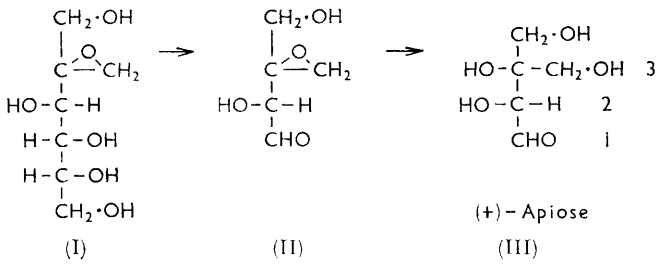
479. *The Synthesis of Branched-chain Sugars. Part I. The Synthesis of (+)-Apiose.*

By A. Khalique.

Apiose, which occurs in widely different species of plants,[1] has the same branched carbon structure as isoprene and its presence in several rubber producing plants [2] suggests a possible metabolic link between sugars and isoprenoid compounds. Its structure and configuration have been determined [3] and confirmed by synthesis of the D(+)-[4] and the L(−)-form.[5] The present work describes a short and easy synthesis of D(+)-apiose from *keto*-D-fructose penta-acetate, providing evidence for the D-structure of naturally occurring apiose and furnishing an alternative proof for the configuration.

The epoxide (I), prepared [6] by the action of diazomethane on *keto*-D-fructose penta-acetate and subsequent deacetylation, is converted by sodium metaperiodate into a syrupy epoxy-aldehyde (II), characterised as its crystalline phenylosazone. Acid-hydrolysis



of the aldehyde (II) produced syrupy D(+)-apiose (III), $[\alpha]_D^{32}$ +4·2° (in H_2O). Its rate of travel on a paper chromatogram was identical with that of rhamnose (cf. Bell *et al.*[1]) and natural D(+)-apiose, $[\alpha]_D^{19}$ +9·1° ± 0·5° (in H_2O).[7] The identity was confirmed by a mixed melting point determination of the *p*-bromophenylosazones and of the crystalline di-*O*-isopropylidene derivative (cf. Bell *et al.*[1]) with the correct specific rotations. The configuration is thus proved and confirms Shafizadeh's designation [1] of the sugar as the D-*glycero*-aldotetrose.

Experimental.—1,3,4,5-*Tetra*-O-*acetyl*-D-*fructose*. This was obtained by Hudson and Brauns's method [8] as monoclinic crystals, m. p. 131—132° (from methanol–ether), $[\alpha]_D^{25}$ −102·5° (*c* 1·15 in chloroform) (Found: C, 48·6; H, 5·6; Ac, 50·3. Calc. for $C_{14}H_{20}O_{10}$: C, 48·3; H, 5·8; Ac, 49·4%) (lit., m. p. 131—132°; $[\alpha]_D^{20}$ −101·6°).

1,3,4,5,6-*Penta*-O-*acetyl*-keto-D-*fructose*, prepared (25%) from the above compound,[8] had m. p. 65—68°, $\lambda_{max.}$ 280 mμ (log ε 1·5), $[\alpha]_D^{30}$ +17·8° (*c* 2·82 in chloroform) (Found: C, 49·5;

[1] Hudson, *Adv. Carbohydrate Chem.*, 1949, **4**, 57; 1948, **3**, 21; Shafizadeh, *ibid.*, 1956, **11**, 275; Nordström and Swain, *J.*, 1953, 2764; Nordström, Swain, and Hamblin, *Chem. and Ind.*, 1953, 85; Farooq, Varshney, and Rahman, *Naturwiss.*, 1957, **44**, 444; Chopra, Badwar, and Ghosh, "Poisonous Plants of India," Government of India Press, Calcutta, 1949, p. 511; Bell, Ishwerwood, and Hardwick, *J.*, 1954, 3702; Patrick, *Nature*, 1956, **178**, 216.

[2] Chrastil, *Chem. Listy*, 1956, **50**, 163; cf. Patrick, ref. 1.

[3] Raphael and Roxburgh, *J.*, 1955, 3405; Raphael, *Angew. Chem.*, 1957, **69**, 516.

[4] Gorin and Perlin, *Canad. J. Chem.*, 1958, **36**, 480.

[5] Weygand and Schmiechen, *Chem. Ber.*, 1959, **92**, 535.

[6] Wolfrom, Weisblat, and Waisbrot, *J. Amer. Chem. Soc.*, 1941, **63**, 632.

[7] Stone (née Hardwick), Ph.D. Thesis, Cambridge, and "Methods of Carbohydrate Chemistry," under the heading of Apiose (in the press).

[8] Hudson and Brauns, *J. Amer. Chem. Soc.*, 1915, **37**, 2736; Pacsu and Rich, *ibid.*, 1933, **55**, 3022; Wolfrom and Thompson, *ibid.*, 1934, **56**, 880; Steele, *J.*, 1918, **113**, 261; Haworth, Hirst, and Learner, *J.*, 1927, 1040.

H, 5·5; Ac, 56·5. Calc. for $C_{16}H_{22}O_{11}$: C, 49·2; H, 5·7; Ac, 55·1%) {lit.,[8,9] m. p. 70°, $[\alpha]_D^{20}$ +34·7°; m. p. 65—68°, $[\alpha]_D^{16}$ +13·0°, $\lambda_{max.}$ 280 mμ (log ε 1·5)}; it reduced hot Fehling's solution and gave a positive Pacsu *keto*-acetate test.[10]

2-*Deoxy*-2,2-*methyleneoxy*-D-arabo-*hexitol penta-acetate*. The last-mentioned compound (3·9 g.)in sodium-dried ether (50 c.c.) was treated with ethereal diazomethane (0·42 g. in 50 c.c.) at 0° for 12 hr. Filtration and evaporation yielded a syrup which crystallised from dried ether at 0° during 2—3 weeks, giving needles (0·85 g., 22%), m. p. 86—87°, $[\alpha]_D^{25}$ +32° (*c* 2 in chloroform) (Found: C, 50·2; H, 5·5. Calc. for $C_{17}H_{24}O_{11}$: C, 50·4; H, 5·9%) {lit.,[6] m. p. 86—87°, $[\alpha]_D^{24}$ +32° (*c* in chloroform)}. It gave a negative Pacsu *keto*-acetate test [10] and produced no colour [6] with hot methanolic potassium hydroxide, but reduced Tollens's reagent in pyridine.

2-*Deoxy*-2,2-*methyleneoxy*-D-arabo-*hexitol* (I). A solution of the preceding acetate (2·76 g.) in absolute methyl alcohol (20 c.c.) was deacetylated with barium methoxide (3·4 g., 1 equiv.) in the same solvent (40 c.c.) at 0° for 90 min., then diluted with water (40 c.c.); part (61%) of the barium was removed by carbonation, and the rest by adding the calculated amount of oxalic acid; deionisation, evaporation under reduced pressure to a syrup (1·19 g., 96%), and crystallisation from absolute alcohol gave the compound (I) (0·35 g., 27%), m. p. 135—136° (Found: C, 42·8; H, 7·5. Calc. for $C_7H_{14}O_6$: C, 43·3; H, 7·3%) (lit.,[6] m. p. 136°).

3-*Deoxy*-3,3-*methyleneoxy*-D-glycero-*tetrose* (II). The compound (I) (1·9 g.), in water (10 c.c.), was treated with sodium metaperiodate (4·2 g., 2 equiv.) and sodium hydrogen carbonate (0·8 g.) in water (40 c.c.) for 2 hr. at room temperature; the mixture was then deionised over mixed-bed exchange resin (V; Merck). The effluent and washings (80 c.c.) were evaporated to dryness under reduced pressure, and the residue extracted with warm absolute alcohol (3 × 20 c.c.); evaporation of the extracts under reduced pressure gave the epoxy-aldehyde (1 g., 80%) as a thin syrup.

This syrup (1 g.) was heated with phenylhydrazine (3·2 g.) in alcohol (15 c.c.) under reflux for 90 min. Evaporation gave a brownish-black tar that was extracted with boiling water (3 × 20 c.c.). Concentration of the extracts to *ca.* 10 c.c. and cooling afforded an *osazone* (350 mg., 16%) that recrystallised from water in needles, m. p. 124—125° (Found: C, 65·4; H, 6·1; N, 18·2. $C_{17}H_{18}O_2N_4$ requires C, 65·8; H, 5·8; N, 18·1%).

(+)-*Apiose* (III). The epoxy-aldehyde (II) (0·8 g.), in alcohol (25 c.c.), was treated with N-hydrochloric acid (5 c.c.) at room temperature for 3 hr. The mixture was then diluted with water (20 c.c.), deionised over an anion-exchange resin (II; Merck; 25 g.) presaturated with carbon dioxide. The effluent (80 c.c.), on evaporation under reduced pressure, gave a brown syrup (0·27 g., 29%). This was dissolved in a little methanol, filtered twice through charcoal, and recovered under reduced pressure, giving (+)-apiose as a colourless syrup. This gave a positive Fehling's test and a cherry-red colour in Tauber's test, and had $[\alpha]_D^{32}$ ±4·2° (*c* 0·48 in H_2O). The *p*-bromophenylosazone formed bright yellow needles (from hot dilute ethanol), m. p. and mixed m. p. 206—208° (lit.,[3] 206—208°). The di-*O*-isopropylidene derivative formed plates, m. p. and mixed m. p. 81—83°, $[\alpha]_D^{30}$ +55·5° (*c* 1·1 in EtOH) (Found: C, 57·5; H, 7·6. Calc. for $C_{11}H_{18}O_5$: C, 57·4; H, 7·9%) (lit.,[1] m. p. 81—83°; $[\alpha]_D^{19}$ +56·4°). The product (III) was chromatographed on Whatman No. 1 paper with benzene–butanol–pyridine–water (1 : 5 : 3 : 3), and the paper was sprayed with aniline hydrogen phthalate and dried at 105°. The spot produced was the same as that given by rhamnose (Merck) or authentic natural D(+)-apiose.

The author expresses his gratitude to Dr. S. Trippett for advice and encouragement, to Professor B. Lythgoe, F.R.S., for suggestions, to Professor R. A. Raphael for helpful discussions, and to Dr. S. Siddiqui, F.R.S., and Dr. M. Q. Khuda of Pakistan Council of Scientific and Industrial Research for the facilities of work in their laboratories.

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[*Received, September 29th*, 1961.]

[9] Bredereck, Horschele and Huber, *Chem. Ber.*, 1953, **86**, 1271; Bourne and Stephens, *J.*, 1954, 4009.

[10] Pacsu and Rich, *J. Amer. Chem. Soc.*, 1933, **55**, 3018; Cramer and Pacsu, *ibid.*, 1937, **59**, 1468.

480. *Introduction of a Sulphonamido-group by Means of Benzenesulphonyl Azide: An Unusual Substitution Pattern for Anthracene.*

By J. F. Tilney-Bassett.

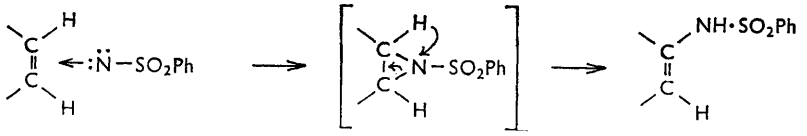
The decomposition of arenesulphonyl azides in aromatic solvents results in the introduction of a sulphonamido-group into the aromatic nucleus of the solvent:[1,2]

$$Ar{\cdot}SO_2{\cdot}N_3 \longrightarrow Ar{\cdot}SO_2{\cdot}N\!< + N_2$$
$$Ar{\cdot}SO_2{\cdot}N\!< + Ar'H \longrightarrow Ar{\cdot}SO_2{\cdot}NHAr'$$

Edmisson and his co-workers [2] have shown that benzenesulphonyl azide behaves as a free radical since various monosubstituted benzene derivatives show little difference in reactivity towards it, and that the free radical is electrophilic in character because of the predominant *ortho–para*-substitution of toluene, chlorobenzene, phenol, and anisole and *meta*-substitution of methyl benzoate.

