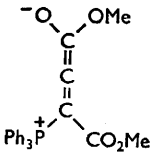
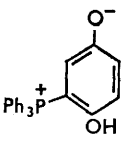
NOTES.

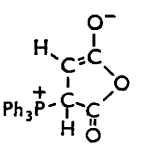
224. *The Isomerisation of Dimethyl Maleate by Triphenylphosphine.*

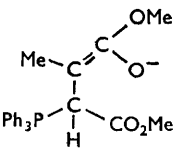
By A. R. HANDS.

THE isomerisation of a dialkyl maleate to the corresponding fumarate is known to be catalysed by many agents, most of which are general catalysts for the *cis–trans*-isomerisation of olefinic bonds. It has now been found that dimethyl maleate in the presence of 10% of triphenylphosphine is a almost completely converted into dimethyl fumarate in 1 hour at 150° (see Figure), whereas dimethyl citraconate is not isomerised under these conditions.


(I)


(II)

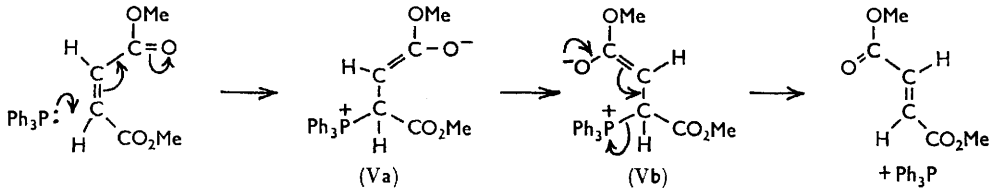

(III)


(IV)

Dimethyl acetylenedicarboxylate and triphenylphosphine have been shown [1] to give initially the adduct (I). *p*-Benzoquinone gives [2] the adduct (II), and maleic anhydride gives [3] the adduct (III). Dimethyl maleate might by analogy be expected to give the

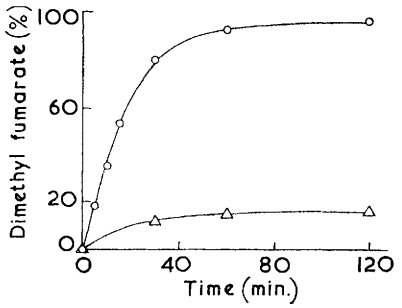
[1] Horner and Hoffmann, *Angew. Chem.*, 1956, **68**, 473.
[2] Ramirez and Dershowitz, *Chem. and Ind.*, 1956, 665.
[3] Hands, unpublished work.

compound (Va); examination of a molecular model shows that there is little steric hindrance to rotation about the C–C bond to give the more stable configuration (Vb) in which the charge separation is far less. Elimination of triphenylphosphine from structure (Vb) will give dimethyl fumarate.



The hypothetical adduct (IV) from triphenylphosphine and dimethyl citraconate is shown by a molecular model to be more strained than structure (Va), and rotation about the C–C bond is hindered by collision between the *C*-methyl group and the triphenylphosphonium and methoxycarbonyl groups, thus preventing isomerisation to the *trans*-configuration.

Experimental.—Dimethyl maleate (9·0 g.) and triphenylphosphine (1·0 g.) were heated together at 150° for periods of up to 120 min. Acetone (10 ml.) was added to the cooled mixture, and after 8 hr. at 0° the crystals were filtered off and washed with ice-cold acetone



The isomerisation of dimethyl maleate to dimethyl fumarate when heated with ○ 10% and △ 1% of triphenylphosphine for different periods.

(5 ml.). The combined filtrate and washings were evaporated to 13 ml., and left at 0° for 8 hr., and the crystals were filtered off and washed as before. Recrystallisation from the minimum amount of acetone gave dimethyl fumarate, m. p. 101—102° (Figure). Mixtures of dimethyl maleate (10·0 g.) and triphenylphosphine (0·1 g.) were treated similarly (Figure). No dimethyl fumarate was isolated when dimethyl maleate was heated alone at 150° for 2 hr.

Dimethyl citraconate (9·0 g.) and triphenylphosphine (1·0 g.) were heated together at 150° for periods of up to 2 hr. The mixture was hydrolysed at 60° for 2 hr. with 10% potassium hydroxide in aqueous methanol (1 : 1 v/v; 25 ml.), evaporated to 15 ml. under reduced pressure, extracted with ether (25 ml.), acidified with 2N-hydrochloric acid (30 ml.), and re-extracted with ether (6 × 30 ml.). The latter extracts were dried (Na_2SO_4), and evaporated to dryness, and the residue was recrystallised from ether–light petroleum (b. p. 40—60°; 1 : 1), to give citraconic acid (7·8—8·3 g., 87—92%), m. p. 89—90° (decomp.).

Department of Biochemistry, University of Oxford. [*Received, April 8th,* 1963.]

225. *A Substituted Naphthoic Acid Analogue to 4-Aminosalicylic Acid.*

By E. N. Gabali, Y. M. Abouzeid, and E. M. Abdallah.

We report here the synthesis of the naphthalene analogue to 4-aminosalicyclic acid namely 4-amino-2-hydroxy-1-naphthamide, from 1-naphthylamine, *via* 2,4-dinitro-1-naphthylamine. The 1,2-diazo-oxide obtained by the diazotisation of that amine was converted into the 1-cyano-2-hydroxy-compound by the modification of the Sandmeyer's reaction reported earlier [1] but by using potassium cyanonickelate instead of cuprous cyanide, the yield of the cyano-compound was thereby raised to 80%.[1] The cyano-derivative, by hydrolysis with sulphuric acid and subsequent reduction of the amide, with alkaline ferrous sulphate afforded 4-amino-2-hydroxy-1-naphthamide. 2-Hydroxy-4-nitro-1-naphthonitrile, on the other hand, was converted by alkaline ferrous sulphate into 4-amino-2-hydroxy-1-naphthonitrile.

Experimental.—2,4-Dinitro-1-naphthylamine and 4-nitronaphthalene-1,2-diazo-oxide were prepared according to the methods reported by Morgan *et al.*[2]

2-*Hydroxy*-4-*nitro*-1-*naphthonitrile*. The 1,2-diazo-oxide (21·5 g.) in freshly distilled pyridine (110 ml.) was added to a cooled solution of potassium cyanonickelate (35 g. of potassium cyanide in 150 ml. of water, added to 30 g. of nickel sulphate in 50 ml. of water). The mixture was kept at 0° until it did not give a blue to alkaline resorcinol. The mixture was then warmed to 50—60° for 2 hr., and poured into 1 : 1-hydrochloric acid. The precipitate crystallised from boiling water as yellow needles, m. p. 212—213° (decomp.) (lit.,[1] m. p. 212—213°). The filtrate was concentrated under reduced pressure and extracted with ether, the extract treated with sodium hydroxide and then hydrochloric acid, and the total isolated (17·2 g.).

The nitrile was hydrolysed with sulphuric acid to 2-hydroxy-4-nitro-1-naphthamide as already reported.[1]

4-*Amino*-2-*hydroxy*-1-*naphthamide*. The amide (2 g.) was dissolved in hot dilute ammonia (100 ml.) and poured into a boiling solution of ferrous sulphate (16 g.) in water (40 ml.). Ammonia solution (4 g., 0·88) was added (3 × 5 ml.) followed by vigorous agitation after each addition. The mixture was then boiled for 5 min. and filtered hot, and the clear filtrate acidified with dilute acetic acid (1 : 1) yielding a precipitate which was extracted with ether; the ether was evaporated under reduced pressure and the residue (1 g.) crystallised from 75% aqueous methanol, forming brown plates of the *amide*, m. p. 184—186° (decomp.) (Found: C, 64·6; H, 5·4; N, 14·2. $C_{11}H_{10}N_2O_2$ requires C, 65·3; H, 4·9; N, 13·85%).

4-*Amino*-2-*hydroxy*-1-*naphthonitrile*. 2-Hydroxy-4-nitro-1-naphthonitrile (3 g.) in hot dilute ammonia solution (100 ml.) was poured into a boiling solution of ferrous sulphate (24·2 g.) in water (60 ml.). The solution was then treated with ammonia solution (s.g. 0·88), boiled for 5 min., and filtered hot. The filtrate was acidified with 1 : 1-acetic acid, and the precipitate (1·4 g.) crystallised from dilute acetic acid; the *nitrile* formed long needles, m. p. 242—243° (decomp.) (Found: C, 71·7; H, 4·3; N, 15·2. $C_{11}H_8N_2O$ requires C, 71·7; H, 4·3; N, 15·21%).

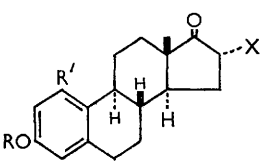
Organic Chemistry Department,
Faculty of Pharmacy, Cairo University, Egypt. [*Received, June 28th,* 1963.]

[1] Gabali and Abdallah, *J.*, 1963, 3465.
[2] Morgan and Evens, *J.*, 1919, **115**, 1126.

226. *Modified Steroid Œstrogens.*

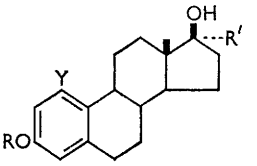
By D. D. Evans, D. E. Evans, and R. W. J. Williams.

