# NOTES.

## 720. *The Pyrolysis of* N-*Methylaniline, and the* N–H *Bond Strength in Aniline.*

By G. L. Esteban, J. A. Kerr, and A. F. Trotman-Dickenson.

Results of the pyrolysis of *N*-methylaniline by the aniline carrier technique are recorded in the Table. First-order rate constants for the decomposition were derived from the yields of methane in accordance with the scheme:

$$Ph{\cdot}NH{\cdot}CH_3 = Ph{\cdot}NH{\cdot} + CH_3{\cdot}$$
$$CH_3{\cdot} + Ph{\cdot}NH_2 = CH_4 + Ph{\cdot}NH{\cdot}$$
$$2Ph{\cdot}NH{\cdot} = (Ph{\cdot}NH)_2$$

Pyrolysis of methylaniline.

| Temp. (°K) | Total pressure (mm.) | Contact time (sec.) | Methyl-aniline ($10^{-5}$ mole) | $H_2$ ($10^{-5}$ mole) | $CH_4$ ($10^{-5}$ mole) | $10^2k$ (sec.$^{-1}$) |
|---|---|---|---|---|---|---|
| 812·1 | 12·17 | 2·300 | 78·95 | 0·074 | 0·488 | 0·270 |
| 824·8 | 11·73 | 1·260 | 84·54 | 0·097 | 0·387 | 0·383 |
| 828·5 | 12·06 | 1·280 | 77·80 | 0·068 | 0·445 | 0·448 |
| 828·8 | 10·43 | 1·380 | 31·17 | 0·050 | 0·373 | 0·501 |
| 829·7 | 11·30 | 2·250 | 73·91 | 0·079 | 0·449 | 0·478 |
| 838·2 | 11·19 | 2·270 | 43·48 | 0·158 | 0·741 | 0·749 |
| 839·6 | 10·87 | 2·360 | 30·42 | 0·135 | 0·586 | 0·817 |
| 841·7 | 11·96 | 2·270 | 76·89 | 0·443 | 1·241 | 0·708 |
| 844·9 | 12·17 | 2·260 | 54·68 | 0·310 | 1·040 | 0·842 |
| 848·7 | 9·04 | 0·614 | 103·40 | 0·037 | 0·597 | 0·936 |
| 850·7 | 8·50 | 0·622 | 92·01 | 0·040 | 0·564 | 0·997 |
| 851·7 | 11·85 | 1·245 | 45·50 | 0·188 | 0·676 | 1·20 |
| 852·0 | 11·52 | 2·270 | 54·50 | 0·582 | 1·258 | 1·03 |
| 869·4 | 9·04 | 0·596 | 67·00 | 0·101 | 0·911 | 2·27 |
| 870·8 | 8·48 | 0·628 | 110·60 | 0·230 | 1·728 | 2·49 |
| 885·5 | 7·82 | 0·636 | 76·33 | 0·176 | 2·145 | 4·48 |
| 889·5 P | 7·06 | 0·470 | 37·70 | 0·050 | 0·851 | 4·77 |
| 890·9 | 6·85 | 0·663 | 29·11 | 0·064 | 0·937 | 4·92 |
| 900·7 | 8·14 | 0·595 | 82·50 | 0·432 | 3·692 | 7·69 |
| 900·8 | 8·97 | 0·606 | 74·30 | 0·554 | 3·282 | 7·44 |
| 912·3 P | 7·82 | 0·470 | 84·73 | 0·660 | 3·835 | 9·81 |
| 915·7 | 8·67 | 0·584 | 63·08 | 0·464 | 4·547 | 12·8 |
| 915·7 P | 7·06 | 0·470 | 42·74 | 0·117 | 2·374 | 12·2 |
| 916·3 | 8·91 | 0·571 | 11·57 | 0·047 | 0·926 | 14·5 |
| 924·7 P | 7·00 | 0·460 | 18·10 | 0·074 | 1·386 | 17·4 |
| 935·3 | 8·48 | 0·513 | 44·40 | 0·667 | 5·656 | 26·5 |
| 937·3 | 8·58 | 0·588 | 34·10 | 0·741 | 4·470 | 23·8 |
| 946·9 | 11·30 | 0·484 | 27·06 | 0·560 | 4·932 | 41·5 |
| 948·5 | 11·76 | 0·337 | 38·82 | 1·373 | 6·350 | 52·8 |

P, packed reaction vessel.

A variable amount of hydrogen (average 15% of the methane) was formed and attributed to a reaction analogous to that by which styrene is formed from ethylbenzene. The rate constants were unaffected by (i) packing the reaction vessel so as to increase its surface : volume ratio by six, (ii) altering the partial pressure of reactants, (iii) varying the contact time by a factor of four, or (iv) slight changes in the pressure of aniline. The reaction appears to be homogeneous and unimolecular. Its rate constant is given by

$$\log k\ (\text{sec.}^{-1}) = (13{\cdot}40 \pm 0{\cdot}06) - (60{,}000 \pm 200/2{\cdot}3\boldsymbol{R}T).$$

The error limits were determined by least mean squares and are an indication of reproducibility.

The activation energy of the reaction can be identified with the heat of dissociation of the N–C bond. Hence, from the heats of formation of methylaniline [1] (21·6 kcal. mole$^{-1}$) and the methyl radical [2] (33·9 kcal. mole$^{-1}$), $\Delta H_f°$(Ph·NH) = 47·7 kcal. mole$^{-1}$. Since the heat of formation of aniline vapour is also known [3] (19·6 kcal. mole$^{-1}$), it can be shown that $D$(Ph·NH–H) = 80·1 kcal. mole$^{-1}$. It is evident that the N–H bond is weaker than the bond in ammonia [4] by roughly the same amount that the C–H bond in toluene [5] (84·6 kcal. mole$^{-1}$) is weaker than that in methane [2] (103·9 kcal. mole$^{-1}$). This conclusion is of interest because Kerr, Sekhar, and Trotman-Dickenson [4] found that alkyl substitution affected N–H bonds in methylamines more strongly that it did the corresponding C–H bonds in alkanes.

*Experimental.*—Methylaniline was twice distilled, tested by gas chromatography, and stored under a vacuum.

The apparatus and procedure previously described [5] were used, apart from the method of introduction of the methylaniline. Convenient amounts of aniline and methylaniline were distilled from weighed storage vessels into a trap. The exact composition of the mixture was determined by further weighings. The mixture was then distilled through the reaction vessel. The boiling points of the compounds are close together; therefore the composition of the vapour entering the reaction zone probably varied little during the run. It would be no disadvantage if some variation did occur as the decomposition is a first-order reaction. The end of the run was seen by the sudden decline of the pressure in the system. This procedure, which is thought to be novel, is extremely convenient for handling high-boiling substances.

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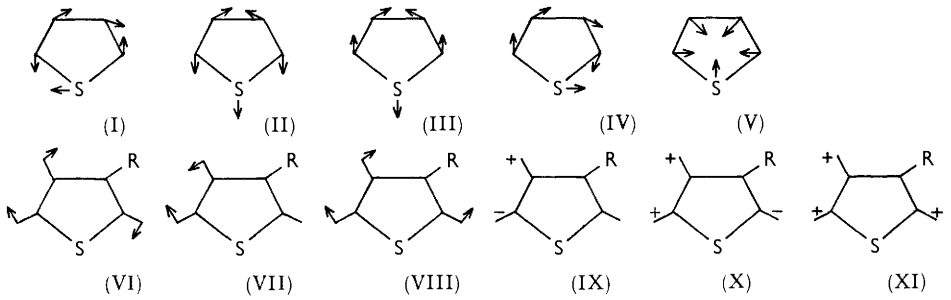
[1] Garner and Abernethy, *Proc. Roy. Soc.*, 1921, *A*, **99**, 213; Klages, *Chem. Ber.*, 1949, **82**, 358.
[2] Fettis and Trotman-Dickenson, *J.*, 1961, 3037.
[3] Anderson and Gilbert, *J. Amer. Chem. Soc.*, 1942, **64**, 2369.
[4] Kerr, Sekhar, and Trotman-Dickenson, *J.*, 1963, 3217.
[5] Esteban, Kerr, and Trotman-Dickenson, preceding paper.

## 721. *Infrared Absorption of Heteroaromatic, Five-membered, Monocyclic Nuclei. Part IV.*[1] *3-Monosubstituted Thiophens.*

By S. Gronowitz, A. R. Katritzky, and R. E. Reavill.

2-Monosubstituted thiophens were previously examined in this series of papers;[2] we have now studied the 3-substituted derivatives: some infrared spectra were recorded earlier,[3] without systematic investigation. In the 2000—700 cm.$^{-1}$ region of the spectrum, absorption corresponding to modes (I—XI) is expected. Ring-stretching (I—IV) and -breathing (V) mode frequencies should resemble those for the 2-substituted analogues and thiophen itself; in-plane (VI—VIII) and out-of-plane CH deformation mode frequencies (IX—XI) should parallel those for 1,2,4-trisubstituted benzenes.




Eighteen compounds (see ref. 3) were investigated, with the following substituents: NHAc, OMe, SMe, Br, I, $S_2$-thienyl, SCN, CHMe·OH, CHEt·OH, $SO_2$·Me, CN, CO·$NH_2$, $CO_2H$, $CO_2Me$, CHO, Ac, COEt, $NO_2$. Full spectra will be published in the D.M.S. scheme. 0·195M-Chloroform solutions were measured[4] in a 0·1025 mm. compensated cell, and apparent extinction coefficients were recorded: the errors and approximations involved have been noted.[4]

*Ring-stretching Frequencies at* 1600—1200 *cm.*$^{-1}$.—Bands shown by the 3-substituted thiophens at 1555—1481 [1512 ± 17],* 1443—1392 [1413 ± 15], 1374—1355 [1365 ± 11], and 1235—1193 [1210 ± 12] are assigned to modes (I—IV), respectively, as these frequencies correspond closely to those shown by the 2-substituted analogues.[2] The frequencies for all these modes are often considerably lower for compounds with a " heavy " atom (Cl, Br, I, S) attached directly to the thiophen ring than for the other compounds: this behaviour is often found for ring-stretching modes.[5]

For the first two bands, the intensity is usually greater for compounds with strong electron-acceptor substituents {*e.g.*, $\varepsilon_A$ = (90—240) [(135 ± 50)] and (65—135) [(100 ± 50)]}. However, the differentiation is less pronounced than for the corresponding 2-substituted compounds, and high intensities for the methoxy-compound are noteworthy. The third band is generally much weaker (5—45) [(25 ± 10)]. The fourth band occurs in a region obscured by chloroform absorption: frequencies were obtained from liquid films or mulls.

* Apparent extinction coefficients are in parentheses and arithmetic means and standard deviations in brackets. The intensities of shoulders and superposed bands, and the position of shoulders are not treated statistically.

[1] Part III, Katritzky and Boulton, *Spectrochim. Acta*, 1961, **17**, 238.
[2] Part II, Katritzky and Boulton, *J.*, 1959, 3500.
[3] For references see Gronowitz in " Advances in Heterocyclic Chemistry," Vol. I, p. 1, Academic Press, New York, 1963.
[4] Katritzky, Monro, Beard, Dearnaley, and Earl, *J.*, 1958, 2182.
[5] Cf. Katritzky, *Quart. Rev.*, 1959, **13**, 353.

*Hydrogen In-plane Deformation.*—A band of medium intensity at 1098—1070 cm.$^{-1}$ (10—50) [1083 ± 10 (25 ± 10)], assigned to mode (VII), is to be compared with the absorption found [6] for 1,2,4-trisubstituted benzenes at 1127 ± 10 cm.$^{-1}$ (m). Weak absorption at *ca.* 1155 cm.$^{-1}$ may correspond to mode (VIII) and the absorption found [6] for 1,2,4-trisubstituted benzenes at 1151 ± 8 cm.$^{-1}$ (m).

700—1000 *cm.*$^{-1}$ *Region.*—Weak absorption near 930 cm.$^{-1}$, medium bands at 895—850 cm.$^{-1}$ (35—105) [872 ± 10 (65 ± 25)] and 854—817 cm.$^{-1}$ (15—150) [832 ± 12 (60 ± 30)], and a strong band at 795—745 [789 ± 9] cm.$^{-1}$ (below solvent cut-off) [6] probably correspond, respectively, to the out-of-plane CH-bending mode (IX), to the ring-breathing mode (V), and the two out-of-plane CH-bending modes (X) and (XI). For comparison, mode (V) occurs at 831 cm.$^{-1}$ (95) in thiophen and at 839—790 cm.$^{-1}$ (25—85) in 2-substituted derivatives: 1,2,4-trisubstituted benzenes absorb [7] at 929 ± 11 (w), 868 ± 11 (m), and 816 ± 14 cm.$^{-1}$ (vs).

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[6] Randle and Whiffen, Paper No. 12, Report on Conference of Molecular Spectroscopy, 1954, Institute of Petroleum.
[7] Cf. Gronowitz, *Arkiv Kemi*, 1957, **12**, 239.

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## 722. *The Mechanism of Electrophilic Substitution of Heteroaromatic Compounds. Part II.*[1] *Nitration of Bis-*1,2,4,6*-tetramethylpyridinium Sulphate.*

By A. R. KATRITZKY and B. J. RIDGEWELL.

IN Part I,[1] comparison of the rates of acid-catalysed hydrogen exchange of 2,4,6-collidine and its 1-methyl cation formed part of the evidence that the former underwent electrophilic substitution as the protonated cation rather than the free base.

If these conclusions are valid for other electrophilic substitutions of pyridines in acidic media, it should follow that the corresponding 1-methylpyridinium cations undergo substitution under the same conditions. No such reactions appear to have been previously reported, but we have now justified this speculation for the nitration of 2,4,6-collidine. Nitration of bis-1,2,4,6-tetramethylpyridinium sulphate afforded a picrate in good yield which was identical with that made from the methiodide of 2,4,6-trimethyl-3-nitropyridine.

*Experimental.*—2,4,6-*Trimethyl-3-nitropyridine.*[2] Purified 2,4,6-collidine [3] (5 g.), " AnalaR " fuming nitric acid (*d* 1·5; 25 ml.), and 20% oleum (20 ml.) were heated at 100° for 4 hr. After cooling and basification with 10% aqueous sodium hydroxide, the mixture was extracted with ether. The ether was evaporated at 100°, and the residue fractionally distilled; the fraction of b. p. 113—114°/14 mm. (*ca.* 2 g., 30%) solidified and had m. p. *ca.* 28° (lit.,[2] m. p. 38°).

1,2,4,6-*Tetramethyl-3-nitropyridinium iodide.* 2,4,6-Trimethyl-3-nitropyridine (0·5 g.) and methyl iodide (5 g.) were heated (sealed tube) at 100° for 4 hr. The contents were filtered, and the solid residue was shaken with water (20 ml.) and filtered again to remove carbonaceous material. The yellow solution was evaporated to dryness at 70°/14 mm. The residue crystallised from ethanol as yellow plates (0·5 g., 55%), m. p. 232° (decomp.) (unchanged by

[1] Katritzky and Ridgewell, *J.*, 1963, 3753.
[2] Van Rijn, *Rec. trav. chim.*, 1926, **45**, 267.
[3] Engel, U.S.P. 2,426,442.

recrystallisation) (lit.,[2] m.p. 210—211°) (Found: C, 35·0; H, 4·1. Calc. for $C_9H_{13}IN_2O_2$: C, 35·1; H, 4·2%).

The *picrate* was prepared in aqueous solution (for reasons given in ref. 4 with sodium picrate) and formed yellow plates, m. p. 171·5—172·5 (decomp.) (Found: C, 44·4; H, 3·9; N, 17·3. $C_{15}H_{15}N_5O_9$ requires C, 44·0; H, 3·7; N, 17·1%).

*Nitration of 1,2,4,6-tetramethylpyridinium cation.* Bis-1,2,4,6-tetramethylpyridinium sulphate (1 g.), " AnalaR " fuming nitric acid (*d* 1·5; 5 ml.), and 20% oleum (4 ml.) were heated at 100° for 4 hr. After cooling and dilution with water (50 ml.), the mixture was neutralised with Dowex-3 ion-exchange resin ($OH^-$ form). Saturated aqueous sodium picrate (35 ml.) was added to the neutral solution at 80° and the resulting picrate (1·6 g., 73%) recrystallised from water. It had m. p. 171—171·5° (decomp.), unchanged by further recrystallisation and not depressed on admixture with the picrate prepared as above (Found: C, 43·8; H, 3·8; N, 17·4).

We thank D.S.I.R. for a research studentship to B. J. R.

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[4] Baker and Mann, *J.*, 1961, 3845.

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## 723. *Optically Active Phosphorus Compounds. Part III.* Displacement Reactions of (+)-Diethyl Pyromethylphosphonothionate and (+)-S-Methyl Ethylphenylphosphinothiolate.*

By M. GREEN and R. F. HUDSON.

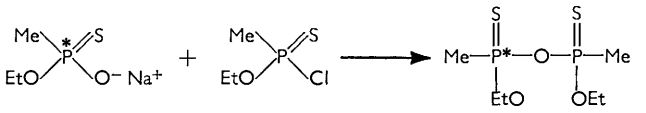
IN spite of the growing interest in the stereochemistry of displacement reactions at asymmetric phosphoryl and thiophosphoryl centres, attempts to devise stereochemical Walden cycles of the kind which first established inversion of configuration for $S_N2$ reactions at saturated carbon centres have so far been unsuccessful. The experiments described below, however, lead to such a cycle for the thiophosphoryl centre and show that alkaline hydrolysis of an optically active thiopyrophosphate proceeds almost exclusively with inversion of configuration.

Phosphonothioic acids, which can be readily resolved into their optical enantiomorphs,[1] undergo *S*-alkylation exclusively, but give the *O*-phosphorylated product with phosphoryl

$$\text{Me·PO(OEt)·SR} \xleftarrow{RX} \text{Me·PO(OEt)·S}^- \text{Na}^+ \xrightarrow{RR'POCl} \text{Me·PS(OEt)·O·P(O)RR'}$$

chlorides.[2] Michalski *et al.*[3] recently used optically active thiopyrophosphates to show that *O*-phosphorylation does not proceed through an *S*-phosphorylated product which subsequently rearranges.

We have found that optically active (−)-sodium *O*-ethyl methylphosphonothioate (I) reacts with racemic *O*-ethyl methylphosphonochloridothionate (II) to give the corresponding optically active (+)-pyrophosphonothioate (III) in high yield:



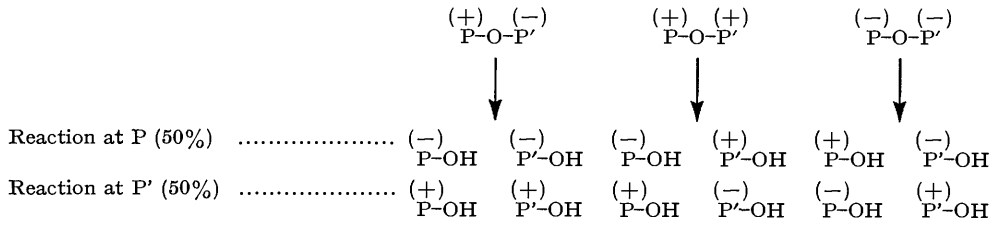
(I) (II) (III)

The (+)-pyrophosphonothionate (III) with only one optically active phosphorus atom was hydrolysed in an excess of aqueous hydroxide to give, after acidification, *O*-ethyl hydrogen

* Part II, *J.*, 1963, 540.

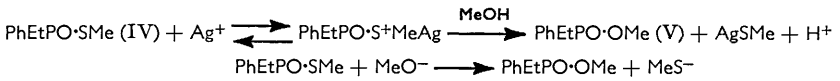
[1] Aaron, Braun, Shryne, Frack, Smith, Uyeda, and Miller, *J. Amer. Chem. Soc.*, 1960, **82**, 596.
[2] McIvor, McCarthy, and Grant, *Canad. J. Chem.*, 1956, **34**, 1819.
[3] Michalski, Mikolajczyk, and Ratajczak, *Chem. and Ind.*, 1962, 819.

methylphosphonothioate with zero rotation. Since the hydrolysis proceeds with equal probability at the two thiophosphoryl centres, an acid with a rotation of the same sign as the initial acid would be obtained if each act of substitution proceeded with retention of configuration. If, however, each act of substitution proceeded with inversion, a totally racemic product would be obtained, as shown by the following scheme. The optically active pyrophosphate occurs in *meso*-(+)-, and -(−)-forms the second predominating. Reaction with hydroxide ions gives the following changes at the two phosphorus atoms:




This scheme shows that an inversion mechanism would give an acid of zero activity, whatever the optical purity of the pyrophosphonate, whereas other stereochemical courses would give an acid with some (+)-activity. The experiment described above therefore shows that the alkaline hydrolysis proceeds with at least 99% inversion. We have recently found that the symmetrical exchange of a phosphinate ester similarly proceeds with inversion of configuration.[4]

Since the transition-state structure may change with the charge on it (*d*-orbital participation is sensitive to the charge on the phosphorus atom [5]), we tried to follow the acid-catalysed hydrolysis of the pyrophosphonate, but these experiments were unsuccessful owing to loss of sulphur by hydrolysis. In further experiments, the alcoholysis of *S*-methyl ethylphenylphosphinothiolate (IV), catalysed by silver ions, which proceeds similarly to silver-catalysed hydrolysis,[6] was compared with the displacement by methoxide ions previously reported:




Treatment of the ester (IV), $[\alpha]_D^{20}$ +1·0°, with silver nitrate in methanol gave a product (V), $[\alpha]_D^{20}$ −0·31° (*c* 25 in MeOH) by the above silver reaction. Treatment of an ester (IV), $[\alpha]_D^{20}$ +10·4°, gave a product (V) $[\alpha]_D^{20}$ −3·49° (homogeneous), $[\alpha]_D^{20}$ −3·45° (*c* 13 in MeOH), by the alkaline reaction.[7] If the latter reaction is assumed to proceed with inversion, by analogy with the alkaline hydrolysis of the pyrophosphonothioate and the transesterification of methyl ethylphenylphosphinate, it follows that the silver reaction also proceeds with predominant inversion (*ca.* 94% optical purity). We conclude therefore that, in this case, the stereochemistry of the transition state is not modified significantly by electrostatic factors.