The reaction of benzenesulphonyl azide with anthracene, which is described in this Note, was carried out in order to gain further insight into the nature of the initial attack. Reaction of benzenesulphonyl azide with a refluxing saturated solution of anthracene in chlorobenzene yielded a mixture of anthracenemonosulphonamides from which all three isomers were obtained, together with comparable amounts of *o*- and *p*-chlorobenzenesulphonamide. 1-Benzenesulphonamidoanthracene was isolated in 55% yield, based on anthracene lost in the reaction. The 9-isomer was obtained in 15% yield. The 2-isomer was isolated but was not completely separated from *N*-*p*-chlorophenylbenzenesulphonamide; its yield is estimated as 5—15%.

Normal free-radical substitution of anthracene, as well as electrophilic and nucleophilic substitution, take place exclusively at position 9. However, theoretical calculations of double-bond localisation energies [3] indicate that double-bond reagents should attack anthracene at the 1,2-bond, and this has been confirmed for attack by osmium tetroxide. The preponderance of attack at position 1 by benzenesulphonyl azide is thus more consistent with the reagent's behaving as a double-bond reagent than as a free radical. The formation of substitution rather than addition products could be explained by the supposition that any intermediate or transition state formed by attack on a localised double bond could readily rearrange to a substitution product.



Such a mechanism would be consistent with Edmisson's results [2] since the direction of the rearrangement step would be expected to be strongly influenced by polar factors.

Experimental.—A mixture of benzenesulphonyl azide (6·0 g.) with chlorobenzene (10 c.c.) was added dropwise during 1 hr. to a refluxing solution of anthracene (30 g.) in chlorobenzene (50 c.c.) under nitrogen. Refluxing was continued for 10 hr., then the mixture was allowed to cool. The anthracene which crystallised was filtered off and recrystallised from toluene. The mother-liquors were combined and the solvents removed, leaving a residue which was

[1] Curtius, *J. prakt. Chem.*, 1930, **125**, 303.
[2] Dermer and Edmisson, *J. Amer. Chem. Soc.*, 1955, **77**, 70; Heacock and Edmisson, *ibid.*, 1960, **82**, 3460.
[3] Brown, *J.*, 1950, 3249; Scherr, *J. Chem. Phys.*, 1953, **21**, 1582.

extracted with boiling benzene (200 c.c.). This left a residue (1·16 g.) of 1-*benzenesulphonamidoanthracene* which after recrystallisation from ethyl acetate had m. p. and mixed m. p. 233° (cf. below) (Found: C, 71·6; H, 4·7. $C_{20}H_{15}NSO_2$ requires C, 72·0; H, 4·5%). The benzene solution was extracted with 2N-sodium hydroxide (2 × 100 c.c.). The organic layer was evaporated, giving anthracene, m. p. 213—215° after crystallisation. No sulphonamides were obtained by chromatography of this fraction. The total recovery of anthracene was 27·3 g. The alkaline extract was acidified and extracted with ether. The ethereal solution was dried and the ether removed, leaving a gum (6·4 g.). This was boiled with benzene, leaving a residue (0·43 g.) of the 1-isomer, and the solution was chromatographed on alumina. Elution with benzene yielded *N-p*-chlorophenylbenzenesulphonamide, m. p. 131° (1·49 g.), followed by 9-*benzenesulphonamidoanthracene* (0·75 g.), m. p. and mixed m. p. 250° (Found: C, 71·7; H, 4·7%). Further elution with benzene gave the 1-isomer (1·14 g.; total yield 2·72 g.), followed by a mixture (1·65 g.) which, when extracted with ether, gave a residue that on crystallisation from acetone–ligroin gave 2-*benzenesulphonamidoanthracene*, m. p. and mixed m. p. 184° (Found: C, 72·2; H, 4·6%), and an extract yielding *N-p*-chlorophenylbenzenesulphonamide, m. p. 121°. No other products were obtained on further elution.

The amidoanthracene isomers were identified by comparison with specimens prepared by treating anthracene-1-, -2-, and -9-amine, respectively, with benzenesulphonyl chloride and pyridine. This method gave the 1-amide, m. p. 232·5—233·5° (from wet methanol or ethyl acetate), the 2-amide, m. p. 183—184° (from methanol), and the 9-amide, needles, m. p. 250° (from ethyl acetate–ligroin).

The author thanks the University of Sheffield for an Imperial Chemical Industries Research Fellowship.

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[*Received, October 26th*, 1961.]

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481. *Preparation of Quinolines by Reductive Cyclisation by Means of Cyclohexene and Palladium–Charcoal.*

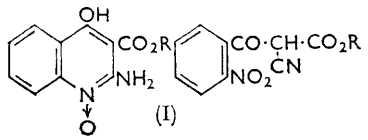
By R. T. Coutts and D. G. Wibberley.

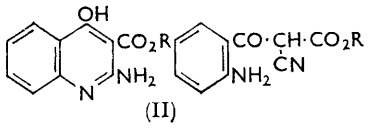
The preparation of hydroxamic acids related to quinoline by reductive cyclisation of suitable *o*-nitrobenzoylacetates with hydrazine hydrate and palladium–charcoal [1] was only partly successful. Hydrogen-transfer by means of cyclohexene and palladium–charcoal [2] has now been applied to a similar series of esters. Even with a short reflux time no 1,2-dihydro-1-hydroxy-2-oxoquinolines were formed; instead quinolines were obtained in good yield (cf. Table). Partial reduction of the nitro-group, with formation of *N*-oxides, occurred in three cases. The m. p. of ethyl 4-hydroxy-2-methylquinoline-3-carboxylate differed from that previously quoted [3] but the structure of our product was proved by conversion into 4-hydroxy-2-methylquinoline.

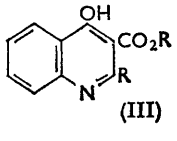
In the reductive cyclisation of ethyl α-cyano-α-*o*-nitrobenzoylacetate an expected product, ethyl 2-amino-4-hydroxyquinoline-3-carboxylate was formed, but in low yield. Major products were the adducts (I and II; R = Et). The structure of the adduct (I; R = Et) was proved by its conversion into, and re-formation from, its component

[1] Coutts, Hooper, and Wibberley, *J.*, 1961, 5058.
[2] Braude, Linstead, and Woolridge, *J.*, 1954, 3586.
[3] Gould and Jacobs, *J. Amer. Chem. Soc.*, 1939, **61**, 2890; Bangdivala and Desai, *J. Indian Chem. Soc.*, 1954, **31**, 553.

oxide and benzoylacetate. The latter yielded a similar adduct with 2-aminopyridine. Ethyl 2-amino-4-hydroxyquinoline-3-carboxylate was produced on reduction of this *N*-oxide, or of the adduct (I; R = Et), and on hydrolysis of the


(I)


(II)


(III)

adduct (II; R = Et). Attempts to isolate ethyl α-anthraniloyl-α-cyanoacetate resulted in lactamisation to 3-cyano-1,2-dihydro-4-hydroxy-2-oxoquinoline. Similar adducts (I and II; R = Me) and derived compounds were isolated from methyl α-cyano-α-*o*-nitrobenzoylacetate.

X in *o*-NO_2·C_6H_4X	Reflux time (hr.)	Product	Yield (%)
CO·CH_2Ac	9	4-Hydroxy-2-methylquinoline 1-oxide	61
CO·CHAc·CO_2Me	20	III; R = R′ = Me	74
CO·CHAc·CO_2Et	20	III; R = Et, R′ = Me	60
CO·CHAc·CO_2Et	3	III; R = Et, R′ = Me	26
		Corresponding 1-oxide	14
CO·CH_2·CO_2Me	20	1,2-Dihydro-4-hydroxy-2-oxoquinoline	87
CO·CH(CO_2Et)$_2$	24	Et 1,2-dihydro-4-hydroxy-2-oxoquinoline-3-carboxylate	30
CH:C(CO_2Et)$_2$	24	Et 1,2-dihydro-2-oxoquinoline-3-carboxylate	47
CH:CH·CO_2Me	3	1,2,3,4-Tetrahydro-2-oxoquinoline	54
	20	1,2,3,4-Tetrahydro-2-oxoquinoline	81
CH_2·CO·CO_2Me	3	Me indole-2-carboxylate	72
CO·CH(CN)·CO_2Et	3	Adduct (II; R = Et)	16
		Adduct (I; R = Et)	43
CO·CH(CN)·CO_2Et	24	Adduct (II; R = Et)	32
		III; R = Et, R′ = NH_2	15
CO·CH(CN)·CO_2Me	3	Adduct (II; R = Me)	10
		Adduct (I; R = Me)	51
CO·CH(CN)·CO_2Me	20	Adduct (II; R = Me)	39
		Adduct (I; R = Me)	3
		III; R = Me, R′ = NH_2	4

Experimental.—Infrared spectra (potassium chloride discs) were determined on a Perkin–Elmer " Infracord " spectrophotometer. Equivalent weights were determined, except where otherwise stated, by non-aqueous titration with perchloric acid.

General method of reductive cyclisation. The *o*-nitro-compound (1·0 g.), redistilled cyclohexene (3·0 ml.), 10% palladium–charcoal (0·1 g.), and ethanol (10 ml.) were refluxed for the stated time. Any compound which separated with the charcoal was isolated by extraction with acid, or a suitable solvent, and further crops, or additional products were obtained by concentration of the filtrate. The known compounds recorded in the Table gave correct analyses for carbon, hydrogen, and nitrogen and, with the exception of ethyl 4-hydroxy-2-methylquinoline-3-carboxylate, had the m. p.s quoted in the literature.

Methyl 4-hydroxy-2-methylquinoline-3-carboxylate separated in needles (from ethanol), m. p. 238—239° (Found: C, 66·4; H, 5·0; N, 6·3%; equiv., 221. $C_{12}H_{11}NO_3$ requires C, 66·4; H, 5·1; N, 6·45%; equiv., 217). Alkaline hydrolysis yielded the corresponding acid, m. p. 243—244° (decomp.),[4] which was decarboxylated at 250° to 4-hydroxy-2-methylquinoline,[5] m. p. 240—241°.

Ethyl 4-hydroxy-2-methylquinoline-3-carboxylate separated in needles (from ethanol), m. p. 229—230° (Found: C, 67·35; H, 5·9; N, 6·1%; equiv., 226. $C_{13}H_{13}NO_3$ requires C, 67·5;

[4] McCluskey, *J. Amer. Chem. Soc.*, 1922, **44**, 1573.
[5] Gabriel and Gerhard, *Ber.*, 1921, **54**, 1069.

H, 5·6; N, 6·05%; equiv., 231). 4-Hydroxy-2-methylquinoline and the 3-carboxylic acid were isolated as described for the methyl ester. Acetylation of the ester gave a derivative, m. p. 90—91°, which may be the product which previous authors [3] have isolated in the attempted preparation of this ester.

Ethyl 1,2,-*dihydro*-2-*oxoquinoline*-3-*carboxylate* separated in prisms (from ethanol), m. p. 163—164° (Found: C, 66·2; H, 4·5. $C_{12}H_{11}NO_3$ requires C, 66·4; H, 5·1%), and yielded 1,2-dihydro-2-oxoquinoline-3-carboxylic acid,[6] m. p. 332° (decomp.), on hydrolysis.