The use of steroid œstrogens in treatment of coronary heart disease results in a return of the blood lipid pattern towards normal,[1] but during treatment œstrogenic effects are usually severe [2] and a serious disadvantage.[3] In an effort to obtain compounds with low œstrogenicity but potentiated lipodiatic activity, we have prepared analogues of œstrone (Ia), œstradiol (IIa), 1-hydroxy-4-methylœstra-1,3,5(10)-trien-17-one (IIIa) [4] and 17β-hydroxy-17α-methylœstr-5(10)-en-3-one (IVa).[5]



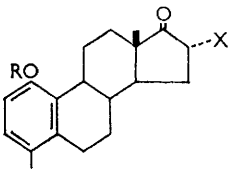
(I)

(Ia: R = R′ = X = H)
(Ib: R = R′ = Me; X = H)
(Ic: R = R′ = Me; X = CH·OH)
(Id: R = R′ = Me; X = Cl)
(Ie: R = R′ = Me; X = Br)



(II)

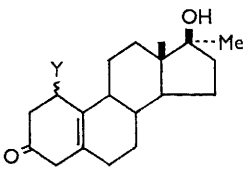
(IIa: R = R′ = Y = H)
(IIb: R = Y = Me; R′ = H)
(IIc: R = R′ = Y = Me)
(IId: R = Y = Me; R′ = C≡CH)
(IIe: R = Y = Me; R′ = Et)



(III)

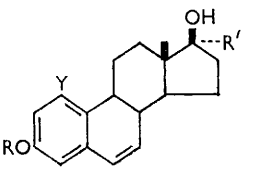
(IIIa: R = X = H)
(IIIb: R = Me; X = Cl)
(IIIc: R = Me; X = Br)
(IIId: R = Me; X = H)

The diol (Va) [6] was converted into its 3-methyl ether (Vb) with dimethyl sulphate, and subsequently, by hydrogenation, into 3-methoxy-1-methylœstra-1,3,5(10)-trien-17β-ol (IIb).[7] Oxidation of the 17β-alcohol (IIb) with Jones chromic acid [8] yielded the 17-ketone (Ib), which reacted with methyl-lithium to give 3-methoxy-1,17α-dimethylœstra-1,3,5(10)-trien-17β-ol (IIc). Birch reduction of the ether (IIc), and subsequent mild acid hydrolysis of the crude 3-methoxy-1ξ,17α-dimethylœstra-2,5(10)-dien-17β-ol, gave 17β-hydroxy-1ξ,17α-dimethylœstr-5(10)-en-3-one (IVb).



(IV)

(IVa: Y = H)
(IVb: Y = Me)



(V)

(Va: R = R′ = H; Y = Me)
(Vb: R = Y = Me; R′ = H)

Ethynylation of the ketone (Ib) gave 17α-ethynyl-3-methoxy-1-methylœstra-1,3,5(10)-trien-17β-ol (IId), which by hydrogenation yielded the 17α-ethyl analogue (IIe). Since the initiation of this work, the syntheses of the 17α-ethynyl- (IId) and the 17α-ethyl-analogue (IIe) have been claimed [9] but the compounds were not characterised, other than by melting point.

[1] Oliver and Boyd, *Lancet*, 1956, (ii), 1273; Marmorston, Magidson, Kuzma, and Moore, *J. Amer. Med. Assoc.*, 1960, **174**, 241.
[2] Bedford and Lodge, *J. Amer. Geriat. Soc.*, 1959, **7**, 911.
[3] Eder in "Hormones and Atherosclerosis," ed. Pincus, Academic Press, New York, 1959, p. 339.
[4] Dreiding and Voltman, *J. Amer. Chem. Soc.*, 1954, **76**, 537; Djerassi and Scholz, *J. Org. Chem.*, 1948, **13**, 697.
[5] Cook, Edgren, and Saunders, *Endocrinology*, 1958, **62**, 798 (U.S.P., 2,905,676).
[6] Djerassi, Rosenkranz, Romo, Pataki, and Kaufmann, *J. Amer. Chem. Soc.*, 1952, **72**, 4540.
[7] British Drug Houses, B.P. 807,225 (*Chem. Abs.*, 1959, **53**, 13,208).
[8] Djerassi, Engle, and Bowers, *J. Org. Chem.*, 1956, **21**, 1547.
[9] G. D. Searle and Co., B.P. 842,303 (*Chem. Abs.*, 1961, **55**, 4592).

Hydroxymethylation of the ketone (Ib) with ethyl formate in the presence of sodium hydride gave 16-hydroxymethylene-3-methoxy-1-methylœstra-1,3,5(10)-trien-17-one (Ic), and a similar reaction with 3-methoxyœstra-1,3,5(10)-trien-17-one gave the previously reported [10] 16-hydroxymethylene-3-methoxyœstra-1,3,5(10)-trien-17-one.

Substitution at C-16 was also achieved by halogenation [11] of the 17-enol acetates of the ketones (Ib) and (IIId), to give 16α-chloro- (Id) and 16α-bromo-3-methoxy-1-methylœstra-1,3,5(10)-trien-17-one (Ie) and 16α-chloro- (IIIb) and 16α-bromo-1-methoxy-4-methylœstra-1,3,5(10)-trien-17-one (IIIc). The 16α-configuration was assigned to these halogenated compounds by analogy with other compounds prepared previously by halogenation of 17-enol acetates.[12,13]

Experimental

For general experimental details, see *J.*, 1963, 3578.

3-*Methoxy*-1-*methylœstra*-1,3,5(10),6-*tetraen*-17β-*ol* (Vb).—Reaction of the diol (Va) [6] (15·0 g.) with dimethyl sulphate (150 ml.) in methanolic potassium hydroxide at 35° gave the *alcohol* (Vb) (9·2 g.), m. p. 117—120° (from acetone–light petroleum), $[\alpha]_D$ −137° (*c* 1·215), $\nu_{max.}$ 3505, 1630, 1587, 1130 cm.$^{-1}$ (Found: C, 80·3; H, 8·95. $C_{20}H_{26}O_2$ requires C, 80·5; H, 8·8%).

3-*Methoxy*-1-*methylœstra*-1,3,5(10)-*trien*-17β-*ol* (IIb).—The alcohol (Vb) (9·2 g.) was hydrogenated in ethyl acetate over 10% palladised charcoal (2·0 g.), to give the alcohol (IIb), m. p. 118—120° (from acetone–light petroleum), $[\alpha]_D$ +158° (*c* 0·96) (lit.,[7] m. p. 117—118°, $[\alpha]_D$ +157°) (Found: C, 80·3; H, 9·6. Calc. for $C_{20}H_{28}O_2$: C, 79·95; H, 9·4%).

3-*Methoxy*-1-*methylœstra*-1,3,5(10)-*trien*-17-*one* (Ib).[14]—Oxidation of the alcohol (IIb) (3·0 g.) in acetone (300 ml.) (freshly distilled from potassium permanganate) at 15—20° with Jones chromic acid solution [8] (3 ml.) gave the ketone (Ib) (2·5 g.), m. p. 126—130° (from ethanol) (lit.,[14] 129—130°).

3-*Methoxy*-1,17α-*dimethylœstra*-1,3,5(10)-*trien*-17β-*ol* (IIc).—A solution of methyl-lithium [from methyl iodide (25 ml.) and lithium (4·5 g.)] in ether (100 ml.) was added to a stirred solution of the foregoing ketone (Ib) (3·9 g.) in anhydrous ether (250 ml.) under argon. The mixture was set aside for 2 hr., refluxed for 2 hr., left for 50 hr., and worked up in the usual way, to give the *alcohol* (IIc) (2·8 g.), m. p. 172—174° (from acetone), $[\alpha]_D$ +128° (*c* 0·98), $\nu_{max.}$ 3474, 3378, 1595, 1577, 1145 cm.$^{-1}$ (Found: C, 80·4; H, 9·8. $C_{21}H_{30}O_2$ requires C, 80·2; H, 9·6%).

17β-*Hydroxy*-1ξ,17α-*dimethylœstr*-5(10)-*en*-3-*one* (IVb).—Lithium wire (8·5 g.) was added to a stirred mixture of anhydrous ether (500 ml.) and liquid ammonia (1500 ml.). After ten minutes' stirring, a solution of the alcohol (IIc) (6·45 g.) in anhydrous ether (650 ml.) was added dropwise during 15 min. Stirring was continued for a further 20 min., then ethanol (200 ml.) was added dropwise during 20 min., and the ammonia allowed to evaporate. The product was isolated in the usual way with ether, dissolved in methanol (600 ml.), and treated, under nitrogen, with a mixture of acetic acid (6 ml.) and water (90 ml.). After 22 hr. at room temperature the mixture was poured into sodium chloride solution, and worked up in the usual way. Concentration of the ethereal extract gave a white solid (2·15 g.), m. p. 184—195°, $[\alpha]_D$ −39° (*c* 0·65). Further concentration yielded a second crop of crystals (390 mg.), m. p. 185—195°, $[\alpha]_D$ −48° (*c* 1·09). The first solid gave the *ketone* (IVb), m. p. 185—195° (from ether) $[\alpha]_D$ −48° (*c* 1·12), $\nu_{max.}$ 3474, 1701, 1648sh cm.$^{-1}$. The ultraviolet spectrum showed only end-absorption (Found: C, 79·2; H, 9·8. $C_{20}H_{30}O_2$ requires C, 79·4; H, 10·0%). Since isomerisation of $\Delta^{5(10)}$-3-keto-steroids is reported [15] to occur on heating, the m. p. reported is for samples placed on the Kofler block at 170°.

17α-*Ethynyl*-3-*methoxy*-1-*methylœstra*-1,3,5(10)-*trien*-17β-*ol* (IId).—Acetylene was bubbled through a stirred solution of potassium (8·0 g.) in anhydrous t-pentyl alcohol (180 ml.) and ether (180 ml.) at 0° for 1 hr. before the addition of 3-methoxy-1-methylœstra-1,3,5(10)-trien-17-one (Ib) (7·9 g.), and for 4 hr. afterwards. After the mixture had reached room temperature, it

[10] Bardhan, *J.*, 1936, 1848.
[11] Johnson and Johns, *J. Amer. Chem. Soc.*, 1957, **79**, 2005.
[12] Fishman and Biggerstaff, *J. Org. Chem.*, 1958, **23**, 1190.
[13] Mueller and Johns, *J. Org. Chem.*, 1961, **26**, 2403; Mueller, Johns, Cook, and Edgren, *J. Amer. Chem. Soc.*, 1958, **80**, 1769.
[14] Ringold, Rosenkranz, and Sondheimer, *J. Amer. Chem. Soc.*, 1956, **78**, 2477.
[15] Wilds and Nelson, *J. Amer. Chem. Soc.*, 1953, **75**, 5366.

was stirred for a further 18 hr., treated with 10% ammonium chloride solution (100 ml.), and steam-distilled. Isolation in the usual way with ethyl acetate–ether gave the *alcohol* (IId) (6·28 g.), m. p. 128·5—130·5 (from acetone–light petroleum) (lit.,[9] 128—131°), $[\alpha]_D$ +63·5° (*c* 1·03), $\nu_{max.}$ 3580, 3310, 1594, 1547, 1144 cm.$^{-1}$ (Found: C, 81·2; H, 8·7. $C_{22}H_{28}O_2$ requires C, 81·4; H, 8·7%).

