NOTES.

913. *Organic Fluorine Compounds. Part XXVI.* Synthesis of α-Fluoro-β-alanine.*

By Ernst D. Bergmann and Sasson Cohen.

α-Fluoro-β-alanine (I) was isolated by Heidelberger [1] as a metabolic product of 5-fluorouracil. Its potential value as an antimetabolite of β-alanine and its derivatives made a synthesis of this amino-acid desirable. The synthesis was to be based on the hydroxymethylation of ethyl fluoroacetate or a congener of this substance, after it had been shown [2,3] that ethyl fluoro-oxaloacetate condenses easily with formaldehyde. Ethyl

* Part XXV, *J.*, 1961, 4033.

[1] Heidelberger, *J. Biol. Chem.*, 1960, **235**, 433.
[2] Gault, Rouge, and Gordon, *Compt. rend.*, 1960, **250**, 1073.
[3] Bergmann and Shahak, *J.*, 1960, 5261.

αγ-difluoroacetoacetate, ethyl γγ-dichloro-α-fluoroacetoacetate, diethyl fluoromalonate and, with exceptional ease, fluoromalondiamide condense similarly with formaldehyde to give the compounds (II; R = CH_2F, R′ = OEt, R = $CHCl_2$, R′ = OEt, R = R′ = OEt and R = R′ = NH_2). Alkaline cleavage of the ester (II; R = $CHCl_2$, R′ = OEt) gave the expected ethyl α-fluoro-β-hydroxypropionate (III) which was converted, without isolation, into its methanesulphonate. However, reaction of the latter with potassiophthalimide in dimethylformamide only decomposed the methanesulphonate to ethyl α-fluoroacrylate (IV). On the other hand, reaction of potassiophthalimide with the methanesulphonate from the hydroxymethyl derivative (II; R = R′ = OEt) proceeded normally; hydrolysis of the product (V) with hydrochloric acid gave the desired amino-acid (I) in the form of its hydrochloride. Chromatography showed that the acid was homogeneous and that its R_F values in two solvent systems were identical with those found for Heidelberger's product.[1] A sample was kindly put at the disposal of Dr. Th. Winnick (Weizmann Institute of Science) by Dr. C. Heidelberger. We are indebted to Dr. Th. Winnick for the chromatographic identification.

(I) $NH_2{\cdot}CH_2{\cdot}CHF{\cdot}CO_2H$ (II) $R{\cdot}CO{\cdot}CF(CH_2{\cdot}OH){\cdot}COR'$ (III) $HO{\cdot}CH_2{\cdot}CHF{\cdot}CO_2Et$

(IV) $CH_2{:}CF{\cdot}CO_2Et$ (V) $p\text{-}C_6H_4(CO)_2N{\cdot}CH_2{\cdot}CF(CO_2Et)_2$

Experimental.—Ethyl γγ-dichloro-α-fluoroacetoacetate. To a stirred suspension of sodium hydride (12 g.) in anhydrous ether (350 ml.) a mixture of ethyl fluoroacetate (53 g.) and ethyl dichloroacetate (109 g.) was added dropwise at such a rate that the mixture refluxed gently. Heating was continued on a water-bath for 4 hr.; then the mixture was cooled and poured on sulphuric acid (50 g.) and ice. The ethereal layer was separated and the aqueous phase extracted twice with ether. The combined ether extracts were washed with sodium hydrogen carbonate solution, dried (Na_2SO_4), and distilled. The *product* (64 g., 59%) distilled at 75—80°/0·2 mm. and had n_D^{26} 1·4555 (Found: C, 33·3; H, 3·3; F, 8·7. $C_6H_7Cl_2FO_3$ requires C, 33·2; H, 3·2; F, 8·7%).

Fluoromalondiamide. The following recipe is based on previous [4] observations. Ethyl chloroformate (217 g.) was added, dropwise and with stirring, to a cooled suspension of the sodio-enolate of ethyl fluoroacetate [from the ester (212 g.) and sodium hydride (48 g.)] in ether (1 l.), and the mixture was refluxed for 5 hr. After addition of water, the ether layer was separated and the aqueous phase extracted twice with ether. Distillation of the combined ethereal solutions permitted the recovery of unchanged ethyl fluoroacetate (80 g., 38%). The oily residue (ethyl fluoromalonate and fluoro-fluoroacetylmalonate) was added, at 5—10°, to a stirred aqueous 28% ammonia solution (500 ml.). After 21 hr. at the same temperature, the precipitate (50 g., 21%, or 34% calc. on the unrecovered fluoroacetate) was filtered off, washed with methanol, acetone, and ether and dried. The product melted at 202—204°.

Ethyl γγ-dichloro-α-fluoro-α-hydroxymethyl-β-oxobutyrate (II; R = $CHCl_2$, R′ = OEt). Piperidine (1 ml.) and formic acid (6 drops) were added to a stirred mixture of ethyl γγ-dichloro-α-fluoroacetoacetate (115 g.) and paraformaldehyde (16 g.). The mixture was heated on a boiling-water bath until a clear solution resulted, then cooled and distilled. The *hydroxymethyl compound* (95 g., 73%) distilled at 120—130°/0·5 mm. and on redistillation at 115—120°/0·2 mm. it had n_D^{24} 1·4655 (Found: C, 33·8; H, 3·7; F, 8·0. $C_7H_9Cl_2FO_4$ requires C, 34·0; H, 3·6; F, 7·7%).

Ethyl αγ-difluoro-α-hydroxymethyl-β-oxobutyrate (II; R = CH_2F, R′ = OEt). Piperidine (1 ml.), formic acid (5 drops), ethyl αγ-difluoroacetoacetate, (35 g.) [5] and paraformaldehyde (5 g.) gave, as above, the *hydroxy-ester* (11 g., 38%), b. p. 95—100°/0·2 mm. (and considerable tar) (Found: C, 43·2; H, 5·4; F, 19·6. $C_7H_{10}F_2O_4$ requires C, 42·9; H, 5·1; F, 19·4%).

Diethyl α-fluoro-α-hydroxymethylmalonate (II; R = R′ = OEt). Piperidine (2 ml.) and formic acid (10 drops) were added to a stirred mixture of ethyl fluoromalonate [4] (70 g.), paraformaldehyde (18 g.), and ethanol (4 ml.). The mixture was heated on a boiling-water bath

[4] Bergmann, Cohen, and Shahak, *J.*, 1959, 3286.
[5] McBee, Pierce, Kilbourne, and Wilson, *J. Amer. Chem. Soc.*, 1953, **75**, 3152.

until it had become clear (4—5 hr.), and then distilled. Some ethyl fluoromalonate (10 g., 14%) was recovered; the *hydroxy-diester* (50 g., 61%) had b. p. 98—100°/0·2 mm. (Found: C, 46·4; H, 6·4; F, 9·2. $C_8H_{13}FO_5$ requires C, 46·2; H, 6·3; F, 9·1%).

α-Fluoro-α-hydroxymethylmalonamide (II; R = R′ = NH_2). (*a*) The foregoing ester (15 g.) was added to cold aqueous 28% ammonia (50 ml.) and kept at 0° for 48 hr. with occasional shaking. When the mass had become homogeneous, the solvent was removed under reduced pressure and the semisolid residue taken up with ethanol. The amide (5 g., 45%) separated in pure form, m. p. 180—182° (Found: C, 32·0; H, 4·8; F, 13·2. Calc. for $C_4H_7FN_2O_3$: C, 32·0; H, 4·7; F, 12·7%).

(*b*) 38% Formaldehyde solution (5 ml.) was added dropwise, with shaking, to a suspension of fluoromalonamide (3 g.) in 28% aqueous ammonia (20 ml.). The resulting clear solution was brought to dryness under reduced pressure and the residue recrystallized from hot aqueous ethanol (yield, 2 g., 58%).

Ethyl α-fluoro-β-methanesulphonyloxypropionate. Crude ethyl γγ-dichloro-α-fluoro-α-hydroxymethyl-β-oxobutyrate [from ethyl γγ-dichloro-α-fluoroacetoacetate (212 g.) and paraformaldehyde (22 g.)] was added dropwise to a stirred solution of sodium carbonate (106 g.) in water (1 l.). Stirring was continued for 1 hr., then the mixture was extracted with ether. Distillation of the ether extract gave the *ester* (III) (30 g., 23%), b. p. 70—72°/0·5 mm., n_D^{25} 1·4251.

Pyridine (17·6 g.) was added dropwise to a mixture of the ester (28 g.), methanesulphonyl chloride (22·5 g.), and benzene (100 ml.), and the mixture was refluxed for 2 hr., diluted with water, and extracted with benzene. The benzene extract was distilled, to yield 20 g. (45%) of the *methanesulphonate*, b. p. 120—125°/0·1 mm., n_D^{25} 1·4467 (Found: C, 33·9; H, 4·9. $C_6H_{11}FO_5S$ requires C, 33·6; H, 5·1%).

Diethyl α-fluoro-α-methanesulphonyloxymethylmalonate. Pyridine (30 g.) was added dropwise and with stirring to a solution of ester (II; R = R′ = OEt) (76 g.) and methanesulphonyl chloride (44 g.) in benzene (100 ml.), and the mixture was refluxed for 2 hr., then cooled and extracted with water. The benzene solution gave, upon fractionation, the *sulphonate* (67 g., 64%), b. p. 140—145°/0·5 mm. (Found: C, 36·6; H, 5·4; F, 7·2. $C_9H_{15}FO_7S$ requires C, 37·8; H, 5·2; F, 6·7%).

Diethyl α-fluoro-α-phthalimidomethylmalonate (V). The foregoing methanesulphonate (40 g.), potassiophthalimide (26 g.), and dimethylformamide (120 ml.) were refluxed, with stirring, for 2 hr., diluted with ether (500 ml.), and extracted with ether (3 × 150 ml.). The combined ether extracts were washed with water, dried (Na_2SO_4), concentrated to about 80 ml., and chilled for 12 hr. The *phthalimido-compound* (19 g., 40%), m. p. 60—80°, was filtered off and could be used in the next step without further purification. For analysis, it was purified by recrystallization from cold methanol, then from toluene–light petroleum and had m. p. 93—94° (Found: C, 58·6; H, 5·1. $C_{16}H_{16}FNO_6$ requires C, 57·0; H, 4·8%).

β-Amino-α-fluoropropionic acid hydrochloride. The ester (V) (23 g.) was refluxed in 36% hydrochloric acid (110 ml.) and water (40 ml.) with stirring for 8 hr., then left overnight at room temperature. The filtered solution was brought to dryness *in vacuo* and the residue taken up again in water (50 ml.), filtered, and brought to dryness again. The solid residue was taken up in methanol, and the insoluble (4 g., 41%) *salt* was filtered off and washed with methanol and anhydrous ether. The yield of the air-dried hydrochloride, m. p. 190—915° (decomp., after sintering at 180°), was 4 g. (41%) (Found: C, 24·8; H, 5·4; Cl, 24·5; F, 13·5; N, 9·5. $C_3H_7ClFNO_2$ requires C, 25·1; H, 4·9; Cl, 24·8; F, 13·3; N, 9·8%).

On Whatman paper (No. 1), with butanol–acetic acid–water (75 : 15 : 10) and phenol, saturated with water, as moving phases, respectively, the following R_F values were found: (I) 0·08 and 0·37; Heidelberger's preparation 0·08 and 0·37; unsubstituted β-alanine 0·23 and 0·57.

INSTITUTE FOR BIOLOGICAL RESEARCH,
NESS-ZIONA, ISRAEL.

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914. *Heterocyclic Derivatives of Guanidine. Part IV.*[1]

By J. E. Banfield.

Preparation of a number of new guanidino-2*H*-pyrroles required for spectroscopic study is described.

Experimental.—Ultraviolet absorption spectra were determined for 95% EtOH solutions on a Unicam S.P. 500 spectrophotometer by Mrs. J. E. Banfield, B.Sc. General methods, referred to below, correspond to analogous preparations described in Part I.[2] For a description and correlation of spectra referred to below, for convenience, as Type E or Type I, see Part I; [2] " points of inflection " for shoulders are taken as points of maximum upwards curvature [$d^3(\log \varepsilon)/d\lambda^3 = 0$], as points where $d^2(\log \varepsilon)/d\lambda^2 = 0$ (two per shoulder) are widely separated and difficult to locate for curves of this type. Microanalyses were carried out by Dr. K. W. Zimmermann and his staff.

5-N-*Ethylguanidino*-2-*imino*-3,4-*diphenyl*-2H-*pyrrole*. *N*-Ethylguanidinium sulphate (4·5 g.), sodium (0·9 g.), and *trans*-αβ-dicyanostilbene (6 g.) gave, by the previous method, the 2H-*pyrrole* (6·7 g.), m. p. 202° (decomp.) (Found: C, 72·3; H, 6·0; N, 22·0. $C_{19}H_{19}N_5$ requires C, 71·9; H, 6·0; N, 22·1%), which recrystallised from ethanol in yellow prisms (Found: C, 71·6; H, 5·9; N, 22·2%); however, when heating during this recrystallisation was prolonged, the compound separated in brown crystals of lower purity. It had $\lambda_{max.}$ 311, 230, $\lambda_{infl.}$ 374, 214 mμ (log ε 4·262, 4·301, 3·40, 4·28) changed by acetic acid to $\lambda_{max.}$ at 307, $\lambda_{infl.}$ 380 mμ (log ε 4·259, 3·21), both spectra being of Type E.[2]

N′-*Acetylguanidino*-2-*acetylimino*-5-N-*ethyl*-3,4-*diphenyl*-2H-*pyrrole*. 5-*N*-Ethylguanidino-2-imino-3,4-diphenyl-2*H*-pyrrole (1·0 g.) in acetic anhydride (15 ml.) and stirred at 80—90° until homogeneous yielded the *diacetyl derivative* (from benzene–light petroleum) in orange-yellow needles, m. p. 205·5—209·5° (decomp.) [Found: C, 68·6; H, 5·85; N, 17·15; O, 8·8; Ac, *ca.* 23% (MeOH–NaOH used; the microanalyst reported distillation of a solid). $C_{23}H_{23}N_5O_2$ requires C, 68·8; H, 5·8; N, 17·45; O, 8·0; 2Ac, 21·4%], $\lambda_{max.}$ 344, 235, $\lambda_{infl.}$ 394, 250 mμ (log ε 4·429, 4·416, 3·40, 4·31), and changed by acetic acid to $\lambda_{max.}$ 344, $\lambda_{infl.}$ 384, 250 mμ (log ε 4·341, 3·52, 4·28), both spectra of Type E.