The *adduct* (I; R = Et) separated in yellow prisms (from ethanol), m. p. 150—151° (decomp.) [Found: C, 56·2; H, 4·45; N, 10·9%; *M* (Rast), 476; equiv., 508; equiv. (aqueous back-titration), 251. $C_{24}H_{22}N_4O_9$ requires C, 56·5; H, 4·3; N, 11·0%; *M*, 510], $\nu_{max.}$ 3390w, 3270w (N–H and O–H); 2200m (C≡N), 1680s, 1670s, 1620m (C=O); 1530m, 1340m, 850w cm.$^{-1}$ (NO_2). This adduct (1·3 g.) was stirred with 2N-hydrochloric acid (5·0 ml.), to yield ethyl α-cyano-α-*o*-nitrobenzoylacetate (0·57 g.) and *ethyl* 2-*amino*-4-*hydroxyquinoline*-3-*carboxylate* 1-*oxide hydrochloride* (0·53 g.), m. p. 261—262° (decomp.) (from alcohol–ether) [Found: C, 51·1; H, 4·7 N, 9·4; Cl, 12·5%; equiv. (aqueous back-titration), 142. $C_{12}H_{12}N_2O_4$,HCl requires C, 50·6; H, 4·6; N, 9·8; Cl, 12·5%; equiv., 142·5], $\nu_{max.}$ 3410m, 3080m (N–H and O–H); 1660s, 1625s (C=O); 1570m, 1360m cm.$^{-1}$ (*N*-oxide). The free N-*oxide* had m. p. 189—190° (from ethanol) (Found: N, 11·0%; equiv., 252. $C_{12}H_{12}N_2O_4$ requires N, 11·3%; equiv., 248). Treatment of the *N*-oxide (0·03 g.) in ethanol (0·5 ml.) with ethyl α-cyano-α-*o*-nitrobenzoylacetate (0·04 g.) in ethanol (0·5 ml.) gave an immediate precipitate of the yellow adduct (I; R = Et).

The *adduct* (II; R = Et) separated in prisms (from acetic acid), m. p. 198—199° (decomp.) (Found: C, 61·7; H, 4·7; N, 12·0%; equiv., 458. $C_{24}H_{24}N_4O_6$ requires C, 62·05; H, 5·2; N, 12·05%; equiv., 464), $\nu_{max.}$ 3450w, 3100—2780bm (N–H and O–H); 2220m (C≡N); 1680s, 1640sh, 1610m (C=O); 1530s, 1310m cm.$^{-1}$ (*N*-oxide).

Ethyl 2-*amino*-4-*hydroxyquinoline*-3-*carboxylate*. (*a*) This *ester* was obtained on reductive cyclisation of ethyl α-cyano-α-*o*-nitrobenzoylacetate by cooling the filtrate from the adduct (II; R = Et); it formed pale yellow prisms (from ethanol), m. p. 271—272° (Found: C, 61·7; H, 5·2; N, 11·7%; equiv., 230. $C_{12}H_{12}N_2O_3$ requires C, 62·05; H, 5·2; N, 12·05%; equiv., 232), $\nu_{max.}$ 3330—3030bs (N–H and O–H); 1670s, 1630s, 1610s cm.$^{-1}$ (C=O). (*b*) The yellow adduct (I; R = Et) (1·67 g.) was reduced by the general method to give the ester (0·57 g.). (*c*) Ethyl 2-amino-4-hydroxyquinoline-3-carboxylate 1-oxide (0·14 g.) similarly yielded the same ester (0·1 g.). (*d*) The adduct (II; R = Et) (0·48 g.) was stirred with N-sodium hydroxide (10 ml.) at room temperature. The clear solution (0·5 hr.) was adjusted to pH 8·0, the ester (0·2 g.; m. p. and mixed m. p. 271—272°) being precipitated. The filtrate, on treatment with an excess of hydrochloric acid, gave 3-cyano-1,2-dihydro-4-hydroxy-2-oxoquinoline (0·18 g.), m. p. 292—295° (decomp.) (from ethanol) [lit.,[7] m. p. " around 300° " (decomp.)] (Found: C, 63·9; H, 4·1; N, 14·8%; equiv. (aqueous back-titration), 184. Calc. for $C_{10}H_6N_2O_2$: C, 64·5; H, 3·2; N, 15·05%; equiv., 186).

The ester (0·42 g.), on treatment with hydriodic acid by Gabriel's method,[7] yielded 2-amino-4-hydroxyquinoline, prisms (from ethanol), m. p. and mixed m. p. 305—307°.

Adduct of 2-*aminopyridine with ethyl* α-*cyano*-α-*o*-*nitrobenzoylacetate*. A yellow *adduct* (1·3 g.), m. p. 156—157° (decomp.), separated immediately on mixing of solutions of 2-aminopyridine (0·5 g.) in ethanol (5·0 ml.) and ethyl α-cyano-α-*o*-nitrobenzoylacetate (1·0 g.) in ethanol (5·0 ml.) (Found: C, 57·0; H, 4·4 N, 15·9%; equiv., 353. $C_{17}H_{16}N_4O_5$ requires C, 57·3; H, 4·5 N, 15·7%; equiv., 356); it had $\nu_{max.}$ 3330m, 3180w, 2980w (N–H and O–H); 2230m (C≡N); 1700s, 1690s, 1660s (C=O); 1530s, 1350m, 850w cm.$^{-1}$ (NO_2).

Methyl α-*cyano*-α-*o*-*nitrobenzoylacetate* was prepared as described by Gabriel [7] for the ethyl ester. It separated in prisms (from ethanol), m. p. 105—106° (Found: C, 53·0; H, 3·5; N, 11·3. $C_{11}H_8N_2O_5$ requires C, 53·2; H, 3·2; N, 11·3%).

Reductive cyclisation with cyclohexene and palladium–charcoal gave a series of compounds similar to those described above for the ethyl ester, the structures of which were proved in the same manner.

Adduct (I; R = Me), yellow prisms (from ethanol), m. p. 158—159° (decomp.), separated on concentration of the filtrate from the adduct (II; R = Me) (Found: C, 55·25; H, 4·2; N, 11·7%; equiv., 486. $C_{22}H_{18}N_4O_9$ requires C, 54·8; H, 3·75; N, 11·6%; equiv., 482); it had

[6] Rupe and Heckendorn, *Helv. Chim. Acta*, 1926, **9**, 987.
[7] Gabriel, *Ber.*, 1918, **51**, 1500.

$\nu_{max.}$ 3390w, 3280m (N–H and O–H); 2220s (C≡N); 1690s, 1630s (C=O); 1540s, 1340s, 855w cm.$^{-1}$ (NO_2).

Adduct (II; R = Me), prisms (from acetic acid), m. p. 189—191° (decomp.) (Found: C, 60·7; H, 4·5; N, 12·6%; equiv., 432. $C_{22}H_{20}N_4O_6$ requires C, 60·55; H, 4·6; N, 12·8%; equiv., 436), $\nu_{max.}$ 3340m, 3100—2600bs (N–H and O–H); 2210m (C≡N); 1720s, 1650s, 1630s cm.$^{-1}$ (C=O).

Methyl 2-amino-4-hydroxyquinoline-3-carboxylate, prisms (from ethanol), m. p. 286—287° (Found: C, 60·5; H, 5·1; N, 13·1. $C_{11}H_{10}N_2O_3$ requires C, 60·6; H, 4·6; N, 12·8%), $\nu_{max.}$ 3310m, 3250m, 3100s (N–H and O–H); 1670s, 1630 cm.$^{-1}$ (C=O).

2-Amino-4-hydroxy-3-methoxycarbonylquinoline 1-oxide hydrochloride, m. p. 230—232° (decomp.) (Found: C, 48·8; H, 3·8. $C_{11}H_{10}N_2O_4$,HCl requires C, 48·8; H, 4·1%).

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[*Received, December 4th*, 1961.]

482. *A Simple Preparation of Alkyl Ammonium Phosphonates and Some Comments on the Reaction.*

By P. R. HAMMOND.

ACTION of aqueous ammonia on dialkyl phosphonates $HPO(OR)_2$ has been found to be an excellent method for making crystalline ammonium alkyl phosphonates RO·PHO·ONH_4 in high yield, and more convenient than others described in the literature.[1] Dialkyl phosphonates are easily prepared, so this reaction, coupled with oxidation by potassium permanganate, provides an easy route to monoalkyl phosphates. It should also be noted that the use of aqueous ammonia or other strongly basic systems in the chromatography of dialkyl phosphonates is to be avoided.

No amine was detected in the reactions with ammonia. Diphenyl phosphonate reacted vigorously and phenol was liberated. Decomposition of an alkyl benzyl phosphonate produced approximately equal proportions of the alkyl ammonium phosphonate and the alkyl alcohol. Thus, the hydrolytic step is probably P–O bond cleavage.

The success of the method must depend on the rapid * hydrolysis of the dialkyl phosphonates in the presence of hydroxide ion, as reported by Nylen.[2,3] It is of interest that hydrolyses of dialkyl alkyl- and aryl-phosphonates are known to be slow under similar conditions [4] and heating is necessary.[5] From the data reported [4] for hydrolysis of diethyl methyl- and phenyl-phosphonate second-order rate constants at 25° of 3×10^{-4} and 8×10^{-4} l. mole^{-1} sec.$^{-1}$, respectively, may be estimated. Thus replacement of phosphorus-bound hydrogen by methyl or phenyl in a phosphonate decreases the rate by a factor of 5×10^5. This marked contrast is unlikely to arise from a difference in steric or polar effects on the phosphorus atom or on other parts of the molecule, for the changes in alkyl groups of alkylphosphonates cause comparatively small alterations in hydrolysis rates. Participation of the phosphite structure $(RO)_2P$·OH is possible although the stability of

* A check on the rate of hydrolysis of diethyl phosphonate in a pH-controlled apparatus gave a second-order rate constant of 130 l. mole^{-1} sec.$^{-1}$ for hydroxide ion (25°; μ ~0·01). This is comparable with the value found in studies with buffered solutions,[2] 77 l. mole^{-1} sec.$^{-1}$ (25°; μ 1·5).

[1] Nylen, *Svensk kem. Tidskr.*, 1936, **48**, 2; Baddiley, Clark, Michalski, and Todd, *J.*, 1949, 815; Christie, Kenner, Todd, and Weymouth, *J.*, 1953, 2947; Smith, *J.*, 1961, 5050.
[2] Nylen, *Svensk kem. Tidskr.*, 1937, **49**, 29.
[3] Nylen, *Z. anorg. Chem.*, 1938, **235**, 161.
[4] Hudson and Keay, *J.*, 1956, 2463.
[5] Rabinowitz, *J. Amer. Chem. Soc.*, 1960, **82**, 4564.

the triesters under basic conditions [6] may preclude this. A known difference between the PH(O) and PR(O) structures as applied to the dialkyl phosphonates is that the P–H bond can ionise as revealed by iodination,[3] deuteration,[7] and other studies, and it must be concluded that this property is in some way connected with the rapid hydrolysis.

Experimental.—Ammonium alkyl phosphonates. Diethyl phosphonate (5·0 g.) was dissolved in concentrated, aqueous ammonia (25 ml.) and left for an hour. The solution was evaporated on a water-bath under reduced pressure, a colourless gum, which rapidly crystallised, being left. One crystallisation from ethanol–acetone gave the pure *ammonium salt* as needles.

Ammonium alkyl phosphonates, $RO{\cdot}PHO{\cdot}ONH_4$.

