543. *Metal Complexes of Histamine and Some Structural Analogues. Part II.*[1] *Metal Complexes of 2-2′-Aminoethylimidazole.*

By F. Holmes and F. Jones.

2-2′-Aminoethylimidazole differs structurally from histamine only in the position of the side-chain, but it is devoid of histamine activity.[2] However, it still has the configuration necessary to form six-membered chelated rings with metal ions. Formation constants have therefore been obtained for a few of its metal complexes as a comparison with those already found for histamine.[1]

Experimental and Results.—2-2′-Aminoethylimidazole was prepared as its dihydrochloride by Jones's method.[3] Potentiometric titrations were carried out at 25·0° and 0·0° and formation constants calculated as previously described.[1] Results, together with those for histamine, are summarised in the Table.

Logarithms of formation constants of metal complexes.

				Cu(II)			Ni(II)				
Ligand		pK_1'	pK_2'	β_1	β_2	K_1/K_2	β_1	β_2	β_3	K_1/K_2	K_2/K_3
Histamine	0°	6·37	10·42	10·10	17·00	3·20	—	—	—	—	—
,, ...	25°	5·94	9·80	9·55	16·04	3·06	6·84	11·92	14·98	1·76	2·02
2-2′-Aminoethyl-imidazole	0°	6·02	10·04	9·09	16·57	1·61	—	—	—	—	—
,, ,,	25°	5·59	9·32	8·56	15·60	1·52	5·99	11·10	15·16	0·88	1·05

Discussion.—Histamine is slightly the more basic ligand and as expected its complexes are rather more stable (except β_3 for nickel). However, values of log (K_1/K_2) and log (K_2/K_3) for 2-2′-aminoethylimidazole are only about half the corresponding values for histamine. The histamine ratios are among the highest known for six-membered rings, but the ratios now found for 2-2′-aminoethylimidazole are low and are nearer those normally expected for five-membered rings. Such ratios are very responsive to errors in the constants themselves but the differences in the case of these two similar ligands are very marked.

Inspection of the electron densities, bond orders, and bond lengths calculated by Brown [4] does not suggest any pronounced difference between the 2- and the 4-position; an aminomethyl group at position 4 gives values of log(K_1/K_2) reasonable for a 5-membered ring,[1] as it does for the 2-position of benzimidazole,[5] no figures being available for imidazole itself.

The entropy and free-energy terms have been discussed for the Cu(II)–histamine complex [6] in relation to the suggestion that the very high value of log(K_1/K_2) is due to a *trans*-configuration. Values of ΔH^0 and ΔS^0 calculated from the data of the Table for the formation of the ions [Cu(histamine)]$^{2+}$ and [Cu(histamine)$_2$]$^{2+}$ from their components are −8 and −14 kcal. mole^{-1} and 16 and 25 cal. mole^{-1} deg.$^{-1}$ at 25°, respectively. Corresponding values for [Cu(2-2′-aminoethylimidazole)]$^{2+}$ and [Cu(2-2′-aminoethylimidazole)$_2$]$^{2+}$ are −8 and −15, and 13 and 23, respectively. Although data so derived may be seriously in error the figures are of the same order with both ligands.

[1] Holmes and Jones, *J.*, 1960, 2398.
[2] Lee and Jones, *J. Pharmacol.*, 1949, **95**, 71.
[3] Jones, *J. Amer. Chem. Soc.*, 1949, **71**, 383.
[4] Brown and Hefferman, *Austral. J. Chem.*, 1959, **12**, 543.
[5] Irving and Weber, *J.*, 1959, 2560.
[6] Mickel and Andrews, *J. Amer. Chem. Soc.*, 1955, **77**, 5291.

Unfortunately this work cannot be continued. We thank Professor S. Peat, F.R.S., for his interest, and Dr. J. E. McKail for advice on the synthesis. One of us (F. J.) is grateful to the Department of Scientific and Industrial Research for a grant.

UNIVERSITY COLLEGE OF NORTH WALES,
BANGOR, CAERNARVONSHIRE. [*Received, November 2nd,* 1961.]

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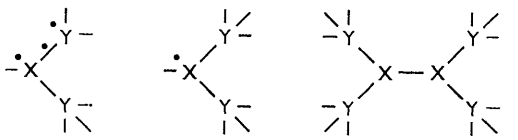
544. *Triatomic Molecules and Ions Containing Nineteen Valency Electrons.*

By MICHAEL GREEN.

THE behaviour of various triatomic molecules and ions containing 17 valency electrons has been discussed by Green and Linnett [1] in an earlier paper, in which particular attention was paid to the tendency of such compounds to dimerize. In this note, nineteen-valency electron systems are considered. As in the earlier paper, the discussion is confined to elements from the first two Periods.

When the arguments of the earlier paper [1] are applied to a molecule XY_2, containing nineteen valency electrons, three possibilities arise: (*A*) X and Y are approximately equal in electronegativity, so that the principal resonant hybrid is (I), which has an overall bond order of $2\frac{1}{2}$. (*B*) The electronegativity of Y is greater than that of X by one or more (on



(I) (II) (III)

Pauling's scale [2]), so that the main hybrid is (II), which has a total bond order of 2. (*C*) The electronegativity of X is greater than that of Y by one or more; however, such systems are very uncommon and are not considered here.