5-N-*Ethylguanidino*-2-*oxo*-3,4-*diphenyl*-2H-*pyrrole*. 5-*N*-Ethylguanidino-2-imino-3,4-diphenyl-2*H*-pyrrole (2 g.) was treated in ethanolic-aqueous acetic acid with sodium nitrite (4 g.) to yield, after 3 days at 0—5° 5-imino-2-oxo-3,4-diphenyl-3-pyrroline, m. p. 233—236° (0·45 g.), which, purified from ethanol, had m. p. and mixed m. p. 242—245° (decomp.) (Found: C, 77·1; H, 4·8%), and, by basification of the mother liquors, the *oxopyrrole* (1·4 g.), m. p. 214° (decomp.) (Found: N, 17·3%), which (from ethanol) crystallised in bright yellow needles, m. p. 217° (decomp.) (Found: C, 71·65; H, 5·7; N, 17·6; O, 6·1. $C_{19}H_{18}N_4O$ requires C, 71·7; H, 5·7; N, 17·6; O, 5·0%), $\lambda_{max.}$ 316, 230, $\lambda_{infl.}$ 364, 244 mμ (log ε 4·269, 4·228, 3·38, 4·18), changed by alkali to $\lambda_{max.}$ 315, $\lambda_{infl.}$ 364, 237 mμ (log ε 4·275, 3·35, 4·23), both of Type E, and by acetic acid to $\lambda_{max.}$ 351, 277, $\lambda_{infl.}$ 250 mμ (log ε 3·651, 4·140, 4·09), of Type I.

N-*Cyclohexylguanidine*. The sulphate [3] from cyclohexylamine and *S*-methylisothiouronium sulphate afforded a *picrate*, m. p. 230—231° (from ethanol) (Found: C, 42·3; H, 5·1; N, 22·1. $C_{13}H_{18}N_6O_7$ requires C, 42·2; H, 4·9; N, 22·7%).

5-N-*Cyclohexylguanidino*-2-*imino*-3,4-*diphenyl*-2H-*pyrrole*. *N*-Cyclohexylguanidine sulphate (7·5 g.), sodium ethoxide (from sodium, 0·9 g.), and *trans*-αβ-dicyanostilbene (6 g.) afforded (after one week) the 2H-*pyrrole* (7·7 g.), m. p. 215° (decomp.) (Found: C, 74·5; H, 6·9; N, 18·7. $C_{23}H_{25}N_5$ requires C, 74·4; H, 6·8; N, 18·85%), $\lambda_{max.}$ 234, 319, $\lambda_{infl.}$ 367 mμ (log ε 4·331, 4·314, 3·59), changed by acetic acid to $\lambda_{max.}$ 310, $\lambda_{infl.}$ at 384 mμ (log ε 4·260, 3·25), both spectra of Type E, which (from ethanol) formed yellow needles, m. p. 214° (decomp.), of the *monoethanol solvate* (Found: C, 72·3; H, 7·2; N, 17·1. $C_{25}H_{31}N_5O$ requires C, 71·9; H, 7·5; N, 16·8%), $\lambda_{max.}$ 234, 318, $\lambda_{infl.}$ 369 mμ (log ε 4·343, 4·331, 3·59), changed by acetic acid to $\lambda_{max.}$ 310, $\lambda_{infl.}$ 385 mμ (log ε 4·284, 3·26), both spectra of Type E.

[1] Part III, Banfield, *J.*, 1961, 4332.
[2] Banfield, *J.*, 1960, 2108.
[3] McGuinness, unpublished work.

Reaction of the above components for 10 min. on the steam-bath afforded an amorphous yellow-green solid (2·3 g.), which crystallised from ethanol in yellow needles, m. p. 214—216° (decomp.).

The 2*H*-pyrrole and ethyl cyanoacetate afforded 2,5-di-(α-cyano-α-ethoxycarbonylmethylene)-3,4-diphenyl-3-pyrroline (from butan-1-ol), m. p. and mixed m. p. 254—256°.

2-*Acetylimino*-5-N-*cyclohexylguanidino*-3,4-*diphenyl*-2H-*pyrrole*. 5-*N*-Cyclohexylguanidino-2-imino-3,4-diphenyl-2*H*-pyrrole (1 g.), stirred with acetic anhydride (15 ml.) at 60—70° and then at 0°, yielded the *monoacetyl derivative* (0·95 g.), m. p. 175—178°, which recrystallised from benzene–light petroleum in orange-yellow needles, m. p. 173—176° (decomp.) (Found: C, 71·3; H, 6·3; N, 15·1; O, 7·9. $C_{27}H_{29}N_5O_2$ requires C, 71·2; H, 6·4; N, 15·4; O, 7·0%), $\lambda_{max.}$ 347, 233, $\lambda_{infl.}$ 390, 250, 217 mμ (log ε 4·474, 4·376, 3·49, 4·29, 4·42), changed by acetic acid to $\lambda_{max.}$ 346, $\lambda_{infl.}$ 390, 250 mμ (log ε 4·393, 3·46, 4·26), both spectra of Type E.

5-N-*Cyclohexylguanidino*-2-*oxo*-3,4-*diphenyl*-2H-*pyrrole*. (*a*) The imino-compound (2·0 g.) and sodium nitrite (4 g.) gave a nitrite salt (2·0 g.), m. p. 142° (decomp.) (Found: N, 15·3%), of unknown constitution. This (0·4 g.) was dissolved in ethanolic acetic acid, and the solution was basified with aqueous sodium carbonate, giving a solid (0·34 g.), m. p. 159—163° (decomp.), which (from methanol) gave the *monomethanol solvate* of 5-N-*cyclohexylguanidino*-2-*imino*-3,4-*diphenyl*-2H-*pyrrole* in yellow needles, m. p. 194° (decomp.) (Found: C, 71·3; H, 7·0; N, 17·4; O, 3·4. $C_{24}H_{29}N_5O$ requires C, 71·4; H, 7·2; N, 17·4; O, 4·0%), $\lambda_{max.}$ 322, 237, $\lambda_{infl.}$ 367 mμ (log ε 4·343, 4·365, 3·59), changed by acetic acid to $\lambda_{max.}$ 309, $\lambda_{infl.}$ 384 mμ (log ε 4·259, 3·27), both spectra of Type E.

Thus the imino-compound has (partly) survived these conditions. The nitrite salt (0·5 g.) was taken up in warm chloroform and diluted with ether, to yield yellow needles of a nitrite salt (0·23 g.), m. p. 154—160° (decomp.) (Found: C, 59·0; H, 6·1; N, 18·8. Calc. for $C_{23}H_{24}N_4O,2HNO_2$: C, 59·0; H, 6·0; N, 17·9. Calc. for $C_{23}H_{25}N_5,HNO_2,2H_2O$: C, 60·8; H, 6·65; N, 18·5%), $\lambda_{max.}$ 311, $\lambda_{infl.}$ 387, 230 mμ (log ε 4·258, 3·224, 4·25), changed by alkali to $\lambda_{max.}$ 322, 234, $\lambda_{infl.}$ 370 mμ (log ε 4·345, 4·420, 3·54), and by acetic acid to $\lambda_{max.}$ 307, $\lambda_{infl.}$ 387 mμ (log ε 3·253, 3·21); all three spectra being of Type E which argues against formulation as the nitrite of the oxo-compound.

(*b*) The imino-compound (1·7 g.) was treated with acidified sodium nitrite (3 g.) at 15—20°; a solid was deposited immediately (probably the nitrite salt of the starting material) which dissolved during 0·5 hr. at *ca.* 40°. The mixture was set aside for 1 week and then refrigerated to yield what is possibly a high-melting *modification* of diphenylmaleinimide, m. p. 222°, thick yellow needles (Found: C, 77·3; H, 4·8; N, 5·9. $C_{16}H_{11}NO_2$ requires C, 77·1; H, 4·45; N, 5·6%). The mother-liquors were basified to give the *oxo-pyrrole* in yellow prisms, m. p. 214—216° (decomp.) (Found: C, 73·8; H, 6·5; N, 15·4%), which crystallised from ethanol in yellow needles, m. p. 213—214° (decomp.) (Found: 73·7; H, 6·5; N, 14·8; O, 5·4. $C_{23}H_{24}N_4O$ requires C, 74·2; H, 6·5; N, 15·0; O, 4·3%), $\lambda_{max.}$ 318, 242, 231, $\lambda_{infl.}$ 374 mμ (log ε 4·338, 4·206, 4·235, 3·32), of Type E, changed by acetic acid to $\lambda_{max.}$ 353, 277, $\lambda_{infl.}$ 247 mμ (log ε 3·712, 4·191, 4·12) of Type I and by alkali to $\lambda_{max.}$ 318, $\lambda_{infl.}$ 227, 240, 365 mμ (log ε 4·353, 4·269, 4·23, 3·49), of Type E.

5-N-*Methylguanidino*-2-*oxo*-3,4-*diphenyl*-2H-*pyrrole*. 2-Imino-5-*N*-methylguanidino-3,4-diphenyl-2*H*-pyrrole [2] (1 g.) and sodium nitrite (2 g.) at 0—5° gave in 6 days a solid (0·5 g.) which afforded 5-imino-2-oxo-3,4-diphenyl-3-pyrroline (0·35 g.), m. p. 246—250° (from ethanol), and, by basification, the *dihydrate* of the *oxo-compound*, m. p. 210° (decomp.) (Found: C, 64·0; H, 6·0; N, 16·6. $C_{18}H_{16}N_4O,2H_2O$ requires C, 64·5; H, 5·9; N, 16·5%), $\lambda_{max.}$ 316, 230, $\lambda_{infl.}$ 364, 237 mμ (log ε 4·291, 4·243, 3·41, 4·22) of Type E, changed by acetic acid to $\lambda_{max.}$ 357, 276; $\lambda_{infl.}$ 250 mμ (log ε 3·712, 4·182, 4·12) of Type I, and by alkali to $\lambda_{max.}$ 315, $\lambda_{infl.}$ at 364, 237 mμ (log ε 4·317, 3·44, 4·28), of Type E. This, when dried at 150°/0·05 mm., gave the anhydrous *oxo-compound*, m. p. 212° (decomp.) (Found: C, 70·5; H, 4·9; N, 18·7; O, 6·2. $C_{18}H_{16}N_4O$ requires C, 71·0; H, 5·3; N, 18·4; O, 5·3%).

2-*Acetylimino*-5-NN-*dimethylguanidino*-3,4-*diphenyl*-2H-*pyrrole*. 5-*NN*-Dimethylguanidino-2-imino-3,4-diphenyl-2*H*-pyrrole [2] (1·0 g.) was warmed gently with acetic anhydride (10 ml.) and the solution was cooled in ice, giving the yellow *monoacetyl derivative* (0·75 g.) (from benzene–light petroleum), m. p. 218—219° (decomp.) (Found: C, 70·3; H, 6·1; N, 19·25; O, 5·1; Ac, 13·9, but with unsatisfactory saponification. $C_{21}H_{21}N_5O$ requires C, 70·2; H, 5·9; N, 19·5; O, 4·5; Ac, 12·0%), $\lambda_{max.}$ 237, 338, $\lambda_{infl.}$ 384 mμ (log ε 4·402, 4·390, 3·62) of Type E, changed by acetic acid to $\lambda_{max.}$ 297, $\lambda_{infl.}$ 334 mμ (log ε 4·285, 3·98), of Type intermediate between E and I.

5-NN-*Dimethylguanidino*-2-*oxo*-3,4-*diphenyl*-2H-*pyrrole*. The imino-compound (2·0 g.) and sodium nitrite (4·0 g.), when mixed and acidified at 0—5° and refrigerated for 4 days, afforded the *nitrite* (1·25 g.), m. p. 200—208° (decomp.) (Found: C, 62·75; H, 5·54; N, 19·05; O, 12·8. $C_{19}H_{19}N_5O_3$ requires C, 62·45; H, 5·2; N, 19·2; O, 13·1%), $\lambda_{max.}$ 309, $\lambda_{infl.}$ 362 mμ (log ε 4·193, 3·71), changed by alkali to $\lambda_{max.}$ 311, $\lambda_{infl.}$ 370 mμ (log ε 4·298, 3·50), both spectra of Type E and by acid to $\lambda_{max.}$ 279, $\lambda_{infl.}$ 332 mμ (log ε 4·174, 3·81), essentially of Type I; although the acid concentration was apparently less than that used below. The filtrate was basified to yield a yellow solid (0·8 g.) which (from ethanol) afforded (probably) the oxo-compound, m. p. 251° decomp.) (Found: C, 71·2; H, 5·8%), $\lambda_{max.}$ 230, 317, $\lambda_{infl.}$ 380 mμ (log ε 4·266, 4·267, 3·33), changed by acetic acid to $\lambda_{max.}$ 282, 354 mμ (log ε 4·134, 3·707).

This (0·2 g.) was taken up in ethanolic acetic acid and added to aqueous sodium carbonate solution, giving a solid, m. p. 249—250° (decomp.) (0·2 g.), which, dissolved in acetic acid and treated with ethanolic triethylamine, gave the *oxo-compound* in yellow needles, m. p. 252—253° (decomp.) (Found: C, 71·7; H, 5·8; N, 18·0; O, 5·1. $C_{19}H_{18}N_4O$ requires C, 71·7; H, 5·7; N, 17·6; O, 5·0%), $\lambda_{max.}$ 314, 234, $\lambda_{infl.}$ 374 mμ (log *D* 0·279, 0·788, Ī·40), of Type E, changed by acetic acid to $\lambda_{max.}$ 278, 353, 234, 374 mμ (log *D* 0·296, 0·367, Ī·440), of Type E in a nearly saturated solution, the base being almost insoluble in ethanol.

2-*Methylthio*-2-*imidazoline sulphate*. A mixture of 2-thioimidazoline (72 g.), dimethyl sulphate (35 ml.), and water (20 ml.) was refluxed for 3 hr., then diluted with water; a solid, m. p. 198—200°, and probably unchanged thioimidazoline, was collected and the filtrate was evaporated; the residue was taken up in a little water and stirred into acetone, giving the sulphate (64 g.) in hygroscopic crystals which, although slightly wet, were suitable for the succeeding preparation. A further amount of the sulphate (13 g.) was obtained from the mother-liquors. The sulphate afforded a picrate, m. p. 183—186° (lit.,[4] 180°).

2-*Amino*-2-*imidazoline sulphate*. The above-mentioned sulphate (20 g.) and aqueous ammonia (*d* 0·880; 40 ml.) were mixed and refluxed for 1·5 hr., the solvent was removed, and the residual oil was dissolved in a minimum of water and added to acetone. The precipitated oil slowly crystallised and the solid recrystallised from methanol–acetone to give the sulphate (11 g., not thoroughly dried), m. p. 248° (lit.,[4] 281°). The picrate, as first prepared, had m. p. 217—221° (lit.,[4] 217, 219°); however, when purified from water it had m. p. 220—220·5° (Found: C, 34·5; H, 3·2; N, 26·35. Calc. for $C_9H_{10}N_6O_7$: C, 34·4; H, 3·2; N, 26·75%); recrystallisation of the impure picrate from ethanol gave a solid of m. p. 259—261° (decomp.).