	Yield		Found (%)				Required (%)		
R	(%)	M. p.	C	H	N	Formula	C	H	N
Methyl.....	89	110—111°	11·1	6·8	12·1	CH_8NO_3P	10·6	7·1	12·4
Ethyl	86	99—100	19·4	8·3	10·8	$C_2H_{10}NO_3P$	18·9	7·9	11·0
n-Propyl	92	91—92	25·9	8·2	9·6	$C_3H_{12}NO_3P$	25·5	8·5	9·9
Isopropyl ...	72	131—132	26·0	8·4	9·7	$C_3H_{12}NO_3P$	25·5	8·5	9·9
Benzyl.....	82	150—151	43·8	6·0	7·3	$C_7H_{12}NO_3P$	44·4	6·3	7·4
Phenyl	95	172—173	41·2	5·9	7·8	$C_6H_{10}NO_3P$	41·1	5·7	8·0

Other *ammonium salts* (see Table) were similarly prepared, except that ethanol (10 ml.) was added to the reaction mixture to dissolve dibenzyl and diphenyl phosphonate and ammonium phenyl phosphonate was recrystallised from ethanol–ether.

The first four compounds have recently been described by Smith.[1] Our m. p.s are close to his except for the isopropyl ester. The ethyl derivative has been described but no properties has been given; [8] a product, m. p. 95°, has been said to be the ethyl compound from its analysis.[9] The benzyl compound has been described.[10] The phenyl is new.

Decomposition of benzyl thymidine phosphonate [*with* Dr. H. PAULUS]. A sample of this compound,[11] used successfully in a later synthesis, was chromatographed on paper with a solvent system of propan-2-ol–ammonia (*d* 0·88)–water (6 : 3 : 1). Two phosphorus-containing products of approximately equal intensity ran parallel with benzyl ammonium phosphonate and thymidine ammonium phosphonate; two approximately equal ultraviolet absorbing spots could be similarly ascribed to thymidine ammonium phosphonate and thymidine.

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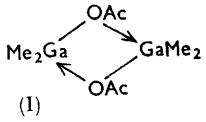
[*Received, December 12th*, 1961.]

[6] Arbuzov and Imaev, *Doklady Akad. Nauk S.S.S.R.*, 1957, **112**, 856.
[7] Hammond, *J.*, 1962, 1365.
[8] Dimroth and Ploch, *Chem. Ber.*, 1957, **90**, 812.
[9] Medved and Kabachnik, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1954, 314.
[10] Christie, Elmore, Kenner, Todd, and Weymouth, *J.*, 1953, 2947.
[11] Corby, Kenner, and Todd, *J.*, 1952, **3669**.

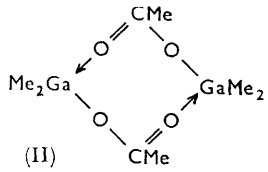
483. *Cobalt*(II) *Methyl- and Phenyl-phosphinates.*

By G. E. Coates and D. S. Golightly.

There is abundant evidence that oxyacid groups such as carbonate, sulphate, and phosphate can act as chelate groups in octahedral co-ordination complexes, thus forming four-membered rings.[1] Four-membered rings are also readily formed by some thio-acids, for example, in the *NN*-diethyldithiocarbamates of metals of planar, tetrahedral, or octahedral stereochemistry.[2] There is little evidence that oxyacids can form four-membered rings with elements of tetrahedral stereochemistry; the steric strain, in the sense of deformation of bond angles from their normal values, would be greater when the metal is in a tetrahedral rather than a planar or octahedral environment. The acetate group does not act as a chelating ligand in the gallium compound $(Me_2GaOAc)_2$; both a four-membered ring (I) and an eight-membered ring (II) have been considered as



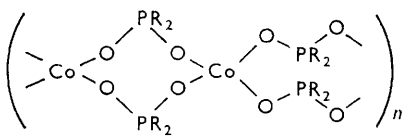
(I)



(II)

possible structures.[3] Molybdenum(II) forms insoluble and almost involatile carboxylates, $[(R{\cdot}CO_2)_2Mo]_x$, for which a polymeric structure involving eight-membered rings analogous to those in compound (II) has been proposed.[4]

We have prepared some cobalt(II) derivatives of phosphinic acids, R_2PO_2H. These compounds, $(R_2PO_2)_2Co$, have the bright blue colour typical of spin-free cobalt(II) complexes in which the metal atom has a tetrahedral environment. They are insoluble in common organic solvents with the exception of the lower alcohols and mixed solvents containing pyridine and similar bases. In these solvents, as in water, the cobalt(II) phosphinates form pink solutions indicative of octahedral co-ordination, and their solubility generally decreases with increasing temperature. When the pink aqueous solution is heated, blue crystals of the anhydrous phosphinate are deposited. These observations are consistent with a strain-free polymeric structure (III) for the blue anhydrous com-



(III)

pounds. Pink solutions, in which cryoscopic measurements (water) show there is extensive dissociation, would then result from the attack of donor molecules on the blue polymer. Ammonia and pyridine adducts were obtained as pink crystals; the ammine lost base so rapidly that it could not be analyzed and it became blue as soon as the material was dried other than in an ammonia atmosphere or was washed with a solvent which did not contain

[1] Martell and Calvin, "Chemistry of the Metal Chelate Compounds," Prentice Hall, New York, 1952, p. 134; "The Chemistry of the Co-ordination Compounds," ed. Bailar, Reinhold Publ. Inc., New York, 1956, p. 226.
[2] Chatt, Duncanson, and Venanzi, *Suomen Kem.*, 1956, **29**, *B*, 75.
[3] Coates and Hayter, *J.*, 1953, 2519.
[4] Bannister and Wilkinson, *Chem. and Ind.*, 1960, 319.

an excess of ammonia. The pyridine adduct did not decompose quite so readily, though it lost pyridine when exposed to the air (rapidly when in a vacuum). It is remarkable that the analysis of the most stable pyridine adduct examined, that of the diphenylphosphinate, though not satisfactory on account of its instability, indicated a 1 : 1 formula $(Ph_2PO_2)_2Co$ py instead of 1 : 2 as expected.

Cobalt(II) diphenylarsinate resembled the analogous phosphinate, but is not soluble in pyridine.

None of these compounds, except the unstable adducts with bases, melted below 350°, nor was any decomposition observed up to that temperature. The presumably polymeric molybdenum(II) carboxylates [4] are apparently stable to about 300°.

Infrared Spectra.—Compounds were examined by the potassium bromide disc method, and the following bands (500—2000 cm.$^{-1}$) were observed:

$Co(Me_2PO_2)_2$: 1441m, 1424m, 1309s, 1297s, 1196s, 1118vs, 1060vs, 935w, 911w, 873s, 752m, 709w.

$Co(MePhPO_2)_2$: 1603w, 1495vw, 1447m, 1376w, 1302m, 1220m, 1136vs, 1054vs, 1028s, 1000m, 928vw, 878s, 778s, 742s, 695s, 520m.

$Co(Ph_2PO_2)_2$: 1605w, 1492w, 1447s, 1220sh, 1130vs, 1058vs, 1027s, 1002m, 756m, 729s, 694s, 565s, 536s.

Bands due to the Ph–P system can be identified at 1603, 1495, and 1447 cm.$^{-1}$ (methylphenylphosphinate) and at 1605, 1492, and 1447 cm.$^{-1}$ (diphenylphosphinate). The doublet due to P–CH_3 sysmmetrical deformation observed in various salts of dimethylphosphinic acid,[5] appears at 1309 and 1297 cm.$^{-1}$ for cobalt(II) dimethylphosphinate, and becomes a single band at 1302 cm.$^{-1}$ for the methylphenylphosphinate. Bands due to P–O stretching are very strong and are in the region 1220—1000 cm.$^{-1}$, two particularly strong bands appearing in the three compounds at 1130, 1136, 1118 and 1058, 1054, 1060 cm.$^{-1}$. These are rather lower than the P=O stretching frequencies observed for numerous metal complexes of tertiary phosphine oxides,[6] but for the cobalt(II) phosphinates P–O bond orders of about 1·5 would be expected. Bands at 878 (methylphenyl) and 873 cm.$^{-1}$ (dimethyl) may be assigned to P–CH_3 rocking by comparison with analyses of various other compounds containing this group.[7] Except for the weak band at 521 cm.$^{-1}$ (methylphenyl) we detected no bands in the 500—600 cm.$^{-1}$ region attributable to Co–O stretching (see ref. 6 for a discussion of metal–OSi frequencies in this range); the 565 and 536 cm.$^{-1}$ bands of the diphenylphosphinate are present, at slightly different frequencies, in the spectrum of diphenylphosphinic acid.

Experimental.—General methods. (A) A solution of the sodium phosphinate (0·02 mole) in water (~30 c.c.) was added to cobalt(II) chloride (0·01 mole) in water (50 c.c.). The mixture was heated and filtered while hot. (B) The phosphinic acid (0·02 mole) was added to anhydrous cobalt(II) chloride (0·01 mole) dissolved in ethanol or tetrahydrofuran. Addition of a slight excess of triethylamine then precipitated the cobalt phosphinate, which was separated by filtration of the heated solution, triethylammonium chloride remaining dissolved. The following salts were obtained by the method indicated.

Cobalt(II) *dimethylphosphinate* (55% A; 72% B) crystallized from hot water as very fine blue needles, very soluble in cold water [Found: C, 19·2; H, 5·0; Co, 23·8, 23·8%; *M* (cryoscopically in 0·718, 1·04, 1·38% aqueous solution), 78·4, 85·1, 86·2. $C_4H_{12}CoO_4P_2$ requires C, 19·6; H, 5·0; Co, 24·1%; *M*, 245].

Cobalt(II) *methylphenylphosphinate* (92% A), from hot water, in which it is sparingly soluble, formed blue needles [Found: C, 45·2; H, 4·4; Co, 15·8%; *M* (cryoscopically in 0·638, 1·05, 1·33, 1·53% aqueous solution), 148, 181, 160, 160. $C_{14}H_{16}CoO_4P_2$ requires C, 45·5; H, 4·3;

[5] Corbridge and Lowe, *J.*, 1954, 4555.
[6] Cotton, Barnes, and Bannister, *J.*, 1960, 2199; Goodgame and Cotton, *J.*, 1961, 3735.
[7] Goubeau and Berger, *Z. anorg. Chem.*, 1960, **304**, 147; Goubeau and Baumgartner, *Z. Elektrochem.*, 1960, **64**, 598.

Co, 15·9%; *M*, 369], insoluble in common organic solvents except pyridine, moderately soluble in cold water, readily soluble in aqueous ammonia.

Cobalt(II) *diphenylphosphinate* (100% A) is only sparingly soluble in cold water and almost insoluble in hot water from which it crystallized as very fine blue needles (Found: Co, 11·7. $C_{24}H_{20}CoO_4P_2$ requires Co, 11·8%), readily soluble in pyridine at room temperature to a pink solution, very sparingly soluble in hot pyridine and benzene (hot or cold) to pale blue solutions.

Cobalt(II) *diphenylarsinate*. This *salt*, prepared quantitatively by a method analogous to (A), closely resembled the analogous phosphinate and crystallized as deep blue needles (Found: Co, 10·1. $C_{24}H_{20}As_2CoO_4$ requires Co, 10·1%). It differs from the diphenylphosphinate in being insoluble in pyridine.

Adducts with bases. The brownish-pink ammonia adduct separated when concentrated aqueous ammonia was added to a suspension of the diphenylphosphinate in acetone, and the resulting solution was filtered and then cooled. The dry diphenylphosphinate (1 g.), suspended in dry benzene (100 c.c.), dissolved when dry pyridine (5 mol.) was added. Addition of cyclohexane precipitated the pink pyridine adduct, which reverted to blue starting material if washed with benzene though not when washed with benzene containing pyridine (Found: Co, 10·5; C_5H_5N, 11·7, 11·7. Calc. for $C_{29}H_{25}CoNO_4P_2$: Co, 10·3; C_5H_5N, 13·8%). Pyridine was determined by keeping the adduct in a vacuum and titrating the pyridine condensed in a trap.

Cobalt(II) methylphenylphosphinate, suspended in dry benzene, dissolved to a brown solution when bipyridyl was added, but was deposited unchanged as blue needles when the solution was concentrated.