17α-*Ethyl*-3-*methoxy*-1-*methylœstra*-1,3,5(10)-*trien*-17β-*ol* (IIe).—The alcohol (IId) (5·84 g.) was hydrogenated in ethanol (130 ml.) over 5% palladised charcoal (600 mg.), to give the *alcohol* (IIe) (5·3 g.), m. p. 157—159° (from acetone–light petroleum), $[\alpha]_D$ +125° (*c* 0·975), $\nu_{max.}$ 3535, 1598, 1574, 1147 cm.$^{-1}$ (Found: C, 80·2; H, 9·7. $C_{22}H_{32}O_2$ requires C, 80·4; H, 9·8%).

16-*Hydroxymethylene*-3-*methoxy*-1-*methylœstra*-1,3,5(10)-*trien*-17-*one* (Ic).—A stirred solution of 3-methoxy-1-methylœstra-1,3,5(10)-trien-17-one (Ib) (2·84 g.) in anhydrous benzene (25 ml.) was treated with sodium hydride (950 mg.; 50% dispersion in oil) and ethyl formate (16 ml.) under nitrogen. Stirring was continued for 2 hr., and the mixture then refluxed for 90 min. The cooled mixture was poured into ether, and the sodium salt of the 16-hydroxymethylene derivative extracted with water. The aqueous extract was washed with ether, acidified, and the product extracted with ether in the usual way. A solution of the oily residue in ether (10 ml.) was refrigerated overnight, to give the *ketone* (Ic), m. p. 120—125° (decomp.) (from acetone–ether), $[\alpha]_D$ +223° (*c* 1·0), $\lambda_{max.}$ 268 (ε 10,700) 303 mμ (ε 6300), $\nu_{max.}$ 3225, 1701, 1632, 1595, 1140 cm.$^{-1}$ (Found: C, 77·3; H, 8·1. $C_{21}H_{26}O_3$ requires C, 77·3; H, 8·0%).

16-Hydroxymethylene-3-methoxyœstra-1,3,5(10)-trien-17-one [10] was prepared similarly; m. p. 169—172° (lit.,[10] 170—171°), $[\alpha]_D$ +136° (*c* 1·02), $\lambda_{max.}$ 270 (10,820), 304 mμ (ε 6730), $\nu_{max.}$ 1699, 1618, 1605, 1500, 1235 cm.$^{-1}$ (Found: C, 77·2; H, 7·8. Calc. for $C_{20}H_{24}O_3$: C, 76·9; H, 7·7%).

16α-*Bromo*-3-*methoxy*-1-*methylœstra*-1,3,5(10)-*trien*-17-*one* (Ie).—A solution of bromine (500 mg.) in carbon tetrachloride (7 ml.) was added during 15 min. to a cooled (−5 to −10°) stirred solution of 3-methoxy-1-methylœstra-1,3,5(10),16-tetraen-17-yl acetate (1·03 g.) in anhydrous carbon tetrachloride (140 ml.) containing suspended anhydrous potassium carbonate (2 g.). The pale yellow mixture was poured into sodium hydrogen sulphite solution and the product isolated in the usual way with methylene chloride. Boiling ethyl acetate (5 ml.) was added to the solid product (1·2 g.), and the solution quickly re-boiled and rapidly cooled to −5°; a solid (560 mg.), m. p. 154—158°, crystallised out. Recrystallisation gave the *bromo-ketone* (Ie), m. p. 157—160°, $[\alpha]_D$ +185° (*c* 1·51), $\nu_{max.}$ 1745, 1599, 1577, 1148 cm.$^{-1}$ (Found: C, 63·8; H, 7·1; Br, 20·95. $C_{20}H_{25}BrO_2$ requires C, 63·7; H, 6·7; Br, 21·2%).

The chloro-ketone (Id) was prepared similarly; it had m. p. 152—155° (from ethyl acetate), $[\alpha]_D$ +230 (*c* 1·14), $\nu_{max.}$ 1754, 1599, 1574, 1148 cm.$^{-1}$ (Found: C, 72·0; H, 8·0; Cl, 10·4. $C_{20}H_{25}ClO_2$ requires C, 72·2; H, 7·6; Cl, 10·65%).

Halogenation of 1-methoxy-4-methylœstra-1,3,5(10),16-tetraen-17-yl acetate gave the *bromo-ketone* (IIIc), m. p. 137—139°, $[\alpha]_D$ +221° (*c* 1·08), $\nu_{max.}$ 1748, 1581, 1081 cm.$^{-1}$ (Found: C, 64·0; H, 6·9; Br, 20·6%), and the *chloro-ketone* (IIIb), m. p. 144—146°, $[\alpha]_D$ +284° (*c* 1·08), $\nu_{max.}$ 1750, 1577, 1079 cm.$^{-1}$ (Found: C, 72·3; H, 7·5; Cl, 10·4%).

3-*Methoxy*-1-*methylœstra*-1,3,5(10),16-*tetraen*-17-*yl Acetate*.—A mixture of 3-methoxy-1-methylœstra-1,3,5(10)-trien-17-one (Ib) (10·7 g.), toluene-*p*-sulphonic acid (1·8 g.), and isopropenyl acetate (160 ml.) was distilled slowly. After 12 hr. (90 ml. of distillate), more isopropenyl acetate (50 ml.) was added, and distillation continued for a further 5 hr. (15 ml. of distillate). The mixture was cooled, and the oily product isolated in the usual way and chromatographed on neutral alumina, to give the *acetate* (8·24 g.), m. p. 88—89·5° (from acetone–methanol), $\nu_{max.}$ 1750, 1624sh, 1605, 1577, 1148 cm.$^{-1}$ (Found: C, 77·5; H, 8·35. $C_{22}H_{28}O_3$ requires C, 77·6; H, 8·3%).

Reaction of the 17-ketone (IIId) [4] under similar conditions gave 1-*methoxy*-4-*methylœstra*-1,3,5(10),16-*tetraen*-17-*yl acetate* (4·3 g.), m. p. 126—128°, $[\alpha]_D$ +229° (*c* 0·97), $\nu_{max.}$ 1754, 1628, 1615, 1584, 1100 cm.$^{-1}$ (Found: C, 77·9; H, 8·6%).

The authors thank Dr. R. E. Bowman for his encouragement, Miss E. M. Tanner for determination of rotations and spectra, and Mr. F. H. Oliver for microanalyses.

PARKE, DAVIS AND CO., HOUNSLOW, MIDDLESEX. [*Received, July 11th,* 1963.]

227. *Transition-metal Complexes of Bipyrazinyl: An Analogue of 2,2′-Bipyridyl.*

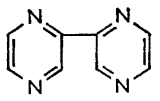
By A. B. P. Lever, J. Lewis, and R. S. Nyholm.

Recently we have studied the transition-metal co-ordination chemistry of pyrazine as a ligand.[1-3] Evidence presented indicated that, although pyrazine is a very much weaker base than pyridine, it is a very much better π-electron acceptor and occupies a position higher in the spectrochemical series than pyridine.[4]

We now present some preliminary data on the properties of the hitherto unknown chelate compound bipyrazinyl, a bidentate ligand analogous to 2,2′-dipyridyl and *o*-phenanthroline. Bipyrazinyl (I) (Bpz), prepared[5] by the pyrolysis of di-2-pyraninylacetocopper(II),[6] forms white crystals, m. p. 190°, and is almost insoluble in water and dilute acid, but is readily soluble in chloroform.

In the Table, are listed the properties of some bipyrazinyl complexes of Cr(III), Fe(II), Co(II), Ni(II), and Cu(I). They were prepared, in general, by the direct interaction of bipyrazinyl with the appropriate metal salt in an organic solvent. All the perchlorates explode when heated but do not appear to be sensitive to mechanical shock. They also tend to be precipitated with several molecules of solvent of crystallisation (ethanol, water, acetone, etc.), which are often very strongly held.

The stoicheiometries of the complexes formed are similar to those obtainable with 2,2′-bipyridyl, *i.e.*, complexes with one, two, or three molecules of ligand per metal atom can be prepared. However, the presence of two further potential donor nitrogen atoms allows additional co-ordination, and compounds of uncertain structure containing two metal atoms per molecule of bipyrazinyl have been isolated; thus, in the case of nickel, it is possible to isolate a yellow compound of the empirical formula $Bpz{\cdot}Ni_2Cl_4$. Complexes with three metal atoms per bipyrazinyl unit are also known. The reaction of cupric salts with bipyrazinyl in the presence of a reducing agent gave complexes of the type $Bpz{\cdot}Cu_3X_3$, containing univalent copper, similar to those formed by pyrazine.[3] The complex has two infrared-active cyanide stretching frequencies at 2110 and 2060 cm.$^{-1}$, the latter with about half the intensity of the former. The complex is insoluble in all solvents investigated and hence we cannot deduce the structure by the normal physicochemical techniques. However, the complex may be formulated, either as a monomer involving trico-ordinated copper and bico-ordinated copper, or as a polymer involving bridging cyanide groups. It is difficult to say, in the case of the cyanide group, the exact range of infrared stretching frequencies expected for a bridging group, although we might expect that the bridging group would absorb at higher frequencies than those we observed.



(I) Bpz

The trisbipyrazinyl complexes presumably have an octahedral arrangement of the bipyrazinyl groups about the metal atom. All the complexes exhibit strong absorption between 350 and 400 mμ, which is probably charge-transfer in origin. This absorption band tails into the visible region and tends to obscure metal *d*–*d* transitions.