2-(5-*Imino*-3,4-*diphenyl*-5H-2-*pyrrolylimino*)*imidazolidine*. 2-Amino-2-imidazoline sulphate (5·5 g.), sodium (0·9 g.), and *trans*-αβ-dicyanostilbene (5·5 g.) were caused to react, initially at 50° and subsequently at room temperature, yellow crystals of an *ethanol solvate*, m. p. 172° (decomp.), separating (Found: C, 71·6; H, 6·0%). This recrystallised from ethanol in yellow needles, decomp. *ca.* 208°, but not molten below 250° (Found: C, 72·15; H, 5·6; N, 18·8; O, 1·5%). Another sample, dried at 100°/0·05 mm., decomposed similarly at *ca.* 210° (Found: C, 71·1; H, 5·85; N, 21·3; O, 1·3. $C_{19}H_{17}N_5,\frac{1}{2}C_2H_6O$ requires C, 71·1; H, 5·9; N, 20·6; O, 2·4%), $\lambda_{max.}$ 321, 234, $\lambda_{infl.}$ 367 mμ (log ε 4·324, 4·324, 3·49), changed by acetic acid to $\lambda_{max.}$ 321, $\lambda_{infl.}$ 387 mμ (log ε 4·257, 3·25), both spectra of Type E.[2] This sample lost *ca.* 10% by weight at 140—160°/0·05 mm. to give the *base* (Found: C, 72·4; H, 5·5; N, 21·85. $C_{19}H_{17}N_5$ requires C, 72·4; H, 5·4; N, 22·2%).

The iminopyrrole, heated with ethyl cyanoacetate, gave 2,5-di-(α-cyano-α-ethoxycarbonylmethylene)-3,4-diphenyl-3-pyrroline (m. p. and mixed m. p.).

The iminopyrrole (0·5 g.) was taken up in ethanolic acetic acid, diluted with water, and basified with sodium carbonate, giving a yellow solid (0·42 g.), which afforded unchanged iminopyrrole as yellow needles, darken at 207°, not melted by 273°. However, treatment of the ethanolic acetic acid solution with sodium nitrite gave at 3° (after 5 min.) a 27% yield of 5-imino-2-oxo-3,4-diphenyl-3-pyrroline, m. p. 248—252° (decomp.) (Found: C, 76·7; H, 5·0; N, 11·0%), and longer reaction times gave both this and diphenylmaleinimide; none of the expected 2-(5-oxo-3,4-diphenyl-5*H*-2-pyrrolylimino)imidazoline being obtained.

The iminopyrrole (1·0 g.) was covered with acetic anhydride (5 ml.), set aside at room temperature and then refrigerated; it gave colourless rhombs of *diacetyl derivative* (0·39 g.), m. p. 188—190° (from benzene) (Found: C, 68·5; H, 5·3; N, 17·7; O, 8·7; Ac, 21·6. $C_{23}H_{21}N_5O_2$ requires 69·15; H, 5·3; N, 17·5; O, 8·0; 2Ac, 21·6%), $\lambda_{max.}$ 262, 215 mμ (log ε

[4] Beilstein's " Handbuch der Organischen Chemie," Springer Verlag, Berlin.

3·817, 4·450), changed but slightly by acetic acid to $\lambda_{max.}$ 262 mμ (log ε 3·820). The structure of this derivative is being further investigated.

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UNIVERSITY OF NEW ENGLAND,
N.S.W., AUSTRALIA.

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915. *The Characterisation of Amines by Use of (−)-Di-O-p-toluoyltartaric Acid.*

By D. A. A. KIDD.

(−)-DI-*O*-*p*-TOLUOYLTARTARIC ACID, first prepared by Stoll and Hofmann [1] for the resolution of racemic lysergic hydrazide, was later used in the separation of the ergotoxine group of alkaloids,[2] for characterisation of minor alkaloids of the *Rauwolfia* genus,[3] and for resolution of an intermediate in the synthesis of reserpine.[4] Incidentally to its use for *Rauwolfia* alkaloids,[5] this acid, now commercially available, has been found invaluable in the characterisation and purification of a variety of synthetic amines, many of which give hygroscopic or non-crystalline salts with most acids. We have prepared its salts with

				Found (%)		Required (%)	
Base	M. p.	Recryst. from	Formula	C	H	C	H
n-Propylamine	186—188°	Aq.MeOH	$C_{26}H_{26}N_2O_8$	61·9	7·1	61·9	7·2 [b]
Isopropylamine	202—204 [a]	Aq.MeOH	$C_{23}H_{27}NO_8$	62·0	6·05	62·0	6·1
n-Butylamine	191—192	MeOH	$C_{24}H_{29}NO_8$	62·8	6·4	62·7	6·4
s-Butylamine	201—202 [a]	MeOH	$C_{24}H_{29}NO_8$	62·8	6·6	62·7	6·4
Dimethylamine	186—188	EtOH	$C_{22}H_{25}NO_8$	60·95	5·75	61·2	5·8
Di-n-propylamine	170—171	EtOH	$C_{26}H_{33}NO_8$	64·25	6·9	64·1	6·8
Di-n-butylamine	174—175	Aq.EtOH	$C_{28}H_{37}NO_8$	64·9	7·2	65·2	7·2
Dicyclohexylamine	186—187 [a]	EtOH	$C_{32}H_{41}NO_8$	67·75	7·25	67·7	7·3
Triethylamine	157—157·5 [a]	EtOH	$C_{26}H_{33}NO_8$	64·2	6·85	64·1	6·8
Benzylamine	195—197	MeOH	$C_{27}H_{27}NO_8$	65·6	5·7	65·7	5·5
Dibenzylamine	150—150·5	Aq.EtOH	$C_{34}H_{33}NO_8$	70·1	5·8	70·0	5·7
Aniline	159—161	EtOAc	$C_{26}H_{25}NO_8$	65·3	5·2	65·2	5·3
o-Toluidine	167—169	EtOAc	$C_{27}H_{27}NO_8$	65·5	5·8 [c]	65·7	5·5
m-Toluidine	164—164·5	C_6H_6–EtOAc	$C_{27}H_{27}NO_8$	66·2	5·55 [d]	65·7	5·5
p-Toluidine	167—168	C_6H_6–EtOAc	$C_{27}H_{27}NO_8$	65·6	5·5 [e]	65·7	5·5
p-Chloroaniline	171·5—173·5	Pet [f]–EtOAc	$C_{26}H_{24}ClNO_8$	60·9	4·6	60·8	4·7
α-Naphthylamine	168—170	Pet [f]–EtOAc	$C_{30}H_{27}NO_8$	68·2	5·25	68·0	5·1
β-Naphthylamine	186—187	EtOH	$C_{30}H_{27}NO_8$	68·3	5·3	68·0	5·1
Pyridine	143—145 [a]	Aq.EtOH	$C_{25}H_{23}NO_8$	64·5	5·0	64·5	5·0
α-Picoline	157—158 [a]	EtOH	$C_{26}H_{25}NO_8$	65·7	5·3	65·2	5·3
β-Picoline	174—175 [a]	EtOH–EtOAc	$C_{26}H_{25}NO_8$	65·4	5·65	65·2	5·3
γ-Picoline	140—141·5 [a]	EtOH	$C_{26}H_{25}NO_8$	64·9	5·1	65·2	5·3
2-Ethylpyridine	147·5—148·5 [a]	EtOH	$C_{27}H_{27}NO_8$	66·1	5·7	65·7	5·5
4-Ethylpyridine	150—151 [a]	EtOH	$C_{27}H_{27}NO_8$	65·5	5·4	65·7	5·5
4-Benzylpyridine	123·5—125 [a]	EtOH	$C_{32}H_{29}NO_8$	69·3	5·5	69·2	5·3
Piperidine	172—173 [a]	EtOH	$C_{25}H_{29}NO_8$	63·5	6·25	63·7	6·2
Pyrrolidine	184—186 [a]	EtOH	$C_{24}H_{27}NO_8$	63·1	6·1	63·0	5·95
Morpholine	183—184·5 [a]	EtOH	$C_{24}H_{27}NO_9$	60·8	5·7	60·9	5·75

[a] With decomp. [b] Found: N, 5·6. Required: N, 5·55%. [c] Found: N, 2·8. Required: N, 2·8%. [d] Found: N, 2·9. Required: N, 2·8%. [e] Found: N, 3·05. Required: N, 2·8%. [f] Pet. is light petroleum (b. p. 60—80°).

a number of common amines (see Table). Salt formation, which normally results in an acid (1 : 1) salt although a few neutral (2 : 1) salts were obtained, can be carried out in organic solvents or by double decomposition in water, but use of ether solutions has the

[1] Stoll and Hofmann, *Helv. Chim. Acta*, 1943, **26**, 922.
[2] Stoll and Hofmann, *Helv. Chim. Acta*, 1943, **26**, 1570.
[3] Hofmann, *Helv. Chim. Acta*, 1954, **37**, 314; Stoll, Hofmann, and Brunner, *ibid.*, 1955, **38**, 270.
[4] Woodward, Bader, Bickel, Frey, and Kierstead, *Tetrahedron*, 1958, **2**, 50.
[5] Kidd, *J.*, 1958, 2432.

advantage that all the salts are insoluble whereas the acid, and usually the amine, are soluble. The salts are normally stable and crystalline, have definite melting points, and recrystallise from the usual solvents without decomposition. The substantial increase in molecular weight is useful in characterising small quantities of amine, which can be regenerated, for example, by shaking a solution of the salt in chloroform–methanol with aqueous alkali. For identification the fact that the melting points appear to fall within a range of about 60° is a disadvantage, although useful separations occur in certain groups of related amines, such as the picolines.

Experimental.—(−)-*Di*-O-p-*toluoyltartaric anhydride*. Stoll and Hofmann's method [1] was modified by the use of a solvent: A mixture of (+)-tartaric acid (164 g.), *p*-toluoyl chloride (575 g.), and xylene (825 ml.) was stirred under reflux with exclusion of moisture. After 3 hr., the clear hot solution was poured into cold benzene (2 l.). The anhydride, after being washed with hot benzene, and recrystallised if necessary from ethyl acetate, melted at 204—205°.

(−)-*Di*-O-p-*toluoyltartaric acid*. Prepared essentially by Stoll and Hofmann's method,[1] the acid had m. p. 169—171°, $[\alpha]_D^{22}$ −141° (*c* 1·0 in EtOH), but some samples showed pronounced earlier softening, or even complete melting, at ~150° without change in optical rotation or microanalysis. The dextrorotatory form behaves similarly [6] in exhibiting a double m. p. (148°, 172°).

Salts. The *salts* (see Table) were prepared by mixing ethereal solutions of equimolecular quantities of acid and base. Analyses indicated 1 : 1 salts except in the one case noted. Several other salts have been described elsewhere.[7]

The author thanks Mr. B. W. Sharp for technical assistance.

The Research Laboratories,
May & Baker Ltd., Dagenham, Essex. [*Received, April 26th*, 1961.]

[6] Hunt, *J.*, 1957, 1926.
[7] Collins, *J.*, 1960, 2053.

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916. *Steroids of Unnatural Configuration. Part VI.* Oxidation and Reduction of Epilumisterol.*

By G. D. Meakins and M. W. Pemberton.

Previous work in this series established that oxidation [1] and reduction [2] of the 5,6-double bond in lumisterol (I) generally lead to products formed by attack at the front (β) face of the molecule. Since inversion of the 3-hydroxyl group in lumisterol from the β- to the α-configuration should accentuate this difference from normal steroid behaviour we have investigated the corresponding reactions of epilumisterol (lumista-5,7,22-trien-3α-ol) (II; R = H).[3]

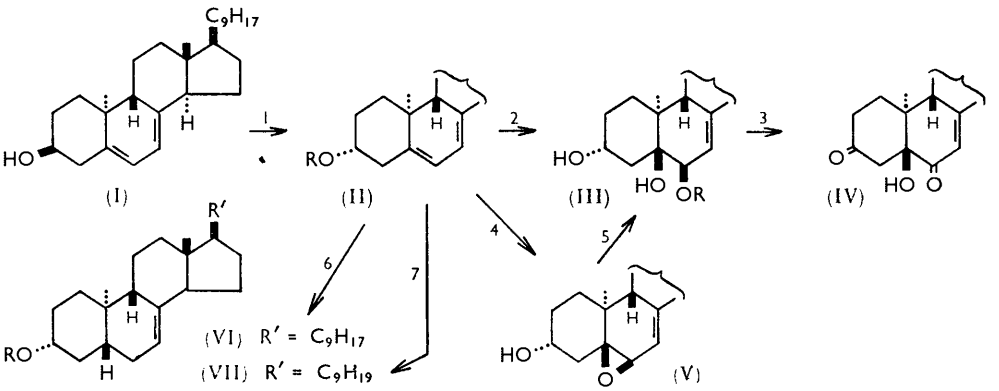
The lumisterol–epilumisterol complex, obtained from lumisterol with aluminium isopropoxide in boiling xylene, was separated with digitonin,[3] to give epilumisterol which was purified through its 3,5-dinitrobenzoate. Although ring A of lumisterol and epilumisterol is somewhat distorted from the chair form by the ring B diene system the substituents at position 3 retain characteristic conformations (3β-axial,3α-equatorial).

With osmium tetroxide epilumisterol gave a triol shown to be the 3α,5β,6β-compound (III; R = H) by oxidation with chromic acid to the 5β-hydroxy-3,6-dione (IV).[1] The 5β,6β-epoxide (V) was the first product formed from epilumisterol and 1 mol. of perbenzoic acid: a longer reaction time in the presence of added benzoic acid led to an

* Part V, *J.*, 1960, 2800.

[1] Mayor and Meakins, *J.*, 1960, 2792.
[2] Castells, Fletcher, Jones, Meakins, and Swindells, *J.*, 1960, 2785.
[3] Barnett, Heilbron, Jones, and Verrill, *J.*, 1940, 1390.

intermediate, presumably the triol monobenzoate (III; R = Bz), which was reduced with lithium aluminium hydride to triol (III; R = H). Reduction of epilumisterol with lithium and ethanol in liquid ammonia afforded the 5β-dihydro-compound [2] (VI; R = H) while catalytic reduction produced the 5β-tetrahydro-compound [2] (VII; R = H), both



Reagents: 1, $Al(OPr^i)_3$. 2, OsO_4. 3, CrO_3 in $COMe_2$. 4, BzO_2H–C_6H_6. 5, BzO_2H–BzOH–C_6H_6. 6, Li–NH_3–EtOH. 7, H_2–Pt in AcOH.

reactions giving high yields. These results correspond closely with those established for lumisterol, except that catalytic reduction of lumisterol yielded approximately equal proportions of products containing the 5α- and the 5β-configuration.