The authors thank the Durham County Council for a maintenance award (to D. S. G.).

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[*Received, December 14th*, 1961.]

484. *A High-temperature Form of Strontium Carbonate.*

By E. H. BAKER.

STRONTIUM CARBONATE undergoes a solid-state transition from orthorhombic to hexagonal at ~925°.[1,2] The present work has shown that by further heating of the hexagonal form, a second endothermic transition can be detected at 1416°, provided that a carbon dioxide atmosphere is employed at a pressure greater than about 20 atm. to prevent decomposition of the carbonate to an oxide–carbonate melt.

Barium carbonate, which has been shown to exist in forms isomorphous with those of strontium carbonate, exhibits the transitions, orthorhombic to hexagonal at 806° and hexagonal to cubic at 968°.[2,3] By analogy therefore, the form of strontium carbonate which is stable above 1416° is probably a cubic modification.

Experimental.—Two grades of strontium carbonate were used: Specpure supplied by Johnson Matthey and Co., and Reagent Quality supplied by Hopkin and Williams.

A pressure-vessel containing a resistance furnace of platinum alloy was used for heating under pressure. The furnace was equipped with booster windings at the top and the bottom of the main winding to enable a good constant-temperature zone in the region of the sample. The bore of the furnace tube was 2 cm. and the free space in the tube was filled by solid alumina cylinders to eliminate gas turbulence. For thermal detection of the transition point, twin platinum crucibles and differential thermocouples were employed; the latter were connected

[1] Eitel, *Z. Kryst.*, 1925, **61**, 596; U.S. Nat. Bur. Stand., Circular No. 500, Washington D.C., 1952, pp. 785, 1150.
[2] Lander, *J. Amer. Chem. Soc.*, 1951, **73**, 5794.
[3] Lander, *J. Chem. Phys.*, 1949, **17**, 892.

to a two-channel recorder. A fuller description of the equipment is to be found elsewhere.[4] The crucibles had semicircular cross-sections of 1·2 cm. diameter and were mounted alongside each other, 1 mm. apart. One crucible contained the carbonate, and the other alumina powder. Both materials were packed to a depth of 1·7 cm. and the platinum-sheathed thermocouples were buried centrally in them.

With heating and cooling rates of 2° per min. the transition at the higher temperature was shown by a marked inflection of the differential plot, a characteristic triangular loop being obtained. The transition temperatures were 1416° ± 1° and 1410° ± 2° for the Specpure and Reagent Quality carbonate, respectively. The slightly lower transition temperature of the latter material can be attributed to the small amount of impurity present. With both materials, the respective temperatures were reproducible within the stated limits on both heating and cooling, and were independent of pressure in the range 20—50 atm.

For a given set of experimental conditions, the area of a D.T.A. loop should be proportional to the heat change involved. Discrepancies are, however, occasionally encountered, such as those discussed by Sewell and Honeyborne,[5] particularly with respect to the dehydration of minerals. With solid-state transitions, no loss of material is involved, so that it was considered that measurement of the ratio of the loop areas for the transitions at 925° and 1410—1416° would give approximately the ratio of the two heats of transition. The areas of the D.T.A. loops for the upper and the lower transition were therefore determined from several runs at 30 atm. pressure, with a constant weight (1·49 g.) of carbonate and a heating rate of 2° per min. At this pressure, the ratios of the loop areas of the upper and the lower transition were reproducible within ±8% for both brands of carbonate.

For the heat of transition at 925° Lander [2] gives 4·70 kcal. mole^{-1}. On this basis, the ratio of the loop areas shows the heat of transition at 1416° to be 800 cal. mole^{-1}. For the isomorphous barium carbonate, Kelley [6] gives the heats of transition for orthorhombic to hexagonal, and hexagonal to cubic, as 4·49 kcal. mole^{-1} and 730 cal. mole^{-1}, respectively. These values are nearly in the same ratio as those for strontium carbonate, which suggests that a heat change of 800 cal. mole^{-1} would be approximately correct for a transition from a hexagonal to a cubic form.

X-Ray powder photographs of strontium carbonate quenched from above 1416° by the method previously described [4] did not differ detectably from those of the orthorhombic form. It is likely, however, that conversion from the probable cubic form back to the orthorhombic form had occurred during quenching.

The author thanks Mr. J. Butler for assistance and the D.S.I.R. for financing the work.

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[4] Baker, *J.*, 1962, 464.
[5] Sewell and Honeyborne, " The Differential Thermal Investigation of Clays," ed. R. C. MacKenzie, Mineralogical Soc., London, 1957, Chapter 3.
[6] Kelley, Bull. No. 584, U.S. Bur. Min., Washington D.C., 1960, p. 23.

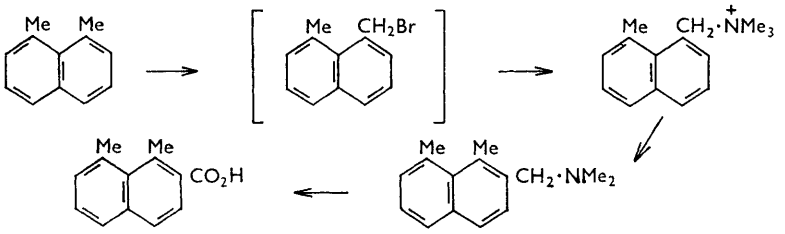
485. 1,8-*Dimethylnaphthoic Acids.*

By W. J. Mitchell, R. D. Topsom, and J. Vaughan.

Recent satisfactory preparations of 1,8-dimethylnaphthalene [1,2] have opened the way to the three previously unreported 1,8-dimethylnaphthoic acids, preparations of which are the subject of this Note. An improved two-stage process for the preparation of the hydrocarbon from naphthalic anhydride is also reported. The preparative scheme for

[1] Ghilardi and Kalopissis, *Bull. Soc. chim. France*, 1952, 217.
[2] Ried and Bodem, *Chem. Ber.*, 1958, **91**, 1354.

1,8-dimethyl-2-naphthoic acid is shown. The key step was thus a Hauser rearrangement of *NNN*-trimethyl-(8-methyl-1-naphthyl)methylammonium bromide, but this was sometimes difficult to induce and, even when sucessful, resulted in yields below 30%. With



simpler naphthalene derivatives Hauser and his co-workers [3] have found that the rearrangement is less successful than with the corresponding benzene derivatives.

4,5-Dimethyl-1-naphthoic acid was obtained without difficulty from the dimethylnaphthalene *via* the 1-bromo-compound and the corresponding lithium derivative.

4,5-Dimethyl-2-naphthoic acid was prepared from 3-bromonaphthalic anhydride, the two-stage reduction mentioned above being used. In the preparation of the starting material from naphthalic anhydride, Rule and Thompson's method [4] was, in our hands, far less satisfactory than one based on Derbyshire and Waters's bromination procedure.[5]

Experimental.—1,8-*Bishydroxymethylnaphthalene.* A suspension of naphthalic anhydride (100 g.) in benzene (250 ml.) was added during 2 hr. to a stirred solution of lithium aluminium hydride (50 g.) in ether (1 l.) and benzene (200 ml.). Stirring was continued for a further 3 hr. (reflux) and most of the ether was then distilled off. The excess of metal hydride was destroyed by dropwise addition of ethyl acetate. Addition of concentrated potassium hydroxide solution (50 ml.) gave a white precipitate. Liquid was decanted off and the solid was extracted with benzene (2 × 500 ml.) containing ether (50 ml.). The volume of the combined extracts was reduced to 250 ml., ethanol (250 ml.) was added, and the solution was evaporated to *ca.* 200 ml. 10% Aqueous sulphuric acid was added and the precipitated dialcohol was filtered off, washed well with water, and dried. The yield was 76·5 g. (81%). It had m. p. 155°, raised to 158° after recrystallisation from ethanol.

1,8-*Dimethylnaphthalene.*—Phosphorus tribromide (60 g.) in ether (200 ml.) was added during 2 hr. to a stirred solution of 1,8-bishydroxymethylnaphthalene (60 g.) in benzene (1 l.) and ether (400 ml.). The mixture was refluxed for 1 hr. and poured on crushed ice (2 kg.). The organic layer was washed with cold saturated sodium hydrogen carbonate solution and with water. It was dried ($MgSO_4$), most of the solvent was removed, and sufficient ether was added to prevent precipitation of the bisbromomethylnaphthalene. This solution was added during 2 hr. to a stirred solution of lithium aluminium hydride (20 g.) in ether (2 l.), and the mixture was refluxed for 3 hr. The excess of metal hydride was destroyed with ethyl acetate, and an excess of concentrated potassium hydroxide solution was added. The organic layer was decanted and the residue was washed with the benzene–ether mixture (see above; 3 × 400 ml.). The combined organic extracts were washed well with water, and dried ($MgSO_4$). The solution was distilled almost to dryness, the residue was taken up in ethanol, and this solution was cooled. The precipitated hydrocarbon was filtered off and recrystallised from ethanol. The yield was 44·9 g. (90%); m. p. 62·5°.

4,5-*Dimethyl*-1-*naphthoic Acid.*—1,8-Dimethylnaphthalene (7·5 g.) was brominated [6] to give 1-bromo-4,5-dimethylnaphthalene (72%), b. p. 204—207°/30 mm., m. p. 30·5° (from ethanol). The bromo-compound (6·0 g.) was converted, *via* the lithium compound, into the required *acid*

[3] Hauser, Van Eenam, and Bayless, *J. Org. Chem.*, 1958, **23**, 354.
[4] Rule and Thompson, *J.*, 1937, 1764.
[5] Derbyshire and Waters, *J.*, 1950, 573.
[6] Topsom and Vaughan, *J.*, 1957, 2842.

(72%), m. p. 191—194°. Successive recrystallisations from aqueous ethanol and aqueous dioxan gave needles, m. p. 195° (Found: C, 77·75; H, 5·9. $C_{13}H_{12}O_2$ requires C, 78·0; H, 6·0%).

NNN-*Trimethyl*-(8-*methyl*-1-*naphthyl*)*methylammonium Bromide*.—A mixture of 1,8-dimethylnaphthalene (22·5 g.), *N*-bromosuccinimide (25·7 g.), benzoyl peroxide (0·25 g.), and carbon tetrachloride (110 ml.) was refluxed for 3 hr. It proved advisable to insert a splash-head between the reaction flask and the condenser, because initial reaction was very vigorous. After filtration, the liquid was washed successively with 1% sodium hydroxide solution and water, and dried ($MgSO_4$). The solvent was evaporated off and the crude 1-bromomethyl-8-methylnaphthalene was added to trimethylamine (10 g.) in methanol (100 ml.). After 24 hr. the solvent was removed. The *salt* was washed with ether and recrystallised from acetonitrile. The yield was 19·5 g. (46%); m. p. 210—212° (decomp.) (Found: C, 60·35; H, 6·5; Br, 28·4. $C_{15}H_{20}BrN$ requires C, 60·0; H, 6·5; Br, 28·5%).

2-*Dimethylaminomethyl*-1,8-*dimethylnaphthalene*.—The quaternary ammonium salt (8·7 g.) was converted, by Hauser's method,[3] into the required *amine* (2·2 g., 35%), b. p. 138—140°/1 mm., m. p. 32—34° (raised to 36·5° by recrystallisation from light petroleum) (Found: C, 84·65; H, 8·8; N, 6·8. $C_{15}H_{19}N$ requires C, 84·5; H, 9·0; N, 6·6%).

1,8-*Dimethyl*-2-*naphthoic Acid*.—Finely powdered potassium permanganate (3·8 g.) was added during 3 hr. to a stirred suspension of 2-dimethylaminomethyl-1,8-dimethylnaphthalene (1·9 g.) in water (60 ml.). Stirring was continued for a further 2 hr., and manganese dioxide was then filtered off. Acidification of the filtrate furnished 1,8-*dimethyl*-2-*naphthoic acid*, m. p. 122—123° (from aqueous ethanol). Yield was 0·33 g. (18%) (Found: C, 78·0; H, 5·6. $C_{13}H_{12}O_2$ requires C, 78·0; H, 6·0%).

