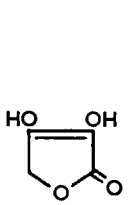
894. *Tetronic Acids and Related Compounds. Part III.* The Claisen Ester Condensation of Ethyl Tetrahydro-2-pyranyloxyacetate.*

By L. J. Haynes and J. R. Plimmer.

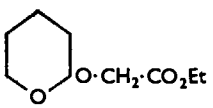
The Claisen ester condensation of benzoylglycollic ester has been employed for the preparation of α-hydroxytetronic acid (I) by Micheel and Jung.[1] However, it seemed likely that improved yields and a cleaner reaction might be obtained by protection of the hydroxyl group of glycollic ester as its dihydropyran adduct,[2] and we now report an examination of this route.

Ethyl tetrahydro-2-pyranyloxyacetate (II) was prepared in good yield by reaction of ethyl glycollate with 2 : 3-dihydropyran in presence of a trace of hydrochloric acid or when an acid ion-exchange resin [Amberlite IR-120 (H)] was used as catalyst. The product was characterised as the amide.

The ester reacted smoothly with sodium and a trace of ethanol in ether to give a syrup which could not be distilled under ordinary conditions without decomposition, but by short-path distillation yielded ethyl αγ-di(tetrahydro-2-pyranyloxy)acetoacetate (III)



(I)



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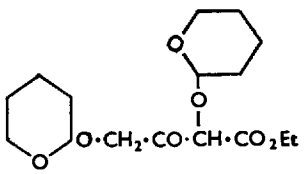
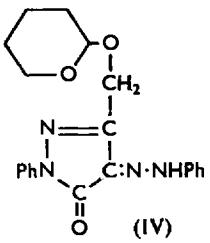


(III)



(IV)

which gave a lilac colour with ferric chloride solution and had $\lambda_{max.}$ 2620 Å (ε 700) in ethanol, shifted to longer wavelengths by addition of sodium ethoxide. The crude product also contained a slightly lower-boiling material which gave a red-brown colour with ferric chloride and a purple colour, indicative of an ene-diol system, with saturated aqueous *o*-dinitrobenzene followed by a few drops of alkali.[3] It was presumably ethyl α-hydroxy-γ-tetrahydropyranyloxy- or γ-hydroxy-α-tetrahydropyranyloxy-acetoacetate formed by hydrolysis, but was not examined further. The bistetrahydropyranyl ester was characterised by the formation of a derivative with phenylhydrazine. The bright orange product was expected to be the corresponding pyrazolone, but its molecular formula, $C_{21}H_{22}O_3N_4$, suggests that it has the structure (IV).

Hydrolysis of the ester (III), first with dilute sulphuric acid to remove the tetrahydropyranyl groups and then with concentrated hydrochloric acid, gave a brown syrup which in one experiment crystallised. On paper chromatography this syrup showed as a single spot (2 : 6-dichlorophenolindophenol spray) in the position expected for hydroxytetronic acid. It gave hydroxytetronic acid bisphenylhydrazone on treatment with phenylhydrazine.

Alkaline hydrolysis of the ester (III) gave the expected 1 : 3-di(tetrahydro-2-pyranyloxy)acetone as an oil.

Experimental.—Ethyl tetrahydro-2-pyranyloxyacetate. (*a*) One drop of concentrated hydrochloric acid was added to a mixture of redistilled 2 : 3-dihydropyran (29·5 g.) and ethyl glycollate (19·5 g.). The temperature rose rapidly but was kept below 40° by cooling. The mixture was set aside for 3 hr., a few pellets of potassium hydroxide were added to remove the acid, and the liquid was distilled under reduced pressure. *Ethyl tetrahydro-2-pyranyloxyacetate* (30 g., 80%)

* Part II, preceding paper.

[1] Micheel and Jung, *Ber.*, 1933, **66**, 1291; 1934, **67**, 1660.

[2] Paul, *Bull. Soc. chim. France*, 1934, **1**, 971; Woods and Kramer, *J. Amer. Chem. Soc.*, 1947, **69**, 2246.

[3] Fearon and Kawerau, *Biochem. J.*, 1943, **37**, 326.

was thus obtained as a liquid, b. p. 73°/0·4 mm., n_D^{16} 1·4440 (Found : C, 57·4; H, 8·4. $C_9H_{16}O_4$ requires C, 57·4; H, 8·5%).

(*b*) Amberlite IR-120(H) ion-exchange resin (0·5 g., dried) was added to a mixture of redistilled 2 : 3-dihydropyran (17 g.) and ethyl glycollate (10 g.). The temperature rose slowly from 22° to 26°. The mixture was kept for 20 hr. at room temperature, then filtered, and the filtrate was distilled as before. The yield of adduct was 12·2 g. (70%).

The *amide* was prepared by treatment of the ester with an excess of ammonia solution (*d* 0·880) overnight. It crystallised after removal of solvent under reduced pressure and recrystallised from benzene as prisms, m. p. 66·5° (Found : C, 53·0; H, 8·2; N, 8·7. $C_7H_{13}O_3N$ requires C, 52·8; H, 8·2; N, 8·8%).

Ethyl αγ-di(tetrahydro-2-pyranyloxy)acetoacetate. Ethyl tetrahydropyranyloxyacetate (20 g.) in dry ether (20 ml.) was added to sodium wire (2·7 g.) in dry ether (200 ml.) whilst a stream of dry nitrogen was passed through the liquid. The mixture was left at room temperature for 24 hr., the sodium slowly dissolving with slight effervescence and a yellow sodio-derivative separating. The reaction was completed on the water-bath (1 hr.). A little ethanol was then added to destroy unchanged sodium, and the mixture was then cooled to 0°, treated with ice and aqueous tartaric acid, and extracted with ether. The ether extract was dried (Na_2SO_4) and evaporated under reduced pressure. The red-brown oil when distilled in a short-path distillation apparatus gave three main fractions : (i) b. p. 75—98°/0·05 mm., $n_D^{13·5}$ 1·4620 (2·47 g.); (ii) b. p. 98—113°/0·05 mm., $n_D^{13·5}$ 1·4674 (1·70 g.); and (iii) b. p. 113—122°/0·05 mm., $n_D^{13·5}$ 1·4730 (1·70 g.). Fraction (i) in ethanol gave a red-brown colour with ferric chloride and was probably a mixture of unchanged starting material and fraction (ii). Fraction (ii) gave a red-brown colour with ferric chloride and a purple colour on addition of aqueous *o*-dinitrobenzene followed by a few drops of alkali. Fraction (iii) was *ethyl αγ-di(tetrahydro-2-pyranyloxy)acetoacetate* which in ethanol slowly gave a purple-lilac colour with ferric chloride (Found : C, 57·8; H, 8·0. $C_{16}H_{26}O_7$ requires C, 58·2; H, 7·9%). The ester (0·5 g.) and phenylhydrazine (0·5 g.) were kept at 100° during 1 hr. The resultant red gum did not crystallise on treatment with light petroleum but after chromatography on alumina formed orange prisms, m. p. 123° (Found : C, 66·7; H, 5·8; N, 14·4. $C_{21}H_{22}O_3N_4$ requires C, 66·7; H, 5·8; N, 14·8%), presumably 4 : 5-*dioxo*-1-*phenyl*-3-(*tetrahydro*-2-*pyranyloxymethyl*)*pyrazolidine*-4-*phenylhydrazone* (IV).

Acid hydrolysis of ethyl αγ-di(tetrahydro-2-pyranyloxy)acetoacetate. Hydroxytetronic acid bisphenylhydrazone. The ester (2·85 g.) and 0·2N-sulphuric acid (10 ml.) were shaken in an inert atmosphere during 3 days. Sulphuric acid was removed by addition of the theoretical amount of 0·1N-barium hydroxide, and the solution was freeze-dried. A pale yellow oil remained. This was kept for 20 hr. in concentrated hydrochloric acid (2 ml.) and water (2 ml.). Solvent was then removed over potassium hydroxide *in vacuo*. The residue was a brown gum : in one experiment the gum crystallised partly but could not be recrystallised. A sample of the gum was examined by paper chromatography with butan-1-ol–glacial acetic acid–water (4 : 1 : 5) as the solvent system, and ascorbic acid as a reference compound, the paper being subsequently sprayed with a solution of 2 : 6-dichlorophenolindophenol. Ascorbic acid had R_F 0·39 and the gum gave a single spot at R_F 0·66. Mapson and Partridge [4] give ascorbic acid R_F 0·37, hydroxytetronic acid R_F 0·63. The gum (0·5 g.) was left at room temperature with phenylhydrazine (1·5 g.) and a drop of glacial acetic acid for 48 hr. Hydroxytetronic acid bisphenylhydrazone (0·7 g.) separated as a red solid which on recrystallisation from ethanol had m. p.s 168° and 215° (decomp.) (Found : C, 65·3; H, 5·0; N, 19·1. Calc. for $C_{16}H_{14}O_2N_4$: C, 65·30; H, 4·7; N, 19·1%). Micheel and Jung [1] give m. p.s 180° and 238°.

Alkaline hydrolysis of ethyl αγ-di(tetrahydro-2-pyranyloxy)acetoacetate. 1 : 3-*Di*(*tetrahydro*-2-*pyranyloxy*)*acetone*. The ester (4·5 g.) was kept in aqueous-methanolic sodium hydroxide (1·0 g. in 100 ml. of methanol and 10 ml. of water) for 24 hr. Water (100 ml.) was added, the solution was extracted several times with ether, and the ether extract dried (Na_2SO_4) and evaporated under reduced pressure. The residual pale yellow oil on short-path distillation gave 1 : 3-*di*(*tetrahydro*-2-*pyranyloxy*)*acetone*, b. p. 85—90° (bath-temp.)/0·01 mm., $n_D^{17·5}$ 1·4748 (Found : C, 60·6; H, 8·5. $C_{13}H_{22}O_5$ requires C, 60·4; H, 8·5%).

We thank Professor E. L. Hirst for advice and encouragement, and Trinity College, Dublin, for the award of a John Winthrop Hackett prize (to J. R. P.).

UNIVERSITY OF EDINBURGH. [*Received, June 25th*, 1956.]

[4] Mapson and Partridge, *Nature*, 1949, **164**, 479.

895. 4-*Benzoyldiphenylamine.*

By M. P. Lippner and Muriel L. Tomlinson.

Plant and Worthing [1] found that benzoyl groups could not be introduced into the benzene nuclei of diphenylamine by the Friedel–Crafts method. 4-Benzoyldiphenylamine has now been made by the Chapman rearrangement of *p*-benzoylphenyl *N*-phenylbenzimidoate.

Experimental.—p-*Benzoylphenyl* N-*phenylbenzimidoate.* Benzanilide (9·8 g.), dried at 100° for 5 hr., was suspended in dry toluene (50 c.c.) and treated with phosphorus pentachloride (10·42 g.). After being heated at 100° until evolution of hydrogen chloride ceased (1 hr.), the colourless solution formed was evaporated under reduced pressure. The resulting *N*-phenylbenzimidoyl chloride, which solidified, was dissolved in dry ether (40 c.c.) and filtered slowly into a solution made by adding *p*-hydroxybenzophenone (10·1 g.) to absolute ethanol (50 c.c.) in which sodium (1·9 g.) had been previously dissolved. Sodium chloride separated, and, after storage overnight in a stoppered vessel, the solvents were removed by distillation and the resulting oil was thoroughly washed with water, extracted with ether, and dried ($MgSO_4$). When the ether had been distilled, the residue solidified after prolonged cooling and rubbing with ethanol. p-*Benzoylphenyl N-phenylbenzimidoate* (8·3 g., 82%) separated from ethanol as colourless prisms, m. p. 98—99° (Found: C, 83·1; H, 5·0. $C_{26}H_{19}O_2N$ requires C, 82·8; H, 5·0%).

4-*Benzoyldiphenylamine.* *p*-Benzoylphenyl *N*-phenylbenzimidoate (8 g.) was heated for 40 min. at 270—280°; the melt was cooled and formed a brown glass which crystallised when rubbed with alcohol. N : 4-*Dibenzoyldiphenylamine* (7·2 g., 90%) separated from ethanol as colourless prisms, m. p. 138° (Found: C, 83·0; H, 5·2. $C_{26}H_{19}O_2N$ requires C, 82·8; H, 5·0%). Hydrolysis with aqueous-alcoholic potassium hydroxide (1 hr.) afforded 4-*benzoyldiphenylamine* (4·7 g., 89%), which crystallised from ethanol as yellow plates, m. p. 155° (Found: C, 83·4; H, 5·4. $C_{19}H_{15}ON$ requires C, 83·5; H, 5·5%). It formed a 2 : 4-*dinitrophenylhydrazone* (red prisms), m. p. 196° (Found: C, 66·2; H, 4·2. $C_{25}H_{19}O_4N_5$ requires C, 66·2; H, 4·4%). Treatment of a solution of 4-benzoyldiphenylamine in acetic acid with 1 equiv. of aqueous sodium nitrite gave 4-*benzoyl*-N-*nitrosodiphenylamine*, m. p. 82°, as yellow prisms (from methanol) (Found: C, 75·8; H, 4·7. $C_{19}H_{14}O_2N_2$ requires C, 75·5; H, 4·6%). N-*Acetyl*-4-*benzoyldiphenylamine* was obtained by boiling 4-benzoyldiphenylamine with acetic anhydride for 5 hr. It crystallised from ethanol as prisms, m. p. 119—120° (Found: C, 80·1; H, 5·4. $C_{21}H_{17}O_2N$ requires C, 80·0; H, 5·4%).

The Dyson Perrins Laboratory, Oxford University. [*Received, July 12th,* 1956.]

[1] Plant and Worthing, *J.*, 1955, 1278.

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896. *Carbamoylglyoxaline.*

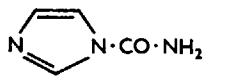
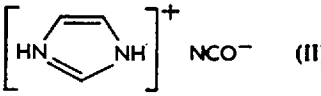
By J. M. Lowenstein.

Mixing a solution of potassium cyanate with a neutralized solution of glyoxaline yields a precipitate which might be carbamoylglyoxaline (I) or glyoxalinium cyanate (II). We show below that the former structure is correct.

A saturated solution of the compound was prepared by stirring an excess of it with water at 0° for 10 minutes and filtering off the undissolved solid. One drop of 1% aqueous cobaltous nitrate, added to 0·2 ml. of such a solution, freshly prepared, gave a very pale grey colour which changed rapidly to a deep blue colour if the solution was boiled. The blue colour also developed if the solution was kept at room temperature overnight. When the cobalt reagent was added to a day-old solution of the compound or to an aqueous solution of potassium cyanate of comparable amount and concentration, the blue colour was at once formed. Glyoxaline itself gave a pink colour and the solution became turbid when boiled. (Ammonium chloride and urea also gave no blue colour, in the cold or when boiled.)

1 ml. of 2N-nitric acid was added to 0·2 ml. of a freshly prepared solution of carbamoylglyoxaline. There was no immediate liberation of gas; from a day-old solution carbon dioxide was liberated immediately. Under similar conditions potassium cyanate liberated carbon dioxide immediately.

The infrared absorption spectrum of the compound, in a potassium bromide disc, did not show the strong absorption maximum of 4·55 μ characteristic of the cyanate ion.

(I)   (II)

The chemical tests and the spectrum indicate the absence, or virtual absence, of free cyanate and this is interpreted as support for structure (I). The chemical tests indicate further that the compound decomposes in water, probably *via* the cyanate (II). From the mode of synthesis and decomposition it may be assumed that there is an equilibrium in aqueous solution of the type carbamoylglyoxaline ⇌ glyoxalinium cyanate.

Citrulline is formed enzymically from carbamoyl phosphate and ornithine.[1] Potassium cyanate can replace carbamoyl phosphate in this reaction. The rate of reaction with potassium cyanate is stimulated by the addition of orthophosphate. This indicates that potassium cyanate first forms carbamoyl phosphate, which then reacts in the usual manner. Carbamoylglyoxaline can also replace carbamoyl phosphate in the enzymic formation of citrulline from ornithine. The rate of its reaction is also stimulated by the addition of orthophosphate (see Table), which suggests that carbamoylglyoxaline affords carbamoyl phosphate, which then reacts in the usual manner. Since either compound (I) or (II) might act in this way, the experiments cannot be taken as evidence for either structure, but the results are of interest from the point of view of possible enzyme mechanisms.

Addition	Citrulline formed (μmole)
None	0·01
Enzyme + phosphate	0·02
Carbamoylglyoxaline	0·07
Carbamoylglyoxaline + enzyme	0·27
Carbamoylglyoxaline + enzyme + phosphate	3·69
Potassium cyanate	0·02
Potassium cyanate + enzyme	0·40
Potassium cyanate + enzyme + phosphate	6·24

Experimental.—Carbamoylglyoxaline. Glyoxaline (3·40 g.) was dissolved in 2N-hydrochloric acid (17 ml.). The solution had pH ~7 (external indicator). A solution of potassium cyanate (4·06 g.) in water (5 ml.) was added at 20°. A heavy white precipitate formed after 4—5 min. The mixture was stirred for 1 hr. at 20°, then filtered. The moist precipitate was extracted with absolute ethanol (100 ml.) at 20°, the extract filtered, and anhydrous ether (150 ml.) added. The resulting solution was stored at −18° for 5 days. The precipitated needles were filtered off and washed with absolute ethanol (20 ml.), 1 : 1 ethanol–ether (20 ml.), and ether (50 ml.). The *compound* was dried *in vacuo* over anhydrous magnesium perchlorate, and was stored similarly (yield 0·9 g.) (Found: C, 43·2; H, 4·4. $C_4H_6ON_2$ requires C, 43·3; H, 4·5%). In the preparation, hydrochloric acid may be replaced by nitric acid. Carbamoylgloxaline sublimes above 200°. At room temperature it is insoluble in ethanol, chloroform, carbon tetrachloride, and carbon disulphide, and is sparingly soluble in water and in ethanol–water (95 : 5, v/v). It dissolves readily in hot water but probably decomposes in the process, since no precipitate is formed on subsequent cooling.

Enzymic formation of citrulline. Each tube contained 0·5M-maleic acid–potassium hydroxide buffer (0·1 ml.; pH 6·8), 0·1M-ornithine (0·2 ml.), sufficient water to make the final volume 1·0 ml., and, where indicated, an aqueous extract of an acetone powder of rat-liver mitochrondria (0·1 ml.; 0·8 mg. of protein), 0·5M-potassium phosphate buffer (0·2 ml.; pH 6·8), 0·05M-carbamoylglyoxaline (0·4 ml.) or 0·05M-potassium cyanate (0·4 ml.). The reaction was started by the addition of carbamoylglyoxaline or cyanate. The tubes were incubated at 38°

[1] Jones, Spector, and Lipmann, *J. Amer. Chem. Soc.*, 1955, **77**, 819; Hall, Marshall, and Cohen, *Biochim. Biophys. Acta*, 1955, **17**, 279.

for 15 min. and the reaction was stopped by the addition of ice-cold 0·5N-perchloric acid (5 ml.). The denatured protein was removed by centrifugation, and aliquot parts of the supernatant solution were analysed for citrulline[2]. Results are tabulated.

The author is grateful for a Beit Memorial Fellowship.

BIOCHEMISTRY DEPARTMENT, UNIVERSITY OF OXFORD. [*Received, June 27th*, 1956.]

[2] Archibald, *J. Biol. Chem.*, 1944, **156**, 121.

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897. *Organic Peroxides. Part VII.* The Alkylation of Hydrogen Peroxide and Alkyl Hydroperoxides with Ethers.*

By ALWYN G. DAVIES and R. FELD.

ALKYL halides, sulphates, and sulphonates, alcohols, esters, and olefins have all been used for alkylating hydrogen peroxide and alkyl hydroperoxides to form alkyl hydroperoxides and dialkyl peroxides, respectively.[1] We now describe the analogous alkylation with ethers.

The mechanism of these reactions is undoubtedly similar to that which has been described for the analogous reaction of alcohols,[1] and involves nucleophilic attack of the peroxide molecule at a carbon atom, probably by an S_N1 or S_Ni mechanism.

Experimental.—In the following experiments precautions were taken against explosion.

Reactions of ethers with hydrogen peroxide. (i) *Ethyl 1-phenylethyl ether.* The ether (0·5 g.) was added at 0° with stirring to 90% hydrogen peroxide (8 c.c.) containing concentrated sulphuric acid (0·1 g.). The mixture was allowed to warm to room temperature and stirring was continued for a total of 6 hr. Water (25 c.c.) was then added and the organic layer was extracted with ether, washed with aqueous sodium hydrogen carbonate and with water, and dried (Na_2SO_4). Evaporation of the ether left an oil (0·1 g.) which was identified as 1-phenylethyl hydroperoxide by the preparation of its triphenylmethyl derivative,[2] m. p. 78—80°, mixed m. p. 79—81°. In the absence of sulphuric acid the ether was recovered after treatment with hydrogen peroxide for 1 hr.

(ii) *Ethyl triphenylmethyl ether.* A mixture of ethyl triphenylmethyl ether (0·6 g.) dissolved in the minimum of ether, and 90% hydrogen peroxide (4 c.c.) containing concentrated sulphuric acid (0·1 g.) likewise yielded triphenylmethyl hydroperoxide (0·48 g.), m. p. 86° (from light petroleum) (Found: C, 82·3; H, 5·8. Calc. for $C_{19}H_{16}O_2$: C, 82·6; H, 5·8%). Bisdiphenylmethyl ether was recovered after similar treatment. Bis-1-phenylethyl ether gave an oil, b. p. 165°/20 mm., which was mainly starting material but gave a strong peroxide test on starch–iodide paper.