Experimental.—For general directions see *J.*, 1958, 2156.

Lumista-5,7,22-trien-3α-ol (epilumisterol) (II; R = H). The lumisterol–epilumisterol complex [3] (5 g.; m. p. 157—159°, $[\alpha]_D$ +195°) in ethanol (450 ml.) and water (50 ml.) was added to digitonin (8·5 g.) in ethanol (765 ml.) and water (85 ml.) at 60°. The digitonide of epilumisterol, which separated as the mixture cooled, was collected and the dried material (9 g.) heated in pyridine (150 ml.) at 90° for 90 min. Evaporation at 100°/15 mm. followed by two extractions (Soxhlet) of the residue with dry ether gave epilumisterol (2·2 g.; soluble in ether) which was purified as the 3,5-dinitrobenzoate (2·8 g.), m. p. 185—186° (from ethyl acetate–ethanol), $[\alpha]_D$ +131° (*c* 1·1) {lit.,[4] m. p. 184—185°, $[\alpha]_D$ +134° (in benzene)}. Hydrolysis on alkaline alumina afforded epilumisterol (1·7 g.), m. p. 112—113° (from acetone–methanol), $[\alpha]_D$ +221° (*c* 1·0), $\nu_{max.}$ 3540 and 1052 cm.$^{-1}$ (lit.,[4] m. p. 112—113°, $[\alpha]_D$ +227°). The acetate (II; R = Ac) had m. p. 115—116° (from ethanol), $[\alpha]_D$ +129° (*c* 0·8), $\nu_{max.}$ 1730 and 1242 (simple acetate band) cm.$^{-1}$ (lit.,[5] m. p. 114—115°, $[\alpha]_D$ +175°).

Oxidation of lumista-5,7,22-trien-3α-ol. (*a*) A solution of epilumisterol (500 mg.) and osmium tetroxide (500 mg.) in dry ether (40 ml.) and pyridine (2 ml.) was kept at 20° for 3 days, and then refluxed with lithium aluminium hydride (400 mg.) for 2 hr. Standard treatment gave *lumista-7,22-diene-3α,5β,6β-triol* (III; R = H) (350 mg.), m. p. 228—231° (from aqueous methanol), $[\alpha]_D$ −21° (*c* 0·6) (Found: C, 78·3; H, 11·0. $C_{28}H_{46}O_3$ requires C, 78·1; H, 10·8%). Oxidation of the triol (100 mg.) in acetone with 8N-chromic acid gave 5β-hydroxylumista-7,22-diene-3,6-dione (IV) (50 mg.), m. p. 182—184°, $[\alpha]_D$ −20° (*c* 0·8), identified by comparison with authentic material.[1]

(*b*) Epilumisterol (210 mg.) in benzene (15 ml.) and xylene (1·5 ml.) was oxidised with 0·068M-perbenzoic acid in benzene (7·9 ml.) for 20 hr. at 5° and the solution was then poured on a column of deactivated alumina (25 g.). Elution with benzene–ether (9 : 1) gave 5β,6β-*epoxylumista-7,22-dien-3α-ol* (V) (100 mg.), m. p. 160—161° (from acetone), $[\alpha]_D$ +76° (*c* 1·1) (Found: C, 81·65; H, 10·9. $C_{28}H_{44}O_2$ requires C, 81·5; H, 10·75%), $\nu_{max.}$ 3590 and 1047 cm.$^{-1}$.

Benzoic acid (85 mg.) was added to a solution containing epilumisterol and perbenzoic acid in the quantities specified above. The mixture was kept at 5° for 4 days and then chromatographed. Ether eluted material [assumed from spectroscopic examination to be the triol

[4] Harrison, Hurst, Lythgoe, and Williams, *J.*, 1960, 5176.
[5] Heilbron, Kennedy, Spring, and Swain, *J.*, 1938, 869.

monobenzoate (III; R = Bz)] which was reduced with lithium aluminium hydride to the 3α,5β,6β-triol (III; R = H) (35 mg.), m. p. and mixed m. p. 226—229°, $[\alpha]_D$ −20° (*c* 0·6).

Reduction of lumista-5,7,22-trien-3α-ol. (*a*) Lithium (200 mg.) was added to a stirred solution of epilumisterol (250 mg.) in dry ether (20 ml.) and liquid ammonia (40 ml.), and after 30 min. ethanol (~4 ml.) was added slowly. Chromatography of the product on deactivated alumina (20 g.) gave 5β-lumista-7,22-dien-3α-ol (VI; R = H) [200 mg.; eluted with benzene–ether (4 : 1; 50 ml.)], m. p. 137—139° (from ethanol), $[\alpha]_D$ +47° (*c* 0·8), identified by comparison with authentic material [2] and preparation of the 3,5-dinitrobenzoate,[2] m. p. 166—168°.

(*b*) A solution of epilumisterol (775 mg.) in glacial acetic acid was shaken in hydrogen with Adams catalyst (95 mg.). The product, isolated after the absorption of *ca.* 2·1 mol. of hydrogen, was treated with lithium aluminium hydride (to remove acetylated material) and then chromatographed, giving 5β-lumist-7-en-3α-ol (VII; R = H) (500 mg.), m. p. 144—145° (from ethanol), $[\alpha]_D$ +60° (*c* 0·7), identified by comparison with authentic material [2] and preparation of the acetate (VII; R = Ac), m. p. 115—119°, $[\alpha]_D$ +5° (*c* 0·5).[2]

The authors are indebted to Professor E. R. H. Jones, F.R.S., for his interest and advice, to the Department of Scientific and Industrial Research for a maintenance grant (to M. W. P.), and to Mrs. I. E. Croxon for technical assistance.

THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, April 27th,* 1961.]

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917. *The First Acid Dissociation Constant of Hydrogen Sulphide at High Pressures.*

By A. J. ELLIS and D. W. ANDERSON.

PREVIOUS papers [1-3] showed the large effect of pressure on the ionisation of weak acids of the hydrated gas type such as " carbonic acid " and " sulphurous acid," compared with simple weak acids such as acetic and phosphoric acid. The work on carbon dioxide was part of a programme on the chemistry of mineral deposition under high pressures and high temperatures. Results are now given from conductance measurements at 25° of the effect of pressure on the ionisation of hydrogen sulphide, also a dissolved gas weak acid and important in natural mineral-forming processes.

Experimental.—Materials and apparatus. Hydrogen sulphide was prepared by the reaction of " AnalaR " sodium sulphide with dilute sulphuric acid. Pure nitrogen was passed for an hour through the distilled water (specific conductance $1{\cdot}4 \times 10^{-6}$ ohm^{-1} cm.$^{-1}$) used for making the sulphide solutions. Potassium hydrogen sulphide solutions were prepared by titrating hydrogen sulphide solutions to pH 9·3 with potassium hydroxide.

The apparatus used was similar to that described previously.[1]

Method. Previous values [1] for the conductance of potassium chloride and hydrochloric acid were combined with the present results for hydrogen sulphide and potassium hydrogen sulphide to provide values of K_a for hydrogen sulphide.

Corrections for the conductance of the distilled water were made as before.[1]

At the concentrations of hydrogen sulphide used (0·01—0·001m), ionization is less than 1%. Within this degree of accuracy the concentrations of un-ionized hydrogen sulphide can be equated to the total sulphide in solution. The first molal dissociation constant, K_a, was obtained from the equation

$$K_a = m^{-1}\gamma_\pm^2 (1000L'/\Lambda'\rho_r)^2,$$

i.e.,

$$L' = 10^{-3}\Lambda'\rho_r K_a^{\frac{1}{2}} m^{\frac{1}{2}}/\gamma_\pm.$$

The symbols are as defined in the previous papers.

At the low ion concentrations (~10^{-5}m) the value for the sum of the molar conductances

[1] Ellis, *J.*, 1959, 3689.
[2] Clark and Ellis, *J.*, 1960, 247.
[3] Ellis and Anderson, *J.*, 1961, 1765.

Λ' of the H^+ and HS^- ions can be taken as constant at each pressure, and the value of $\gamma_\pm$ equated to unity.

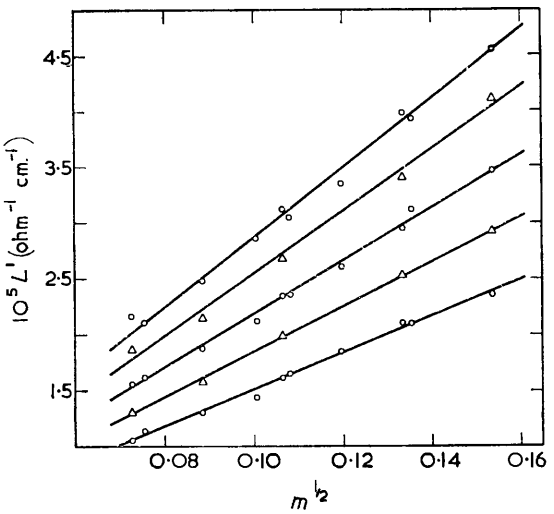
By plotting L' against $m^{\frac{1}{2}}$, a line of slope $10^{-3}\Lambda'\rho_r K_a^{\frac{1}{2}}$ was obtained for each pressure, and hence the value of K_a obtained.

Bright platinum electrodes were used in the conductance cell as it was considered this would minimize their interaction with the sulphide solutions. To check any polarisation effects, results were obtained for several different oscillator frequencies. Table 1 gives typical values of L' (ohm^{-1} cm.$^{-1}$) for a solution of hydrogen sulphide.

TABLE 1.

Hydrogen sulphide: variation in L' with oscillator frequency (values of 10^{-5} L').

Frequency (cycles/sec.)	P (atm.) 1	1000	2000	Frequency (cycles/sec.)	P (atm.) 1	1000	2000
500	2·07	2·86	3·80	2000	2·16	3·01	4·06
1000	2·10	2·95	3·99	5000	2·18	3·05	4·12



Specific conductance (L' in ohm^{-1} cm.$^{-1}$) for hydrogen sulphide as a function of $m^{\frac{1}{2}}$.

Curves relate, reading downwards, to 2000, 1500, 1000, 500, and 1 atm.

The ratios of high- and low-pressure L' values are constant above 1000 cycles and this frequency was used throughout, for convenience. Similar small frequency effects were observed with bright gold electrodes.

Results.—Table 2 gives for potassium hydrogen sulphide the values of $\Lambda^P\rho_r/\Lambda^1$, which within experimental error were constant at concentrations below 10^{-2}m. Table 3 contains the values of $\Lambda'\rho_r$ used for calculating K_a.

The Figure presents the specific conductance of hydrogen sulphide solutions as a function of $m^{\frac{1}{2}}$ at the different pressures. Table 4 contains the values of K_a derived from the results shown in the Figure, and the change in partial molar volume on ionization at one atmosphere (ΔV^1).

TABLE 2.

Potassium hydrogen sulphide: values of $\Lambda^P\rho_r/\Lambda^1$ at 25° for 10^{-3}m-solutions.

(Value of Λ^1 in parentheses.)

P (atm.)	1	500	1000	1500	2000
$\Lambda^P\rho_r/\Lambda^1$	(139)	1·030	1·045	1·055	1·065

TABLE 3.

Values of $\Lambda^1\rho_r$ used in calculation of K_a.

P (atm.)	1	500	1000	1500	2000
$\Lambda'\rho_r$	417	439	454	467	480

TABLE 4.

First acid dissociation constant, K_a, for hydrogen sulphide at 25°.

P (atm.)	1	500	1000	1500	2000
$10^7 K_a$	1·54	2·10	2·76	3·56	4·25

$\Delta V^1 = -15{\cdot}0$ c.c. mole^{-1}.

Discussion.—The effect of pressure on the first dissociation constant of hydrogen sulphide is less than that for the dissolved gases carbon dioxide [1] ($\Delta V^1 = -26{\cdot}5$), sulphur dioxide [3] ($\Delta V^1 = -19{\cdot}7$), and ammonia [4] ($\Delta V^1 = -28{\cdot}9$). ΔV^1 for hydrogen sulphide is similar to that for other simple weak acids, for which the values range from about −7 to −16 c.c. mole^{-1} (*e.g.*, salicylic,[2] formic,[4] benzoic,[2] acetic,[3] and phosphoric acid:[3] −7·2, −8·8, −10·6, −12·1, and −15·5 c.c. mole^{-1}, respectively). It is therefore confirmed that large negative ΔV^1 values arise only where hydration equilibria are involved in the ionization processes, for example, with carbon dioxide, sulphur dioxide, and ammonia.

DOMINION LABORATORY, DEPARTMENT OF SCIENTIFIC AND INDUSTRIAL RESEARCH,
WELLINGTON, NEW ZEALAND. [*Received, May 8th*, 1961.]

[4] Hamann, " Physico-chemical Effects of Pressure," Butterworths, London, 1957.

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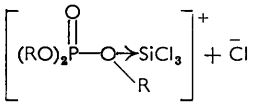
918. *Interaction of Trialkyl Phosphates with Silicon Chlorides.*

By M. J. FRAZER, W. GERRARD, and A. P. SINGH.

RELEVANT to studies of the factors influencing the formation of mixed anhydride links in the development of inorganic or semi-inorganic polymers [1] is the observation that triethyl phosphate and silicon tetrachloride gave ethyl chloride and silicon phosphate,[2] and we now give additional examples.

Silicon tetrachloride (3 mol.) and the trialkyl (Pr^i, Bu^i, Bu^s) phosphate (4 mol.) reacted very slowly at 20° (Table 1), and had to be heated for effective evolution of alkyl chloride and formation of Si–O–P links. The methyl ester reacted vigorously at 20°, and with the n-propyl and n-butyl esters reaction was well advanced in 24 hr. The removal of alkyl from the phosphorus–oxygen bond would appear to be by an S_N2 reaction (end-on approach) involving the chlorine anion, which could be formed by attachment of oxygen to silicon as shown. Attachment by the phosphoryl-oxygen appears less likely; because, although trialkyl phosphates [3] and triphenyl phosphate [4] readily form complexes with boron trichloride at that oxygen atom, triphenyl phosphate did not react with silicon tetrachloride, in accordance with low electron density on the aryloxy-oxygen atom owing to mesomeric interaction of that atom with the phenyl group.