3-*Bromonaphthalic Anhydride*.—To stirred sulphuric acid (1 l.) were added naphthalic anhydride (50 g.), silver sulphate (40 g.), and bromine (50 g.). Stirring was continued for 6 hr. at 50—60°. The cooled mixture was filtered (disc). Careful addition of the filtrate to water (8 l.) afforded a precipitate which was washed with water and ethanol, and dried in a vacuum. The bromonaphthalic anhydride (56·4 g., 81%) had m. p. 246—252° (from acetic acid).

1,8-*Bishydroxymethyl*-3-*bromonaphthalene and* 3-*Bromo*-1,8-*dimethylnaphthalene*.—The two-stage procedure, described above for the preparation of 1,8-dimethylnaphthalene, was followed, and only in the extraction of products were there any differences. In the first step, from 3-bromonaphthalic anhydride (10 g.) solvent was removed from the benzene–ether extracts and light petroleum was added to the residue. The deposited *dialcohol* (8·0 g., 83%) had m. p. 162—163° (from ethanol) (Found: C, 54·3; H, 4·0; Br, 29·8. $C_{12}H_{11}BrO_2$ requires C, 53·95; H, 4·15; Br, 29·9%). In the second step, from the dialcohol (6·5 g.), addition of potassium hydroxide solution was followed by extraction with ether–acetone. Solvent was removed at atmospheric pressure and a fraction, b. p. 202—205°/17 mm. (4·1 g., 77%), was collected. The 3-*bromo*-1,8-*dimethylnaphthalene* had m. p. 83° (from ethanol) (Found: C, 60·9; H, 4·6; Br, 34·5. $C_{12}H_{11}Br$ requires C, 61·3; H, 4·7; Br, 34·0%).

4,5-*Dimethyl*-2-*naphthoic Acid*.—3-Bromo-1,8-dimethylnaphthalene (2·9 g.) was converted (see above) into the *acid* (1·6 g., 65%), m. p. 215—217° (from acetic acid) (Found: C, 78·4; H, 6·2. $C_{13}H_{12}O_2$ requires C, 78·0; H, 6·0%).

We thank Dr. A. D. Campbell, University of Otago, for the microanalyses.

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[*Received, December 18th*, 1961.]

486. *The Preparation and Properties of Trifluoromethylthio- and Trifluoromethylseleno-bis(trifluoromethyl)-phosphine and -arsine and of Heptafluoropropylselenobis(trifluoromethyl)arsine.*

By H. J. Emeléus, K. J. Packer, and N. Welcman.

Bis(trifluoromethylthio)mercury reacts with phosphorus and arsenic chlorides to form compounds of the type R_3M, R_2MCl, and $RMCl_2$ ($R = CF_3{\cdot}S{\cdot}$, $M = P$ or As).[1] The substituted phosphines $(CF_3{\cdot}S)_2PH$ and $(CF_3{\cdot}S)_3P$ have also been isolated from the product of the reaction of trifluoromethanesulphenyl chloride with phosphine.[2] It has now been shown that bis(trifluoromethylthio)mercury and bis(trifluoromethylseleno)mercury react readily at room temperature with iodobis(trifluoromethyl)-phosphine and -arsine to form the compounds $(CF_3)_2P{\cdot}S{\cdot}CF_3$, $(CF_3)_2As{\cdot}S{\cdot}CF_3$, $(CF_3)_2P{\cdot}Se{\cdot}CF_3$, and $(CF_3)_2As{\cdot}Se{\cdot}CF_3$. The corresponding reaction of iodobis(trifluoromethyl)arsine with bis(heptafluoropropylseleno)mercury yields $(CF_3)_2As{\cdot}Se{\cdot}C_3F_7$. The other product in all these reactions was mercuric iodide.

These compounds are colourless mobile liquids, though heptafluoropropylselenobis(trifluoromethyl)arsine becomes yellow on storage. The selenium derivatives are of special interest as being among the few known covalent compounds in which selenium is bonded to phosphorus or arsenic. All the compounds lose two trifluoromethyl groups as fluoroform on treatment with 20% aqueous alkali. A similar reaction occurs when iodobis(trifluoromethyl)-phosphine or -arsine is treated with alkali. This reaction was used in analysis, the fluoroform being dried and weighed. Phosphorus or arsenic was determined in the hydrolysate as magnesium ammonium phosphate or arsenate after oxidation with hydrogen peroxide, sulphur being determined as barium sulphate and selenium as the element. The infrared spectra show weak absorption at 2200—2400 cm.$^{-1}$, these bands being overtones of the strong absorption in the carbon–fluorine stretching region (1000—1300 cm.$^{-1}$). The compounds containing only trifluoromethyl groups have only four main bands in this region, but for the heptafluoropropyl compound there are many more. All of the compounds show strong absorption at 725—780 cm.$^{-1}$, associated with the deformation modes of perfluoroalkyl groups. The ^{19}F nuclear magnetic resonance spectra of the compounds containing only trifluoromethyl groups, which will be reported in detail elsewhere, show for the phosphines, a doublet of quartets and a doublet of septets, the doublets arising from spin–spin coupling with the phosphorus nucleus. The spectra of the arsines show a quartet and a septet. Arsenic, having a nuclear spin of 3/2, has a nuclear electric quadrupole moment, which prevents any arsenic–fluorine coupling from being observed, especially in unsymmetrical molecules such as these. There was, however, a slight broadening of the lines compared with those of the phosphorus compounds.

Experimental.—Iodobis(trifluoromethyl)-phosphine and -arsine were prepared by known methods [3,4] and their purities checked by molecular-weight determinations and infrared spectroscopy. Bis(trifluoromethylthio)mercury was prepared by the reaction of carbon disulphide and mercuric fluoride.[5] Bis(trifluoromethylseleno)mercury and bis(heptafluoropropylseleno)mercury were prepared from bis(trifluoromethyl) and bis(heptafluoropropyl) diselenide and mercury.[6,7]

Bis(trifluoromethyl)trifluoromethylthiophosphine. Iodobis(trifluoromethyl)phosphine (2·7

[1] Emeléus and Pugh, *J.*, 1960, 1108.
[2] Emeléus and Nabi *J.*, 1960, 1103.
[3] Bennett, Emeléus, and Haszeldine, *J.*, 1953, 1565.
[4] Brandt, Emeléus, and Haszeldine, *J.*, 1952, 2198.
[5] Man, Coffman, and Muetterties, *J. Amer. Chem. Soc.*, 1959, **81**, 3575.
[6] Dale, Emeléus, and Haszeldine, *J.*, 1958, 2939.
[7] Welcman, Ph.D. Thesis, Cambridge, 1961.

mmoles) and bis(trifluoromethylthio)mercury (1·5 mmoles) were sealed in a Pyrex ampoule. After 48 hr. red mercuric iodide had separated. Vacuum-fractionation of the volatile products gave *bis(trifluoromethyl)trifluoromethylthiophosphine* (2·61 mmoles) which collected in a trap at −95° [Found: C, 13·0; CF_3 (attached to P, estimated as CHF_3), 51·2; P, 11·4; S, 12·0%; *M*, 269. C_3F_9PS requires C, 13·3; CF_3, 51·1; P, 11·5; S, 11·9%; *M*, 270]. It was a colourless liquid, m. p. −107°, the vapour pressure of which (−32° to 20°) was given by $\log_{10} p$ (mm.) = $-1695/T + 8{\cdot}12$, giving an extrapolated b. p. of 50·3°. Mercuric iodide (1·3 mmoles) was recovered.

Bis(trifluoromethyl)trifluoromethylthioarsine. Iodobis(trifluoromethyl)arsine (6·2 mmoles) and bis(trifluoromethylthio)mercury (3·8 mmoles) were sealed in a Pyrex ampoule. After 48 hr. red mercuric iodide had separated. Vacuum-fractionation of the volatile products gave *bis(trifluoromethyl)trifluoromethylthioarsine* (5·6 mmoles) which collected in a trap cooled to −65° [Found: C, 12·4; CF_3 (attached to As, measured as CHF_3), 42·6; As, 22·3; S, 10·0%; *M*, 311. C_3AsF_9S requires C, 11·4; CF_3, 43·9; As, 23·9; S, 10·2%; *M*, 314]. Although the carbon and arsenic analyses are not very accurate the ratio of S : As : CF_3 obtained is 1·04 : 1·0 : 2·06. This, combined with the molecular weight and infrared and nuclear magnetic resonance spectra, was considered sufficient evidence as to the structure and formula of this molecule. It was a colourless, mobile liquid, m. p. −107°, the vapour pressure of which, over the range −10° to 39°, was given by $\log_{10} p$ (mm.) = $-1776/T + 8{\cdot}16$, giving an extrapolated b. p. of 63·0°.

Bis(trifluoromethyl)trifluoromethylselenophosphine. Iodobis(trifluoromethyl)phosphine (2·1 mmoles) and bis(trifluoromethylseleno)mercury (1·5 mmoles) were sealed in a Pyrex ampoule. After 72 hr., separation of the red mercuric iodide was complete and vacuum-fractionation of the volatile products gave *bis(trifluoromethyl)trifluoromethylselenophosphine* (2·1 mmoles) which collected in a trap at −65° [Found: C, 11·5; CF_3 (attached to P, measured as CHF_3), 42·6; P, 9·7; Se, 24·9%; *M*, 316. C_3F_9PSe requires C, 11·3; CF_3, 43·5; P, 9·8; Se, 24·9%; *M*, 317]. It is a colourless liquid, m. p. −98°, the vapour pressure of which (−37° to 17°) was given by $\log_{10} p$ (mm.) = $-1875/T + 8{\cdot}47$, giving an extrapolated b. p. of 62°.

Bis(trifluoromethyl)trifluoromethylselenoarsine. Iodobis(trifluoromethyl)arsine (3·7 mmoles) and bis(trifluoromethylseleno)mercury (1·9 mmoles) were sealed in a Pyrex ampule. After 72 hr., separation of red mercuric iodide was complete. Vacuum-fractionation of the volatile products gave *bis(trifluoromethyl)trifluoromethylselenoarsine* (3·1 mmoles) which collected in a trap at −65° [Found: CF_3 (attached to As, measured as CHF_3), 38·7; As, 20·4; Se, 21·5%; *M*, 359. C_3AsF_9Se requires CF_3, 38·8; As, 20·8; Se, 21·9%; *M*, 361]. It is a colourless liquid, m. p. −143°, the vapour pressure of which (−46° to 22°) was given by $\log_{10} p$ (mm.) = $-1818/T + 8{\cdot}03$, giving an extrapolated b. p. of 80°. The m. p. of this compound is the lowest recorded for this type of compound and is exceptionally low for a compound of such a molecular weight.

Heptafluoropropylselenobistrifluoromethylarsine. Iodobis(trifluoromethyl)arsine (2·6 mmoles) and bis(heptafluoropropylseleno)mercury (1·3 mmoles) were sealed in a Pyrex ampoule. After 72 hr., separation of the red mercuric iodide was complete and vacuum-fractionation of the volatile products gave *heptafluoropropylselenobistrifluoromethylarsine*, which collected in a trap at −65° [Found: CF_3 (attached to As, measured as CHF_3), 29·9; As, 16·0; Se, 16·9%; *M*, 460. $C_5F_{13}AsSe$ requires CF_3, 30·4; As, 16·3; Se, 17·1%; *M*, 461]. It is a colourless liquid, m. p. −67°, the vapour pressure of which (4° to 75°) is given by $\log_{10} p$ (mm.) = $-2103/T + 8{\cdot}26$, giving an extrapolated b. p. of 118°.

