NOTES.

The Exchange of Iodine Atoms between Iodine and Methyl Iodide in the Temperature Range 150—375°.

By DOUGLAS CLARK, H. O. PRITCHARD, and A. F. TROTMAN-DICKENSON.

[Reprint Order No. 4863.]

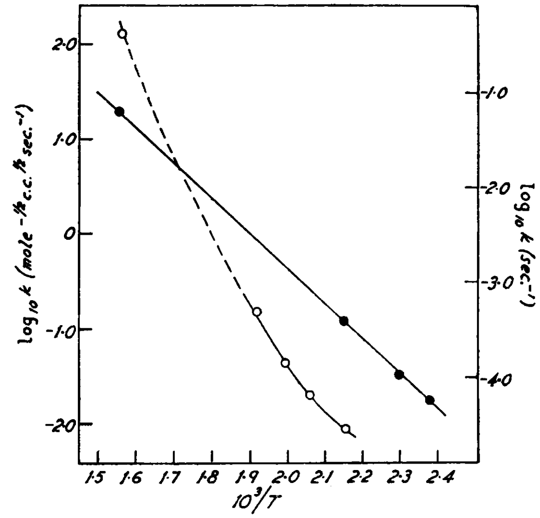
OGG and POLANYI (*Trans. Faraday Soc.*, 1935, **31**, 482) showed that the reaction between iodine atoms and *sec.*-butyl iodide leads to optical inversion of the butyl iodide molecule. They found that below 200° the racemisation was a heterogeneous reaction of low activation energy (8 kcal./mole), but that in the temperature range 240—280° the homogeneous inversion by iodine atoms predominated because of its considerably higher activation energy (32·2 kcal./mole); the investigation was complicated, however, by the fact that at these temperatures the butyl iodide molecule is unstable. In an attempt to gain a better understanding of the factors affecting these inversion reactions, we have studied the exchange of ^{131}I atoms between iodine and methyl iodide vapours, hoping to follow the very simplest example of an inversion reaction, *i.e.*,

$$I^* + H_3C{-}I \longrightarrow I^*{-}CH_3 + I$$

The reaction was studied over the temperature range 185—250° in a Pyrex bulb of about 1 l. capacity: known pressures of methyl iodide (*ca.* 50 cm.) and of radio-iodine (*ca.* 1 cm.) were introduced into the bulb (at constant temperature; thermostat) and allowed to react; after a known time, the reaction was terminated by condensation of the iodine–methyl iodide mixture in liquid air. The reaction products were shaken with mercury and a little acetone to remove free iodine, and the remaining mixture of methyl iodide and acetone was distilled off and made up to a standard volume with acetone; the mercuric iodide left was dissolved in 10% sodium iodide solution and made up to the standard volume with water. The extent to which the reaction had occurred was then determined from the ratio of the γ-ray activities of the two solutions (tests showed only a minute difference between the γ-ray assay obtained when a known quantity of iodine was counted in either aqueous or acetone solution).

It was found that the rate of transference of radioactivity from the iodine to the methyl iodide was represented by the equation Rate $= k[\mathrm{MeI}][\mathrm{I_2}]^{\frac{1}{2}}$, as is required for the inversion reaction, but that a plot of log k against $1/T$ was not a straight line (see Figure), suggesting that the reaction might be partly heterogeneous. When the reaction vessel was packed with Pyrex tubes, increasing the surface to volume ratio by a factor of about 8, the reaction rate increased 30-fold; the reaction remained of first order in methyl iodide concentration, but became independent of iodine concentration over a three-fold variation. The Arrhenius plot of these first-order, heterogeneous rate constants gives a straight line, roughly parallel to the lower portion of the plot for the unpacked vessel, corresponding to an activation energy of about 17 kcal./mole.

By analogy with Ogg and Polanyi's results, we assumed that the reaction occurred by two mechanisms, one heterogeneous having an activation energy of about 17 kcal./mole, the other homogeneous having a higher activation energy; if this were the case, higher temperatures would favour the latter reaction, and in order to try to isolate this reaction, experiments were carried out at 375° in a conventional flow pyrolysis apparatus (Leigh, Sehon, and Szwarc, *Proc. Roy. Soc.*, 1951, *A*, **209**, 97). The reactants were introduced into the reaction zone, methyl iodide vapour at about 8 mm. pressure being used as a carrier for the iodine; the rate of flow of methyl iodide was adjusted to give a contact time of about ¾ sec., and the iodine pressure was adjusted to give about the same ratio of $[MeI]/[I_2]$ as in the static experiments. A point representing the mean of several bimolecular rate constants is shown in the Figure as a continuation of the Arrhenius curve, since the surface to volume ratios for the two unpacked reaction vessels were not very different. However, packing the reaction vessel showed that even at this temperature the reaction was largely heterogeneous, and the heterogeneous rate was still dependent only on the methyl iodide concentration. Two types of packing were used in testing for heterogeneity in the flow system. In one set of experiments the reaction zone was packed completely with short lengths of Pyrex tube, resulting in a 6-fold increase in surface to volume ratio; the rate of the reaction increased by a factor of 6 as a result. The rate constants obtained were scaled up in the ratio of 8 to 6 to allow for the disparity in surface to volume ratios of the two packed reaction vessels, and the mean point thus obtained was found to lie very close to the continuation of the Arrhenius plot for the heterogeneous reaction observed at lower temperatures; the best line through all these points represents an activation energy of 17·0 kcal./mole.



Arrhenius plots for the exchange of radio-iodine with methyl iodide :
○ *in an unpacked reaction vessel,*
● *in a packed reaction vessel.*

A second type of packing, which has sometimes been used in kinetic studies, was also tried : enough quartz fibre to increase the surface area of the effective reaction zone by a factor of 4—5 was introduced into the vessel; the volume of this packing was quite small and it lay on the floor of the reaction vessel, occupying only about one-fifth of the volume of the reaction zone. No increase in reaction rate was observed under these conditions, suggesting that with contact times as short as those used here, the main body of the gas streams through the reaction vessel without coming into contact with the fibre packing. Such observations must cast some doubt on the interpretation of those kinetic measurements in which this type of packing was used, as it seems only to provide a stringent test for heterogeneity when it is distributed throughout the whole cross-section of the reaction zone.

These experiments show that it is not possible to isolate the reaction of higher activation energy, which probably represents the inversion of methyl iodide by iodine atoms (because of the nature of the kinetics in the unpacked vessels) at temperatures at which methyl iodide is stable; the only conclusion we can draw is that, from the slope of the upper portion of the Arrhenius curve, the activation energy is certainly not less than the 32·2 kcal./mole observed by Ogg and Polanyi for *sec.*-butyl iodide.

We thank Professor Geoffrey Gee, F.R.S., for his interest, Manchester University for the award of an I.C.I. Fellowship to one of us (A. F. T.-D.), and the D.S.I.R. for the award of a maintenance grant (D. C.).

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The Magnetic Susceptibility of Lanthanum.

By O. M. HILAL and F. A. SALEH.

[Reprint Order No. 5050.]

EGYPTIAN monazite, after separation of thorium and most of the cerium, was split into four fractions by the sodium nitrite separation (Hilal and El-Abbady, *J.*, 1952, 2935). The tail fraction contained most of the lanthanum. Its apparent atomic weight was 141·51 and bands of praseodymium, neodymium, and samarium were observed in the visible region. It was converted into nitrate and fractionated by the nitrite precipitation (*loc. cit.*) 179 times in 14 series, coloured head fractions being discarded. The last series was split into 16 fractions. The χ value of the lanthanum ion was determined and the last nine fractions gave the same value, within the experimental error, so they were mixed together (80·6 g. of oxide) and fractionally precipitated by ammonia carried in a current of air (Hilal and Sugden, *J.*, 1949, 135). After systematic separation involving 23 precipitations, 12 fractions were obtained, representing 21·2% of the crude lanthana. The magnetic susceptibility of the lanthanum ion from these fractions showed no substantial change from the previous values and so they were regarded as pure lanthana; they had $10^6 \chi^{20}_{\text{La}^{\cdots}} = -0{\cdot}17 \pm 0{\cdot}01$.

Two determinations of the apparent atomic weight of this oxide gave 138·97, 138·88; mean 138·92. The emission spectrum of the pure oxide, a copper–graphite arc and a small quartz spectrograph being used, showed no lines other than those of lanthanum. In particular the persistent lines of cerium and praseodymium were absent.

The nitrite precipitation method for the purification of lanthanum is therefore satisfactory when the yield and purity are compared with those obtained on precipitation by air-borne ammonia (Vickery, *J.*, 1952, 2506), and cerium, if present, is concentrated in the head fractions more easily than by the latter method.

For comparison, a solution of mixed rare-earth nitrates (80 g. of oxide/l.), containing a small percentage of cerium, was fractionated by both methods. In the first, the filtrate after the fourth fraction was found to be free from cerium, and contained 21% of the total weight of the original oxide, whereas by the second method a cerium-free filtrate was not obtained until after the fifth fraction, and contained 12%. Moreover, cerium is automatically eliminated during the nitrite precipitations, as its precipitate does not easily dissolve in cold dilute nitric acid.

The precipitate obtained on treating chemically pure lanthanum nitrate solution with sodium nitrite, as detailed above, contained La_2O_3, 71·29; N_2O_3, 16·56; H_2O (by diff.), 12·15%. The absence of N_2O_5 was confirmed colorimetrically. The composition is therefore $La_2O_3,N_2O_3,3H_2O$, the ratio $La_2O_3 : N_2O_3$ being the same as that found by Sherwood (*J. Amer. Chem. Soc.*, 1944, **66**, 1228).

The apparent atomic weight was determined by Hilal and Sugden's method (*loc. cit.*) within 0·1 unit. The titration was carried out potentiometrically and approximately 0·5N-ammonium oxalate solution was used as a precipitant, as its pH coincides with the pH at the neutralisation point.