Tri-n-butyl phosphite and silicon tetrachloride react by the mutual exchange of alkoxyl and chlorine,[5] phosphorus and silicon remaining separate in chloro-esters. Similarly, the n-butoxysilanes and boron trichloride react by the mutual exchange of alkoxyl and chlorine, although for the s-butyl compounds formation of Si–O–B links is evident.[6]

In conformity, there was no significant interaction between ethyl phosphorodichloridate and silicon tetrachloride under the conditions stated, electron density on the oxygen atoms

[1] Gerrard, " Reports of Progress in Applied Chemistry," 1960, *J. Oil Colour Chemists' Assoc.*, 1959, **42**, 625.
[2] Gerrard and Jeacocke, *Chem. and Ind.*, 1959, 704.
[3] Gerrard and Griffey, *J.*, 1960, 3170.
[4] Frazer, Gerrard, and Patel, *J.*, 1960, 726.
[5] Gerrard and Honey, unpublished work.
[6] Frazer, Gerrard, and Strickson, *J.*, 1960, 4701.

being effectively reduced by the two chlorine atoms attached to phosphorus. On the other hand, tri-n-butoxychlorosilane (*n* mol.) afforded a silyl phosphate, probably $[(Bu^nO)_3SiO]_nP(O)(OR)_{3-n}$, and alkyl chloride (Table 2), when heated with a trialkyl phosphate (1 mol.) (for Me or Et, instead of Bu^n when $n = 1$, see ref. 7). Some tetra-alkoxysilane was found; this could arise from the monochlorosilane by mutual exchange of groups, and the polymeric non-volatile residue is accounted for by interaction of the resulting dichlorosilane and the phosphate.

Experimental.—Trialkyl phosphate–silicon tetrachloride systems. The trialkyl phosphate (4 mol.) was added to silicon tetrachloride (3 mol.) at 20°. Trimethyl phosphate reacted vigorously at 20°: methyl chloride and silicon tetrachloride were evolved and were condensed at −80°. The mixture became a gel within 2 hr. Gel formation occurred overnight in experiments 2 and 4 (Table 1). The progress of the reaction at 20° was followed by determining the easily hydrolysable chlorine (e.h.Cl) in samples (0·2 g.). After 195 hr., at 20°, alkyl chloride, unchanged phosphate, and silicon tetrachloride were removed at the stated temperature and pressure. Volatile products were separated by distillation and characterised by their physical constants, analysis, and gas chromatography. Propene (4·20 g.) and butene (3·80 g.) were detected in experiments 2 and 4, and in all the experiments (except no. 1), hydrogen chloride (0·5—1·5 g.) was evolved during the heating. After the removal of the volatile matter, part of the residual black solid was heated at 900° in air, a white powder corresponding to $Si_3P_4O_{16}$ being formed.

TABLE 1.

Experiment no.	1	2	3	4	5	6
R in $(RO)_3PO$	Me	Pr^n	Pr^i	Bu^n	Bu^i	Bu^s
e.h.Cl (%) in mixtures at 20°: 2 hr.	—	—	—	25·5	—	—
e.h.Cl (%) in mixtures at 20°: 24 hr.	0	11·3	30·4	12·3	27·1	25·9
e.h.Cl (%) in mixtures at 20°: 48 hr.	—	8·7	30·4	11·6	27·1	24·6
e.h.Cl (%) in mixtures at 20°: 195 hr.	—	8·4	30·4	11·0	26·9	20·7
Calc. e.h.Cl (%) for orig. mixture	39·8	30·3	30·3	27·1	27·1	27·1
RCl was removed at:	20° [a]	20°/15 mm.	85°/10 mm. (5 hr.)	20°/13 mm.	130° (8 hr.)	150°/10 mm. (5 hr.)
Total RCl (mol.)	4·4 [b]	9·29	8·01	8·91	8·94	9·90
Unchanged $SiCl_4$ (mol.)	1·75 [b]	0·29	0·52	0·33	0·60	0·29
Solid [d] obtained at 900° (P, %)	28·2	27·1	26·6	27·9	27·3	25·4
Solid [d] obtained at 900° (Si, %)	17·1	19·4	17·2	17·5	17·6	18·2

[a] Unchanged phosphate (1·30 mol.) obtained at 130°/15 mm. [b] Evolved during the initial exothermal reaction. [c] Bu^iCl 95%, and Bu^tCl 5%. [d] Calc. for $O_{16}P_4Si_3$: P, 26·7; Si, 18·1%.

TABLE 2.

R in $(RO)_3PO$ (*n* mol.)	Et	Bu^n	Et	Bu^n
$(Bu^nO)_3SiCl$ (*n* mol.), *n* =	1	1	2	3
RCl (mol.)	0·86	0·97	2·0	2·75
Silyl phosphate, yield (%)	69·8 [a]	56·5 [b]	20·1 [b]	25·0 [b]
B. p. at 0·1 mm.	148—150°	168—172°	160—166°	170—185°
$[R]_D$, Found: [c]	100 (99)	117 (117)	163 (156)	220 (213)
P (%), Found: [c]	7·9 (7·7)	6·6 (6·8)	3·7 (5·0)	2·1 (3·7)
Si (%), Found: [c]	7·1 (7·0)	5·9 (6·1)	8·2 (9·0)	8·7 (10·0)
M, Found: [c]	398 (400)	462 (456)	—	—

[a] Also $(Bu^nO)_4Si$ (24·0%), b. p. 110°/12 mm. (Found: Si, 8·5%). [b] Other fractions were obtained. Physical constants and analysis showed these to be mixtures of the tetra-alkoxysilane and the silyl phosphate, but they could not be separated by ordinary distillation. [c] Calc. values for $[(Bu^nO)_3SiO]_nPO(OR)_{3-n}$ are in parentheses.

Triphenyl phosphate–silicon tetrachloride. A mixture of triphenyl phosphate (58·60 g., 1 mol.) and silicon tetrachloride (1 mol.) was heated under reflux at 160° for 20 hr. Silicon tetrachloride was recovered at 20°/18 mm., and triphenyl phosphate (99·8%), m. p. 48° (Found: P, 9·0. Calc. for $C_{18}H_{15}O_4P$: P, 9·5%), remained.

[7] Feher, Kühlborsch, Blümcke, Keller, and Lippert, *Chem. Ber.*, 1957, **90**, 134.

Ethyl phosphorodichloridate and silicon tetrachloride. Ethyl phosphorodichloridate (51·40 g., 1 mol.) and silicon tetrachloride (1 mol.) were heated under reflux at 90° for 35 hr. Ethyl chloride (1·50 g.) (gas chromatography), silicon tetrachloride (97·3% recovery), b. p. 56° (Found: Cl, 82·9%), and the phosphorodichloridate (45·80 g., 89·1% recovery), b. p. 62°/10 mm., n_D^{20} 1·4336 (Found: Cl, 43·1. Calc. for $C_2H_5Cl_2O_2P$: Cl, 43·5%), were obtained.

Trialkyl phosphates and tri-n-butoxychlorosilane. Tri-n-butoxychlorosilane (1, 2, and 3 mol.) and the phosphate (1 mol., see Table 2) were heated under reflux at 150—155° for 6 hr. Alkyl chloride, and then fractions containing the tetra-alkoxysilane, and the alkyl butoxysilyl phosphates, and a residue containing silicon and phosphorus were obtained.

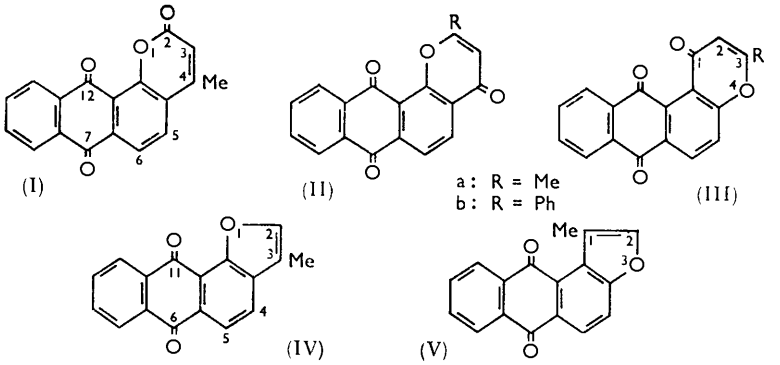
THE NORTHERN POLYTECHNIC, HOLLOWAY ROAD,
LONDON, N.7.

[*Received, May 11th*, 1961.]

919. *Hydroxyanthracene Series. Part IV.*[1] *Synthesis of Some Anthraquinone Derivatives.*

By N. H. SHAH and SURESH SETHNA.

THE quinonopyrones (I—III) have been prepared by oxidising the corresponding anthrapyrones with chromic acid or sodium dichromate in acetic acid; yields were good. Kostanecki–Robinson benzoylation of 2-acetyl-1-hydroxy- and 1-acetyl-2-hydroxy-anthraquinone yielded the 2- and the 3-benzoyl derivative of compounds (IIIb and IIb, respectively); Kostanecki–Robinson acetylation gave resins.



Attempts to synthesise ketones by Fries migration of 1- and 2-acetoxyanthraquinone or Friedel–Crafts acetylation of 1- and 2-hydroxyanthraquinone did not succeed. These ketones were, however, obtained in good yield by oxidation of 2-acetyl-1-acetoxy- and 1-acetyl-2-acetoxy-anthracene with chromic acid in acetic acid and subsequent hydrolysis with sulphuric acid.

3-Methylanthra[1,2-*b*]furan [1] on oxidation gave 2-acetyl-1-hydroxyanthraquinone instead of the quinono-furan (IV). The desired furan derivatives (IV and V) were, however, synthesised by oxidising the intermediate compounds, ethyl 2-acetyl-1- and ethyl 1-acetyl-2-anthryloxyacetate [1,2] to the corresponding anthraquinone derivatives, hydrolysis of the esters to the corresponding acids, and simultaneous cyclisation and decarboxylation by hot sodium acetate and acetic anhydride.

Experimental.—Oxidations (see Table). To a stirred solution of the anthracene derivative (0·01 mole) in acetic acid at 60—65° was added, during 10 min., a 10% solution of chromic acid or sodium dichromate (0·04 mole) in 90% acetic acid. After 3 hours' stirring at this temperature the mixture was left overnight at room temperature. The *products* obtained on dilution were washed with cold dilute alkali and the residue crystallised from acetic acid.

[1] Part III, Shah and Sethna, *J. Indian Chem. Soc.*, 1960, **37**, 699.
[2] Shah and Sethna, *J. Org. Chem.*, 1959, **24**, 1783.

Products formed by chromic oxidation.

Product [a]	M. p.	Yield (%)	Found (%) C	Found (%) H	Formula	Reqd. (%) C	Reqd. (%) H
Anthraquinones							
1-Acetoxy-2-acetyl [b]	167—168°	35	70·4	3·6	$C_{18}H_{12}O_5$	70·1	3·9
2-Acetoxy-1-acetyl [b]	200—202	45	70·2	4·1	,,	,,	,,
1-Acetyl-2-methoxy [c]	215—216	45	73·2	4·1	$C_{17}H_{12}O_4$	72·9	4·3
Et x-*acetyl*-9,10-*dihydro*-9,10-*dioxo*-y-*anthryloxyacetates*							
$x = 2, y = 1$	145—146	46	68·0	4·6	$C_{20}H_{16}O_6$	68·2	4·6
$x = 1, y = 2$	164—165	46	68·4	4·8	,,	,,	,,
7,12-Dihydro-4-methyl-2,7,12-trioxo-2*H*-anthra[1,2-*b*]pyran (I)	319—320	54	74·3	3·1	$C_{18}H_{10}O_4$	74·5	3·5
7,12-*Dihydro*-4,7,12-*trioxo*-4H-*anthra*[1,2-*b*]*pyrans* (II)							
2-Methyl	293 [d]	36	74·7	4·0	,,	,,	,,
2-Phenyl	325	37	78·8	3·7	$C_{23}H_{12}O_4$	78·4	3·4
7,12-*Dihydro*-1,7,12-*trioxo*-1H-*anthra*[2,1-*b*]*pyrans* (III)							
2-Methyl	251	27	74·2	3·4	$C_{18}H_{10}O_4$	74·5	3·5
2-Phenyl	266—267	27	78·0	3·8	$C_{23}H_{12}O_4$	78·4	3·4

[a] Insol. in alkali; give a red colour with Zn dust and alkali. [b] As the reaction caused partial hydrolysis the crude product was treated with acetic anhydride and pyridine for 24 hr. at room temperature. [c] Also obtained by methylation of 1-acetyl-2-hydroxyanthraquinone. [d] With decomp.

1-*Acetoxy*-2-*acetylanthracene*, prepared from 2-acetyl-1-anthrol,[3] acetic anhydride, and pyridine overnight at room temperature, crystallised from dilute alcohol in yellow needles, m. p. 140—142° (Found: C, 77·7; H, 4·9. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·0%).

2-*Acetoxy*-1-*acetylanthracene*, prepared as above from 1-acetyl-2-anthrol,[2] crystallised from dilute alcohol in colourless needles, m. p. 130° (Found: C, 77·5; H, 4·5%).

2-*Acetyl*-1-*hydroxyanthraquinone*. 1-Acetoxy-2-acetylanthraquinone (0·1 g.) was hydrolysed by concentrated sulphuric acid (5 ml.) at room temperature in 4 hr. The product crystallised from dilute acetic acid in reddish-yellow needles, m. p. 166° (Spruit [4] gave the same m. p.) (Found: C, 72·1; H, 3·9. Calc. for $C_{16}H_{10}O_4$: C, 72·2; H, 3·8%). It gave a green colour with alcoholic ferric chloride. Its 2,4-*dinitrophenylhydrazone* crystallised from acetic acid in reddish needles, m. p. 276° (Found: N, 12·7. $C_{22}H_{14}N_4O_7$ requires N, 12·6%).

3-*Benzoyl*-7,12-*dihydro*-4,7,12-*trioxo*-2-*phenyl*-4H-*anthra*[1,2-*b*]*pyran*. A mixture of 2-acetyl-1-hydroxyanthraquinone (0·6 g.), fused sodium benzoate (1·8 g.), and benzoic anhydride (6 g.) was heated at 180—190° for 8 hr. The *product* obtained on removal of the excess of benzoic anhydride and sodium benzoate with hot water crystallised from acetic acid in yellow needles (0·15 g.), m. p. 275—276°. (Found: C, 78·5; H, 3·9. $C_{30}H_{16}O_5$ requires C, 78·9; H, 3·5%).

This compound (0·1 g.) with boiling 70% w/v sulphuric acid (10 ml.) (2 hr.) gave the debenzoylated product that crystallised from acetic acid as yellow needles, m. p. and mixed m. p. 325° (cf. Table).

1-*Acetyl*-2-*hydroxyanthraquinone*. 1-Acetyl-2-acetoxyanthraquinone (0·25 g.) was hydrolysed with sulphuric acid as above. The *product* crystallised from dilute acetic acid in brown needles, m. p. 249—250°, giving a pale green colour with alcoholic ferric chloride (Found: C, 72·0; H, 3·6%). Its 2,4-*dinitrophenylhydrazone* crystallised from alcohol in red needles, m. p. 260° (Found: N, 12·8%).