(iii) *Bisdiphenylmethyl ether.* The ether (1·0 g.) was dissolved in a mixture of acetic acid (5 c.c.), 90% hydrogen peroxide (1 c.c.), and concentrated sulphuric acid (0·2 c.c.). After 4 hr. at room temperature the mixture yielded diphenylmethyl hydroperoxide (0·63 g.), m. p. 46·5—47° (from light petroleum) (Found: C, 77·6; H, 5·6. Calc. for $C_{13}H_{12}O_2$: C, 78·0; H, 6·0%); triphenylmethyl derivative,[2] m. p. 84—86°; 9-xanthenyl derivative,[2] m. p. 115—117°.

Reactions of ethers with alkyl hydroperoxides. (i) *Ethyl triphenylmethyl ether.* Ethyl triphenylmethyl ether (0·37 g.), *tert.*-butyl hydroperoxide (0·12 g.), acetic acid (3 c.c.), and concentrated sulphuric acid (0·05 c.c.) were mixed. After 6 hr. at room temperature the mixture was poured into water, yielding *tert.*-butyl triphenylmethyl peroxide[2] (0·24 g.), m. p. and mixed m. p. 69—71°.

(ii) iso*Propyl triphenylmethyl ether.* The ether (0·54 g.), acetic acid (5 c.c.), concentrated sulphuric acid (0·05 c.c.), and αα-dimethylbenzyl hydroperoxide (0·29 g.) were mixed. After 3 hr. the mixture was diluted with water, yielding a solid (0·44 g.) which was insoluble in the common organic solvents. It was purified by washing it with a large volume of hot ethanol, giving αα-dimethylbenzyl triphenylmethyl peroxide,[2] m. p. and mixed m. p. 169—170°.

(iii) *Bisdiphenylmethyl ether.* The ether (2·0 g.) and *tert.*-butyl hydroperoxide (1·04 g.) were dissolved in acetic acid (20 c.c.) containing concentrated sulphuric acid (0·8 g.). After 6 hr.

* Part VI, *J.*, 1956, 665.

[1] References are given in Part VI, Davies and Feld, *J.*, 1956, 665.
[2] Davies, Foster, and White, *J.*, 1954, 2200.

the mixture was poured into water yielding tert.-*butyl diphenylmethyl peroxide* (1·46 g.), b. p. 85° (bath)/0·001 mm., n_D^{25} 1·5463 (Found : C, 79·5; H, 7·2. $C_{17}H_{20}O_2$ requires C, 79·7; H, 7·85%).

We are indebted to Professors E. D. Hughes, F.R.S., and C. K. Ingold, F.R.S., for their interest and encouragement, to Laporte Chemicals Limited for the gift of concentrated hydrogen peroxide, and to the Governing Body of Battersea Polytechnic for the award of an Edwin Tate and Holl Scholarship (to R. F.).

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[*Received, July 19th,* 1956.]

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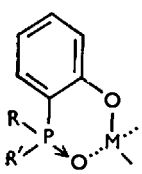
898. *Organic Complex-forming Agents for Metals. Part III.* Compounds containing the o-Hydroxyphenylphosphine Oxide Group.*

By J. KENNEDY, E. S. LANE, and J. L. WILLANS.

THERE is some evidence to suggest that the phosphine oxide group can form complexes with certain metals, *e.g.*, uranium,[1] by donation of two electrons from the oxygen atom. If this is so, a compound containing the *o*-hydroxyphenylphosphine oxide group should chelate with metals, as in (I), as " oxine " does. Since it represents a completely new chelating system some compounds containing such ligands were prepared and examined.



(I)

Di-(*o*-methoxyphenyl)methylphosphine was obtained in 70% yield by treatment of methylphosphonous dichloride with *o*-methoxyphenylmagnesium bromide, and was characterised as the sulphide and as a phosphonium salt; it oxidised to the phosphine oxide with hydrogen peroxide. It was also prepared (84% yield) by alkaline hydrolysis of tri-(*o*-methoxyphenyl)methylphosphonium iodide, itself prepared by quaternisation of tri-(*o*-methoxyphenyl)phosphine with methyl iodide. Di-(*o*-hydroxyphenyl)methylphosphine oxide was obtained on dealkylation of the dimethoxy-oxide with aluminium chloride or pyridine hydrochloride and was characterised as the diacetate.

Tri-(*o*-hydroxyphenyl)phosphine oxide was similarly obtained (79% yield), with aluminium chloride, and was characterised as the triacetate.

In contradistinction to the methoxy-derivatives, both compounds containing the *o*-hydroxyphenylphosphine oxide group gave precipitates with solutions containing Fe^{3+}, UO_2^{2+}, and Hg^{2+}, but apart from establishing this grouping as a chelating system this ligand is unlikely to be of analytical interest because of its low sensitivity and lack of selectivity.

We were unable to prepare the related *o*-hydroxyphenylphosphonic acid, the phosphorus analogue of salicylic acid. Attempts to demethylate *o*-methoxyphenylphosphonic acid caused breakage of the C–P bond, and *o*-benzyloxyaniline (which we hoped to debenzylate later by hydrogenation) did not undergo the Freeman–Doak reaction for replacement of the amino-group by phosphonic acid.

Experimental.—Determination of phosphorus in aromatic phosphines, phosphine oxides, and phosphonium salts. Wet oxidation methods were ineffective for the digestion of these classes of compounds to orthophosphate. Fusion with sodium peroxide (cf. Stanley *et al.*[2]) was satisfactory.

Determination of the equivalent weight of organo-phosphorus compounds. Phosphines and phosphonium salts were titrated with perchloric acid in acetic acid (see Parts I and II). Phosphine oxides were insufficiently basic for this technique. *o*-Hydroxyphenylphosphine oxides were titrated as phenols in ethylenediamine.

Tri-(o-methoxyphenyl)methylphosphonium iodide, prepared quantitatively from methyl iodide

* Part II, *J.*, 1956, 569.

[1] Blake, Brown, and Coleman, ORNL 1946 (Chemistry), 1955.
[2] Stanley, Vannier, Freeman, and Doak, *Analyt. Chem.*, 1955, **27**, 474.

and the parent tertiary phosphine,[3] had m. p. 212—213° (Found: C, 53·0; H, 4·7; I, 26·1. $C_{32}H_{24}O_3IP$ requires C, 53·4; H, 4·9; I, 25·7%).

Tri-(o-hydroxyphenyl)phosphine oxide. To tri-(*o*-methoxyphosphine) oxide[4] (50 g.) and anhydrous aluminium chloride (72·5 g.), benzene (150 ml.) was added with stirring. Methyl chloride was evolved. The mixture was kept at 95—100° for 4 hr., evolution of methyl chloride then ceasing. After acidification with 20% hydrochloric acid (250 ml.) the benzene was removed in steam, leaving a solid. This was filtered off and recrystallisation (alcohol) gave a colourless *iodide* (35 g.), m. p. 214·5—216° (Found: C, 66·2; H, 4·8; P, 9·1%; equiv., 107. $C_{18}H_{15}O_4P$ requires C, 66·25; H, 4·6; P, 9·5%; equiv., 109). The *triacetate* had m. p. 197—199° (Found: C, 64·5; H, 5·0; P, 6·7. $C_{24}H_{21}O_7P$ requires C, 63·7; H, 4·6; P, 6·9%).

Di-(o-methoxyphenyl)methylphosphine. Methylphosphonous dichloride (13·1 g.) in dry ether (50 ml.) was added dropwise to a cooled, stirred solution of *o*-methoxyphenylmagnesium bromide (from 47 g. of *o*-bromoanisole) in ether (150 ml.). After 1 hr. the mixture was decomposed by saturated aqueous ammonium chloride, and the ether layer was evaporated. The residue recrystallised from alcohol, giving the *phosphine* (20·1 g.), m. p. 128—129° (Found: C, 69·4; H, 6·6; P, 11·5%; equiv., 262. $C_{15}H_{17}O_2P$ requires C, 69·3; H, 6·5; P, 11·9%; equiv., 260). With methyl and ethyl iodide respectively it gave quantitative yields of the corresponding *phosphonium iodides*, m. p. 215—216·5° (Found: equiv., 402. $C_{16}H_{20}O_2IP$ requires equiv., 402), and m. p. 157—160° (Found: C, 48·9; H, 4·9; P, 7·45%; equiv., 418. $C_{17}H_{22}O_2IP$ requires C, 49·0; H, 5·3; P, 7·45%; equiv., 416).

Di-(o-methoxyphenyl)methylphosphine oxide. (*a*) The preceding phosphine (14·1 g.) in water (20 ml.) at 60° was treated with hydrogen peroxide (15 ml.; 100-vol.) dropwise. The mixture was refluxed for 10 min., then cooled; the lower oily layer solidified and recrystallised from alcohol, giving a quantitative yield of the *oxide*, m. p. 150° (Found: C, 64·9; H, 6·25; P, 11·2. $C_{15}H_{17}O_3P$ requires C, 65·2; H, 6·2; P, 11·2%).

(*b*) Tri-(*o*-methoxyphenyl)methylphosphonium iodide (9·88 g.) was refluxed for 2 hr. with 20% aqueous potassium hydroxide (40 ml.), then steam-distilled to remove anisole, and the residue was filtered off and recrystallised from benzene, giving the oxide, m. p. 150—151·5° (Found: C, 65·4; H, 6·5%).

The corresponding *phosphine sulphide*, obtained by the exothermic reaction between sulphur and the parent phosphine in ether, had m. p. 87—88° (from ethanol) (Found: P, 15·1; S, 16·0. $C_9H_{12}OSP$ requires P, 15·5; S, 16·0%).

Di-(o-hydroxyphenyl)methylphosphine oxide. (*a*) Di-(*o*-methoxyphenyl)methylphosphine oxide (13·8 g.) was refluxed for 1 hr. with benzene and aluminium chloride (70·0 g.). Evaporation of the benzene layer, followed by recrystallisation from alcohol, gave the *phenol* (5·8 g.), m. p. 204·5—206° (Found: P, 12·5. $C_{13}H_{13}O_3P$ requires P, 12·5%). The *diacetate* had m. p. 201—203° (Found: C, 61·6; H, 5·25; P, 9·15%; equiv., 164. $C_{17}H_{17}O_5P$ requires C, 61·5; H, 5·1; P, 9·35%; equiv., 168).

(*b*) Di-(*o*-methoxyphenyl)methylphosphine oxide (6·5 g.) and pyridine hydrochloride (15 g.) were heated together at 200° for 4 hr., then poured into water. The phenol separated (3·0 g.). The m. p. was raised to 210·5—211·5° by alternate dissolution in alkali and precipitation with acid (Found: P, 12·5%).

Sensitivity and selectivity tests. The method of Irving *et al.*[5] was used. The results are expressed as volumes of standard metal solutions which (*a*) gave a perceptible precipitate (V_1) and (*b*) failed to give a precipitate (V_2). The larger volume V_1 was taken as a conservative estimate of the sensitivity. The results are expressed in terms of pL [$-\log_{10}$ (limiting concentration in g.-equivs. per l.)] for the volumes V_1 and V_2 respectively. The following ions were tested: Cu^{2+}, Fe^{3+}, UO_2^{2+}, Mg^{2+}, Hg^{2+}, Ni^{2+}, and Co^{2+}.

Tri(*o*-hydroxyphenyl)phosphine oxide at pH 5·3: Fe^{3+}, 4·24—4·54; UO_2^{2+}, 3·24—3·54; Hg^{2+}, 2·24—3·24.

Di-(*o*-hydroxyphenyl)methylphosphine oxide at pH 5·3: Fe^{3+} 3·24—4·24; UO_2^{2+} 2·24—2·73; Hg^{2+} 2·24—2·84; and at pH 8·5: Fe^{3+}, 3·24—4·24; UO_2^{2+}, 3·24—4·24.

The colours of the precipitates obtained with both compounds and Fe^{3+}, UO_2^{2+}, and Hg^{2+} were red-brown, pale brown, and white respectively.

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[3] Mann and Chaplin, *J.*, 1937, 527.
[4] Dawson and Burger, *J. Org. Chem.*, 1953, **18**, 207.
[5] Irving, Butler, and Ring, *J.*, 1949, 1489; cf. Hollingshead, *Chem. and Ind.*, 1944, 440; Irving, Hollingshead, and Harris, *Analyst*, 1955, **80**, 260; Hollingshead, *Analyt. Chim. Acta*, 1955, **12**, 201.

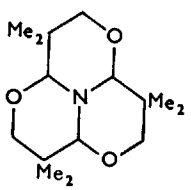
899. *The Reaction of Ammonium Acetate with β-Hydroxy-αα-dimethylpropaldehyde.*

By J. F. CAVALLA.

SOME two years ago [1] a by-product $C_{15}H_{27}O_3N$ was obtained during preparation of 2-cyano-5-hydroxy-4 : 4-dimethylpent-2-enolactone from β-hydroxy-αα-dimethylpropaldehyde, ammonium acetate, and acetic acid in benzene (cf. Cope [2]). Further work has shown that the nitrogen atom in the by-product came from the ammonium acetate rather than from the ethyl cyanoacetate. Acetic acid in stoicheiometric amounts had also to be present to give good yields.

The compound was remarkably stable to all except drastic conditions. It was recovered unchanged from boiling dilute hydrochloric acid or 5% ethanolic sodium hydroxide (3 hr.); acetic anhydride at the b. p. or in pyridine at 95°, and methyl iodide alone or in boiling nitromethane or acetonitrile had no effect, the compound crystallising well from the anhydride or iodide.

The absence of carbonyl groups, indicated by the compound's inertness to the common reagents, was confirmed by the lack of both ultraviolet and infrared absorption. When refluxed with constant-boiling hydrochloric acid or phosphorus in phosphoric–hydriodic acid the substance decomposed to give formaldehyde, *iso*butyraldehyde, and β-hydroxy-αα-dimethylpropaldehyde, identified by paper chromatography. The molecular formula, preparation, and properties indicate a probable structure (I) and this view is shared by Lynn [3] who has isolated what is almost certainly the same compound by treating β-hydroxy-αα-dimethylpropaldehyde with ammonia.



(I)

However, whilst the compound can be titrated with perchloric acid in acetic acid its pK_a is remarkably low (<2); it yields a perchlorate but not a hydrochloride. Unlike the oxazolidines,[4] which resemble the postulated formula, the compound resisted hydrogenation even under forcing conditions (5% palladised charcoal in ethanol at 100°/80 atm.). It also did not react with ethereal methylmagnesium iodide which is known to react with the grouping $NR_2{\cdot}C(OR)<$.[4,5]

Experimental.—Reaction of β-hydroxy-αα-dimethylpropaldehyde with ammonium acetate and acetic acid. The aldehyde (30·6 g., 0·3 mol.), ammonium acetate (15·4 g., 0·2 mol.), and acetic acid (12 g., 0·2 mol.) in benzene (100 ml.) were refluxed under a Dean and Stark head. After 3 hr., 9 ml. of water had collected and refluxing was stopped. On cooling, needles separated (15·6 g., m. p. 183—186°). The mother-liquor on dilution with light petroleum (200 ml.) gave a less pure product (3·5 g; m. p. 165—180°). One crystallisation from chloroform–ethanol gave *dodecahydro-3 : 3 : 6 : 6 : 9 : 9-hexamethyl-1 : 4 : 7-trioxa-9b-azaphenalene* (I), m. p. 185—187° (71%) (Found : C, 66·9; H, 10·4; N, 5·2; O, 17·7%; *M*, 256. $C_{15}H_{27}O_3N$ requires C, 66·9; H, 10·1; N, 5·2; O, 17·8%; *M* 269), which had no significant absorption above 215 mμ and gave infrared max. at 2950, 2850, 2800, 2700, 2590, 1478, 1461, 1396, 1374, 1365, 1317, 1300, 1246, 1222, 1204, 1138, 1087, 1048, 1020, 998, 965, 952, 938, 926, 907, 808, and 698 cm.$^{-1}$ in a potassium bromide disc.

If the acetic acid was omitted from the above reaction mixture no product was obtained; addition of small quantities (0·2 g.) of acid gave only 0·4 g. of product.

Reactions. The substance (0·4 g.) in ether (50 ml.) was treated with a dilute solution of perchloric acid in ether (50 ml.); the *perchlorate* separated as needles (0·4 g.), m. p. 248° (decomp.). Crystallisation from ethanol–ether gave prisms, m. p. 250° (decomp.) (Found : C, 49·1; H, 7·6; N, 3·7. $C_{15}H_{27}O_3N,HClO_4$ requires C, 48·7; H, 7·6; N, 3·8%).

The substance (1·5 g.) was refluxed for 1 hr. with constant-boiling hydrochloric acid (150 ml.),

[1] Bowman and Cavalla, *J.*, 1954, 1171.
[2] Cope, *J. Amer. Chem. Soc.*, 1941, **63**, 3452.
[3] Lynn, *ibid.*, 1955, **77**, 6067.
[4] Senkus, *ibid.*, 1945, **67**, 1515.
[5] Robinson and Robinson, *J.*, 1923, 532.

then distilled, the first 10 ml. of distillate being collected. Treatment with Brady's solution gave an immediate precipitate, m. p. 145—160°. This was run upwards on chromatography paper with the top layer of a light petroleum (b. p. 100—120°)–methanol mixture : three spots were obtained, having R_F 0·15, 0·26, and 0·58 and shown to be those for the 2 : 4-dinitrophenylhydrazones of β-hydroxy-αα-dimethylpropaldehyde, formaldehyde, and *iso*butyraldehyde respectively. Basification or dilution of the acid solution remaining from the distillation gave some unchanged starting material.

The compound did not react with lithium aluminium hydride in boiling ether during 4 hr.

The author thanks Mr. A. J. Durre of this laboratory and Frau E. Pascher (Bonn) for the microanalyses and Miss E. Tanner for the physical measurements, also Dr. R. E. Bowman for many helpful discussions.

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900. 2 : 6-*Dimethylacetophenone.*

By (the late) E. A. BRAUDE and R. L. ERSKINE.

2 : 6-DIMETHYLACETOPHENONE (I) has been prepared by several methods, *inter alia* from 2 : 6-dimethylbenzonitrile,[1] 2 : 6-dimethylbenzoic acid,[2,3] and 2-iodo-1 : 3-dimethylbenzene,[4] but some of the physical properties recorded for it by different workers are not in good agreement. Since the ketone is liquid and does not readily furnish crystalline derivatives, the discrepancies could conceivably be due to the presence of isomers. The spectral properties are of importance in connection with the theory of steric hindrance in conjugated systems [3] and we have therefore re-investigated this compound.

2 : 6-Dimethylacetophenone was prepared from the nitrile by reaction with methylmagnesium iodide in anisole, followed by acid hydrolysis. The ketone, which is somewhat unstable in air, shows ultraviolet absorption with an inflexion at about 2400 Å (ε 2000) in ethanol, and infrared absorption with intense peaks at 1700 (CO stretching) and 773 cm.$^{-1}$ (1 : 2 : 3-trisubstituted benzene). When heated with Brady's reagent, it furnished a 2 : 4-dinitrophenylhydrazone, m. p. 158°, identical with that previously described,[1,3] but the yield was only 30% under the best conditions tried. The structure and homogeneity of the ketone was confirmed by conversion [4] with potassium hypochlorite into 1 : 3-dimethyl-2-trichloroacetylbenzene (II), followed by alkaline hydrolysis in a *glass* vessel to 2 : 6-dimethylbenzoic acid (III).

When the hydrolysis of the trichloro-ketone was conducted in a copper flask, the acid (III) was obtained in lower yield, together with a second acid $C_{10}H_{12}O_3$, m. p. 152°. This must be 2 : 6-dimethylmandelic acid (IV), since the infrared spectrum indicates the presence of a hydroxyl group and a non-conjugated carboxyl group, and the acid is converted by chromic oxide into 2 : 6-dimethylbenzaldehyde (VI), presumably *via* 2 : 6-dimethylglyoxylic acid (V) followed by decarboxylation. 2 : 6-Dimethylmandelic acid has been reported by Ando [5] to have m. p. 115°, but his product, obtained by the reaction between *m*-xylene and oxomalonic ester, was actually 2 : 4-dimethylmandelic acid.[6] The formation of the mandelic acid (IV) from the ketone (II) can be rationalized either by a copper-catalysed reduction of the carbonyl group at some stage in the hydrolysis or by an initial hydrogenolysis of one C–Cl bond followed by hydrolysis and rearrangement [7] of the resulting 2 : 6-dimethylphenylglyoxal.

These results, which have been duplicated several times, suggest that some of the samples of 2 : 6-dimethylacetophenone previously used for spectral measurements were impure.

[1] Pearson and Greer, *J. Amer. Chem. Soc.*, 1955, **77**, 1294; cf. Charlton and Hughes, *J.*, 1954, 2939.
[2] De Jong, *Rec. Trav. chim.*, 1942, **61**, 539.
[3] Braude and Sondheimer, *J.*, 1955, 3754.
[4] Schwartzman and Corson, *J. Amer. Chem. Soc.*, 1954, **76**, 781.
[5] Toshio Ando, *J. Chem. Soc. Japan*, 1935, **56**, 745.
[6] Riebsomer, Irvine, and Andrews, *J. Amer. Chem. Soc.*, 1938, **60**, 1015.
[7] Evans, *Amer. Chem. J.*, 1906, **35**, 115.