The dimer X_2Y_4, unless the octet rule is violated, has to be represented by structure (III), which has an overall bond order of 5. (It is assumed that dimerization occurs by formation of an X–X bond, for this is normally the case.) During dimerization of two molecules (I), there is no rise in bond order. In the case of (II), however, there is an increase of one. According to the argument of the previous paper,[1] therefore, if X and Y are nearly equal in electronegativity (case A), the dimer X_2Y_4 will be either of low stability or non-existent, while if the difference in electronegativity of X and Y is greater than one, as in case (*B*), X_2Y_4 will be stable. Examples of cases (*A*) and (*B*) in 17—34 electron systems are N_2O_4 and $C_2O_4^{2-}$.

ClO_2, O_3^-, and NO_2^{2-} are all nineteen-electron examples of case (*A*), for the differences in electronegativities [2] of the atoms involved are small (N = 3·0, O = 3·5, Cl = 3·0). The dimer of ClO_2, *i.e.*, Cl_2O_4, is unknown. The ozonide ion is now fairly well characterized,[3,4] but no dimer O_6^{2-} has been detected. NO_2^{2-} may be present in equilibrium with $N_2O_4^{4-}$ in $Na_4N_2O_4$, a substance shown by Asmussen [5] to be paramagnetic. The change in magnetic susceptibility of this compound with temperature has been investigated by Klemm and Pauli.[6] These workers used the solid salt and it is possible

[1] Green and Linnett, *J.*, 1960, 4959.
[2] Pauling, " The Nature of the Chemical Bond," Cornell Univ. Press, 1960, p. 88 ff.
[3] Whaley and Kleinberg, *J. Amer. Chem. Soc.*, 1951, **73**, 79.
[4] McLachlan, Symons, and Townsend, *J.*, 1959, 952.
[5] Asmussen, *Kem. Maanedsblad*, 1941, **6**, 81; *Acta Chem. Scand.*, 1958, **12**, 578.
[6] Klemm and Pauli, *Z. anorg. Chem.*, 1951, **266**, 30.

that equilibrium was not reached as their results do not show a linear relationship between $\ln K$ and $1/T$. Nevertheless, their results would indicate an energy of dissociation between 0·75 and 1·5 kcal. mole^{-1}, pointing to an example of case (*A*). However, the evidence for NO_2^{2-} is somewhat tentative.[7]

Case (*B*) is more complicated in a 19—38-electron system than in the 17—34-particle analogue. In a 17-electron system, theoretical considerations by Mulliken,[8] by Walsh,[9] and by Green and Linnett [10] indicate that the unpaired electron lies in a $4a_1$ orbital. This fact has been verified in the case of NO_2 by Bird, Baird, and Williams.[11] On dimerization, pairing of electrons of this type leads primarily to a σ-bond, which is however accompanied by some π-conjugation,[12,13] that causes the planar configuration. In the nineteen-electron dimer, however, two complications arise. First, there are the lone pairs on each X atom in X_2Y_4 in the 38-electron system, which are not present in N_2O_4 or $C_2O_4^{2-}$. Repulsion between these lone pairs will weaken the X–X bond in X_2Y_4 particularly if X belongs to the first Period,* so that in case (*B*) a stable dimer will not necessarily be found (cf. $C_2O_4^{2-}$).

NF_2 provides an example of case (*B*), for the difference in electronegativity between the atoms involved is unity [2] (N = 3·0, F = 4·0). Colburn and Johnson [14] have shown that the energy of dimerization is relatively low, namely, 19·2 kcal. mole^{-1}.

In the dithionite ion $S_2O_4^{2-}$, the central atoms (*i.e.*, X) no longer come from the first Period, hence lone pair repulsion ought to be diminished. The 19-electron system SO_2^-, therefore, should be an example of case (*B*), in which the tendency to dimerize is stronger (electronegativities: [2] S = 2·5, O = 3·5). Clark, Horsfield, and Symons [7] have verified that in a solution of sodium dithionite only small quantities of SO_2^- exist. However, the S–S bond in sodium dithionite is abnormally long, namely, 2·39 Å [15] compared with 2·05 Å [16] in H_2S_2. An explanation of this phenomenon is offered below.

The second complication in 19-electron systems is that the unpaired electron lies in a $2b_1$ orbital,[8,9,10] which has a node in the plane of the molecule. An electron in this level, at least, in a planar dimer, would lead to a bond which was essentially π in character. (The pure π-bond was suggested by Coulson and Duchesne [17] to explain the properties of N_2O_4.) However, it is unlikely that overlap of two *p*-orbitals alone in a bond would lead to the most stable configuration. N_2F_4 has been shown by Lide and Mann [18] to have a hydrazine-like structure, rather than a planar form. (Incidentally in view of the weak N–N link, one wonders if they are justified in assuming that the bond has a normal length of 1·47 Å in determining the structure.) On the other hand, the dithionite ion in $Na_2S_2O_4$ is planar,[15] which might be attributed to a pure π-bond. This idea precludes the possibility of some electronic excitation from the $4a_1$- to the $2b_1$-orbital of the SO_2^- ion during dimerization. In this species, provided that the electronic distribution is $(4a_1)^2(2b_1)$, the apex angle ought to be near in size to $118\frac{1}{2}°$, the value [19] observed in ClO_2. However Walsh's correlation diagram [9] indicates that a configuration $(4a_1)(2b_1)^2$ would have a considerably larger apex angle. The OSO angle in $Na_2S_2O_4$ is 163°,[15] a size which indicates that this sort of excitation probably occurs. Nevertheless, some π-bonding must occur in the anion

* Compare the dissociation energies in the sequence: F_2 = 36, Cl_2 = 57, Br_2 = 45, I_2 = 36 kcal. mole^{-1} (Cottrell, " Strength of Chemical Bonds," Butterworths Scientific Publns., London, 1958).