2-*Benzoyl*-7,12-*dihydro*-1,7,12-*trioxo*-3-*phenyl*-1H-*anthra*[2,1-*b*]*pyran*. 1-Acetyl-2-hydroxyanthraquinone (0·8 g.), sodium benzoate (2·4 g.), and benzoic anhydride (8 g.) gave as above the *quinono-pyran* as yellow needles (0·1 g.), m. p. 253—254° (from acetic acid) (Found: C, 78·7; H, 3·5%).

The same product was obtained on oxidation of 2-benzoyl-1-oxo-3-phenylanthra[2,1-*b*]-pyran [2] (0·1 g.) in acetic acid with sodium dichromate at room temperature.

2-*Acetyl*-9,10-*dihydro*-9,10-*dioxo*-1-*anthryloxyacetic acid*. Ethyl 2-acetyl-1-(9,10-dihydro-9,10-dioxoanthryloxy)acetate (0·25 g.) was hydrolysed by 4% sodium hydroxide solution (25 ml.) at 50° for about an hour. The *acid* obtained on acidification crystallised from dilute

[3] Lele, Shah, and Sethna, *J. Org. Chem.*, 1956, **21**, 1293.
[4] Spruit, *Rec. Trav. chim.*, 1949, **68**, 304.

acetic acid in yellow needles (0·2 g.), m. p. 189—190° (Found: C, 66·2; H, 3·9. $C_{18}H_{12}O_6$ requires C, 66·7; H, 3·7%).

6,11-*Dihydro*-3-*methyl*-6,11-*dioxoanthra*[1,2-*b*]*furan*. The above acid (0·2 g.) and anhydrous sodium acetate (1 g.) were boiled in acetic anhydride (10 ml.) for 45 min. The *product* was washed with alkali and crystallised from dilute acetic acid in reddish-yellow needles, m. p. 226—227° (Found: C, 77·9; H, 3·7. $C_{17}H_{10}O_3$ requires C, 77·9; H, 3·8%).

1-*Acetyl*-9,10-*dihydro*-9,10-*dioxo*-2-*anthryloxyacetic acid*. Ethyl 1-acetyl-2-(9,10-dihydro-9,10-dioxoanthryloxy)acetate (0·15 g.) on hydrolysis as above gave the corresponding acid, yellowish-green plates (0·1 g.) (from dilute alcohol), m. p. 256—257° (decomp.) (Found: C, 66·4; H, 3·8%).

6,11-*Dihydro*-1-*methyl*-6,11-*dioxoanthra*[2,1-*b*]*furan*. The preceding acid (0·2 g.), acetic anhydride (10 ml.) and anhydrous sodium acetate (1 g.) were boiled for 45 min. The *product* was washed with cold dilute alkali and crystallised from alcohol in pale yellow plates, m. p. 198—199° (Found: C, 77·4; H, 3·9%).

CHEMISTRY DEPARTMENT, FACULTY OF SCIENCE, M.S. UNIVERSITY OF BARODA, BARODA, INDIA. [*Received, May 16th*, 1961.]

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920. *Constituents of* Eugenia maire *A. Cunn. Part II.*[1] *Identification of Mairin and Constituents of the Leaves.*

By LINDSAY H. BRIGGS and R. C. CAMBIE.

IN Part I[1] there was reported the isolation of 3,3′,4-tri-*O*-methylellagic acid and an alleged dihydroxytriterpene, mairin, from the bark of *Eugenia maire*. Continued investigation of mairin has now shown its identity with betulic acid.

The leaves of *E. maire* also afforded betulic acid, and, in minor amount, oleanolic acid; gallic acid, methyl gallate, and β-sitosterol were also isolated but not 3,3′,4-tri-*O*-methylellagic acid or leucoanthocyanins. Oleanolic acid has been isolated by other workers from *E. caryophyllata* Thunbg.[2]

Experimental.—Analyses were by Dr. A. D. Campbell and his associates, University of Otago, New Zealand. Infrared spectra were measured for KBr discs with a Beckman IR2 instrument; optical rotations were measured for $CHCl_3$ solutions.

Betulic acid. "Mairin," m. p. 295—296°, in benzene solution, was chromatographed on silica gel. Fractions eluted from the column with benzene and crystallised from methanol gave betulic acid, m. p. and mixed m. p. 312—314°, $[\alpha]_D^{25}$ +10·8° (*c* 1·2) (correct infrared spectrum). The acetate had m. p. and mixed m. p. 291—292° [Found (for sample dried to constant wt.): C, 77·35; H, 9·7; Ac, 8·0. Calc. for $C_{32}H_{50}O_4$: C, 77·1; H, 10·1; Ac, 8·6%]. The benzoate had m. p. and mixed m. p. 339—341° [Found (for sample dried to constant wt.): C, 79·0; H, 9·35. Calc. for $C_{37}H_{52}O_4$: C, 79·2; H, 9·35%].

Further working-up of the initial extract of the bark of *E. maire* and chromatography on silica gel of the fraction soluble in benzene gave additional betulic acid (7·14 g. from 7·1 kg.).

Leaves. Dried, finely ground leaves (1 kg.) were extracted (Soxhlet) with methanol and the residue, after removal of solvent, was re-extracted with hot ether. The ether concentrate was treated with 20% aqueous sodium hydroxide (3 × 200 c.c.) and acidic material isolated through the insoluble sodium salts by Corbett and McDowall's procedure.[3] Repeated crystallisation from methanol gave betulic acid (6·4 g.), m. p. and mixed m. p. 310—312°, $[\alpha]_D^{25}$ +10·6° (*c* 0·89) (correct infrared spectrum). The acetate had m. p. and mixed m. p. 290—292° [Found (for sample dried to constant wt.): C, 77·3; H, 10·0; Ac, 8·9%]; the methyl ester had m. p. and mixed m. p. 225—226°.

Oleanolic acid. Acidification of the aqueous alkaline solution above gave amorphous acids which were washed with hot water and chromatographed in benzene on silica gel. Elution

[1] Part I, Briggs, Cambie, Lowry, and Seelye, *J.*, 1961, 642.
[2] Karrer, "Konstitution und Vorkommen der Organischen Pflanzenstoffe," Birkhäuser Verlag, Basle, 1958, p. 806.
[3] Corbett and McDowall, *J.*, 1958, 3715.

with benzene gave, first, further betulic acid (1·8 g.), then oleanolic acid (38 mg.), $[\alpha]_D^{25}$ +71·3° (*c* 0·87), m. p. and mixed m. p. 297—299° (correct infrared spectrum). The methyl ester had m. p. and mixed m. p. 198—200°.

Gallic acid. The aqueous washings and the acidified aqueous solution remaining after separation of amorphous acids were continuously extracted with ether for 30 hr. The concentrated ether solution was extracted with 10% aqueous sodium hydrogen carbonate, and the extract was acidified and re-extracted with ether. Removal of solvent and repeated crystallisation from water gave gallic acid (1·1 g.), m. p. and mixed m. p. 256—258° (decomp.) after drying at 125° (Found: C, 49·5; H, 3·7. Calc. for $C_7H_6O_5$: C, 49·4; H, 3·6%).

Methyl gallate. Purification of the neutral fraction obtained from the ether solution above by Jurd's method,[4] followed by repeated crystallisation from water, gave methyl gallate (65 mg.), m. p. and mixed m. p. 197—198° (decomp.) (Found: C, 52·2; H, 4·2. Calc. for $C_8H_8O_5$: C, 52·2; H, 4·4%).

β-*Sitosterol.* Chromatography of the neutral fraction of the initial ether extract in light petroleum on alumina (P. Spence and Co., grade H) and crystallisation from methanol of fractions eluted from the column with benzene gave β-sitosterol (125 mg.), m. p. and mixed m. p. 137—138°, $[\alpha]_D^{25}$ −34·6° (*c* 0·61) [Found (for sample dried to constant wt.): C, 84·2; H, 12·3. Calc. for $C_{29}H_{50}O$: C, 84·0; H, 12·15%] (correct infrared spectrum). The acetate had m. p. and mixed m. p. 126—127° (Found: C, 81·6; H, 11·35. Calc. for $C_{31}H_{52}O_2$: C, 81·5; H, 11·5%).

We are indebted to Dr. R. E. Corbett, University of Otago, for samples of betulic acid and methyl oleanolate and to Professor D. E. White, University of Western Australia, for a sample of oleanolic acid. Assistance is gratefully acknowledged from the Chemical Society, the Rockefeller Foundation of New York, the Australian and New Zealand Association for the Advancement of Science, and the Research Grants Committee of the University of New Zealand.

Department of Chemistry,
University of Auckland, New Zealand. [*Received, May 24th*, 1961.]

[4] Jurd, *J. Amer. Chem. Soc.*, 1956, **78**, 3445.

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921. *The Direct Amination of Mesitylene by Hydrazoic Acid in Concentrated Sulphuric Acid.*

By G. M. Hoop and J. M. Tedder.

The recent papers by Kovacic and Bennett on "Direct Amination" [1] prompt us to report some uncompleted work carried out in these laboratories two years ago and since set aside. Schmidt was the first to report the direct amination of benzene by sodium azide in concentrated sulphuric acid.[2] He suggested that the NH-radical was involved. It seemed to us more likely that in very strong acids hydrazoic acid would become protonated to yield the -onium ion ($NH=\overset{+}{N}=NH$ or $N\equiv\overset{+}{N}-NH_2$) and that this ion was responsible for the amination. Cryoscopic examination in 99·8% sulphuric acid showed that sodium azide gives an *i* factor of ~4: $NaN_3 + 2H_2SO_4 \longrightarrow H_2N_3^+ + HSO_4^- + Na^+ + HSO_4^-$.

Solutions of sodium azide in concentrated sulphuric acid were found to aminate a wide variety of aromatic nuclei, but the yields of amine were very small. Mesitylene proved exceptional and three amino-compounds, mesidine, diaminomesitylene, and 3-amino-2,4,6-trimethylbenzenesulphonic acid, were isolated together with some polymeric material which had the properties of an aromatic amine. When a solution of sodium azide in concentrated sulphuric acid at 60° was used the main product was the amino-sulphonic acid (42%), and the basic material was mainly diaminomesitylene and polymer. In 90% sulphuric acid under the same conditions no sulphonic acid was formed and the basic product was mainly mesidine. *m*-Xylene yielded only traces of sulphonated amine when treated with sodium azide in concentrated sulphuric acid, and with 87% sulphuric acid the

[1] Kovacic and Bennett, *J. Amer. Chem. Soc.*, 1961, **83**, 221, 743.
[2] Schmidt, *Ber.*, 1924, **57**, 704.

yield of crude *m*-xylidene was only 2%. Other aromatic hydrocarbons gave similar yields. It seems possible that the exceptional behaviour of mesitylene is due to the formation of mesitylenesulphonic acid which is hydrolysed to yield mesitylene dispersed in acid solution. Treatment of mesitylenesulphonic acid with a similar solution of sodium azide in 90% sulphuric acid gave an even larger yield of basic material (corresponding to about 80% of the starting acid), but toluene-*p*-sulphonic acid, which is less easily hydrolysed, yielded only 3-amino-4-methylbenzenesulphonic acid (5%).

The only other aromatic compound which gave more than a few percent of an amino-compound was *p*-nitrotoluene. When treated with a slight excess of sodium azide in concentrated sulphuric acid at 100° for 2 hr. it afforded a moderate yield of a crystalline amine. This product proved to be similar in properties and derivatives to the product that Bamberger isolated on reaction of *p*-tolyl azide with *p*-nitrotoluene and sulphuric acid,[3] and Gattermann obtained on electrolytic reduction of *p*-nitrotoluene.[4] These workers described their product as 4-amino-2′-methyl-5′-nitrodiphenylmethane, and the analysis of the present product and its derivatives are consistent with this structure, although it is not easy to explain its formation.

In an attempt to achieve amination in a more homogeneous medium, benzene and several other aromatic compounds were treated with a solution of toluene-*p*-sulphonyl azide and only a slight excess of sulphuric acid. This mixture gave slightly better yields of aminated product with benzene but more than one compound was produced. With other aromatic compounds the yields were no better than with sodium azide.

The present results show that, except with mesitylene, solutions of hydrazoic acid in sulphuric acid have little value as aminating agents. The results are consistent with a mechanism involving electrophilic substitution, although the exact nature of the acting species remains obscure. The reaction cannot involve hydroxylamine because sodium azide in anhydrous hydrogen fluoride was found to be weakly effective. It seems possible that the -onium ion ($N\equiv\overset{+}{N}-NH_2$) reacts with an aromatic nucleus to yield nitrogen and NH_2^+ as the transient electrophile which partakes in the substitution.[1,5]

Experimental.—Some hydrazoic acid is evolved when sodium azide is dissolved in concentrated sulphuric acid and the solution heated. In all the experiments described the reaction was carried out in an open vessel behind the safety screen of a fume cupboard with a good draught. So long as the vessel is open there is no danger, but in one experiment in a closed vessel fitted with a condenser there was a very violent explosion.

Amination of mesitylene. (*a*) In concentrated sulphuric acid. Sodium azide (8·1 g.) was dissolved in concentrated sulphuric acid (100 c.c.) and the solution was heated at 60°. Mesitylene (6 g.) was added dropwise during 20 min. to the rapidly stirred mixture (heat was evolved during the addition and the temperature was maintained without external heating). Further sodium azide (8·1 g.) was then added slowly and mixture was stirred for a further hour at 60—70°. The acid solution was poured on ice; the precipitate (4·47 g.) formed recrystallised from hot water to yield white crystals of 3-*amino*-2,4,6-*trimethylbenzenesulphonic acid* which charred at about 400° without melting. It was soluble in alkali and treatment with nitrous acid yielded a diazonium salt (Found: C, 50·2; H, 6·5; N, 6·5; S, 15·7%; equiv., 213. $C_9H_{13}NO_3S$ requires C, 50·2; H, 6·1; N, 6·5; S, 14·9%; equiv., 215). The main aqueous filtrate was rendered alkaline and extracted with ether. Evaporation gave an oil (3·36 g.; N, 12·4%) which on diazotisation and coupling gave a mixture of dyes. Distillation gave no clear fractions but one fraction (0·40 g.; b. p. 130—180°/16 mm.) gave an oil (N, 17·7%) from which 1,3-*dibenzamido*-2,4,6-*trimethylbenzene*, m. p. 278°, was obtained (Found: C, 76·2; H, 6·1; N, 7·4. $C_{23}H_{22}N_2O_2$ requires C, 77·0; H, 6·1; N, 7·8%). In another experiment crystalline 1,2-diamino-2,4,6-trimethylbenzene, m. p. 89°, was obtained. A higher-boiling fraction (1·82 g.; b. p. 180—200°; N, 9·2%) became a glass on cooling but still exhibited the properties of an aromatic amine and could be diazotised and coupled.