The present results correspond closely to those reported by Schwartzman and Corson,[4] except that their material showed a peak at 1658 cm.$^{-1}$, possibly due to 2 : 6-dimethylstyrene. It is surprising that Schwartzman and Corson's ketone did not furnish [4] the 2 : 4-dinitrophenylhydrazone, m. p. 158°, but afforded [3] instead an unidentified derivative,

$$\underset{(I)}{R\cdot CO\cdot CH_3} \longrightarrow \underset{(II)}{R\cdot CO\cdot CCl_3} \longrightarrow \underset{(III)}{R\cdot CO_2H} \qquad \underset{(IV)}{R\cdot CH(OH)\cdot CO_2H} \longrightarrow \underset{(V)}{R\cdot CO\cdot CO_2H} \longrightarrow \underset{(VI)}{R\cdot CHO}$$

$$(R = 2:6\text{-}C_6H_3Me_2)$$

m. p. 223°; it is difficult to account for this except by prior decomposition of the ketone. We have been unable to repeat the preparation [3] of 2 : 6-dimethylacetophenone by the action of methyl-lithium on 2 : 6-dimethylbenzoic acid, mostly unchanged acid being recovered in each attempt; although the ketone previously obtained gave a 2 : 4-dinitrophenylhydrazone, m. p. 155°, the ultraviolet light absorption of the product, $\lambda_{max.}$ 2510 Å (ε 5600) is not that of 2 : 6-dimethylacetophenone.

The present results necessitate some revision of the earlier discussion.[3] The ultraviolet light absorption of 2 : 6-dimethylacetophenone is very similar to that of 2 : 4 : 6-trimethylacetophenone; application of the equation $\cos^2\theta = \varepsilon/\varepsilon_0$ to the reduction in intensity of the characteristic band relative to acetophenone leads to values of 70° and 63°, respectively, for the interplanar angle θ between the phenyl and the carbonyl chromophore, showing that the steric effects of the two *o*-methyl substituents are comparable in the two compounds. The influence of the *p*-methyl substituent is to reduce θ slightly; the same effect is observed in comparing 2-methyl- and 2 : 4-dimethyl-acetophenone and may be ascribed to the hyperconjugative increase in the bond order of the bond between the substituted phenyl and the carbonyl group which will promote the planarity of the conjugated system. It may be noted that the decreases in intensity are accompanied by small, but by no means negligible, displacements to shorter wavelengths; if it is assumed that, in the absence of steric effects, *o*-methyl groups would produce bathochromic shifts similar to those observed with *p*-methyl groups ($\Delta\lambda$ = 90 Å), the $\Delta\lambda$ values due to steric effects are *ca.* −210 Å for 2 : 6-dimethyl- and −280 Å for 2 : 4 : 6-trimethyl-acetophenone, corresponding to increases of *ca.* 12—14 kcal. in transition energy compared with that of acetophenone. Acetophenones carrying two *o*-methyl substituents thus represent border-line cases between what have been termed steric effects of type (1) and type (2).

Experimental.—*2 : 6-Dimethylacetophenone.* 2 : 6-Dimethylbenzonitrile (8·7 g.; m. p. 90—91°, $\lambda_{max.}$ 2310 Å, ε 10,000 in EtOH) in dry anisole (120 ml.) was added to methylmagnesium iodide (1·1 mol.) in ether (100 ml.). The ether was distilled off and the residual solution was refluxed for 3 hr. Excess of saturated aqueous ammonium chloride was then added, the mixture was extracted with ether, the ether solution was extracted with N-sulphuric acid (3 × 50 ml.), and the acid solution was refluxed with toluene (50 ml.) for 12 hr. The toluene layer was separated, the aqueous layer was extracted with ether, and the combined toluene–ether solutions were washed with 2N-sodium carbonate solution and water, dried (Na_2SO_4), and distilled, to give 2 : 6-dimethylacetophenone (5·2 g., 44%) as a colourless oil, b. p. 106°/17 mm., n_D^{27} 1·5141 (Found: C, 81·0; H, 8·3. Calc. for $C_{10}H_{12}O$: C, 81·0; H, 8·1%). Infrared spectrum (liquid film): $\nu_{max.}$ 1700 s, 1592 m, 1461 m, 1420 m, 1381 w, 1350 s, 1254 s, 1165 w, 1106 w, 1054 m, 959 m, 773 s, and 744 m cm.$^{-1}$.

The ketone (0·3 g.) was heated under reflux with 2 : 4-dinitrophenylhydrazine (0·5 g.), ethanol (10 ml.), and sulphuric acid (1 ml.). The 2 : 4-dinitrophenylhydrazone (0·23 g., 30%) crystallised from methyl*cyclo*hexane as yellow needles, m. p. 158°, $\lambda_{max.}$ 3640 Å (ε 23,000) in $CHCl_3$ (Found: C, 59·0; H, 5·1; N, 16·8. Calc. for $C_{16}H_{16}O_4N_4$: C, 58·5; H, 4·9; N, 17·1%). When hydrochloric acid was used [1] in place of sulphuric acid, the yield of derivative was slightly lower.

Oxidation. The ketone was converted by potassium hypochlorite at 55° (3 hr.) into the 1 : 3-dimethyl-2-trichloroacetylbenzene (75%), b. p. 139°/11 mm., n_D^{23} 1·5412. Hydrolysis by refluxing 2N-sodium hydroxide (6 hr.) in a glass vessel gave 2 : 6-dimethylbenzoic acid (85%), m. p. 115°. Hydrolysis in a copper flask under otherwise identical conditions gave 2 : 6-dimethylbenzoic acid (56%) and 2 : 6-dimethylmandelic acid (33%) which were separated

by partition between benzene and water. After sublimation at 140°/15 mm., the very water-soluble 2 : 6-*dimethylmandelic acid* crystallised from benzene in needles, m. p. 152° (Found : C, 66·5; H, 6·8. $C_{10}H_{12}O_3$ requires C, 66·6; H, 6·7%). Infrared spectrum (in paraffin mull) : $\nu_{max.}$ 3400 m (OH), 1709 s (CO_2H), and 1590 w, 1168 m, 1078 m, 891 w, and 777 s cm.$^{-1}$ (1 : 2 : 3-trisubstituted benzene ring).

A stirred mixture of 2 : 6-dimethylmandelic acid (0·21 g.), pyridine (5 ml.), and chromic oxide (0·28 g.) was kept for 12 hr. at 20°. Water (20 ml.) was added and the mixture was continuously extracted with ether. The ether extract was concentrated and treated with Brady's reagent, giving the 2 : 4-dinitrophenylhydrazone of 2 : 6-dimethylbenzaldehyde (0·13 g.) as red prisms, m. p. and mixed m. p. 255°, $\lambda_{max.}$ 3780 Å (ε 26,500) in $CHCl_3$ (Found : C, 57·7; H, 4·7; N, 17·7. Calc. for $C_{15}H_{14}O_4N_4$: C, 57·3; H, 4·5; N, 17·8%). The infrared spectrum (KBr disc) was indistinguishable from that of an authentic sample and showed bands with $\nu_{max.}$ 3240 w, 1615 s, 1590 s, 1505 s, 1327 s, 1255 m, 1215 m, 1127 s, 836 m, 788 m, 780 m, 739 m cm.$^{-1}$.

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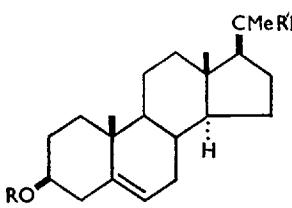
901. 20ξ-*Hydroxycholesterol.*

By VLADIMIR PETROW and (MRS.) ISOBEL A. STUART-WEBB.

PRESUMPTIVE evidence exists [1] that 20-hydroxycholesterol (Ia) is an intermediate in corticosteroid biogenesis. We have, therefore, prepared a 20ξ-hydroxycholesterol (Ib) and some simpler analogues for biological study.

A previous attempt [2] to prepare the compound (Ib) by reacting *iso*hexylmagnesium bromide with 3β-acetoxypregn-5-en-20-one (Ic) gave "unsatisfactory results." In our hands, however, smooth condensation occurred to give, after acetylation, 3β-acetoxy-20ξ-hydroxycholesterol (Id) in *ca.* 45% yield. The constitution assigned to this product was supported by its infrared absorption spectrum, for which we are indebted to Mr. R. F. Branch, B.Sc. (Ministry of Supply), which showed the presence of a non-hydrogen-bonded hydroxyl group in the molecule. Alkaline hydrolysis at room temperature yielded 20ξ-hydroxycholesterol (Ib), which was converted by the Oppenauer route into 20ξ-hydroxycholest-4-en-3-one.



(Ia): R=H, R'= ▬ OH, R''= ⋯ $[CH_2]_3 \cdot CHMe_2$

(Ib): R=H, R'= ~~OH, R''= ~~ $[CH_2]_3 \cdot CHMe_2$

(Ic): R = Ac, R'R''= O

(Id): R=Ac, R'= ~~OH, R''= ~~ $[CH_2]_3 \cdot CHMe_2$

Some simpler analogues of (Ib), prepared in similar manner, are listed in the Table.

In no case was there any evidence for the formation of more than one $C_{(20)}$-stereoisomer. The stereochemistry of the products remains unestablished. Discussion of this point with Dr. W. Klyne, however, leads us to believe that the compounds have probably the same configuration at $C_{(20)}$ as has cholesterol.[4]

Experimental.—Optical rotations were measured in chloroform in a 1-dm. tube. The ultraviolet absorption spectrum was kindly determined by Mr. M. T. Davies, B.Sc.

4-Methylpentan-1-ol was prepared essentially as described by Cardwell *et al.*[2] It was converted into *iso*hexyl bromide by Sabetay and Bléger's method.[3]

3β-*Acetoxycholest-5-en-20ξ-ol* (Id). 3β-Acetoxypregn-5-en-20-one (3·58 g.) in benzene (150

[1] Cf. for example, Lynn, jun., Staple, and Gurin, *Fed. Proc.*, 1955, **14**, 783.
[2] Cardwell, Cornforth, Duff, Holtermann, and Robinson, *J.*, 1953, 361.
[3] Sabetay and Bléger, *Bull. Soc. chim. France*, 1930, **47**, 885.
[4] Cf. Klyne, "Ciba Foundation Colloquia on Endocrinology," Vol. VII, p. 130.

ml.) was added to the Grignard solution prepared from magnesium (2·4 g.), *iso*hexyl bromide (1·65 g.), and ether (100 ml.). The mixture was distilled until the distillate temperature reached 78° and gently refluxed thereafter for a further 3 hr. After cooling, the mixture was decomposed with ammonium chloride solution, and the product isolated with benzene. The resulting oil was acetylated (acetic anhydride–pyridine for 1 hr. on the water-bath), and a benzene solution of the product was chromatographed on alumina (100 g.; B.D.H. chromatography grade). The benzene–ether (6·5 : 1) eluates yielded 3β-*acetoxycholest*-5-*en*-20ξ-*ol*, needles (from methanol), m. p. 155—156°, $[\alpha]_D^{23}$ −58° (*c*, 0·455) (Found: C, 78·8; H, 11·0. $C_{29}H_{48}O_3$ requires C, 78·4; H, 10·8%).

Cholest-5-*ene*-3β : 20ξ-*diol* (Ib). The acetate (220 mg.) in methanol (20 ml.) was treated with potassium carbonate (140 mg.) in water (2 ml.) overnight at room temperature. The product was isolated with chloroform and crystallised from acetone–hexane, giving *cholest*-5-*ene*-3β : 20ξ-*diol*, m. p. 123—125°, $[\alpha]_D^{22}$ −52° (*c*, 0·369) (Found: C, 80·4; H, 11·5. $C_{27}H_{46}O_2$ requires C, 80·6; H, 11·4%).

20ξ-*Hydroxycholest*-4-*en*-3-*one*. 20ξ-Hydroxycholesterol (1 g.) in *cyclo*hexanone (13 ml.) was oxidised with aluminium *tert.*-butoxide (1 g.) in toluene (8 ml.) under reflux for 40 min. Crystallisation from aqueous methanol furnished 20ξ-*hydroxycholest*-4-*en*-3-*one*, needles, m. p. 137—138°, $[\alpha]_D^{22}$ +66° (*c*, 0·592), $\lambda_{max.}$ 241 mμ (log ε 4·23) (Found: C, 80·5; H, 11·0. $C_{27}H_{44}O_2$ requires C, 81·0; H, 11·0%).

Condensation of 3β-acetoxypregn-5-en-20-one with alkyl halides followed the general pattern employed for the preparation of compound (Ic). The products obtained are listed in the Table (the hydroxyl group and the 20-substituent are of unknown orientation).

					Analysis				
(I; R′ = OH)					Found, %			Reqd., %	
R	R″	M. p.	$[\alpha]_D^t$	*c*	C	H	Formula	C	H
H	Me	187°	−65° [a]	0·291	79·3	10·4	$C_{22}H_{36}O_2$	79·5	10·8 *
H	Et	167—168	−65 [b]	0·46	77·5	10·8	$C_{23}H_{38}O_2,\frac{1}{2}H_2O$	77·8	11·0
Ac	Et	172—173	−64 [a]	0·823	77·5	10·6	$C_{25}H_{40}O_3$	77·3	10·3
H	*n*-Bu	112—114	—	—	76·0	11·1	$C_{25}H_{42}O_2,H_2O$	76·5	11·2
H	*n*-C_5H_{11}	123	−61 [b]	0·604	80·7	11·2	$C_{26}H_{44}O_2$	80·4	11·3
Ac	*n*-C_5H_{11}	155	−57 [c]	0·402	77·8	10·6	$C_{28}H_{46}O_3$	78·1	10·7

[a] t = 23°. [b] t = 24°. [c] t = 22°. * Cf. ref. 5.

The authors thank the Directors of The British Drug Houses Ltd. for permission to publish this work.

CHEMICAL RESEARCH LABORATORIES,
THE BRITISH DRUG HOUSES LTD., LONDON, N.1. [*Received, June 14th*, 1956.]

[5] Marker, Crooks, Jones, and Shabica, *J. Amer. Chem. Soc.*, 1942, **64**, 1276.

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902. *The Kinetics of Alkyl–Oxygen Fission in Ester Hydrolysis. Part VI.* Olefin Formation.*

By J. G. HAWKE and V. R. STIMSON.

BUNTON [1] has shown that *iso*butene is formed in the acid-catalysed methanolysis of *tert.*-butyl benzoate. The present results (Tables 1 and 2) show that olefin is produced according to first-order kinetics during hydrolyses of *tert.*-butyl benzoate and 2 : 4 : 6-trimethylbenzoate, and *tert.*-amyl benzoate for which mechanism $A_{AL}1$ has been proposed.[2] The ratios of olefin-producing reaction to total reactions are independent of the nature of R′ in R′·CO_2R and, with allowance for the change in temperature, are closely comparable with the values found by Hughes *et al.*[3] for the *tert.*-butyl and *tert.*-amyl halides. Such results for olefin production indicate the formation of the carbonium ion R^+ and are further evidence for the unimolecular nature of these hydrolyses.

* Part V, *J.*, 1956, 3629.

[1] See Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 780.
[2] Stimson, *Nature*, 1955, **175**, 47; Parts I and III, *J.*, 1954, 2848: 1955, 2673.
[3] Hughes and MacNulty, *J.*, 1937, 1283; Cooper, Hughes, and Ingold, *J.*, 1937, 1280.

Rate of Hydrolysis and Acidity Function.—On a number of occasions [4] it has been shown that for a unimolecular acid-catalysed reaction the rate is proportional to the Hammett acidity function H_0, whereas for a bimolecular reaction involving a molecule of water the

TABLE 1. *Olefin produced from* tert.*-butyl 2 : 4 : 6-trimethylbenzoate.* C_A *and* C_E *are the concentrations of hydrochloric acid and ester respectively.*

Solvent: 80% ethanol. $C_A = 1{\cdot}03$; $C_E = 0{\cdot}086$; $Na_2S_2O_3 = 0{\cdot}01970$N; ester $= 4{\cdot}29 \times 10^{-3}$ mole; $\tau = 24$ and 48 hr.

Time (t, hr.)	3	6	9	12	15	24	27	30	33
Titre (T, c.c.)	9·13	17·34	24·43	29·52	34·03	42·97	45·00	47·22	48·71
$\text{Log}_{10}(T_{t+\tau} - T_t)$ ...	—	—	—	—	—	1·633	1·555	1·475	1·385
Time (t, hr.)	36	39	48	51	54	57	60	63	
Titre (T, c.c.)	50·05	51·04	54·44	55·05	55·65	56·31	56·88	57·42	
$\text{Log}_{10}(T_{t+\tau} - T_t)$ ...	1·312	1·231	1·736	1·662	1·583	1·503	1·437	1·369	

TABLE 2. *Olefin production in* 80% *ethanol at* 49°.

$C_A = 1{\cdot}03$.

	Ester (10^{-3}mole)	$10C_E$	10^2k_1 (hr.$^{-1}$)	$10^2k_1/C_A$ (hr.$^{-1}$ l. mole^{-1})	Olefin (10^{-3}mole)	Olefin (proportion)
But^t benzoate	5·55	1·11	6·4	6·2	0·75	0·13
But^t 2 : 4 : 6-trimethyl-benzoate	4·29	0·86	6·0	5·8	0·57	0·13
tert.-Amyl benzoate	4·92	0·97	8·4	8·2	1·88	0·38
	5·06	1·00	8·2	8·0	2·06	0·40

TABLE 3. *First-order rate constants for acid-catalysed hydrolyses.*

Temp. 50·0°. Solvent: 80% ethanol. $C_E = 0{\cdot}28$ mole/l.

C_A (mole/l.)	0·1	1·0	Factor
But^t benzoate (min.$^{-1}$)	$7{\cdot}5 \times 10^{-5}$	$1{\cdot}45 \times 10^{-3}$	19
But^t 2 : 4 : 6-trimethylbenzoate (min.$^{-1}$)	$5{\cdot}5 \times 10^{-5}$	$1{\cdot}27 \times 10^{-3}$	23

rate is proportional to the stoicheiometric concentration of hydrogen ion.[5] Acidity function (H_0) measurements in 80% ethanol are available for 0·1 and 1M-hydrochloric acid [6] and indicate a ratio in rate of 20·4 between these concentrations if H_0 be followed, whereas the factor would be 10 if the rate were proportional to the stoicheiometric concentration. The former is more nearly the case (Table 3), which substantiates the proposal of a unimolecular mechanism.

Experimental.—Olefin estimation. Nitrogen (20 c.c./min.), saturated with 80% ethanol at room temperature, was bubbled through a solution of the ester (*ca.* 1 g.) and hydrogen chloride (N concentration) in 80% ethanol (50 c.c.), then passed through a narrow water-condenser and three bubblers (*a*, *b*, and *c*), wrapped in black paper and each containing 1 : 1 carbon tetrachloride–chloroform (20 c.c.) at −78°. The olefin trapped in *a* and *b* was estimated at certain times by the method of Cooper, Hughes, and Ingold.[3] In no case did olefin reach *c*. The first-order rate constants and infinity titres were calculated by Guggenheim's method.[7]

Hydrolyses. Ethanol (8 vols.) was mixed with the ester, and hydrochloric acid (2 vols.) added to produce a 0·1 or 1N-solution. The runs were followed as described [2] in Part I. In the case of *tert.*-butyl benzoate the integrated first-order rate constants fell during the reaction, $k_1^{(0\cdot25)}/k_1^{(0)}$ being *ca.* 0·9. This is doubtless due to esterification of benzoic acid, as k_1/C_A for loss of benzoic acid in 80% ethanol is $2{\cdot}8 \times 10^{-4}$ min.$^{-1}$ l. mole^{-1} at 50° in 1 and 0·1N-hydrochloric acid for an initial concentration of 0·14M. The rate constants were obtained by extrapolation to zero reaction.

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[*Received, March 28th,* 1956.]

[4] Long and Purchase, *J. Amer. Chem. Soc.*, 1950, **72**, 3267; Paul, *ibid.*, 1952, **74**, 141; Taft, *ibid.*, p. 5372; McIntyre and Long, *ibid.*, 1954, **76**, 3240; Bell and Brown, *J.*, 1954, 774; Bunton, Konasiewicz, and Llewellyn, *J.*, 1955, 604; Gold and Hilton, *J.*, 1955, 843.

[5] Long, McDevit, and Dunkle, *J. Phys. Chem.*, 1951, **55**, 829; Bell, Dowding, and Noble, *J.*, 1955, 3106.

[6] Braude and Stern, *J.*, 1948, 1978.

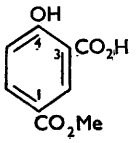
[7] Guggenheim, *Phil. Mag.*, 1926, **2**, 538.

903. *The Partial Hydrolysis of Dialkyl Esters of 4-Hydroxyisophthalic Acid.*

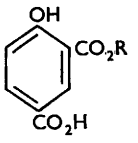
By J. M. Z. Gladych and E. P. Taylor.

It has been shown by Hunt, Idris Jones, and Lindsey [1] that Fischer–Speier esterification of 4-hydroxy*iso*phthalic acid yields diesters together with small amounts of the corresponding monoesters; the orientation of the monomethyl ester so obtained was established as (I). The same authors have also shown that partial hydrolysis of the dimethyl ester by potassium hydroxide in boiling aqueous methanol yields the same monomethyl ester (I).

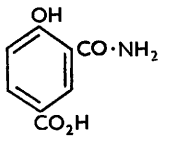
We have confirmed these results, but have found that hydrolysis of dialkyl 4-hydroxy-*iso*phthalates with excess of aqueous sodium hydroxide at room temperature gives the isomeric monoalkyl ester (II). This has been effected with the dimethyl, diethyl, and di-*n*-propyl esters. In addition to the fact that the resulting monoesters were different from those obtained by Hunt *et al.*, their structure is confirmed by their ammonolysis to the known mono-3-amide [2] (III).