The magnetic susceptibility was determined at 20° ± 0·02° by Gouy's method with the specimen in a fixed position (Hilal and Fredericks, *J.*, 1954, 785), Hilal and Sugden's procedure (*loc. cit.*) being used. Strict additivity of the susceptibilities of the constituents in a chloride solution being assumed, the χ value of the $La^{\cdots}$ could be calculated. The value of $10^6 \chi_{\text{Soln.}}$ could be determined to within 0·001 and the consequent error in $10^6 \chi_{\text{La}^{\cdots}}$ was not more than ±0·01.

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2 : 2′ : 4 : 4′ : 5 : 5′-*Hexamethoxydiphenyl.*

By W. I. Taylor.

[Reprint Order No. 5138.]

2 : 2′ : 4 : 4′ : 5 : 5′-HEXAMETHOXYDIPHENYL has been isolated as a by-product in the preparation of large quantities of 1 : 2 : 4-trimethoxybenzene by methylation of crude methoxyquinol. Since methylation of purified methoxyquinol afforded no hexamethoxydiphenyl, the latter must be derived mainly from the unknown 2 : 2′ : 5 : 5′-tetrahydroxy-4 : 4′-dimethoxydiphenyl formed during the alkaline hydrogen peroxide oxidation of the vanillin to methoxyquinol. We have not, however, been able to isolate pure tetrahydroxydimethoxydiphenyl from the tar left after the methoxyquinol had been purified.

Experimental.—Crude methoxyquinol (350 g.) (Dakin, *Amer. Chem. J.*, 1909, **42**, 477) was methylated by methyl sulphate and alkali. The crude 1 : 2 : 4-trimethoxybenzene was extracted with ether, which was washed with water until neutral and dried (Na_2SO_4). After the ether had been removed and about one-third of the 1 : 2 : 4-trimethoxybenzene (b. p. 96°/0·4 mm.) had been distilled off, there appeared in the distillation flask a voluminous crystalline precipitate which was filtered off and washed with ethanol, to yield pure 2 : 2′ : 4 : 4′ : 5 : 5′-hexamethoxydiphenyl (12 g.), m. p. and mixed m. p. 176—177° (Found : C, 64·4; H, 6·7; MeO, 55·6. Calc. for $C_{18}H_{22}O_6$: C, 64·5; H, 6·6; MeO, 55·6%), ultra-violet absorption maximum in 95% EtOH at 298 mμ (log ε 4·06).

Chemical Laboratories, University of New Brunswick. [*Received, February 20th*, 1954.]

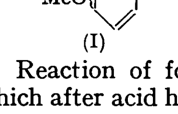
Condensation of α-Keto-acids with 2-3′ : 4′-Dihydroxyphenylethylamine.

By J. S. Little, A. G. Smith, W. I. Taylor, and B. R. Thomas.

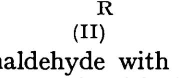
[Reprint Order No. 5139.]

SYNTHESIS by Belleau (*J. Amer. Chem. Soc.*, 1953, **75**, 5765) of the tetracyclic ring system present in some of the *Erythrina* alkaloids, *e.g.*, erysodine (I) (Karmack, McKusick, and Prelog, *Helv. Chim. Acta*, 1951, **34**, 1601), prompts us to report some work carried out some time ago.

Hahn and Stiehl (*Ber.*, 1936, **69**, 2645) showed that α-oxoglutaric acid reacted readily with 2-3′ : 4′-dihydroxyphenylethylamine hydrochloride in aqueous solution to yield (II; R = H) and we attempted to extend this reaction to the preparation of (II; R = $[CH_2]_2\cdot CO_2H$) from which erysodine (I) might be elaborated. For this purpose β-oxaloadipic acid was required. Ethyl β-iodopropionate and diethyl sodiooxalosuccinate afforded diethyl β-ethoxalyl-β-ethoxycarbonyladipate which, however, on acid hydrolysis furnished butane-1 : 2 : 4-tricarboxylic acid : hindrance of the tertiary ethoxycarbonyl group allows more rapid hydrolysis and consequent elimination of oxalo-group. In spite of this, successful preparations of disubstituted pyruvic acids have been recorded by this general route (*e.g.*, 3-methyl-2-oxopentanoic acid from ethyl ethoxalylpropionate; Mebus, *Monatsh.*, 1905, **26**, 483). The method developed by Schreiber (*Ann. Chim.*, 1947, **2**, 84) for the preparation of α-keto-acids from aliphatic α-ethoxalyl esters *via* the internal anhydrides was applied to the present case but the only tractable product was the above-mentioned tricarboxylic acid. We were also unable to make β-ethyl-α-oxoglutaric acid from ethoxalylsuccinic ester by similar methods : instead, ethylsuccinic acid was formed. A model β-monosubstituted α-oxoglutaric acid was prepared to see whether a disubstituted pyruvic acid of this type would condense with 2-3′ : 4′-dihydroxyphenylethylamine.



(I)



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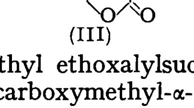

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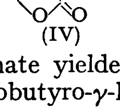
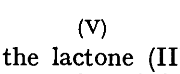


(IV)



(V)

Reaction of formaldehyde with diethyl ethoxalylsuccinate yielded the lactone (III) which after acid hydrolysis furnished β-carboxymethyl-α-oxobutyro-γ-lactone whose infrared spectrum indicated that the keto-group was completely enolised (cf. IV). However this did not condense with 2-3′ : 4′-dihydroxylphenylethylamine. Hahn, Bärwarld, Schales, and Werner (*Annalen*, 1935, **520**, 107) found no reaction to occur with either trimethylpyruvic acid or phenylglyoxylic acid and suggested that for condensation to take place the α-keto-group must be enolisable; the lack of reactivity of our acid (IV) must be due to another cause. We were also unable to effect condensation of the amine, under neutral or strongly acidic conditions, with *cyclo*hexanone, ethyl 2-oxo*cyclo*hexanecarboxylate or 2-oxo*cyclo*hexylglyoxylate, or 2-oxo*cyclo*hexylacetic acid.

The lactam (II; R = H) has been methylated with diazomethane and reduced directly with lithium aluminium hydride to 9-hydroxymethyl-2′ : 3′-dimethoxy-7 : 8-benzopyrrocoline (V) whose physiological properties will be described elsewhere.

*Experimental.—Butane-*1 : 2 : 4*-tricarboxylic acid.* Condensation of ethyl β-iodopropionate (43·4 g.) and diethyl sodio-oxalosuccinate (54 g.) furnished crude diethyl β-ethoxalyl-β-ethoxycarbonyladipate (50·6 g.), b. p. 165—167°/2 mm. (Found: C, 55·6; H, 7·4; OEt, 49·2. Calc. for $C_{17}H_{26}O_9$: C, 54·6; H, 7·0; 4OEt, 48·1%). The crude ester (20 g.) was refluxed overnight with 20% sulphuric acid (200 c.c.), then extracted exhaustively with ether, to yield crude butane-1 : 2 : 4-tricarboxylic acid (12·5 g.) which after two crystallisations from ether–chloroform melted constantly at 120—122° (lit., 116—119°) (Found: C, 43·9; H, 5·2. Calc. for $C_7H_{10}O_6$: C, 44·2; H, 5·3%). The crude ester (9·7 g.) and sulphuric acid (10 g.) were set aside for 2 weeks after which the solution was diluted with four volumes of water and saturated with hydrogen chloride under reflux. Cooling and exhaustive extraction with ether gave a crude oily acid (5·6 g.) which afforded pure butane-1 : 2 : 4-tricarboxylic acid, m. p. 120—121°, after several crystallisations from ether–chloroform (Found: C, 43·9; H, 5·3%). From the mother-liquors from both acid hydrolyses, and from those of other experiments, no α-keto-acid could be isolated.

Ethylsuccinic acid. Condensation of ethyl bromide with diethyl sodioethoxalylsuccinate afforded diethyl ethylethoxalylsuccinate (50 g.), b. p. 140—144°/1·5 mm., which with 10% sulphuric acid furnished, after ether-extraction, ethylsuccinic acid (17·6 g., 90%), m. p. 98° (lit., 98°) (Found: C, 49·2; H, 6·9. Calc. for $C_6H_{10}O_4$: C, 49·3; H, 6·9%). No other compounds could be isolated and the mother-liquors gave a negative test for ketones with 2 : 4-dinitrophenylhydrazine.

β-Carboxymethyl-α-oxobutyro-γ-lactone (IV). Potassium carbonate (2·5 g.) was added portionwise during 1 hr. to a cooled well-stirred mixture of formaldehyde (3 c.c. of 36% solution) and diethyl ethoxalylsuccinate (10 g.) in water (15 c.c.). The clear solution was saturated with ammonium sulphate, extracted three times with ether (50 c.c.), dried (Na_2SO_4), and concentrated to dryness, to yield on distillation a low-boiling fraction (not further investigated) and a crude lactone (III) (4·5 g.) as a viscous oil, b. p. 140—145°/2·5 mm. (strong bands in the carbonyl region at 1810 cm.$^{-1}$, γ-lactone; 1750 cm.$^{-1}$, keto-group in a five-membered ring; and 1735 cm.$^{-1}$, carboxylic ester). The lactone (III) (2·5 g.) was heated at 110° for 3 hr. in acetic acid (10 c.c.), water (7 c.c.), and hydrochloric acid (10 c.c.), then extracted with ether to furnish a crystalline product which after two crystallisations from ethyl acetate gave *β-carboxymethyl-α-oxobutyro-γ-lactone* (280 mg.), m. p. 155—157° (Found: C, 45·7; H, 4·0. $C_6H_6O_5$ requires C, 45·6; H, 3·8%) (infra-red bands at 1710 and 1735 cm.$^{-1}$ due to carbonyl stretching frequencies of a carboxyl group, and an αβ-unsaturated γ-lactone slightly lower than usual because of the 2-hydroxy-group).