[7] Clark, Horsfield, and Symons, *J.*, 1961, 7.
[8] Mulliken, *Canad. J. Chem.*, 1958, **36**, 10.
[9] Walsh, *J.*, 1953, 2266.
[10] Green and Linnett, *Trans. Faraday Soc.*, 1961, **57**, 1.
[11] Bird, Baird, and Williams, *J. Chem. Phys.*, 1958, **28**, 738; for a fuller discussion, see ref. 10.
[12] Green and Linnett, *Trans. Faraday Soc.*, 1961, **57**, 10.
[13] Brown and Harcourt, *Proc. Chem. Soc.*, 1961, 216.
[14] Colburn and Johnson, *J. Chem. Phys.*, 1960, **33**, 1869.
[15] Dunitz, *J. Amer. Chem. Soc.*, 1956, **78**, 878.
[16] Stevenson and Beach, *J. Amer. Chem. Soc.*, 1938, **60**, 2872.
[17] Coulson and Duchesne, *Bull. Classe Sci., Acad. roy. Belg.*, 1957, **43**, 522.
[18] Lide and Mann, *J. Chem. Phys.*, 1959, **31**, 1129.
[19] Nielsen and Woltz, *J. Chem. Phys.*, 1952, **20**, 1878.

because of its planarity. It is therefore suggested that configurational interaction occurs between

$$(4a_1)^2(4a_1')^2(2b_{3u})^2,\ ^1A_g \text{ " } \pi \text{ "-bond}$$

and

$$(4a_g)^2(2b_1)^2(2b_1')^2,\ ^1A_g \text{ " } \sigma \text{ "-bond}$$

where $2b_{3u}$ is the bonding combination of $2b_1$ and $2b_1'$, and $4a_g$ is the bonding combination of $4a_1$ and $4a_1'$.

This does not happen in N_2F_4 because of the greater separation in energy of 2*s*- and 2*p*-orbitals than of 3*s*- and 3*p*-orbitals.

I thank Drs. M. J. S. Dewar and Henry Taube for interesting and helpful discussions.

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545. *Infrared Spectra and Structure of the Deuterated Propene Complex* $K[PtCl_3(C_3D_6)],H_2O$.

By D. M. Adams and J. Chatt.

In 1953 Chatt and Duncanson [1] reported the infrared spectra of five olefin co-ordination complexes and concluded that the olefin in the complex retained a large part of its double-bond character. A band near 1500 cm.$^{-1}$ was assigned to the C=C bond stretching mode ($\nu_{C=C}$) in the co-ordinated olefin. This assignment has been challenged by Babushkin, Gribov, and Gel'man [2] who, arguing by analogy with the spectrum of ethylene oxide, said that the 1500 cm.$^{-1}$ band was due to a CH_2 deformation mode. Adams and Chatt,[3] however, found absorption near 1500 cm.$^{-1}$ in complexes of substituted olefins having no CH_2 group. Powell and Sheppard [4] published similar infrared evidence, and from a study of the nuclear magnetic resonance spectrum also concluded that the co-ordinated olefin retained most of its double-bond character.

To confirm the assignment of the 1500 cm.$^{-1}$ band to a lowered $\nu_{C=C}$ mode we have now prepared the salt $K[PtCl_3(C_3D_6)],H_2O$, and recorded its infrared spectrum from 2·5 to 50 μ (see Table).

Absorption frequencies (cm.$^{-1}$) of $K[PtCl_3(C_3X_6)],H_2O$ (X = H or D).

X = H	X = D	X = H	X = D	X = H	X = D	X = H	X = D
*3538s	*3538s	2971sh	2208vw	1365s	1000sh	830w	580sh
*3480s	*3480s	2965m	2203sh	1252vw	934w	809w	*(535)vs, broad
*3262w	*3262w	2911vw	*1621vs	1175w	864vs	635vw	370m
*3205w	*3205w	*1621vs	1416s	1049s	780w	*(530)vs, broad	330vs
3068m	2252w	1504s	1144m	1010m	762m	393m	306s
3034w	2242sh	1449s	1048m	990m	721m	330vs	
3010m		1429s	1038m	932m	686w	306s	
		1392m		899m			

* Frequencies due to water of crystallisation.

In a full assignment of the vibrational spectra of propene and hexadeuteriopropene, Lord and Venkateswarlu [5] found $\nu_{C=C}$ at 1651·6 and 1587·6 cm.$^{-1}$, respectively. The drop

[1] Chatt and Duncanson, *J.*, 1953, 2939.
[2] Babushkin, Gribov, and Gel'man, *Russ. J. Inorg. Chem.*, 1959, **4**, 695.
[3] Adams and Chatt, *Chem. and Ind.*, 1960, 149.
[4] Powell and Sheppard, *J.*, 1960, 2519.
[5] Lord and Venkateswarlu, *J. Opt. Soc. Amer.*, 1953, **43**, 1079.

in frequency upon deuteration, $\Delta\nu$, is 64 cm.$^{-1}$. For the CH_2 deformation mode, $\Delta\nu$ = 286 cm.$^{-1}$ (1298; 1012 cm.$^{-1}$). Other C–H deformation vibrations drop by 200—400 cm.$^{-1}$ upon deuteration.