*Experimental.—Partial resolution of* O*-ethyl hydrogen methylphosphonothioate.*[1] The quinine salt was fractionally crystallised from acetone–ether. The acid (cf. I) was liberated from it by alkali and removal of the quinine in ether. Acidification of the alkaline solution gave the acid, which was purified by distillation. The fraction, b. p. 69—70°/0·3 mm. (lit.,[8] b. p. 63°/0·2 mm.), $[\alpha]_D^{20}$ −8° (homogeneous), was used in the following experiment.

[4] Green and Hudson, *Proc. Chem. Soc.*, 1962, 307.
[5] Craig, Maccoll, Nyholm, Orgel, and Sutton, *J.*, 1954, 332.
[6] Saville, *J.*, 1961, 4624.
[7] Green and Hudson, *Proc. Chem. Soc.*, 1961, 145.
[8] Hoffmann, Kagan, and Canfield, *J. Amer. Chem. Soc.*, 1959, **81**, 148.

*Preparation of* (+)-*diethyl pyromethylphosphonothionate* (III). *O*-Ethyl hydrogen methylphosphonothioate (6·4 g.), $[\alpha]_D^{20}$ −8° (homogeneous), in dry 1,2-dimethoxyethane (20 ml.) was added dropwise to a suspension of sodium hydride (2·19 g., 50% in oil) in 1,2-dimethoxyethane (75 ml.). *O*-Ethyl methylphosphonochloridothionate (II) (14·5 g.) in 1,2-dimethoxyethane (20 ml.) was then added all at once. The mixture was stirred overnight and the 1,2-dimethoxyethane removed under reduced pressure. Ether (200 ml.) was added, and the precipitated sodium chloride removed by filtration. Evaporation under reduced pressure and distillation of the residue gave unchanged phosphonochloridothionate [9] (4 g.) and *di*-O-*ethyl pyromethylphosphonothionate* (10·4 g.), b. p. 80—81°/0·1 mm., $[\alpha]_D^{20}$ +24·2° (homogeneous) [Found: C, 27·8; H, 6·2; P, 22·9; S, 24·2%; *M* (cryoscopic in benzene), 259. $C_5H_{16}O_3P_2S_2$ requires C, 27·5; H, 6·2; P, 23·6; S, 24·5%; *M*, 262]. The infrared spectrum showed no peaks between 7·7 and 8·7 μ, but showed peaks at 8·7 and 9·7 μ (P–O–Et). The pyrophosphonothioate was shown to be homogeneous by gas chromatography on a Perkin-Elmer type " O " Silicone column.

*Alkaline hydrolysis of the ester* (III). A solution of the ester (5 g.), $[\alpha]_D^{20}$ +24·2° (homogeneous), in dioxan (20 ml.) was added dropwise with stirring to sodium hydroxide (18 g.) in water (150 ml.). The clear solution was stirred overnight, then extracted with ether (3 × 75 ml.). The alkaline layer was acidified with concentrated hydrochloric acid and continuously extracted with ether overnight. The extract was dried ($MgSO_4$), and the ether removed. The residue was distilled, to give *O*-ethyl hydrogen methylphosphonothioate (I) (4·1 g.), b. p. 69°/0·3 mm., whose infrared spectrum was identical with that of an authentic sample. The optical rotation of the pure acid was zero (±0·01°) when measured in a 1 dm. tube on a Zeiss polarimeter.

*Reaction of* (±)-*methyl ethylphenylphosphinothiolate* (IV) *with methanol in the presence of silver perchlorate.* A solution of the ester (IV) (9·0 g.), $[\alpha]_D^{20}$ +1·00° (homogeneous), in 1,2-dimethoxyethane (10 ml.) was added dropwise with stirring to a solution of anhydrous silver perchlorate (9·36 g.), in dry methanol (100 ml.). After several minutes, a thick yellow precipitate was formed. The mixture was stirred for 0·5 hr. at room temperature and then neutralised with triethylamine (4·5 g.). The precipitate was filtered off and the solvent removed. Distillation of the residue gave methyl ethylphenylphosphinate (5·5 g.), b. p. 76°/0·03 mm., $[\alpha]_D^{20}$ −0·31° (*c* 25 in MeOH), whose infrared spectrum was identical with that of an authentic sample.[5] The optical rotations were measured by an E.T.L. photoelectric polarimeter (sensitivity ±0·0002°).

*Attempted Reaction of ester* (I) *with di-n-butylmercury.* Di-n-butylmercury (3·4 g.) was boiled with the ester (2·09 g.) in benzene (10 ml.) overnight. The benzene was removed and the residue distilled, giving di-n-butylmercury (2·8 g.), b. p. 50—52°/0·2 mm., and unchanged ester (1·6 g.), b. p. 110—112°/0·2 mm.

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[9] Hoffmann, Wadsworth, and Weiss, *J. Amer. Chem. Soc.*, 1958, **80**, 3945.

## 724. *Synthesis of 2-Amino-2,6-dideoxy-L-talopyranose (Pneumosamine).*

By J. S. Brimacombe and M. J. How.

2-Amino-2,6-dideoxy-L-talopyranose (pneumosamine) has been isolated from acid hydrolysates of type V *Pneumococcus* capsular polysaccharide.[1,2] We have recently reported [3] a synthesis of the D-enantiomorph *via* hydrazinolysis of methyl 6-deoxy-3,4-*O*-isopropylidene-2-*O*-tosyl-α-D-galactopyranoside. The following reaction sequence yields 2-amino-2,6-dideoxy-L-talopyranose in slightly improved yield.*

Oxidation of methyl 6-deoxy-3,4-*O*-isopropylidene-α-L-galactopyranoside [4] with chromium trioxide in pyridine [5] yielded methyl 6-deoxy-3,4-*O*-isopropylidene-α-L-*lyxo*-hexosuloside † which on treatment with hydroxylamine was converted into the oxime in almost quantitative yield. Reduction of the oxime with hydrogen in the presence of platinum gave a mixture of epimeric amino-sugars in which the derivative having the L-*talo*-configuration predominated. Several workers [6] have observed that catalytic reduction of oximes and hydrazones attached to cyclohexane or pyranose ring systems leads to a preponderance of the epimer having an axial amino-group in the stable chair form.

The mixture of epimeric amino-sugars was *N*-acetylated, the protecting groups removed by acid hydrolysis, and the product mixture fractionated on Dowex 50($H^+$) to yield, *inter alia*, 2-amino-2,6-dideoxy-α-L-talopyranose hydrochloride. The melting point and chromatographic and electrophoretic properties of the synthetic sugar were indistinguishable from those of pneumosamine hydrochloride [2] and 2-amino-2,6-dideoxy-α-D-talose hydrochloride.[3] The infrared spectra and the *X*-ray powder photographs of the D- and the L-enantiomorphs were also identical.

*Experimental.*—M. p.s are corrected. Paper chromatograms were run on Whatman No. 1 paper by downward irrigation with the organic phase of one of the following solvent systems: (a) butan-1-ol–ethanol–water (4 : 1 : 5), (b) butan-1-ol–acetic acid–water (4 : 1 : 5).

*Methyl 6-deoxy-3,4-O-isopropylidene-α-L-galactopyranoside.* This compound, b. p. 99—100°/0·02 mm., $n_D^{19}$ 1·4620, was prepared by the method described by Percival and Percival [4] who record b. p. 95°/0·01 mm., $n_D^{18}$ 1·4621.

*Methyl 6-deoxy-3,4-O-isopropylidene-α-L-lyxo-hexosuloside.*—Powdered chromium trioxide (15 g.) was added cautiously, under an atmosphere of nitrogen, to a stirred and cooled (10°) solution of pyridine (150 ml.). The suspension of the yellow complex was allowed to attain room temperature and a solution of the foregoing glycoside (10 g.) in pyridine (100 ml.) was then added dropwise with stirring. Stirring was continued for 20 hr. at room temperature. Most of the pyridine was removed under reduced pressure below 40°, the resulting brown residue dissolved in water (50 ml.), and the aqueous layer extracted with ether (4 × 200 ml.), followed by continuous ether extraction for 24 hr. The combined and dried ($MgSO_4$) ether extracts were evaporated to a syrup which was oxidised twice more by the above procedure. The *product* (2·35 g.) which crystallised on evaporation of the solvent had m. p. 73·5—75° (from di-isopropyl ether), $[\alpha]_D^{29}$ −107° (*c* 3·0 in chloroform) (Found: C, 55·8; H, 7·3. $C_{10}H_{16}O_5$

* A similar synthesis has been reported recently by Collins and Overend, *Chem. and Ind.*, 1963, 375.

† The name is based on Rule 7 of the U.S.–British Rules of Carbohydrate Nomenclature, cf. *J.*, 1962, 5307.

[1] Barker, Stacey, and Williams, *Bull. Soc. Chim. biol.*, 1960, **12**, 1611.
[2] Barker, Brimacombe, How, Stacey, and Williams, *Nature*, 1961, **189**, 303.
[3] Brimacombe and How, *Chem. and Ind.*, 1962, 1382; *J.*, 1962, 5037.
[4] Percival and Percival, *J.*, 1950, 690.
[5] Poos, Arth, Beyler, and Sarett, *J. Amer. Chem. Soc.*, 1953, **75**, 422; Walton, Rodin, Stammer, Holly, and Folkers, *ibid.*, 1958, **80**, 5168; Burton, Overend, and Williams, *Chem. and Ind.*, 1961, 175.
[6] Lindberg and Theander, *Acta Chem. Scand.*, 1959, **13**, 1226; Posternack, *Helv. Chim. Acta*, 1950, **33**, 1597; Anderson and Lardy, *J. Amer. Chem. Soc.*, 1950, **72**, 3141.

requires C, 55·5; H, 7·4%). The infrared spectrum showed absorption at 1730 cm.$^{-1}$ (C=O stretching) but no absorption due to hydroxyl stretching at *ca.* 3600 cm.$^{-1}$.

*Oximation and reduction of oxime.* A solution of methyl 6-deoxy-3,4-*O*-isopropylidene-α-L-*lyxo*hexosuloside (2 g.) in ethanol (60 ml.) was added in portions to a stirred solution of hydroxylamine hydrochloride (6·2 g.) in water (90 ml.) which had been previously adjusted to pH 4. The temperature was kept at 10° by external cooling and pH maintained at 4 by addition of 0·1N-sodium hydroxide solution. After 5 hr. the solution was adjusted to pH 7, concentrated to *ca.* 50 ml., and extracted with ether (4 × 200 ml.). Removal of the solvent gave a syrup (2·15 g.) which was dissolved in butan-1-ol (75 ml.) and reduced with a slight overpressure of hydrogen in the presence of Adams catalyst (0·2 g.) for 20 hr. at room temperature. The filtered solution was concentrated under reduced pressure to yield a syrup (1·98 g.) which would not crystallise. Chromatograms (solvent a) revealed two components at *R* (glucose) 4·35 (major), and 3·03 (minor) which were detected with ninhydrin reagent.[7]

N-*Acetylation and hydrolysis.* To a stirred and cooled (0°) solution of the foregoing syrup (1·98 g.) in water (80 ml.) and methanol (5·6 ml.) was added Dowex-1 ($CO_3^{2-}$) (140 ml.) and redistilled acetic anhydride (2·8 ml.); the reaction was allowed to proceed for 90 min. The combined filtrate and washings were stirred for 10 min. with Amberlite IR-120($H^+$), the solution was filtered, and the resin was thoroughly washed with water. The combined filtrate and washings were freeze-dried to give a syrup (1·4 g.) which was hydrolysed with 2N-hydrochloric acid (80 ml.) for 8 hr. at 95°. The cooled solution was neutralised with silver carbonate, the insoluble silver salts were removed by centrifugation and washed with water (3 × 100 ml.), and hydrogen sulphide was bubbled through the combined supernatant liquid and washings. The filtered solution was then concentrated to *ca.* 250 ml. and D-glucosamine hydrochloride (40 mg.) was added as a marker.

*Fractionation on Dowex-*50($H^+$). The foregoing solution was applied to a freshly regenerated column of Dowex-50($H^+$) (23 × 6 cm.; 200—400 mesh) and the column eluted with 0·3N-hydrochloric acid. Fractions (25 ml.) were collected automatically. A portion (2 ml.) of each of the fractions was analysed for amino-sugars with the Elson–Morgan reagent.[8] The fraction eluted from the column between 5·75 and 7 l. was neutralised with Deacidite-FF($CO_3^{2-}$), filtered, and freeze-dried. The residue was treated with an equivalent amount of 0·3N-hydrochloric acid and freeze-dried to give a crystalline residue (0·34 g.), which was washed with cold dry methanol and dried. 2-Amino-2,6-dideoxy-L-talopyranose hydrochloride had m. p. 162—163° (decomp.), $[\alpha]_D^{30}$ +9° (final, *c* 0·8 in water) (Found: N, 7·3. $C_6H_{14}ClNO_4$ requires N, 7·0%).

The chromatographic and electrophoretic properties (acetate buffer, pH 5) of the amino-sugar were indistinguishable from those of pneumosamine hydrochloride [1,2] and the D-enantiomorph.[3] The infrared spectra (Nujol mulls) of the L- and D-enantiomorphs were indistinguishable, as were their *X*-ray powder photographs.

The authors thank Professor M. Stacey, F.R.S., and Dr. S. A. Barker for their interest, and Mr. R. Brueton for experimental assistance. One of them (M. J. H.) thanks the Ramsay Memorial Fellowships Trust for a maintenance grant.

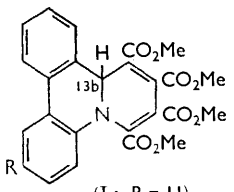
CHEMISTRY DEPARTMENT, THE UNIVERSITY, BIRMINGHAM 15. [*Received, November 30th*, 1962.]

[7] Consden, Gordon, and Martin, *Biochem. J.*, 1944, **38**, 224.
[8] Partridge, *Biochem. J.*, 1948, **42**, 238.

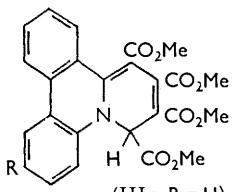
## 725. *Addition Reactions of Heterocyclic Compounds. Part XVI.* Some Dibenzo[a,c]quinolizine Derivatives.*

By R. M. Acheson, G. R. Miller, and A. O. Plunkett.

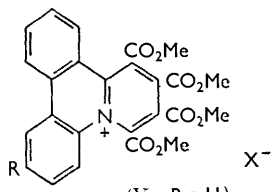
Structures (I) and (III) have been suggested,[1] respectively, for the " labile " adduct obtained from phenanthridine and dimethyl acetylenedicarboxylate, and for its " stable " isomer. A similar pair of isomers (II) and (IV) with analogous ultraviolet and infrared absorption spectra has now been obtained from 2-bromophenanthridine and the ester.




(I: R = H)
(II: R = Br)




(III: R = H)
(IV: R = Br)




(V: R = H)
(VI: R = Br)

The significant feature of the proton magnetic resonance spectrum of the " labile " adduct (II) is the chemical shift of the 13b-hydrogen atom which occurs at 4·30 p.p.m. on the $\tau$ scale, about 0·55 p.p.m. below the resonance of the comparable proton of the " labile " quinoline adduct, tetramethyl 11a*H*-benzo[*c*]quinolizine-1,2,3,4-tetracarboxylate.[2] The chemical shift of this bridgehead proton is expected to change on going from the quinoline adduct to the phenanthridine adduct because of the ring current in the additional aromatic ring of the latter. Using ideal bond lengths and bond angles for the suggested structure of this adduct (II) and the calculations of Johnson and Bovey [3] on the effect of a ring current on a nucleus situated at an arbitrary distance and direction from the aromatic ring one can predict a shift of 0·6 p.p.m. to low field for the 13b-hydrogen atom relative to the 11a-hydrogen atom in the quinoline adduct. The agreement between the calculated and the experimental result supports the above formulation of the " labile " adducts.

The limited solubility of the " stable " phenanthridine adducts (III) and (IV) in suitable solvents prevented a satisfactory study of their proton magnetic resonance spectra but the absence of a hydrogen atom corresponding to that at position 13b of the adduct (II) was established.

The 13b*H*-quinolizines (I) and (II) and the 4*H*-quinolizine (IV) with hot bromine in acetic acid gave quinolizinium perbromides which with perchloric acid yielded the perchlorates (V and VI; X = $ClO_4$). Surprisingly, the 4*H*-quinolizines (III and IV) with bromine in cold acetic acid gave immediate precipitates of the quinolizinium perbromide hydrobromides (V and VI; X = $Br_3$, HBr), almost identical in ultraviolet absorption spectra with the corresponding perchlorates, into which they were converted. All these compounds decomposed on attempted crystallisation and were analysed without purification. The ultraviolet absorption spectra of the perchlorates generally resembled that of triphenylene [4] and were not affected by alkali. The infrared absorption spectra of the perbromide hydrobromides showed maxima at 5·68—5·70 $\mu$ not possessed by the

* Part XV, *J.*, 1963, 2082.

[1] Acheson and Plunkett, *J.*, 1962, 3758.
[2] van Tamelen, Aldrich, Bender, and Miller, *Proc. Chem. Soc.*, 1959, 309; Acheson, Earl, Higham, Richards, Taylor, and Vernon, *ibid.*, 1960, 281.
[3] Johnson and Bovey, *J. Chem. Phys.*, 1958, **29**, 1012.
[4] Friedel and Orchin, " Ultraviolet Spectra of Aromatic Compounds," spectrum no. 445, John Wiley Inc., New York, 1951.

perbromides themselves. α-Halogenated esters also absorb in this range,[5] so it appears that in the solid phase the perbromide hydrobromides are more correctly formulated as the 1(or 3)-bromo-1,4(or 3,4)-dihydroquinolizinium perbromides while in methanol, used for the ultraviolet spectroscopy, hydrogen bromide is lost giving salts derived from the cations (V) and (VI).

*Experimental.*—Infrared absorption spectra were measured for paraffin paste (P) or chloroform solutions (C) and are given for the 5—7 μ region. Ultraviolet absorption spectra are for methanol solutions; $10^{-4}\varepsilon$ are given in parentheses. Inflexions are marked with asterisks. Proton magnetic resonance spectra were measured for chloroform and deuterochloroform solutions at 29·92 Mc./sec., as described elsewhere.[6]

*Tetramethyl* 8-*bromo*-13bH-*dibenzo*[a,c]*quinolizine*-1,2,3,4-*tetracarboxylate* (II). 2-Bromophenanthridine (10·32 g.), dimethyl acetylenedicarboxylate (11·36 g.), and dry benzene (160 ml.) were refluxed for 2½ hr. and left at 18° for 48 hr. Evaporation to small volume gave an oily precipitate which crystallised on trituration with ether (10 ml.). The precipitate (9·3 g.) was washed with ether and dried; crystallisation from acetonitrile (300 ml.) gave the *quinolizine* as yellow needles (7·23 g.), m. p. 246—247° (decomp.) (Found: C, 55·1; H, 3·8; Br, 15·1; N, 3·0; OMe, 23·1. $C_{25}H_{20}BrNO_8$ requires C, 55·4; H, 3·7; Br, 14·8; N, 2·6; 4OMe, 22·9%), $\nu_{max.}$ (C) 5·74, 5·84, 5·88, 6·20, 6·41, 6·60, 6·75, 6·89, and 6·98 μ, $\lambda_{max.}$ 406 (0·80), 295* (1·14), and 258 mμ (3·94).

*Tetramethyl* 8-*bromo*-4H-*dibenzo*[a,c]*quinolizine*-1,2,3,4-*tetracarboxylate* (IV). The above 13b*H*-quinolizine (2·0 g.) and redistilled quinoline (4 ml.) were heated at 120—125° for 25 min. and the hot solution was poured into stirred concentrated hydrochloric acid (5 ml.) and ice (60 ml.). The precipitate (2·06 g.) was washed successively with dilute hydrochloric acid and water and dried. Crystallisation from acetonitrile (50 ml.) gave the 4H-*quinolizine* (0·64 g.) as red needles, m. p. 237° (Found: C, 55·6; H, 3·7; N, 2·6; OMe, 23·4. $C_{25}H_{20}BrNO_8$ requires C, 55·4; H, 3·7; N, 2·6; 4OMe, 22·9%), $\nu_{max.}$ (P) 5·74, 5·86, 5·96, 6·24*, 6·27*, 6·33, 6·43, 6·69, 6·88, and 7·01 μ, $\lambda_{max.}$ 466 (1·57), 323* (1·08), 303 (1·57), and 260 mμ (5·62).

*Oxidation with bromine.* (i) Tetramethyl 13b*H*-dibenzo[*a,c*]quinolizine-1,2,3,4-tetracarboxylate (I) (0·2 g.) was dissolved in hot glacial acetic acid (20 ml.), bromine (0·24 g.) in acetic acid (20 ml.) was added, and the mixture was heated to 100° and filtered hot. Cooling precipitated 1,2,3,4-*tetramethoxycarbonyldibenzo*[a,c]*quinolizinium perbromide* (V; X = $Br_3$) as yellow needles (0·13 g.) which after being washed with acetic acid and dried over sodium hydroxide *in vacuo* had m. p. 152° (decomp.) (Found: C, 43·0; H, 3·1; Br, 34·5; OMe, 17·5. $C_{25}H_{20}Br_3NO_8$ requires C, 42·8; H, 2·9; Br, 34·2; 4OMe, 17·7%), $\nu_{max.}$ (P) 5·75, 6·22, 6·31, 6·37, 6·52, 6·75, 6·88, 6·94, and 6·99* μ.

This compound (68 mg.) and 72% perchloric acid (0·8 ml.) in methanol (8 ml.) were heated on a steam-bath for 10 min. and after filtration cooling gave the corresponding *perchlorate* (42 mg.), m. p. 250° (decomp.), in yellow rhombs, which were washed with methanol and dried (Found: C, 52·6; H, 3·7; Br, 0·0; Cl, 5·7; N, 2·8; OMe, 21·3. $C_{25}H_{20}ClNO_{12},\frac{1}{2}H_2O$ requires C, 52·6; H, 3·7; Cl, 6·35; N, 2·5; 4OMe, 22·7%), $\nu_{max.}$ (P) 5·75, 6·22, 6·29, 6·38, 6·54, 6·71, 6·85, and 6·91 μ, $\lambda_{max.}$ 380 (0·55), 287* (1·24), and 256 mμ (3·14), and after acidification 410—430* (0·44), 380* (0·62), 335* (1·05), 300 (1·86), and 256 mμ (3·16).