9*-Hydroxymethyl-*2′ : 3′*-dimethoxy-*7 : 8*-benzopyrrocoline* (V). The lactam (II; R = H) (760 mg.) was kept with excess of diazomethane in methanol–ether, then evaporated *in vacuo*. The gummy product was taken up in a little methanol, absorbed into a filtration accelerator pad, dried *in vacuo*, then extracted (Soxhlet) into a solution of lithium aluminium hydride in absolute ether. After addition of ethyl acetate, the ethereal solution was shaken vigorously with 10% sodium hydroxide solution and with water, dried (Na_2SO_4), and concentrated, to furnish an oily base purified as its *picrate* (730 mg.), m. p. 201—202° (Found: C, 51·1; H, 5·0; N, 11·2. $C_{21}H_{24}O_{10}N_4$ requires C, 51·2; H, 4·9; N, 11·4%). The *base*, regenerated from the picrate, was an oil (Found, on a sample sublimed at 140°/0·5 mm.: C, 68·5; H, 8·2; N, 5·5. $C_{15}H_{21}O_3N$ requires C, 68·4; H, 8·0; N, 5·3%).

We are indebted to the National Research Council of Canada, for a grant and for a N.C.R. studentship (to J. S. L.), and for a N.R.C. post-doctorate fellowship (to B. R. T.).

CHEMICAL LABORATORIES, UNIVERSITY OF NEW BRUNSWICK. [*Received, February 20th,* 1954.]

The Methanolysis of Some Acetyl Derivatives of Cevine.

By W. J. ROSENFELDER.

[Reprint Order No. 5164.]

THE methanolysis of esters of the tertiary steroidal alkaloids has been widely reported (*inter al.*, Fried, White, and Wintersteiner, *J. Amer. Chem. Soc.*, 1950, **72**, 4621; Fried, Numerof, and Coy, *ibid.*, 1952, **74**, 3041; Kupchan and Deliwala, *ibid.*, 1952, **74**, 3202; Stoll and Seebeck, *Helv. Chim. Acta*, 1952, **35**, 1942). In principle this methanolysis could be a selective neighbouring group effect (cf. Winstein *et al.*, *J. Amer. Chem. Soc.*, 1953, **75**, 2297, and earlier papers there cited) or simply a consequence of the basicity of the medium due to the tertiary nitrogen atom. In either event, the reaction should be inhibited by quaternisation of the nitrogen atom: this was shown to be true, it being observed that whereas cevine di- and tetra-acetate were readily methanolysed, conversion into a methiodide or into an *N*-oxide afforded a product that was stable to aqueous methanol. However, it was found that addition of one mole of triethylamine to cevine tetra-acetate methiodide in methanol caused the methanolysis to proceed again quite rapidly, thus indicating that it is merely the basic property of the tertiary nitrogen atom of the cevine ester that is necessary to catalyse the reaction.

An interesting observation in the reaction of cevine di- and tetra-acetate with hydrogen peroxide (cf. Freund, *Ber.*, 1904, **37**, 1946; Stoll and Seebeck, *Helv. Chim. Acta*, 1952, **35**, 1270, for the preparation of cevine and cevagenin *N*-oxides) was the loss of one acetate residue giving cevine monoacetate *N*-oxide and cevine triacetate *N*-oxide, respectively. The structures of these two compounds, which had been assigned on the basis of their acetyl values, were confirmed by conversion into the *N*-oxides of cevine di- and tetra-acetate. This conversion was readily effected by mild treatment with acetic anhydride, authentic samples of the di- and tetra-acetate *N*-oxides being obtained by the action of one mol. of perphthalic acid on the corresponding tertiary bases. The *N*-oxides of all these four acetates of cevine proved to be stable to aqueous methanol.

Experimental. Values of $[\alpha]_D$ have been approximated to the nearest degree. Cevine has $[\alpha]_D$ $-19°$ (*c*, 2·00 in methanol). Acetyl values were determined by the method described in Roth, "Quantitative Organic Micro-analysis of Fritz Pregl," 3rd English Edn., J. and A. Churchill Ltd., p. 191 *et seq.*

The methanolysis of cevine diacetate. Cevine diacetate (Freund, *Ber.*, 1904, **37**, 1946; Barton and Eastham, *J.*, 1953, 424) (0·1242 g.) was dissolved in 90% aqueous methanol (3 ml.). The initial value of $[\alpha]_D$ was $-1°$, changing to $-12°$ (2 days), $-13·5°$ (4 days), and $-15°$ (9 days) at room temperature.

The methanolysis of cevine tetra-acetate. Cevine tetra-acetate (Stoll and Seebeck, *Helv. Chim. Acta*, 1952, **35**, 1270; Barton and Eastham, *loc. cit.*) (0·0196 g.) was dissolved in 90% aqueous methanol (2 ml.). The initial value of $[\alpha]_D$ was $+41°$, changing to $+26°$ (3 days) and $+20°$ (9 days) at room temperature.

Cevine diacetate N-*oxide.* Cevine diacetate (500 mg.) was dissolved in pure dry dioxan (10 ml.) and benzene (7 ml.), and a solution of perphthalic acid (110% of theory for 1 mol.) in ether was added. The reaction was followed by withdrawing 1-ml. samples of the solution from time to time, adding an excess of aqueous potassium iodide solution, and titrating the iodine liberated against 0·01N-sodium thiosulphate solution. After about 40 min. at room temperature, one mol. of perphthalic acid had reacted; the solution was taken up in a large volume of chloroform, washed with dilute ammonia, water, dilute acetic acid, and again with water, and was then dried and distilled. The residue was twice crystallised from aqueous methanol. *Cevine diacetate* N-*oxide* formed prisms, m. p. 219—220° (decomp.), $[\alpha]_D$ $-1°$ (*c*, 2·46), from 90% aqueous methanol (Found: C, 59·1; H, 7·8; Ac, 11·8. $C_{31}H_{47}O_{11}N,H_2O$ requires C, 59·3; H, 7·9; Ac, 13·7%).

No change in rotation was observed at room temperature in a solution of cevine diacetate *N*-oxide (0·0734 g.) in 3 ml. of 90% aqueous methanol during 3 days, and on concentration of the solution, prisms of cevine diacetate *N*-oxide, m. p. and mixed m. p. 219—220° (decomp.), were recovered.

Cevine tetra-acetate N-*oxide* (with Dr. J. S. FAWCETT). Cevine tetra-acetate (420 mg.) was treated with one mol. of perphthalic acid in an analogous manner to the diacetate (see above).

The product after two recrystallisations from aqueous methanol afforded needles of *cevine tetra-acetate* N-*oxide*, m. p. 223—226° (decomp. and softening above 215°), $[\alpha]_D$ +18° (*c*, 1·46), +20° (*c*, 1·87) in chloroform; $[\alpha]_D$ +40° (*c*, 1·86) in 90% aqueous methanol (Found: C, 57·1; H, 7·5; Ac, 24·5. $C_{35}H_{51}O_{13}N,2H_2O$ requires C, 57·6; H, 7·6; Ac, 23·6%). A solution (0·0558 g.) in aqueous methanol (90%; 3 ml.) still had a specific rotation of +40° after 3 days at room temperature.

Cevine monoacetate N-*oxide*. A suspension of cevine diacetate (300 mg.) in 30% hydrogen peroxide (1·5 ml.) was warmed on a steam-bath for 3—5 min. The resulting solution was evaporated to dryness *in vacuo* and the residue taken up in hot ethanol, and the solution treated with charcoal and concentrated, and a little water added. After 5 days crystals (130 mg.) were obtained which after one more recrystallisation from aqueous ethanol afforded *cevine monoacetate* N-*oxide*, m. p. 264—265° (decomp. above 230°), $[\alpha]_D$ −15° (*c*, 2·19 in 90% MeOH–H_2O) (Found: C, 59·1; H, 8·1; N, 2·1; Ac, 8·1. $C_{29}H_{45}O_{10}N,H_2O$ requires C, 59·5; H, 8·1; N, 2·4; Ac, 7·4%). After 3 days at room temperature a solution in 90% aqueous methanol still had $[\alpha]_D$ −15° and on concentration *in vacuo* of this solution cevine monoacetate *N*-oxide, m. p. and mixed m. p. 262—263° (decomp. above 225°), was recovered.

Mild acetylation of cevine monoacetate N-*oxide*. Cevine monoacetate *N*-oxide (65 mg.) and acetic anhydride (1 ml.) were warmed on a steam-bath for 5 min. Water was now added and the solution evaporated to dryness *in vacuo*. The product, upon recrystallisation from aqueous methanol, had m. p. 219—220° (decomp.), $[\alpha]_D$ −2° (*c*, 1·34 in 90% MeOH–H_2O) and did not depress the m. p. of an authentic sample of the diacetate *N*-oxide.

Cevine triacetate N-*oxide*. Cevine tetra-acetate (300 mg.) was treated with 30% hydrogen peroxide (1·5 ml.) in a manner analogous to the conversion of cevine diacetate into cevine monoacetate *N*-oxide (see above). The product after one crystallisation from aqueous methanol and one from aqueous ethanol gave *cevine triacetate* N-*oxide*, m. p. 230—232° (decomp., after softening at 217°), $[\alpha]_D$ +29° (*c*, 4·00 in 90% MeOH–H_2O) (Found: C, 57·2; H, 7·6; N, 2·1; Ac, 17·4. $C_{33}H_{49}O_{12}N,2H_2O$ requires C, 57·6; H, 7·6; N, 2·0; Ac, 18·8%). After four days at room temperature a solution of cevine triacetate *N*-oxide (0·0873 g.) in 90% aqueous methanol (5 ml.) still had $[\alpha]_D$ +29°.