[3] Bamberger, *Annalen*, 1925, **443**, 194.
[4] Gattermann, *Ber.*, 1893, **26**, 1844.
[5] Keller and Smith, *J. Amer. Chem. Soc.*, 1944, **66**, 1122; 1946, **68**, 899.

(*b*) In 90% sulphuric acid. Sodium azide (8·1 g.) was dissolved in a mixture of concentrated sulphuric acid (187 g.) and water (14 g.). Mesitylene (6 g.) was added gradually and the whole was heated to 100°. The mesitylene was followed by further sodium azide (8·1 g.), and the mixture was heated at 100° for 2 hr. The products were isolated as before. No precipitate was formed when the reaction mass was poured on ice. The basic product (4·06 g.) was distilled at atmospheric pressure; the main fraction boiled at 230° and was readily converted into a crystalline acetyl derivative, m. p. 213° (mesidine [6] has b. p. 230° and *N*-acetylmesidine has m. p. 210—212°).

Amination of m-*xylene*. (*a*) In concentrated sulphuric acid. *m*-Xylene (5·3 g.) was added to a solution of sodium azide in concentrated sulphuric acid in the conditions used for mesitylene. There was no basic product although there was a small amount of an amino-sulphonic acid as indicated by addition of sodium nitrite to the aqueous mother liquor and coupling of the resultant diazonium salt with β-naphthol.

(*b*) In 87% sulphuric acid. *m*-Xylene (5·3 g.) was added to a solution of sodium azide (8·1 g.) in a mixture of concentrated sulphuric acid (130 g.) and water (14·8 g.). Then further sodium azide (8·1 g.) was added and the mixture heated at 100° for 2 hr. and worked up as before. The aqueous phase contained traces of an amino-sulphonic acid. A crude basic oil (0·13 g.) was also obtained. This was diazotised and coupled with β-naphthol and the resultant dye purified by chromatography to yield 1-(2,4-dimethylphenylazo)-2-naphthol,[7] m. p. 155°, alone or in admixture with an authentic specimen.

Amination of p-*nitrotoluene*. *p*-Nitrotoluene (12·1 g.) was added to a solution of sodium azide (7·8 g.) in concentrated sulphuric acid (50 c.c.). The mixture was heated for 2·5 hr., then poured on ice. Unchanged *p*-nitrotoluene (5·83 g.) was precipitated. The filtrate was rendered alkaline and extracted with ether continuously for 12 hr. Evaporation left dark-yellow crystals (1·28 g.). Two recrystallisations from aqueous alcohol gave yellow needles, m. p. 117° (Found: C, 69·3; H, 6·2; N, 11·7. Calc. for $C_{14}H_{14}N_2O_2$: C, 69·4; H, 5·8; N, 11·6%). Bamberger [3] reports 4-amino-2′-methyl-5′-nitrodiphenylmethane to melt at 117—118°. A portion of the product was treated with acetic anhydride: the resultant *N*-acetyl derivative had m. p. 174° (Gattermann [4] reports m. p. 174°). The product was diazotised and coupled with β-naphthol, to yield 1-[p-(2-*methyl*-5-*nitrobenzyl*)*phenylazo*]-2-*naphthol*, m. p. 157—158° (Found: C, 71·8; H, 5·3; N, 11·1. $C_{24}H_{19}N_3O_3$ requires C, 72·5; H, 4·8; N, 10·7%).

Amination of mesitylenesulphonic acid. Mesitylenesulphonic acid dihydrate (5·9 g.) was added gradually to a solution of sodium azide (4·1 g.) in 90% sulphuric acid (100 g.). Further sodium azide (4·1 g.) was added and the mixture stirred at 100° for 2 hr., then poured on ice and rendered alkaline. Extraction with ether and evaporation left a basic oil (2·85 g.). Distillation at atmospheric pressure gave no discrete fractions but one fraction (b. p. <230°, 0·15 g.) corresponded to mesidine and treatment with acetic anhydride gave 2,4,6-trimethylacetanilide (m. p. 210—212°). A second fraction (b. p. 230—260°; 0·9 g.) was mainly diaminomesitylene, from which the benzoyl derivative, m. p. and mixed m. p. 278°, was obtained.

The authors thank Dr. D. Jaques for measuring the *i*-factor.

THE UNIVERSITY, SHEFFIELD, 10. [*Received, May 26th*, 1961.]

[6] Ingold and Piggott, *J.*, 1924, **125**, 168.
[7] Niementowski, *Anz. Akad. Wiss. Krakau*, 1902, 413 (*Chem. Zentr.*, 1902, II, 938).

922. *Some Compounds Derived from* o-2-*Carboxyethylbenzoic Acid.*

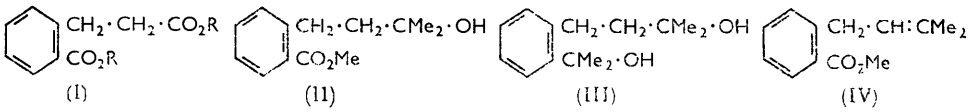
By E. D. ANDREWS and W. E. HARVEY.

o-2-CARBOXYETHYLBENZOIC ACID (I; R = H) is readily available from β-naphthol [1] and we have investigated it with a view to its use in the synthesis of certain *ortho*-substituted isopentylbenzenes.

Nitration of the acid (I; R = H) proceeds normally to give the 5-nitro-compound which was converted into the corresponding amine and bromo-compound. With methylmagnesium iodide the dimethyl ester (I; R = Me) was converted, in good yield, into the

[1] Page and Tarbell, *Org. Synth.*, 1954, **34**, 8.

hydroxy-ester (II), although with a large excess of the Grignard reagent some of the diol (III), isolated as the crystalline hemihydrate, was also formed. Dehydration of the ester (II) with sulphuric acid gave the unsaturated ester (IV), identified by hydrogenation



(I) (II) (III) (IV)

and hydrolysis to *o*-isopentylbenzoic acid, which is more conveniently prepared by this method than by that previously described.[2]

Experimental.—o-2-*Carboxyethylbenzoic acid.* This acid [1] with methanolic hydrogen chloride gave its *dimethyl ester*, b. p. 124°/2·5 mm., n_D^{25} 1·5115 (Found: C, 65·05; H, 6·5. $C_{12}H_{14}O_4$ requires C, 64·85; H, 6·35%).

2-2′-*Carboxyethyl-5-nitrobenzoic acid.* A mixture of fuming nitric acid (3·25 g., 1 mol.) and concentrated sulphuric acid (6 g.) was added dropwise with stirring to an ice-cold solution of *o*-2-carboxyethylbenzoic acid (15 g.) in concentrated sulphuric acid (50 g.). Stirring was continued for a further 2 hr., then the solution was poured on ice. The *nitro-acid* (16·25 g., 88%) crystallised from water as pale yellow plates, m. p. 180—182° (Found: C, 50·6; H, 3·7; N, 5·7. $C_{10}H_9NO_6$ requires C, 50·2; H, 3·8; N, 5·9%). Treatment with methanol containing 5% of dry hydrogen chloride on the water-bath for 3 hr. and working up in the usual manner gave *methyl* 2-2′-*methoxycarbonylethyl-5-nitrobenzoate* (60%), pale yellow needles (from methanol), m. p. 51—52° (Found: C, 54·3; H, 4·6; N, 5·0. $C_{12}H_{13}NO_6$ requires C, 53·9; H, 4·9; N, 5·2%), and 2-2′*methoxycarbonylethyl-5-nitrobenzoic acid* (30%), colourless prisms (from methanol), m. p. 124—125° (Found: C, 51·6; H, 4·1; N, 5·5. $C_{11}H_{11}NO_6$ requires C, 52·1; H, 4·4; N, 5·5%).

5-*Amino*-2-2′-*carboxyethylbenzoic acid.* The nitro-acid, in methanol, was hydrogenated at 50°/50 atm. in presence of Raney nickel. The *amino-acid* (86%) crystallised from water as plates, m. p. 200—201° (Found: C, 58·1; H, 5·2; N, 6·3. $C_{10}H_{11}NO_4$ requires C, 57·4; H, 5·3; N, 6·7%). The *dimethyl ester* prepared analogously in 95% yield crystallised from methanol as plates, m. p. 75—76° (Found: C, 60·9; H, 6·1; N, 5·95. $C_{12}H_{15}NO_4$ requires C, 60·75; H, 6·4; N, 5·9%).

5-*Bromo*-2-2′-*carboxyethylbenzoic acid.* Potassium nitrite (5 g.) in water (15 ml.) was added dropwise to a cooled suspension of the amino-acid (10 g.) in 40% hydrobromic acid (50 g.) and water (5 ml.) in a flask which was stoppered after each addition of the nitrite solution and shaken until all the nitrous fumes were absorbed. The temperature was kept below 10°; when most of the nitrite solution had been added a yellow precipitate was formed. Copper bronze (2 g.) was added, and, after the initial reaction, the mixture was allowed to warm to room temperature, then heated on a steam bath for 1 hr. during which the bromo-compound was precipitated. The mixture was treated with 10% sodium carbonate solution and the resulting dark red solution was filtered and acidified with hydrochloric acid. The brown material which separated (8 g., 62%) was sublimed in a high vacuum at 150° to give the colourless *bromo-acid*, m. p. 160—162° (Found: C, 44·3; H, 3·3; Br, 28·8. $C_{10}H_9BrO_4$ requires C, 44·0; H, 3·7; Br, 29·3%).

Reaction of methyl 2-2′-*methoxycarbonylethylbenzoate with methylmagnesium iodide.* The di-ester (48 g., 1 mol.) in dry ether (250 ml.) was added dropwise with stirring during 1 hr. to methylmagnesium iodide (2·5 mol.) in ether (250 ml.). The resulting suspension was heated under reflux with stirring for 1·5 hr., then poured on ice and ammonium chloride. The ethereal solution was washed with water, dried (Na_2SO_4), and concentrated, to yield *methyl* o-(3-*hydroxy*-3-*methylbutyl*)*benzoate* (II) (41 g., 85%), b. p. 115°/1 mm., n_D^{25} 1·5181 (Found: C, 70·05; H, 8·1. $C_{13}H_{18}O_3$ requires C, 70·2; H, 8·2%). When the amount of methylmagnesium iodide was increased to 5·5 mol. and heating was extended to 3 hr., working up as before gave the above material together with 15% of crystalline material which separated from the crude product and recrystallised from moist light petroleum (b. p. 45—60°) as needles of 4-[o-(1-*hydroxy*-1-*methylethyl*)*phenyl*]-2-*methylbutan*-2-*ol hemihydrate*, m. p. 78—79° [Found (air-dried material): C, 72·5; H, 10·0. $C_{14}H_{22}O_2,\frac{1}{2}H_2O$ requires C, 72·7; H, 10·0%]. When this material was dried in a high vacuum over phosphorus pentoxide at room temperature it formed a viscous

[2] Harvey, *J.*, 1958, 2060.

gum from which the crystalline material was regenerated by crystallisation from moist light petroleum.

o-(3-*Hydroxy*-3-*methylbutyl*)*benzoic acid*. Alkaline hydrolysis of the ester (II) gave the *acid* which crystallised from light petroleum as plates, m. p. 81—82° (Found: C, 69·3; H, 7·7. $C_{12}H_{16}O_3$ requires C, 69·2; H, 7·7%).

o-(3-*Methylbut*-2-*enyl*)*benzoic acid*. The above hydroxy-acid was heated under reflux with vigorous stirring with 40% w/v sulphuric acid for 3·5 hr. The product was isolated with ether and distilled, giving the *acid*, b. p. 140—143°/1 mm., which solidified and after sublimation in a vacuum had m. p. 83—83·5° (Found: C, 76·0; H, 7·6. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%).

Methyl o-(3-*methylbut*-2-*enyl*)*benzoate* (IV). Dehydration of the ester (II) with sulphuric acid as above gave, in 70% yield, the unsaturated *ester*, b. p. 100—102°/1 mm., n_D^{25} 1·5220 (Found: C, 76·5; H, 8·2. $C_{13}H_{16}O_2$ requires C, 76·4; H, 7·9%).

o-*Isopentylbenzoic acid*. The unsaturated ester above, in methanol, was hydrogenated at 50°/50 atm. in presence of Raney nickel, to give methyl *o*-isopentylbenzoate, b. p. 92—93°/1 mm., n_D^{25} 1·4997, identified by alkaline hydrolysis to *o*-isopentylbenzoic acid, m. p. and mixed m. p. 42—43°.

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VICTORIA UNIVERSITY OF WELLINGTON,
WELLINGTON, NEW ZEALAND. [*Received, May 29th*, 1961.]

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923. *The Preparation of Silver Fluoroborate and Silver Hexafluorophosphate.*

By D. R. RUSSELL and D. W. A. SHARP.

SILVER salts of complex fluoro-acids are interesting because of their solubility in organic solvents and because of their potential use in organic and inorganic syntheses.[1] Silver fluoroborate has previously been prepared by the use of bromine trifluoride [2] or sulphur tetrafluoride [3] and from silver(I) fluoride and boron trifluoride in nitromethane,[4] hydrogen fluoride,[5] and benzene.[6] Silver hexafluorophosphate has been prepared by use of bromine trifluoride.[7] These salts tenaciously retain organic and other solvents, and the products of these reactions have to be heated to remove excess of solvent.

Both silver salts are readily obtained pure from silver(I) fluoride and boron trifluoride or phosphorus pentafluoride by use of sulphur dioxide as solvent. The solvent may easily be removed without heating by use of a simple vacuum line and the salts are obtained as clean dry products.

Experimental.—Silver fluoride was prepared by the method of Andersen, Bak, and Hillebert.[8] Boron trifluoride was a gift from the Imperial Smelting Corporation and was dried and purified by passage through a suspension of boric oxide in sulphuric acid. Phosphorus pentafluoride was obtained by heating a diazonium hexafluorophosphate (Phosfluorogen A). Sulphur dioxide was dried by passage over phosphorus pentoxide.

The gaseous fluoride was bubbled through a suspension of silver fluoride in liquid sulphur dioxide. When dissolution was complete the liquid was filtered free from insoluble impurities and evaporated to dryness *in vacuo*; no external heating was necessary. *X*-Ray powder photographs confirmed the identity of the products [(*a*) Found: Ag, 55·6. Calc. for $AgBF_4$: Ag, 55·4. (*b*) Found: Ag, 43·0. Calc. for $AgPF_6$: Ag, 42·7%].