(ii) The 8-bromo-13b*H*- or -4*H*-quinolizine (II or IV) (116 mg.) in hot acetic acid (5 ml.) was treated with bromine (150 mg.) in acetic acid (2·5 ml.) as in (i) and gave *the* 8-*bromoquinolizinium perbromide* (VI; X = $Br_3$) as yellow needles (43 mg.), m. p. 148—150° (decomp.) (Found: C, 39·1; H, 2·8; Br, 40·2; N, 2·0; OMe, 16·1. $C_{25}H_{19}Br_4NO_8$ requires C, 38·4; H, 2·4; Br, 41·0; N, 1·8; 4OMe, 15·9%), $\nu_{max.}$ (P) 5·75, 6·22*, 6·27, 6·37, 6·53, 6·86, 6·90, and 7·00 μ. 60% Perchloric acid (1 ml.) was added to the mother-liquor and after evaporation to small volume at room temperature the corresponding *perchlorate* separated as a yellow microcrystalline powder (25 mg.), m. p. 260° (decomp.) (Found: C, 46·8; H, 3·0; Br, 12·3; Cl, 5·6; OMe, 19·5. $C_{25}H_{19}BrClNO_{12}$ requires C, 46·8; H, 3·0; Br, 12·5; Cl, 5·7; 4OMe, 19·40%), $\nu_{max.}$ (P) 5·75, 6·25, 6·39, 6·55, 6·77, and 6·93 μ, $\lambda_{max.}$ 375 (0·53), 289* (1·26), and 258 (3·20), and after acidification 430* (0·38), 380* (0·71), 340* (1·00), 306 (1·70), and 253 mμ (3·41).

(iii) Bromine (60 mg.) in acetic acid (1 ml.) was added to a cold soution of tetramethyl

[5] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1958, p. 182.
[6] Leane, Richards, and Schaefer, *J. Sci. Instr.*, 1959, **36**, 230.

4*H*-dibenzo[*a*,*c*]quinolizine-1,2,3,4-tetracarboxylate (III) (60 mg.) in acetic acid (5·0 ml.). The corresponding *quinolizinium perbromide hydrobromide* (V; X = $Br_3$,HBr) (74 mg.) was precipitated and had m. p. 163° (decomp.) (Found: C, 38·45; H, 2·9; Br, 41·5. $C_{25}H_{21}Br_4NO_8$ requires C, 38·4; H, 2·7; Br, 40·7%), $\nu_{max.}$ (P) 5·70, 5·77, 6·22, 6·32, 6·41, 6·59, 6·70, 6·89, and 6·99 μ. This compound (40 mg.) with 60% perchloric acid (0·65 ml.) and methanol (5 ml.) were heated on a steam-bath for 10 min.; filtration and cooling gave the perchlorate, m. p. 254° (decomp.), identical in infrared absorption spectrum with the specimen obtained in experiment (i).

(iv) The 8-bromo-4*H*-quinolizine (IV) (36 mg.) was treated as for compound (III) in (iii) and gave 8-*bromo*-1,2,3,4-*tetramethoxycarbonyldibenzo*[a,c]*quinolizinium perbromide hydrobromide* (VI; X = $Br_3$,HBr) (35 mg.), m. p. 148—150° (decomp.) (Found: C, 35·1; H, 2·4; Br, 46·4; N, 1·6; OMe, 14·5. $C_{25}H_{20}Br_5NO_8$ requires C, 34·9; H, 2·3; Br, 46·5; N, 1·6; 4OMe, 14·4%), $\nu_{max.}$ (P) 5·68, 5·75, 6·23, 6·35, 6·42, 6·63*, 6·84*, 6·90, and 6·98* μ. With perchloric acid, as in (iii), it gave the corresponding perchlorate, m. p. 259° (decomp.) (Found: C, 46·3; H, 3·1; OMe, 19·5%), identical in infrared absorption spectrum with the specimen described under (ii). The perchlorate was also obtained from the quinolizine (IV) in hot acetic acid by addition of bromine, then perchloric acid.

One of us (G. R. M.) thanks the United States National Science Foundation for a post-doctoral fellowship and Dr. R. E. Richards, F.R.S., for the hospitality of his laboratory. This work was supported in part by grants from the Rockefeller Foundation and from the United States Public Health Service to the Department of Biochemistry, University of Oxford.

Department of Biochemistry, and the Physical Chemistry Laboratory,
University of Oxford. [*Received, January 7th*, 1963.]

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## 726. *Thermochemistry of Vanadium Tetrachloride and the Vanadyl Ion.*

By R. G. Cavell and H. C. Clark.

During a thermochemical study of the vanadium fluorides,[1] a value for the heat of hydrolysis of vanadium tetrachloride was required for inclusion in a thermochemical cycle. Ruff and Freidrich [2] found the heat of hydrolysis of vanadium tetrachloride, according to the equation

$$VCl_4(l) + 9/2\ OH^-(aq) + 1/2\ O_2H^-(aq) \longrightarrow VO_3^-(aq) + 5/2\ H_2O + 4Cl^-(aq),$$

to be −161 kcal. mole$^{-1}$. However, this reaction was not applicable since the equation is that for hydrolysis in an alkaline peroxide solution, while the present study has been concerned with hydrolysis in distilled water. Measurements have therefore been made of the heat of hydrolysis of vanadium tetrachloride in water, and the previously unknown heat of formation of the vanadyl ion, $VO^{2+}$, has been calculated.

*Experimental.*—Vanadium tetrachloride was prepared by direct chlorination of vanadium metal at 300—350°, followed by distillation of the product in an all-glass still, the fraction of b. p. 152—154° (lit.,[3] 154°) being collected (Found: Cl, 73·5; V, 26·4. Calc. for $VCl_4$: Cl, 73·6; V, 26·4%).

The calorimeter used in the determination of the heat of hydrolysis will be described elsewhere.[1] The weighed sample was contained in a glass bulb of about 3 c.c. capacity, with a fragile glass tip at the bottom and a break-seal at the top. The break-seal was sealed to a 25 cm. length of 8-mm. glass tubing and the sample container was then inserted into the hollow shaft of the calorimeter stirrer so that the top of the long 8 mm. tube emerged from the hollow

[1] Cavell and Clark, unpublished results.
[2] Ruff and Freidrich, *Z. anorg. Chem.*, 1914, **89**, 279.
[3] Simons and Powell, *J. Amer. Chem. Soc.*, 1945, **67**, 75.

shaft. The bulb containing the vanadium tetrachloride was then immersed in the calorimeter vessel, which contained a tared amount of water, and the system allowed to reach thermal equilibrium. A slight pressure of nitrogen was applied through the 8-mm. tube, the break-seal was broken, and, by jerking the sample tube upwards against the end of the stirrer shaft, the fragile tip of the sample bulb was broken. After the nitrogen pressure had forced the tetrachloride into the water, the pressure was released so that water flowed back into the sample container to remove any last traces of the tetrachloride.

Four determinations of the heat of hydrolysis were made. The specific heat of each resultant vanadyl chloride solution was determined immediately after the hydrolysis experiment and the average value for six determinations, 0·980 ± 0·005 cal. g.$^{-1}$ deg.$^{-1}$, was used in the subsequent calculations. The solutions were analysed after each experiment and the results were in satisfactory agreement with the theoretical value of 26·4% of vanadium expected for vanadium tetrachloride.

| | Wt. $VCl_4$ (g.) | Wt. water (g.) | Water equiv. (cal. deg.$^{-1}$) | $\Delta T$ (°C) | Vanadium concn. in soln. (%) | Heat liberated by $VCl_4$ (cal.) | Heat liberated per mole of $VCl_4$ (cal.) |
|---|---|---|---|---|---|---|---|
| 1. | 2·5098 | 900·0 | 99·0 | 0·899 | 26·6 | 884·1 | 67,994 |
| 2. | 2·3686 | 900·0 | 95·3 | 0·858 | 27·0 | 840·5 | 68,488 |
| 3. | 2·5000 | 900·0 | 95·3 | 0·903 | 26·6 | 884·7 | 68,302 |
| 4. | 2·0053 | 900·0 | 95·3 | 0·740 | 26·4 | 724·9 | 69,650 |

The average heat of hydrolysis of vanadium tetrachloride is $\Delta H_{hyd} = -68{,}630$ cal. mole$^{-1}$ with a standard deviation of ±440 cal. Unevaluated errors probably double this error, hence the results are considered reliable to ±1000 cal. Heats of solution have not been corrected to infinite dilution, but such correction would contribute not more than 0·1 kcal. mole$^{-1}$.

*Discussion.*—Assuming that the hydrolysis of vanadium tetrachloride in water proceeds according to the equation

$$VCl_4(l) + H_2O(l) \longrightarrow VO^{2+}(aq) + 2H^+(aq) + 4Cl^-(aq),$$

the heat of this reaction can be combined with the standard heat of formation of vanadium tetrachloride,[4] and with other thermochemical data,[5] to complete the thermochemical cycle giving the standard heat of formation of the $VO^{2+}(aq)$ ion. The heat of formation of the vanadyl ion at 298°K is $\Delta H_f°[VO^{2+}(aq)] = -113 \pm 1$ kcal. mole$^{-1}$. The standard free energy of formation of $VO^{2+}(aq)$ obtained from measurements of electrochemical cell potentials [6] is $\Delta G_f°[(VO^{2+}(aq)] = -109$ kcal. mole$^{-1}$. Hence the entropy change of formation, $\Delta S_f°$, has a value of −13·4 e.u. at 298°K. The corresponding value for the vanadate ion is not known, so comparisons are not possible.

By addition of the equation for the hydrolysis of vanadium tetrachloride in an alkaline peroxide solution [2] to the reverse of the equation for the present hydrolysis reaction, the equation

$$VO^{2+}(aq) + 5/2\ OH^-(aq) + 1/2\ O_2H^-(aq) \longrightarrow VO_3^-(aq) + 3/2\ H_2O(l)$$

is obtained. This represents the oxidation of quadrivalent vanadium to quinquevalent vanadium in alkaline peroxide solution, and $\Delta H$ for this reaction is −92·4 kcal. mole$^{-1}$.

The support of the U.S. Office of Naval Research is gratefully acknowledged, and also the award of a studentship (to R. G. C.) by the National Research Council, Ottawa.

Department of Chemistry, University of British Columbia,
Vancouver 8, B.C., Canada. [*Received, January 14th*, 1963.]

[4] Gross, personal communication.
[5] "Selected Values of Chemical Thermodynamic Properties," Circular 500, National Bureau of Standards, Washington, 1952.
[6] Latimer, "Oxidation Potentials," 2nd edn., Prentice-Hall, New York, 1952.

## 727. *Ruthenium Tetrafluoride.*

By J. H. Holloway and R. D. Peacock.

Before the present work three binary fluorides of ruthenium were known. The hexafluoride has only recently been discovered.[1] The pentafluoride was prepared in 1925 [2] but its properties were not thoroughly reinvestigated until our own recent work.[3] In 1952 Aynsley, Peacock, and Robinson discovered that iodine or sulphur reduced the pentafluoride at 150—200° to ruthenium trifluoride.[4] The crystal structure was determined by Hepworth *et al.*[5] and they observed that there were changes in the size of the unit cell according to the proportions of iodine and sulphur used in the reaction. They considered that the " ideal " ruthenium trifluoride was formed only when an excess of the reducing agent was employed and that otherwise some ruthenium atoms remained in the quadrivalent or quinquevalent state. It seemed reasonable to us, therefore, to expect that reaction of ruthenium pentafluoride with iodine under milder conditions might result in the formation of the tetrafluoride.

When an excess of ruthenium pentafluoride, dissolved in pure iodine pentafluoride, is allowed to react with iodine, reduction takes place according to the equation: $10RuF_5 + I_2 \longrightarrow 10RuF_4 + 2IF_5$. Little heat is evolved, and, after the iodine pentafluoride and the excess of ruthenium pentafluoride have been removed, a non-volatile, sandy-yellow residue remains which is pure ruthenium tetrafluoride. The compound is blackened immediately by moist air, and so is much more reactive than the trifluoride, but it can be conveniently handled in Pyrex glass apparatus under dry conditions. It reacts violently with water, depositing ruthenium dioxide. No tetroxide is formed (cf. $RuF_5$). Samples of the tetrafluoride heated to 280° in Pyrex glass do not melt, but above 280° they attack glass, forming a volatile compound and a black residue which is probably ruthenium dioxide. When prepared in this way the tetrafluoride is poorly crystalline, but *X*-ray diffraction powder photographs suggest that it may have a simple structure.

The magnetic properties of ruthenium tetrafluoride, over a temperature range 90—300°K, are presented in the Table. The observed effective magnetic moment at ordinary temperatures is higher than the spin-only value for two unpaired electrons (μ 2·83 B.M.)

Magnetic moment of ruthenium tetrafluoride.

| Temp. (K) ... | 291° | 281° | 270° | 259° | 251° | 243° | 236° | 232° | 225° | 211° | 207° |
|---|---|---|---|---|---|---|---|---|---|---|---|
| $10^6\chi_A$ ..... | 3959 | 4067 | 4184 | 4321 | 4457 | 4560 | 4701 | 4775 | 4882 | 5121 | 5228 |
| $\mu_{eff}$ ..... | 3·04 | 3·03 | 3·01 | 2·99 | 2·99 | 2·98 | 2·98 | 2·98 | 2·97 | 2·94 | 2·94 |
| Temp. (K) ... | 184° | 178° | 164° | 156° | 143° | 137° | 123° | 116° | 104° | 101° | 88° |
| $10^6\chi_A$ ..... | 5701 | 5853 | 6189 | 6389 | 6780 | 6926 | 7414 | 7638 | 8599 | 8072 | 8941 |
| $\mu_{eff}$ ..... | 2·90 | 2·86 | 2·85 | 2·83 | 2·79 | 2·76 | 2·70 | 2·66 | 2·68 | 2·56 | 2·51 |

Curie temperature ($\theta$) = 74°.

and also higher than the moment expected from the Kotani theory for a $d\varepsilon_4$ ruthenium compound [6] such as the complex $K_2RuF_6$ for which the moment, measured over the same temperature range, reaches a maximum of about 2·9 B.M. at 200°K.[7] The Kotani theory requires that a plot of $\mu_{eff}$ against $\sqrt{T}$ should give a straight line for the $d\varepsilon_4$ configuration, and this requirement is not met by our measurements. If six-co-ordination of ruthenium atoms is present in the tetrafluoride, as in the pentafluoride [3] and trifluoride,[4] it follows that four out of six fluorine atoms will be bonded to more than one metal atom. Such

[1] Claassen, Selig, Malm, Chernick, and Weinstock, *J. Amer. Chem. Soc.*, 1961, **83**, 2390.
[2] Ruff and Vidic, *Z. anorg. Chem.*, 1925, **143**, 171.
[3] Holloway and Peacock, *J.*, 1963, 527.
[4] Aynsley, Peacock, and Robinson, *Chem. and Ind.*, 1952, 1002.
[5] Hepworth, Jack, Peacock, and Westland, *Acta Cryst.*, 1957, **10**, 63.
[6] Kotani, *J. Phys. Soc. Japan*, 1949, **4**, 293; Griffith, *Trans. Faraday Soc.*, 1958, **54**, 1109.
[7] Earnshaw, Figgis, Lewis, and Peacock, *J.*, 1961, 3132.

fluorine bonds might well be the cause of the observed departure from theory. Unfortunately the magnetic moment of the trifluoride, which is completely fluorine-bonded, has not been measured.

*Experimental.—Reagents.* Iodine pentafluoride was prepared from the elements and purified by distillation under a vacuum.

*Ruthenium tetrafluoride.* Ruthenium pentafluoride (1 g.) was dissolved in freshly purified iodine pentafluoride (5 ml.), and to the yellow-green solution was added a sufficient quantity of dry, resublimed iodine to reduce most of the ruthenium pentafluoride to the quadrivalent state. The mixture was warmed gently for a few minutes to complete the reaction. The iodine pentafluoride and the excess of ruthenium pentafluoride were distilled off under a high vacuum. The residual *ruthenium tetrafluoride* was sealed under a vacuum (Found: Ru, 57·0; F, 42·6%. $RuF_4$ requires Ru, 57·3; F, 42·7%).

*Magnetic moment.* This was determined between 90° and 300°K by the Gouy method; the apparatus was similar to that described by Figgis and Nyholm.[8] The powdered solid was introduced into the sample tube under a vacuum.

*Debye X-ray photographs.* Specimens were mounted in evacuated Pyrex capillaries and photographed in Cu-$K_\alpha$ nickel-filtered radiation on a 19 cm. camera.

*Analyses.* The tetrafluoride was decomposed in 2N-sodium hydroxide. Ruthenium was precipitated as the hydrated dioxide and estimated as metal after reduction by hydrogen. Fluorine was precipitated as lead chloride fluoride and determined as the chloride equivalent by the Volhard procedure.

We are indebted to Imperial Chemical Industries Limited for the loan of a fluorine cell, to the Royal Society for the magnetic balance, and to the Department of Scientific and Industrial Research for a maintenance grant (to J. H. H.).

Department of Chemistry,
The University, Birmingham, 15. [*Received, January 18th,* 1963.]

[8] Figgis and Nyholm, *J.*, 1959, 331.

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## 728. *The Preparation and Properties of Silyl Isoselenocyanate.*

By E. A. V. Ebsworth and M. J. Mays.

Silyl isocyanate has recently been prepared by passage of iodosilane vapour, diluted with nitrogen gas, over silver cyanate.[1] This same technique gives silyl isoselenocyanate from the corresponding silver salt in 70% yield. Attempts to effect the preparation with undiluted iodosilane vapour [2] failed.

Silyl isoselenocyanate is a colourless liquid which polymerises slowly at room temperature in sealed glass apparatus even in the dark; the liquid became yellow in a week and then quickly solidified, suggesting that the polymerisation may be autocatalytic. Heat or irradiation accelerate decomposition; under these conditions, monosilane, silyl cyanide, and disilyl selenide are among the decomposition products. Traces of boron trifluoride or silver selenocyanate also accelerate decomposition at room temperature.

The thermal instability of the compound means that no accurate value of the entropy of vaporisation at the boiling point could be obtained; the value from an extrapolated vapour-pressure curve implies that there may be association in the liquid phase, and this is to some extent borne out by the large proton-resonance dilution shift, though large dilution shifts are often observed in molecules containing such heavy elements as

[1] Ebsworth and Mays, *J.*, 1962, 4844.
[2] MacDiarmid, *J. Inorg. Nuclear Chem.*, 1956, **2**, 88.

selenium.[2, 3a] The proton-resonance chemical shift and SiH coupling constant are close to those for silyl isothiocyanate.[3b]

Many silyl–nitrogen compounds take up equimolar quantities of boron trifluoride at −78°, forming adducts which decompose irreversibly at higher temperatures.[4] At this temperature silyl isoselenocyanate is a solid and does not react with boron trifluoride; at room temperature the two substances react, but the reaction is complicated by the formation of unreactive polymers containing SiH bonds, so that non-stoicheiometric results are obtained.

Attempts to determine the place of the isoselenocyanate group, –NCSe, in MacDiarmid's conversion series for silyl compounds [5] have been complicated by the instability of silyl isoselenocyanate (like some other analogous silyl compounds) in the presence of certain silver salts. It appears, however, that isoselenocyanate must lie close to bromide in the series. Since isocyanate and isothiocyanate lie appreciably to the right, the shift from thiocyanate to selenocyanate implies either that the energy of the Si–N bond is reduced by the substitution of selenium for sulphur, or that the lattice energy of silver selenocyanate is higher than that of silver thiocyanate. The lower solubility product of silver selenocyanate [6] favours the latter possibility, though both effects may be involved.

At the same time, in these solid–gas reactions the nature of the solid may play an important part in determining the rate at which equilibrium is attained; therefore it is not possible to be sure that the composition of the products of a single experiment represents an equilibrium mixture. We have tried to avoid this difficulty by studying each conversion in both directions, *i.e.*, by treating the silver salt AgX with the silyl compound $SiH_3Y$, and AgY with $SiH_3X$; nevertheless, a purely thermodynamic explanation of our results must be regarded with some reserve.

*Experimental.—Preparation.* In a typical experiment a slow stream of nitogen gas, dried by passage through concentrated sulphuric acid and molecular sieve, was bubbled through iodosilane (1·5 g.) at −46°, and then over a mixture of silver selenocyanate and powdered glass. The volatile products were condensed at −196°, while the non-condensable gases were pumped away continuously. From the volatile products, *silyl isoselenocyanate* (0·93 g.) was obtained (Found: N, 10·5; Se, 58·1; SiH, 2·3%; *M*, 135. $CH_3NSeSi$ requires N, 10·3; Se, 58·1; SiH, 2·2%; *M*, 136). It was the only volatile product condensing in a trap at −46°. The other volatile products included hydrogen cyanide and silane (identified spectroscopically). The yield based on the amount of silyl iodide taken was 70%.

*Physical properties.* Silyl isoselenocyanate melts at −15·1° ± 0·5°; the estimated b. p. (extrapolated over 50°) is 111° ± 5°; between 0° and 60° the vapour pressure is related to the temperature by the expression $\log_{10} p$ (mm.) = 8·968 − 2345/*T* (9·6 mm. at 20°). The latent heat of vaporisation between 0° and 60° is 10,800 cal. mole$^{-1}$, and Trouton's constant (estimated from the extrapolated vapour-pressure curve) is 28 cal. mole$^{-1}$ degree$^{-1}$. Infrared bands were observed at 2210, 2068, 935, 868, and 710 cm.$^{-1}$; the infrared spectrum being studied under high resolution.