Infrared absorption spectra. The spectra were recorded in the region 4000—400 $cm.^{-1}$ on a Perkin–Elmer model 21, double-beam, recording spectrophotometer, with sodium chloride and potassium bromide prisms. The frequencies ($cm.^{-1}$) and intensities are tabulated. The spectra of the compounds marked * were recorded on Infracord spectrophotometers, and only the strongest bands are given.

$(CF_3)_2(CF_3S)P$: 2370w, 2340w, 2295m, 2260m, 2285w, 2080w, 2063w, 1878w, 1413vw, 1378m, 1367m, 1358m, 1262m, 1199s, 1178vs, 1131s, 1110vs, 841vw, 753s, 743s, 583—570bs, 556s, 535m, 514s, 443s (doublet).

$(CF_3)_2(CF_3S)As$: 2350vw, 2290w, 2260w, 2220w, 1928vw, 1885vw, 1866vw, 1844vw, 1320w, 1302w, 1267m, 1262m, 1205m, 1218ms, 1190s, 1165vs, 1135s, 1106vs, 755s, 731s, 576w, 560w, 534w, 523w, 463w, 436m,

*$(CF_3)_2(CF_3Se)P$: 1195m, 1180vs, 1140m, 1110s, 1080m, 750s.

*$(CF_3)_2(CF_3Se)As$: 1255m, 1185vs, 1160vs, 1130vs, 1100vs, 1060m, 800m, 740m.
*$(CF_3)_2(C_3F_7Se)As$: 1335s, 1280m, 1240vs, 1225vs, 1200s, 1180vs, 1160vs, 1140vs, 1110vs, 1080m, 1045m, 900m, 837vs, 800vw, 750w, 740vs, 672m.

One of the authors (K. J. P.) thanks the Department of Scientific and Industrial Research for a maintenance grant, and another (N. W.) thanks the Israel Institute of Technology for a Scholarship.

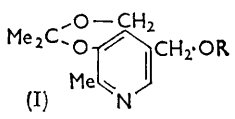
UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, January 10th*, 1962.]

487. *A Convenient Method for the Preparation of Isopropylidenepyridoxine and Some Esters of Pyridoxine.*

By W. KORYTNYK and W. WIEDEMAN.

ISOPROPYLIDENEPYRIDOXINE (I; R = H) has previously been obtained by two methods,[1,2] one of which has been patented.[3] The compound served as the key intermediate in the synthesis of codecarboxylase (pyridoxal phosphate) by Baddiley and Mathias.[1] Since then, it has been used in preparing a number of potential antimetabolites of pyridoxine,[2,4] and more recently in preparing isopyridoxal.[5] In an attempt to find a method which could be adapted for large-scale preparation of isopropylidenepyridoxine, we saturated an acetone suspension of pyridoxine hydrochloride with anhydrous hydrogen chloride at 0°. After 1 hour's shaking at room temperature an almost quantitative yield of pure isopropylidenepyridoxine hydrochloride was obtained. It has been stated[6] that this reaction is "not catalysed by dry hydrogen chloride, at least at room temperature;" in our experiments, about 14% of anhydrous hydrogen chloride was introduced by saturation, but when the concentration of hydrogen chloride was only 4% no detectable amount of isopropylidenepyridoxine hydrochloride was formed.

Isopropylidenepyridoxine has been readily esterified with acyl chlorides[1,6] in the presence of pyridine to give monoesters (I; R = acyl), but the toluene-*p*-sulphonate nor methanesulphonate could not be obtained.[1] As part of our study on the influence of modification of the pyridoxine molecule on biological activity, we have obtained the *p*-nitrobenzoate, benzoate, and hydrogen succinate (I; R = $CO{\cdot}CH_2{\cdot}CO_2H$) of isopropylidenepyridoxine. The isopropylidene group has been selectively hydrolyzed with dilute formic acid, yielding the corresponding monoesters of pyridoxine. Acyl migration is excluded as the three pyridoxine monoesters give characteristic shifts in their ultraviolet absorption maxima which are associated with the formation of a boric acid complex with the unsubstituted phenolic and the 4-hydroxymethyl group.[7]



(I)

Experimental.—Isopropylidenepyridoxine hydrochloride. Pyridoxine hydrochloride (12·0 g., dried in a moderate vacuum at 100°) was suspended in dry, freshly distilled acetone (250 ml.) and cooled in ice. Hydrogen chloride was passed into the suspension with protection from moisture. After about an hour, 35 g. of hydrogen chloride were taken up, and the mixture was

[1] Baddiley and Mathias, *J.*, 1952, 2583.
[2] Cohen and Hughes, *J.*, 1952, 4384.
[3] Cohen, B.P. 715,212.
[4] Bennett, Burger, and Umbreit, *J. Medicin. Pharmaceut. Chem.*, 1959, **1**, 213.
[5] Korytnyk and Kris, *Chem. and Ind.* 1961, 1834.
[6] Sakuragi and Kummerow, *J. Amer. Chem. Soc.*, 1956, **78**, 839.
[7] Scudi, Bastedo, and Webb, *J. Biol. Chem.*, 1940, **136**, 399.

saturated. The flask was stoppered (Teflon) and shaken at room temperature for 1 hr. Crystallisation had by then begun and was complete after storage at −10° to −20° for 2 hr. The crystals were quickly filtered off and immediately washed with dry ether. The colourless product (12·1 g.) had m. p. 210—212° (decomp.) [lit.,[2] 217—218° (decomp.)] (Found: C, 53·4; H, 6·6. Calc. for $C_{11}H_{16}ClNO_3$: C, 53·8; H, 6·6%). Addition of anhydrous ether to the mother-liquors and keeping the mixture at −20° yielded a further 1·9 g. of identical material (negative Gibbs's test).

The procedure has been readily adapted for 100 g. or more of starting material. Isopropylidenepyridoxine, obtained from its hydrochloride by treatment with aqueous potassium carbonate solution, had m. p. 111—112° (lit., m. p. 108—109°,[1] 113—115° [2]).

O^3O^4-*Isopropylidene*-O^5-p-*nitrobenzoylpyridoxine*. Isopropylidenepyridoxine (5·5 g.) was added to a solution of *p*-nitrobenzoyl chloride (5·1 g.) in anhydrous pyridine (40 ml.). After 3 hr., water (75 ml.) was added, and the solid was filtered off, washed with water, and recrystallized from ethanol, yielding 7·2 g. (77%) of needles, m. p. 185—187° (Found: C, 60·2; H, 5·2; N, 8·05. Calc. for $C_{18}H_{18}N_2O_6$: C, 60·3; H, 5·1; N, 7·8%). Baddiley and Mathias [1] gave m. p. 178—179°; their molecular formula and analyses were consistent with each other, but not with the structure assigned to the compound.

The *benzoate*, prepared similarly, had m. p. 85—87° [from light petroleum ether (b. p. 40—60°)] (Found: C, 69·1; H, 6·25. $C_{18}H_{19}NO_4$ requires C, 69·0; H, 6·1%).

O^5-p-*Nitrobenzoylpyridoxine*. O^3O^4-Isopropylidene-O^5-*p*-nitrobenzoylpyridoxine (6·2 g.) was suspended in 9% aqueous formic acid (300 ml.) and heated for 30 min. on a steam-bath. The solution was evaporated *in vacuo*, and some methanol was added. Recrystallization of the crystalline precipitate from hot acetone gave the O^5-p-*nitrobenzoate*, m. p. 197—198·5° (decomp.) (4·5 g., 81%) (Found: C, 56·9; H, 4·6. $C_{15}H_{14}N_2O_6$ requires C, 56·6; H, 4·4%).

O^5-*Benzoylpyridoxine*, obtained by an analogous method, had m. p. 172—174° (decomp.) (Found: C, 65·7; H, 5·6. $C_{15}H_{15}NO_4$ requires C, 65·9; H, 5·5%).

O^5-2′-*Carboxyethyl*-O^3O^4-*isopropylidenepyridoxime*. Isopropylidenepyridoxine (2·0 g.) was heated with succinic anhydride (1·0 g.) at 120° for 3 hr. Two crystallizations from acetone gave the *hydrogen succinate* (2·1 g., 70%), m. p. 180—181° (Found: C, 58·0; H, 6·2; N, 4·6. $C_{15}H_{19}NO_6$ requires C, 58·2; H, 6·2; N, 4·5%).

O^5-2′-*Carboxyethylpyridoxine*. The last-mentioned compound (1·5 g.) was suspended in 1% aqueous formic acid (70 ml.). Ethanol (10 ml.) was added, and the solution was heated on a steam-bath for 30 min., after which most of the liquid was removed *in vacuo*. Ethanol was added and evaporated, and the process was repeated. The oil was taken up in a little ethanol, and was kept at −20° overnight, the *ester* product (0·6 g., 46%) then crystallizing as needles, m. p. 143—146° (Found: C, 53·4; H, 5·8; N, 5·4. $C_{12}H_{15}NO_6$ requires C, 53·5; H, 5·6; N, 5·2%).

Ultraviolet spectra. These were determined with a Cary recording spectrophotometer. Phosphate buffer (pH 6·8; 0·1M-ionic strength) was used. Borate complexes were formed by saturation with boric acid of the solution of the compound in phosphate buffer and adjustment of the pH to its original value (6·8) by addition of sodium hydroxide solution. 3-Deoxypyridoxine and 4-deoxypyridoxine gave no shifts of absorption maxima under these conditions. O^5-2′-Carboxyethylpyridoxine had maxima at 254, 290, and 325 mμ at pH 6·8. Addition of boric acid resulted in a single absorption maximum at 296 mμ. Similar shifts were observed for the other two monoesters.

This work was supported in part by the National Cancer Institute, U.S. Public Health Service. We thank Dr. Charles A. Nichol for his interest and encouragement.

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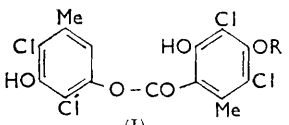
[*Received, January 15th,* 1962.]

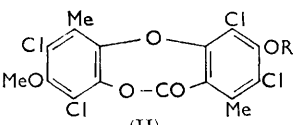
488. *Oxidative Coupling of* o-*Phenoxybenzoic Acid.*

By J. R. Lewis.

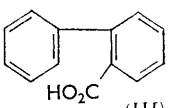
Recent work on the oxidative coupling of phenolic intermediates to yield natural products has been extended to show that depsidones may be produced from the appropriate depsides, since Ollis and his co-workers have successfully synthesised diploicin (II; R = H) from the depside (I; R = CH_2Ph) by treatment with manganese dioxide.[1] An alternative method for producing the depside linkage would be through carbon–carboxyl coupling and in this context the work of Kenner and his colleagues [2] on the cyclisation of diphenyl-2-carboxylic acid (III) to the lactone (IV) suggested that the appropriate *o*-phenoxybenzoic acid (V) might, under similar oxidative conditions, yield the simple depsidone (VI).



(I)



(II)



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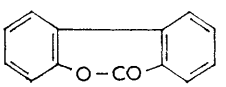
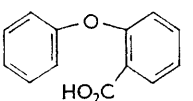


(IV)



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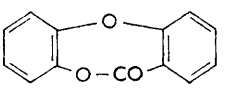

(VI)

Treatment of *o*-phenoxybenzoic acid (V) with manganese dioxide in boiling chloroform for 2 hours gave the depsidone (VI) in ~2% yield. The use of chromium trioxide in glacial acetic acid at 100° also gave ~2% of the depsidone. The identity of the product of oxidation was confirmed by unambiguous synthesis: dehydration of *o*-*o*′-hydroxphenoxybenzoic acid [3] gave the lactone (VI). Although Ungnade and Rubin reported the production of a neutral compound by acidification of an alkaline solution of this phenoxy-acid,[3] we were unable to obtain it by this method; their material differed from our lactone in m. p. and analysis.