Mild acetylation of cevine triacetate N-*oxide*. The product of reaction of cevine triacetate *N*-oxide (24 mg.) and acetic anhydride (1 ml.) was worked up by dilution with water and concentration to dryness. The residue, upon recrystallisation from aqueous methanol, did not depress the m. p. of an authentic sample of cevine tetra-acetate *N*-oxide, and had $[\alpha]_D$ +20° (*c*, 1·77 in $CHCl_3$).

Cevine tetra-acetate methiodide. Cevine tetra-acetate (300 mg.) was dissolved in anhydrous acetone (3 ml.), and methyl iodide (3 ml.) added. After 24 hr. at room temperature in a stoppered flask, the solution was evaporated to dryness *in vacuo* at room temperature. The residue was crystallised twice from water (2—3 ml.) affording *cevine tetra-acetate methiodide*, m. p. 227—227·5° (decomp.), $[\alpha]_D$ +37° (*c*, 1·75), +36° (*c*, 1·38) in 90% aqueous methanol (Found: C, 48·7; H, 7·0; N, 1·7; I, 14·2. $C_{36}H_{54}O_{12}NI,4H_2O$ requires C, 48·5; H, 7·0; N, 1·6; I, 14·2%). A solution of cevine tetra-acetate methiodide (0·0873 g.) in 90% aqueous methanol (5 ml.) had $[\alpha]_D$ +37° (zero time), +36° (9 days at room temperature). On concentration *in vacuo* and crystallisation from aqueous methanol, cevine tetra-acetate methiodide, m. p. and mixed m. p. 227—227·5° (decomp., after softening at 225°) was recovered.

Methanolysis of cevine tetra-acetate methiodide in presence of 1 *mol. of triethylamine*. Cevine tetra-acetate methiodide (0·0804 g.) was dissolved in methanol (4 ml.), and a solution (1 ml.) of triethylamine (0·125 ml. in 10 ml. of water) added. The mixture was set aside at room temperature; the variation of the specific rotation with time is given in the following table:

Time	18 hr.	24 hr.	4 days	6 days	8 days	12 days	20 days	28 days
$[\alpha]_D$	+24°	+20·5°	+14°	+9°	+7°	+4°	−1°	−3°

After 28 days the solution was evaporated to dryness *in vacuo* and the residue recrystallised from water giving cevine methiodide (Freund and Schwarz, *J. pr. Chem.*, 1917, **96**, 236; Jacobs and Craig, *J. Biol. Chem.*, 1938, **135**, 625; Barton and Eastham, *loc. cit.*), m. p. and mixed m. p. with an authentic sample, kindly supplied by Professor D. H. R. Barton, F.R.S., 247—252° (decomp.).

The author is grateful to Professor D. H. R. Barton, Dr. C. J. W. Brooks, and Dr. J. S. Fawcett for their interest in this work.

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The Surface Tension of Antimony Pentafluoride.

By D. R. Hub and P. L. Robinson.

[Reprint Order No. 5176.]

Antimony pentafluoride differs remarkably in both physical and chemical properties from arsenic pentafluoride. Its boiling point and liquid density (Ruff, Graf, Heller, Knoch, and Plato, *Ber.*, 1904, **37**, 673; 1906, **39**, 4310), (appreciable) electrical conductivity and (abnormally high) viscosity (Woolf and Greenwood, *J.*, 1950, 2200), vapour pressure and liquid density (Schair and Schurig, *Ind. Eng. Chem.*, 1951, **43**, 1624) have been measured. Vapour density measurements made here (G. J. Falconer) by a modified Dumas method gave at 180° a value of 296, suggesting a molecular weight of 592 and a molecular association corresponding to $(SbF_5)_{2\cdot7}$. Other measurements made here indicated a complexity approximating to $(SbF_5)_3$ at 150° and $(SbF_5)_2$ at 250°. Attempts were made to determine the surface tension of the liquid by measuring the differential capillary rise in a closed system (Mills and Robinson, *J.*, 1927, 1823), but the result was too low to be considered probable, owing to the high viscosity and possibly also to the angle of contact. So far as we know the surface tension of antimony pentafluoride has not been otherwise measured, and we now give values obtained between 0° and 138° with a maximum bubble pressure apparatus (Sugden, *J.*, 1922, **121**, 858; Mills and Robinson, *J.*, 1931, 1629) suitably modified to protect a hygroscopic liquid and using dried air.

T (°c)	0·5	1·0	1·75	2·3	18·9	19·6	39·8	82·6	106·3	119·5	138·4
γ (dynes cm.$^{-1}$)	51·5	47·0	50·6	48·7	45·7	44·5	39·9	31·8	28·4	26·4	23·1

The parachor derived from these surface tensions, $(P)_{\text{obs.}} = 169{\cdot}5$, is low compared with that calculated, $\Sigma(P) = 194{\cdot}5$, from Sugden's data ("The Parachor and Valency," Routledge, London, 1930, p. 181). That calculated of the basis of Walden's boiling-point rule, $P_W = 185{\cdot}8$, is closer to the theoretical value. The low figure found above conforms with the fact that liquid antimony pentafluoride is highly associated.

The Katayama plot of $\gamma/(D - d)^{2/3}$ against T is slightly curved which, again, is due to association; the slope of the best straight line through the points between 60° and 138° gives the critical temperature $T_c = 324{\cdot}6°$.

Experimental.—Preparation. Antimony trioxide, dried just below its melting point in an evacuated Pyrex glass tube, was fluorinated with a 4 : 1 mixture of fluorine and nitrogen. It was thrice fractionated with rejection on each occasion of head and tail fractions.

Measurement. The resulting liquid was distilled into the all-glass surface-tension vessel in which the jets, protected from atmospheric moisture by guard traps cooled in liquid oxygen, were sealed in position. The vessel was mounted in a bath at the required temperature, and the difference in pressure needed to produce bubbles at the respective jets was measured with a water-manometer. The surface tension was calculated by Sugden's method (*J.*, 1922, **121**, 858; 1924, **125**, 27), but as neither of his approximations can be used, owing to the low specific cohesion, a, his original method was employed which involved calculation of further values for $X/r_{\text{min.}}$, namely, 0·3640, 0·3484, 0·3351 corresponding respectively to values of $r/a = 1{\cdot}70, 1{\cdot}80, 1{\cdot}88$. The last is the highest value for which the tables of Bashforth and Adams ("An Attempt to Test the Theory of Capillary Action," Cambridge Univ. Press, 1883) can be used.

It was difficult to obtain consistent pressures at low temperatures owing to the high viscosity of the liquid, but a rapidly-tapering jet was better than one of uniform bore. Some hours were allowed at these temperatures for the attainment of thermal equilibrium in the sluggish liquid which was meanwhile gently stirred by a stream of air. The maximum bubble pressure was taken as that required to produce the first bubble after a momentary interruption of a stream of bubbles : bubbles subsequent to the first tended to merge into one another with a consequent fall in pressure. Even despite these precautions the readings for the supercooled liquid, *i.e.*, the first four above, are scattered.

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The Reduction of 4-Amino- and 4-Acetamido-salicylic Acids.

By A. A. Goldberg and R. S. Theobald.

[Reprint Order No. 5194.]

During a search for an easy route to 4-aminosalicylaldehyde one method presenting itself was sodium amalgam reduction of the easily accessible 4-aminosalicylic acid; Weil (*Ber.*, 1908, **41**, 4147) obtained a 60% yield of salicylaldehyde from salicylic acid by this reaction.

It was found, however, that treatment of 4-aminosalicylic acid with sodium amalgam in the presence of *p*-toluidine and boric acid effected reduction of the carboxyl and simultaneous hydrogenolysis of the amino-group; salicylidene-*p*-toluidine was the only product which could be isolated. Reduction of 4-acetamidosalicylic acid, on the other hand, yielded 4-acetamidosalicylaldehyde although in small yield.

Experimental.—Reduction of 4-*aminosalicylic acid.* A solution of sodium 4-aminosalicylate (20 g.) in water (650 c.c.) was stirred with sodium chloride (250 g.), finely powdered *p*-toluidine (20 g.), and boric acid (20 g.). Portionwise and alternate additions of sodium amalgam (150 g.; 4%) and boric acid (150 g.) were made during 1 hr. and the mixture stirred for a further 3 hr. This suspension was decanted from mercury, the insoluble material collected, and *p*-toluidine removed by heating it to 70° with water (1000 c.c.), cooling to 25°, and then filtering. Crystallisation of the yellow residue from alcohol (20 c.c.) gave pure salicylidene-*p*-toluidine (2·5 g.) as bright yellow needles, m. p. 92° (Found: C, 79·4; H, 6·1; N, 6·8. Calc. for $C_{14}H_{13}ON$: C, 79·7; H, 6·2; N, 6·6%). Heating the Schiff's base (2 g.) with thiosemicarbazide (2 g.) in 50% aqueous alcohol gave salicylaldehyde thiosemicarbazone (0·8 g.) which separated in almost colourless prisms, m. p. 233° (decomp.) alone and mixed with authentic material (Found: C, 48·8; H, 4·6; N, 21·3. Calc. for $C_8H_9ON_3S$: C, 49·2; H, 4·6; N, 21·5%).