The nuclear magnetic resonance spectrum was recorded on a Varian Associates V 4300B spectrometer, with flux stabiliser and sample spinning, operating at 40 Mc./sec. The proton-resonance spectrum of the compound in cyclohexane consisted of the expected single peak with satellites due to $^{29}SiH$ groups; the chemical shift $\tau$ measured relative to cyclohexane as solvent is $\tau$ 5·33 for 95% solution and 5·50 for 5% solution, giving $\tau$ = 5·52 ± 0·02 p.p.m. for infinite dilution; the $^{29}SiH$ coupling constant is 243·2 ± 0·4 c./sec.

In the vapour phase the compound had $\lambda_{max.}$ = 268 ($\log_{10} \varepsilon$ 3·29) and 199 mμ ($\log_{10} \varepsilon > 4·3$); no vibrational fine structure was resolved on either of these bands.

*Decomposition.* When a sample of silyl isoselenocyanate was sealed in a Pyrex tube, the

[3] (*a*) Bothner-By and Glick, *J. Chem. Phys.*, 1957, **26**, 1647; (*b*) Ebsworth and Turner, *J. Phys. Chem.*, 1963, **67**, 805.

[4] Sujishi and Witz, *J. Amer. Chem. Soc.*, 1957, **79**, 2447; Ebsworth and Emeléus, *J.*, 1958, 2150; Evers, Freitag, Kriner, MacDiarmid, and Sujishi, *J. Inorg. Nuclear Chem.*, 1960, **13**, 239.

[5] MacDiarmid, *Quart. Rev.*, 1956, **10**, 208.

[6] Birckenbach and Huttner, *Z. anorg. Chem.*, 1930, **190**, 26.

colourless liquid became yellow after one day, underwent no apparent further change for a week, and then rapidly solidified to a brick-red solid. No non-condensable gas had been formed and the only volatile product was a trace of silane (identified spectroscopically). Warming the brick-red solid to 100° gave further traces of silane and hydrogen cyanide (identified spectroscopically). The residue was shown qualitatively to contain Si–H bonds. These results were confirmed in a second experiment in which, however, the brick-red solid appeared after 2 days.

After 1 hr. at 80° in a sealed tube, silyl isoselenocyanate (0·122 g.) gave a spongy pale orange solid. A trace of hydrogen had been formed and the other volatile products were small quantities of silane, silyl cyanide, disilyl selenide, and hydrogen cyanide (identified by infra-red and proton-resonance spectra). No starting material was recovered: the solid contained 90% of the selenium originally present in the isoselenocyanate.

When a sample was irradiated with ultraviolet light, a red deposit was soon formed on the walls of the Pyrex tube; small quantities of silane, silyl cyanide, disilyl selenide, and hydrogen cyanide, with some unchanged isoselenocyanate (all identified spectroscopically), were obtained after an hour.

*Reactions.* (*a*) Boron trifluoride (1·654 mmole) was recovered quantitatively when kept with silyl isoselenocyanate (0·535 mmole) for 18 hr. at −78°; the absence of silyl fluoride was confirmed spectroscopically and by alkaline hydrolysis of the boron trifluoride. When the white solid was allowed to warm to room temperature, it melted to a colourless liquid, which immediately deposited a red solid; 0·128 mmole of volatile products recovered at this stage was shown spectroscopically to be a mixture of silyl cyanide and hydrogen cyanide. When silyl isoselenocyanate (0·548 mmole) was kept with boron trifluoride (1·382 mmole) for 4 hr. at room temperature, the volatile products were identified spectroscopically as a mixture of silyl fluoride and boron trifluoride; on the assumption that these substances alone are present, this mixture was shown by hydrolysis to consist of 1·237 mmole of boron trifluoride and 0·355 mmole of silyl fluoride, corresponding to consumption of 0·145 mmole of boron trifluoride. The red solid left in the reaction tube effervesced vigorously on treatment with cold sodium hydroxide solution.

(*b*) Silyl isoselenocyanate (0·733 mmole) was kept with water (1·872 mmole) at room temperature (½ hr.). A thick red deposit was quickly formed in the reaction tube, and non-condensable gas (0·236 mmole) was evolved. Fractionation of the volatile products yielded disiloxane (0·235 mmole) (v. p. at −80°, 19 mm.; lit.,[7] 19 mm.), and a mixture of water and hydrogen cyanide (identified spectroscopically).

(*c*) (i) When disilyl sulphide (103·6 mg.) was passed as vapour over silver selenocyanate (5·0 g.) the silver salt blackened and hydrogen cyanide (12 mg.) was recovered (Found: *M*, 28·5; v. p. at −46°, 14 mm. Calc: *M*, 27; v. p.,[8] 10 mm.; identification confirmed spectroscopically), with traces of silane and disiloxane (identified spectroscopically).

In a similar experiment with only 1 g. of the silver salt, silyl isoselenocyanate (Found: v. p. at 20°, 9·5 mm.; identification confirmed spectroscopically) and some unchanged disilyl sulphide (identified spectroscopically) were recovered in addition to the above products.

No measurable quantity of disilyl sulphide was obtained when the reaction was carried out in the reverse direction.

(ii) When silyl bromide (682 mg.) was passed as vapour over silver selenocyanate (10 g.) the reaction tube became warm and the solid yellow-red. Silyl isoselenocyanate (217 mg.) (Found: v. p. at 21°, 11 mm. Calc.: 10 mm.; identification confirmed spectroscopically) was recovered. This represents a 26% yield based on the silyl bromide taken. The remaining volatile products consisted of 40 mg. of a mixture of silane, silyl cyanide, hydrogen cyanide, and unchanged silyl bromide (identified spectroscopically).

When silyl isoselenocyanate (189 mg.) was passed over silver bromide (5 g.) a mixture of hydrogen cyanide and silyl bromide (19·9 mg.) (*M*, 102; identification confirmed spectroscopically) was recovered, with unchanged silyl isoselenocyanate (31·2 mg.) (Found: v. p. at 20°, 9·4 mm.) and the usual decomposition products of silyl isoselenocyanate.

(iii) When silyl isoselenocyanate (156 mg.) was passed over silver chloride (5 g.), silyl chloride (23·1 mg.) (Found: *M*, 67; v. p. at −66°, 120 mm. Calc.: *M*, 66·5; v. p.,[9] 123 mm.) was

[7] Stock, Somieski, and Wintgen, *Ber.*, 1917, **50**, 1754.
[8] Lewis and Schutz, *J. Amer. Chem. Soc.*, 1934, **56**, 1002.
[9] Stock and Somieski, *Ber.*, 1919, **52**, 695.

recovered, with the usual decomposition products of silyl isoselenocyanate and 13·9 mg. of starting material. When the reaction was carried out in the reverse direction, 98% of the silyl chloride was recovered unchanged.

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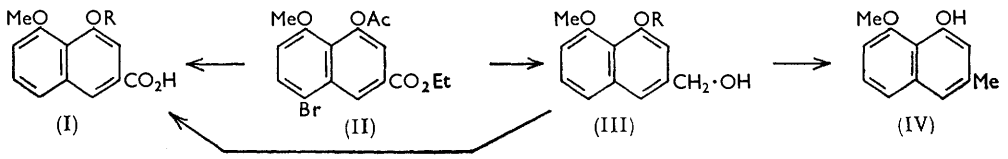
## 729. *Syntheses of Eleutherolic Acid.*

By B. O. HANDFORD and W. B. WHALLEY.

ELEUTHEROLIC ACID (4-hydroxy-5-methoxy-2-naphthoic acid) (I; R = H) is a key intermediate in the degradation and synthesis of the benzophthalide, (+)-eleutherol, isolated [1] from the tubers of *Eleutherine bulbosa* (Mill) Urb. We describe two syntheses of eleutherolic acid which, in contrast to the only process previously available, make this acid readily accessible.

Condensation of 2-bromo-5-methoxybenzaldehyde with ethyl succinate, followed by cyclisation, gives ethyl 4-acetoxy-8-bromo-5-methoxy-2-naphthoate (II) which is reduced by lithium aluminium hydride to 3-hydroxymethyl-8-methoxy-1-naphthol (III; R = H). Oxidation of the benzyl ether (III; R = Ph·$CH_2$) yields the acid (I; R = Ph·$CH_2$) which on debenzylation gives eleutherolic acid (I; R = H).




Alternatively, catalytic reduction of the naphthoate (II) with Raney nickel in alkaline solution, followed by hydrolysis of the crude ester, gives eleutherolic acid in high yield.

Raney nickel reduction of the alcohol (III; R = H) gives the hitherto unknown 8-methoxy-3-methyl-1-naphthol (IV) (cf. Covell, King, and Morgan [2]).

*Experimental.*—*2-Bromo-5-methoxybenzaldehyde.* This was prepared more readily and in much higher yield by bromination of *m*-methoxybenzaldehyde than by methylation of 2-bromo-5-hydroxybenzaldehyde (cf. Pschorr [3]). The calculated quantity of 2N-bromine–chloroform solution was added to *m*-methoxybenzaldehyde (86 g.) in chloroform (1 l.), and the mixture was refluxed for 6 hr. Then the solvent was removed under reduced pressure. When purified by steam-distillation or by crystallisation from light petroleum (b. p. 40—60°) 2-bromo-5-methoxybenzaldehyde formed needles (82 g.), m. p. 76°.

*4-Hydroxy-5-methoxy-2-naphthoic acid* (I; R = H). (*a*) Condensation of 2-bromo-5-methoxybenzaldehyde (33 g.) with ethyl succinate (80 ml.) by means of sodium hydride (9·9 g.), followed by cyclisation of the resultant crude ethyl hydrogen 2-bromo-5-methoxybenzylidenesuccinate, as previously described,[4] gave *ethyl 4-acetoxy-8-bromo-5-methoxy-2-naphthoate* which

[1] Schmid, Meijer, and Ebnother, *Helv. Chim. Acta*, 1950, **33**, 595; Schmid, Ebnother, and Burger, *ibid.*, p. 609; Schmid and Ebnother, *ibid.*, 1951, **34**, 1041; Haber, Ebnother, and Schmid, *ibid.*, 1956, **39**, 1529.
[2] Covell, King, and Morgan, *J.*, 1961, 702.
[3] Pschorr, *Annalen*, 1912, **391**, 23.
[4] Loder, Mongolsuk, Robertson, and Whalley, *J.*, 1957, 2233.

separated from alcohol in yellow prisms (11·7 g.), m. p. 114° (Found: C, 52·4; H, 4·2. $C_{16}H_{15}BrO_5$ requires C, 52·3; H, 4·1%).

This ester (19 g.) was extracted during 50 hr. from a Soxhlet thimble by boiling ether (2·5 l.) containing lithium aluminium hydride (50 g.). After isolation in the usual manner, *3-hydroxymethyl-8-methoxy-1-naphthol* separated from benzene–light petroleum (b. p. 60—80°) in needles (7·6 g.), m. p. 135° (Found: C, 70·4; H, 5·9; OMe, 14·9. $C_{11}H_9O_2$·OMe requires C, 70·6; H, 5·9; OMe, 15·2%).

Raney nickel alloy (10 g.) was added gradually, with agitation, to a solution of this naphthol (4·6 g.) in 10% aqueous sodium hydroxide (150 ml.) at 100°. When reaction ceased the solid precipitate was collected, washed, and exhaustively extracted with ether. Evaporation of the extract furnished *8-methoxy-3-methyl-1-naphthol* which formed prisms (1·4 g.), m. p. 91° [from light petroleum (b. p. 60—80°)], $\lambda_{max.}$ 230, 304, 319, and 333 mμ (log ε 4·78, 3·80, 3·80, and 3·87, respectively) (Found: C, 76·6; H, 6·5; OMe, 16·4. $C_{11}H_9O$·OMe requires C, 76·6; H, 6·4; OMe, 16·5%).

Prepared by reaction of 3-hydroxymethyl-8-methoxy-1-naphthol (6 g.) with benzyl bromide (5·1 g.) in boiling acetone (500 ml.) containing potassium carbonate (25 g.) during 48 hr., *1-benzyloxy-3-hydroxymethyl-8-methoxynaphthalene* separated from benzene in needles, m. p. 140°, in almost quantitative yield (Found: C, 77·1; H, 6·2. $C_{19}H_{18}O_3$ requires C, 77·5; H, 6·2%).

A solution of potassium permanganate (0·9 g.) in water (25 ml.) was added gradually to a stirred solution of this benzyl ether (1 g.) in acetone (250 ml.). Next day the mixture was clarified with sulphur dioxide and poured into water (1 l.) at 0°. The precipitate crystallised from acetic acid, to yield *4-benzyloxy-5-methoxy-2-naphthoic acid* in needles (0·6 g.), m. p. 129° (Found: C, 73·5; H, 5·1. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2%).

Debenzylation of this acid (0·9 g.) in acetic acid (45 ml.) containing hydrochloric acid (2 ml.) occurred during 2 hr. at 100°; then the mixture was added to water (500 ml.) at 0°. From methanol 4-hydroxy-5-methoxy-2-naphthoic acid formed cream-coloured needles (0·5 g.), m. p. 250—251° (decomp.), identical (m. p. and mixed m. p.) with an authentic specimen and having the requisite infrared spectrum (Found: C, 66·0; H, 4·7. Calc. for $C_{12}H_{10}O_4$: C, 66·1; H, 4·6%).

(*b*) A solution of ethyl 4-acetoxy-8-bromo-5-methoxy-2-naphthoate (1 g.) in alcohol (300 ml.) containing Raney nickel (0·2 g.) and 2N-sodium hydroxide (3 ml.) was shaken in hydrogen for 3 hr. (absorption, 72 ml.; calc., 70 ml.). The filtered solution was made alkaline by addition of potassium hydroxide (6 g.), refluxed for 12 hr., and poured into excess of ice-cold 2N-hydrochloric acid. Purification of the precipitate from methanol gave 4-hydroxy-5-methoxy-2-naphthoic acid in almost quantitative yield, identical with the product prepared by method (*a*).

After removal of the nickel, steam-distillation, adjustment of the pH, and removal of the alcohol under reduced pressure gave *ethyl 4-hydroxy-5-methoxy-2-naphthoate*, plates (from a large volume of water), m. p. 88° (Found: C, 68·2; H, 5·6. $C_{14}H_{14}O_4$ requires C, 68·3; H, 5·7%).

The ultraviolet absorption spectra were determined for alcohol solutions in a Unicam S.P. 500 spectrophotometer. The analyses were by Mr. C. Tomlinson, Mr. D. Newman, and their associates of this Department. The work was carried out during the tenure of a Smith, Kline and French Laboratories Research Grant (by B. O. H.). Professor H. Schmid (Zürich) kindly supplied the authentic 4-hydroxy-5-methoxy-2-naphthoic acid.

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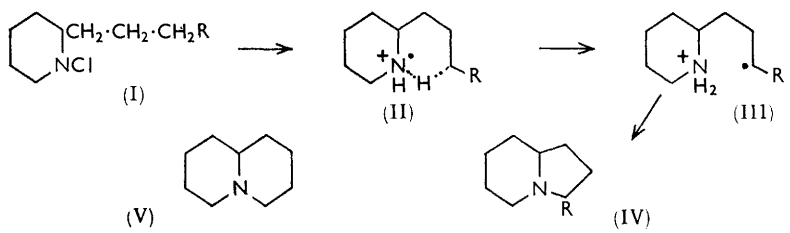
## 730. *Octahydro-3-methylindolizine.*

By M. F. Grundon and B. E. Reynolds.

Octahydroindolizine (IV; R = H) was obtained[1] by heating 1-bromo-2-propylpiperidine (*N*-bromoconiine) with concentrated sulphuric acid, but the reaction has not been used for the preparation of substituted octahydroindolizines, perhaps because of the poor yield obtained in the earlier experiment. In accord with recent views on the Hofmann–Freytag–Loeffler reaction,[2] the formation of octahydroindolizines (I—IV) involves abstraction of hydrogen from a δ-carbon atom and it should proceed readily since the preferred six-membered ring transition state (II) can be accommodated easily. However, the reaction of 1-bromo-2-propylpiperidine is an unfavourable example because it demands the removal of hydrogen from a methyl group. Terminal substitution of the propyl group should facilitate the formation of an octahydroindolizine. Further, a competitive reaction leading to an octahydroquinolizine (V) is unlikely if the piperidine does not contain an ε-methylene or methine group. We have tested these predictions by studying the irradiation of 2-n-butyl-1-chloropiperidine (I; R = Me).




2-n-Butylpiperidine and *N*-chlorosuccinimide afforded 2-n-butyl-1-chloropiperidine, which was transformed by irradiation in sulphuric acid solution into octahydro-3-methylindolizine (IV; R = Me) (64%). Leonard and Pines[3] prepared the latter product by reduction of perhydro-3-methylindolizin-2-one and showed that the racemates (A and B) were formed in the ratio 9 : 1. Reductive rearrangement of perhydroquinolizin-3-one also produced racemate A predominantly.[3] In contrast, chromatography of our octahydro-3-methylindolizine on alumina gave racemate B as the major component (76%) and furnished racemate A in only 2% yield. The isomers were identified by comparing their picrolonates with authentic samples. The Hofmann–Freytag–Loeffler reaction leads, therefore, to a promising stereospecific synthesis of 3-substituted octahydroindolizines.

Fractional crystallisation of the crude picrolonate and vapour-phase chromatography of the total irradiation product suggested that octahydroquinolizine (V) was absent, but since the latter technique failed to detect the presence of racemate A of octahydro-3-methylindolizine the formation of a small percentage of octahydroquinolizine is not excluded.

*Experimental.*—*2-n-Butyl-1-chloropiperidine.* A mixture of 2-n-butyl-piperidine (9·87 g.), *N*-chlorosuccinimide (9·5 g.), and ether (250 c.c.) was stirred under nitrogen for 24 hr. Water was added, and the ether solution was separated and evaporated. Distillation of the residue gave *2-n-butyl-1-chloropiperidine* (8·7 g., 71%), b. p. 83—85°/5·5 mm., $n_D^{20}$ 1·4785 (Found: C, 61·3; H, 9·8. $C_9H_{18}ClN$ requires C, 61·5; H, 10·3%).

*Octahydro-3-methylindolizine.* 2-n-Butyl-1-chloropiperidine (5·84 g.) was added to 80% aqueous sulphuric acid (70 c.c.) at 0°, and the solution under nitrogen was irradiated with ultraviolet light for 20 hr. with shaking, and then ice and water were added. The solution was

[1] Hofmann, *Ber.*, 1885, **18**, 109.
[2] Wawzonek and Culbertson, *J. Amer. Chem. Soc.*, 1960, **82**, 441; Corey and Hertler, *ibid.*, p. 1657; Barton and Morgan, *J.*, 1962, 622.
[3] Leonard and Pines, *J. Amer. Chem. Soc.*, 1950, **72**, 4931.

saturated with potassium hydroxide and extracted with ether continuously for 60 hr. The ether was evaporated. Vapour-phase chromatography of the residue (Silicone; 100°) gave a single peak (retention time, 11·5 min.), and distillation furnished octahydro-3-methylindolizine (2·98 g., 64%), b. p. 40—50° (bath)/16 mm., $n_D^{22}$ 1·4700.

A sample (937 mg.) was separated by chromatography on alumina [3] into racemate A (22 mg., 2%) and racemate B (702 mg., 75%). Racemate A gave a picrolonate in orange prisms (from ethanol), m. p. 209—213° (decomp.), undepressed on admixture with an authentic sample of m. p. 210—214° (decomp.). The picrolonate of racemate B crystallised from ethanol in yellow rods, m. p. 168—169°, alone or mixed with an authentic sample of the same m. p. (Found: C, 56·4; H, 6·2. Calc. for $C_{19}H_{25}N_5O_5$: C, 56·6; H, 6·3%).

The authors thank Professor N. J. Leonard for samples of octahydro-3-methylindolizine picrolonates.

THE QUEEN'S UNIVERSITY OF BELFAST, N. IRELAND. [*Received, January 25th,* 1963.]

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## 731. 3-*Methoxy*-4-*nitrophenylacetic Acid and Related Compounds.*

By A. A. R. SAYIGH, HENRI ULRICH, and J. RUBINFELD.

WE here report the first synthesis of 3-methoxy-4-nitrophenylacetic acid, the isomeric 3-methoxy-2-nitro- and 5-methoxy-2-nitro-acid being known.[1,2]

Nitration of *m*-methoxyphenylacetic acid under conditions favouring *ortho*-nitration gave the 5-methoxy-2-nitro-acid in 35% yield and an inseparable mixture of the 3-methoxy-4- and (mainly) the 3-methoxy-2-nitro-isomer.

The second approach was a vain attempt to effect methoxide displacement of the bromine from the previously unknown 3-bromo-4-nitrophenylacetic acid or its ethyl ester, prepared from 4-amino-3-bromophenylacetic acid [3] and its ethyl ester, respectively, by Emmons's method.[4]

We synthesized 3-methoxy-4-nitrophenylacetic acid from a product of nitration of *m*-methoxybenzoic acid. Our nitration results are in disagreement with those of Froelicher and Cohen.[5] They reported predominant formation of the 4-nitro- over the 2-nitro-acid, but we have found a 2 : 1 ratio in favour of the latter. Froelicher and Cohen assumed material of m. p. 208—211° to be 3-methoxy-4-nitrobenzoic acid, but reported no mixed m. p. with Rieche's product.* We find this material to be a mixture of the isomers, as shown by infrared studies as well as fractional crystallization; pure 3-methoxy-4-nitrobenzoic acid melted at 232—233°, and the pure 2-nitro-isomer melted at 258—259° (cf. refs. 6 and 7).

These two benzoic acids were converted into the corresponding phenylacetic acids by the Arndt–Eistert method, Newman and Beal's improvement [8] of the Wolff rearrangement procedure being used.

*Experimental.—Nitration of* m-*methoxyphenylacetic acid.* Fuming nitric acid (54 g.) in glacial acetic acid (150 ml.) was added at −20° to *m*-methoxyphenylacetic acid (82·3 g., 0·49 mole) in acetic anhydride (500 ml.), and the temperature was kept at −15° to −20° for 2 hr.

* Rieche,[6] made the two acids by nitration of *m*-methoxybenzaldehyde followed by oxidation. Chakravarti *et al.*[7] prepared the pure 4-nitro-acid, m. p. 233°, by oxidation of 3-methoxy-4-nitrocinnamic acid.