The only absorption found (see Table) for our deuterio-salt between 1621 (δH_2O) and 1114 cm.$^{-1}$ is a band at 1416 cm.$^{-1}$. This we assign to $\nu_{C=C}$, corresponding to the 1504 cm.$^{-1}$ band in the protium analogue. Thus, for co-ordinated propene, $\Delta\nu$ = 88 cm.$^{-1}$ for $\nu_{C=C}$, which proves that the 1504 cm.$^{-1}$ band originates, essentially, in a C=C stretching mode, lowered by co-ordination by some 148 cm.$^{-1}$ from the normal value, and cannot be associated with any essentially hydrogenic vibration.

The frequencies were assigned for Zeise's salt $K[PtCl_3(C_2H_4)]$ by Powell and Sheppard [6] by comparison with the spectra of ethylene and ethylene sulphide. A similar treatment for the propene analogue leads to equivocal assignments, and a normal co-ordinate calculation is necessary. Bands in the far-infrared region can be assigned more confidently. Both complexes give two bands near 320 cm.$^{-1}$, that of higher frequency being the stronger and broader. These may be attributed to platinum–chlorine stretching modes (ν_{Pt-Cl}). (K_2PtCl_6 has infrared absorption at 345 cm.$^{-1}$.[7]) The Pt–Cl bond *trans* to the olefin is expected to be weaker than each of the other Pt–Cl bonds, owing to the higher *trans*-effect of propene than of chlorine. The 306 cm.$^{-1}$ band is therefore assigned to ν_{Pt-Cl} of the bond *trans* to propene and the higher-frequency band to the antisymmetric stretching vibration of the linear Cl–Pt–Cl unit.

Bands at 393 and 370 cm.$^{-1}$ in the spectra of the propene and deuteriopropene salt, respectively, may be assigned to a torsional mode of the olefin, with respect to the rest of the molecule.

Experimental.—Potassium trichloro[$^2H_6$]*propeneplatinite monohydrate*, $K[PtCl_3(C_3D_6)],H_2O$. This was prepared analogously to $K[PtCl_3(C_3H_6)],H_2O$ by the reaction of the olefin with aqueous potassium tetrachloroplatinite.[1] The reaction is slow (3 weeks), and to avoid the rather remote possibility of deuterium–hydrogen exchange with the olefin the reaction was carried out in heavy water. A sealed vessel was used to avoid loss of deuteriopropene. Potassium tetrachloroplatinite (2·5 g.), and a 3% solution of hydrogen chloride in deuterium oxide (12·5 ml.) were introduced into a bulb of ~200-ml. capacity, fitted with two high-vacuum taps in series. The mixture was frozen in liquid nitrogen, and the bulb evacuated and then warmed to room temperature to release trapped air bubbles. This procedure was repeated. [$^2H_6$]Propene (0·33 l.) was admitted to the vessel which was cooled in liquid nitrogen. The bulb was then removed from the vacuum-line and shaken for 3 weeks, during which the colour lightened, then cooled in iced water. The solution was filtered, and the yellow residue dried *in vacuo*. This material was recrystallised from a very small quantity of 3% aqueous hydrochloric acid by slow evaporation from a covered vessel in a desiccator. This caused the deposition of fairly large yellow crystals of the *product* and small brownish-red crystals of potassium tetrachloroplatinite. The yellow crystals were selected by hand and shown to be pure $K[PtCl_3(C_3D_6)],H_2O$ by analysis and the infrared spectrum [Found (D : H ratio assumed to be 3 : 1): C, 8·9; D, 3·0; H, 0·5. $C_3H_2Cl_3D_6KOPt$ requires C, 8·7; D, 2·9; H, 0·5%]. The infrared spectrum proved that the propene in the complex is fully deuterated, that the solvent of crystallisation is H_2O, and that neither HOD nor D_2O is present.

Infrared spectra were recorded for Nujol and hexachlorobutadiene mulls on a Grubb–Parsons GS2A spectrometer. Spectra in the 20—50 μ region were recorded on Nujol mulls with an evacuated grating spectrometer.

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[6] Powell and Sheppard, *Spectrochim. Acta*, 1958, **13**, 69.
[7] Adams, *Proc. Chem. Soc.*, 1961, 335.

546. *The Purification of Acetylglycosyl Bromides.*

By P. A. Finan and C. D. Warren.

The poly-*O*-acetylglycosyl bromides are readily prepared by treatment of the fully acetylated sugars with hydrogen bromide in glacial acetic acid.[1] Yields are usually good although difficulty in purification is sometimes experienced. These compounds do not keep well however and the recrystallisation of partly decomposed material usually results in considerable loss. We have found that chromatography on silica gel using anhydrous ether as developing solvent provides an excellent method for purification of the crude material arising either from reaction or from decomposition on storage. A number of examples of the use of this technique is given in the Table. In the case of the two disaccharides, elution from the column was accelerated by the use of anhydrous ether containing 5% anhydrous acetone.

Preparation of poly-*O*-acetylglycosyl bromides and their purification by using silica-gel chromatography.