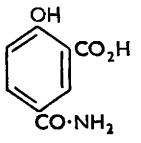
(I)



(II)



(III)



(IV)

The di-*n*-butyl ester appeared to form a sodium salt which was very sparingly soluble in water and resisted hydrolysis with aqueous alkali, regenerating the original ester on acidification. This salt, however, when refluxed with 50% aqueous methanol for 3 hours (without the addition of more alkali), gave the 1-monobutyl ester in good yield; the orientation was confirmed by ammonolysis to the known mono-1-amide [2] (IV).

Experimental.—Partial hydrolysis of dialkyl esters (general method). The dialkyl ester was dissolved in 0·5N-aqueous sodium hydroxide and kept at room temperature for 2—3½ hr. (see Table 1). The pH was then adjusted to 8·4—8·7 with 2N-hydrochloric acid. Any unchanged dialkyl ester was filtered off, washed with water, dried, and identified by m. p. and mixed m. p. determinations. [The di-*n*-propyl ester, which separated as a liquid, was extracted with benzene, the extract washed with water, the solvent recovered, and the identity confirmed by refractive index determination (n_D^{22} 1·5105).] The filtrate obtained after removal of the dialkyl ester was then acidified with 2N-hydrochloric acid to pH 4·8—5·0, and the resulting 3-monoalkyl ester was filtered off, washed with water, and dried. Acidification of the filtrate to Congo-red yielded 4-hydroxy*iso*phthalic acid. The results are in Table 1.

Table 1. *Hydrolysis with aqueous alkali at room temperature.*

Ester	Molar ratio, NaOH : ester	Time (hr.)	Yield (%) of crude product: Unchanged dialkyl ester	3-Monoalkyl ester	Acid
Me_2	2 : 1	2·5	42	23·5	29
Me_2	3 : 1	2·0	11	42	30
Me_2	4 : 1	2·0	2·5	38·5	55
Me_2	4 : 1 *	2·0	7	38	50
Et_2	4 : 1	2·0	6	50·5	35
Pr^n_2	4 : 1	2·0	38	25	36
Bu^n_2	4 : 1	3·5	82	—	10

* KOH used in this experiment.

Hydrolyses in aqueous methanol are recorded in Table 2.

Paper electrophoresis in 2N-acetic acid of a sample of the crude hydrolysis product of the dimethyl ester (obtained by complete acidification of the reaction mixture) indicated that the

[1] Hunt, Idris Jones, and Lindsey, *J.*, 1956, 3099.
[2] *Idem, Chem. and Ind.*, 1955, 417.

1-monomethyl ester was formed in very small quantity when the molar ratio of alkali to ester was not more than 3 : 1.

The following 3-monoalkyl esters (crystallised from alcohol) of 4-hydroxy*iso*phthalic acid are new: 3-*Methyl*, needles, m. p. 253—254° (Found: C, 54·8; H, 3·9. $C_9H_8O_5$ requires

TABLE 2. *Hydrolysis of dimethyl* 4-*hydroxy*iso*phthalate with* 1·5% *of alkali in boiling* 50% *aqueous methanol for* 3 *hours.*

Molar ratio, alkali : ester	Yield (%) of crude product: 1-Monoalkyl ester	Yield (%) of crude product: Acid	Molar ratio, alkali : ester	Yield (%) of crude product: 1-Monoalkyl ester	Yield (%) of crude product: Acid
3·75 : 1 (KOH)	—	91	1·57 : 1 (NaOH)	—	97
* 1·12 : 1 ,,	78	—	1·12 : 1 ,,	73	—

* Proportions used by Hunt *et al.*[1]

C, 55·1; H, 4·1%). 3-*Ethyl*, needles, m. p. 205—205·5° (Found: C, 57·1; H, 4·6. $C_{10}H_{10}O_5$ requires C, 57·1; H, 4·8%). 3-n-*Propyl*, prisms, m. p. 171—171·5° (Found: C, 58·9; H, 5·5. $C_{11}H_{12}O_5$ requires C, 58·9; H, 5·4%).

Confirmation of structure. The monoalkyl ester (2 g.) and aqueous ammonia (*d* 0·880.; 10 ml.) were heated in a sealed tube at 110—115° for 4·5 hr. After concentration to drive off the bulk of the ammonia, the residue was cooled and acidified with 2N-hydrochloric acid to Congo-red, and the resulting mono-3-amide filtered off, washed with water, and dried. Yields of crude amide, m. p. 296° (decomp.) (lit.,[2] 297°), exceeded 90%. After recrystallisation from aqueous dimethyl formamide, the m. p. rose to 297° (decomp.) (Found: C, 52·6; H, 3·9; N, 7·8. Calc. for $C_8H_7O_4N$: C, 53·1; H, 3·9; N, 7·7%).

The 1-n-*butyl* 3-*hydrogen* 4-*hydroxy*iso*phthalate* crystallised from aqueous methanol as needles, m. p. 141—142° (Found: C, 60·5; H, 5·8. $C_{12}H_{14}O_5$ requires C, 60·5; H, 5·9%). On ammonolysis, this gave an excellent yield of the mono-1-amide, m. p. and mixed m. p. 276° (decomp.) [lit.,[2] 275° (decomp.)].

We are grateful to Mr. S. E. Hunt, Dr. J. Idris Jones, and Dr. A. S. Lindsey of the Chemical Research Laboratory, Teddington, for communicating their results before publication. We thank the Directors of Messrs. Allen & Hanburys Ltd. for permission to publish this note.

RESEARCH DIVISION, ALLEN AND HANBURYS LTD.,
WARE, HERTS.

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904. *Compounds Derived from Cholestenone.*

By G. D. MEAKINS and O. R. RODIG.

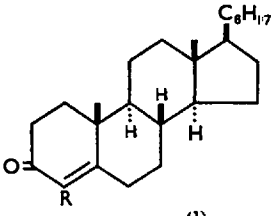
IN work concerned with ring A of the steroids we required derivatives of cholestenone with substituents at position 4. This note describes the preparation of 4-methyl- (I; R = Me) and 4-2′-carboxyethyl-cholest-4-en-3-one (I; R = CH_2·CH_2·CO_2H).

Preliminary experiments showed that the methyl compound could not be prepared satisfactorily by direct methylation of cholestenone (I; R = H),[1] and attention was turned to a method based on the enol-lactone [2] (III). Conversion of this compound into cholestenone by treatment with methylmagnesium iodide and cyclisation of the resulting diketone is well known: [3] the use of ethylmagnesium iodide led to the required methylcholestenone (I; R = Me).

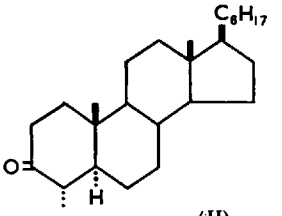
Reduction of the conjugated ketone with lithium in liquid ammonia produced 4α-methylcholestan-3-one (II), which had been prepared previously by methylation of cholestanone derivatives.[1] Hydrogenation in acetic acid resulted in the rapid uptake of two mols. of hydrogen, and chromic acid oxidation of the product gave a mixture of ketones from which a small quantity of the saturated ketone (II) was isolated. Presumably the 4α-methyl compound arises by isomerisation of the 4β-methyl derivative which was expected as the product of *cis*-addition of hydrogen to the 4 : 5-bond.

[1] Beton, Halsall, Jones, and Phillips, unpublished work.
[2] Turner, *J. Amer. Chem. Soc.*, 1950, **72**, 579.
[3] Fujimoto, *ibid.*, 1951, **73**, 1856, and later papers.

The keto-acid (I; R = $CH_2 \cdot CH_2 \cdot CO_2H$) was obtained by addition of methyl acrylate to cholestenone in the presence of potassium *tert.*-butoxide and subsequent hydrolysis. Later experiments showed that extensive hydrolysis occurs during the acrylate addition and that the acid can be isolated directly in 40% yield.



(I)



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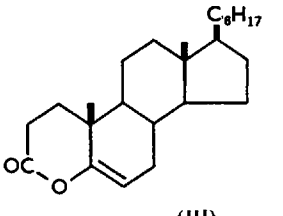

(III)

Experimental.—Rotations were measured in $CHCl_3$. J. Crosfield's silica, " Woelm " alumina, and light petroleum (b. p. 60—80°) were used for chromatography.

4-Methylcholest-4-en-3-one.—Ethylmagnesium iodide was prepared under nitrogen by refluxing ethyl iodide (3·3 g.) in ether (80 c.c.) with magnesium (0·8 g.) for 1·5 hr., and the concentration of the solution was determined by titration with standard hydrochloric acid. A portion (*ca.* 19 c.c.; 0·73 g. of ethylmagnesium iodide) was added to a solution of the enol-lactone (1·5 g.) in ether (15 c.c.) at 0° under nitrogen. The mixture was kept at 0° for 13 hr., acidified with 6N-hydrochloric acid, and extracted with ether. The residue obtained after the removal of ether was refluxed in methanol (60 c.c.) for 3 hr. under nitrogen with a solution of sodium hydroxide (2·05 g.) in water (10 c.c.). Concentration, dilution with water, and extraction with ether yielded an oil (1·3 g.) which was dissolved in benzene and adsorbed on alumina (50 g.). The product eluted with benzene (300 c.c.) crystallised from methanol, to give 4-methylcholest-4-en-3-one (1·06 g.), m. p. 94—98°. Recrystallisation afforded material (0·75 g.), m. p. 102—103°, $[\alpha]_D$ −108° (*c*, 0·9) (Found: C, 84·45; H, 11·5. $C_{28}H_{46}O$ requires C, 84·35; H, 11·6%), light absorption max. in EtOH at 2500 Å (ε 15,600), $\nu_{max.}$ 1671 cm.$^{-1}$ in CS_2.

Reduction of 4-Methylcholest-4-en-3-one.—(*a*) The methylcholestenone (190 mg.) in dry ether (35 c.c.) was added slowly to a stirred solution of lithium (100 mg.) in liquid ammonia (75 c.c.). After 20 min. ammonium chloride was added, the ammonia was allowed to evaporate, and the mixture was worked up by dilution with water and ether-extraction. The product (190 mg.) was chromatographed from benzene on alumina (20 g.). Benzene–ether (19 : 1; 150 c.c.) eluted an oil (130 mg.) which crystallised from methanol to give 4α-methylcholestan-3-one (102 mg.), m. p. and mixed m. p. 123—124°, $[\alpha]_D$ +26° (*c*, 1·1), $\nu_{max.}$ 1708 cm.$^{-1}$ in CS_2.

(*b*) A solution of methylcholestenone (500 mg.) in glacial acetic acid (10 c.c.) was shaken with Adams catalyst (150 mg.) in hydrogen for 1 hr. (uptake, 98 c.c.). The residue obtained after removal of catalyst and solvent was oxidised in acetone (40 c.c.) with 8N-chromic acid. The product (420 mg.) was adsorbed from light petroleum on alumina (40 g.). The fractions eluted with light petroleum–benzene and with benzene (100 c.c.) were discarded. Elution with benzene–ether (49 : 1; 250 c.c.) gave an oil (210 mg.) which, after three crystallisations from methanol, yielded 4α-methylcholestan-3-one (85 mg.), m. p. 120—122°, identified as above.

4-2′-Carboxyethylcholest-4-en-3-one. (*a*) A M-solution of potassium *tert.*-butoxide in *tert.*-butyl alcohol (7 c.c.) was added under nitrogen to a stirred solution of cholestenone (2 g.) in ether (20 c.c.). After 15 min. the mixture was cooled to 0°, and freshly distilled methyl acrylate (0·6 g.) in ether (10 c.c.) was added during 5 min. Stirring was continued for 1·5 hr. at 0°, then for 1 hr. at 20°. Water (5 c.c.) was added, the organic solvents were removed under reduced pressure, and the residue was refluxed under nitrogen for 2·5 hr. with potassium hydroxide (10 g.) in 50% aqueous methanol (60 c.c.). The mixture was concentrated *in vacuo*, diluted with water, and washed with ether. Acidification with hydrochloric acid and extraction with ether gave an oil (2·1 g.). A small part of this oil was chromatographed on silica gel. Benzene–ether (4 : 1) eluted material which crystallised on titration with acetone. These crystals were used as seeds in the crystallisation from acetone of the main part of the product. The *keto-acid* was obtained as plates (1·3 g.), m. p. 136—138°, $[\alpha]_D$ −88° (*c*, 1·0) (Found: C, 78·8; H, 10·6. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%), light absorption max. in EtOH at 2500 Å (ε = 14,200), $\nu_{max.}$ 1714, 1672 cm.$^{-1}$ in CS_2.

(*b*) The preceding experiment was repeated as far as the addition of water (5 c.c.). The organic layer was separated and extracted with aqueous sodium hydrogen carbonate. Acidification of the alkaline solution and extraction with ether afforded the keto-acid (0·94 g.), m. p. 135—137°.

THE UNIVERSITY, MANCHESTER, 13. [*Received, June 22nd,* 1956.]

905. *The Preparation and Manipulation of Molybdenum Hexafluoride.*

By T. A. O'DONNELL.

ALTHOUGH there are several reports of the preparation of molybdenum hexafluoride by direct fluorination of the metal, it is not generally recognised that the compound can be prepared, and its physical and chemical properties studied, in relatively simple vacuum-apparatus. Thus the original preparation [1] was performed in platinum and several authors refer to nickel–copper or Teflon systems.[2] Gaunt [3] describes the storage in glass at −80° of a purified sample used for structural analysis and the handling of the sample in an all-glass apparatus which had been exhaustively dried beforehand and in which a fully fluorinated tap-grease was used. However, his system was very different from those needed for most chemical investigations. Preparation of the hexafluoride is usually accompanied by the formation of hydrogen fluoride and reaction of the latter with glass leads to autocatalytic hydrolysis of the hexafluoride. In the present work the product was collected in glass traps which had been carefully cleaned and " flamed " *in vacuo* and to which sodium fluoride was added as a " getter " for the hydrogen fluoride. The hexafluoride could then be purified and stored in glass break-seal tubes, as Gaunt states; but prolonged manipulation of the hexafluoride and its reaction products in glass systems with greased taps and joints was found to be impossible even though fluorinated greases were used. This was due presumably to the difficulty of drying the systems adequately. Conventional greased taps and tapered joints have been replaced by specially designed valves and joints.

The techniques described here for the handling of molybdenum hexafluoride could be applied to other volatile reactive fluorides.

Experimental.—The reaction between fluorine and metallic molybdenum, which had been previously heated in hydrogen and cooled in nitrogen, was performed in a copper tube, and the product was collected in a series of three glass traps. Each trap was provided with a break-off seal and between each was a capillary constriction. Initially, powdered sodium fluoride was added to the clean dry traps, which were then flamed while connected to a high-vacuum system. Dried air was admitted before connection of the traps to the copper tube. The reaction was initiated at about 100° and then became self-sustaining. Most of the hexafluoride, together with the less volatile oxyfluoride which was also formed, condensed in the first trap at −78°. The other two traps were maintained at −196° as guard traps. There was considerable loss of hexafluoride as " smoke " if the first trap was at −196°. When reaction was complete, excess of fluorine was swept from the system with dry nitrogen, and the trap at −78° was sealed off.

This trap was then joined through its break-off seal with a system of several break-seal traps in series, the latter system being connected through a capillary tube to a pumping system. These traps were flamed *in vacuo* but no " getter " was added. The crude hexafluoride was cooled to −196° and the seal broken. Residual nitrogen in the system was pumped away and the capillary tube between the traps and the pumping system was sealed, providing an all-glass greaseless system. The first of the clean traps was then cooled to −78° and the last to −196°. The crude hexafluoride was allowed to distil at room temperature, almost all of the hexafluoride being deposited as colourless crystals in the trap at −78°. Small amounts of silicon tetrafluoride from the preparation condensed in the trap at −196°, and the sodium fluoride " getter " and the relatively involatile molybdenum oxyfluoride remained in the original trap. The first

[1] Ruff and Eisner, *Z. anorg. Chem.*, 1907, **52**, 256.
[2] Burke, Smith, and Neilson, *J. Chem. Phys.*, 1952, **20**, 447.
[3] Gaunt, *Trans. Faraday Soc.*, 1953, **49**, 1122.

and last traps were sealed off and the pure hexafluoride was distributed equally by distillation between the remaining traps to give samples of convenient size. These samples could be stored indefinitely in glass at room temperature without sodium fluoride. They underwent no visible change and no silicon tetrafluoride was formed after three months. The reactions of the hexafluoride are being studied by using similar techniques.

Molybdenum hexafluoride was characterised by its m. p. and molecular weight. The m. p. was 17·4° in a sealed trap, in agreement with the value of 17·5° given by Ruff and Ascher.[4] However, since the compound reacts with mercury and with grease, the conventional apparatus for determination of molecular weights by the Dumas method, in which greased taps and joints are used, was modified. Glass taps in the manifold of the vacuum-system were replaced by metal valves. To each end of a Hoke valve No. 431, a brass-bodied valve with stainless-steel needle and bronze bellows was silver-soldered a copper–Pyrex seal (General Electric Co.'s thimble SE5), and the valves so made were resistant to reactive fluorides and maintained a vacuum for pressures down to 10^{-3}—10^{-4} mm. Hg. Instead of a mercury manometer's being used, a sensitive Pyrex spiral gauge was sealed directly to the manifold. A mirror was fitted to the spiral, and the gauge was used as a null-point instrument. The molecular-weight bulb, of about 350 ml. capacity and as light as possible, was connected by a copper–Pyrex seal to one end of a Hoke valve, which had been stripped of excess of metal, and to the other end was silver-soldered a B14 brass cone. The vacuum-seal between this cone and a B14 glass socket on the manifold was made by a tapered Teflon sleeve lightly smeared on its upper edge with a completely fluorinated hydrocarbon grease.

The molecular weight was determined in the usual way, except that, since it is inadvisable to flame the spiral gauge, the whole system was flushed several times before and after the determination with dry air to ensure that no moisture entered the system. If this were to happen, the gauge and bulb would be contaminated with hydrolysis products and the valves would be corroded. It was found that virtually all of the sample could be recovered after a determination and values of 211 and 212 (calc., 210) were obtained for the hexafluoride.

The author, who carried out this work while on leave from the University of Melbourne, thanks Professor H. J. Emeléus for advice and the Officers of the Royal Society for the award of a Royal Society and Nuffield Foundation Commonwealth Bursary.

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Pembroke Street, Cambridge. [*Received, January 16th,* 1956.]

[4] Ruff and Ascher, *Z. anorg. Chem.*, 1931, **196**, 146.

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906. *Vapour–Liquid Equilibrium Data for the Benzene–Fluorobenzene System.*

By R. E. Banks and W. K. R. Musgrave.

In view of continued failure to separate mixtures of benzene and fluorobenzene by use of improved fractionating columns, and the well-known propensity of fluorine-containing organic compounds to form azeotropes [1] we investigated the system more closely and have now obtained vapour–liquid equilibrium data which show that no azeotrope formation occurs and, by using Fenske's [2] equation and assuming mixtures of benzene and fluorobenzene to form ideal solutions, we have calculated that 66 theoretical plates would be required to separate a mixture into a distillate containing 99 mole % of benzene and a residue containing 99 mole % of fluorobenzene. In practice this means that such a separation would require about 130 theoretical plates [3] and explains why earlier efforts failed.

The graph of log α against mole fraction of benzene shows that, subject to experimental error, the system is ideal. The average value of α is 1·176 compared with a theoretical value of 1·145.

[1] Evans and Tatlow, *J.*, 1955, 1184.
[2] Fenske, *Ind. Eng. Chem.*, 1932, **24**, 482.
[3] Carney, "Laboratory Fractional Distillation," Macmillan, New York, 1949, p. 40.

EXPERIMENTAL.—" AnalaR " benzene was dried over sodium wire, distilled over fresh sodium wire, and then redistilled through a 60-plate concentric-tube column. A fraction of b. p. 80°/759 mm., n_D^{20} 1·5013, was collected.

Fluorobenzene was dried ($MgSO_4$), distilled, and then redistilled through the concentric-tube column. The fraction of b. p. 84°/760 mm., n_D^{20} 1·4653, was collected.

Mixtures of benzene and fluorobenzene of known composition were prepared by weighing and their refractive indices measured on an Abbé refractometer at 20° ± 0·1°. A composition–refractive index graph was constructed from the results (Table 1).

TABLE 1. *Refractive index–composition data for benzene–fluorobenzene mixtures.*

n_D^{20}	1·4653	1·4690	1·4720	1·4756	1·4818	1·4860	1·4900	1·4944	1·4970	1·5013
Benzene (mole %) ...	—	12·16	20·80	32·0	50·01	61·65	72·33	84·73	91·65	100·00

TABLE 2. *Vapour–liquid equilibrium data.*

Atm. pressure (mm. Hg)	Vapour temp. (° c)	Mole fraction of benzene: liquid	vapour	Atm. pressure (mm. Hg)	Vapour temp. (°c)	Mole fraction of benzene: liquid	vapour
753·8	79·35	1	1	755·5	81·2	0·54	0·57
754·2	79·45	0·97	0·98	754·0	82·1	0·31	0·37
754·2	79·77	0·90	0·92	753·8	82·42	0·25	0·29
754·2	79·8	0·895	0·91	754·2	82·87	0·22	0·24
755·5	80·83	0·63	0·66	753·8	83·5	0·09	0·10
755·5	80·99	0·59	0·63	753·8	84·0	—	—

Vapour–liquid equilibria were determined at atmospheric pressure with a still of the Othmer type,[4] which had a condenser on the outlet tube. No manostat was used but all the experiments were carried out on the same day during which the barometric pressure did not vary by more than 2 mm. The still was charged with 60 ml. of each mixture and maintained at equilibrium, as shown by an N.P.L. thermometer, for 30 min. before samples of distillate and distilland were taken for analysis. The results, from which the b. p.–composition and vapour–liquid equilibrium diagrams were drawn, are given in Table 2.