Reduction of 4-*acetamidosalicylic acid.* A solution of 4-acetamidosalicylic acid (40 g.) and sodium carbonate (21·2 g.) in water (1 l.) and alcohol (500 c.c.) was stirred at room temperature with sodium chloride (450 g.), *p*-toluidine (40 g.), and boric acid (64 g.). Sodium amalgam (4%; 320 g.) and boric acid (320 g.) were added portionwise during 1 hr. and stirring continued for a further 4 hr. The mercury was separated, the aqueous-alcoholic suspension filtered, and the insoluble material freed from inorganic material by washing with hot water; crystallisation from alcohol gave 4-*acetamido*-2-*hydroxybenzylidene*-p-*toluidine* (8·6 g.) in yellow needles, m. p. 212° (Found: N, 10·5. $C_{16}H_{16}O_2N_2$ requires N, 10·4%). The Schiff's base (2 g.) was refluxed with acetic anhydride (20 c.c.) for 15 min., excess of the reagent decomposed with hot water (60 c.c.), and the cooled suspension basified with aqueous ammonia. After removal of the insoluble *p*-acetotoluidide, the filtrate was acidified with acetic acid, and the precipitate of 4-*acetamidosalicylaldehyde* (1 g.; m. p. 182°) collected; a sample crystallised from dilute alcohol in fine colourless needles, m. p. 184° (Found: N, 7·9. $C_9H_9O_3N$ requires N, 7·8%). The *oxime* separated from dilute alcohol in small colourless needles, m. p. 226° (decomp.) (Found: N, 14·6. $C_9H_{10}O_3N_2$ requires N, 14·4%).

A solution of the foregoing azomethine (2 g.) in boiling alcohol (100 c.c.) was mixed with a solution of thiosemicarbazide (2 g.) in water (100 c.c.); 4-*acetamidosalicylaldehyde thiosemicarbazone* (1·5 g.) rapidly separated in small orange leaflets, m. p. 258—260° (decomp.) alone and on admixture with material obtained by the method of Goldberg and Walker (*J.*, 1954, 2540) (Found: N, 22·4; S, 12·8. $C_{10}H_{12}O_2N_4S$ requires N, 22·2; S, 12·7%). Hydrolysis of this (1 g.) with 2N-sodium hydroxide (50 c.c.) on the water-bath for 1 hr., followed by acidification with acetic acid, gave 4-*aminosalicylaldehyde thiosemicarbazone*; this crystallised from aqueous alcohol in pale orange needles, m. p. 218—220° (Found: N, 26·6; S, 15·1. $C_8H_{10}ON_4S$ requires N, 26·7; S, 15·3%).

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Methylation of Indoles.

By K. T. Potts and J. E. Saxton.

[Reprint Order No. 5227.]

1-Methylindoles have been of interest in our studies related to alkaloid chemistry and were not readily available. 1-Methylindole itself can be prepared from the *as*-methylphenylhydrazone of pyruvic acid (Fischer and Hess, *Ber.*, 1884, **17**, 561) or by the action of sodamide or sodium hydride followed by methyl iodide on indole at elevated temperatures (Weissgerber, *Ber.*, 1910, **43**, 3522; Gray, *J. Amer. Chem. Soc.*, 1953, **75**, 1253). A more recent method (Shirley and Roussel, *ibid.*, p. 375) involves the treatment of indole with methyl toluene-*p*-sulphonate and anhydrous sodium carbonate in boiling xylene. The method now reported for the methylation of indole derivatives has been used in this laboratory for a number of years (see, *e.g.*, Robinson and Stephen, *Nature*, 1948, **162**, 177) and has given very satisfactory results. Originally, the *N*-sodio-derivative was prepared in liquid ammonia and then allowed to react with methyl iodide after removal of the solvent. Harman and harmine have been converted into *ind-N*-methylharman and *ind-N*-methylharmine respectively (Anet, Chakravarti, Robinson, and Schlitter, *J.*, 1954, 1242) in this manner. A logical extension of this method involved carrying out the whole reaction in liquid ammonia. The product was then isolated by means of ether after the ammonia had been allowed to evaporate. Indole, 2-methylindole, ethyl α-3-indolyl*iso*butyrate, and 3-2′-aminoethylindole (tryptamine) have been methylated in this fashion. It is interesting that the reaction can be employed in the presence of a basic amino-group; a similar type of methylation has been found to occur with phenylhydrazines (Audrieth, Weisiger, and Carter, *J. Org. Chem.*, 1941, **6**, 417).

Experimental.—1-*Methylindole.* Sodium (2·5 g.) was added in small pieces to liquid ammonia (200 c.c.) containing ferric nitrate (0·1 g.). When dissolution was complete, indole (11·7 g.) in ether (20 c.c.) was added to the stirred mixture. After 10 min., methyl iodide (16 g.) was added dropwise, and stirring was continued for a further 15 min. The ammonia was allowed to evaporate, water (50 c.c.) and ether (50 c.c.) were added, the ethereal layer was separated and dried, and the solvent removed. The crude oil ($n_D^{18\cdot5}$ 1·6078) was purified by distillation, and 1-methylindole obtained as a colourless oil, b. p. 133°/26 mm., $n_D^{18\cdot5}$ 1·6082. The yield was almost quantitative. Snyder and Eliel (*J. Amer. Chem. Soc.*, 1948, **70**, 1703) report b. p. 134—135°/31 mm. and n_D^{20} 1·6062.

The picrate was obtained from benzene as red prisms, m. p. 149—150°, alone and when mixed with a specimen prepared by the method of Fischer and Hess (*loc. cit.*).

1 : 2-*Dimethylindole.* 2-Methylindole was alkylated as above, and the product obtained as colourless plates (90%) from light petroleum (b. p. 40—60°), m. p. 56°, alone and when mixed with an authentic specimen prepared from acetone methylphenylhydrazone. The picrate was obtained from benzene as red needles, m. p. 125°, alone and when mixed with authentic 1 : 2-dimethylindole picrate (Marion and Oldfield, *Canad. J. Res.*, 1947, **25**, *B*, 1, also report m. p. 125°).

Ethyl α-(1-*methyl*-3-*indolyl*)iso*butyrate.* Ethyl α-3-indolyl*iso*butyrate (3·5 g.; Erdtman and Jonsson, *Acta Chem. Scand.*, 1954, **8**, 119) in ether (25 c.c.) was added to a stirred solution of sodamide (from 0·4 g. of sodium) in liquid ammonia (100 c.c.). Methyl iodide (2·5 g.) was then added dropwise, and the stirring continued for 30 min. The ammonia was allowed to evaporate, and the residue treated with ether (75 c.c.) and water (50 c.c.). The ethereal layer was separated, dried, and evaporated, and the residue crystallized from light petroleum (b. p. 60—80°). *Ethyl* α-(1-*methyl*-3-*indolyl*)iso*butyrate* (3·5 g.) was obtained as colourless needles, m. p. 83° (Found: C, 73·5; H, 7·55; N, 5·7. $C_{15}H_{19}O_2N$ requires C, 73·5; H, 7·75; N, 5·7%). In contrast to the starting material, this substance shows no absorption at 2·95 μ, indicating the absence of an >NH group in the molecule.

3-2′-*Aminoethyl*-1-*methylindole.* Finely powdered tryptamine (4·1 g.) was added to a solution of sodamide in liquid ammonia (from 0·6 g. of sodium in *ca.* 100 c.c. of ammonia), with efficient stirring throughout the reaction. After 5 min., methyl iodide (4·0 g.) was added carefully and the solution kept at room temperature until all the ammonia had evaporated. Water (20 c.c.) was added to the residue, the mixture extracted with ether (5 × 20 c.c.), and the ethereal layer washed with water, dried, and evaporated. Distillation of the residue gave a colourless, mobile oil (2·7 g., 60%) with a typical indole-amine odour, b. p. 112—113°/0·2 mm., n_D^{21} 1·6050 (Snyder and Eliel, *loc. cit.*, report b. p. *ca.* 108—110°/0·1 mm.) (Found: C, 75·5; H, 7·9. Calc. for $C_{11}H_{14}N_2$: C, 75·8; H, 8·1%).

The phthalimido-derivative separated as cream needles, m. p. 177°, from methanol (Manske, *Canad. J. Res.*, 1931, **5**, 597, reports m. p. 177·5°). No colour was obtained with Ehrlich's reagent even on prolonged heating.

The *picrate* separated from methanol as scarlet, rectangular plates, which lost solvent above 100° to give the yellow form, m. p. 178—179° (Found: C, 49·8; H, 4·6; N, 15·9. $C_{17}H_{17}O_7N_5,CH_3\cdot OH$ requires C, 49·7; H, 4·8; N, 16·1%). Snyder and Eliel (*loc. cit.*) report m. p. 178—179°. The solvated derivative shows intense absorption at 2·85 μ, showing the presence of an OH group; a specimen dried at 100° for 6 hr. showed no absorption at this wavelength. Preparation of the picrate in acetone solution and recrystallization from the same solvent gave *1-methyl-*N-iso*propylidenetryptamine picrate*, yellow-orange needles, m. p. 177—179°, mixed m. p. with 1-methyltryptamine picrate 160—170° (Found: C, 54·2; H, 4·8; N, 15·4. $C_{14}H_{18}N_2,C_6H_3O_7N_3$ requires C, 54·2; H, 4·8; N, 15·8%).

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The Preparation and Freezing Point of Pure Naphthalene.

By E. F. G. HERINGTON, A. B. DENSHAM, and P. J. MALDEN.

[Reprint Order No. 5267.]

MAIR and STREIFF (*J. Res. Nat. Bur. Stand.*, 1940, **24**, 395) have described the preparation, by crystallization from ethyl alcohol and by distillation, of a sample of naphthalene of purity 99·94 ± 0·04 moles % and freezing point 80·24°. These workers estimated the freezing point of the 100% pure material as 80·27° ± 0·02°. Mathieu (*Mém. Acad. roy. Belg.*, 1953, **28**, No. 2) prepared a sample of naphthalene of $99{\cdot}99_1$ ± 0·002 moles % purity by fractional crystallization from alcohol and acetone, followed by simple distillation and recrystallization from the liquid melt. The freezing points of the sample and of the 100% pure material were recorded as 80·279° and 80·284° ± 0·003° respectively.