With the nickel complex it has been possible to detect an absorption band at 12,900 cm.$^{-1}$ which may be assigned as the $^3T_{2g} \leftarrow {}^3A_{2g}$ transition, *i.e.*, as $10Dq$. This is slightly

[1] Lever, Lewis, and Nyholm, *Nature*, 1961, **189**, 58; "Advances in the Chemistry of the Coordination Compounds," ed. Kirschner, Macmillan, New York, 1961, p. 419.
[2] Lever, Lewis, and Nyholm, *J.*, 1962, 1235.
[3] Lever, Lewis, and Nyholm, *J.*, 1963, 3156.
[4] Lever, Lewis, and Nyholm, *J.*, 1963, 5042.
[5] Lever, to be published elsewhere.
[6] Friesen, Lever, Lewis, and Nyholm, unpublished work.

higher than in the analogous trisbipyridylnickel cation (12650 cm.$^{-1}$). If the shoulder at 20,000 cm.$^{-1}$ is assigned to the $^3T_{1g} \leftarrow {}^3A_{2g}$ transition, then the Racah parameter B is 855 cm.$^{-1}$, compared with 744 cm.$^{-1}$ in the bipyrazinyl compound.[7]

The magnetic moment of the trisbipyrazinylcobalt(II) cation is low for an octahedral complex.[8] It is, however, close to the moment observed for the trisbipyridylcobalt(II) cation (4·85 B.M.). The magnetic properties of the bipyridyl complex over a temperature range have been interpreted[9] on the basis of a reasonable amount of electron delocalisation and distortion. The low moment probably arises from either the splitting of the ground orbital triplet, since the molecule belongs strictly to the C_{3v} point group, rather than to 0_h, or to electron delocalisation on to the ligand. Dibromodibipyrazinylcobalt(II) has a diffuse reflectance spectrum ($\nu_{max.}$ 395, 515, and 540 mμ), and a magnetic moment (Table) consistent with octahedral symmetry in the solid state. It is a nonelectrolyte in nitromethane, but its solution spectrum therein (Table) is more remininiscent of tetrahedral than of octahedral symmetry—based on the band position, although the small extinction coefficient of the band is difficult to correlate with tetrahedral symmetry. The spectrum depends markedly upon the solvent; these solutions probably involve a variety of different substituted species depending upon the nature of the solvent.

Bipyrazinyl reacts with iron(II) to give the intense red colour typical of ligands of this type (cf. the intense red colour of bipyridyl- and *o*-phenanthroline-ferrous complexes). Unlike these complexes, the diamagnetic trisbipyrazinylferrous cation appears to dissociate slowly in water, as the red colour fades with time. However, the stabilisation of the ferrous state by bipyrazinyl is so strong towards oxidation that the complexes cannot be oxidised by ceric ions or dichromate ions, both of which will oxidise the bipyridyl- or phenanthroline-ferrous complexes to the ferric state. The trisbipyrazinylferrous cation has an absorption spectrum (Table) closely similar to that of the trisbipyridyl analogue[10] (peaks at 19,100 and 28,500 cm.$^{-1}$ and shoulders at 20,200, 24,100, and 25,000 cm.$^{-1}$ although no shoulder was observed near 25,000 cm.$^{-1}$).

Reaction of hydrated chromic perchlorate with bipyrazinyl in propan-2-ol leads to the substitution of two of the water molecules by the ligand. The yield is, however, very small, and the complex difficult to purify. Only the lower of the two *d–d* transitions expected[8] can be observed, the other being undoubtedly obscured by the very intense charge-transfer absorption and this absorption is assigned as equivalent to the $^4T_{1g} \leftarrow {}^4A_{2g}$ of an octahedral (0_h) environment. This *d–d* band is split into two components separated by about 1200 cm.$^{-1}$. The molecule had C_{2v} symmetry, under which the $^4T_{2g}$ of the octahedral group transforms to $A_2 + B_1 + B_2$. The double band may be assigned as due to transitions from the $^4A_2$ ground state to these levels.

No.		Colour	Mol.* cond.	μ_{eff} (B.M.) at 20°	Absorption spectra in $MeNO_2$ [ν, cm.$^{-1}$ (ε)]
1	$(Bpz)Cr(H_2O)_4(ClO_4)_3$	Pale red	298 †	3·9 ¶	27,940(3900); 19,620(600); 18,430(590)
2	$(Bpz)_3Fe(ClO_4)_2$	Dark red	204	0	26,830(2450); 21,000(3300); 19,673(4270)
3	$(Bpz)_3Co(ClO_4)_2$	Yellow	191	4·75	26,400(3280); 15,750(15)
4	$(Bpz)_2CoBr_2$	Red	11	4·91	26,000(1560); 16,150(36); 14,500(34)
5	$(Bpz)_3Ni(ClO_4)_2$	Pale yellow	181	3·3 ‡	27,600(750); 20,000sh(29); 12,900(12)
6	$(Bpz)Cu_3(CN)_3$	Dark brown	§	0	—

* Molecular conductivity (in ohm^{-1}) of 0·0005M-solution in $MeNO_2$. † Conductivity in water. ‡ Packs very badly in magnetic tube—accuracy ±5% (cobalt values ±1%). § Insoluble (for infrared data, see text). ¶ Difficult to obtain sample of sufficient purity for accurate magnetic determinations.

Analytical Data. Bipyrazinyl (Bpz) (Found: C, 60·7; H, 3·8; N, 35·5. $C_8H_6N_4$ requires C, 60·7; H, 3·8; N, 35·4%). 1. $[CrBpz(H_2O)_4]ClO_4$ (Found: Cr. 8·8; N, 9·7.

[7] Jorgensen, *Acta Chem. Scand.*, 1955, **9**, 1362.
[8] "Modern Coordination Chemistry," ed. Lewis and Wilkins, Interscience, New York, 1960.
[9] Burstall and Nyholm, *J.*, 1952, 3570.
[10] Jorgensen, *Acta Chem. Scand.*, 1957, **11**, 166.

$C_8H_{14}CrN_4O_{16}$ requires Cr, 8·9; N, 9·6%). 2. $[Fe(Bpz)_3][ClO_4]_2,2C_2H_5{\cdot}OH$ (Found: C, 40·4; H, 3·8; Cl, 8·3; Fe, 7·0. $C_{28}H_{38}Cl_2FeN_{12}O_{10}$ requires C, 40·9; H, 3·5; Cl, 8·6; Fe, 6·8%). 3. $[Co(Bpz)_3][ClO_4]_2,(CH_3)_2CO,H_2O$ (Found: Cl, 8·8; Co, 7·3; N, 20·8. $C_{27}H_{44}Cl_2CoN_{12}O_{10}$ requires Cl, 9·1; Co, 7·3; N, 20·8%). 4. $[Co(Bpz)_2]Br_2$ (Found: C, 35·9; H, 1·9; Br, 29·8. $C_{16}H_{12}Br_2CoN_8$ requires C, 35·9; H, 2·2; Br, 29·9%). 5. $[NI(Bpz)_3][ClO_4]_2,C_2H_5{\cdot}OH,H_2O$ (Found: Cl, 9·6; N, 21·1; Ni, 7·4. $C_{26}H_{20}Cl_2N_{12}O_{10}Ni$ requires Cl, 8·9; N, 21·0; Ni, 7·3%). 6. $[Cu_3Bpz][CN]_3$ (Found: C, 31·8; H, 1·7; Cu, 44·2. $C_{11}H_6Cu_3N_{17}$ requires C, 31·0; H, 1·4; Cu, 44·6%).

We are grateful to the Wyandotte Chemicals Corp. (U.S.A.) for special chemicals and for financial support for one of us (A. B. P. L.).

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[*Received, August 13th,* 1963.]

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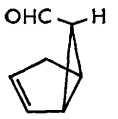
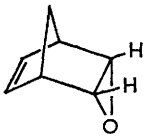
228. *The Reaction of Norbornadiene with Peracids.*

By J. T. LUMB and G. H. WHITHAM.

THE Paper by Meinwald, Labana, and Chada [1] on the reaction of peracids with norbornadiene prompts us to record our own findings on the same reaction.

We have treated norbornadiene with, *e.g.*, perbenzoic, monoperphthalic, and peracetimidic acid,[2] and in each case have obtained the bicyclic aldehyde (I) [1*] together with a second, relatively minor product. The latter material, which had a shorter retention time on gas chromatography than the aldehyde (I), could be obtained fairly pure by oxidation

(I) 



(II)

of the crude product with alkaline silver oxide. In this way the aldehyde (I) was oxidised to the corresponding acid which could be readily removed. The neutral fraction, which was gas chromatographically identical with the minor constituent of the crude product, was identified as the previously unknown *endo*-2,3-epoxynorborn-5-ene (II) in the following way. The infrared spectrum showed bands at 3030 and 737 cm.$^{-1}$, attributable to a norbornene double bond, and the compound could be extracted by aqueous silver nitrate; norbornenes are known to form strong complexes with silver ion.[3] Reduction of the epoxide (II) with lithium in ethylamine gave *endo*-norbornan-2-ol, a reaction clearly involving reduction of the double bond along with the epoxide ring; norbornene is known to be readily reduced to norbornane with lithium in ethylamine.[4]

Reduction of the epoxide (II) with lithium aluminium hydride appeared to give largely *endo*-norborn-2-en-5-ol, as judged by gas chromatography, but another product of closely similar retention time prevented satisfactory identification. Apparently the reduction

* Since our work on the structure and stereochemistry of (I) essentially duplicates that of Meinwald *et al.* it will not be described here.

[1] Meinwald, Labana, and Chada, *J. Amer. Chem. Soc.*, 1963, **85**, 582.
[2] Payne, Denning, and Williams, *J. Org. Chem.*, 1961, **26**, 659; Payne, *Tetrahedron*, 1962, **18**, 763.
[3] Muhs and Weiss, *J. Amer. Chem. Soc.*, 1962, **84**, 4697.
[4] Traynham, *J. Org. Chem.*, 1960, **25**, 833.

with lithium aluminium hydride is complicated by rearrangement, cf., the reduction of *exo*-2,3-epoxynorbornane.[5]

Experimental.—A Pye Argon Chromatograph equipped with a column of polyethylene glycol on Celite (at 100°) was used for gas chromatography.

Oxidation of norbornadiene with peracetimidic acid. 30% Hydrogen peroxide (85 ml., 0·75 mol) was added during 15 min. to a stirred suspension of potassium hydrogen carbonate (20 g.) in acetonitrile (32·5 g., 0·75 mol.), norbornadiene (69 g., 0·75 mol.), and methanol (450 ml.). After 18 hr. at 20° the mixture was heated to 45° for 2 hr. and then poured into water. Isolation of the product with dichloromethane gave a dark liquid (22 g.) shown by gas chromatography to contain the epoxide (II) (13%) and the aldehyde (I) (77%), together with very volatile material (10%), probably unchanged norbornadiene.