One of us (R. E. B.) thanks the Department of Scientific and Industrial Research for a maintenance grant.

THE UNIVERSITY, SOUTH ROAD, DURHAM. [*Received, May 30th,* 1956.]

[4] Othmer, *Ind. Eng. Chem. Anal.*, 1932, **4**, 232.

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907. *The Lability of* 1 : 4 : 6-*Triazanaphthalene.*

By ADRIEN ALBERT and CHRISTIAN PEDERSEN.

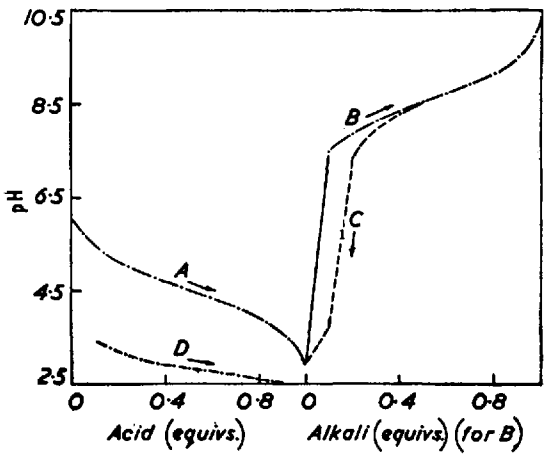
1 : 4 : 6-TRIAZANAPHTHALENE (I) (1-deazapteridine) is unaffected by aqueous alkali, but when it was titrated with acid the potential drifted for about 15 minutes after each addition. The trend was to higher pH, indicating that a stronger base was formed. Whereas curve *D* shows that 1 : 4 : 6-triazanaphthalene is a very weak base of pK_a about 2·5, curve *A*, obtained after equilibration at each addition, corresponds throughout to a stronger base (pK_a 4·52 ± 0·01), which will be called Base A.

When the equilibrated solution was back-titrated with one equivalent of alkali (curve *B*), much higher pH values were obtained, showing that yet another and far stronger base (pK_a 8·53 ± 0·05) had been formed. This will be called Base B, and its formation was almost instantaneous. Curve *B* is of theoretical shape for this p*K* from the point of 20% neutralization onwards.

Finally, the solution was re-titrated with an equivalent of acid. Instead of duplicating curve *A*, this titration (curve *C*) at first followed curve *B* (for 0·6 equiv. of acid). Thence slightly lower pH values were obtained until 0·8 equiv. of acid had been added. At this stage, the figures showed that about 10% of Base B had disappeared, and the intense mouse-like odour of 1 : 4 : 6-triazanaphthalene became evident. The next 0·1 equiv. of

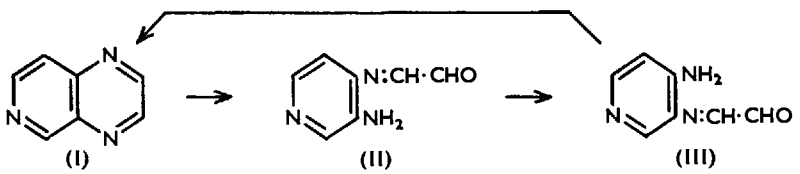
acid caused a sudden drop in pH, and the last two points of curve *C* (at 0·1 and 0 on the abscissa) were first observed about 0·5 pH lower, but within 15 minutes became steady at the values shown. This behaviour suggests that, below pH 8·5, Base B is in rapid equilibrium with 1 : 4 : 6-triazanaphthalene, which is slowly converted into Base A. A weighed quantity of the triazanaphthalene was submitted to three cycles of curves *B* + *C*, and the same curves were re-traced, showing the absence of side-reactions.

A likely interpretation of these curves is that 1 : 4 : 6-triazanaphthalene is hydrolytically ring-opened by acid, the pyrazine ring (higher N : C ratio) being the more sensitive.[1] Thus Base A with its pK_a of 4·5 should be 3-amino-4-glyoxylideneaminopyridine (II) rather than the isomer (III), because 3-aminopyridine has pK_a 5·98, but 4-aminopyridine is a much stronger base (pK_a 9·17).[2] To examine this matter more fundamentally, 4 : 5-diaminopyridine was titrated and found to have pK_a 9·08 (± 0·01, at 0·05M and 20°) and no



Titration of 1 : 4 : 6-*triazanaphthalene* (0·05M).
A, Titration with N-*hydrochloric acid* (*added by micrometer syringe*) *after* 15 *minutes for equilibration.*
B, Further titration of A *by* 0·1N-*potassium hydroxide.*
C, Further titration of B *with* N-*hydrochloric acid.*
D, As A, *but additions made at* 0·5 *minute intervals.*

second constant above 1·0. Thus the structure of the anil (II) is compatible with a base of about pK_a 5, in so far as the strongly basic nature of 4 : 5-diaminopyridine is due to the vinylogous amidine formed by the ring-nitrogen and the 4-amino-group :[2] in the anil (II),



this amidine is blocked by an electron-attracting group. However the isomeric 4-amino-3-glyoxylideneaminopyridine (III) should be only a little weaker than 4 : 5-diaminopyridine, and hence Base B (pK_a 8·5) would appear to be this isomer. That Base B is not 4 : 5-diaminopyridine was confirmed by paper chromatography. It appears that catalysis by falling drops of alkali during the titration converts (II) into (III). Finally, when neutrality is restored the triazanaphthalene (I) is re-formed. In fact it can be obtained almost quantitatively from a solution of Base B at pH 9 by extraction with ether, or by evaporation, so that the compound (III) must cyclize easily in the absence of water.

Because of the lability of the two anils, they have not yet been obtained in the dry state, or as derivatives. The isomeric 1 : 4 : 6-triazanaphthalene[3] behaved normally on titration

[1] Albert, in "Recent Work on naturally occurring Nitrogen Heterocyclic Compounds," *Chem. Soc. Special Publ.* No. 3, 1955.
[2] Albert, Goldacre, and Phillips, *J.*, 1948, 2240.
[3] Leese and Rydon, *J.*, 1955, 303.

with acid (pK_a 1·20 ± 0·02). Pteridine gave a steady basic constant, although acid or alkali eventually degraded it to 2-amino-3-formylpyrazine.[4]

1 : 4 : 6-Triazanaphthalene, first prepared in 1936,[5] was more conveniently made as follows. 3 : 4-Diaminopyridine [5] (1 g.), glyoxal hydrate (0·8 g., solid), and alcohol (50 ml.) were refluxed for an hour. The alcohol was removed *in vacuo*, and the residue sublimed at 65°/0·01 mm., then recrystallised from light petroleum, giving 50% of 1 : 4 : 6-triazanaphthalene, m. p. 97° (Found : C, 64·25; H, 3·8; N, 31·4. Calc. for $C_7H_5N_3$: C, 64·1; H, 3·8; N, 32·1%).

1 : 3 : 5-*Triazaindene*.—3 : 4-Diaminopyridine (0·7 g.) was refluxed for an hour with formic acid (1 ml.) and the excess of acid removed *in vacuo*. This gave 52% of 1 : 3 : 5-triazaindene (3-deazapurine), m. p. 168—169°, pK_a (basic) 6·10 ± 0·02, (acidic) 10·88 ± 0·04 (cf. 3·95 and 11·08 for 1 : 3 : 4-triazaindene [6]) (Found : C, 60·55; H, 4·3; N, 34·9. Calc. for $C_6H_5N_3$: C, 60·5; H, 4·2; N, 35·3%). Weidenhagen and Weeden [7] failed to produce the 1 : 3 : 5-isomer similarly, and resorted to a less direct method.

We thank Mr. E. P. Serjeant for the physical measurements.

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Australian National University, Canberra. [*Received, June 27th*, 1956.]

[4] Albert, Brown, and Wood, *J.*, 1956, 2066.
[5] Koenigs, Bueren, and Jung, *Ber.*, 1936, **69**, 2690.
[6] Mason, *J.*, 1954, 2071.
[7] Weidenhagen and Weeden, *Ber.*, 1938, **71**, 2347.

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908. *Oxidation of Organic Compounds by Solid Manganese Dioxide.*

By M. Z. Barakat, M. F. Abdel-Wahab, and M. M. El-Sadr.

Manganese dioxide has been used to oxidise polyene alcohols,[1] steroidal allylic alcohols,[2] benzyl alcohols, and secondary aromatic alcohols [3] to the corresponding carbonyl compounds; in addition three amines have been oxidised to their Schiff bases, an aminoethanol to a lactam, and two hemiacetals to lactones.[4] We have oxidised a wide variety of organic substances with manganese dioxide. The results given in the Table show clearly that the solid cannot be regarded as a specific oxidising agent for particular groupings, *e.g.*, allylic alcohols only.

Hydroxy-compounds, with the exception of triphenylmethanol which did not react, were oxidised to carbonyl compounds, and aromatic aldehydes gave the corresponding carboxylic acids. Polybasic hydroxy-acids, *e.g.*, tartaric acid [5] in ice-cold solution and malic acid in hot solution gave carbon dioxide and acetaldehyde. In these cases it is probable that acetylene is first formed and is hydrated. Hydrogen peroxide was detected by its liberation of iodine from potassium iodide in dilute acetic acid (starch–iodide) :

$$HO_2C{\cdot}[CH{\cdot}OH]_2{\cdot}CO_2H + O \longrightarrow C_2H_2 + H_2O_2 + H_2O + 2CO_2$$
$$HO_2C{\cdot}CH(OH){\cdot}CH_2{\cdot}CO_2H + O \longrightarrow C_2H_2 + 2H_2O + 2CO_2$$
$$C_2H_2 + H_2O \longrightarrow Me{\cdot}CHO$$

Citric acid yields acetone [6] and malonic acid ethylene, and carbon dioxide. The latter reaction is probably :

$$CH_2(CO_2H)_2 + O \longrightarrow CH_2{:} + 2CO_2 + H_2O$$
$$2CH_2{:} \longrightarrow CH_2{:}CH_2$$

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[1] Ball, Goodwin, and Morton, *Biochem. J.*, 1948, **42**, 516; Attenburrow, Cameron, Chapman, Evans, Hems, Jansen, and Walker, *J.*, 1952, 1094.
[2] Sondheimer, Amendolla, and Rosenkranz, *J. Amer. Chem. Soc.*, 1953, **75**, 5930, 5932.
[3] Turner, *ibid.*, 1954, **76**, 5175.
[4] Highet and Wildman, *ibid.*, 1955, **77**, 4399.
[5] Cf. Leoncini, *Staz. sper. agr. stat.*, 1910, **43**, 33; *Chem. Zentr.*, 1910, I, 1655.
[6] Cf. Kuyper, *J. Amer. Chem. Soc.*, 1933, **55**, 1722.

α-Hydroxy-acids and α-amino-acids react readily in hot aqueous solution to give the corresponding aldehyde or ketone with one carbon atom less. They all lose carbon dioxide, and amino-acids lose ammonia in addition. Leoncini [7] reported that amino-acids did not give nitric acid with manganese dioxide.

Reactant	Solvent *	Time of reaction (min.)	Yield (%) †	Product.
EtOH	N	20	50	Me·CHO
Pr^{i}OH	N	20	50	Me_2CO
Bu^{i}OH	N	20	50	Pr^{i}·CHO
$(CH_2·OH)_2$	W	20	—	CO_2
$HO·CH(CH_2·OH)_2$	W	20	—	CO_2
Mannitol	W	20	—	CO_2
Inositol	W	20	—	CO_2
Ph·CO·CH(OH)·Ph	C	60	80	Ph·CO·CO·Ph
$C_6H_4(OMe)·CO·CH(OH)·C_6H_4(OMe)$	C	60	52	$C_6H_4(OMe)·CO·CO·C_6H_4(OMe)$
$Ph_2CH·OH$	E	20	88	$(Ph_2·CH)_2O$
,,	B	120	87	Ph·CO·Ph
9-Hydroxyxanthene	E	20	91	Xanthone
9-Hydroxyfluorene	E	60	86	Fluorenone
$Ph_3C·OH$	B	120	—	No oxidation ‡
p-$C_6H_4(OH)_2$	E	30	38	*p*-$C_6H_4O_2$
Ph·CHO	P	24	75	$Ph·CO_2H$
$C_6H_4(OMe)·CHO$	P	24	44	$C_6H_4(OMe)·CO_2H$
o-$C_6H_4(OH)·CHO$	P	24	40	*o*-$C_6H_4(OH)·CO_2H$
$H·CO_2H$	W	Inst.	—	CO_2
$Ph·CH_2·CO_2H$	W	10	50	Ph·CHO + CO_2 [a]
$(CO_2H)_2$	W	Inst.	—	CO_2
$CH_2(CO_2H)_2$	W	20	—	$C_2H_4 + CO_2$
$HO_2C·CH_2·CH_2·CO_2H$	W	20	—	$C_2H_4 + CO_2$
Maleic acid	W	20	—	$C_2H_2 + CO_2$
Fumaric acid	W	20	—	$C_2H_2 + CO_2$
$HO_2C·[CH(OH)]_2·CO_2H$	W	10	66	Me·CHO + CO_2 [b]
$HO_2C·CH(OH)·CH_2·CO_2H$	W	15	45	Me·CHO + CO_2
Citric acid	W	15	45	Me_2CO
$HO·CH_2·CO_2H$	W	10	—	CO_2
$Me·CH(OH)·CO_2H$	W	10	50	Me·CHO + CO_2
$Ph·CH(OH)·CO_2H$	W	10	50	Ph·CHO + CO_2
$Ph_2C(OH)·CO_2H$	W	30	52	PhCOPh + CO_2 [c]
$H_2N·CH_2·CO_2H$	W	10	—	$CO_2 + NH_3$
$Me·CH(NH_2)·CO_2H$	W	10	—	Me·CHO + $CO_2 + NH_3$
$Pr^{i}·CH(NH_2)·CO_2H$	W	10	—	Pr^{i}·CHO + $CO_2 + NH_3$
$Bu^{i}·CH(NH_2)·CO_2H$	W	10	—	Bu^{i}·CHO + $CO_2 + NH_3$
$HO_2C·CH_2·CH(NH_2)·CO_2H$	W	10	—	Me·CHO + $CO_2 + NH_3$
$Et·NH_2$	W	15	50	Me·CHO + NH_3
$Ph·NH_2$	P	6 hr.	87	Ph·N:N·Ph
o-$C_6H_4Cl·NH_2$	P	6 hr.	87	*o*-$C_6H_4Cl·N{:}N·C_6H_4Cl$-*o*
p-$C_6H_4Cl·NH_2$	P	6 hr.	87	*p*-$C_6H_4Cl·N{:}N·C_6H_4Cl$-*p*
p-$C_6H_4Me·NH_2$	B	6 hr.	87	*p*-$C_6H_4Me·N{:}N·C_6H_4Me$-*p*
α- or β-$C_{10}H_7·NH_2$	P	24 hr.	—	No oxidation ‡
o-, *m*-, or *p*-$C_6H_4NO_2·NH_2$	P	24 hr.	—	No oxidation ‡
Benzophenone hydrazone	E	24 hr.	52	*s*-Diphenylketazine
Fluorenone hydrazone	E	24 hr.	58	*s*-Difluorenylketazine
2 : 4-Dinitrophenylhydrazine	B	5 hr.	50	*m*-$C_6H_4(NO_2)_2$
Ph_2CH_2	P	2 hr.	49	$Ph_2·CH·CHPh_2$ [d]
Ph_3P	P	5 hr.	75	Ph_3PO

* W, water; C, chloroform; E, ether; B, benzene; P, light petroleum (b. p. >120°); N, no solvent.

† Refers to solid or liquid products only.

‡ At least 95% of starting material recovered.

[a] After refluxing, the mixture was cooled, and filtered into ice-cold alcoholic 2 : 4-dinitrophenylhydrazine sulphate solution. [b] Not refluxed. The mixture, cooled in ice, was treated with manganese dioxide, and after 10 min. filtered into ice-cold alcoholic 2 : 4-dinitrophenylhydrazine sulphate solution. [c] After refluxing, the mixture was filtered hot and the residue washed with hot alcohol. Benzophenone separated from the combined filtrates as an oil which solidified on being kept. [d] M. p. 211—212° (from $CHCl_3$) (Found : C, 93·1; H, 6·5. Calc. for $C_{26}H_{22}$: C, 93·4; H, 6·6%).

[7] Leoncini, *Staz. sper. agr. ital.*, 1913, **45**, 224; *Chem. Abs.*, 1913, **7**, 2824.

Aromatic primary amines yielded the corresponding azo-compounds. Previously, however, quinone was obtained from aniline by use of manganese dioxide.[8] Hydrazones yielded the symmetrical diarylketazines. We found that in the oxidation of benzophenone hydrazone, diphenyldiazomethane was an intermediate; it was detected by the violet colour of its ethereal solution.[9]

Experimental.—Water as solvent. The reactant (0·01 mole) and manganese dioxide (B.D.H. Laboratory Reagent, MnO_2 precipitated) (0·05 mole) in distilled water (20—35 ml.) were refluxed in the apparatus described by Schönberg *et al.*[10] in a stream of carbon dioxide. The products were collected in ice-cold alcoholic 2 : 4-dinitrophenylhydrazine sulphate solution. Carbonyl compounds thus precipitated were identified as their 2 : 4-dinitrophenylhydrazones. In separate experiments formation of ammonia or carbon dioxide was tested by use of Nessler's reagent or barium hydroxide solution respectively.

Unsaturated hydrocarbons were detected by decolorising acidified potassium permanganate solution (1/1000) or bromine water. It proved impossible to distinguish between ethylene and acetylene by the copper acetylide test, probably because of simultaneous oxidation of the ammoniacal cuprous chloride solution. However, where acetylene is indicated in the Table, its formation is inferred from the analogous reaction of *N*-bromosuccinimide with maleic and fumaric acids,[11] any other product being unlikely : no acetaldehyde was detected in these cases.

Dry solvents other than ether. The reactant (0·01 mole) and manganese dioxide (0·06 mole) were refluxed in the dry solvent (50 ml.). After filtration the product was isolated by concentration of solvent, except as indicated in the Table, and identified by m. p. and mixed m. p. after recrystallisation.

Ether as solvent. The reactant (0·01 mole), manganese dioxide (0·1 mole), and dry ether were shaken mechanically or allowed to stand with occasional shaking for 24 hr. After filtration, the ether was evaporated off and the product identified by m. p. and mixed m. p. after recrystallisation.

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EIN-SHAMS UNIVERSITY, CAIRO. [*Received, April 4th*, 1956.]

[8] Kimijima and Kishino, *J. Soc. Chem. Ind., Japan*, 1944, **47**, 274.
[9] Staudinger and Kupfer, *Ber.*, 1911, **44**, 2197.
[10] Schönberg, Moubacher, and Mostafa, *J.*, 1948, 176.
[11] Barakat, *J. Pharm. Pharmacol.*, 1952, **4**, 582.

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909. *Retardation of the Chain-decomposition of Benzoyl Peroxide by Polycyclic Aromatic Hydrocarbons.*

By J. J. BATTEN.

DURING work on the reaction between benzoyl peroxide and phenols [1,2] some observations were made on the relative retarding effects of several polycyclic aromatic hydrocarbons on the chain decomposition of benzoyl peroxide in dioxan solution. Since the observations support the general order of reactivity of the hydrocarbons towards free radicals indicated by other investigations,[3,4,5] and since it is not intended to continue this work, it seems worthwhile placing the results on record (for procedure and analysis see ref. 1; for preparations see ref. 4). The retarding effects of six aromatic hydrocarbons on the decomposition at 80·65° are shown in Fig. 1 in which the amount of peroxide which decomposed in a fixed time is plotted against the initial concentration of hydrocarbon. The effects range from that of diphenyl, which is only just appreciable in the concentration range, to that of anthracene which suppresses the amount of decomposition to a limit. The limit (30%) is only slightly higher than that found under the same conditions for *p*-benzoquinone [1] (28%) or picric acid [2] (27%) as inhibitor and therefore corresponds to almost complete

[1] Batten and Mulcahy, *J.*, 1956, 2948.
[2] Batten, *J.*, 1956, 2959.
[3] Roitt and Waters, *J.*, 1952, 2695.
[4] Kooyman and Farenhorst, *Trans. Faraday Soc.*, 1953, **49**, 58.
[5] Dunn, Waters, and Roitt, *J.*, 1954, 580.

suppression of the chain decomposition. Benzene has no detectable effect at these concentrations, but at higher concentrations is in fact a very weak retarder.[6]

The order of reactivity of the hydrocarbons is : benzene < diphenyl < naphthalene < pyrene < 1 : 2-5 : 6-dibenzanthracene < stilbene < anthracene. This is derived from the results at the high end of the concentration range shown in Fig. 1 : the different order at lower concentrations probably arises from the effects of reaction products. The kinetic behaviour of pyrene, however, appears to be different from that of the other compounds, and it is also anomalous as an antioxidant.[5] The relative reactivities of anthracene and 1 : 2 - 5 : 6-dibenzanthracene are in agreement with the results of Roitt and Waters [3] which were derived from analyses of the products. The order of reactivity of the seven hydrocarbons towards the radicals involved in this reaction thus agrees with that found by Kooyman and Farenhorst [4] for the reactivity towards trichloromethyl radicals, except

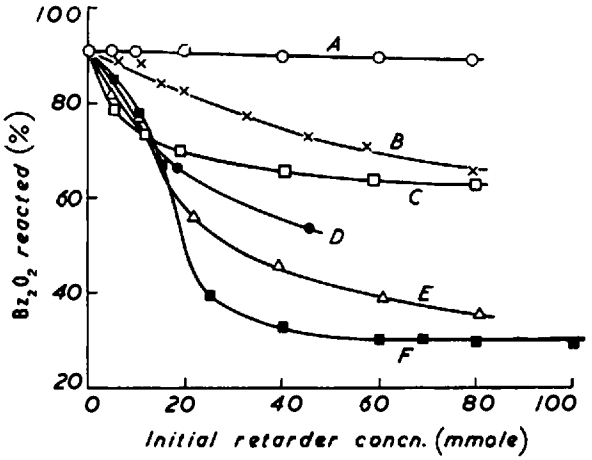
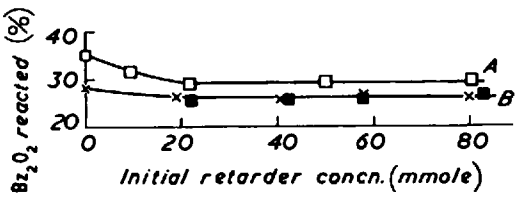


FIG. 1. *Effects of initial concentrations of hydrocarbons on amount of benzoyl peroxide which has reacted in* 135 *min. in dioxan. For Figs.* 1 *and* 2 *initial benzoyl peroxide concn.* = 5 *mmole, and temperature* = 80·65°.