The present note describes the preparation of a sample of naphthalene of low sulphur content and 99·978 ± 0·10 moles % purity. The freezing point of the actual sample and of the 100% pure material were shown to be 80·287° ± 0·002° and 80·300° ± 0·006° respectively. This figure for the freezing point of the 100% pure material is in agreement with the values given above when consideration is given to the standard deviations of the various measurements. However, since the freezing point of our actual specimen (*viz.*, 80·287° ± 0·002°) is higher than that ascribed to the 100% pure material by Mathieu (80·284° ± 0·003°) the latter is probably a little low. The best value for the freezing point of 100% pure naphthalene, *viz.*, 80·287° ± 0·003° is obtained by combining Mathieu's and our value into a grand mean and weighting the individual measurements by the squares of the reciprocals of their standard deviations in the usual manner.

Experimental.—Preparation. Thionaphthen, first isolated from a coal tar fraction by reaction with sodamide (Weissberger and Krüber, *Ber.*, 1920, **53**, 1551), is the main impurity in commercially pure crystal naphthalene (Armstrong, Densham, and Gough, *J.*, 1950, 3359). Preliminary experiments showed that recrystallization and simple distillation did not remove this sulphur compound very effectively: for example, crystal naphthalene, after two recrystallizations from methanol and fractionation, still had a sulphur content of 0·08% by weight. The following procedure was therefore adopted.

Commercial crystal naphthalene was kept overnight at 140° under a stream of nitrogen in order to remove water, and the product was then stirred at 140° for a further 24 hr. with 5% of sodamide powder. The naphthalene was decanted and was then stirred at 180° with 1% of sodamide for a further 24 hr. The melt was filtered through glass wool and was fractionated in an adiabatic column, packed with glass helices, of 10 theoretical-plate efficiency. The middle fraction was twice recrystallized from redistilled methanol and redistilled. The distillate after solidification was broken up in an agate mortar. The sulphur content, determined by Grote-Krekeler's quartz-tube method (*Angew. Chem.*, 1933, **46**, 106), was less than 0·002% by weight.

Purity and freezing-point determinations. The purity and the f. p. of the sample were measured by means of the apparatus described by Herington and Handley (*J.*, 1950, 199). Further details of this technique and of the calculations have been given recently (Biddiscombe, Coulson, Handley, and Herington, *J.*, 1954, 1957). This method of analysis of the f. p. curves necessitates the addition of known amounts of impurity and for this purpose anthracene was chosen because Mathews (*J. Amer. Chem. Soc.*, 1917, **39**, 1125) has established that anthracene produces the theoretical cryoscopic depression when dissolved in naphthalene. The anthracene employed in the present experiments was a synthetic specimen of high purity.

We express our thanks to Mr. R. Handley and Mr. D. Harrop for assistance with the freezing-point measurements. We also thank the Director of the Chemical Research Laboratory and the North Thames Gas Board for permission to publish this paper.

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Methyl 3β-*Iodochol*-5-*enate.*

By W. KLYNE.

[Reprint Order No. 5278.]

METHYL 3β-IODOCHOL-5-ENATE has been prepared from the corresponding 3β-hydroxy-ester by the method used by Beynon, Heilbron, and Spring (*J.*, 1936, 737) in the cholesterol series. The toluene-*p*-sulphonate of methyl 3β-hydroxychol-5-enate was treated with potassium acetate in methanol to give the 6β-methoxy-3 : 5-*cyclo*-compound, which with hydriodic acid in acetic acid yielded methyl 3β-iodochol-5-enate. The β-configuration of the iodine atom is allotted by analogy with that for cholesteryl iodide (Carlisle and Crowfoot, *Proc. Roy. Soc.*, 1945, *A*, **184**, 64). Molecular-rotation differences in the cholenic ester series show satisfactory agreement with those in the cholesterol series (cf. Barton and Brooks, *J.*, 1949, 2596).

Experimental.—M. p.'s are corrected. Optical rotations were determined in $CHCl_3$ at 20—25° (*c*, 1—2%). The " usual working up " followed Barton and Brooks, *J.*, 1951, 257, except that ethereal solutions of products were dried with Na_2SO_4 before distillation. Light petroleum was the fraction of b. p. 60—80°.

Methyl 3β-*toluene*-p-*sulphonyloxychol*-5-*enate.* This *ester* was obtained by treating the hydroxy-ester (m. p. 141—143°) with toluene-*p*-sulphonyl chloride in pyridine, and crystallised from light petroleum, containing a little ethyl acetate or chloroform, as rosettes of stout prisms, m. p. 121—123°, $[\alpha]_D$ −40°, $[M]_D$ −215° (Found: C, 70·7; H, 8·5; S, 6·3. $C_{32}H_{46}O_5S$ requires C, 70·8; H, 8·5; S, 5·9%).

Methyl 6β-*methoxy*-3 : 5-cyclo*cholanate.* The above ester (3·8 g.) and anhydrous potassium acetate (5·0 g.) were refluxed in methanol (200 ml.) for 2 hr. The usual working up yielded a gum (2·6 g.), which crystallised on long standing. The cyclo-*compound* after two recrystallisations from methanol had m. p. 62—65° (decomp.), $[\alpha]_D$ +43°, $[M]_D$ +173° (Found: C, 77·3; H, 10·2. $C_{26}H_{42}O_3$ requires C, 77·6; H, 10·5%).

Methyl 3β-*iodochol*-5-*enate.* The *cyclo*-compound (1·27 g.) was allowed to stand overnight with glacial acetic acid (100 ml.) and aqueous hydriodic acid (*d* 1·7; 12 ml.). Addition of aqueous sodium sulphite (100 ml.; 10%) precipitated the crude product which was chromatographed on alumina; light petroleum–benzene (4 : 1 v/v) eluted a white solid which crystallised from light petroleum. The *iodo*-compound formed large prisms (420 mg.), m. p. 110—112° (the supercooled liquid showed a striking bluish-violet or bluish-green fluorescence), $[\alpha]_D$ −15°, $[M]_D$ −75° (Found: C, 60·3; H, 8·1; I, 25·1. $C_{25}H_{39}O_2I$ requires C, 60·2; H, 7·9; I, 25·5%).

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The Structure of the Oxazoline Derivatives of Glucose and Galactose.

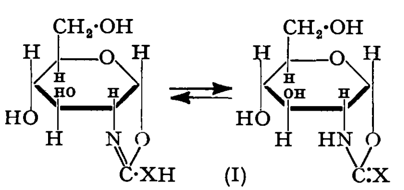
By J. C. P. SCHWARZ.

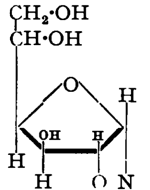
[Reprint Order No. 5280.]

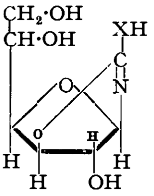
ZEMPLÉN, GERECS, and RADOS (*Ber.*, 1936, **69**, 748) obtained a compound from the reaction of D-glucose with potassium thiocyanate, to which they gave the name " μ-thiolglucoxazoline " and the structure (I; X = S). Oxidation with hydrogen peroxide in alkaline solution converted this compound into μ-hydroxyglucoxazoline, which was given the structure (I; X = O). Similar structures have also been suggested for the compounds obtained by the action of thiocyanic acid on D-fructose (Zemplén, Gerecs, and Illés, *Ber.*, 1938, **71**, 590), D-galactose, D-xylose, and L-arabinose (Bromund and Herbst, *J. Org. Chem.*, 1945, **10**, 267).

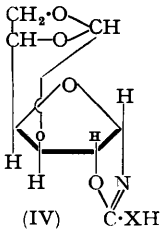
More recently Edward and Martlew (*Chem. and Ind.*, 1952, 1034) hydrolysed μ-thiolglucoxazoline with concentrated hydrochloric acid. Using paper chromatography they were able to demonstrate the presence of 1-aminoglucose and diglucosylamine in the products, but no glucosamine could be detected. This suggests that the nitrogen atom in the above oxazolines is attached to $C_{(1)}$ and not to $C_{(2)}$.

μ-Hydroxyglucoxazoline has now been oxidised with sodium periodate. It consumed 1 mol. of periodate with production of 0·94 mol. of formaldehyde and no formic acid. μ-Thiolglucoxazoline gave 0·7 mol. of formaldehyde. These results are consistent only with the furanose structures (II and III; X = S or O) and their tautomers. μ-Thiolglucoxazoline readily gave an orthoformate when shaken with ethyl orthoformate in methanol in the presence of a little hydrogen chloride. This derivative has the structure (IV; X = S) as the formation of an orthoformate from (III; X = S) is sterically impossible. The glucoxazolines therefore have the structure (II; X = S or O). Oxidation with hydrogen peroxide converted the orthoformate (IV; X = S) into its oxygen analogue (IV; X = O).


(I)


(II)

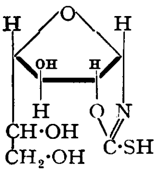

(III)

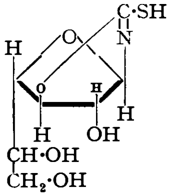

(IV)

μ-Thiolgalactoxazoline (Bromund and Herbst, *loc. cit.*) also gave formaldehyde (0·6 mol.) on oxidation with sodium periodate. By analogy with the glucose compounds, the structure (V) seems more probable than (VI). An attempt to verify this by methylation was abandoned, as the compound was sensitive to alkali and practically insoluble in non-polar solvents.

The reaction of μ-thiolglucoxazoline and μ-thiolgalactoxazoline with sodium periodate is complicated by the oxidation of the sulphur atom. In both cases iodine was liberated and the formation of sulphate could be demonstrated. During the oxidation of the μ-thiolglucoxazoline the solution became cloudy (sulphur?); this also occurred at higher concentrations in the oxidation of μ-thiolgalactoxazoline. The production of iodine is probably due to the reduction of iodate by the thioloxazolines. Titration with sodium thiosulphate after the addition of potassium iodide and sulphuric acid showed that about 9·6 equivs. of oxidising agent (periodate and iodate) had been consumed by the thioloxazolines. Theoretically 10 equivs. of oxidant are required to oxidise the thioloxazolines to the hydroxyoxazolines and sulphuric acid, and to bring about one glycol fission.