[1] Blaikie and Perkin, *J.*, 1924, 296.
[2] Blair and Newbold, *J.*, 1955, 2871.
[3] Gabriel, *Ber.*, 1882, **15**, 834.
[4] Emmons, *J. Amer. Chem. Soc.*, 1954, **76**, 3470; 1957, **79**, 5528.
[5] Froelicher and Cohen, *J.*, 1921, **119**, 1425.
[6] Rieche, *Ber.*, 1889, **22**, 2347.
[7] Chakravarti, Ganapati, and Aravamudhachari, *J.*, 1938, 171.
[8] Newman and Beal, III, *J. Amer. Chem. Soc.*, 1950, **72**, 5163.

The solution was concentrated *in vacuo* to achieve separation of a solid (a) (13 g.), which was collected. Addition of water to the filtrate precipitated solid (b) (27·5 g.); when recrystallized from ethanol–water solids (*a*) and (*b*) gave 5-methoxy-2-nitrophenylacetic acid (35 g., 35%), m. p. 176—178° (lit.,[1] 176°), $\lambda_{max.}$ (in Nujol) 5·82, 6·18, 6·3, 6·62, 6·82, 7·25, and 9·2 μ. Concentration of chloroform extracts afforded 58 g. of a mixture (58 g., 56%), m. p. 100—111°, which could not be separated into its components. The infrared spectrum indicated that the mixture consisted mainly of the 2-nitro-acid.

*3-Bromo-4-nitrophenylacetic acid.* To trifluoroacetic acid (30 g.) and 4-amino-3-bromophenylacetic acid (made essentially by Gabriel's procedure [3]) (3·0 g.), 90% hydrogen peroxide (1·8 g.) was added with ice-cooling. The temperature was gradually raised to the b. p. whereupon all the material dissolved. After refluxing for 2 hr. and cooling to room temperature, it was poured on ice. The crude nitro-acid, m. p. 97—101°, was recrystallized from water–acetone, to afford slightly yellow needles of *3-bromo-4-nitrophenylacetic acid* (1·4 g., 41%), m. p. 117—118° (Found: N, 5·6. $C_{10}H_6BrNO_4$ requires N, 5·4%).

*Ethyl 3-bromo-4-nitrophenylacetate.* To 90% hydrogen peroxide (9·9 g.) in methylene chloride (100 ml.), trifluoroacetic anhydride (76 g.) was added with ice-cooling. After removal of the bath, ethyl 4-amino-3-bromophenylacetate (18·8 g.; prepared by saturation of an alcoholic solution of the acid with hydrogen chloride) in methylene chloride (50 ml.) was added dropwise with stirring. After 2 hours' refluxing the mixture was poured into water, and the methylene chloride was separated, washed with water, and dried ($Na_2SO_4$). Evaporation and distillation afforded *ethyl 3-bromo-4-nitrophenylacetate* (14·2 g., 68%), b. p. 173—178°/2 mm., m. p. 42—43° (Found: C, 41·8; H, 3·6; N, 4·7. $C_{10}H_{10}BrNO_4$ requires C, 41·7; H, 3·5; N, 4·9%).

*3-Methoxy-2- and -4-nitrobenzoic acid.* *m*-Methoxybenzoic acid,[9] was nitrated essentially by the procedure of Froelicher and Cohen.[5] The solid obtained (48 g., 74%) was exhaustively extracted with boiling chloroform; the chloroform-insoluble material was recrystallized from absolute ethanol, to yield 3-methoxy-2-nitrobenzoic acid (19·5 g.). Concentration of the chloroform extract deposited a solid which on recrystallization from absolute ethanol gave the same acid (7·8 g.; total 42%), m. p. 258—259° (decomp.) (lit.,[6,7,10] m. p. 251°, 253—255°, 248—250°), $\lambda_{max.}$ (in Nujol) 5·9, 6·3, 6·45, 6·82, 7·23, 7·67, 7·8, 9·45, 11·0, 11·69, 12·22, 13·0, 13·18, and 14·5 μ. Further concentration of the chloroform extract deposited a solid which on recrystallization from 95% ethanol gave 3-methoxy-4-nitrobenzoic acid (15·0 g., 23%), m. p. 232—233° (lit.,[7] 233°), $\lambda_{max.}$ (in Nujol) 5·88, 6·18, 6·25, 6·48, 6·55, 6·8, 7·22, 7·3, 7·62, 7·93, 9·75, 11·3, 11·88, 13·03, and 13·33 μ.

*3-Methoxy-4-nitrophenylacetic acid.* A mixture of 3-methoxy-4-nitrobenzoic acid (13·8 g., 0·107 mole) and thionyl chloride (33 g., 0·28 mole) was heated on a steam-bath for 90 min. The excess of thionyl chloride was removed under reduced pressure and the residue was recrystallized from carbon tetrachloride–ligroin, to yield 3-methoxy-4-nitrobenzoyl chloride (12·1 g., 80%), m. p. 60—62° (lit.,[11] 63—63·5°).

To a solution of diazomethane (from 37 g. of methyl-*N*-nitrosourea) in ether (400 ml.), 3-methoxy-4-nitrobenzoyl chloride (12 g.) in ether (250 ml.) was added during 1 hr. with stirring at 0°. Next morning the ether was evaporated *in vacuo* and the residue was washed with cold ether and ligroin. Thus, ω-diazo-3-methoxy-4-nitroacetophenone (10 g., 81%), m. p. 78—80° (decomp. 110—118°), was obtained.

A filtered solution of silver benzoate (2 g.) in triethylamine (12 g.) was added during 60 min. to a refluxing solution of the diazo-ketone (6·85 g.) in t-butyl alcohol (140 ml.). After 45 minutes' refluxing and addition of charcoal, the solution was filtered hot and evaporated *in vacuo* to a residue which was dissolved in benzene. This was washed with dilute sodium hydrogen carbonate solution and evaporated, yielding a residue which was dissolved in t-butyl alcohol (40 ml.) to which concentrated hydrochloric acid (100 ml.) was added. The mixture was refluxed for 2 hr. with distillation of the solvent and, after addition of water, was extracted with chloroform; the extract was dried and evaporated, leaving a residue which was dissolved in dilute aqueous sodium hydrogen carbonate and acidified with dilute hydrochloric acid, to give an acid (3·5 g.), m. p. 128—130°. Recrystallization from benzene afforded *3-methoxy-4-nitrophenylacetic acid* (3·2 g., 48%), m. p. 130·5—131·5°, $\lambda_{max.}$ (in $CHCl_3$) 5·8, 6·18, 6·25, 6·55,

[9] Graebe, *Annalen*, 1905, **340**, 204.
[10] Ewins, *J.*, 1912, **101**, 544.
[11] Liss, *J. Amer. Chem. Soc.*, 1952, **74**, 4968.

6·8, 7·05, 7·38, 7·6, 7·8, 8·5, 9·68, and 11·82 μ (Found: C, 51·3; H, 4·5; N, 6·8. $C_9H_9NO_5$ requires C, 51·2; H, 4·3; N, 6·6%).

*3-Methoxy-2-nitrophenylacetic acid.* By the above procedure, 3-methoxy-2-nitrobenzoic acid was converted into 3-methoxy-2-nitrophenylacetic acid, m. p. 133—137° (decomp.), in 53% yield. Recrystallization from 1 : 1 ethanol–water gave acid of m. p. 136·5—137° (lit., 137—138°,[1] 136—137° [2]), $\lambda_{max.}$ (in $CHCl_3$) 5·78, 6·18, 6·27, 6·5, 6·75, 6·92, 7·28, 7·78, 9·22, and 11·7 μ.

THE CARWIN COMPANY, DIVISION OF THE UPJOHN COMPANY,
NORTH HAVEN, CONNECTICUT, U.S.A. [*Received, January 28th*, 1963.]

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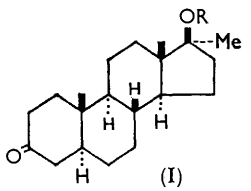
## 732. *The Formylation of Some 5α-Androstan-3-ones.*

By P. J. PALMER.

CLINTON and his co-workers [1] showed that, in the presence of anhydrous sodium methoxide, ethyl formate condensed readily with saturated and αβ-unsaturated 3-keto-steroids in pyridine, to give the corresponding 2-hydroxymethylene derivatives. No evidence was obtained by them for the simultaneous formation of the tautomeric 2-formyl compounds. In contrast, condensation of 17α-methyl-17β-(β-phenylpropionyloxy)-5α-androstan-3-one [2] (I; R = $CO{\cdot}CH_2{\cdot}CH_2Ph$) with ethyl formate under conditions similar to those used by Clinton *et al.*[1] has given, in our hands, both the 2-hydroxymethylene (II; R = $CO{\cdot}CH_2{\cdot}CH_2Ph$) and the 2-formyl compound (III; R = $CO{\cdot}CH_2{\cdot}CH_2Ph$). The structures assigned to these two compounds were based on the following data. The 2-hydroxymethylene compound had maximal ultraviolet absorption at 283 mμ (ε 9110), shifting to 315 mμ (ε 16,200) in 0·1N-alkali, and infrared bands at 3625 and 3495 (OH), 1726 (ester), 1640 (αβ-unsaturated β-hydroxy-ketone), and 1587 (C=O; chelate ring) cm.$^{-1}$. An



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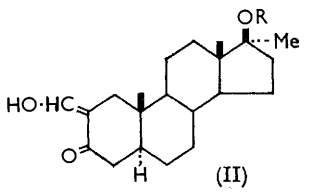

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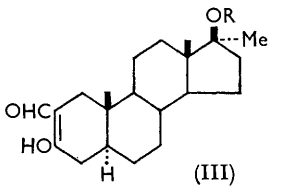

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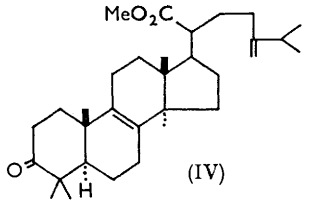

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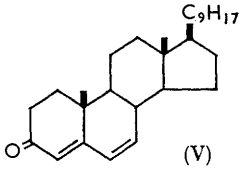


(V)

instantaneous colour reaction was given with ferric chloride. The 2-formyl compound had an ultraviolet absorption maximum at 276 mμ (ε 11,500), shifting in 24 hours in 0·1N-alkali to 297 mμ (ε 12,200), and infrared bands at 3625 and 3435 (OH), 1715 (ester), 1664 (αβ-unsaturated β-hydroxy-aldehyde), and 1577 (C=O; chelate ring) cm.$^{-1}$. A colour developed with ferric chloride after a few seconds. Finally, mineral acid isomerised it to the hydroxymethylene derivative, though the reverse change could not be induced by alkali.

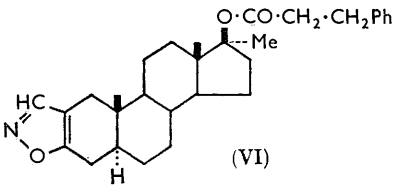
Previous work [3,4] on the formylation of 3-keto-steroids indicated that in the cases of

[1] Clinton, Manson, Stonner, Neumann, Christiansen, Clarke, Ackerman, Page, Dean, Dickinson, and Carabateas, *J. Amer. Chem. Soc.*, 1961, **83**, 1478.
[2] D. D. Evans, D. E. Evans, Lewis, Palmer, and Weyell, *J.*, 1963, 3578.
[3] Holker, Powell, Robertson, Simes, and Wright, *J.*, 1953, 2414.
[4] Tsuda and Nozoe, *Chem. and Pharm. Bull.* (*Japan*), 1959, **7**, 232.

methyl-3-ketoeburic-8-enoate [3] (IV) and ergosta-4,6,22-trien-3-one [4] (V) 2-hydroxymethylene and 2-formyl tautomers were capable of independent existence. There, however, the greater stability of the formyl derivatives was ascribed [1] to the stabilising effect of *gem*-dimethyl groups at C-4 and to additional nuclear double bonds, respectively. The present example is believed to be the first where a simple 3-keto-steroid unsubstituted in the α-position gives rise to both possible tautomers on formylation.

Formylation of 17β-acetoxy-17α-methyl-5α-androstan-3-one (I; R = Ac) under the conditions described gave the expected 2-hydroxymethylene compound (II; R = Ac). No conclusive evidence was obtained for the simultaneous formation of the 2-formyl tautomer (III; R = Ac), though the difficulty experienced in purifying the product could be indicative of its presence.

Condensation of hydroxylamine with the derivative (II; R = $CO{\cdot}CH_2{\cdot}CH_2Ph$) and hydrazine with the derivatives (II; R = Ac or $CO{\cdot}CH_2{\cdot}CH_2Ph$) afforded, respectively, the isoxazole (VI) and the pyrazoles (VII; R = Ac and $CO{\cdot}CH_2{\cdot}CH_2Ph$).

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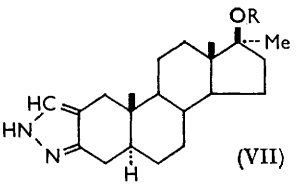


(VII)

*Experimental.*—Rotations are for chloroform solutions. Ultraviolet spectra were determined for ethanol solutions unless otherwise specified, and infrared spectra for chloroform solutions. M. p.s were determined on a Kofler block.

*2-Hydroxymethylene-17α-methyl-17β-(β-phenylpropionyloxy)-5α-androstan-3-one* (II; R = $CO{\cdot}CH_2{\cdot}CH_2Ph$). A solution of 17α-methyl-17β-(β-phenylpropionyloxy)-5α-androstan-3-one (3·946 g., 9·04 mmoles) in anhydrous pyridine (36 ml.) containing freshly distilled ethyl formate (7·2 ml., 90·4 mmoles) was added with stirring to methanol-free sodium methoxide prepared from sodium (416 mg., 18·08 mg.-atoms). The mixture rapidly set to a gel which was set aside under nitrogen for 1·5 hr. at room temperature before dilution with ether. The precipitated sodium salt was collected, washed with ether, dissolved in water, and acidified with dilute sulphuric acid. The product was extracted into ether and the ethereal solution washed to neutrality with water; some solid (682 mg.), m. p. 160—165°, crystallised at this stage and was collected. Concentration of the filtrate and storage at 0° afforded a further crop (2·431 g.) of crystals, m. p. 150—162°. The combined solids were crystallised twice from ether and then from ethyl acetate, to yield the *2-hydroxymethylene derivative*, m. p. 163—165°, $[\alpha]_D$ +38° (*c* 1·06) (Found: C, 77·1; H, 8·4. $C_{30}H_{40}O_4$ requires C, 77·55; H, 8·7%).

*2-Formyl-17α-methyl-17β-(β-phenylpropionyloxy)-5α-androst-2-en-3-ol* (III; R = $CO{\cdot}CH_2{\cdot}CH_2Ph$). In a second experiment conducted essentially as above, crystallisation of the product from methanol, then acetone, and finally light petroleum (b. p. 80—100°) gave the *2-formyl derivative*, m. p. 176—180°, $[\alpha]_D$ +30° (*c* 1·02) (Found: C, 77·3; H, 8·7%).

Treatment of the formyl compound (50 mg.) in acetone (5 ml.) with concentrated hydrochloric acid (2 drops) for 1 hr. at room temperature gave, on precipitation with water, the 2-hydroxymethylene compound (47 mg.), m. p. and mixed m. p. 162—165°. Identity was confirmed by the infrared spectrum.

*17β-Acetoxy-2-hydroxymethylene-17α-methyl-5α-androstan-3-one* (II; R = Ac). 17β-Acetoxy-17α-methyl-5α-androstan-3-one (1·04 g., 3 mmoles) was formylated as in the first example. Isolation of the product as before gave a solid (973 mg.), m. p. 125—145°. Recrystallisation from methanol afforded the required *hydroxymethylene compound* (II; R = Ac), m. p. 132—145° (after drying at 100°/0·1 mm.), $[\alpha]_D$ +43° (*c* 1·02), $\lambda_{max.}$ 282 mμ (ε 8760), $\lambda_{max.}$ (in 0·1N-NaOH) 315 mμ (ε 16,900), $\nu_{max.}$ 3525, 1720, 1636, and 1587 $cm.^{-1}$ (Found: C, 73·4; H, 9·6. $C_{23}H_{34}O_4$ requires C, 73·8; H, 9·2%).

*17α-Methyl-17β-(β-phenylpropionyloxy)-5α-androst-2-eno*[2,3-d]*isoxazole* (VI) (Steroid numbering). Hydroxylamine hydrochloride (104 mg., 1·5 mmoles) was added to a solution of 2-hydroxymethylene-17α-methyl-17β-(β-phenylpropionyloxy)-5α-androstan-3-one (464 mg., 1·0

mmole) in 96% ethanol (25 ml.), and the solution was refluxed for 30 min., then left overnight at room temperature. The precipitate (412 mg.), m. p. 225—235°, was collected. Crystallisation from benzene–light petroleum and then twice from dimethylformamide afforded the *isoxazole* as needles, m. p. 235—242°, $[\alpha]_D$ +37° (*c* 1·115), $\lambda_{max.}$ 228 mμ (ε 5020) (Found: C, 77·7; H, 8·3; N, 3·2. $C_{30}H_{39}NO_3$ requires C, 78·05; H, 8·5; N, 3·0%).

17α-*Methyl*-17β-(β-*phenylpropionyloxy*)-5α-*androstano*[3,2-c]*pyrazole* (VII; R = $CO{\cdot}CH_2{\cdot}CH_2Ph$) (Steroid numbering). 100% Hydrazine hydrate (0·073 ml., 1·5 mmoles) was added to 2-hydroxymethylene-17α-methyl-17β-(β-phenylpropionyloxy)-5α-androstan-3-one (II; R = $CO{\cdot}CH_2{\cdot}CH_2Ph$) (464 mg., 1·0 mmole) in 96% ethanol (15 ml.), and the solution refluxed for 4 hr. Dropwise addition of water to the cooled solution precipitated plates (248 mg.), m. p. 202—205°. Crystallisation from methanol afforded the *pyrazole*, double m. p. 150° and 203—208°. A sample dried at 120°/0·1 mm. had $[\alpha]_D$ +36° (*c* 1·015), $\lambda_{max.}$ 225 mμ (ε 4930), $\lambda_{max.}$ (in 0·01N-HCl) 229 mμ (ε 6340) (Found: C, 78·25; H, 8·8; N, 6·0. $C_{30}H_{40}N_2O_2$ requires C, 78·2; H, 8·75; N, 6·1%).

17β-*Acetoxy*-17α-*methyl*-5α-*androstano*[3,2-c]*pyrazole* (VII; R = Ac) (Steroid numbering). 17β-Acetoxy-2-hydroxymethylene-17α-methyl-5α-androstan-3-one (II; R = Ac) (374·5 mg., 1·0 mmole) was condensed with hydrazine as in the above example to give a solid (357 mg.), m. p. 203—208° (decomp.). Crystallisation from methanol afforded the *pyrazole* as plates, m. p. 218—220° (decomp.), $[\alpha]_D$ +43° (*c* 1·005), $\lambda_{max.}$ 223 mμ (ε 4940), $\lambda_{max.}$ (in 0·01N-HCl) 230 mμ (ε 6830) (Found: C, 74·7; H, 9·2; N, 7·8. $C_{23}H_{34}N_2O_2$ requires C, 74·55; H, 9·25; N, 7·6%).

The author thanks Dr. R. E. Bowman for helpful discussion, Miss E. M. Tanner for interpretation of the physical data, Mr. F. H. Oliver for microanalyses, and Mr. D. J. Weyell for preparation of intermediates.

PARKE, DAVIS AND COMPANY, STAINES ROAD,
HOUNSLOW, MIDDLESEX. [*Received, January 25th,* 1963.]

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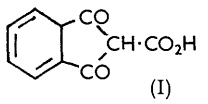
## 733. *Some Lead Salts of* o-*Acetylbenzoic Acid.*

By B. L. HOLLINGSWORTH.

IN an investigation of the lead salts of organic acids, it became of interest to prepare the lead salts of *o*-acetylbenzoic acid. These lead salts have received little attention in the literature. Karslake and Huston [1] described a dihydrate which charred at 130°, but Michael and Gabriel [2] had described the lead salts as syrups which readily formed glasses on dehydration. In the present work, no dihydrate was isolated, nor was any compound which melted or charred at 130°. Three lead salts have been isolated and characterised, the anhydrous normal salt, the normal salt containing one molecule of ethanol of crystallisation, and a basic salt. In addition, two less-defined hydrates have been isolated. The hydrates readily formed uncrystallisable glasses when melted in the presence of a little water.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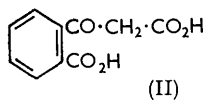
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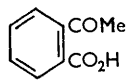
(III)

The required acid (III) was prepared essentially by the methods of Michael and Gabriel [2,3] and Gabriel and Neumann.[4] 1,3-Dioxoindane-2-carboxylic acid (I), prepared by Perkin condensation of phthalic anhydride with acetic anhydride, was hydrolysed to

[1] Karslake and Huston, *J. Amer. Chem. Soc.*, 1909, **31**, 479.
[2] Michael and Gabriel, *Ber.*, 1877, **10**, 392.
[3] Michael and Gabriel, *Ber.*, 1877, **10**, 1522.
[4] Gabriel and Neumann, *Ber.*, 1893, **26**, 951.

*o*-carboxybenzoylacetic acid (II). Decarboxylation to the required acid (III) proceeded smoothly in boiling water.

*Experimental.—Intermediates.* These were prepared by standard methods. M. p.s in parentheses are as recorded in the literature:

1,3-Dioxoindane-2-carboxylic acid, pale yellow needles (from acetic acid), m. p. 290° (decomp.) (Found: C, 63·55; H, 3·15. Calc. for $C_{10}H_6O_4$: C, 63·5; H, 2·6%) [270° (decomp.) [5]] (yield 32%).

*o*-Carboxybenzoylacetic acid, plates (from aqueous alcohol), m. p. 92—93° (decomp.) (Found: C, 57·3; H, 3·9. Calc. for $C_{10}H_8O_5$: C, 57·7; H, 3·8%) [90° (decomp.) [3]] (yield 50%).