A, Diphenyl; B, naphthalene; C, pyrene; D, 1 : 2-5 : 6-*dibenzanthracene; E, stilbene; F, anthracene.*

FIG. 2. *Effects of initial anthracene* (□, ■) *and naphthalene* (×) *concentrations on amount of peroxide reacting in* 135 *min. in* (*A*) *acetophenone and* (*B*) *benzene.*



for the position of stilbene which in their results occupies a position between naphthalene and pyrene. To this extent the present results support the conclusions of these authors concerning the influence of structure on the reactivity of polycyclic aromatic hydrocarbons towards free radicals.

There is no evidence of a direct reaction between these hydrocarbons and the peroxide such as occurs with phenols of comparable retarding efficiency.[1,2] This is confirmed by the influence of anthracene and naphthalene on the decomposition in the " unreactive " solvents benzene and acetophenone (Fig. 2). Here again the rate is suppressed to a limit. This presumably corresponds to complete inhibition of the chain reaction which in these solvents occurs to a relatively small extent.

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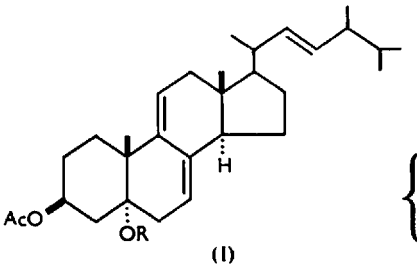
[6] Batten, Thesis, Melbourne, 1955.

910. *Further Experiments on the Epoxidation of Steroids.*

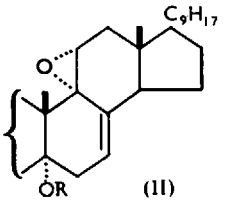
By O. K. Sewell, J. H. Turnbull, and W. Wilson.

The conversion of 5α-hydroxy- and 5α-acetoxy-$\Delta^{7:9:22}$-steroids into 9α : 11α-monoepoxides by reaction with peracids has been discussed in an earlier paper.[1] We now report the isolation of some of the components of the rather complex mixtures produced by epoxidation under more vigorous conditions.

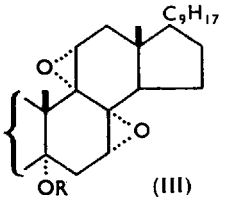
3β-Acetoxyergosta-7 : 9(11) : 22-trien-5α-ol (I; R = H) with performic acid in either "homogeneous" or "heterogeneous" media[2] gave some of the nuclear diepoxide (III; R = H). This was more easily obtained (54% yield) from the 9 : 11-monoepoxide (II; R = H) and excess of monoperphthalic acid; a little triepoxide (IV) was also formed. The latter was readily made from the purified diepoxide and performic acid. Oxidation of the 3 : 5-diacetate (I; R = Ac) with performic acid in heterogeneous media yielded an intractable glass: however, from oxidations in homogeneous media several substances were isolated, including the two diepoxides (III; R = Ac) and (VI), and a substance



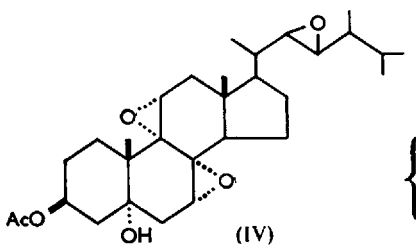
(I)



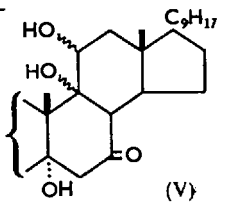
(II)



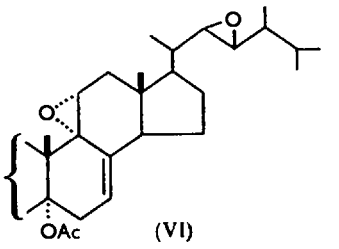
(III)



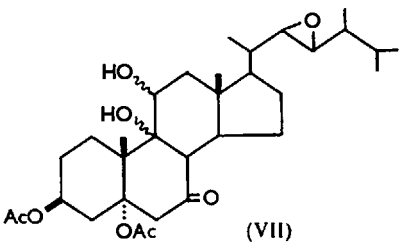
(IV)



(V)



(VI)



(VII)

$C_{32}H_{50}O_8$, which is probably the 9 : 11-dihydroxy-7-oxo-mono-oxide (VII). A related substance $C_{30}H_{48}O_6$, believed to have structure (V), was isolated from the oxidation products of the acetoxy-alcohol (I; R = H) with performic acid in heterogeneous media. Other workers[2,3,4] have isolated 7-oxo-9 : 11-diols similar to (VII) and (V) from the epoxidation products of $\Delta^{7:9}$-steroids. There is considerable chemical evidence[2,4,5] that these substances have the 11α-configuration; however, they are probably formed by way

[1] Burke, Turnbull, and Wilson, *J.*, 1953, 3237.
[2] Cf. Bladon, Henbest, Jones, Wood, Eaton, and Wagland, *J.*, 1953, 2916.
[3] Stork, Romo, Rosenkranz, and Djerassi, *J. Amer. Chem. Soc.*, 1951, **73**, 3546.
[4] Budziarek, Newbold, Stevenson, and Spring, *J.*, 1952, 2892.
[5] Djerassi, Mancera, Romo, and Rosenkranz, *J. Amer. Chem. Soc.*, 1953, **75**, 3505.

of 7-oxo-9α : 11α-epoxides and, according to the " axial rule " [6] for the fission of steroid epoxides, they should have the 9α : 11β-configuration.

It has been noted [2] that a 5α-acetoxy-group markedly hinders the reaction of a 7 : 8-double bond with peracids. This is consistent with our results, which indicate that in the 5α-acetoxy-series, side-chain epoxidation may occur in preference to 7 : 8-epoxidation, as in the formation of (VI). The ergosterol side-chain appears to be rather unreactive to peracids, although other workers [7] obtained isomeric side-chain epoxides in low yields from an ergosterol derivative.

Experimental.—Alumina neutralised with acetic acid [8] was used for chromatography; $[\alpha]_D$ are in chloroform. "P.I. Rectified spirit" was used as solvent for the ultraviolet-absorption measurements.

Oxidation of 3β-*acetoxyergosta*-7 : 9(11) : 22-*trien*-5α-*ol*. (*a*) " Homogeneous." The triene (1·16 g.) in dioxan (360 c.c.) was added to a mixture of 99% formic acid (11 c.c.) and hydrogen peroxide solution (34 c.c.; 100-vol.). After 18 hr. at 25° the solution was poured into water and the product isolated by means of ether. Chromatography gave benzene–light petroleum eluates containing 3β-acetoxy-7α : 8α-9α : 11α-diepoxyergost-22-en-5α-ol (120 mg., 10%), which formed needles, m. p. 223—228°, $[\alpha]_D$ −10° (*c* 0·81), $\lambda_{max.}$ 207 mμ (ε 1300) (Found: C, 74·0; H, 9·4. Calc. for $C_{30}H_{46}O_5$: C, 74·05; H, 9·55%); Burke, Turnbull, and Wilson [1] give m. p. 234—235°, $[\alpha]_D$ −10°, $\lambda_{max.}$ 203 mμ (ε 1020). The product had absorption bands at 1728 (acetyl) and 3600 cm.$^{-1}$ (hydroxyl); it gave no precipitation with 2 : 4-dinitrophenylhydrazine solution, and did not develop ultraviolet absorption bands on treatment with alcoholic alkali. Boron trifluoride–ether complex in benzene at 20° for 4 hr. did not appear to give a 7-ketone, as the product did not develop ultraviolet absorption bands in alkali. The diepoxide was boiled for 2 hr. with 2N-sulphuric acid in aqueous dioxan; chromatography gave fractions having absorption max. at 280 (ε 6700), 229 (ε 7700), and 243 mμ (ε 6300) (cf. ref. 1); the last two bands suggest the formation of 7-oxo-Δ^5- and 7-oxo-$\Delta^{5:8(9)}$-chromophores. The diepoxide (160 mg.), 10% aqueous potassium hydroxide (2 c.c.), and dioxan (40 c.c.) were refluxed for 1 hr. Chromatography and recrystallisation from methanol–benzene yielded 7α : 8α-9α : 11α-diepoxyergost-22-ene-3β : 5α-diol as plates (30%), m. p. 245—247°, $[\alpha]_D$ −17° (*c* 1·15), $\lambda_{max.}$ 203 mμ (ε 970) {Burke, Turnbull, and Wilson [1] give m. p. 251—252°, $[\alpha]_D$ −18°, $\lambda_{max.}$ 206 mμ (ε 1200)}.

(*b*) " Heterogeneous." The triene (1·11 g.) was dissolved in chloroform (20 c.c.), and a mixture of 98% formic acid (5 c.c.) and hydrogen peroxide (5 c.c.; 100-vol.) was added. The two-phase mixture was stirred at 20° for 22 hr. The product from the chloroform layer was chromatographed in 1 : 1 benzene–light petroleum (60 c.c.), yielding the above diepoxide (317 mg.), m. p. 217—221°, $[\alpha]_D$ −5° (*c* 1·15), $\lambda_{max.}$ 207 mμ (ε 525). Benzene–ether eluates yielded (?) impure 3β-acetoxy-5α : 9ξ : 11ξ-trihydroxyergost-22-en-7-one (V) (35 mg.), m. p. 186—192°, $[\alpha]_D$ −34° (*c* 0·93) (Found: C, 72·3; H, 9·95. Calc. for $C_{30}H_{48}O_6$: C, 71·4; H, 9·6%). This product gave a yellow precipitate within 2 hr. with 2 : 4-dinitrophenylhydrazine solution; ethanolic potassium hydroxide at 20° for 16 hr. developed an absorption band at 250 mμ (ε 6700), attributable to the formation of a 7-oxo-$\Delta^{5:8(9)}$-chromophore.

(*c*) Oxidation of the triene with 1·1 mols. of monoperphthalic acid in ether gave a product which contained 10% of unchanged triene and was difficult to purify. 1·3—1·4 Mols. of monoperphthalic acid gave 60% yields of 3β-acetoxy-9α : 11α-epoxyergosta-7 : 22-dien-5α-ol.

3β-*Acetoxy*-7α : 8α-9α : 11α-22 : 23-*triepoxyergostan*-5α-*ol*. (*a*) The above monoepoxide (0·63 g.) was treated with monoperphthalic acid (2 mols.) in ether (140 c.c.) at 20° for 11 days. Recrystallisation from methanol–benzene afforded 3β-acetoxy-7α : 8α-9α : 11α-diepoxyergost-22-en-5α-ol (124 mg., 19%), m. p. 212—219°, $[\alpha]_D$ −12° (*c* 1·34), $\lambda_{max.}$ 202 mμ (ε 1200) (Found: C, 73·5; H, 9·55. Calc. for $C_{30}H_{46}O_5$: C, 74·05; H, 9·55%). The mother-liquors were evaporated and chromatographed. A benzene–ether eluate was recrystallised from methanol–benzene, to afford 3β-*acetoxy*-7α : 8α-9α : 11α-22 : 23-*triepoxyergostan*-5α-*ol* (39 mg.), m. p. 216—224°, $[\alpha]_D$ −7° (*c* 0·77), $\lambda_{max.}$ 202 mμ (ε 375) (Found: C, 71·75; H, 9·0. $C_{30}H_{46}O_6$ requires C, 71·7; H, 9·2%). The triepoxide developed no ultraviolet absorption bands when treated with alcoholic potassium hydroxide.

(*b*) The diepoxide (252 mg.) was dissolved in chloroform (10 c.c.) and dioxan (60 c.c.), and 98% formic acid (20 c.c.) and hydrogen peroxide (20 c.c., 100-vol.) were added. The mixture

[6] Barton, *J.*, 1953, 1033.
[7] Barton and Laws, quoted by Bladon, Clayton, Greenhalgh, Henbest, Jones, Lovell, Silverstone, Wood, and Woods, *J.*, 1952, 4883.
[8] Farrar, Hamlet, Henbest, and Jones, *J.*, 1952, 2665.

was left at 20—22° for 4 days. The crude product (230 mg.; m. p. 220—228°) was recrystallised from methanol–benzene, to yield the triepoxide, m. p. 228—231°, $[\alpha]_D$ −5° (*c* 1·13), $\lambda_{max.}$ 203 mμ (ε 530) (Found: C, 71·8; H, 9·0. Calc. for $C_{30}H_{46}O_6$: C, 71·7; H, 9·2%).

Oxidation of 3β : 5α-*diacetoxyergosta*-7 : 9(11) : 22-*triene*. (*a*) The diacetate (640 mg.) with performic acid in aqueous dioxan at 20° for 17 hr. was largely (70%) recovered unchanged; a small amount of 3β : 5α-acetoxyergosta-8(9) : 22-dien-7-one [9] (10 mg.), m. p. 150—153°, $[\alpha]_D$ −29° (*c* 0·24), $\lambda_{max.}$ 250 mμ (ε 6400), was isolated.

(*b*) The diacetate (2·64 g.), dioxan (280 c.c.), 98% formic acid (23 c.c.), and hydrogen peroxide (68 c.c.; 100-vol.) were mixed and left at 25° for 40 hr. The product was chromatographed in benzene–light petroleum (1 : 19). The first eluates (1·4 g.) were rechromatographed and crystallised from methanol, giving 3β : 5α-*diacetoxy*-9α : 11α-22 : 23-*diepoxyergost*-7-*ene* (225 mg.), m. p. 152—154°, $[\alpha]_D$ +50° (*c* 0·64), $\lambda_{max.}$ 207 mμ (ε 6500) (Found: C, 72·5; H, 9·4. $C_{32}H_{48}O_6$ requires C, 72·7; H, 9·15%). This product had no hydroxyl groups (infrared); there was a very weak band at 968 cm.$^{-1}$, probably indicating the presence of a little Δ^{22}-compound as impurity. With alcoholic potassium hydroxide, no ultraviolet absorption bands were developed; however, treatment with 2N-sulphuric acid in aqueous dioxan at 100° for 2 hr. produced a band [$\lambda_{max.}$ 247 mμ (ε 11,000)] attributed to the formation of a 7-oxo-$\Delta^{5:8(9)}$-chromophore [Burke, Turnbull, and Wilson [1] give $\lambda_{max.}$ 246 (ε 11,000)]. Benzene–ether eluates from the chromatogram were rechromatographed and crystallised from methanol, to afford (?) impure 3β : 5α-diacetoxy-22 : 23-epoxy-9ξ : 11ξ-dihydroxyergostan-7-one (VII) (350 mg.), m. p. 207—210°, $[\alpha]_D$ −13° (*c* 0·91), $\lambda_{max.}$ 207 mμ (ε 180) (Found: C, 67·7; H, 8·95. Calc. for $C_{32}H_{50}O_5$: C, 68·25; H, 8·95%), which had infrared absorption at 1728 (acetyl), 3600 ± 50 (OH), and 971 ± 2 cm.$^{-1}$ (Δ^{22}).[10] With alcoholic potassium hydroxide at 80° for 3½ hr., this product developed absorption bands at 231 (ε 11,000) and 272 mμ (ε 4000), attributed to the formation of 7-oxo-Δ^5- [$\lambda_{max.}$ 234 mμ (ε 12,500) [11]] and 7-oxo-$\Delta^{3:5:8(9)}$-chromophores [$\lambda_{max.}$ 272 mμ (ε 14,600) [9]].

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[9] Elks, Evans, Oughton, and Thomas, *J.*, 1954, 463.
[10] Turnbull, Whiffen, and Wilson, *Chem. and Ind.*, 1950, 626.
[11] Fieser and Fieser, "Natural Products Related to Phenanthrene," Reinhold Publ. Corpn., New York, 1949, p. 191.

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911. *The Preparation of Aliphatic Aldehydes and Ketones from Lithium Alkyls and Dimethylamides.*

By E. A. EVANS.

FORMATION of ethylenic aldehydes from lithium alkenyls by *NN*-dimethylformamide has been recently described,[1] and this reaction has now been extended to the lithium alkyl series: $RLi + NMe_2{\cdot}COR' \longrightarrow NMe_2{\cdot}CRR'{\cdot}OLi \longrightarrow CORR' + NHMe_2$ (R′ = H). The aldehydes were obtained in 50—85% yields (see Table), except *iso*valeraldehyde (37%), and for convenience were usually isolated as their 2 : 4-dinitrophenylhydrazones or semicarbazones. However, *iso*propyl-lithium gave no aldehyde, perhaps owing to steric hindrance. ωω′-Dibromoalkanes, $Br{\cdot}[CH_2]_n{\cdot}Br$ ($n = 2$—5) could not be dimetallated with lithium or cross-metallated with *n*-butyl-lithium.

A number of methyl ketones were similarly prepared by action of *NN*-dimethylacetamide. In general the yields (see Table) were higher than those of the corresponding aldehydes.

R	Yield (%) of R·CHO	Yield (%) of R·COMe	R *	Yield (%) of R·CHO	Yield (%) of R·COMe	R *	Yield (%) of R·CHO	Yield (%) of R·COMe
Et	—	47	Bu^n	52	78	C_8H_{17}	70	—
Pr^n	50	—	C_5H_{11}	67	71	C_9H_{19}	71	—
Pr^i	0	—	C_6H_{13}	85	45	$C_{10}H_{21}$	60	79
Bu^i	37	50	C_7H_{15}	62	—	$C_{11}H_{23}$	—	88

* *n*-Alkyl.

[1] Braude and Evans, *J.*, 1955, 3331.

The reactions of the carboxyamide group with organometallic compounds have also been investigated by Heyns and Pyrus,[2] who found that amides with an excess of a Grignard reagent or with lithium alkyls or aryls give, after hydrolysis, only 20—40% yields of ketones.

Experimental.—M. p.s are corrected. Literature values for m. p.s were taken from " A Textbook of Practical Organic Chemistry " by Vogel, and are given in parentheses after m. p.s.

The lithium alkyls were prepared by Gilman's general procedure [3] in dry oxygen-free nitrogen.

n-*Butyraldehyde.* *NN*-Dimethylformamide (2 g.) was added dropwise to *n*-propyl-lithium [from Li (0·6 g.) and *n*-propyl bromide (6 g.)] in ether (50 ml.) at −20°. The mixture was stirred for 3 hr. while the solution attained room temperature. The solution was then cooled to −10° and an excess of saturated aqueous ammonium chloride added. After 30 minutes' stirring the ether layer was dried (Na_2SO_4) and evaporated under reduced pressure. The residual liquid was dissolved in methanol (5—10 ml.), and an excess of 2 : 4-dinitrophenylhydrazine in methanol–sulphuric acid added. *n*-Butyraldehyde 2 : 4-dinitrophenylhydrazone (3·5 g., 50% based on dimethylformamide) was separated and crystallised from ethyl acetate–methanol in orange needles, m. p. 123° (123°) (Found : N, 22·4. Calc. for $C_{10}H_{12}O_4N_4$: N, 22·2%).

The following aldehydes R·CHO were similarly prepared. (*a*) As 2 : 4-dinitrophenylhydrazones : R = Bu^n, m. p. and mixed m. p. 98—99° (98°) [free aldehyde, b. p. 102—104° (104°)]; Bu^i, m. p. 121—122° (123°); *n*-C_7H_{15}, m. p. 105—106° (106°); *n*-C_8H_{17}, m. p. 100° (100°); *n*-C_9H_{19}, m. p. 102—103° (104°) (Found : N, 16·5. Calc. for $C_{16}H_{24}O_4N_4$: N, 16·4%); *n*-$C_{10}H_{21}$, m. p. 102—103° (104°) (Found : N, 16·2. Calc. for $C_{17}H_{26}O_4N_4$: N, 16·0%). (*b*) As semicarbazones : R = *n*-C_5H_{11}, m. p. 110—111° (106°) (Found : C, 53·8; H, 9·4. Calc. for $C_{17}H_{15}ON_3$: C, 53·5; H, 9·65%); *n*-C_6H_{13}, m. p. 107° (109°).