The crude product, in ether (100 ml.), was added during 15 min. to a stirred suspension of silver oxide obtained from silver nitrate (63·9 g., 0·42 mol.) and aqueous sodium hydroxide (10%; 570 ml.). After a further 2 hr. at 20° the mixture was filtered, and the ethereal layer was removed, washed with aqueous sodium hydroxide and water, and dried. Evaporation gave the epoxide (II) as an oil (3·2 g.) which was homogeneous to gas chromatography; distillation of a portion resulted in partial decomposition, as shown by gas chromatography. Acidification of the aqueous layers gave the carboxylic acid which was isolated with ether.

Reduction of the epoxide (II) *with lithium in ethylamine.* Lithium pieces (200 mg.) were added to a solution of the crude epoxide (520 mg.) in anhydrous ethylamine at −5°. The solution was stirred until the blue colour had persisted for 15 min., and methanol was then added to destroy excess of lithium. After being poured into water the product was isolated with ether as a brown solid which, after chromatography on alumina, and sublimation, had m. p. 147·5—149°. Mixed m. p. with an authentic sample of *endo*-norbornan-2-ol, which had m. p. 146·5—148° (lit.,[6] 151—152°), was 146—148°. The two samples had identical infrared spectra and were inseparable by gas chromatography.

We thank Professor M. Stacey, F.R.S., for encouragement, and the D.S.I.R. for a research studentship (J. T. L.) and a research grant for purchase of the Pye Argon Chromatograph.

CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM 15. [*Received, August 22nd,* 1963.]

[5] Kwart and Takeshita, *J. Org. Chem.*, 1963, **28**, 670.
[6] Bixler and Niemann, *J. Org. Chem.*, 1958, **23**, 742.

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229. *Ethyl* DL-α-*Acetamido*-α-*thiocarbamoylacetate.*

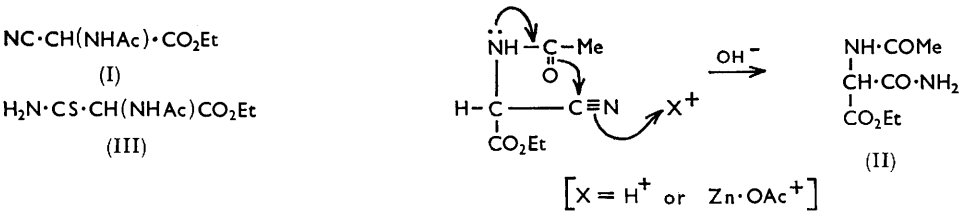
By A. G. LONG and A. TULLEY.

THERE is evidence of difficulty in converting acylamido-cyanides like (I), by means of hydrogen sulphide and ammonia, into the corresponding thioamides.[1] The difficulty does not apply to conversion of ethyl acetamidocyanoacetate (I) into the thioamide (III), which we have achieved with hydrogen sulphide and di- or tri-ethylamine as catalyst;[2] with thioacetamide and dimethylformamidinium chloride[3] the conversion failed, probably because an amino-oxazole was formed.[4]

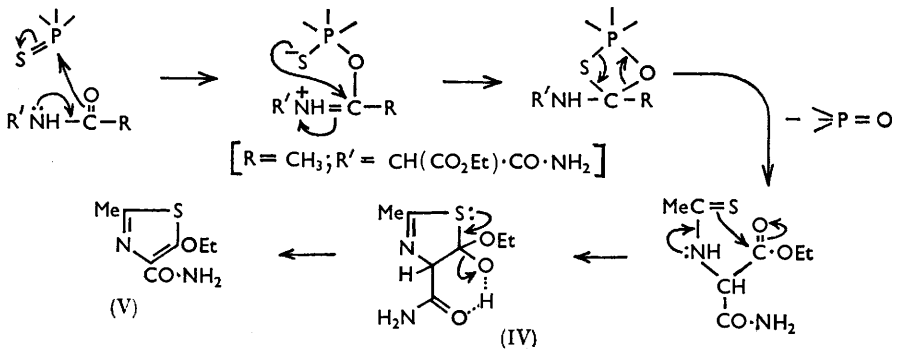
We made the cyanide (I) by reducing ethyl isonitrosocyanoacetate with aluminium

[1] Bentley, Catch, Cook, Heilbron, and Shaw, Committee for Penicillin Synthesis (C.P.S.) report 267 (see Cook, *Quart. Rev.*, 1948, **2**, 203); cf. Gross, Kenner, Sheppard, and Stehr, *J.*, 1963, 2143.
[2] Hurd and DeLaMater, *Chem. Rev.*, 1960, **61**, 45; cf. Eggers, Emerson, Kane, and Lowe, *Proc. Chem. Soc.*, 1963, 248.
[3] Taylor and Zoltewitz, *J. Amer. Chem. Soc.*, 1960, **82**, 2656.
[4] (*a*) Cf. Boon, Carrington, Davies, Jones, Ramage, and Waring, C.P.S. 346; (*b*) Cornforth in "Heterocyclic Compounds," ed. Elderfield, Wiley, New York, 1956, Vol. 5, p. 298.

amalgam and acetylating the amine at 25°.[1] Reduction by activated zinc and acetic acid,[5] with acetylation at 80°, gave ethyl α-acetamido-α-carbamoylacetate (II). Hydrolysis of the cyanide under these conditions probably owes its facility to assistance [6] by the amide group (see the annexed scheme; formation of a 5-amino-oxazole may occur intermediately [4b]):



Attempted preparation of the thioamide (III) by reaction of the carbamoyl compound (II) with phosphorus pentasulphide [2] gave the thiazole (V). The outcome of the reaction indicates completion of the changes summarized in the following scheme.



The infrared spectra indicate that the product is not an amino-ester isomeric with the thiazole (V). Elimination of a hydroxyl rather than an ethoxyl group is probably due to hydrogen-bonding as in (IV).[7]

Experimental.—M. p.s were measured on a Kofler block. Measurements of nuclear magnetic resonance were made on a Varian 40 Mc. spectrometer (for solutions in chloroform) and on a Varian A 60 machine.

Ethyl α-acetamido-α-thiocarbamoylacetate (III). Diethylamine (5 ml.) or triethylamine (5 ml.) was added to ethyl acetamidocyanoacetate (I) (5 g.),[1] in benzene–ethanol (6 : 1; 350 ml.) saturated with hydrogen sulphide. The solution was kept for 48 hr. at 20°, and then evaporated; the resulting solid was washed with a little acetone to give the *thioamide* (III) (3·2 g., 53%), m. p. 121—124°, $\lambda_{max.}$ (in EtOH) 271 mμ (ε 10,220), $\nu_{max.}$ (in $CHBr_3$) 3420 and 3340 (–NH_2), 3170 (–NH–), 1748 (–CO·OR), and 1665 and 1498 cm.$^{-1}$ (CO·NH–), τ (in $CHCl_3$) 8·70 and 5·75 (CH_3·CH_2·O), 7·90 (CH_3·CO), 4·50 (–CS·CH(CO–)·N<), and 1·90 (–NH–) (Found: C, 41·2; H, 5·5; N, 13·8; S, 15·8. $C_7H_{12}N_2O_3S$ requires C, 41·2; H, 5·9; N, 13·7; S, 15·8%).

Ethyl α-acetamido-α-carbamoylacetate (II). Ethyl isonitrosocyanoacetate (100 g.) was reduced in 1 hr. at 25—30° with acid-washed zinc dust (114 g.) and acetic acid (535 ml.), and the resulting amine was acetylated *in situ* during 2 hr. with acetic anhydride (72 ml.) and acetic acid (179 ml.) at 70—80°, to give the *amido-ester* (II) (57 g., 47%), which crystallised from propan-2-ol as rectangular prisms, m. p. 131°, $\nu_{max.}$ (in $CHBr_3$) 3480 and 3380 (–NH_2 and

[5] Wilson, *J.*, 1949, 1157.
[6] Ronwin, *Canad. J. Chem.*, 1957, **35**, 1031.
[7] Cf. Meredith, Ritchie, Walker, and Whiting, *J.*, 1963, 2672.

–NH–), 1742 (–CO·OR), 1672 and 1588 cm.$^{-1}$ (–CO·NH_2), τ (in pyridine) 8·88 and 5·77 (CH_3·CH_2·O–), 7·70 (CH_3·CO–), and 4·06 (–CO·CH·CO–) (Found: C, 44·9; H, 6·6; N, 14·7. $C_7H_{12}N_2O_4$ requires C, 44·7; H, 6·4; N, 14·9%). Reduction with commercial zinc dust, with acetylation at 25—30°, gave ethyl acetamidocyanoacetate (I) (cf. ref. 5).

4-Carbamoyl-5-ethoxy-2-methylthiazole (V). Ethyl α-acetamido-α-carbamoylacetate (II) (2 g.) with phosphorus pentasulphide (2 g.) in tetrahydrofuran (40 ml.) [2] gave, after 2 days at 25°, the *thiazole* (V) (0·49 g., 24%), which separated from ethyl acetate as irregular prisms, m. p. 159°, $\lambda_{max.}$ (in EtOH) 284 mμ (ε 6380), $\nu_{max.}$ (in $CHBr_3$) 3470 and 3340 (–NH_2), 1668 and 1584 (–CO·NH_2), and 1270 cm.$^{-1}$ (–O·C=C–), τ (in $CHCl_3$) 8·63 and 5·63 (CH_3·CH_2·O–), 7·48 (CH_3·C=N–), and 3·50 (–NH_2) (Found: C, 45·3; H, 5·6; S, 17·4; OEt, 24·8. $C_7H_{10}N_2O_2S$ requires C, 45·2; H, 5·4; S, 17·2; OEt, 24·2%).

We thank Professor D. H. R. Barton, F.R.S., for the benefit of a discussion, and Dr. N. Sheppard of Cambridge University for n.m.r. determinations.

GLAXO RESEARCH LTD., GREENFORD, MIDDLESEX. [*Received, August 29th,* 1963.]