*o*-Acetylbenzoic acid, needles (from water) or plates (from benzene), m. p. 119—120° (Found: C, 66·0; H, 4·9. Calc. for $C_9H_8O_3$: C, 65·9; H, 4·9%) (115° [6]) (yield 86%).

*Lead* o-*acetylbenzoate.* (*a*) Lead carbonate (0·28 mole; Pb content 77·3%) was added in portions with stirring to a solution of *o*-acetylbenzoic acid (0·5 mole) in water (1 l.) at 90°. Carbon dioxide was vigorously evolved and, after addition was complete, the solution was boiled for 15 min., and then filtered from lead hydroxide. On cooling, the filtrate deposited small white needles. Recrystallisation from water, and drying over phosphorus pentoxide at room temperature, gave *lead* o-*acetylbenzoate monohydrate* (89%), m. p. 170—175° (decomp.) (sinters from 110°) [Found: C, 38·9; H, 3·0; Pb, 37·4; loss at 100°, 3·4. $(C_9H_7O_3)_2Pb,H_2O$ requires C, 39·2; H, 2·9; Pb, 37·6; $H_2O$, 3·3%]. Drying this hydrate at 50° gave the *hemihydrate* [Found: C, 39·7; H, 2·9; Pb, 38·05. $(C_9H_7O_3)_2Pb,\frac{1}{2}H_2O$ requires C, 39·8; H, 2·8; Pb, 38·2%]. Careful drying of the monohydrate under a high vacuum at 70° gave anhydrous *lead* o-*acetylbenzoate*, needles, m. p. 175° (decomp.) [Found: C, 40·4; H, 2·7; Pb, 38·8. $(C_9H_7O_3)_2Pb$ requires C, 40·5; H, 2·6; Pb, 38·8%].

(*b*) Lead carbonate (0·4 mole) was added in portions with stirring to a solution of *o*-acetylbenzoic acid (0·7 mole) in water (2 l.) at 95°. The solution was boiled for 30 min. after the addition, filtered from lead hydroxide, and concentrated under a vacuum to 250 ml. On cooling, a thick brown syrup was deposited. The aqueous layer was removed, and the syrup was dissolved in hot 80% aqueous ethanol. On evaporation and cooling, a *monoethanol solvate* (80%) was deposited. It formed needles (from aqueous alcohol), m. p. 119—120° (decomp.) [Found: C, 41·4; H, 3·35; Pb, 35·75; loss at 100°, 7·9%. $(C_9H_7O_3)_2Pb,C_2H_5{\cdot}OH$ requires C, 41·4; H, 3·45; Pb, 35·8; $C_2H_5{\cdot}OH$, 8·0%]. After some months in a moist atmosphere, the solvate was decomposed, and the monohydrate, m. p. 170—175° (decomp.), was formed in its place.

*Basic lead* o-*acetylbenzoate.* During the boiling of either lead *o*-acetylbenzoate monohydrate or monoethanol solvate in water at pH 8—9 for 6 hr., white needles were slowly deposited. These were separated and purified by repeated extraction with hot water (yield 40%). The compound was insoluble in the usual organic solvents and water. *Basic lead* o-*acetylbenzoate* formed needles, m. p. >300° (decomp.) [Found: C, 28·5; H, 1·9; Pb, 54·6. $(C_9H_7O_3)_2Pb,PbO$ requires C, 28·6; H, 1·85; Pb, 54·8%].

Attempts to prepare the lead salts by treatment of hot aqueous, aqueous-alcoholic, or alcoholic solutions of *o*-acetylbenzoic acid with lead oxide, or lead acetate and sodium hydrogen carbonate, or by metathesis between sodium *o*-acetylbenzoate and lead acetate or nitrate, proved unsuccessful.

MINISTRY OF AVIATION, EXPLOSIVES RESEARCH AND DEVELOPMENT ESTABLISHMENT,
WALTHAM ABBEY, ESSEX. [*Received, January 30th*, 1963.]

[5] Yale, *J. Amer. Chem. Soc.*, 1947, **69**, 1547.
[6] Benneville, *J. Org. Chem.*, 1941, **6**, 462.

## 734. *Solvent Extraction Studies. Part VI.*[1] *The Viscosities of Extract Solutions of Mineral Acids in Tri-n-butyl Phosphate and Di-isopropyl Ketone.*

By D. G. Tuck.

Extract solutions of some mineral acids in basic organic solvents show comparatively large increases in viscosity with increasing concentration of acid. Earlier work [2,3] on certain tri-n-butyl phosphate (TBP) systems has now been extended to include all those acids on which there is information from solvent-extraction experiments about the nature of the species present in the organic phase.[1,4]

Fig. 1 shows the viscosity of extract solutions of five acids in tributyl phosphate. Where comparable, the present results agree with those of Hesford and McKay,[2] who also

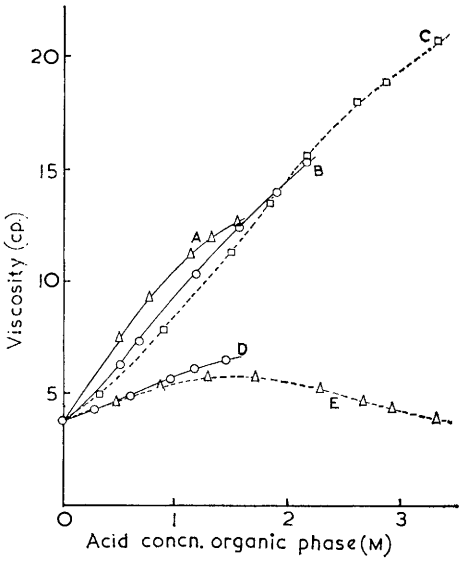


Fig. 1. Viscosities of extract solutions of acids in tributyl phosphate at 25° (results for nitric acid from ref. 3). Value at zero acid is for water-saturated tributyl phosphate. A, $HClO_4$. B, HBr. C, HCl. D, $CCl_3{\cdot}CO_2H$. E, $HNO_3$.

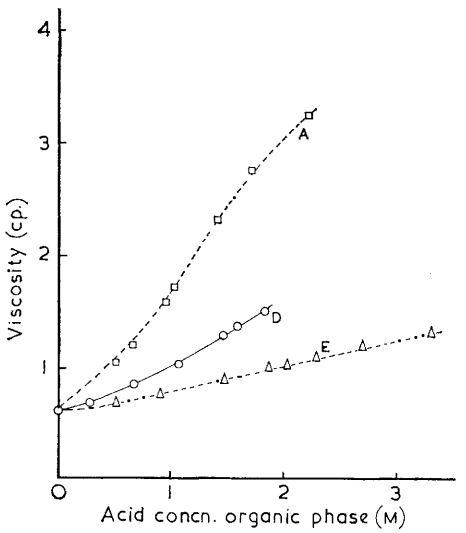


Fig. 2. Viscosities of extract solutions of acids in di-isopropyl ketone at 25°. Value at zero acid is for pure solvent. Key as for Fig. 1.

found that sulphuric acid behaves in a similar manner to perchloric acid. There is a clear difference between (*a*) perchloric, hydrochloric, and hydrobromic acid, which are known to exist in the organic phase as solvated $H_9O_4^+X^-$ at the concentrations studied here, and (*b*) nitric and trichloroacetic acid, which are present as TBP,HX.[1,4] (Sulphuric acid seems to be extracted as a highly aquated species [2] and may well also be present as $H_9O_4^+HSO_4^-$.) The difficulty of interpreting the viscosities of liquid mixtures is well known, but in the present case certain dominating factors can be identified. Although perchloric, hydrochloric (and presumably hydrobromic), and sulphuric acid have different ionisation constants in tributyl phosphate,[2] they must all be extensively, if not completely,

[1] Part V, Tuck, *J.*, 1963, 2736.
[2] Hesford and McKay, *J. Inorg. Nuclear Chem.*, 1960, **13**, 165.
[3] Tuck, *Trans. Faraday Soc.*, 1961, **57**, 1297.
[4] Tuck and Diamond, *J. Phys. Chem.*, 1961, **65**, 193.

ion-paired since the solvated $H_9O_4^+$ cation cannot form a covalent bond to the anion. The high viscosity of these solutions is therefore attributed to an increasing number of strong interactions between these ion-paired species with increasing acid concentration. The bulky cation, solvated $H_9O_4^+$, must also contribute appreciably to the resistance to flow, especially since hydrogen-bonding between neighbouring molecules is possible.

Nitric and trichloroacetic acid, on the other hand, are not hydrated in the extract solution [4] and, in agreement with the above argument, show comparatively little change in viscosity with increasing acid concentration. The interactions in extract solutions of nitric acid in tributyl phosphate have been discussed elsewhere.[3] Differences between trichloroacetic and nitric acid solutions may arise from the larger molar volume of the former.

With di-isopropyl ketone and similar solvents, it is possible to study only perchloric, trichloroacetic, and nitric acid over a significant concentration range because other acids are only slightly extracted.[1] The absolute increases in viscosity are not as large as with tributyl phosphate, but the general pattern (Fig. 2) is the same, with the viscosity of perchloric acid solution increasing more rapidly than that for the two weaker acids. The predominant extracted species here [1] are solvated $H_9O_4^+ClO_4^-$, $H_3O^+CCl_3{\cdot}CO_2^-$, and $H_3O^+NO_3^-$, so that the arguments set out above again fit the experimental results.

*Experimental.*—Materials were as described earlier.[1,3,4] Extract solutions were prepared by equilibration at room temperature and separated after centrifugation, and the organic phase was stored in a 25° thermostat before measurement. Viscosities were determined with an Ostwald viscometer at 25° ± 0·1°; densities were measured with a weight pipette.

Department of Chemistry, University of Nottingham. [*Received, January 30th,* 1963.]

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## 735. *Organogermanium Compounds. Part IV.*[1] *Some Derivatives of* p-*Triethylgermylbenzenesulphonic Acid.*

By R. W. Bott, C. Eaborn, and T. Hashimoto.

We described previously how the cleavage of aryl–silicon bonds by sulphur trioxide could be used in the preparation of sulphoarylsilicon compounds,[2] and we now show that an analogous method applies to organogermanium compounds. Reaction of *p*-bistriethylgermylbenzene with sulphur trioxide in carbon tetrachloride gives triethylgermyl *p*-triethylgermylbenzenesulphonate, $p\text{-}Et_3Ge{\cdot}C_6H_4{\cdot}SO_2{\cdot}O{\cdot}GeEt_3$, from which various derivatives of the parent sulphonic acid can be obtained. The products are the first sulphoarylgermanium compounds to be reported.

Cleavage of the aryl–germanium bond by sulphur dioxide is an electrophilic aromatic substitution; when a sulpho-group has been introduced by cleavage of one aryl–germanium bond of a bistriethylgermylbenzene the remaining bond is strongly deactivated and remains intact.

*Experimental.*—(i) A freshly prepared solution of sulphur trioxide (1·8 g., 0·0225 mole) (obtained by heating 65% oleum) in anhydrous carbon tetrachloride (40 ml.) was added dropwise, with exclusion of moisture, during 15 min. to a stirred solution of *p*-bistriethylgermylbenzene (9·0 g., 0·0227 mole) in carbon tetrachloride (30 ml.) cooled with ice–water. The mixture was refluxed gently for 15 min. and then fractionally distilled through a precision-made Vigreux column (20 plates), to give *triethylgermyl* p-*triethylgermylbenzenesulphonate* (8·0 g., 74%), b. p. 192—194°/0·02 mm., m. p. 41—43° (Found: C, 45·6; H, 7·1. $C_{18}H_{34}Ge_2O_3S$ requires C, 45·4; H, 7·2%). The sulphonate was sensitive to moisture.

[1] Part III, Bott, Eaborn, Pande, and Swaddle, *J.*, 1962, 1217.
[2] Eaborn and Hashimoto, *Chem. and Ind.*, 1961, 1081.

(ii) The sulphonate (2 g.) was dissolved in water (40 ml.), and after 15 min. hexaethyldigermoxane was removed. The filtrate was evaporated below 40° at reduced pressure, and the residue recrystallised from benzene–light petroleum to give *p*-triethylgermylbenzenesulphonic acid hydrate (1·3 g.), m. p. 65—66·5°. [The acid equivalent (by alkali titration) was 332, corresponding to a monohydrate, but the carbon and hydrogen analyses were unsatisfactory (Found: C, 40·4; H, 6·4. Calc. for $C_{12}H_{22}GeO_4S$: C, 43·0; H, 6·6%).] The S-*benzylthiouronium salt*, m. p. 147—148° (from benzene), was prepared in the usual way (Found: C, 49·6; H, 6·3; N, 5·7. $C_{20}H_{30}GeN_2S_2$ requires C, 49·7; H, 6·3; N, 5·8%).

(iii) A solution of triethylgermyl *p*-triethylgermylbenzenesulphonate in water was neutralised (to phenolphthalein) with 5% aqueous sodium hydroxide. The water was removed at reduced pressure, and the sodium *p*-triethylgermylbenzenesulphonate was taken up in a little water and re-precipitated by addition of ethanol. The dried salt (1·6 g.) was heated at 130° for 20 min. with phosphorus pentachloride (1·6 g.), and the mixture was added to ice–water (*ca.* 10 ml.). Extraction with benzene, followed by separation, drying ($Na_2SO_4$), and fractional distillation of the extract gave *p*-triethylgermylbenzenesulphonyl chloride, b. p. 131—132°/0·01 mm., which was added with stirring to a few ml. of aqueous ammonia (*d* 0·88). The solid which separated was dried and recrystallised from benzene–light petroleum, to give p-*triethylgermylbenzenesulphonamide*, m. p. 106—107° (Found: C, 45·2; H, 6·3; N, 4·5. $C_{12}H_{21}GeNO_2S$ requires C, 45·6; H, 6·7; N, 4·4%).

This work was financed by a grant from the Office of Aerospace Research, United States Air Force, through its European Office. We thank Dr. L. Spialter, of the Aeronautical Research Laboratory, Wright Air Development Center, for his interest and encouragement.

Department of Chemistry, The University, Leicester. [*Received, February 4th*, 1963.]

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## 736. *The Synthesis of 2-Phenyl-5-prop-1′-ynylthiophen.*

By J. Cymerman Craig and M. Moyle.

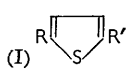
Since the isolation [1] of junipal (Ia) in 1955, other acetylenic thiophens have been found in Nature.[2] The co-existence [2] of thiophen compounds (I) and of the corresponding diacetylenes (II) supports the postulate that the latter function as precursors of the former in Nature, and Schulte *et al.*[3] have recently carried out this conversion *in vitro* by the action of sodium hydrogen sulphide on the diacetylenes.

From *Coreopsis grandiflora*, Sörensen and Sörensen [4] isolated both 2-phenyl-5-prop-1′-ynylthiophen (Ib) and 1-phenylhepta-1,3,5-triyne (IIb). However, an attempted synthesis [3] of the former from the latter gave only the isomeric 2-methyl-5-phenylethynylthiophen (Ic).

We now report the synthesis of the natural product (Ib). Carboxylation of 5-phenyl-2-thienylmagnesium bromide gave 5-phenylthiophen-2-carboxylic acid [5] which was converted into chloromethyl 5-phenyl-2-thienyl ketone by the general method of Ritter and Sokol.[6] Reaction with triethyl phosphite [7] then afforded the unstable diethyl 1-(5-phenyl-2-thienyl)vinyl phosphate (Id) which with sodamide in liquid ammonia [8] gave smoothly 2-ethynyl-5-phenylthiophen (Ie). Methylation of the lithium salt of the latter in dioxan [9] with dimethyl sulphate gave 2-phenyl-5-prop-1′-ynylthiophen (Ib), m. p. 43—44°, identical

[1] Birkinshaw and Chaplen, *Biochem. J.*, 1955, **60**, 255.
[2] Sörensen, *Proc. Chem. Soc.*, 1961, 98.
[3] Schulte, Reisch, and Hörner, *Angew. Chem.*, 1960, **72**, 920; *Chem. Ber.*, 1962, **95**, 1943.
[4] Sörensen and Sörensen, *Acta Chem. Scand.*, 1958, **12**, 765, 771.
[5] Kosak, Palchak, Steele, and Selwitz, *J. Amer. Chem. Soc.*, 1954, **76**, 4450.
[6] Ritter and Sokol, *J. Amer. Chem. Soc.*, 1948, **70**, 3420.
[7] Lichtenthaler, *Chem. Rev.*, 1961, **61**, 607.
[8] Craig and Moyle, *Proc. Chem. Soc.*, 1962, 149.
[9] Elsner and Paul, *J.*, 1951, 893.

in infrared and ultraviolet absorption with the material, m. p. 42—43° obtained [4] from *Coreopsis grandiflora*.



(I)

| R | R′ |
|---|---|
| (a) CHO | C:CMe |
| (b) Ph | C:CMe |
| (c) Ph·C:C | Me |

| R | R′ |
|---|---|
| (d) Ph | $CH_2$:C·O·PO(OEt)$_2$ |
| (e) Ph | C:CH |

(II) R·C:C·C:C·R′

*Experimental.*—Infrared and ultraviolet spectra were recorded on a Beckman I.R.5 and a Cary model 11 spectrophotometer, respectively.

*5-Phenylthiophen-2-carboxylic acid.* 2-Bromo-5-phenylthiophen [5] (29 g.) was heated with magnesium (3·0 g.) in ether (200 ml.) under reflux for 6 hr. After cooling, the mixture was poured on solid carbon dioxide (250 g.) and kept overnight. The magnesium salt was decomposed with ice-cold dilute sulphuric acid, and the precipitated acid was collected and purified through the sodium salt. Crystallization from aqueous ethanol afforded 5-phenylthiophen-2-carboxylic acid (20·1 g., 81%), m. p. 186—188° (lit.,[5] m. p. 186—187°).

*Chloromethyl 5-phenyl-2-thienyl ketone.* 5-Phenylthiophen-2-carboxylic acid (20 g.) and thionyl chloride (60 ml.) were heated under reflux for 1 hr., and the excess of thionyl chloride removed *in vacuo*. A solution of the resulting acid chloride in ether (500 ml.) was cooled to 0° and treated with a dried solution of diazomethane (from 100 g. of *N*-methyl-*N*-nitrosotoluene-*p*-sulphonamide in ether (1 l.). The mixture was kept for 4 hr. at 0°, saturated with dry hydrogen chloride, and kept overnight at room temperature. The ether was removed *in vacuo*, and the residue taken up in chloroform, washed with sodium hydrogen carbonate solution, and dried ($Na_2SO_4$). Evaporation of the solvent and crystallization from ethanol afforded the *chloromethyl ketone* (20·0 g., 86%) as leaflets, m. p. 123—124° (Found: C, 60·55; H, 4·0. $C_{12}H_9ClOS$ requires C, 60·85; H, 3·85%).

*2-Ethynyl-5-phenylthiophen.* The chloromethyl ketone (7·11 g., 0·03 mole) and triethyl phosphite (15 ml.) were heated under nitrogen for 1 hr. at 90° and the excess of triethyl phosphite was then evaporated *in vacuo*. The crude phosphate was added in ether (50 ml.) during 15 min. to a stirred suspension of sodamide (from 3·35 g., 0·15 g.-atom of sodium) in liquid ammonia (250 ml.) at −70°. The mixture was stirred for a further 45 min. at −70°, then ammonium chloride was added and the ammonia allowed to evaporate. The residue was distributed between water and ether, the ether dried ($Na_2SO_4$) and evaporated, and the crude product adsorbed from hexane (50 ml.) on a column of neutral alumina (60 g.; activity I). Elution with hexane (400 ml.) afforded *2-ethynyl-5-phenylthiophen* (3·8 g., 68%), leaflets (from hexane), m. p. 65—67° (Found: C, 78·25; H, 4·4. $C_{12}H_8S$ requires C, 78·25; H, 4·4%), $\nu_{max.}$ 3285 and 2100 (C:CH), 805 cm.$^{-1}$ (2,5-disubstituted thiophen).

*2-Phenyl-5-prop-1′-ynylthiophen* (Ib). 2-Ethynyl-5-phenylthiophen (3·68 g., 0·02 mole) in dioxan (50 ml.) was added during 15 min. to a stirred suspension of lithamide (from 175 mg., 0·025 g.-atom, of lithium) in liquid ammonia (100 ml.). The mixture was stirred under reflux for 1 hr. and the ammonia then evaporated in a stream of nitrogen. Dioxan (75 ml.) was added and the mixture heated under nitrogen at 90° until evolution of ammonia ceased (~30 min.). Dimethyl sulphate (3·8 g., 0·03 mole) was added, the mixture kept at 90° for 1 hr., and the dioxan then evaporated *in vacuo*. The residue was distributed between ether and water, the ethereal layer washed with saturated sodium hydrogen carbonate solution, dried ($Na_2SO_4$), and evaporated, and the product adsorbed from hexane (50 ml.) on neutral alumina (100 g.; activity I). Elution with hexane afforded 2-phenyl-5-prop-1′-ynylthiophen (2·4 g., 60%), as needles [from light petroleum (b. p. 30—60°)], m. p. 43—44° (Found: C, 78·35; H, 5·0. Calc. for $C_{13}H_{10}S$: C, 78·75; H, 5·10%), $\lambda_{max.}$ 310 mμ (broad) (log ε 4·4), $\nu_{max.}$ (in $CS_2$) 2240 (C:C), 805 cm.$^{-1}$ (2,5-disubstituted thiophen). Further elution with hexane–benzene (9 : 1) afforded unchanged 2-ethynyl-5-phenylthiophen (0·40 g.), m. p. 67°.

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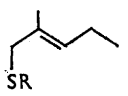
Department of Pharmaceutical Chemistry, University of California,
San Francisco, 22, U.S.A. [*Received, February 9th*, 1963.]

## 737. *A Nuclear Magnetic Resonance Study of* cis–trans-*Isomerism in 2-Methylpent-2-enyl Thiolacetate.*

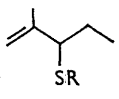
By B. K. Tidd.

In a recent paper [1] the synthesis of 2-methylpent-2-ene-1-thiol was described, and it was shown by gas chromatography to consist of one major and two minor components. The major constituent was considered, on the basis of the probable stereochemistry of the synthetical method employed, to be the *trans*-thiol (I; R = H), and that occurring in the smallest amount to be the iso-allylic thiol (III; R = H). The other minor component was assumed to be the *cis*-thiol (II; R = H).