(V)





(VI)

Experimental.—Periodate oxidations were carried out in the dark with unbuffered sodium periodate (0·05—0·2M). Formaldehyde was estimated by Bell's method (*J.*, 1948, 994). However no phosphate buffer was added and, with the thioloxazolines, a slightly larger quantity of periodate was used.

μ-Hydroxyglucoxazoline. Periodate consumption (arsenite method): 0·99 (5 min.), 0·99 mol. (75 min.). Formaldehyde: 0·94 mol. (25 min.).

μ-Thiolglucoxazoline. Oxidant consumption (periodate and iodate): 9·6 equivs. (10 and 50 min.). Formaldehyde: 0·7 mol. (25 min.).

μ-Thiolgalactoxazoline. Oxidant consumption: 9·6 (15 min.), 9·8 equivs. (40 min.). Formaldehyde: 0·6 mol. (30 min.).

μ-Thiolglucoxazoline orthoformate. Finely powdered μ-thiolglucoxazoline (2 g.) was shaken for 2 hr. with ethyl orthoformate (2·6 c.c.), dry methanol (2 c.c.), and 20% methanolic hydrogen chloride (0·13 c.c.). After filtration the solid product was washed, first, with a little methanol, then with much water. The *orthoformate* (1·9 g.) crystallised from much ethyl acetate as colourless needles, m. p. 255° (decomp.), $[\alpha]_D^{21}$ +20° (*c*, 1·96 in 0·1N-NaOH) (Found: C, 41·9; H, 3·3; S, 13·7. $C_8H_9O_5SN$ requires C, 41·6; H, 3·9; S, 13·9%), and dissolved in cold dilute aqueous sodium hydroxide whence it was recovered on acidification.

μ-Hydroxyglucoxazoline orthoformate. Hydrogen peroxide (100-vol.; 30 c.c.) was added in small portions to μ-thiolglucoxazoline orthoformate (7·3 g.) in 1·05N-sodium hydroxide (70 c.c.) at 25—30° (cooling). After 30 min., the mixture was cooled in the refrigerator and the crude product [m. p. 215—220° (decomp.); 5·7 g.] was filtered off. The *orthoformate* crystallised from ethanol containing a little water as needles, m. p. 220—225° (decomp.), $[\alpha]_D^{19}$ +32° (*c*, 0·396 in H_2O) (Found: C, 44·6; H, 4·2. $C_8H_9O_6N$ requires C, 44·7; H, 4·2%).

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DEPARTMENT OF CHEMISTRY, UNIVERSITY OF EDINBURGH. [*Received, April 5th, 1954.*]

The Dielectric Constant of Trifluoroacetic Anhydride and Related Compounds.

By J. M. TEDDER.

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THE dielectric constant of trifluoroacetic anhydride is of interest, since it has been suggested that certain reactions occurring in this medium are of an ionic character (Bourne, Randles, Tatlow, and Tedder, *Nature*, 1951, **168**, 942; Bourne, Randles, Stacey, Tatlow, and Tedder, *J. Amer. Chem. Soc.*, in the press). The value obtained (ε = 2·7 at 25°) is considerably lower than that for trifluoroacetic acid (ε = 8·2 at 25°), in sharp contrast to their hydrocarbon analogues where the dielectric constant of acetic anhydride (ε = 21 at 25°) is very much higher than that of acetic acid (ε = 6·3 at 25°). The dielectric constants of dichloro- and trichloro-acetic anhydrides have also been measured for comparison and the values obtained for the complete series are tabulated below.

	Anhydride		Acid	
	Conductivity ($\kappa \times 10^7$, mhos)	Dielectric constant ε	Conductivity ($\kappa \times 10^7$, mhos)	Dielectric constant ε
CF_3·CO–	<0·001 (25°) [a]	2·7 (25°) [a]	3·5 (25°) [a]	8·2 (25°) [a]
CCl_3·CO–	0·002 (25°) [a]	5·0 (25°) [a]	0·06 (60°) [c]	4·5 (60°) [d]
$CHCl_2$·CO–	0·4 (25°) [a] *	15·8 (25°) [a] *	—	7·8 (60°) [d]
CH_2Cl·CO–	—	—	14 (60°) [c]	20 (60°) [d]
CH_3·CO–	3·4 (25°) [a] *	21 (25°) [a] *	0·06 (25°) [e]	6·2 (30°) [b]

* These readings of high dielectric constant and appreciable conductivity should be regarded as approximations rather than precise values.

[a] Present investigation. [b] Smyth and Rogers, *J. Amer. Chem. Soc.*, 1930, **52**, 1824. [c] Kendall and Gross, *ibid.*, 1921, **43**, 1426. [d] Walden, *Z. physikal. Chem.*, 1910, **70**, 569. [e] Kolthoff and Willman, *J. Amer. Chem. Soc.*, 1934, **56**, 1007.

There are clearly too many factors involved to permit these values to be analysed. The value obtained for trifluoroacetic acid, ε = 8·2, is in good agreement with that reported by Dannhauser and Cole (*J. Amer. Chem. Soc.*, 1952, **74**, 6105) and confirms their value rather than the earlier one of Simons and Lorentzen (*ibid.*, 1950, **72**, 1426). An attempt was also made to measure the dielectric constant of mixtures of acetic anhydride and trifluoroacetic anhydride. Previous work (Randles, Tatlow, and Tedder, *J.*, 1954, 436) has shown that a conductivity maximum occurs for this system when the mole fraction of trifluoroacetic anhydride is about 0·25. In the present investigation it was found that the equilibrium between the two anhydrides is set up slowly, and apparently a chemical reaction (possibly the attack of acetic anhydride by CH_3·CO^+) also occurs (cf. Randles, Tatlow, and Tedder, *loc. cit.*). These difficulties, coupled with relatively high conductivities (no reasonable balance could be obtained for conductivities greater than 2×10^{-6} mhos with the bridge circuit used), made precise readings impossible. It appeared, however, that there is probably a dielectric-constant maximum as well as conductivity maximum for this system.

Experimental.—The cell and capacitance bridge. The cell, a simplified model of that described by Smyth and Morgan (*J. Amer. Chem. Soc.*, 1928, **50**, 1547), had been designed and previously used by Verhoek and Smith (unpublished work). Capacitance measurements were made with a General Radio Company Type 716-C Capacitance Bridge (substitution method) and a Type 539-B variable condenser as balancing capacitor, and an oscillograph was used as detector. The bridge was most sensitive at 10^5 cycles and the readings reported were made at this frequency. The cell was immersed in an oil-bath maintained at approx. 25°; very rigid temperature control was not attempted. The cell was standardized with carefully redistilled C.P. benzene which was assumed to have a dielectric constant of 2·274 at 25°.

Materials. Trifluoroacetic acid and trifluoroacetic anhydride were prepared as previously described (Randles, Tatlow, and Tedder, *loc. cit.*). Commercial acetic anhydride (Eastman Kodak 99—100%) was purified by fractionation and the centre fraction, b. p. 137—137·5°, was used. Trichloro- and dichloro-acetic anhydride were prepared by distilling the commercial acids over phosphoric oxide, and the crude anhydrides so obtained were then redistilled over fresh phosphoric oxide. Trichloroacetic anhydride had b. p. 220—222° and dichloroacetic anhydride b. p. 210° (the latter compound decomposed slightly at the b. p.). The distillates were tested for phosphorus but none could be detected.

Mixtures of acetic anhydride and trifluoroacetic anhydride. Redistilled acetic anhydride was placed in a receiver, into which trifluoroacetic anhydride was distilled directly. Two mixtures were studied; the first, with the mole fraction of trifluoroacetic anhydride 0·82, gave reasonably constant readings over a period of 2 hr. ($\varepsilon_{23} = 4{\cdot}4$; $\kappa_{23} \approx 1 \times 10^{-8}$ mho). The second mixture with the mole fraction of trifluoroacetic anhydride 0·26, gave values for the dielectric constant and conductivity which increased with time. When the mixture was first added to the cell the values obtained were $\varepsilon_{25} \approx 20$; $\kappa_{25} \approx 6{\cdot}2 \times 10^{-7}$ mho, but after 2 hr. the dielectric constant had risen somewhat ($\varepsilon_{25} \approx 29$) and the conductivity had greatly increased ($\kappa_{25} \approx 1{\cdot}3 \times 10^{-6}$ mho). After 24 hr. the conductivity had risen to such an extent that it was no longer possible to balance the bridge, and some chemical process had taken place causing the mixture to darken.

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The Cryoscopic Behaviour of Non-electrolytes in Sulphuric Acid.

By P. A. H. WYATT.

[Reprint Order No. 5284.]

THE author recently (*J.*, 1953, 1175) drew attention to one source of complication in cryoscopic studies on dissociating solvents, showing that the influence of dissociation heat effects upon the cryoscopic constant (k_f) could be large in the case of a solvent of appreciable dissociation such as nitric acid. An attempt was also made to invoke a thermal effect to explain the behaviour of nitro-compounds in sulphuric acid, but further consideration of Kunzler and Giauque's data (*J. Amer. Chem. Soc.*, 1952, **74**, 3472) shows this explanation to be unlikely. In fact, their Fig. 2 indicates that sulphuric acid is a normal dissociating solvent, with normal partial heat content values corresponding to a heat of dissociation of *ca.* 8 kcal. per mole of H_2O involved in the dissociation reaction. Whatever the form of dissociation, it follows that k_f for sulphuric acid will only vary from 6·12 deg. mole^{-1} kg. in the second place of decimals.

The object of the present Note is to draw attention to another source of complication which has been overlooked in this connexion, namely, the phenomenon of "salting-out." Although well investigated in aqueous systems (see Long and McDevit, *Chem. Reviews*, 1952, **51**, 119), this effect has been somewhat neglected for other solvents. The following observations combine to make a strong case for its importance in the solvent sulphuric acid.