Experimental.—o-o′-*Hydroxyphenoxybenzoic acid lactone* (*dibenzo*-[1,4]-*dioxepin*-11-*one*) (VI). *o*-*o*′-Hydroxyphenoxybenzoic acid [3] (0·2 g.) was treated in dry pyridine (20 ml.) with thionyl chloride (5 ml.) at room temperature overnight, then poured into ice-cold dilute hydrochloric acid and extracted with ether; the ethereal layer was washed with water, dilute sodium hydroxide, and water, dried (Na_2SO_4), and evaporated. The residual *lactone* (0·13 g.) crystallised from pentane, then having m. p. 68° (Found: C, 73·4; H, 3·8; O, 22·7. $C_{13}H_8O_3$ requires C, 73·6; H, 3·8; O, 22·6%).

Oxidative coupling of o-*phenoxybenzoic acid.* (*a*) The acid (1·0 g.) was added in acetic acid (3 ml.) to chromium trioxide (0·3 g.) in water (2 ml.) and heated at 100° for 40 min., then worked up in the usual way to give a neutral fraction (18 mg.), m. p. and mixed m. p. 66—68° (from pentane).

(*b*) The acid (0·5 g.) was treated in chloroform (35 ml.) with manganese dioxide [4] (2 g.) and refluxed for 2 hr. The neutral fraction (8·5 mg.) was the lactone (VI), m. p. and mixed m. p. 66—68°. The acid (0·5 g.) in ether (25 ml.), on treatment with manganese dioxide (1 g.) at room temperature for 17 hr., also gave the lactone (3 mg.), m. p. and mixed m. p. 66—68°.

[1] Brown, Clark, Ollis, and Veal, *Proc. Chem. Soc.*, 1960, 393.
[2] Kenner, Murray, and Taylor, *Tetrahedron*, 1957, **1**, 259.
[3] Ungnade and Rubin, *J. Org. Chem.*, 1951, **16**, 1311.
[4] Mancera, Rosenkranz, and Sondheimer, *J.*, 1953, 2189.

The first part of this work was carried out during the tenure of an I.C.I. Fellowship at University College, Swansea, and the author acknowledges guidance and encouragement by Professor C. H. Hassall.

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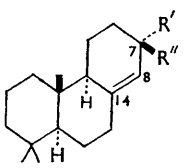
[*Received, January 18th,* 1962.]

489. *The Synthesis of Diterpenes. Part V.* An Intermediate for the Synthesis of the Pimaradienes.*

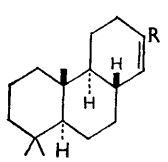
By J. A. BARLTROP, D. GILES, J. R. HANSON, and N. A. J. ROGERS.

(±)-PODOCARP-8(14)-EN-7-ONE (IIa), the synthesis of which has been described elsewhere,[1] seemed to be a starting material well adapted to the synthesis of pimaradienes, one of which, sandaracopimaradiene (Ia), had been reported [2] erroneously [3] to be identical with rimuene. The ketone was transformed into 7-formylpodocarp-7-ene (IIIa) and 13-cyanopodocarp-7-ene (IIIc). It was proposed to complete the synthesis of the pimaradienes by methylating the αβ-unsaturated aldehyde (IIIa) and then condensing the products of this reaction (Ic and Id) with methylenetriphenylphosphorane.

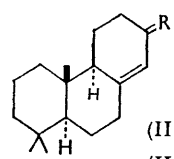
At this point, work on this line was discontinued because of the publication [3] by Ireland and Schiess of a synthesis of (±)-pimaradiene (Ib) and (±)-sandaracopimaradiene (Ia) from one of our intermediates, the unsaturated aldehyde (IIIa).



(Ia: $R' = CH{:}CH_2$, $R'' = Me$)
(Ib: $R' = Me$, $R'' = CH{:}CH_2$)
(Ic: $R' = Me$, $R'' = CHO$)
(Id: $R' = CHO$, $R'' = Me$)



(IIIa: R = CHO)
(IIIb: R = CH:N·OH)
(IIIc: R = CN)



(IIa: R = :O)
(IIb: R = :CH·OMe)

$Ph_3\overset{+}{P}-\overset{-}{C}H\cdot OMe$
(IV)

The unsaturated ketone (IIa) was converted into the unsaturated ether (IIb) by reaction with the ylide (IV). Treatment with alcoholic hydrogen chloride under nitrogen gave (±)-7-formylpodocarp-7-ene (IIIa). The dextrorotatory aldehyde (IIIa) was obtained in similar fashion from (+)-podocarp-8(14)-en-7-one (IIa) which was in turn obtained from manool by an improvement on the published procedure [4] of ozonolysis, followed by acid

* Part IV, Day and Barltrop, *Tetrahedron*, 1961, **14**, 310.

[1] Barltrop and Rogers, *J.*, 1958, 2566.
[2] Galik, Kuthan, and Petrů, *Chem. and Ind.*, 1960, 722.
[3] Ireland and Schiess, *Tetrahedron Letters*, 1960, No. 25, 37.
[4] Hosking, *Ber.*, 1936, **69**, 780.

treatment. (+)-7-Cyanopodocarp-7-ene (IIIc) was obtained by treating the oxime (IIIb) with acetic anhydride.

Experimental.—By " deactivated alumina " is meant Grade H (Peter Spence) alumina that has been deactivated by the addition of 5% v/w of 10% aqueous acetic acid, followed by thorough shaking to ensure homogeneity.

Methoxymethyltriphenylphosphonium chloride. Chloromethyl methyl ether [5] (20 g.) was added, under nitrogen to a stirred solution of triphenylphosphine (32 g.) in dry acetone (50 c.c.) at 40°. Crystals began to separate after 5 min. The mixture was stirred at 40° for a further 6 hr. The crystals were collected and washed with dry ether to give the quaternary salt (47·5 g.) which after crystallisation from methylene dichloride had m. p. 191—192° (cf. lit.,[6] 191—193°).

(±)-7-*Formylpodocarp*-7-*ene* (IIIa). An ethereal solution of n-butyl-lithium (from n-butyl bromide, 5·6 g.) was added, under nitrogen, to a suspension of the above salt (14 g.) in dry ether (50 c.c.). The resulting deep red suspension of the ylide (IV) was stirred for 5 min. and to it was added, with stirring, an ethereal solution of (±)-podocarp-8(14)-en-7-one (1·9 g. in 10 c.c.). The buff-coloured suspension was stirred for a further 3 hr. at room temperature and the complex was then decomposed by heating it under reflux in light petroleum (b. p. 60—80°) for 15 hr. The mixture was cooled and filtered, to give a solution of the products which were adsorbed on deactivated alumina (100 g.). Elution with light petroleum (b. p. 60—80°) gave an oil which was used without further purification.

When shaken in ethereal solution with saturated aqueous mercuric chloride, filtered, evaporated, and subjected to chromatography on deactivated alumina, (±)-7-*methoxymethylenepodocarp*-8(14)-*ene* (IIb) was obtained as an oil, b. p. 145° (bath temp.)/0·05 mm. (Found: C, 82·8; H, 10·6. $C_{19}H_{30}O$ requires C, 83·1; H, 10·9%).

The crude oil from this experiment in ethanol (100 c.c.) was heated under reflux for 1 hr. with 2N-hydrochloric acid (25 c.c.), in an atmosphere of nitrogen. The product was taken up in ether, washed with sodium carbonate solution and water, dried, and evaporated. Adsorption on deactivated alumina, followed by elution with light petroleum (b. p. 60—80°), gave triphenylphosphine, m. p. 80—81°. Further elution with 3 : 10 benzene–light petroleum gave (±)-7-formylpodocarp-7-ene (IIIa) (500 mg.), b. p. 130°/0·1 mm. (Found: C, 82·7: H, 10·5. Calc. for $C_{18}H_{28}O$: C, 83·1; H, 10·8%). The *dinitrophenylhydrazone*, recrystallised from ethanol, had m. p. 215—217° (Found: C, 65·1; H, 7·0. $C_{24}H_{32}N_4O_4$ requires C, 65·1; H, 7·1%). Ireland *et al.* [3] give m. p. 81—83° for the aldehyde.

(+)-*Podocarp*-8(14)-*en*-7-*one* (IIa). Manool (10 g.), dissolved in redistilled ethyl acetate (150 c.c.), was treated with ozonised oxygen (5%; 12 l./hr.) at −10° until the solution no longer decolorised bromine in ethyl acetate. The solvent was removed under reduced pressure at 25°, water (100 c.c.) and zinc dust (2 g.) were added, and the mixture was heated at 100° for 2 hr. with stirring. The products were extracted with ether, and the combined extracts were washed with aqueous sodium hydrogen carbonate, dried, and evaporated to give a yellow oil (6 g.). This was dissolved in benzene and adsorbed on silica gel. Elution with benzene gave (+)-1-(3′-oxobutyl)-5,5,9-trimethyl-*trans*-decal-2-one (3·3 g.). Further elution with 10% ether in benzene gave (+)-podocarpan-14-ol-7-one (0·5 g.), m. p. 215—217° (from light petroleum). These products were combined and dissolved in dry chloroform (50 c.c.), and added to a saturated solution of hydrogen chloride in dry chloroform (150 c.c.). The resulting purple solution was left at room temperature for 15 hr., washed with aqueous sodium carbonate and water, dried, and evaporated. Adsorption on deactivated alumina (200 g.), followed by elution with 2 : 5 benzene–light petroleum (b. p. 60—80°) gave (+)-podocarp-8(14)-en-7-one (IIa) (2·2 g.). Recrystallisation from light petroleum (b. p. 30—40°) gave prisms, m. p. 65—67°, $[\alpha]_D^{22}$ +45° (*c* 1·0 in $CHCl_3$), $\lambda_{max.}$ 242 mμ (ε 17,600) {lit.,[7] m. p. 64—66°, $[\alpha]_D$ +49°, $\lambda_{max.}$ 242·5 mμ (ε16,200)}.

(+)7-*Formylpodocarp*-7-*ene* (IIIa). Prepared according to the directions given for the racemic aldehyde, the *product* crystallised from light petroleum (b. p. 40—60°) as leaflets, m. p. 115—116°, $[\alpha]_D$ +42° (*c* 1·0 in $CHCl_3$), $\lambda_{max.}$ 232·5 mμ (ε 17,800) (Found: C, 82·5; H, 10·9. $C_{18}H_{28}O$ requires C, 83·0; H, 10·8%).

[5] Cf. Marvel, *Org. Synth.*, Coll. Vol. I, 2nd edn., p. 377.
[6] Levine, *J. Amer. Chem. Soc.*, 1958, **80**, 6150.
[7] Grant and Hodges, *Tetrahedron Letters*, 1959, No. 10, 21.

7-Cyanopodocarp-7-ene (IIIc). The dextrorotatory aldehyde (IIIa) (200 mg.) was converted into the *oxime* (IIIb), m. p. 196—197° (from ethanol) (Found: C, 78·0; H, 10·5. $C_{18}H_{29}NO$ requires C, 78·5; H, 10·6%). This (150 mg.) was heated under reflux with acetic anhydride (3 c.c.) for 1 hr., cooled, and poured into dilute sodium hydrogen carbonate solution. The resultant suspension was extracted with ether, washed, dried, and evaporated, to give the crude nitrile (IIIc). Recrystallisation from light petroleum (b. p. 40—60°) gave the *product* as plates, m. p. 127—128°, $\lambda_{max.}$ 212 mμ (ε 13,700) (Found: C, 83·3; H, 10·6. $C_{18}H_{27}N$ requires C, 83·9; H, 10·7%).

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