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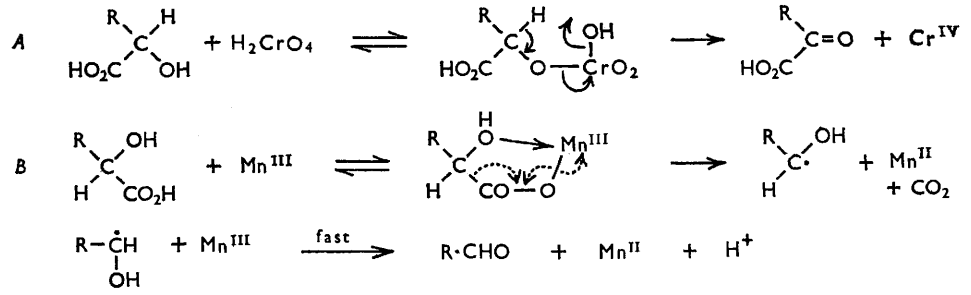
230. *The Mechanisms of Oxidation of α-Hydroxy-acids by Ions of Transition Metals.*

By T. J. KEMP and WILLIAM A. WATERS.

BAKORE and NARAIN [1] have recently suggested that the oxidation by chromic acid of α-hydroxy-acids of the type HO·CHR·CO_2H proceeds by mechanism *A* below, which is similar to that of a secondary alcohol,[2] but their conclusions were based merely on analogies, *viz.*, similarities of reaction rates and activation parameters, retardations of oxidation on addition of manganous ions, and similar rate enhancements on changing the solvent from water to acetic acid.

A different reaction mechanism *B* has been suggested for the one-electron oxidation of α-hydroxy-acids. This was supported in the first instance for oxidation by manganic pyrophosphate,[3] and later for oxidations by quinquevalent vanadium [4] and quadrivalent cerium.[5] Unlike mechanism *A* it does not involve a rate-determining C–H bond cleavage and so can operate with acids, HO·CR_2·CO_2H, that contain no α-hydrogen atom.



We report below experimental evidence to show more conclusively the difference between the 2-electron and the 1-electron mechanisms. Thus, (i) the kinetic isotope

[1] Bakore and Narain, *J.*, 1963, 3419.
[2] Waters, *Quart. Reviews*, 1958, **12**, 277.
[3] Levesley and Waters, *J.*, 1955, 217.
[4] Jones, Waters, and (in part) Littler, *J.*, 1961, 630.
[5] Bhargava, Shanker, and Joshi, *J. Sci. Ind. Res.* (*India*), 1962, **21**, *B*, 573.

TABLE 1.

Kinetic isotope effects for oxidations of mandelic acid.

Chromic Acid

Initial $[Cr^{VI}] = 35{\cdot}0 \times 10^{-4}$M, $[HClO_4] = 0{\cdot}947$M, Temp. 23·2°.

10^2[Mandelic acid] (M)		10^3k_2 (l. mole^{-1} sec.$^{-1}$)	k_H/k_D
Protio	1·165; 2·33	52·1; 56·8 (mean 54·4)	$8{\cdot}6_5$
Deutero	1·105; 2·21	5·81; 6·77 (mean 6·29)	

Ceric Sulphate

Initial $[Ce^{VI}] = 65{\cdot}7 \times 10^{-4}$M, $[H_2SO_4] = 1{\cdot}66$M, Temp. 26·6°.

						k_H/k_D
10^2[Mandelic acid] (M)	1·97	2·95	3·93	4·92	4·92	
10^4k (sec.$^{-1}$)	13·5	20·6	26·7	31·2	31·8	
10^3k/[acid]	6·85	6·99	6·79	6·35	6·47	
10^2[α-Deuteromandelic acid] (M)		0·933	2·80	4·66		$1{\cdot}2_2$ (mean)
10^4k (sec.$^{-1}$)		5·11	15·7	24·9		
10^3k/[acid]		5·48	5·59	5·35		

Manganese Sulphate *

Initial $[Mn^{III}] = 0{\cdot}0329$M, $[Mn^{II}] = 0{\cdot}431$M, $[H_2SO_4] = 3{\cdot}38$M, Temp. = 23·2°.

10^2[Mandelic acid] (M)		k_2 (l. mole^{-1} sec.$^{-1}$)			k_H/k_D
Protio	1·64	175	176	172	1·1
Deutero	1·56	139	139		

Quinquevalent Vanadium *

Initial $[V^V] = 0{\cdot}0645$M, $[H_2SO_4] = 1{\cdot}47$M, Temp. 23·2°.

10^2[Mandelic acid] (M)		10^2k_2 (l. mole^{-1} sec.$^{-1}$)	k_H/k_D
Protio	4·10	11·4	2·0
Deutero	3·89	5·66	

* Values of k_2 found from the initial slopes of log [oxidant]/time plots.

TABLE 2.

Oxidations of α-hydroxyisobutyric acid.

Chromic Acid

(i) Substrate dependence.

Initial $[Cr^{VI}] = 2{\cdot}08 \times 10^{-3}$M, $[HClO_4] = 5{\cdot}00$M, Temp. = 51·8°.

10^3[Hydroxy-acid] (M)	9·50	19·0	28·5	38·0
10^4k (sec.$^{-1}$)	6·57	12·05	16·8	20·6
10^4k/[Acid]	692	635	588	543

(ii) Temperature dependence.

Initial [Hydroxy-acid] = 0·038M, $[HClO_4] = 5{\cdot}00$M, Initial $[Cr^{VI}] = 2{\cdot}08 \times 10^{-3}$M.

Temp. (°c)	25·1	36·0	41·7	51·8
10^4k (sec.$^{-1}$)	2·41	5·87	9·85	25·0

Hence $\Delta E = 16{\cdot}9$ kcal./mole, $\Delta S = -14$ e.u. (Compare Mandelic acid [1]; $\Delta E = 7{\cdot}9$ kcal./mole.)

Manganic Sulphate

Temperature dependence.

Initial [Hydroxy-acid] = 0·0304M, Initial $[Mn^{III}] = 0{\cdot}0297$M, $[Mn^{II}] = 0{\cdot}388$M, $[H_2SO_4] = 3{\cdot}35$M.

Temp. (°c)	21·6	24·4	29·5	33·0	36·0
10^3k (sec.$^{-1}$)	1·13	1·53	2·69	4·00	5·54

Hence $\Delta E = 20{\cdot}0$ kcal./mole, $\Delta S = +5{\cdot}3$ e.u.

Vanadium Perchlorate

Substrate dependence †

$[HClO_4] = 1{\cdot}0$M, total ionic strength = 3·1M, Temp. = 25°.

10^2 [Hydroxy-acid] (M)	9·6	12·1	14·5	19·3	24·1
10^4k (sec.$^{-1}$)	0·628	0·753	0·925	1·27	1·57
10^4k/[Substrate]	6·51	6·25	6·40	6·58	6·51

† Measurements by Dr. J. R. Jones.

effect for the oxidations of mandelic and α-deuteromandelic acids indicates that C–H bond cleavage must occur with chromic acid, but plays only a minor part in oxidations by Mn(III) and Ce(IV) sulphates though it becomes more significant with V(V) (cf., the oxidations of cyclohexanol [6] and acetoin [7]); (ii) α-hydroxyisobutyric acid, $HO{\cdot}CMe_2{\cdot}CO_2H$, is very difficult to oxidise with chromic acid and the reaction has quite different thermodynamic parameters from those found for acids of the type, $HO{\cdot}CHR{\cdot}CO_2H$, (iii) with 1-electron oxidants the oxidation rates for acids $HO{\cdot}CHR{\cdot}CO_2H$ and $HO{\cdot}CR_2{\cdot}CO_2H$ are much more alike, differing only by factors which can easily be attributed to effects of the substituent group, R, in facilitating the formation of radicals $HO{\cdot}CR_2{\cdot}$, *i.e.*, Ph ≫ Me > H.

All our measurements have been carried out spectrophotometrically by methods which have already been described.[8] Unless otherwise indicated the hydroxy-acid was always taken in large excess and it was found in each case that the consumption of the

TABLE 3.

Relative rates of oxidation (k_2 in l. mole^{-1} sec.$^{-1}$).

Acid oxidant	Glycollic	Lactic	Mandelic	α-Hydroxy-isobutyric
Chromic (in 5·0M-$HClO_4$, 24·4°)	—	—	1·7	$5{\cdot}6 \times 10^{-3}$
Manganic sulphate (in 2·47M-H_2SO_4, 24·4°)	$0{\cdot}57 \times 10^{-2}$	$9{\cdot}5 \times 10^{-2}$	1·40	0·61
Ceric sulphate (in 1·66M-H_2SO_4, 26·6°)	$0{\cdot}10 \times 10^{-3}$	$0{\cdot}98 \times 10^{-3}$	70×10^{-3}	$3{\cdot}7 \times 10^{-3}$
Vanadium (V) (in 1·47M-H_2SO_4, 26·6°)	$7{\cdot}3 \times 10^{-3}$	$5{\cdot}2 \times 10^{-3}$	161×10^{-3}	$0{\cdot}76 \times 10^{-3}$

oxidant followed first-order kinetics. The Tables show, where this had not been ascertained by earlier work, that the reaction rate was of the first-order with respect to the organic substrate.

α-Deuteromandelic acid was prepared by equilibrating sodium mandelate three times in a sealed tube at 150° for 7 days with sodium hydroxide (5%) in deuterium oxide (99·8%). Labile hydrogen was then removed by recrystallising the free acid twice from water (m. p. 121°). Analysis showed that 98·5% deuteration had been achieved.

One of us (T. J. K.) thanks the D.S.I.R. for a research studentship.

THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, August 31st*, 1963.]

[6] Littler and Waters, *J.*, 1959, 4046.
[7] Jones and Waters, *J.*, 1962, 1629.
[8] Littler, *J.*, 1962, 827, 832, 2190; Kemp and Waters, *Proc. Roy. Soc.*, 1963, *A*, **274**, 480, and *J.*, 1964, 339.

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231. *Preparation of 3,6-Difluorophthalic Anhydride.*

By ERNST D. BERGMANN, M. BENTOV, and A. LEVY.