	Yield of glycosyl bromide *		Obs.		Lit.		
Poly-*O*-acetate (g.)	(g.)	(%)	M. p.	$[\alpha]_D^{25}$	M. p.	$[\alpha]_D$	Ref.
Penta-*O*-acetyl-β-D-glucopyranose (6·4)...	5·65	80	86—88°	+197°	88—89°	+198°	*a*, 4(*b*)
Penta-*O*-acetyl-β-D-galactopyranose (5)...	4·2	77	83—84	+219	84—85	+217	*b*
Tetra-*O*-acetyl-β-D-xylopyranose (5)	4·2	75	98—99	+219	101—102	+212	*a*
Tetra-*O*-acetyl-β-L-arabinopyranose (4·5)	3·5	71	139	+285	139	+283	*c*
Octa-*O*-acetyl-β-lactose (5·5)	5·2	90	146—147	+109	145	+109	4(*a*)
Octa-*O*-acetyl-β-maltose (5)	4·6	88	Amorphous	+179	112—113	+180	3

* All glycosyl bromides prepared had the α-configuration except tri-*O*-acetyl-β-L-arabinopyranosyl bromide.

a Brauns, *J. Amer. Chem. Soc.*, 1925, **47**, 1280.
b Ohle, Marecek, and Bourjau, *Ber.*, 1929, **62**, 833.
c Gehrke and Aichner, *Ber.*, 1927, **60**, 918.

The hepta-*O*-acety-α-maltosyl bromide obtained by this method was an amorphous powder, $[\alpha]_D^{25}$ +179°. When the bromide was prepared from octa-*O*-acetyl-β-maltose by using titanium tetrabromide in chloroform,[2] the same amorphous product was obtained after chromatography. While Brauns [3] has described the isolation of crystalline hepta-*O*-acetyl-α-maltosyl bromide, m. p. 112—113°, $[\alpha]_D$ +180·1°, many workers [4] have reported the isolation and subsequent synthetical use of the amorphous form. Hudson and Sayre [4d] treated their amorphous hepta-*O*-acetyl-α-maltosyl bromide with silver oxide in methanol and obtained methyl hepta-*O*-acetyl-β-maltoside in good yield. We treated our amorphous product in a similar manner and obtained the same crystalline glycoside (80% yield).

Experimental.—Typical experiment: preparation of 2,3,4-*tri*-O-*acetyl*-α-L-*rhamnopyranosyl bromide.* Tetra-*O*-acetyl-L-rhamnopyranose (anomeric mixture prepared by treatment of L-rhamnose with anhydrous sodium acetate in acetic anhydride in the usual way; syrup, $[\alpha]_D^{25}$ −37·5°; 5 g.) was treated with hydrogen bromide in glacial acetic acid (50% w/v; 10 ml.) at 0° until a clear solution resulted (1 hr.) and for a further 1 hr. The mixture was diluted

[1] For a review see Haynes and Newth, *Adv. Carbohydrate Chem.*, 1955, **10**, 207.
[2] Zemplen and Gerecs, *Ber.*, 1934, **67**, 2049.
[3] Brauns, *J. Amer. Chem. Soc.*, 1929, **51**, 1820.
[4] (*a*) Fischer and Fischer, *Ber.*, 1910, **43**, 2522; (*b*) Fischer, *Ber.*, 1911, **44**, 1898; (*c*) Dale, *J. Amer. Chem. Soc.*, 1915, **37**, 2745; Karrer, *Helv. Chim. Acta*, 1921, **4**, 169, 263, 678; (*d*) Hudson and Sayre, *J. Amer. Chem. Soc.*, 1916, **38**, 1867.

with alcohol-free chloroform (25 ml.) and washed with ice–water until it was no longer acidic to Congo Red. After being dried (Na_2SO_4) the solution was concentrated under reduced pressure. The resulting brown syrup was chromatographed on silica gel (Grade 30/120 as supplied by Silica Gel Ltd., Hounslow, Middlesex; previously dried at 160° for 2 hr., 200 g.), anhydrous ether (300 ml.) being used as eluant. Removal of ether left a pale yellow residue which crystallised immediately, giving 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl bromide (4·2 g., 75%), m. p. 69—70°, $[\alpha]_D^{25}$ −172° (*c* 1 in chloroform) [Previously found [2,5] m. p. 71—72°, $[\alpha]_D^{20}$ −169° (in chloroform)].

We thank the Department of Scientific and Industrial Research for a Maintenance Allowance (to C. D. W.).

THE UNIVERSITY, SHEFFIELD, 10. [*Received, January 22nd,* 1962.]

[5] Fischer, Bergmann, and Rabe, *Ber.*, 1920, **53**, 2362.

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547. *The Preparation of Acid Amides from Acid Chlorides.*

By P. A. FINAN and G. A. FOTHERGILL.

THE examples in the Table show that amides are conveniently prepared by reaction of acid chlorides and ammonium acetate in acetone. The method appears to be milder than that using ammonia.[1] We consider that the reaction takes place through nucleophilic attack on the acid chloride by ammonia molecules which are produced in the dissociation [2] of ammonium acetate.

Experimental.—Typical experiment: preparation of benzamide. A mixture of benzoyl chloride (12 g.) and ammonium acetate (B.D.H. commercial grade; 12 g.) in acetone (100 ml.) was stirred vigorously for 1 hr., the mixture was filtered, and the filtrate was evaporated to dryness.

Preparation of acid amides from acid chlorides.