(1) The solute 2 : 4 : 6-trinitrotoluene gives a greater depression of freezing point in

sulphuric acid containing a little water than would be expected for a non-electrolyte from $k_f = 6{\cdot}12$ (Gillespie, *J.*, 1950, 2544; Wyatt, *loc. cit.*).

(2) Spectrophotometric evidence shows that this nitro-compound is un-ionized in 100% sulphuric acid (Brand, Horning, and Thornley, *J.*, 1952, 1374).

(3) The addition of water reduces the solubility of polynitro-compounds in concentrated sulphuric acid.

(4) For water as solvent, " the depression of the freezing point produced by a salt and a non-electrolyte together is greater than the sum of the depressions produced by each singly " (Butler, " Chemical Thermodynamics," Macmillan, London, 4th Ed., 1946, p. 465).

(5) The high dielectric constant of sulphuric acid may reasonably be expected to lead to important local distribution effects amongst solutes of lower polarity.

(6) Whether salt effects are to be related to molar fractions or to volume concentrations, similar effects to those in water might be expected to occur in sulphuric acid at considerably lower molalities, because of the larger molecular weight and density of the solvent.

(7) Other polynitro-compounds in sulphuric acid behave cryoscopically in the same way as trinitrotoluene, giving molal depressions $>6{\cdot}12$ in the presence of a little water and $<6{\cdot}12$ in the presence of excess of sulphuric anhydride *or of potassium hydrogen sulphate* (Brayford and Wyatt, to be published). The latter observation is important since (i) it is inconsistent with Gillespie's weak-base hypothesis, and (ii) it suggests the possibility that in this solvent salts having activity coefficients less than 1 (H_3O,HSO_4) may salt out nitro-compounds (analogous to the common behaviour of salts in water), whilst salts with activity coefficients greater than 1 ($KHSO_4$) may salt them in (at least for small concentrations of non-electrolyte). Experience with water as solvent does not suggest that all non-electrolytes will behave in the same way, and the behaviour of sulphuryl chloride and chlorosulphonic acid in sulphuric acid (Gillespie, Hughes, and Ingold, *J.*, 1950, 2473) compared with that of the nitro-compounds, may illustrate the variability to be found in this solvent.

It follows from this argument that the design of the standard cryoscopic experiments with sulphuric acid, in which bisulphates are added to suppress solvent dissociation, is not well suited to deciding whether a given solute is a non-electrolyte or not, since the conditions employed are such as to invite complications from salting-out and salting-in. (This type of problem is better solved unambiguously by the spectrophotometric method.) If this assessment of the importance of variations in the activity coefficients of non-electrolytes is correct, it will be of interest in the application of Brønsted's theory of kinetic activity factors to reactions such as nitration and sulphonation in concentrated sulphuric acid.

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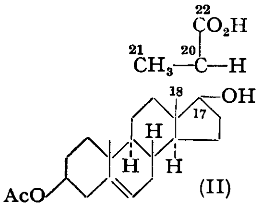
The Steroid Series. Part III. Alteration to Nomenclature.

By D. H. HEY, JOHN HONEYMAN, and W. J. PEAL.

[Reprint Order No. 5286.]

THE names of a number of compounds in our paper " The Steroid Series, Part III " (*J.*, 1954, 185) are not in accordance with the accepted rule for naming steroid acids and their derivatives. For example, the compound illustrated, and identified as (II) in our original paper, was incorrectly named as a derivative of pregnan-20-oic acid. The nomenclature of these compounds should be based on their relationship to bisnorcholanic acid. In this way, (II) is 3β-acetoxy-17β-hydroxy-20β-bisnorchol-5-enic acid. The adoption of this method of nomenclature necessitates the following revised names :



(II)

(*a*) 3-acetoxy-17-hydroxy-20(α or β)-bisnorchol-5-enic acids and esters for 3-acetoxy-17-hydroxy-20(α or β)-pregn-5-en-20-oic acids and esters;

(*b*) 3-acetoxy-20(α or β)-bisnorchola-5 : 16-dienic acids and esters for 3-acetoxy-20(α or β)-pregna-5 : 16-dien-20-oic acids and esters;

(*c*) 3β-acetoxybisnorchola-5 : 17(20)-dienic acid for 3β-acetoxypregna-5 : 17(20)-dien-20-oic acid;

(*d*) 20β-bisnorchola-5 : 16-diene-3β : 22-diol diacetate for 20β-pregna-5 : 16-diene-3β : 22-diol diacetate; and

(*e*) 20β-bisnorchol-5-ene-3β : 17β : 22-triol 3 : 22-diacetate for 20β-pregn-5-ene-3β : 17β : 22-triol 3 : 22-diacetate.

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Synthetic Œstrogens.

By J. GRUNDY.

[Reprint Order No. 5325.]

SINCE work cannot be continued, the preliminary chemical results of an attempt to modify the Schueler hypothesis of œstrogenic activity (*Science*, 1946, **103**, 221) are now reported.

The series of compounds (I)—(VI) was synthesised; these contain two functional groups, at various spacings, capable of reacting *in vivo* with amino-groups. The alkoxycarbonylamino-group in (I)—(IV) was included on the basis of a suggestion in connection with cytotoxic action (Rose, Hendrey, and Walpole, *Nature*, 1950, **165**, 993); compounds (V) and (VI) contain the related alkoxycarbonyloxy-group. Biological tests have not been carried out.

(I) *p*-$MeO_2C{\cdot}NH{\cdot}C_6H_4{\cdot}NH{\cdot}CO_2Me$

(II) *p*-$EtO_2C{\cdot}NH{\cdot}C_6H_4{\cdot}NH{\cdot}CO_2Et$

(III) *p*-$EtO_2C{\cdot}NH{\cdot}C_6H_4{\cdot}O{\cdot}CH_2{\cdot}CO_2H$

p-$MeO_2C{\cdot}NH{\cdot}C_6H_4{\cdot}O{\cdot}CH_2{\cdot}CO_2H$ (IV)

p-$MeO_2C{\cdot}O{\cdot}C_6H_4{\cdot}O{\cdot}CO_2Me$ (V)

p-$EtO_2C{\cdot}O{\cdot}C_6H_4{\cdot}O{\cdot}CO_2Et$ (VI)

p-Nitrophenoxyacetic acid has been prepared in 50% yield by the sodium chloroacetate method (Minton and Stephen, *J.*, 1922, **121**, 1591). It can, however, be obtained in 96% yield by the action of ethyl chloroacetate on sodium *p*-nitrophenoxide in triethylene glycol at 180—200°. The nitro-acid is most satisfactorily reduced by ferrous sulphate–ammonia (Jacobs and Heidelberger, *J. Amer. Chem. Soc.*, 1917, **39**, 1435).

Experimental.—1 : 4-*Dimethoxy- and* 1 : 4-*diethoxy-carbonyloxybenzene*. These were produced by the action of the alkyl chloroformate (0·06 mole) on quinol (0·02 mole) in 20% sodium hydroxide. The products were recrystallised from alcohol. The dimethoxy-compound formed plates (0·019 mole), m. p. 113—114° (Found : C, 54·1; H, 4·6. Calc. for $C_{10}H_{10}O_6$: C, 53·2; H, 4·4%); the diethoxy-compound white needles (0·019 mole), m. p. 100—101° (Found : C, 56·8; H, 5·4. Calc. for $C_{12}H_{14}O_6$: C, 56·7; H, 5·5%).

1 : 4-*Dimethoxy- and* 1 : 4-*diethoxy-carbonylaminobenzene*. Acylation of *p*-phenylenediamine (0·02 mole) in acetic acid–sodium acetate solution with the alkyl chloroformate (0·06 mole) gave the *dimethoxy*-compound as white needles (0·018 mole), m. p. 210—211° (Found : N, 12·4. $C_{10}H_{12}O_4N_2$ requires N, 12·5%), and the diethoxy-compound (also white needles) (0·019 mole), m. p. 195—196° (Found : N, 11·1. Calc. for $C_{12}H_{16}O_4N_2$: N, 11·1%).

p-*Aminophenoxyacetic acid*. Sodium *p*-nitrophenoxide (32·2 g.) in triethylene glycol (40 ml.) was heated to 120°, ethyl chloroacetate (20·9 ml.) was added, and the temperature was raised to 180—200°. Reaction was complete after 1 hr., and the cooled mixture was then poured into excess of 10% sulphuric acid. The mixture was refluxed until homogeneous, and on cooling, pale yellow plates (37·8 g.) of *p*-nitrophenoxyacetic acid, m. p. 187—188° (Found : N, 7·1. Calc. for $C_8H_7O_5$,N : N, 7·7%), were obtained. This acid (20 g.) when reduced with ferrous sulphate–ammonia gave white needles (10 g.), m. p. 250° (decomp.), of the amino-acid (Found : N, 8·8. Calc. for $C_8H_9O_3N$: N, 8·9%).

p-*Methoxy- and* p-*ethoxy-carbonylaminophenoxyacetic acid*. To *p*-aminophenoxyacetic acid (3 g.) in 10% sodium hydrogen carbonate solution (30 ml.) was added in portions, with stirring, a slight excess of the alkyl chloroformate. The cold mixture was acidified with dilute hydrochloric acid, and the coloured solids obtained were treated with charcoal in hot water. The p-*methoxy*-compound formed white plates (4 g.), m. p. 164—165° (Found : C, 53·5; H, 5·1; N, 6·7. $C_{10}H_{11}O_5N$ requires C, 53·3; H, 4·9; N, 6·2%); the p-*ethoxy*-compound white needles (4 g.), m. p. 144—145° (Found : C, 55·4; H, 5·5; N, 6·25. $C_{11}H_{13}O_5N$ requires C, 55·2; H, 5·4; N, 5·9%).

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