(I)

(II)



(III)

These assignments have now been confirmed through a nuclear magnetic resonance investigation of the thiolacetates corresponding to a thiol mixture of the above kind. The thiolacetate mixture used was obtained through quantitative *S*-acetylation of a mixture of thiols considered by Saville from earlier work [1] to consist of (I; R = Ac) 84·5%, (II; R = Ac) 10·9%, and (III; R = Ac) 4·6%.

The thiolacetate mixture, in deuterochloroform solution has a nuclear magnetic resonance spectrum consisting of a triplet ascribed to the vinylic proton *cis* to the acetylthiomethyl group, three singlets due to $=C-CH_2\cdot SAc$, $-S\cdot CO\cdot CH_3$, and $=C-CH_3$, and a triplet due to the saturated $C\cdot CH_3$ (for $\tau$ values see Table). The allylic 4-methylene group appears as a pentuplet, since it is coupled equally to the methyl group on one side and the vinylic proton on the other ($J$ = 7·5 c./sec.). This is in accord with the major component's being compound (I; R = Ac) and/or (II; R = Ac).

Chemical shifts ($\tau$) for protons in allylic thiolacetates.

| Partial structure | $\tau$ | Partial structure | $\tau$ |
|---|---|---|---|
| AcS–C=C–H{*cis* | 4·53 | $-S\cdot CO\cdot CH_3$ | 7·67 |
| AcS–C=C–H{*trans* | 4·66 | $=C-CH_2(CH_3)$ | 7·97 |
| $-C=CH_2$ | 4·98, 5·09 | $=C-CH_3$ | 8·37 |
| $=C-CH_2\cdot SAc$ | 6·43 | $-C-CH_3$ | 9·07 |
| $=C-CH\cdot SAc$ | 5·97 | | |

Using a large spectrum-amplitude setting it was possible to obtain, for the pure liquid, a spectrum in which peaks due to the minor components were clearly visible. A small triplet centred at $\tau$ = 5·97 and a small doublet centred at $\tau$ = 5·04 are ascribed to the secondary thiolacetate proton and to the vinylic protons, respectively, in the minor component (III; R = Ac).

The two outer peaks of the main vinylic proton triplet at $\tau$ = 4·53 have areas which are in the ratio 1 : 1·29, compared with the theoretical [2] value of 1 : 1·017 for the given coupling constant and chemical shift values. This discrepancy together with (*a*) a similar discrepancy relative to the intensity of the central peak, and (*b*) the presence of a small peak at $\tau$ = 4·79, indicates that two overlapping triplets of identical splitting centred at $\tau$ = 4·53 and $\tau$ = 4·66 must be present, with a ratio of intensities equal to 9·14 : 1.

In compounds (I and II; R = Ac) the vinylic proton is *cis* and *trans*, respectively, to the acetylthiomethyl group, and it would therefore be expected that the diamagnetic anisotropy of the carbonyl groups [3] would result in a greater preferential de-shielding of the vinylic proton when this is *cis* to the thiolacetate group. Structure (I; R = Ac) is thus assigned

[1] Evans, Higgins, Saville, and Watson, *J.*, 1962, 5045.
[2] Bernstein, Pople, and Schneider, *Canad. J. Chem.*, 1957, **35**, 65.
[3] Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, London, 1959, Ch. 7.

to the major component ($\tau = 4{\cdot}53$) whilst structure (II; R = Ac) must be assigned to the primary thiolacetate which occurs in small amounts ($\tau = 4{\cdot}66$).

Treatment of the overall integral and the relative integrals for peaks below $\tau = 7{\cdot}5$, according to the method described by Hung Yu Chen,[4] indicates that the mixture contains compounds (I; R = Ac) 83·1%, (II; R = Ac) 8·8%, (III; R = Ac) 5·9%, unchanged starting material 1·9%, and an unidentified compound 0·3%.

Thus, in addition to providing good support for the gas-chromatographic analysis of the thiol mixture, the nuclear magnetic resonance data provide good evidence that the thiolacetate produced in greatest yield is indeed *trans*, as expected.

*Experimental.*—Nuclear magnetic resonance spectra were obtained on a Varian Associates A60 spectrometer and, for the runs in deuterochloroform solution, tetramethylsilane was added as internal standard.

*Preparation of the thiolacetate mixture* (kindly performed by Dr. B. SAVILLE). To a sample (3·42 g., 0·03 mole) of 2-methylpent-2-ene-1-thiol [1] [containing components (I—III); R = H] in dry pyridine (20 ml.) was added acetic anhydride (6·12 g., 0·06 mole). After being left overnight the mixture was poured into water (100 ml.) and extracted with ether (70 ml.). The ether layer was washed with water, dilute acid, and saturated aqueous sodium hydrogen carbonate, and then dried and distilled to afford a thiolacetate mixture (4·5 g., 95%) having b. p. 80—81°/13 mm. and containing 1·9% of unchanged thiol as shown by nuclear magnetic resonance analysis (Found: C, 61·2; H, 9·1; S, 20·5. $C_8H_{14}OS$ requires C, 60·8; H, 8·9; S, 20·3%).

The author is indebted to Mr. M. B. Evans for the gas-chromatographic analysis, and to Mr. J. F. Grove of Imperial Chemical Industries Limited, Akers Research Laboratories, for providing the nuclear magnetic resonance facilities.

THE NATURAL RUBBER PRODUCERS' RESEARCH ASSOCIATION,
48—56 TEWIN ROAD, WELWYN GARDEN CITY, HERTS. [*Received, February 7th*, 1963.]

[4] Hung Yu Chen, *Analyt. Chem.*, 1962, **34**, 1134.

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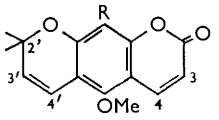
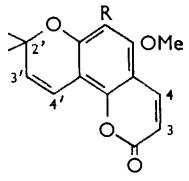
## 738. *A Revised Structure for Avicennin.*

By H. R. ARTHUR and W. D. OLLIS.

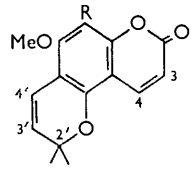
AN earlier study [1] of avicennin, a yellow compound isolated from the bark of *Zanthoxylum avicennae*, suggested that it had the molecular formula $C_{20}H_{22}O_4$, and three alternative structural formulæ (Ia, IIa, and IIIa) were tentatively considered.



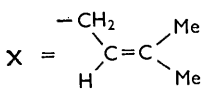
(Ia: R = X)
(Ib: R = Y)
(Ic: R = Z, single bond at 3',4'-position)

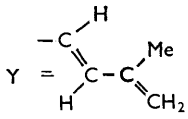


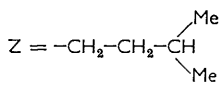
(IIa: R = X)
(IIb: R = Y)
(IIc: R = Z, single bond at 3',4'-position)



(IIIa: R = X)
(IIIb: R = Y)
(IIIc: R = Z, single bond at 3',4'-position)



; 

; 

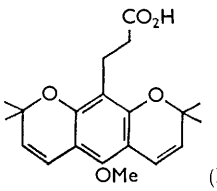
A 5,7-dioxygenated coumarin structure for avicennin was established and the presence of a 2,2-dimethylchromene residue was inferred from the formation of α-hydroxyisobutyric

[1] Arthur and Lee, *J.*, 1960, 4654.

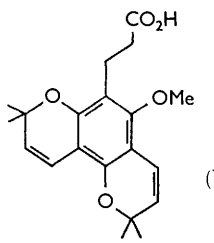
acid by oxidation. The nature of the group R (see Ia, IIa, and IIIa) was not established but the molecular formula, $C_{20}H_{22}O_4$, originally adopted for avicennin required that R be $C_5H_9$ and an isopentenyl group (X) was favoured. Examination of the nuclear magnetic resonance spectrum of avicennin, kindly determined by Professor L. M. Jackman, has established that the molecular formula of avicennin is in fact $C_{20}H_{20}O_4$, and that its reduction product is a hexahydro- rather than a tetrahydro-derivative as previously believed.[1]

The nuclear magnetic resonance spectrum * of avicennin shows signals of the appropriate integrated intensities corresponding to one methoxyl group ($\tau$ 6·24) and a 2,2-dimethylchromene system;[2] the latter is associated with a singlet ($\tau$ 8·52) corresponding to two equivalent methyl groups and a pair of doublets (AB system: 3′-H, $\tau$ 4·37; 4′-H, $\tau$ 3·40; $J$ = 10 c./sec.) assignable to the two *cis*-olefinic protons in positions 3′ and 4′. There are two other AB systems which can be recognised and one of these can be associated with the 3- and 4-protons of the coumarin system[3] (3-H, $\tau$ 3·77; 4-H, $\tau$ 2·0; $J$ = 10 c./sec.). The proton count requires that the group R (see I, II, and III) be $C_5H_7$ and its nature is defined structurally and stereochemically by the nuclear magnetic resonance spectrum. The AB system ($\tau$ 2·58 and 3·30; $J$ = 16 c./sec.) shows no additional splitting and it is characteristic[4] of a *trans*-disubstituted olefin flanked by carbon atoms bearing no hydrogen atoms; the downfield shift suggests that this olefinic group is part of a styrenoid system. This settles the partial structure, $-CH{=}CH-\overset{t}{C}\lessgtr$, within the $C_5H_7$ group and the undefined $C_2H_5$ residue must constitute olefinic methylene and methyl groups. In accord with this analysis, the nuclear magnetic resonance spectrum shows a singlet ($\tau$ 4·85) due to the olefinic methylene group which is broadened because of weak coupling with the methyl group (singlet, $\tau$ 7·98). Thus R in avicennin is uniquely defined as a 3-methyl-*trans*-butadienyl group (Y).

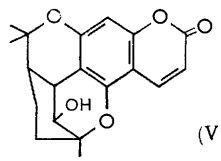
The reduction product of avicennin is the expected hexahydro-derivative (Ic, IIc, or IIIc) containing a 2,2-dimethylchroman residue and an isopentyl group (R = $Bu^i{\cdot}CH_2$). Its nuclear magnetic resonance spectrum * shows a singlet ($\tau$ 6·20) due to the methoxyl group and an AB system (3-H, $\tau$ 3·82; 4-H, $\tau$ 1·97; $J$ = 10 c./sec.) assignable to the protons in positions 3 and 4 of the coumarin system.[3] The absence of aromatic-type protons at low field is clearly established by this spectrum. In the aliphatic proton region, there is a singlet ($\tau$ 8·63) due to the two methyl groups of the 2,2-dimethylchroman residue and a doublet ($\tau$ 9·05; $J$ = 8 c./sec.) due to the two methyl groups of the isopropyl portion



(IV)



(V)



(VI)

of the isopentyl group. There is a multiplet (4 protons; $\tau$ 7·07—7·42) assignable to two benzylic methylene groups and there is another multiplet (5 protons; $\tau$ 8·05—8·56) due to the other aliphatic protons.

* These spectra were determined for deuteriochloroform solutions with tetramethylsilane as internal standard on a Varian A-60 spectrometer.

[2] Burrows, Ollis, and Jackman, *Proc. Chem. Soc.*, 1960, 177.
[3] See spectra 294, 310, and 323, N.M.R. Spectra Catalogue, Varian Associates (1962).
[4] See Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, London, 1959, p. 85.

Many natural phenolic compounds [5] contain $C_5$-residues which are isoprenoid in type and the demonstration that avicennin contains a 3-methyl-*trans*-butadienyl group (Y) represents a hitherto unrecognised variant upon this theme. The evidence at present available does not permit a distinction between the three structures (Ib, IIb, or IIIb) for avicennin which show an interesting structural relationship to eriostoic acid (IV), eriostemoic acid (V), and bruceol (VI) recently isolated [6] from various *Eriostemon* species.

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[5] See Ollis and Sutherland, " Chemistry of Natural Phenolic Compounds," ed. W. D. Ollis, Pergamon Press, London, 1961, p. 74.
[6] Duffield, Jefferies, and Lucich, *Austral. J. Chem.*, 1962, **15**, 812; Duffield and Jefferies, *ibid.*, 1963, **16**, 123; Duffield, Jefferies, Maslen, and Rae, *Tetrahedron*, 1963, **19**, 593; see also spectrum 344, ref. 4.

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## 739. *Unco-ordinated Gallium Hydride.*

By N. N. GREENWOOD and M. G. H. WALLBRIDGE.

IT is doubtful whether unco-ordinated gallium hydride has previously been prepared.[1] Experiments designed to liberate gallium hydride from its adducts usually lead, even at low temperatures, to immediate decomposition into gallium and hydrogen. Evidence is now presented for unco-ordinated gallium hydride prepared as an unstable species by means of the displacement reaction

$$Me_3N,GaH_3(c) + BF_3(g) \xrightarrow{-15^\circ} GaH_3(l) + Me_3N,BF_3(c)$$

*Experimental*—Trimethylamine–gallane (0·262 g., 1·99 mmole) was transferred in a dry, nitrogen-filled glove-box into a tube which was then connected to a vacuum-line, and boron trifluoride (0·171 g., 2·52 mmole) condensed on it at −196°. The tube was allowed to warm slowly and, at −20° to −15°, uptake of boron trifluoride occurred rapidly to yield a colourless viscous liquid and a white solid. After completion of the reaction 0·039 g. (0·574 mmole) of gas was recovered and identified as boron trifluoride by means of its infrared spectrum. Thus, 1·99 mmole of trimethylamine–gallane had reacted with 1·95 mmole of boron trifluoride. The viscous liquid, m. p. −15° to −20°, was stable below −15° but decomposed quantitatively at room temperature into hydrogen and gallium (volume of hydrogen evolved, 64·4 ml., *i.e.*, 2·87 mmole; expected, 2·98 mmole). The residue was a mixture of metallic gallium and a white solid which could be sublimed to give crystals identified as trimethylamine–boron trifluoride m. p. 144—148° (lit.,[2] 146°). In addition, the infrared spectrum of the sublimate in the range 400—4000 cm.$^{-1}$ was identical with that of authentic trimethylamine–boron trifluoride synthesised by direct reaction of the donor and acceptor. Normally there were no other products of the reaction but occasionally a trace of diborane was also observed.

On the basis of the foregoing stoicheiometry the conclusion seems inescapable that the viscous oil was unco-ordinated gallium hydride. In an attempt to determine the molecular weight of gallium hydride the solubility of the oil in non-co-ordinating solvents was investigated. It was immiscible with, and virtually insoluble in, benzene, toluene, light petroleum (various boiling ranges), and carbon tetrachloride; it was partly soluble in chloroform but this solvent also dissolved some of the trimethylamine-boron trifluoride and so was unsuitable. This low solubility in non-co-ordinating solvents is perhaps surprising; it suggests that the molecular complexity of the hydride is greater than that represented by the formulæ $GaH_3$ or $Ga_2H_6$ and may imply some hydrogen-bridged structure in the viscous oil. Gallium hydride was readily soluble in dimethyl sulphide but is known to form an adduct with this ligand.[3]

[1] Shriver, Parry, Greenwood, Storr, and Wallbridge, *Inorg. Chem.*, 1963, **2**, in the press.
[2] Phillips, Hunter, and Sutton, *J.*, 1945, 146.
[3] Greenwood, Storr, and Wallbridge, *Inorg. Chem.*, 1963, **2**, in the press.

Further evidence that the viscous liquid is indeed a hydride of gallium comes from infrared spectroscopy. A low-temperature liquid-film cell with potassium bromide windows (Research and Industrial Instruments Company) was fitted with a 2 mm. spacer and charged with trimethylamine–gallane in a glove-box. The cell was then cooled to −20° and boron trifluoride gas passed in from the vacuum system. As the reaction proceeded, the walls of the cell became covered with a viscous liquid $(GaH_3)_x$ and the solid product ($Me_3N,BF_3$) drained to the bottom of the cell. Simultaneously, strong bands appeared in the Ga–H stretching and Ga–H deformation regions of the spectrum.[4] The Ga–H stretching mode was at 1980 cm.$^{-1}$ and this occurred, as expected, at wave-numbers higher than observed for the corresponding band in gaseous trimethylamine–gallane [4] (1853 cm.$^{-1}$). The half-band width also increased from 23 cm.$^{-1}$ in the adduct [3] to ~130 cm.$^{-1}$ in gallium hydride itself, and this again is consistent with a hydrogen-bridged structure for the viscous liquid. The broad band centred on about 700 cm.$^{-1}$ could not be resolved into the symmetric and the antisymmetric deformation modes which occurred at 715 and 758 cm.$^{-1}$ in the gaseous adduct; there is also the complication of weaker bands from trimethylamine-boron trifluoride in this region.

Evidence for a fugitive gallium hydride species has also been obtained from the gas-phase reaction of trimethylamine–gallane and boron trifluoride at room temperature. A small amount of trimethylamine–gallane was sublimed on to a cold finger attached directly to a 10-cm. infrared gas cell and the spectrum was recorded. The typical sharp bands [4] of the gaseous adduct at 1853 and 758 cm.$^{-1}$ were observed. Gaseous boron trifluoride was then admitted and, as it reacted with the gaseous adduct, these bands disappeared and were replaced by an equally sharp band of about half the intensity at 2000 cm.$^{-1}$. Rapid scanning was necessary as this new band itself decreased in intensity over a period of minutes as the gaseous gallium hydride decomposed to give a deposit of metallic gallium and gaseous hydrogen. By means of repeated experiments, each covering a small range of the spectrum, the region from 400 to 3000 cm.$^{-1}$ was scanned. However, because of the weak intensity of the strongest bands and the complicating presence of the bands due to boron trifluoride in the 700 and the 480 cm.$^{-1}$ region it was impossible to carry out full vibrational assignments and so decide on the molecular complexity of the gaseous hydride ($GaH_3$, $Ga_2H_6$, etc.). Nevertheless, the experiment provides conclusive evidence for the existence of an unstable gaseous gallium hydride which decomposes within minutes at room temperature.

Experiments in which acceptors other than boron trifluoride were used to displace uncoordinated gallium hydride from its adducts failed. Diborane did not react appreciably with trimethylamine–gallane below 40—50° and at this temperature the product decomposed almost instantaneously to gallium and hydrogen. With hydrogen chloride gas the reaction was more complex, but no free gallium hydride was formed.

In summary: Trimethylamine–gallane reacts with an equimolar amount of gaseous boron trifluoride at −20° to give a solid, identified as trimethylamine–boron trifluoride, and a colourless viscous liquid which analyses as $GaH_3$ and has an infrared spectrum comprising two strong bands assignable to the Ga–H stretching and deformation modes. The liquid is stable below −15°, but decomposes quantitatively at room temperature into gallium and hydrogen. The same reaction carried out in the gas-phase at room temperature gives a gaseous gallium hydride species which decomposes rapidly into gallium and hydrogen.

This work was carried out during the tenure of a Fellowship (by M. G. H. W.) at King's College and was supported, in part, by the U.S. Air Force Office of Scientific Research.

KING'S COLLEGE, NEWCASTLE UPON TYNE. [*Received, February 13th*, 1963.]

[4] Greenwood, Storr, and Wallbridge, *Proc. Chem. Soc.*, 1962, 249.

## 740. *The Preparation of 2-Bromo-4,5-dimethoxyphenylacetylene.*

By K. W. Bentley, S. F. Dyke, and (Mrs.) A. R. Marshall.

αβ-Dibromo-β-(2-bromo-4,5-dimethoxyphenyl)propionic acid has been reported[1] to lose hydrogen bromide readily giving, when heated alone, an acid of m. p. 233° or, when heated with alkali, an acid of m. p. 198° and a trace of a neutral product formulated as 1-bromo-2-(2-bromo-4,5-dimethoxyphenyl)ethylene. The acids appear to be *cis–trans*-isomers of α-bromo-β-(2-bromo-4,5-dimethoxyphenyl)acrylic acid, and the lower-melting is converted into the higher-melting form when slowly heated. In our hands treatment of the tribromo-acid with alkali furnished only a trace of the lower-melting acid, together with 78% of a neutral substance different from that previously reported. This is formulated as being *trans*-1-bromo-2-(2-bromo-4,5-dimethoxyphenyl)ethylene (infrared bands at 1610 and 940 cm.$^{-1}$ in Nujol); the lower-melting compound previously reported may well be the *cis*-isomer. We believe that the acid of m. p. 233° has the *trans*-cinnamic acid constitution ($\lambda_{max.}$ 239 and 295 mμ; ε 11,080 and 11,560) and the acid of m. p. 198° the *cis* arrangement ($\lambda_{max.}$ 237 and 290 mμ; ε 11,830 and 8581).

Dehydrobromination of the tribromo-acid and the two isomeric dibromo-acids to the corresponding propiolic acid could not be effected. 1-Bromo-2-(2-bromo-4,5-dimethoxyphenyl)ethylene was recovered unchanged from boiling ethanolic potassium hydroxide but when heated with potassium hydroxide in ethylene glycol at 140° was converted into 1-(2-hydroxyethoxy)-2-(2-bromo-4,5-dimethoxyphenyl)ethylene, which was also obtained from 2-bromo-4,5-dimethoxyphenylacetylene in the same way. This compound shows no acetylenic absorption in the infrared region but does show hydroxyl absorption. On hydrolysis with sulphuric acid it gives what appears to be 2-bromo-4,5-dimethoxyphenylacetaldehyde, giving a yellow 2,4-dinitrophenylhydrazone different from the orange derivative of 2-bromo-4,5-dimethoxyacetophenone prepared by the hydration of 2-bromo-4,5-dimethoxyphenylacetylene.

2-Bromo-4,5-dimethoxyphenylacetylene was successfully prepared in very good yield by heating the bromoethylene with potassium t-butoxide in t-butyl alcohol. We believe this method to be better than that of Barltrop and Nicholson.