Acid chloride (g.)	NH_4·OAc (g.)	Me_2CO (ml.)	Reaction time (min.)	Yield of amide (%)	M. p. (obs.)	M. p. (lit.)	Ref.
Benzoyl (0·5)	0·5	10	30	65	127°		
3,5-Dinitrobenzoyl (5·0)	5·0	70	60	90	183	183°	*a*
,, (0·5)	0·5	10	30	68			
Acetyl (10·0)	10·0	100	60	64	81	82	*b*
,, (0·5)	0·5	10	30	40			
Chloroacetyl (10·0)	10·0	100	60	78	117	119	*c*
,, (0·5)	0·5	10	30	63			
2-Furoyl (5·0)	5·0	70	60	90	140	142	*d*
,, (0·5)	0·5	10	30	55			
Cinnamoyl (3·0)	3·0	50	60	83	146	147	*e*
,, (0·5)	0·5	10	30	79			
Crotonyl (2·0)	2·0	50	60	63	158	158	*f*
,, (0·5)	0·5	10	30	43			

a Heilbron, " Dictionary of Organic Compounds," 1934, Vol. I, p. 620. *b* Ref. 1(*b*). *c* Jacobs and Heidelberger, *Organic Syntheses*, Coll. Vol. I, 1941, p. 153. *d* Schwanert, *Annalen*, 1860, **14**, 63. *e* Galat, *J. Amer. Chem. Soc.*, 1948, **70**, 2596. *f* Stoermer and Stockmann, *Ber.*, 1914, **47**, 1790.

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[1] (*a*) Wohler and Liebig, *Annalen*, 1832, **3**, 249; Krafft and Stauffer, *Ber.*, 1882, **15**, 1728; (*b*) Aschan, *Ber.*, 1898, **31**, 2344; (*c*) Roe, Scanlan, and Swern, *J. Amer. Chem. Soc.*, 1949, **71**, 2215; (*d*) Philbrook, *J. Org. Chem.*, 1954, **19**, 623; B.P. 796,563/1958 (*Chem. Abs.*, 1959, **53**, 20,091).

[2] See Noyes, Kato, and Sosman, *J. Amer. Chem. Soc.*, 1910, **32**, 159; Ray, De, and Dhar, *J.*, 1913, 1565.

The solid residue was crystallised from hot water, giving benzamide (9·5 g., 92%), m. p. and mixed m. p. 124°.

Preparation of other amides. Other amides, made similarly are summarised in the Table.

We thank Monsanto Chemicals Ltd. for a Research Fellowship (to G. A. F.).

THE UNIVERSITY, SHEFFIELD, 10. [*Received, January 25th*, 1962.]

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548. 6-*Fluoroindole and its Derivatives.*

By M. BENTOV, A. KALUSZYNER, and Z. PELCHOWICZ.

FOR the synthesis of 6-fluoroindole, the Reissert synthesis has been employed,[1] starting with 4-fluoro-2-nitrotoluene which has been synthesized repeatedly by the Schiemann reaction from 4-amino-2-nitrotoluene [2,3] and, together with other products, by nitration of *p*-fluorotoluene.[4] The latter method has been improved to give a 60—70% yield of 4-fluoro-2-nitrotoluene. Oxidation thereof with chromic acid in acetic anhydride gave 4-fluoro-2-nitrobenzaldehyde in 35% yield (by reaction of 4-fluoro-2-nitrobenzenediazonium chloride with formaldoxime,[5] we obtained only an 18% yield of this aldehyde). Condensation of the aldehyde with nitromethane proceeded with a 76% yield and the subsequent reduction of 4-fluoro-2,ω-dinitrostyrene to 6-fluoroindole with a 62% yield (overall yield 16%). The conversion of 6-fluoroindole into *N*-substituted 6-fluorotryptamines was carried out as for the 5-fluoro-isomers.[6]

Experimental.—4-Fluoro-2-nitroaniline, m. p. 92—93°, was obtained in 92—96% yield from *p*-fluoroaniline, methyl nitrate, and sulphuric acid at 0—2°.[7]

4-Fluoro-2-nitrobenzaldehyde. A mixture of the foregoing compound (75 g.), concentrated hydrochloric acid (114 ml.), ice–water (300 ml.), and sodium nitrite (35 g.) in water (50 ml.), were added to a solution made up as follows: a mixture of paraformaldehyde (23 g.) and hydroxylamine hydrochloride (52·7 g.) was heated with water (340 ml.) and the clear solution treated with sodium acetate (102 g.), heated under reflux for 15—20 min., cooled at 10°, and mixed with a solution of sodium sulphate (2 g.), copper sulphate (12·5 g.), and sodium acetate (330 g.) in water (360 ml.). The first solution was added below the surface of the second with stirring. After 1 hr., the mixture was acidified to Congo Red and decanted from the precipitate, which then was heated with ferric ammonium sulphate (600 g.) in water (1 l.) for 45 min. and after that steam-distilled. The distillate was extracted with ether. The extract was dried and evaporated to yield the aldehyde (14·7 g., 18%), also obtained as below.

4-Fluoro-2-nitrotoluene. At 0—5°, a mixture of 98% nitric acid (65 g.) and sulphuric acid (100 ml.) was added dropwise to a stirred suspension of *p*-fluorotoluene (99 g.) in cold concentrated sulphuric acid (400 ml.). Cooling was stopped and stirring continued for 1 hr. The mixture was poured into ice–water, and the aqueous layer extracted with ether. The combined organic layers were washed successively with water, sodium carbonate solution, and water, dried, and distilled through a Todd column, to yield 4-fluoro-2-nitrotoluene (81 g., 58%), b. p. 104—105°/22 mm, n_D^{25} 1·5216 (lit.,[2] b. p. 108—109°/23 mm., n_D^{25} 1·5212). The distillation residue was probably the 3-nitro-isomer.