Ketones. These were prepared similarly but with *NN*-dimethylacetamide and, except for butanone, were isolated by distillation. M. p. below are those of 2 : 4-dinitrophenylhydrazones, except as stated. R in R·COMe : Et [m. p. and mixed m. p. 114—115° (117°)]; Bu^n, b. p. 68—70°/200 mm. (128°) [m. p. 105—106° (107°)]; Bu^i, b. p. 115—116° (117°) [m. p. 96—97° (95°) (Found: C, 51·4; H, 5·65. Calc. for $C_{12}H_{16}O_4N_4$: C, 51·4; H, 5·7%)]; *n*-C_5H_{11}, b. p. 70°/60 mm. [m. p. 72—73° (89°) (Found : C, 53·65; H, 6·5; N, 18·8. Calc. for $C_{13}H_{18}O_4N_4$: C, 53·4; H, 6·2; N, 19·2%)]; *n*-C_6H_{13}, b. p. 72—74°/30 mm. [m. p. 57—58° (58°) (Found : C, 54·55; H, 6·3; N, 18·3. Calc. for $C_{14}H_{20}O_4N_4$: C, 54·6; H, 6·5; N, 18·2%)]; *n*-$C_{10}H_{21}$, b. p. 150—155°/18 mm. (lit.,[4] 144°/11 mm.) [semicarbazone, m. p. 123° (lit.,[4] 123°) (Found : C, 64·6; H, 10·8; N, 17·0. Calc. for $C_{13}H_{27}ON_3$: C, 64·7; H, 11·2; N, 17·4%)]; *n*-$C_{11}H_{23}$, b. p. 258—262° (lit.,[5] 260—265°) [m. p. 69° (lit.,[5] 69°].

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The Radiochemical Centre, Amersham, Bucks. [*Received, May 7th*, 1956.]

[2] Heyns and Pyrus, *Chem. Ber.*, 1955, **88**, 678.
[3] Gilman and Jones, *Chem. Rev.*, 1954, **54**, 835; cf. Braude, in Chap. 4 of " Progress in Organic Chemistry," Vol. III, Ed. J. W. Cook, Butterworths, 1955.
[4] Krafft, *Ber.*, 1882, **15**, 1708; Pickard and Kenyon, *J.*, 1911, 57.
[5] Guerin, *Bull. Soc. chim. France*, 1903, **29**, 1128; Morgan and Holmes, *J. Soc. Chem. Ind.*, 1925, **44**, 108T; Pickard and Kenyon, ref. 4.

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912. *The Preparation and Characterisation of* o-*Bromophenylmagnesium Bromide.*

By Harry Heaney, Frederick G. Mann, and Ian T. Millar.

We have recently recorded the results of an investigation on the action of magnesium, lithium, and *n*-butyl-lithium in turn on *o*-di-iodobenzene and of a preliminary investigation on the action of these reagents on *o*-dibromobenzene.[1] In view of the more recent publication by Gilman and Gorsich,[2] describing the preparation of *o*-bromophenyl-lithium in 23% yield by the interaction of ethereal *n*-butyl-lithium and *o*-dibromobenzene for 7 minutes at −110°, we now record our extended work on the preparation of *o*-bromophenylmagnesium bromide, which we have obtained by two alternative methods in 26—30% yield.

[1] Heaney, Mann, and Millar, *J.*, 1956, 1.
[2] Gilman and Gorsich, *J. Amer. Chem. Soc.*, 1956, **78**, 2217.

In contrast with certain aromatic *o*-dibromo-compounds such as 3 : 4-dibromotoluene [3] and 1 : 2-dibromonaphthalene,[4] *o*-dibromobenzene resembles 3 : 4-dibromodiphenyl [5] in failing to react with magnesium alone in ether; [1] it fails to give a simple organometallic derivative with lithium in diethyl ether or with *n*-butyl-lithium in light petroleum at ordinary temperatures,[1] and with *n*-butyl-lithium in diethyl ether gives *o*-bromophenyl-lithium only under the special conditions recorded by Gilman and Gorsich.[2] [In these respects it also differs markedly from *p*-dibromobenzene, which gives both mono- and di-(magnesium halides) [6] and the corresponding lithium derivatives.[7]]

We have, however, been able to bring *o*-dibromobenzene into reaction with magnesium in ether by using ethyl bromide as entraining agent, and have studied the effect of variation of the proportion of bromide from 0·2 to 1·0 mol. per mol. of dihalide.

Optimum yields of *o*-bromophenylmagnesium bromide, assessed by the carboxylation method, were obtained by the use of equimolecular proportions of *o*-dibromobenzene and ethyl bromide, *o*-bromobenzoic acid being then obtained in 30% yield and benzoic acid in 8% yield. The latter acid almost certainly arises from the formation of some *o*-phenylenebis(magnesium bromide), which on reaction with carbon dioxide probably forms a chelated complex which on ultimate hydrolysis would give benzoic acid. A comparable mechanism has been suggested for the reaction of *o*-phenylenebis(magnesium iodide) with carbon dioxide, which similarly gives benzoic acid.[1]

Since the presence of both ethylmagnesium bromide and *o*-phenylenebis(magnesium bromide) in the ethereal solutions of *o*-bromophenylmagnesium bromide might prove inconvenient in the synthetic use of the last reagent, an alternative procedure for its preparation has been investigated. We find that *o*-dibromobenzene reacts with magnesium in tetrahydrofuran, in the absence of ethyl bromide, to give *o*-bromophenylmagnesium bromide. However, in this solvent the reagent failed to give any acidic product on attempted carboxylation, and with benzophenone gave only benzpinacol.[8] The Grignard reagent crystallised from tetrahydrofuran at room temperature, and insolubility at the temperature of carboxylation may account for this failure to react normally: on the other hand, no bromobenzene was isolated on subsequent hydrolysis. Our limited experience of tetrahydrofuran indicates that it may often, like dioxan,[9] cause precipitation of Grignard reagents.

We therefore employed iododimethylarsine as a characterising agent,[1] and obtained a 26% yield of *o*-bromophenyldimethylarsine.

Although the yield of *o*-bromophenylmagnesium bromide obtainable by either of the above procedures is not significantly superior to that of *o*-bromophenyl-lithium obtainable at −100°, the necessity for this low temperature of reaction, which results from the exceptionally high reactivity of *o*-halogenophenyl-lithiums,[2] reduces the practical value of this reagent and suggests that *o*-bromophenylmagnesium bromide may be more valuable as a synthetic intermediate.

We are now investigating the use of *o*-bromophenylmagnesium bromide in the preparation of some *o*-bromophenyl- and *o*-phenylenedi-metallic and metalloidal compounds.

Experimental.—Reactions with magnesium were performed under nitrogen in a standard Grignard assembly; carboxylation was carried out by pouring the reaction product on a slurry of solid carbon dioxide and ether. M. p.s were determined on a Kofler stage.

(a) *Preparation in diethyl ether.* A solution of *o*-dibromobenzene (9·45 g.) and ethyl bromide (4·36 g., 1 mol.) in ether (50 ml.) was added dropwise with stirring to magnesium (1·95 g., 2 atom-equivs.) and ether (15 ml.) at such a rate that the solvent did not boil. After 1 hour's

[3] Zalkind, Kirillowa, and Nikiforowa, *J. Gen. Chem.* (*U.S.S.R.*), 1931, **1**, 193.
[4] Zalkind, *Ber.*, 1934, **67**, 1031.
[5] Case, *J. Amer. Chem. Soc.*, 1936, **58**, 1246.
[6] See, *e.g.*, Gilman, Beaber, and Jones, *Rec. Trav. chim.*, 1929, **48**, 597; Weldon and Wilson, *J.*, 1946, 235.
[7] Gilman, Langham, and Moore, *J. Amer. Chem. Soc.*, 1940, **62**, 2327; Gilman and Melvin, *ibid.*, 1950, **72**, 995.
[8] See Gomberg and Bachmann, *J. Amer. Chem. Soc.*, 1927, **49**, 236, for other examples of the reduction of ketones to pinacols under comparable conditions.
[9] Schlenk and Schlenk, *Ber.*, 1929, **62**, 920; Noller, *J. Amer. Chem. Soc.*, 1931, **53**, 635.

stirring at room temperature the clear yellow solution was decanted from unchanged magnesium (0·24 g., 12%) and carboxylated. The product was hydrolysed with dilute hydrochloric acid, basified, and extracted with aqueous sodium hydroxide, which when acidified deposited a crude crystalline product, m. p. 130—138° (3·1 g.). Distillation of this product in steam gave benzoic acid, m. p. and mixed m. p. 120° (0·4 g., 8%). The residue on sublimation at 140°/0·1 mm. gave *o*-bromobenzoic acid, m. p. and mixed m. p. 150° (2·4 g., 30%). The ethereal layer on evaporation gave *o*-dibromobenzene, b. p. 94—96°/15 mm. (3·0 g., 31·5%), and an unidentified residue. Reactions performed as above but employing 0·2, 0·4, and 0·6 mol. of ethyl bromide gave respectively 2·2 g., 2·5 g., and 2·8 g. of crude acidic product, m. p. 130—138°; magnesium unreacted, 20%, 14·5%. 13% respectively; *o*-dibromobenzene recovered, 39%, 36%, 34% respectively.

(b) *Preparation in tetrahydrofuran.* Tetrahydrofuran was purified by shaking it with aqueous 40% sodium hydroxide, drying ($CaCl_2$), distilling, and prolonged boiling under reflux over sodium; finally it was distilled from sodium into the reaction vessel. A solution of *o*-dibromobenzene (9·45 g.) in tetrahydrofuran (25 ml.) was added dropwise to magnesium (0·97 g., 1 atom-equiv.) and tetrahydrofuran (15 ml.). Then benzene (20 ml.) was added and the mixture stirred at room temperature for 1 hr.; it was then cooled in ice whilst iododimethylarsine (9·28 g., 1 mol.) in benzene (20 ml.) was added dropwise. The resulting clear yellow solution was stirred for 30 min. and then boiled under reflux for 2 hr. before being cooled in ice and hydrolysed with aqueous ammonium chloride.

The organic layer, when dried and distilled in an atmosphere of nitrogen, gave iododimethylarsine, b. p. 30—40°/1 mm. (1 g., 11%), and *o*-bromophenyldimethylarsine, b. p. 93—98°/1 mm. (2·9 g.). The latter fraction when treated with an excess of methyl iodide deposited *o*-bromophenyltrimethylarsonium iodide, which, once recrystallised from methanol, decomposed without melting at *ca.* 240° (4·35 g., 26%) (Found: C, 26·8; H, 3·2. Calc. for $C_9H_{13}BrIAs$: C, 26·8; H, 3·2%). Jones and Mann [10] record identical behaviour on heating.

Treatment of the methiodide with methanolic sodium picrate gave the corresponding *methopicrate*, m. p. 181—182° (from methanol) (Found: C, 35·5; H, 2·95; N, 8·5. $C_{15}H_{15}O_7N_3BrAs$ requires C, 35·75; H, 3·0; N, 8·35%).

An experiment similar to that described above, but employing a benzene solution of benzophenone (1 mol.) as characterising agent in place of iododimethylarsine, gave a dark red solution which after hydrolysis gave on evaporation of the organic layer a crystalline residue of benzpinacol, which, recrystallised from benzene–light petroleum (b. p. 60—80°), had m. p. and mixed m. p. 182—184° (Found: C, 85·1; H, 6·4. Calc. for $C_{26}H_{22}O_2$: C, 85·2; H, 6·05%). In another experiment, the reaction mixture was carboxylated; no acidic material was isolated from the product, and *o*-dibromobenzene (34%) was recovered. In an experiment in which *o*-bromophenylmagnesium bromide was prepared in tetrahydrofuran at 0°, followed by characterisation with iododimethylarsine as above, the yield of recrystallised *o*-bromophenyltrimethylarsonium iodide fell to 15·5%.

We are indebted to the University College of North Staffordshire for a Tutorial Studentship (to H. H.).

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[*Received, June 21st,* 1956.]

[10] Jones and Mann, *J.*, 1955, 4472.

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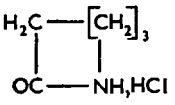
913. *The Beckmann Rearrangement of* cyclo*Pentanone Oxime.*

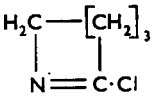
By (MRS.) T. STEPHEN and HENRY STEPHEN.

THE oxime rearranged in chloroform with thionyl chloride to piperid-2-one hydrochloride (I) (47%) and 2-chloro-3 : 4 : 5 : 6-tetrahydropyridine (II) (47%), the yields being in agreement with the mechanism of the Beckmann rearrangement proposed by Stephen and Staskun.[1] Attempts to isolate the pyridine (II) in a pure state were unsuccessful but its formation during the Beckmann rearrangement was established by condensing it with methyl anthranilate to give 6 : 7 : 8 : 9-tetrahydropyrido[2,1-*b*]quinazol-11-one (III).[2]

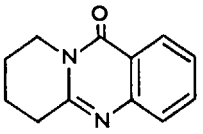
Experimental.—The following improved method gives a 95% yield of *cyclo*pentanone oxime. *cyclo*Pentanone [3] (84 g.) and hydroxylamine hydrochloride (70 g.) in water (250 c.c.) were stirred at room temperature during the addition of sodium hydrogen carbonate (84 g.). The oxime



(I)



(II)



(III)

which crystallised was filtered off, washed with warm water (40°) (150 c.c.), and dried; it was then pure enough for further use.

Rearrangement of the oxime. Thionyl chloride (3·5 c.c.) was added dropwise to the oxime (5 g.) in dry chloroform (100 c.c.) at −5°. The clear green solution was then removed from the freezing mixture; the temperature rose to 15° during the next 5 min., and then rapidly to 38°, its colour changing to yellow with crystallisation of *piperid-2-one hydrochloride*. After being kept at 38° for 5 min. the mixture was cooled at 0° for 30 min., and the hydrochloride filtered off; it crystallised from methanol–ethyl acetate (1 : 1 by vol.) in plates (44%), m. p. 167—169° (decomp.) (Found: Cl, 26·1%; *M*, 140. C_5H_9ON,HCl requires Cl, 26·2%; *M*, 135·5). It also crystallises from thionyl chloride. Piperid-4-one, obtained by rearranging the oxime according to Wallach,[4] was dissolved in chloroform and treated with dry hydrogen chloride, the hydrochloride formed being identical with that described above.

6 : 7 : 8 : 9-*Tetrahydropyrido*[2,1-b]*quinazol*-11-*one* (III). Piperid-2-one hydrochloride (5 g.) was warmed on a water-bath with phosphorus oxychloride (25 c.c.), and after the reaction had subsided the excess of oxychloride was removed under reduced pressure. To the residual oil methyl anthranilate (15 g.) was added and, after the vigorous reaction had ceased, water (150 c.c.) was added, the mixture made alkaline with ammonia, and the excess of methyl anthranilate removed by steam-distillation, leaving an oil which was dissolved in hot dilute hydrochloric acid (charcoal) and filtered. The filtrate, on treatment with ammonia and cooling, deposited white needles (75%) which, recrystallised from hot water, had m. p. 100·5° (Found: C, 72·2; H, 6·2; N, 14·2. $C_{12}H_{12}ON_2$ requires C, 72·0; H, 6·0; N, 14·0%). The *hexachloroplatinate* of the *base* was obtained as orange needles, m. p. 260° (decomp.) [Found: Pt, 24·1%. $(C_{12}H_{12}ON_2)_2,H_2PtCl_6$ requires Pt, 24·1%]. The presence of 2-chloro-3 : 4 : 5 : 6-tetrahydropyridine during the Beckmann rearrangement of *cyclo*pentanone oxime was established as follows: the oxime (4 g., 1 mol.) in chloroform (50 c.c.) was treated as above with thionyl chloride (3 c.c., 1 mol.), and after completion of the rearrangement methyl anthranilate (15 g.) was added, whereupon a vigorous reaction took place with separation of methyl anthranilate hydrochloride, which was removed by filtration. The filtrate was made alkaline with ammonia and stream-distilled to remove chloroform and methyl anthranilate, and the oil remaining was purified as above, yielding needles (40%), m. p. 100·5°, identical with those obtained above.

We thank the South African Council for Scientific and Industrial Research for a grant (to T. S.).

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG. [*Received, May 4th*, 1956.]

[1] Stephen and Staskun, *J.*, 1956, 980.
[2] Stephen and Stephen, *J.*, 1956, 4173.
[3] *Org. Synth.*, 1925, **5**, 37.
[4] Wallach, *Annalen*, 1900, **312**, 179.

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914. *Modification of the Procedure for Converting Nitriles into Aldehydes.*

By (MRS.) T. STEPHEN and HENRY STEPHEN.

THE original method [1] of reducing nitriles to aldehydes assumed the formation of an imidoyl chloride R·CCl(:NH) by addition of hydrogen chloride to the nitrile. Later investigation [2] showed that a nitrilium salt of the type $[R{\cdot}C{:}NH]^+Cl^-$ is probably formed which then undergoes reduction with stannous chloride. The modification of the procedure is the use of ethyl formate or ethyl acetate as solvent instead of anhydrous ether. The advantage is two-fold; anhydrous stannous chloride and nitriles are readily soluble in both solvents at the ordinary temperature and remain in solution after saturation with hydrogen chloride.

[1] Stephen, *J.*, 1925, 1874.
[2] Hantzsch, *Ber.*, 1931, **64**, 661.

Experimental.—A solution of the nitrile (1 mol.) in ethyl acetate saturated with hydrogen chloride at 0° is added to a solution of stannous chloride (1·1 mol.) in ethyl acetate previously saturated with hydrogen chloride at 0°. After several hours at 0° the stannichloride of the aldimine $[R{\cdot}CH{:}NH_2]^+{}_2SnCl_6^{2-}$ separates as pale yellow prisms, and after filtering through a sintered glass filter, washing with anhydrous ether, and drying (NaOH *in vacuo* for several days) is analytically pure. To obtain the aldehyde the product after deposition of the stannichloride is completed is poured into water and steam-distilled, which hydrolyses the stannichloride and removes solvent and aldehyde if the latter is volatile in steam (otherwise the aldehyde is extracted from the residue after steam-distillation). The yields of the following aldehydes were almost quantitative, and they were identified by their *p*-nitrophenylhydrazones, 2 : 4-dinitrophenylhydrazones, and semicarbazones. The tin content of the stannichlorides was determined by hydrolysing a weighed sample (0·5 g.) in boiling water (100 c.c.) and then adding ammonia to precipitate stannic hydroxide, which was collected in a weighed crucible, washed with hot water and with ethanol to remove adhering aldehyde, ignited, and weighed. $(Ph{\cdot}CH{:}NH_2)_2SnCl_6$ (Found : SnO_2, 26·9, 27·1. Required : SnO_2, 27·7%). $(m\text{-}Me{\cdot}C_6H_4{\cdot}CH{:}NH_2)_2SnCl_6$ (Found : SnO_2, 26·8. Required : SnO_2, 26·4%). $(p\text{-}Me{\cdot}C_6H_4CH{:}NH_2)_2SnCl_6$ (Found : SnO_2, 26·9. Required : SnO_2, 26·4%). $(\beta\text{-}C_{10}H_7{\cdot}CH{:}NH_2)_2SnCl_6$ (Found : SnO_2, 22·8, 22·7. Required : SnO_2, 23·4%). $[3:4:5\text{-}(MeO)_3C_6H_2{\cdot}CH{:}NH_2]_2SnCl_6$ (Found : SnO_2, 20·6. Required : SnO_2, 20·8%). *p*-Methoxybenzaldehyde, yield 15% after 12 hr.; *p*-tolualdehyde, 30% after 72 hr.; α-naphthaldehyde, 20% after 24 hr.

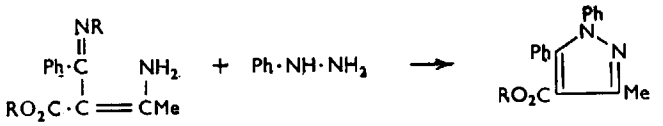
The use of ethyl formate and ethyl acetate as solvents for nitriles in the Hoesch–Houben synthesis of hydroxyaromatic ketones is being investigated.

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG. [*Received, May 24th*, 1956.]

915. *The Preparation of Methyl and Ethyl β-Amino-α-(N-substituted-Benzimidoyl)crotonates, and their Conversion into Methyl and Ethyl 3-Methyl-1 : 5-diphenylpyrazole-4-carboxylates.*

By BENJAMIN STASKUN and HENRY STEPHEN.

METHYL and ethyl β-amino-α-(*N*-substituted benzimidoyl)crotonates (I) are readily obtained by the condensation of *N*-substituted benzimidoyl chlorides with methyl and ethyl β-aminocrotonate. On hydrolysis they yield acetophenone, arylamine, and ammonia, which indicate condensation of the benzimidoyl chlorides at the α-carbon of the



(I) (II)

β-aminocrotonic ester. Similar observations were made by Benary [1] and Grob [2] when investigating the action of acid chlorides on ethyl β-aminocrotonate. Evidence for the structure of compounds (I) is also provided by their reaction with phenylhydrazine which affords the 3-methyl-1 : 5-diphenylpyrazole-4-carboxylates (II). Further, all the methyl esters (I) yield the same methyl ester (II; R = Me), and the ethyl esters yield the ethyl ester (II; R = Et).

Experimental.—General procedure for the condensation of imidoyl chlorides with β-amino-crotonic esters. The ester (0·01 mol.) in dry chloroform (40 c.c.) is treated with the imidoyl chloride (0·01 mol.) at 0° for 3—5 days. At this temperature the hydrogen chloride liberated does not attack the ester. Condensation proceeds slowly, as indicated by the development of a yellow colour in chloroform, and when there is no further change 5% hydrochloric acid (20 c.c.) is added and the chloroform removed by steam-distillation. The aqueous residue is chilled and filtered; the yellow filtrate, after being made alkaline with ammonia, deposits the crude base which crystallises from dilute methanol or ethanol (charcoal). The new compounds are more basic than the β-aminocrotonic esters and are present in the chloroform solutions as the yellow hydrochlorides. The latter are also prepared by passing hydrogen chloride through a chloroform solution of the bases. *Products* are tabulated.