VALKANAS and HOPFF [1] recently described the preparation of 3,6-difluorophthalic anhydride by oxidation of 3,6-difluoro-*o*-xylene. As this anhydride was needed in considerable quantities for another investigation,[2] a convenient preparation (63% yield) has been developed, based on the observation that 3,6-dichlorophthalic anhydride, in the same way

[1] Valkanas and Hopff, *J.*, 1963, 3475.
[2] Bentov and Bergmann, *Bull. Soc. chim. France*, 1961, 1316; 1963, 963.

as 3-chlorophthalic anhydride,[3] exchanges the chlorine atoms for fluorine when treated with potassium fluoride under well-defined conditions. For the preparation of 3,6-dichlorophthalic anhydride, which has been described several times, but always without details of the procedure or yields, the method of Villiger [4] has been used with some improvements.

Experimental.—*3,6-Dichlorophthalic anhydride.* At 60°, chlorine was passed for 15 hr. through a solution of phthalic anhydride (237 g.) and iodine (1 g.) in 20% oleum (1250 g.). Volatile products were removed by heating at 20 mm. pressure (b. p. 86—90°), and the residue was poured on to ice (2 kg.). The precipitate was filtered off, washed with cold water, and discarded, and the filtrate was freed from sulphuric acid by addition of barium chloride (20 g.) and removal of the barium sulphate formed. The solution was neutralised with sodium carbonate, and the zinc salt of the mixture of 3,4- and 4,5-dichlorophthalic acid was precipitated by addition of a concentrated solution of zinc chloride (100 g.). The zinc salts were filtered off, and 3,6-dichlorophthalic acid was obtained as its calcium salt by addition of an excess of calcium chloride to the filtrate. The acid was liberated by means of hydrochloric acid, extracted with ether, and the ether removed; the residue crystallised from acetic anhydride, to give 3,6-dichlorophthalic anhydride (85 g., 25%), m. p. 190° (lit.,[4] 193·5—194·5°).

3,6-Difluorophthalic anhydride. The foregoing compound (5 g.) and anhydrous potassium fluoride (10 g.) was heated at 260—270° for 1 hr. Sublimation of the product at 290—300°(bath)/20 mm. gave 3,6-difluorophthalic anhydride (2·7 g., 63%), which was best recrystallised from benzene, m. p. 212° (lit.,[1] 206—207°) (Calc. for $C_8H_2O_3F_2$: C, 52·2; H, 1·1; F, 20·6. Found: C, 52·2; H, 1·3; F, 20·2%).

ISRAEL INSTITUTE FOR BIOLOGICAL RESEARCH,
NESS-ZIONA, ISRAEL.

[*Received, September 9th,* 1963.]

[3] Heller, *J. Org. Chem.*, 1960, **25**, 834.
[4] Villiger, *Ber.*, 1909, **42**, 353, 3541.

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232. *Digermanyl Iodide.*

By K. M. MACKAY and P. J. ROEBUCK.

DIGERMANE, Ge_2H_6, has been known for forty years,[1] but little is known of its chemistry; no reactions are reported in which the germanium–germanium bond is preserved, and substituted digermanes which retain germanium–hydrogen bonds are unknown. Recently, disilanyl iodide, Si_2H_5I, has been prepared [2] by reaction (1), and

$$Si_2H_6 + HI \xrightarrow{AlI_3} Si_2H_5I + H_2 \quad (1)$$

used to make a variety of substituted disilanes.[3] The corresponding germanium compound has now been prepared, and preliminary work suggests that it may be used to synthesise other substituted digermanes.

The reaction analogous to (1) leads, in the case of digermane, to the complete destruction of the molecule, even at low temperatures. However, digermane reacts smoothly with iodine at −63° to form digermanyl iodide, Ge_2H_5I, according to reaction (2).

$$Ge_2H_6 + I_2 \longrightarrow Ge_2H_5I + HI \quad (2)$$

[1] Dennis, Corey, and Moore, *J. Amer. Chem. Soc.*, 1924, **46**, 657.
[2] Ward and MacDiarmid, *J. Amer. Chem. Soc.*, 1960, **82**, 2151.
[3] Ward and MacDiarmid, *J. Inorg. Nuclear Chem.*, 1961, **20**, 345; **21**, 287; Craig, Urenovitch, and MacDiarmid, *J.*, 1962, 548.

A rough thermodynamic calculation suggests that reaction (3) should occur as well as reaction (2), or even in place of it, but no sign of germyl iodide was found among the reaction products.

$$Ge_2H_6 + I_2 \longrightarrow 2GeH_3I \quad (3)$$

Digermanyl iodide is an unstable liquid at room temperature but it can be handled in a vacuum system and used in reactions with heavy-metal salts.

Experimental.—Digermane (0·152 g., 1·0 mmole) was condensed on to iodine (0·256 g., 1·0 mmole) and held at −63° for 1 hr. No hydrogen was observed when the dark brown mixture was frozen in liquid nitrogen. Monogermane (2·0 mg. at −155°), hydrogen iodide (109·4 mg. at −127°), and digermane (12·5 mg. at −45°) were distilled successively from the reaction mixture. No germyl iodide, GeH_3I, was obtained at −22°. When the mixture was warmed to 0°, *digermanyl iodide* (237·0 mg.) was condensed out, leaving 33·1 mg. of solid residue. These quantities account for 96% of the reactants, and the yields, based on the digermane consumed (0·140 g., 0·93 mmole), were 92·8% for digermanyl iodide and 92·5% for hydrogen iodide. The use of higher temperatures or longer contact times gave lower yields and more decomposition. In a separate experiment, the reaction between digermane and hydrogen iodide at −63° was shown to be negligible. The digermanyl iodide was analysed by decomposing a weighed sample at 300—350° and measuring the hydrogen formed. The solid black residue of germanium and germanium iodides was then dissolved in dilute hydrogen peroxide and analysed for germanium (as the dioxide) and iodine (as silver iodide) (Found: H, 1·75; Ge, 55·4; I, 45·2. H_5Ge_2I requires H, 1·8; Ge, 52·4; I, 45·8%). Small amounts of monogermane (corresponding to 5·6 moles % of the germanium in digermanyl iodide) and hydrogen iodide (corresponding to 4·0 moles % of the iodine) were formed in the thermal decomposition. These were isolated and allowed for in the analysis figures.

Digermanyl iodide is involatile at −22° and melts at about −17°. It is extremely unstable in the liquid state and rapidly turns yellow, evolving hydrogen and depositing solid germanium iodides. It can be distilled in a vacuum system at 0° but decomposition is appreciable at this temperature. A freshly-distilled sample has an apparent vapour pressure of 1—2 mm. at room temperature but part of this must be due to decomposition products. The infrared spectrum of the vapour (measured at 1 mm. pressure in a Perkin-Elmer 137 spectrophotometer; path-length 10 cm.) shows bands in the Ge–H stretching region at 2095sh and 2080s cm.$^{-1}$, and at 860w br, 788s, 780s, 680sh, and 675vs cm.$^{-1}$ in the region of GeH_3 and GeH_2 deformation and rocking. The spectrum resembles that of disilanyl iodide.[2] The decomposition of the vapour was followed by observing the spectrum at intervals. The strong doublet of digermane at 755 cm.$^{-1}$, and the band at 818 cm.$^{-1}$ characteristic of monogermane, appeared within a few minutes, and the digermanyl iodide bands had almost completely disappeared after 3 hr. at room temperature.

Preliminary studies of the reaction of digermanyl iodide with silver chloride at 0° indicated the formation of digermanyl chloride ($\nu_{max.}$ 2100, 790, 730, and 720 cm.$^{-1}$), but monogermane and cyanic acid were the only volatile compounds recovered from the reaction with silver isocyanate. The stabilities of these products parallel the reported properties of the germyl and disilanyl compounds.

We thank the D.S.I.R. for the award of a Research Studentship (to P. J. R.), and the Germanium Research Council for a gift of germanium metal.

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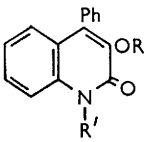
The University of Nottingham. [*Received, September* 13*th*, 1963.]

233. 3-O-*Methylviridicatin, a New Metabolite from* Penicillium puberulum.

By D. J. Austin and M. B. Meyers.

A colourless crystalline nitrogen-containing mixture has been isolated from filtrates from 4—6 week old cultures of *Penicillium puberulum.* This material gave a dark blue-green colour with methanolic ferric chloride, had a very intense broad band in its infra-red spectrum at about 1650 cm.$^{-1}$ indicative of a 2-quinolone,[1] and an ultraviolet spectrum similar to that of viridicatin (I), a metabolite of the genetically related moulds *Penicillium viridicatum* [2] and *Penicillium cyclopium.*[3] Elution of the isolated mixture with 9 : 1 chloroform–methanol on bound silica thin-layer chromatoplates verified the presence of viridicatin (I) (R_F 0·53), and also showed the presence of a less polar compound, *A* (R_F 0·71), which was shown to be 3-*O*-methylviridicatin (II) from the evidence given below. Both compounds exhibited secondary amide bands in about the same position of the infrared spectrum,[4] but compound *A* lacked the OH stretching band at 3359 cm.$^{-1}$ for viridicatin (I), and in addition possessed bands at 2850 2830, and 1017 cm.$^{-1}$ attributable to a methoxyl group.[4] The compounds have similar ultraviolet spectra in neutral solution. However, on the addition of a base, the maxima at 331 and 341 mμ in the



(I : R = H, R′ = H)
(II : R = Me, R′ = H)
(III : R = Me, R′ = Me)
(IV : R = H, R′ = Me)

spectrum of viridicatin (I) undergo a bathochromic shift which is not observed in the corresponding maxima of compound *A*. This, together with the fact that compound *A* gives no colour with ferric chloride, is consistent with a blocking of the 3-hydroxy-group of viridicatin (I).