4-Fluoro-2-nitrobenzaldehyde. To the foregoing substance (81 g.), there were added glacial

[1] Allen, Brunton, and Suschitzky, *J.*, 1955, 1283.
[2] Steck and Fletcher, *J. Amer. Chem. Soc.*, 1941, **70**, 439.
[3] Suschitzky, *J.*, 1953, 3326.
[4] Desirant, *Bull. Sci. Acad. Roy. belges*, 1933, **19**, 325.
[5] Cf. Beech, *J*, 1954, 1297; Woodward, Bader, Bickel, Frey, and Kierstead, *Tetrahedron*, 1958, **2**, 1; Jolad and Rajagopal, *J. Sci. Ind. Res., India*, 1961, **20**, *B*, 399.
[6] Pelchowicz, Kaluszyner, and Bentov, *J.*, 1961, 5418.
[7] Smith and Steinle, *J. Amer. Chem. Soc.*, 1953, **75**, 1292.

acetic acid (815 ml.), acetic anhydride (815 ml.), and concentrated sulphuric acid (152 ml.), followed by chromic anhydride (144 g.). After dilution, the *diacetate* of the aldehyde separated; it had m. p. 70—71° (from methanol) (Found: C, 48·4; H, 4·1; F, 7·0. $C_{11}H_{10}FNO_6$ requires C, 48·7; H, 3·7; F, 7·0%).

The *aldehyde* obtained by saponification of the diacetate was distilled in steam and then in a vacuum. It had m. p. ~30° (29·8 g., 35%) and was characterized as 2,4-*dinitrophenylhydrazone*, m. p. 252—253°, golden plates from ethanol (Found: C, 44·7; H, 2·3; N, 20·3; F, 5·8. $C_{13}H_8FN_5O_6$ requires C, 44·7; H, 2·3; N, 20·1; F, 5·4%), and the yellow *semicarbazone*, m. p. 258—259° (decomp.) (Found: C, 42·5; H, 3·7; N, 25·1. $C_8H_7FN_4O_3$ requires C, 42·5; H, 3·1; N, 24·8%).

4-*Fluoro*-2,ω-*dinitrostyrene*. To a stirred solution of the aldehyde (40 g.) and nitromethane (20 g.) in methanol (200 ml.), potassium hydroxide (21 g.) in water (20 ml.) and methanol (120 ml.) was added dropwise at 5—10°. After 24 hr. the solution was diluted with ice–water and poured into dilute hydrochloric acid, and the oily precipitate was heated with acetic anhydride and anhydrous sodium acetate, cooled, and poured into water. The *product* (38·2 g., 76%), recrystallized from methanol, had m. p. 67—69°. An analytical sample, m. p. 69·0—69·5°, was obtained from light petroleum (Found: N, 13·2. $C_8H_5FN_2O_4$ requires N, 13·2%).

6-*Fluoroindole*. A solution of 4-fluoro-2,ω-dinitrostyrene (10·5 g.) in hot ethyl acetate (150 ml.) and glacial acetic acid (5 ml.) was hydrogenated with 10% palladium–charcoal (1·5 g.) at 60 lb. initial pressure. The required amount of hydrogen was absorbed during 15 min. The mixture was filtered and concentrated and the 6-fluoroindole (4·2 g., 62%) purified by steam-distillation. It melted at 75—76°, in agreement with the literature.[1]

6-*Fluoro*-3-*indolylglyoxalyl chloride*. To an ice-cold solution of 6-fluoroindole (13·5 g.) in dry ether (200 ml.), oxalyl chloride (20 ml.) in dry ether (150 ml.) was added dropwise and with stirring and cooling. The yellow precipitate (23 g., 88%), m. p. 250° (decomp.), was filtered off after 1 hr., washed with cold ether, dried, and used without further purification.

6-*Fluoro*-NN-*dimethyl*-3-*indolylglyoxylamide*. The previous compound (13 g.) was treated with dimethylamine (11 ml.) in cold ether (40 ml.). The precipitated *amide* was filtered off, washed with water, and recrystallized from methanol; it formed needles (10 g., 76%), m. p. 230—231°, which readily sublimed (Found: C, 62·0; H, 4·7; F, 8·0. $C_{12}H_{11}FN_2O_2$ requires C, 61·6; H, 4·7; F, 8·1%).

6-*Fluoro*-NN-*dimethyltryptamine*. A slurry of the foregoing compound (9·3 g.) in tetrahydrofuran (100 ml.) was added slowly to lithium aluminium hydride (12 g.) in tetrahydrofuran (150 ml.) and refluxed with stirring for 3 hr.; the product was decomposed with ethyl acetate and water, and the mixture filtered. The filtrate was concentrated, acidified, and extracted with ether, and the aqueous layer made alkaline and again extracted with ether. Evaporation of the last solvent yielded the *base* (6·5 g., 79%), m. p. 101—102° (from methanol), b. p. 130—140°/0·5 mm. (Found: C, 69·9; H, 7·2; F, 9·3. $C_{12}H_{15}FN_2$ requires C, 69·9; H, 7·3; F, 9·2%). The orange *picrate* had m. p. 196—197° (from methanol) (Found: C, 49·8; H, 4·4; F, 4·5. $C_{18}H_{18}FN_5O_7$ requires C, 49·7; H, 4·2; F, 4·4%).

