diphenylpropane yielded a hydrochloride, m. p. 198—200°, a picrate, m. p. 192° (cf. Rajagopalan, *Proc. Roy. Indian Acad. Sci.*, 1941, *A*, **14**, 127), an *acetyl* derivative, m. p. 105° from benzene–ligroin (Found : C, 80·7; H, 7·25. $C_{17}H_{19}ON$ requires C, 80·6; H, 7·5%), and a *toluene*-p-*sulphonyl* derivative, m. p. 99° from ethanol (Found : C, 72·4; H, 6·2. $C_{22}H_{23}O_2NS$ requires C, 72·3; H, 6·3%). Both acyl derivatives distilled under reduced pressure without decomposition, while the parent amine, recovered as hydrochloride (87%), and the sulphonamide (80% recovered) were unchanged by heating with phosphoric oxide in xylene.

The acetyl compound (0·5 g.) was heated under reflux for 30 minutes with phosphoric oxide (1 g.) in xylene (100 c.c.). Fractional distillation of the xylene layer gave 1 : 3-diphenylpropene (0·06 g.), b. p. 180° (air bath)/10 mm., which with bromine in carbon disulphide yielded the dibromide, m. p. 109°, identical with an authentic specimen prepared from phenylacetaldehyde (Stoermer and Thier, *Ber.*, 1925, **58**, 2611). The phosphoric residue was treated with 10% sodium hydroxide, and the basic portion when recovered in ether, dissolved in dilute hydrochloric acid, and treated with aqueous picric acid gave 3-*benzyl*-1-*methyl*-3 : 4-*dihydroisoquinoline picrate*, m. p. 149° from ethanol (Found : C, 59·5; H, 4·0. $C_{23}H_{20}O_7N_4$ requires C, 59·5; H, 4·3%).

1-Amino-1 : 3-diphenylpropane, isolated as the hydrochloride, m. p. 194°, formed a picrate, lemon-yellow plates, m. p. 183—185° (Found : C, 57·5; H, 4·3. Calc. for $C_{21}H_{20}O_7N_4$: C, 57·3; H, 4·5%) (Henrich, *Annalen*, 1907, **351**, 180, gives m. p. 155° for the picrate), and N-*acetyl* derivative, colourless needles, m. p. 76—77° from benzene–ligroin (Found : C, 80·8; H, 7·5. $C_{17}H_{19}ON$ requires C, 80·6; H, 7·5%).

The *N*-acetyl compound (0·5 g.) was treated with phosphoric oxide (2 g.) in xylene (20 c.c.); the residue obtained from the xylene concentrates yielded 1 : 3-diphenylpropene (0·35 g.), b. p. 140—160° (air bath)/1 mm., which was identified by conversion into the dibromide, m. p. and mixed m. p. 108—110°.

1-*Acetamido*-1-*phenyl*-3-(p-*methoxyphenyl*)*propane* (X), m. p. 117° from aqueous ethanol, was prepared by shaking an aqueous solution of the crude hydrochloride (m. p. 156°) of the base with acetic anhydride and alkali (Found : C, 76·2; H, 7·4. $C_{18}H_{21}O_2N$ requires C, 76·4; H, 7·4%). The acetyl compound (3·8 g.) was heated for 30 minutes with phosphoric oxide (7 g.) in dry xylene (30 c.c.). The xylene solution yielded a volatile product (1·3 g.), b. p. 206—208°/12 mm., and a large amount of non-volatile resin. The volatile product, when titrated with a standard solution of bromine in chloroform, showed the expected titre for a phenylmethoxyphenylpropene, but the last drops of the titration produced a dark green colouration [which was not observed with an authentic sample of (XI) prepared as described by Ingold and Shoppee (*J.*, 1929, 447)]. The gum, obtained from the concentrated chloroform solution, was dissolved in benzene and passed through a short column of alumina which removed most of the colour. The recovered gum was dissolved in warm petroleum (b. p. 60—80°) from which a solid fraction slowly separated, m. p. 87—90°, raised to 94° from methanol, and undepressed by admixture with 2 : 3-dibromo-1-phenyl-3-*p*-methoxyphenylpropane of m. p. 94°. Attempts to obtain crystalline material from the gum remaining in the mother-liquor were unsuccessful.

Aceto*cyclo*hexylamide (12 g.) in dry xylene (35 c.c.) was gently heated with phosphoric oxide (10 g.) under distillation conditions. At 90° (bath temp.) the phosphoric oxide darkened, and a low-boiling fraction began to distil and came over steadily while the temperature was kept at 135° (*i.e.*, below the b. p. of the xylene) for 1 hour (fraction *A*). Thereafter the temperature was raised, and half of the liquid remaining in the flask was distilled (fraction *B*). Fraction *A* was separated into a water-soluble (*C*) and a water-insoluble (*D*) fraction by washing it with water (3 × 10 c.c.). Fraction *C*, recovered from the water by saturating the solution with potassium carbonate, had b. p. 79°/755 mm. and was identified as methyl cyanide (1·35 g., 39%) by reduction with sodium in ethanol to ethylamine, from which the picrate, m. p. and mixed m. p. 168—170°, and 2 : 4-dinitrophenyl derivative, m. p. and mixed m. p. 113—114°, were prepared. Fraction *D* distilled at 81°/760 mm. and had the characteristic smell of *cyclo*hexene (1·36 g.; 19%) : it was unsaturated to bromine, and a portion, oxidised with potassium permanganate, gave adipic acid, m. p. and mixed m. p. 151—152°. Fraction *B* (controls having shown that the procedure was valid) was titrated at −5° with a standard solution of bromine in carbon tetrachloride, and required 2·42 g. of bromine ≡ 1·23 g. of *cyclo*hexene or 17·5%; *cyclo*hexene dibromide, b. p. 88°/10 mm., was obtained by fractional distillation of the resulting solution.

Acetoethylamide (0·5 g.) and phosphoric oxide (1 g.) in xylene (5 c.c.) were heated at 110° (bath temp.) while a slow stream of dry nitrogen was passed to carry the emergent gases through a dilute solution of bromine in ethanol. No ethylene dibromide was obtained [although, in a control experiment with ethanol as source, it was readily produced and was identified by conversion into bis-(2 : 5-dichlorophenylthio)ethane (Loudon and Shulman, *J.*, 1939, 1066)]. The phosphoric residue contained much tar, and basification of a concentrated aqueous extract yielded only a small amount (6%) of ethylamine, identified as 2 : 4-dinitrophenylethylamine, m. p. and mixed m. p. 112—114°.

In a similar experiment no propylene was produced from aceto-*n*-propylamide.

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