*Experimental.*—trans-1-*Bromo*-2-(2-*bromo*-4,5-*dimethoxyphenylethylene*. αβ-Dibromo-β-(2-bromo-4,5-dimethoxyphenyl)propionic acid (4 g.) was stirred as a fine powder into a solution of potassium hydroxide (1·0 g.) in methanol (25 ml.). Colourless needles separated almost immediately. After 30 min. they were collected and recrystallised from aqueous ethanol, being trans-1-*bromo*-2-(2-*bromo*-4,5-*dimethoxyphenyl*)*ethylene*, m. p. 102—103° (2·3 g.) (Found: C, 37·2; H, 3·2; Br, 49·6. $C_{10}H_{10}Br_2O_2$ requires C, 37·3; H, 3·1; Br, 49·6%). M. p. 67° was given for material assigned the same structure (*cis*-form?) by Reimer, Tobin, and Schaffner.[1]

A trace of *cis*-α-bromo-β-(2-bromo-4,5-dimethoxyphenyl)acrylic acid, m. p. 198° (lit.,[1] 198°), was obtained by acidification of the filtrate after isolation of the olefin; this acid was obtained in somewhat better yield by carrying out the dehydrobromination of the tribromo-acid (2·0 g.) with potassium hydroxide (2 g.), ethanol (25 ml.), and water (3 ml.) under reflux for 6 hr. (yield, 0·4 g. of acid and 0·3 g. of bromo-olefin).

2-*Bromo*-4,5-*dimethoxyphenylacetylene*. 1-Bromo-2-(2-bromo-4,5-dimethoxyphenyl)ethylene (10 g.) was heated under reflux for 3 hr. with a solution of potassium (1·5 g.) in t-butyl alcohol (100 ml.), and the solution was then poured into water. The precipitated pale brown solid was collected, washed, and recrystallised from aqueous acetone, the acetylene being obtained as cream coloured needles, m. p. 101—102° (lit.,[2] 101°) (Found: C, 49·5; H, 3·8; Br, 33·3. Calc. for $C_{10}H_9BrO_2$: C, 49·7; H, 3·75; Br, 33·2%). The same material was obtained by dehydrobromination of the bromo-olefin (2 g.) with potassium hydroxide (5·6 g.) and dimethylformamide (25 ml.) under reflux for 3 hr. The mixture was poured into water, and the solid was collected, dissolved in ethanol, and treated with silver nitrate. The precipitated silver acetylide was collected, washed, and decomposed by boiling under reflux with aqueous sodium cyanide for

[1] Reimer, Tobin, and Schaffner, *J. Amer. Chem. Soc.*, 1933, **57**, 211.
[2] Barltrop and Nicholson, *J.*, 1951, 2524.

3 hr. The product was then isolated by ether-extraction and recrystallised from aqueous acetic acid (yield, 0·7 g.; m. p. 100—101°).

1-(2-*Bromo*-4,5-*dimethoxyphenyl*)-2-(2-*hydroxyethoxy*)*ethylene*. (*a*) 1-Bromo-2-(2-bromo-4,5-dimethoxyphenyl)ethylene (2 g.), potassium hydroxide (5·6 g.), and ethylene glycol (25 ml.) were heated together at 140° for 3 hr., then cooled and poured into water. The yellow precipitate was collected and crystallised from aqueous acetone; 1-(2-*bromo*-4,5-*dimethoxyphenyl*)-2-(2-*hydroxyethoxy*)*ethylene* (1·0 g.) was obtained as cream-coloured flakes, m. p. 67—68° (Found: C, 45·1; H, 5·4; Br, 25·2. $C_{12}H_{15}BrO_4,H_2O$ requires C, 44·9; H, 5·3; Br, 24·9%). (*b*) 2-Bromo-4,5-dimethoxyphenylacetylene (0·75 g.), potassium hydroxide (2·8 g.), and ethylene glycol (12·5 ml.) were heated together at 140° for 3 hr. The mixture was cooled and poured into water to give material identical with that prepared as in (*a*) above.

*Hydrolysis of* 1-(2-*bromo*-4,5-*dimethoxyphenyl*)-2-(2-*hydroxyethoxy*)*ethylene*. 1-(2-Bromo-4,5-dimethoxyphenyl)-2-(2-hydroxyethoxy)ethylene (1·0 g.), ethanol (25 ml.), and sulphuric acid (2·0 ml.; 50% v/v) were kept together at room temperature for 90 min. The mixture was poured into water and the precipitated material isolated by ether-extraction. In this way a yellow gum was obtained; this appeared to be 2-bromo-4,5-dimethoxyphenylacetaldehyde; it had $\nu_{max.}$ 1735 cm.$^{-1}$, and gave a yellow 2,4-*dinitrophenylhydrazone* as prisms, m. p. 170—171° (from acetic acid) (Found: C, 43·6; H, 3·65; N, 12·4. $C_{16}H_{15}BrN_4O_5$ requires C, 43·7; H, 3·4; N, 12·8%). The same 2,4-dinitrophenylhydrazone was obtained from the original enol ether after five minutes' treatment with 2,4-dinitrophenylhydrazine in methanolic sulphuric acid at 60°.

2-*Bromo*-4,5-*dimethoxyacetophenone*. 2-Bromo-4,5-dimethoxyphenylacetylene (0·5 g.), 70% aqueous methanol (12 ml.), concentrated sulphuric acid (0·04 g.), and mercuric sulphate (0·04 g.) were heated together on the steam-bath for 3 hr. The mixture was cooled and poured into water containing sodium hydrogen carbonate. The precipitated material was isolated by ether-extraction and was so obtained as a gum (0·62 g.) that solidified later; it recrystallised from ethanol and gave 2-*bromo*-3,5-*dimethoxyacetophenone* as cream-coloured needles, m. p. 106° (Found: C, 46·2; H, 4·1; Br, 30·9. $C_{10}H_{11}BrO_3$ requires C, 46·4; H, 4·25; Br, 30·9%). This material gave an orange 2,4-*dinitrophenylhydrazone*, m. p. 185—186° (Found: C, 44·0; H, 3·6; N, 12·75; Br, 18·6. $C_{16}H_{15}BrN_4O_5$ requires C, 43·7; H, 3·4; N, 12·75; Br, 18·2%).

THE CHEMISTRY DEPARTMENT, BRISTOL COLLEGE OF SCIENCE AND TECHNOLOGY.
J. F. MACFARLAN & CO., LTD., EDINBURGH. [*Received, February* 14*th*, 1963.]

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## 741. *Methylation Analysis of Panose* (4-α-*Isomaltosylglucose*).

By E. E. SMITH and W. J. WHELAN.

THE crystalline glucose trisaccharide, panose, was first isolated by Pan and his co-workers [1] from a submerged culture of *Aspergillus niger* growing on maltose. Subsequently it was synthesized from maltose [2] by several cell-free enzyme systems; it is also a product of the partial hydrolysis of amylopectin [3] and glycogen.[4] We have recently found an improved method of preparing panose,[5] taking advantage of a panose-synthesizing enzyme in commercial specimens of glucose oxidase.

The structure of panose was established as 4-α-isomaltosylglucose, by French [6] by paper-chromatographic examination of the disaccharides formed on partial acid hydrolysis of the sugar and of the aldonic acid formed by hypoiodite oxidation. Wolfrom, Thompson, and Galkowski [7] confirmed this structure by isolation of isomaltose and maltitol from a

[1] Pan, Andreason, and Kolachov, *Science*, 1950, **112**, 115; Pan, Nicholson, and Kolachov, *J. Amer. Chem. Soc.*, 1951, **73**, 2547.
[2] Reviewed by Hassid and Neufeld, in Boyer, Lardy, and Myrbäck's " The Enzymes," Academic Press, Inc., New York, 1946, Vol. VI, p. 292.
[3] Thompson and Wolfrom, *J. Amer. Chem. Soc.*, 1951, **73**, 5849.
[4] Peat, Whelan, and Edwards, *J.*, 1955, 355.
[5] Smith and Whelan, *Biochem. Prep.*, 1963, **10**, in the press.
[6] French, *Science*, 1951, **113**, 352.
[7] Wolfrom, Thompson, and Galkowski, *J. Amer. Chem. Soc.*, 1951, **73**, 4093.

partial acid hydrolysate of borohydride-reduced panose (panitol). Confirmation by methylation analysis was thought desirable since it provides quantitative information about the glycosidic bonds not provided by the partial hydrolysis studies.

Accordingly panose was methylated and hydrolysed, and the products were fractionated on charcoal.[8] These were identified as 2,3,6-tri-, 2,3,4-tri-, and 2,3,4,6-tetra-*O*-methyl-D-glucose in the molar ratio 1·02 : 1·00 : 1. These are the products and the yields expected on the basis of the structure previously assigned to panose,[6,7] *i.e.*, *O*-α-D-glucopyranosyl-(1→6)-*O*-α-D-glucopyranosyl-(1→4)-D-glucopyranose.

*Experimental.—Methylation of panose.* Panose was prepared as by Smith and Whelan [5] and crystallized twice from aqueous methanol.[1] The finely ground sugar (1·0 g.) was methylated [9] by shaking it in the dark with methyl iodide (6 ml.) and freshly prepared silver oxide (6 g.) in dry dimethylformamide (30 ml.) with a second addition of the same quantities of reactants and amide (10 ml.) after 96 hr. After a further 24 hr. the mixture was centrifuged and the silver residue washed twice with hot dimethylformamide (10 ml. each). 4% Potassium cyanide solution (100 ml.) was added to the combined solutions, which were exhaustively extracted with chloroform, and the syrup obtained on evaporation was dissolved in water and de-ionized (Biodeminrolit mixed-bed ion-exchange resin, 20 g., carbonate form,[10] Permutit Co. Ltd.). The filtrate was passed through barium sulphate on an asbestos pad to remove colloidal silver, and evaporated to dryness. The syrup (1·10 g.) had OMe 46·1% (calc. for undeca-*O*-methylpanose: OMe, 51·8%). After a second methylation, without a renewal of the reactants, the product weighed 921 mg. and had OMe 50·3%. Acid hydrolysis of a portion (10 mg.) as by Croon *et al.*[11] and paper chromatography revealed some di-*O*-methylhexose. A third methylation yielded a syrup (821 mg.) having OMe 51·2% and giving only a trace of di-*O*-methylglucose on hydrolysis.

*Hydrolysis of methylated panose and fractionation of the products.* Methylated panose (750 mg.) was hydrolysed,[11] neutralized, and adsorbed on a column (1 × 22 in.) of charcoal (50 g.; British Drug Houses, Ltd., "Activated charcoal for decolorising purposes") mixed with Celite 535 (50 g.; Johns-Manville Co. Ltd.) and previously washed with aqueous $10^{-2}$N-formic acid until the eluate had pH 3·0.[12] A gradient elution [13] with $10^{-2}$N-formic acid (4 l.)—30% (v/v) ethanol in aqueous $10^{-2}$N-formic acid displaced three separate zones of optically active material in fractions (50 ml. each) 49—66, 67—86, and 101—118. These were evaporated and dissolved in water (25 ml.) for determination of optical rotation and concentration (by oxidation of 0·2 ml. portions with sodium hypoiodite at pH 11·4 [14]). The specific optical rotation and yield of each sugar were thereby determined.

Each sugar behaved as a single substance when examined by paper chromatography. The products in fractions 49—66 and 101—118 were crystallized from chloroform–di-isopropyl ether (1 : 9, v/v) and diethyl ether–light petroleum (b. p. 40—60°) (1 : 9, v/v), respectively. The crystalline anilides of the latter sugar and that in fractions 67—86 were also prepared. The results are tabulated.

Properties of *O*-methylglucoses from methylated panose.*

| Fraction | Methyl-glucose | Wt. (mg.) | M. p. | $[\alpha]_D$ in water † | Anilide M. p. | Anilide $[\alpha]_D$ in EtOH |
|---|---|---|---|---|---|---|
| 49—66 | 2,3,6 | 195 | 121—121·5° (121—122°) | 74·8° (70·5°) | — | — |
| 67—86 | 2,3,4 | 190 | — | 76·0 (79·0) | 145—146° (145—145·5°) | −98·0° (−102°) |
| 101—118 | 2,3,4,6 | 202 | 74—76 (96) | 80·7 (84·0) | 137·5—138 (136—137) | 236 (235) |

* Values for authentic materials are given in parentheses. † Determined on the basis of concentrations measured by hypoiodite oxidation. When fractions 49—66 and 101—118 were crystallized and weighed for determination of $[\alpha]_D$ the values were 73·0° and 83·7°, respectively.

[8] Whelan and Morgan, *Chem. and Ind.*, 1954, 78.
[9] Kuhn, Trischmann, and Löw, *Angew. Chem.*, 1955, **67**, 32.
[10] Woolf, *Nature*, 1953, **171**, 841.
[11] Croon, Herrström, Kull, and Lindberg, *Acta Chem. Scand.*, 1960, **14**, 1338.
[12] Taylor and Whelan, *Chem. and Ind.*, 1962, 44.
[13] Alm, Williams, and Tiselius, *Acta. Chem. Scand.*, 1952, **6**, 826.
[14] Ingles and Israel, *J.*, 1948, 810.

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## 742. *A Convenient Preparation of 2,5-Bishydroxymethylfuran.*

By P. A. FINAN.

THE recent synthesis [1] of furan-2,5-dicarboxylic acid through methyl 5-chloromethyl-2-furoate prompts us to record a similar route [2] to 2,5-bishydroxymethylfuran, which is more convenient than those [3,4] from 5-hydroxymethylfurfuraldehyde.

Methyl 5-chloromethyl-2-furoate [5] was treated with methanolic potassium hydroxide as described [5] for its conversion into methyl 5-hydroxymethyl-2-furoate; however, much unchanged chloro-ester was obtained. Treatment with boiling water [6] also gave a product with a weakly positive halogen test. Pure hydroxymethyl derivative was obtained, however, by treatment of the chloro-compound with sodium acetate in acetic acid, to afford methyl 5-acetoxymethyl-2-furoate, which was deacetylated by Zemplen's method.[7] Reduction of the hydroxymethyl ester, or (more conveniently) of the acetoxymethyl compound, with lithium aluminium hydride followed by acetylation *in situ* gave 2,5-bis-acetoxymethylfuran which on deacetylation gave 2,5-bishydroxymethylfuran.

*Experimental.—Methyl 5-acetoxymethyl-2-furoate.* Methyl 5-chloromethyl-2-furoate (prepared in 80% yield by Andrisano's method; [5] plates, m. p. 33°; 12·5 g.), anhydrous sodium acetate (25 g.), and acetic acid (50 ml.) containing a little acetic anhydride (5 ml.) were heated under reflux for 1 hr. After cooling, the mixture was diluted with ether and neutralised with aqueous sodium hydrogen carbonate. Working-up in the usual way gave methyl 5-acetoxymethyl-2-furoate (11·2 g., 92%), b. p. 96°/0·2 mm., $n_D^{25}$ 1·4910 (Found: C, 54·5; H, 5·2. Calc. for $C_9H_{10}O_5$: C, 54·5; H, 5·1%) (lit.,[1] b. p. 135—137/5 mm., m. p. 142—143°).

*Methyl 5-hydroxymethyl-2-furoate.* The preceding compound (4 g.) was treated with methanolic 0·2% sodium methoxide (25 ml.) at room temperature for 24 hr. The solution was passed through IRC-50 cation-exchange resin and concentrated *in vacuo*. Methyl 5-hydroxymethyl-2-furoate (2·75 g., 87%) was obtained as an oil, b. p. 62°/0·02 mm., $n_D^{25}$ 1·4922 (Found: C, 53·7; H, 5·25. Calc. for $C_7H_8O_4$: C, 53·8; 5·1%) (Andrisano [5] gives b. p. 146°/29 mm.).

*2.5-Bishydroxymethylfuran.* Methyl 5-acetoxymethyl-2-furoate (6 g., 0·03 mole) [or methyl 5-hydroxymethyl-2-furoate (5·2 g., 0·03 mole)] in ether (25 ml.) was added dropwise to lithium aluminium hydride (2 g., 0·05 mole) in ether (100 ml.). The mixture was stirred at room temperature for 1 hr., then acetic anhydride (20 ml.) was slowly added. The ether was evaporated and the residue was stirred vigorously at 125° for 2 hr. After cooling, the mixture was diluted with ether and neutralised with aqueous sodium hydrogen carbonate. 2,5-Bis-acetoxymethylfuran (4·8 g., 75%) was obtained as needles (from light petroleum b. p. 60—80°), m. p. 64° (lit.,[3a] 64°).

Treatment of this product with methanolic 0·2% sodium methoxide at room temperature for 24 hr. gave a quantitative yield of 2,5-bishydroxymethylfuran, plates (from ethyl acetate), m. p. 76° (lit.,[4] 77·5—77°) (Found: C, 56·1; H, 6·3. Calc. for $C_6H_8O_3$: C, 56·2; H, 6·25%). The diol (0·5 g.) in 10% aqueous sodium hydroxide was treated with benzoyl chloride;

[1] Gonis and Amstutz, *J. Org. Chem.*, 1962, **27**, 2946.
[2] Finan, Ph.D. Thesis, The Queen's University of Belfast, 1960.
[3] (*a*) Blanksma, *Rec. Trav. chim.*, 1910, **29**, 403; (*b*) Middendorp, *ibid.*, 1919, **38**, 1.
[4] Newth and Wiggins, *Research*, 1950, **3**, S 50.
[5] Andrisano, *Ann. Chim.* (*Italy*), 1950, **40**, 30.
[6] Cf. Cooper and Nuttall, *J.*, 1912, 1075.
[7] Zemplen, *Ber.*, 1926, **59**, 1258.

a dibenzoate (1·05 g., 80%) was obtained, forming prisms (from methanol), m. p. 76° (lit.,[4] 76—77°) (Found: C, 71·7; H, 4·9. Calc. for $C_{20}H_{16}O_5$: C, 71·4; H, 4·8%).

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## 743. *Reaction between Oxalyl Chloride and Saturated Hydrocarbons Induced by Ultraviolet Light and γ-Rays.*

By M. T. AHMED and A. J. SWALLOW.

KHARASCH and BROWN have reported the formation of acid chlorides in the photolysis of oxalyl chloride in the presence of paraffin hydrocarbons.[1] Low conversions were obtained in some cases, even when appreciable amounts of unchanged reactants were still present, and were attributed to the formation of coloured products which prevented further reaction by absorbing light. We have now compared the effects of γ-rays and ultraviolet light on the reaction.

The results (Figs. 1 and 2) show that the two reactions follow a similar course. This strongly suggests that the formation of coloured products does not account for the limited

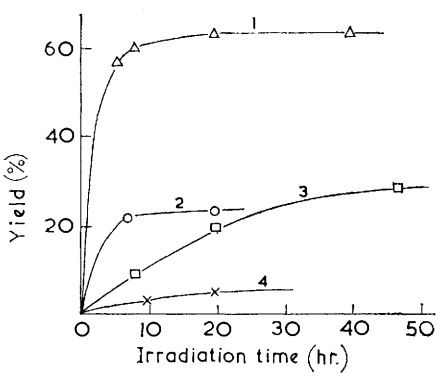


FIG. 1. Yield (%) of acid chloride on irradiation with ultraviolet light.

1, Cyclohexane. 2, Methylcyclohexane. 3, Methylcyclopentane. 4, 2,2,4-Trimethylcyclopentane.

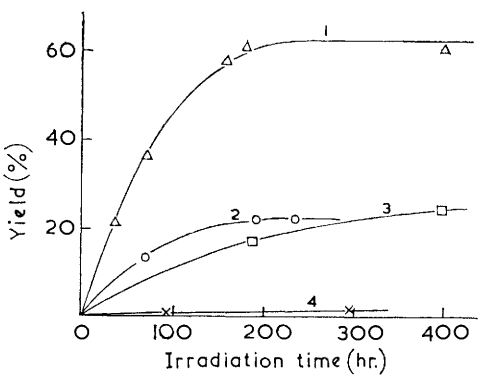


FIG. 2. Yield (%) of acid chloride on irradiation with γ-rays.

1—4, As for Fig. 1.

conversions. Also we have noted a lack of correlation between the colour of the reaction mixture and the extent of reaction. Kharasch and Brown found that the addition of coloured residues to a reaction mixture strongly inhibited the reaction, and also that higher conversions could be obtained by the illumination of freshly distilled reactants in a continuous process. Both these experiments and our own are consistent with inhibition of reaction through the formation of involatile compounds which are more susceptible to radical attack than is the original hydrocarbon.

*Experimental.*—Oxalyl chloride was prepared by Staudinger's method [2] from finely powdered " AnalaR " phosphorus pentachloride and anhydrous oxalic acid. Cyclohexane,

[1] Kharasch and Brown, *J. Amer. Chem. Soc.*, 1942, **64**, 329.
[2] Staudinger, *Ber.*, 1908, **41**, 3558.

methylcyclohexane, and 2,2,4-trimethylpentane were the best available grades from B.D.H., and methylcyclopentane was obtained from Aldrich Chemical Co. The molar ratios of oxalyl chloride to hydrocarbon were 0·05 : 0·1. Experiments were carried out in B24 test tubes fitted with efficient condensers. Ultraviolet illumination was with a 400-w Hanovia U.V.S. 220 lamp and was restricted to the liquid phase of the mixture. The distance from the lamp to the vessel was 10 cm. The intensity was kept as constant as possibly by using an intensity stabiliser. The maximum temperatures of mixtures during the reactions were 40° for cyclohexane, 42° for methylcyclohexane, 48° for methylcyclopentane, and 50° for 2,2,4-trimethylpentane. A kilocurie $^{60}Co$ source was used for $\gamma$-irradiations. The distance between the reactants and the source was constant at 5·5 cm., the dose-rate being $1·2 \times 10^5$/rad/hr.

After reaction the mixture of unchanged oxalyl chloride and hydrocarbon (excess) was distilled off at atmospheric pressure in a conventional micro-distillation unit. Acid chloride was then separated, distilled at 60 mm., weighed, and identified by neutralisation equivalent and preparation of the amide.

In a typical experiment, oxalyl chloride (6·35 g., 0·05 mole) and cyclohexane (8·4 g., 0·1 mole), after 20 hours' exposure to ultraviolet light, yielded 4·6 g. (63%) of acid chloride. 180 hours $\gamma$-irradiation gave 4·46 g. of acid chloride ($G = 93$). The acid chloride, b. p. 106—108°/60 mm., had an equivalent weight of 146 and gave an amide which melted at 185°.

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