[1] See, *e.g.*, Sharp, *Adv. Fluorine Chem.*, 1960, **1**, 68.
[2] Sharpe, *J.*, 1952, 4538.
[3] Kemmitt and Sharp, *J.*, 1961, 2496.
[4] Olah and Quinn, *J. Inorg. Nuclear Chem.*, 1960, **14**, 295.
[5] Clifford and Kongpricha, *J. Inorg. Nuclear Chem.*, 1957, **5**, 76.
[6] Heyns and Paulsen, *Angew. Chem.*, 1960, **72**, 349.
[7] Woolf and Emeléus, *J.*, 1950, 1050.
[8] Andersen, Bak, and Hillebert, *Acta Chem. Scand.*, 1953, **7**, 236.

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INORGANIC CHEMISTRY RESEARCH LABORATORIES,
IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
LONDON, S.W.7.

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924. *The Reaction between Furfuryl Alcohol and 2,4-Dinitrophenylhydrazine in Methanolic Hydrochloric Acid.*

By K. G. LEWIS.

THE rearrangement of furfuryl alcohol by hydrogen chloride in methanol has been shown [1] to yield, among other substances, α-methoxylævulaldehyde dimethyl acetal, and not δ-methoxylævulaldehyde dimethyl acetal as previously suggested.[2,3] In a preliminary attempt to prepare the bis-2,4-dinitrophenylhydrazone of the supposed δ-methoxyaldehyde [3] for comparison with synthetic material of this structure, furfuryl alcohol was refluxed with a solution of 2,4-dinitrophenylhydrazine in methanolic hydrochloric acid. The mixture that formed was separable into substances (I), (II), and (III). Substance (I) was methyl lævulate 2,4-dinitrophenylhydrazone. Substance (II) was yellow and had m. p. 217—218°. The possibility that it was furfuraldehyde 2,4-dinitrophenylhydrazone (yellow form,[4] m. p. 212—214°), formed by oxidation of the furfuryl alcohol by 2,4-dinitrophenylhydrazine as suggested for certain unsaturated alcohols by Braude and Forbes,[5] was eliminated by comparison with the authentic furfuraldehyde derivative and by analysis. Analysis also showed that this material, although of similar m. p. to that recorded by Deriaz *et al.*[3] for the supposed δ-methoxylævulaldehyde bis-2,4-dinitrophenylhydrazone, could not have this structure. The derived molecular formula, $C_{17}H_{16}N_8O_9$, agreed with a formulation as lævulic acid 2,4-dinitrophenylhydrazide 2,4-dinitrophenylhydrazone and this was confirmed by a synthesis of this substance from lævuloyl chloride and 2,4-dinitrophenylhydrazine. Some lævulic acid derivatives may exist in cyclic form,[6] but it is likely that bis-derivatives, *e.g.*, the anil-anilide,[7] are derivatives of the open-chain form. While ultraviolet absorption spectra of compound (II) gave little useful information concerning the structure, the infrared spectrum (KCl disc) showed, in addition to the usual peak characteristic of the C=N grouping, a peak at 1680 cm.$^{-1}$ assigned to the carbonyl group of the acid hydrazide (Barton and Hendricksen [8] record 1678 cm.$^{-1}$ for an analogous group). Thus substance (II) must have the open-chain structure, R·NH·N:CMe·$[CH_2]_2$·CO·NH·NHR, where R = 2,4-$(NO_2)_2C_6H_3$.

The red substance (III), $C_{17}H_{14}N_8O_8$, was sparingly soluble in most solvents except nitrobenzene. It gave a very intense, broad ultraviolet maximum at 400—460 mμ characteristic of the bis-2,4-dinitrophenylhydrazones of conjugated alkenediones [9] and was shown by comparison to be 4-oxopent-2-enal bis-2,4-dinitrophenylhydrazone which has been observed to be formed [1] when α-methoxylævulaldehyde dimethyl acetal is treated with 2,4-dinitrophenylhydrazine in methanolic acid.

Experimental.—Reaction between furfuryl alcohol and 2,4-dinitrophenylhydrazine. Freshly distilled furfuryl alcohol (1 g.) was added to a boiling solution of 2,4-dinitrophenylhydrazine

[1] Lewis, *J.*, 1957, 531; Birkofer and Dutz, *Annalen*, 1957, **608**, 7.
[2] Pummerer and Gump, *Ber.*, 1923, **56**, 999; Pummerer, Guyot, and Birkofer, *Ber.*, 1935, **68**, 480.
[3] Deriaz, Stacey, Teece, and Wiggins, *J.*, 1949, 1222.
[4] Bredereck, *Ber.*, 1932, **65**, 1833.
[5] Braude and Forbes, *J.*, 1951, 1762.
[6] Cason and Reist, *J. Org. Chem.*, 1958, **23**, 1492; Lukes and Prelog, *Chem. Listy*, 1930, **24**, 251 (*Chem. Abs.*, 1930, **24**, 4762).
[7] Lukes and Linhartova, *Coll. Czech. Chem. Comm.*, 1960, **25**, 502.
[8] Barton and Hendrickson, *J.*, 1956, 1028.
[9] Lewis, *J.*, 1956, 1083.

(4 g.) in methanol (400 ml.) containing hydrochloric acid (4 ml.), and the mixture was refluxed for 2 hr. The precipitated material was filtered off and washed with cold methanol. The combined filtrate and washings were evaporated to 100 ml. and chilled. The brown crystals that separated were filtered off and recrystallised from methanol–dioxan, to give methyl lævulate 2,4-dinitrophenylhydrazone (I), m. p. and mixed m. p. 139—141°. The crude residue (*ca.* 2·5 g.) was boiled with methanol (500 ml.), and the boiling solution was filtered. The filtrate, on cooling, deposited small yellow crystals (m. p. 215°) of substance (II). This methanol extraction was repeated until the insoluble residue (III) appeared clear red. The combined crops of compound (II) were recrystallised from ethyl acetate, to give *lævulic acid* 2,4-*dinitrophenylhydrazide* 2,4-*dinitrophenylhydrazone*, m. p. 217—218° (decomp.) (Found: C, 42·9; H, 3·5; N, 23·1; OMe, 0. $C_{17}H_{16}N_8O_9$ requires C, 42·85; H, 3·4; N, 23·5%), $\lambda_{max.}$ 350 mμ (log ε 4·47) in dioxan. In the same solvent lævulic acid 2,4-dinitrophenylhydrazone showed $\lambda_{max.}$ 358 mμ (log ε 4·24), and *N*-acetyl-2,4-dinitrophenylhydrazine $\lambda_{max.}$ 330 mμ (log ε 4·17). The red residue (III) on recrystallisation from nitrobenzene–tetrachloroethane gave 4-oxopent-2-enal bis-2,4-dinitrophenylhydrazone, m. p. 265—266° (decomp.) (Found: C, 44·9; H, 3·3; O, 27·9; N, 24·6. Calc. for $C_{17}H_{14}N_8O_8$: C, 44·5; H, 3·1; O, 27·95; N, 24·45%). There was no depression of m. p. on admixture with authentic material.

Synthes's of lævulic acid 2,4-*dinitrophenylhydrazide* 2,4-*dinitrophenylhydrazone*. Lævuloyl chloride [10] (0·5 ml.), b. p. 74—78°/11 mm., was added to 2,4-dinitrophenylhydrazine (2 g.) in tetralin (50 ml.; distilled over sodium) at 160°. The temperature was kept at 150° for 30 min. and the mixture then left overnight. The product which had separated was filtered off and washed with benzene. The crude material was digested with ethyl acetate and crystallised thrice from acetic acid, to yield lævulic acid 2,4-dinitrophenylhydrazide 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 218° (decomp.) (Found: C, 42·9; H, 3·4; N, 23·5%).

THE UNIVERSITY OF NEW ENGLAND,
ARMIDALE, N.S.W., AUSTRALIA.

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[10] Clemo and Ramage, *J.*, 1931, 54.

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925. *The Synthesis of* 4,5,7-*Trimethoxy*-2-*propylanthraquinone.*

By A. J. BIRCH and C. J. MOYE.

NALGIOVENSIN has been formulated [1] as 4,5-dihydroxy-2-2′-hydroxypropyl-7-methoxyanthraquinone, and to provide further support for this structure we have synthesised the substance named in the title, which is obtainable by a series of processes from nalgiovensin.

The process followed closely that used for the corresponding 2-methylanthraquinone derivative.[2] 3,5-Dimethoxyphthalic anhydride was condensed with 3-propylphenol by the Friedel–Crafts procedure and the product was brominated and cyclised in the standard manner.[3] Refluxing the cyclised product with hydriodic acid removed the bromine and gave the anthrone, which was oxidised by chromic acid to 4,5,7-trihydroxy-2-propylanthraquinone with the m. p. recorded [4] for the substance obtained similarly from nalgiovensin. Methylation to 4,5,7-trimethoxy-2-propylanthraquinone gave a compound identical in infrared spectrum with the compound from nalgiovensin and undepressed in m. p. by it. Nalgiovensin therefore certainly contains a 2-n-propyl group, as predicted [1] by the acetic acid theory of biosynthesis.

Experimental.—4,5,7-*Trimethoxy*-2-*propylanthraquinone*. (i) To aluminium chloride (10 g.) suspended in stirred benzene was slowly added a warm solution of 3,5-dimethoxyphthalic anhydride (4 g.) in *m*-propylphenol (16 c.c.). After 12 hr. the mixture was stirred for 3 hr. at 50°, 2 hr. at 60°, and 3 hr. at 70° and then poured on ice (50 g.) and 2N-hydrochloric acid (50 c.c.). The product was taken up in ether and extracted with sodium hydrogen carbonate solution. Acidification of the extract, followed by crystallisation of the precipitate from aqueous methanol, gave 3,5-*dimethoxy*-2-(2-*hydroxy*-4-*propylbenzoyl*)*benzoic acid* (0·9 g.), m. p.

[1] Birch and Massy-Westropp, *J.*, 1957, 2215.
[2] Brockmann, Kluge, and Muxfeldt, *Chem. Ber.*, 1957, **90**, 2302.
[3] Anslow and Raistrick, *Biochem. J.*, 1941, **35**, 1008.
[4] Raistrick and Ziffer, *Biochem. J.*, 1951, **49**, 563.

229—233° (Found: C, 66·1; H, 5·9. $C_{19}H_{20}O_6$ requires C, 66·3; H, 5·8%). This was brominated by the procedure of Anslow and Raistrick [3] for the corresponding methyl compound, *i.e.*, in 10% w/v acetic acid, finally at 50° (2 hr.). The oily product crystallised under light petroleum (b. p. 30—40°) but melted unsharply at ~220°. The crystalline product (190 mg. from 250 mg.) was directly cyclised with oleum (3·5 c.c.; 7% of SO_3) and boric acid (0·35 g.) at 90° for 15 min. Addition of ice and filtration gave a red solid that crystallised from chloroform–methanol as tan-coloured needles (75 mg.), m. p. 166—174°. This product (35 mg.) in acetic acid (2 c.c.) was refluxed with hydriodic acid (*d* 1·7; 0·2 c.c.) and red phosphorus (30 mg.) for 3 hr. Filtration and cooling gave yellow needles (20 mg.). This anthranol in acetic acid (5 c.c.) was treated with chromium trioxide (20 mg.) in 50% acetic acid (0·6 c.c.) for 0·5 hr. at 60°. Extraction with chloroform and crystallisation from benzene gave orange-yellow crystals (10 mg.), m. p. 213—217° (recorded m. p. for 4,5,7-trihydroxy-2-propylanthraquinone, 216·5—217°). Methylation with potassium carbonate and methyl sulphate in acetone, chromatography on alumina in ether, and crystallisation from benzene–light petroleum (b. p. 40—60°) gave 4,5,7-*trimethoxy*-2-*propylanthraquinone* (5 mg.), m. p. 169—170°, undepressed by the substance described below and identical with it in infrared spectrum (Found: C, 70·7; H, 6·1. $C_{20}H_{20}O_5$ requires C, 70·6; H, 5·9%).

(ii) Reduction of nalgiovensin as described in the literature,[4] oxidation with chromic acid (4 equiv.) in acetic acid, and methylation of the product with a large excess of methyl sulphate and aqueous sodium hydroxide gave a brown gum. This was taken up in benzene; tar was precipitated on addition of light petroleum (b. p. 40—60°). The product then obtained by evaporation was chromatographed in ether on alumina (grade H; neutralised with acetic acid) and recrystallised from light petroleum (b. p. 60—80°). 4,5,7-Trimethoxy-2-propylanthraquinone had m. p. 169—170°.

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Department of Chemistry, University of Manchester. [*Received, June 7th*, 1961.]

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926. *The Synthesis of* (±)-S-3-*Methylbut*-2-*enylhomocysteine.*

By A. J. Birch and M. Slaytor.

We have postulated [1] the biochemical introduction of isoprenoid groups (including isopentenyl groups) into phenolic and related compounds by a process analogous to biological *C*-methylation. Since the latter undoubtedly results from the action of "active" methionine,[2] which acts as a methyl-cation donor, we were led to postulate a similar source of isopentenyl cations. This now appears to be isopentenyl pyrophosphate,[3] from which, however, the group could conceivably be transferred to other biologically active centres containing thiol groups. We have accordingly synthesised the isopentenyl analogue of methionine, namely, (±)-*S*-3-methylbut-2-enylhomocysteine.

Experimental.—3-Methylbut-2-enyl bromide [4] (1·5 g., 0·01 mole) was added to a solution of (±)-*S*-benzylhomocysteine [5] (2·25 g., 0·01 mole) in liquid ammonia (50 c.c.) to which enough sodium had been added to give a permanent blue colour.[6] The ammonia was allowed to evaporate, water (10 c.c.) was added, and the solution neutralised with hydriodic acid until it was alkaline to Congo Red but acid to litmus paper; (±)-S-3-*methylbut*-2-*enylhomocysteine* crystallised. It recrystallised from water as plates (1·25 g., 64%), m. p. 207° (Found: C, 53·2; H, 8·15. $C_9H_{17}NO_2S$ requires C, 53·2; H, 8·43%).

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[1] Birch, Elliott, and Penfold, *Austral. J. Chem.*, 1954, **7**, 169.
[2] Birch, English, Massy-Westropp, Slaytor, and Smith, *J.*, 1958, 365.
[3] See, *e.g.*, Lynen, Eggerer, Henning, and Kessel, *Angew. Chem.*, 1958, **70**, 738.
[4] Staudinger, Kreis, and Schilt, *Helv. Chim. Acta*, 1922, **5**, 750.
[5] Patterson and du Vigneaud, *J. Biol. Chem.*, 1935, **111**, 393.
[6] Challenger and Dransfield, *J.*, 1955, 1153.