3-*O*-Methylviridicatin (II) was reported by Cunningham and Freeman [2] to have m. p. 239°, which is somewhat lower than the purified compound *A* from *Penicillium puberulum* (m. p. 248—249°). In an attempt to obtain the methyl ether (II) the procedure of these authors was repeated, but treatment of the silver salt of viridicatin with methyl iodide produced none of the desired ether, the principal product being the *ON*-dimethyl compound (III) and a trace of material, m. p. 204°, probably the mono-*N*-methyl derivative (IV) (lit.,[2] m. p. 208°). A synthetic sample of 3-*O*-methylviridicatin (II) was finally obtained in poor yield by methylation of viridicatin (I) with methyl toluene-*p*-sulphonate.[5]

The co-occurrence of viridicatin (I) and its 3-*O*-methyl ether (II) may be of interest with respect to the biosynthetic study carried out on this quinoline system by Luckner and Mothes.[6]

Experimental.—Infrared spectra were recorded by Mrs. F. Lawrie on a Unicam S.P. 100 spectrophotometer fitted with an S.P. 130 grating.

Isolation of 3-O-*methylviridicatin* (II) *from* Penicillium puberulum. A culture of *Penicillium*

[1] McCorkindale, *Tetrahedron*, 1961, **14**, 223.
[2] Cunningham and Freeman, *Biochem. J.*, 1953, **53**, 330.
[3] Bracken, Pocker, and Raistrick, *Biochem. J.*, 1954, **57**, 587.
[4] Cross, " Introduction to Practical Infrared Spectroscopy," Butterworths, London, 1960, pp. 60 and 66.
[5] Fales and Wildman, *J. Amer. Chem. Soc.*, 1960, **82**, 3368.
[6] Luckner and Mothes, *Tetrahedron Letters*, 1962, 1035.

puberulum (Strain P-47, obtained from the Department of Biochemistry, London School of Hygiene and Tropical Medicine) was grown on agar and then innoculated into 150 " Glaxo " bottles containing 500 ml. of Czapeck-Dox medium with added " Corn Steep Liquor " (10 ml. per litre). After 4—6 weeks the crumbly mycelium was filtered off and the culture filtrate treated with bone charcoal (5—10 g./litre) which was then continuously extracted with acetone for 2 days. The acetone extracts were evaporated to a brown tar which was partitioned between water and ethyl acetate. The ethyl acetate extracts were washed and evaporated, and the residue triturated with boiling light petroleum (b. p. 60—80°). After filtration the petroleum was concentrated to small volume and an equal volume of ether added. Two crops (30·5 and 32·2 mg.) of 3-O-*methylviridicatin* (II) were obtained. The mother-liquors were chromatographed on deactivated alumina (80 g.) and elution with ether produced a further 147 mg. of compound (II). Several recrystallisations from methanol gave prisms, m. p. 248—249°, $\lambda_{max.}$ (in EtOH) 223 (ε 40,500), 281 (8200), 313 (7300), 324·5 (9100), and 337 mμ (6400), $\nu_{max.}$ (in KBr) 2850—2830, 1654, 1610, 1595, 1561, 1285, 1225, 1017, 760, and 700 cm.$^{-1}$ (Found: C, 76·1; H, 5·3; N, 5·72. $C_{16}H_{13}NO_2$ requires C, 76·5; H, 5·2; N, 5·57%).

Preparation of 3-O-*methylviridicatin* (II) *from viridicatin* (I). A solution of viridicatin [7] (I) (1·0 g.) and methyl toluene-*p*-sulphonate (0·90 g.) in dioxan (25 ml.) was heated under reflux for 4 hr. The solvent was removed at the water pump and the residue dissolved in cold dilute aqueous sodium hydroxide (50 ml.). The solution was extracted with ether and chloroform. The organic extracts were combined, dried, and evaporated, producing ON-*dimethylviridicatin* (III) (0·420 g.), m. p. 195—197° (lit.,[2] 197—198°). The alkaline aqueous extract was acidified with dilute hydrochloric acid and extracted with ether. Evaporation of the ether extracts produced 3-*O*-methylviridicatin (II) (0·060 g.) which, after two recrystallisations from methanol, had m. p. and mixed m. p. 247—249°; the ultraviolet and infrared spectra were identical with those of the naturally occurring compound.

We thank the D.S.I.R. for a research studentship (to D. J. A.), Imperial Chemical Industries Limited for a Fellowship (to M. B. M.) and Miss J. Brown and Miss M. McKenzie for the growing and harvesting of the mould cultures.

CHEMISTRY DEPARTMENT, THE UNIVERSITY, GLASGOW. [*Received, September 13th*, 1963.]

[7] Eistert and Selzer, *Z. Naturforsch.*, 1962, **17**b, 202.

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234. *Organosilicon Compounds. Part XXVI.*[1] *The Preparation of* o-*Chloro- and* o-*Fluoro-phenyltrimethylsilane.*

By C. EABORN, K. L. JAURA, and D. R. M. WALTON.

THE usual method of making *m*- and *p*-halogenophenyl-silicon compounds, involving coupling of silicon halides with preformed *m*- or *p*-halogenophenyl Grignard reagents or lithium compounds, is not directly applicable to *ortho*-isomers because the intermediate organometallic compounds are unstable.[2] (They can be made at low temperatures, but do not, in our experience, couple satisfactorily with silicon chlorides at these temperatures.) We have now made *o*-fluoro- and *o*-chloro-phenyltrimethylsilane by addition of the appropriate *o*-halogenoiodobenzene to a mixture of chlorotrimethylsilane and magnesium in refluxing diethyl ether. Since no *o*-chlorophenyltrimethylsilane was formed in the reaction involving *o*-fluoroiodobenzene, we conclude that the reactions do not involve benzyne formation followed by addition of chlorotrimethylsilane across the triple bond,

[1] Part XXV, Baker, Bott, Eaborn, and Jones, *J. Organometallic Chem.*, 1963, **1**, 37.
[2] Millar and Heaney, *Quart. Rev.*, 1957, **11**, 109; Huisgen and Sauer, *Angew. Chem.*, 1960, **72**, 91.

and it seems that, under the conditions we use, *o*-halogenophenylmagnesium iodide is formed and couples with the silicon halide rather than decomposing to benzyne.

Since the above work was finished, a similar technique, but with tetrahydrofuran as solvent, has been described for the preparation of organosilicon compounds from polyhalogenoalkyl compounds.[3]

Experimental.—o-*Chlorophenyltrimethylsilane.* A mixture of chlorotrimethylsilane (0·93 mole), *o*-chloroiodobenzene (*ca.* 5 ml.), magnesium turnings (0·64 g.-atom), and diethyl ether (250 ml.) was warmed; after a few minutes a vigorous reaction began. The remaining *o*-chloroiodobenzene (total 0·62 mole) was added during 40 min. at such a rate as to maintain gentle reflux, and the mixture was refluxed for 1 hr. more, cooled, and treated with saturated aqueous ammonium chloride. Separation, drying (Na_2SO_4), and fractionation of the ethereal layer gave hexamethyldisiloxane (0·12 mole) and *o*-chlorophenyltrimethylsilane (0·46 mole, 74%), b. p. 89°/15 mm., n_D^{25} 1·5122 (lit.,[4] b. p. 207—208°/740 mm., n_D^{25} 1·512). Vapour-phase chromatography showed that the product contained no *m*- or *p*-isomer.

o-*Fluorotrimethylsilane.* By the same method, from *o*-fluoroiodobenzene, o-*fluorophenyltrimethylsilane* (50%), b. p. 167—168°, n_D^{25} 1·4834, was obtained (Found: C, 64·1; H, 7·7. $C_9H_{13}FSi$ requires C, 64·3; H, 7·7%). Vapour-phase chromatography showed the product to contain no *m*- or *p*-isomers, or *o*-chlorophenyltrimethylsilane.

This work was supported by a grant from the Office of Aerospace Research, United States Air Force, through its European Office.

The Chemical Laboratory,
University of Sussex, Brighton. [*Received, October 7th*, 1963.]

[3] Merker and Scott, *J. Amer. Chem. Soc.*, 1963, **85**, 2243.
[4] Clark, Gordon, Young, and Hunter, *J. Amer. Chem. Soc.*, 1951, **73**, 3798.

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235. *The Formylation of Some 5α-Androstan-3-ones. A Correction.*

By P. J. Palmer.

In a previous publication [1] the condensation of ethyl formate with 17α-methyl-17β-(β-phenylpropionyloxy)-5α-androstan-3-one to give the expected 2-hydroxymethylene derivative was described. A second compound, m. p. 176—180°, resulting from a repetition of the condensation under similar conditions, was formulated as the isomeric 2-formyl-17α-methyl-17β-(β-phenylpropionyloxy)-5α-androst-2-en-3-ol. It was suggested [2] that this compound could be the 2-methoxymethylene derivative, arising by autocatalytic etherification during crystallisation of the condensation product from methanol. The spectral and microanalytical data would also be tenable for the enol ether.

No reaction was observed when a suspension of 2-hydroxymethylene-17α-methyl-17β-(β-phenylpropionyloxy)-5α-androstan-3-one in ether containing a few drops of methanol was treated with ethereal diazomethane.[3] Addition of one drop of boron trifluoride etherate led to a vigorous reaction and dissolution of the solid upon further addition of diazomethane. Isolation of the product in the presence of pyridine gave, unexpectedly, unchanged starting material as the only isolable crystalline solid. Crystallisation of the 2-hydroxymethylene derivative from methanol similarly afforded unchanged

[1] Palmer, *J.*, 1963, 3901.
[2] Alvarez, personal communication.
[3] Knox and Velarde, *J. Org. Chem.*, 1962, **27**, 3925.

starting material (75%). However, by treatment with refluxing methanol containing a trace of perchloric acid,[3] a solid, m. p. 150—177°, was obtained, whose infrared spectrum was virtually identical with that of the compound, m. p. 176—180°, to which the 2-formyl structure had originally been assigned. A methoxyl determination and the original elemental data (Found: C, 77·3; H, 8·7; OMe, 6·3. $C_{31}H_{42}O_4$ requires C, 77·8; H, 8·8; OMe, 6·5%) confirmed its structure as *2-methoxymethylene-17α-methyl-17β-(β-phenylpropionyloxy)-5α-androstan-3-one.*

These results suggest that in the original work [1] a trace of acid present in the crude product after work-up led to partial etherification during the initial crystallisation from methanol, and that subsequent crystallisations from inert solvents led to the selective isolation of the methyl ether.

PARKE, DAVIS AND CO., HOUNSLOW, MIDDLESEX. [*Received, November 8th,* 1963.]