[1] Benary, *Ber.*, 1909, **42**, 3912 ; Benary *et al.*, *Ber.*, 1917, **50**, 65.
[2] Grob, *Helv. Chim. Acta*, 1950, **33**, 1787.

R in Ph·CCl:NR	X in NH_2·CMe:CH·CO_2X	Product (I)	Yield (%)	M. p.	Found: N (%)	Reqd.: N (%)
Ph	Me	$C_{19}H_{18}O_2N_2$ *	67	144°	9·65	9·5
	Et	$C_{19}H_{20}O_2N_2$ *	64	101	9·2	9·1
o-Tolyl	Me	$C_{19}H_{20}O_2N_2$ *	73	156	8·9	9·1
	Et	$C_{20}H_{22}O_2N_2$ *	24	101	8·45	8·7
m-Tolyl	Me	$C_{19}H_{20}O_2N_2$ *	55	127	9·0	9·1
p-Tolyl	Me	$C_{19}H_{20}O_2N_2$ *	73	159	9·1	9·1
o-Xylyl	Me	$C_{20}H_{22}O_2N_2$ *	88	163	8·8	8·7
	Et	$C_{21}H_{24}O_2N_2$	84	176	8·3	8·3
α-Naphthyl	Me	$C_{23}H_{20}O_2N_2$ *	52	174	8·35	8·1
β-Naphthyl	Et	$C_{23}H_{22}O_2N_2$ *	50	141	8·0	7·8
Me	Me	$C_{13}H_{16}O_2N_2$	38	137	12·0	12·1
Et	Me	$C_{14}H_{16}O_2N_2$	68	105	11·3	11·4
	Et	$C_{15}H_{20}O_2N_2$	75	107	10·6	10·8
N-3 : 4 : 5-Trimethoxyphenylbenzimidoyl chloride	Me	$C_{21}H_{24}O_5N_2$	26	171	7·45	7·3
	Et	$C_{22}H_{26}O_5N_2$	35	154	6·8	7·0

* These compounds are yellow needles from methanol or ethanol; others are colourless needles.

Methyl β-N-*acetamido*-α-N-*phenylbenzimidoylcrotonate*. This *ester* was obtained from the base and acetic anhydride. It crystallises in colourless needles (from methanol), m. p. 163° [Found: N, 8·8 (Dumas), 8·6 (Middleton and Stuckey [3]). $C_{20}H_{20}O_3N_2$ requires N, 8·3%]. The *ethyl ester* was similarly obtained as colourless needles (from ethanol), m. p. 123° [Found: N, 8·2 (D.), N, 8·2 (M. and S.). $C_{21}H_{22}O_3N_2$ requires N, 8·0%].

Ethyl N-β-*benzamido*-α-N-*phenylbenzimidoylcrotonate*. The base (0·7 g.) was suspended in 10% aqueous sodium hydroxide (20 c.c.) and treated with benzoyl chloride (2 c.c.) for ½ hr. at room temperature. The *product* crystallises in colourless needles (from dilute ethanol), m. p. 120° (Found: N, 6·9. $C_{26}H_{24}O_3N_2$ requires N, 6·8%).

Hydrolysis. The base (0·5 g.) was refluxed in 70% sulphuric acid (10 c.c.) for ½ hr., cooled, and diluted with water (50 c.c.), and the acetophenone extracted with ether and identified as the 2 : 4-dinitrophenylhydrazone, m. p. 240°. The acidic layer was made alkaline and the amine extracted with ether and in each case identified as the benzoyl derivative.

Methyl 3-*methyl*-1 : 5-*diphenylpyrazole*-4-*carboxylate*. Methyl β-amino-α-*N*-phenylbenzimidoylcrotonate (0·5 g.) and phenylhydrazine (0·2 c.c.) in 50% acetic acid (20 c.c.) were refluxed for 3 hr. and the mixture, after cooling, was treated with water (20 c.c.). The precipitated *pyrazole derivative* crystallised from dilute ethanol (charcoal) in colourless needles, m. p. 132° (Found: N, 9·8. $C_{18}H_{16}O_2N_2$ requires N, 9·6%). The same compound was obtained by treating methyl β-amino-α-*N*-*m*-xylylbenzimidoylcrotonate with phenylhydrazine.

Ethyl 3-*methyl*-1 : 5-*diphenylpyrazole*-4-*carboxylate*. This was prepared by the action of phenylhydrazine on ethyl β-amino-α-*N*-phenylbenzimidoylcrotonate and ethyl β-amino-α-*N*-*o*-tolylbenzimidoylcrotonate. It formed colourless needles (from methanol), m. p. 122° as recorded in the literature.

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG. [*Received, May 24th*, 1956.]

[3] Middleton and Stuckey, *J. Pharm. Pharmacol.*, 1951, **3**, 829.

916. *The Preparation and Characterising Constants of the Phenylboron Chlorides.*

By E. W. ABEL, S. H. DANDEGAONKER, W. GERRARD, and M. F. LAPPERT.

FOR investigations of the diphenylboronous (Ph_2BX), and phenylboronic (Ph·BXX') series, diphenylboron chloride, Ph_2BCl, and phenylboron dichloride, $Ph·BCl_2$, were required in moderate quantities as synthetic intermediates. The methods described herein were developed, which we believe have advantages over earlier ones.

Diphenylboron chloride has previously been prepared, in low yield, by the interaction of diphenylmercury and phenylboron dichloride; [1] it was not characterised. The most recent preparation of phenylboron dichloride involved the interaction of a dialkyl phenylboronate and boron trichloride [2] (for earlier methods, see ref. 3), and subsequent separation of the dichloride from the alkyl dichloroboronite, $RO·BCl_2$, formed concurrently. The present method involves the interaction of boron trichloride with the appropriate anhydride in an inert solvent at −80° :

$$(Ph_2B)_2O + BCl_3 \longrightarrow 2Ph_2BCl + BOCl$$
$$Ph·BO + BCl_3 \longrightarrow Ph·BCl_2 + BOCl$$

[1] Michaelis and Becker, *Ber.*, 1894, **27**, 244.
[2] Brindley, Gerrard, and Lappert, *J.*, 1956, 824.
[3] Lappert, *Chem. Rev.*, 1956, in the press.

The boron oxychloride decomposed to boron trichloride and boron trioxide. The yields obtained were high and the method has the advantage that the required chlorides are the only liquid components. Further, the starting compounds, the anhydrides, are readily accessible. For the previous method of preparing phenylboron dichloride, the dialkyl phenylboronate which was starting material was most conveniently prepared from the anhydride [4] or the acid [4,5] and thus the present method eliminates one step.

Under similar conditions, there was no reaction between boron trifluoride and either anhydride.

Diphenylboronous anhydride was prepared from diphenylboronous acid, obtained by Letsinger and Skoog's method.[6] Physical constants for the acid have not previously been recorded, except for some erroneous early work (see ref. 6). Dehydration to the anhydride was effected at room temperature, by application of a vacuum: previous procedure [6,7] has involved heating (>200°), which we find leads to partial decomposition. Phenylboronic anhydride was obtained similarly by dehydration of the acid, which was obtained by Bean and Johnson's method.[8]

Each of the chlorides was chemically characterised by nearly quantitative hydrolysis to the appropriate anhydride. Phenylboron dichloride was also converted into *n*-butyl phenylchloroboronite, Ph·BCl·OBu, by equimolecular interaction [9] with di-*n*-butyl phenylboronate.

$$2Ph_2B{\cdot}Cl + H_2O \longrightarrow (Ph_2B)_2O + 2HCl$$
$$Ph{\cdot}BCl_2 + H_2O \longrightarrow PhBO + 2HCl$$

The characterising constants of the two chlorides and of diphenylboronous acid are shown in the Table. The value for the refractive index of phenylboron dichloride, quoted previously,[2] shows a misprint in the first decimal place. Both the chlorides were unimolecular, as shown by cryoscopy in *cyclo*hexane under anhydrous conditions with a pulse of dry nitrogen for agitation.[9]

The molecular refractivities for the two chlorides and for diphenylboronous acid are in fair agreement (see Table) with the values calculated from Vogel's data [10] on the phenyl group, hydroxylic oxygen, hydrogen, and chlorine, and Torssell's figures [5] on the atomic refractivity of boron in boronic (for $Ph{\cdot}BCl_2$) and boronous esters (for $Ph_2B{\cdot}Cl$ and $Ph_2B{\cdot}OH$).

Compound	B. p. (°/mm.)	n_D^{20}	d_4^{20}	Found: $[R_L]_D$	Calc.: $[R_L]_D$
$Ph_2B{\cdot}Cl$	98/0·1	1·6118	1·116	62·27	62·03
$Ph{\cdot}BCl_2$	66—66·5/11	1·5430	1·202	41·69	42·41
$Ph_2B{\cdot}OH$	Decomp.	1·5913	1·074	57·25	58·75

Experimental.—Preparation of anhydrides. Diphenylboronous acid (15·9 g.) (Found: C, 77·8; H, 6·0; B, 5·9. $C_{12}H_{11}OB$ requires C, 79·1; H, 6·0; B, 5·9%) was mechanically agitated at 20°/0·005 mm. for 2 hr. The white, crystalline residue (15·01 g., 99%) was diphenylboronous anhydride, which after recrystallisation from *n*-pentane had m. p. 116° (Found: C, 82·9; H, 5·5; B, 6·26. Calc. for $C_{24}H_{20}OB_2$: C, 83·3; H, 5·8; B, 6·24%). Water (0·78 g., 98%) had been evolved and was trapped as a condensate at −80°.

Phenylboronic anhydride, m. p. 218° (Found: B, 10·4. Calc. for C_6H_5OB: B, 10·4%), was obtained by heating the acid at 110—115°/760 mm. for 8—10 hr.

Diphenylboron chloride. Diphenylboronous anhydride (26·0 g., 1 mol.) in methylene dichloride (80 c.c.) was slowly (½ hr.) added to boron trichloride (8·8 g., 1 mol.) in the same solvent (30 c.c.) at −80°. Volatile matter was removed at 20°/10 mm. The resultant mixture comprised a suspension of a white solid, which was filtered off, in a liquid. The filtrate on distillation afforded *diphenylboron chloride* (22·57 g., 76%) (for constants see above) (Found: C, 72·6; H, 5·1; Cl, 17·6; B, 5·4%; *M*, 197. $C_{12}H_{10}ClB$ requires C, 72·0; H, 5·0; Cl, 17·7; B, 5·4%; *M*, 200) as a slightly fuming, colourless liquid.

Water (0·102 g., 1 mol.) in anhydrous diethyl ether (20 c.c.) was added during ¼ hr. to the chloride (2·26 g., 2 mols.) in the same solvent (30 c.c.). Volatile matter was removed at 15 mm.

[4] Brindley, Gerrard, and Lappert, *J.*, 1955, 2956.
[5] Torssell, *Acta Chem. Scand.*, 1954, 8, 1779.
[6] Letsinger and Skoog, *J. Amer. Chem. Soc.*, 1955, **77**, 2491.
[7] Neu, *Chem. Ber.*, 1955, **88**, 1761.
[8] Bean and Johnson, *J. Amer. Chem. Soc.*, 1932, **54**, 4415.
[9] Brindley, Gerrard, and Lappert, *J.*, 1956, 824.
[10] Vogel, *J.*, 1946, 133; 1948, 616, 644, 654.

The white crystalline solid which remained was washed with *n*-pentane (10 c.c.) and freed from solvent in a vacuum-desiccator. This product was diphenylboronous anhydride (1·87 g., 96%), m. p. 114° (Found : B, 6·3%).

Phenylboron dichloride. Boron trichloride (11·75 g., 1 mol.) at −39° was added dropwise to phenylboronic anhydride (10·10 g., 1 mol.) in methylene dichloride (150 c.c.) at −80°. The mixture was slowly (12 hr.) allowed to attain room temperature. Fractional distillation afforded a fore-run of solvent and then phenylboron dichloride (6·17 g.) (Found : Cl, 44·4; B, 6·9%; *M*, 155. Calc. for $C_6H_5Cl_2B$: Cl, 44·6; B, 6·9%; *M*, 159), as a violently fuming, colourless liquid. The residue contained unchanged anhydride (5·64 g.), m. p. 217—218° (Found : B, 10·4%). The overall yield of phenylboron dichloride was 90%. Substantially similar results were obtained when chloroform, benzene, or *n*-pentane was the solvent and when the molar ratio of anhydride to trichloride was 1·5 : 1. The recovery of unchanged anhydride is probably due to its low solubility.

The dichloride (2·346 g.) was hydrolysed by water (0·27 g.) in the presence of *n*-pentane (10 c.c.). Volatile matter was removed under vacuum. The resultant crystalline residue was washed with *n*-pentane and freed from solvent in a vacuum-desiccator. This product was phenylboronic anhydride (1·45 g., 94·5%), m. p. 217—218° (Found : B, 10·3%).

The dichloride afforded *n*-butyl phenylchloroboronite (92%), b. p. 82°/0·1 mm., $n_D^{22\cdot5}$ 1·4960 (Found : Cl, 17·8; B, 5·5. Calc. for $C_{10}H_{14}OClB$: Cl, 18·0; B, 5·5%), by interaction in equimolecular proportions with di-*n*-butyl phenylboronate.

Lack of reaction between boron trifluoride and the anhydrides. Neither anhydride when dissolved in methylene dichloride (same concentration as for BCl_3 reaction) reacted with boron trifluoride [11] at −80° or at 20°. This was demonstrated by passage of the gas for 1 hr., removal of volatile matter, and quantitative isolation of the appropriate anhydride, which was then characterised.

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[11] Booth and Willson, *Inorg. Synth.*, 1939, **1**, 21.

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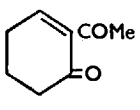
917. *Attempts at the Meyer–Schuster Rearrangement on 2-Ethynyl-2-hydroxycyclohexanone.*

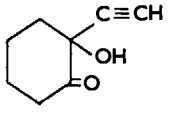
By (Miss) M. E. MCENTEE, A. R. PINDER, HERCHEL SMITH, and R. E. THORNTON.

WE [1] have recently been interested in the problem of preparing 2-acetyl*cyclo*hex-2-en-1-one (I) a much sought-after compound in these laboratories, because of its obvious potentialities as an intermediate in steroid synthesis.[2]

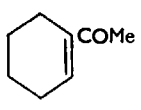
A superficial view might indicate that the alcohol (II) should provide it by a Meyer–Schuster rearrangement (*e.g.*, in formic acid [3] or with an acid-treated ion-exchange resin in acetic acid [4]) or by dehydration to an intermediate enyne followed by hydration of the triple bond. Such processes, which all depend on the readiness with which the carbon atom initially carrying the hydroxyl group becomes cationic,[3,4] will, however, be strongly disfavoured in the compound (II) by the electron-withdrawal from carbon to oxygen in the carbonyl group. Accordingly, our chief efforts to obtain the ketone (I) or its relatives have been directed into other channels.[1,5] However, the ready availability of the alcohol



(I)



(II)



(III)

(II) from *cyclo*hexane-1 : 2-dione and sodium acetylide or the bismagnesium iodide of acetylene has prompted us to study its reaction to Meyer–Schuster conditions.

The alcohol (II) failed to rearrange in formic acid under the Newman conditions [4]

[1] Smith, *J.*, 1953, 803; Pinder and Smith, *J.*, 1954, 113.
[2] Cf. Peak and Robinson, *J.*, 1937, 1581.
[3] Hamlet, Henbest, and Jones, *J.*, 1951, 2652.
[4] Newman, *J. Amer. Chem. Soc.*, 1953, **75**, 4740.
[5] Jaeger and Smith, *J.*, 1955, 646.

or with phosphoric anhydride in benzene.[6] Prolonged heating gave low yields of 1-acetyl-*cyclo*hexene (III) the formation of which in the reactions not involving formic acid, may possibly involve disproportionation.

We have found it convenient to prepare *cyclo*hexane-1 : 2-dione from 2-chloro*cyclo*-hexanone by hydrolysis with boiling water and oxidation with ferric chloride without isolation of the intermediate 2-hydroxy*cyclo*hexanone. The overall yield from *cyclo*-hexanone is higher than that obtained by the standard method,[7] and the process is rapid and avoids the use of selenium dioxide. A similar method has been used to prepare *cyclo*pentane-1 : 2-dione from 2-chloro*cyclo*pentanone.[8]

Experimental.—cyclo*Hexane*-1 : 2-*dione*. 2-Chloro*cyclo*hexanone (90 g.) was refluxed in water (800 c.c.) with stirring until all had dissolved. Ferric chloride (333 g.) in water (167 c.c.) was added during 90 min. and when the solution had cooled to 40° ammonium sulphate (240 g.) was added. Continuous ether-extraction for 6 hr. gave a residue (69 g.), distillation of which gave *cyclo*hexane-1 : 2-dione (33 g., 43%), b. p. 96—100°/24 mm.

2-*Ethynyl*-2-*hydroxy*cyclo*hexanone* (II). (*a*) *cyclo*Hexane-1 : 2-dione (16 g.) in dry ether (25 c.c.) was added during 30 min. with stirring to a solution of sodium acetylide (from the metal, 7 g.) in liquid ammonia (300 c.c.) through which acetylene was passing. The mixture was stirred for a further 2—3 hr., ammonium chloride (16 g.) was added, and the ammonia allowed to evaporate. Water (200 c.c.) was added and the mixture thoroughly extracted with ether. Evaporation of the dried extracts gave an oil (12 g.) which distilled (short Vigreux column) at 104—106°/25 mm. The distillate (9·6 g.) soon solidified; a portion separated from light petroleum (b. p. 40—60°) in needles, m. p. 51·5—52·5° (Jaeger and Smith [5] give 50—52°). The ethynyl group was determined by Hanna and Siggia's method [9] (Found : C, 69·2; H, 7·4; C:CH, 17·6. Calc. for $C_6H_{10}O_2$: C, 69·5, H, 7·3; C:CH, 18·1%). Infrared absorption : bands at 3390, 3250, 2130, and 1710 cm.$^{-1}$. The alcohol was fairly soluble in water with neutral reaction and gave no colour with ferric chloride.

The 2 : 4-*dinitrophenylhydrazone* separated from ethanol as needles, m. p. 161° (Found : C, 52·5; H, 4·6; N, 17·7. $C_{14}H_{14}O_5N_4$ requires C, 52·8; H, 4·4; N, 17·6%), absorption max. in $CHCl_3$ at 360 mμ (ε 16,700). The *phenylhydrazone* separated from methanol as needles, m. p. 146° (Found : C, 73·6; H, 7·05. $C_{14}H_{16}ON_2$ requires C, 73·7; H, 7·05%).

(*b*) *cyclo*Hexane-1 : 2-dione (10 g.) in benzene (100 c.c.) was added dropwise with stirring to the bismagnesium iodide derivative [10] from acetylene [from ethylmagnesium iodide (330 g.) and gaseous acetylene] in benzene (450 c.c.) under nitrogen. After 12 hr. at room temperature the mixture was refluxed for 2 hr. Ice-cold saturated aqueous ammonium chloride (103 g.) was added to the cooled solution, and the organic layer was separated, washed with aqueous sodium hydroxide, dried, and evaporated to an oil (5 g.), distillation of which gave a fraction, b. p. 85°/12 mm. Crystallisation from light petroleum (b. p. 40—60°) gave the 2-ethynyl-2-hydroxy*cyclo*hexanone (2·0 g.), m. p. 53—54° (Found : C, 69·4; H, 7·2. Calc. for $C_8H_{10}O_2$: C, 69·5; H, 7·3%).

The alcohol (II) was recovered unchanged after treatment with formic acid as described by Chanley [11] and with acid-treated Dowex-50 as described by Newman.[4] Heating for 5—5·5 hr. gave products which were mostly involatile tars, but in each case 1-acetyl*cyclo*hexene (III) (*ca.* 10%), b. p. 65—70°/10 mm., was also obtained (Found : C, 77·1; H, 9·6. Calc. for $C_8H_{12}O$: C, 77·4; H, 9·7%). The 2 : 4-dinitrophenylhydrazone of this had m. p. and mixed m. p. 200—201° (Found : C, 55·1; H, 5·0. Calc. for $C_{14}H_{16}O_4N_4$: C, 55·25; H, 5·3%). Treatment of the alcohol (II) with phosphoric anhydride as described by Saunders [6] also gave 1-acetyl-*cyclo*hexene (25%).

2-Ethynyl-2-hydroxy*cyclo*pentanone,[12] b. p. 86°/12 mm., prepared as described under (*b*), had infrared absorption bands at 3390, 3279, 2101, and 1745 cm.$^{-1}$ and failed to rearrange in formic acid.

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[6] Saunders, *Org. Synth.*, 1949, **29**, 1.
[7] Hach, Banks, and Diehl, *ibid.*, 1952, **32**, 35.
[8] Dutch P. 58,279; *Chem. Abs.*, 1947, **41**, 4807; Inhoffen and Kramer, *Chem. Ber.*, 1954, **87**, 488.
[9] Hanna and Siggia, *Analyt. Chem.*, 1949, **21**, 1469.
[10] Bachmann and Chemerda, *J. Amer. Chem. Soc.*, 1948, **70**, 1468.
[11] Chanley, *ibid.*, p. 244.
[12] Dane, Höss, Eder, Schmitt, and Schön, *Annalen*, 1938, **536**, 183.