NN-*Diethyl*-6-*fluoro*-3-*indolylglyoxylamide*. 6-Fluoro-3-indolylglyoxalyl chloride (6 g.) was treated with diethylamine (5 ml.) in cold ether (50 ml.). The precipitated *amide* (5·2 g., 75%), when recrystallized from methanol, had m. p. 189° (Found: C, 64·2; H, 6·1; F, 7·7; N, 11·2. $C_{14}H_{15}FN_2O_2$ requires C, 64·2; H, 5·7; F, 7·3; N, 10·8%).

NN-*Diethyl*-6-*fluorotryptamine*. A solution of the foregoing compound (4·5 g.) in tetrahydrofuran (200 ml.) was added dropwise to lithium aluminium hydride (5 g.) in tetrahydrofuran (200 ml.) and refluxed with stirring for 3 hr. and the product decomposed with ethyl acetate and water and filtered. The fluorescent organic layer was concentrated, acidified, and extracted with ether, and the aqueous layer made alkaline and again extracted with ether. Evaporation of the last solvent gave a paste (3·9 g., 75%) which was purified by vacuum-distillation (b. p. 156—159°/0·08 mm.). The product gave a crystalline *hydrochloride*, m. p. 139—140° (from methanol–ether) (Found: C, 62·5; H, 7·2; F, 6·9; N, 10·0. $C_{14}H_{20}ClFN_2$ requires C, 62·2; H, 7·4; F, 7·0; N, 10·4%).

6-*Fluoro*-3-*indolylglyoxylpiperidide*, prepared as above from the chloride (3 g.) and piperidine (6 ml.) and recrystallized from methanol, melted at 222° (2·8 g., 77%) (Found: 66·1; H, 5·2; F, 6·9; N, 10·1. $C_{15}H_{15}FN_2O_2$ requires C, 65·7; H, 5·5; F, 7·0; N, 10·2%).

6-*Fluoro*-3-2′-*piperidinoethylindole* was obtained by reduction of the foregoing compound (2·1 g.) with lithium aluminium hydride (4·5 g.). The brown product (0·9 g., 50%), when

recrystallized from methanol, had m. p. 110° and gave a *picrate*, m. p. 208—212° (from methanol) (Found: C, 52·9; H, 4·6; F, 4·5; N, 14·2. $C_{21}H_{22}FN_5O_7$ requires C, 53·0; H, 4·6; F, 4·0; N, 14·7%).

6-*Fluoro*-3-*indolylglyoxylmorpholide* (6·5 g., 93%), m. p. 236°, was obtained from the chloride (5·8 g.) and morpholine (7 ml.): it recrystallized from methanol (Found: C, 60·8; H, 4·7; F, 7·1; N, 9·8. $C_{14}H_{13}FN_2O_3$ requires C, 61·0; H, 4·7; F, 6·9; N, 10·1%).

6-*Fluoro*-3-2′-*morpholinoethylindole* (4·1 g., 70%), m. p. 137° (from methanol), was obtained from the foregoing compound (6·5 g.) by reduction with lithium aluminium hydride (12 g.) (Found: C, 67·2; H, 7·3; F, 7·8; N, 11·4. $C_{14}H_{17}FN_2O$ requires C, 67·8; H, 6·9; F, 7·7; N, 11·3%). The *picrate* melted at 230° (from methanol) (Found: C, 50·3; H, 4·0; F, 4·2; N, 14·8. $C_{20}H_{20}FN_5O_8$ requires C, 50·3; H, 4·2; F, 4·0; N, 14·7%).

For their technical assistance we are grateful to Mr. D. Baldermann and Mrs. L. Zelik.

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549. 6-*Fluoro*-, 6-*Methoxy*-, *and* 7-*Methoxy-tryptophan.*

By ERNST D. BERGMANN and ELIAHU HOFFMANN.

THE biochemical properties of 6-fluorotryptophan have been studied recently [1] but its synthesis has not yet been described. It appears both to inhibit tryptophan utilisation and to be a substrate for tryptophan-metabolising enzymes.

The preparation chosen was the condensation of diethyl acetamido- or formamido-malonate with 6-fluorogramine, which in turn was prepared from 6-fluoroindole.[2]

By the same method, the known [3] 6-methoxytryptophan was obtained. For the synthesis of 7-methoxytryptophan,[4] the Fischer indole synthesis applied to γ-acetamido-γγ-diethoxycarbonylbutyraldehyde *o*-methoxyphenylhydrazone [5] proved less cumbersome than the gramine method, though the yield in the cyclisation was low.

Experimental.—6-*Fluorogramine.* (*a*) Dimethylamine (1·08 g., 55% aqueous solution) in cold glacial acetic acid (7·8 ml.) and formaldehyde (0·97 g., 40% aqueous solution) were added successively to 6-fluoroindole (1·7 g.). After 4 hr. the clear solution was made alkaline with 10% sodium hydroxide solution, and the precipitate was filtered off. The product (1·2 g., 50%) had m. p. 138° (from aqueous ethanol).

(*b*) With vigorous agitation and cooling, 6-fluoroindole (4 g.) in dioxan (29·5 ml.) was added during 30 min. to a mixture of dioxan (29·5 ml.), glacial acetic acid (29·5 ml.), formalin solution (2·35 ml.), and aqueous 55% dimethylamine solution (3·5 ml.). After 12 hr. at room temperature, the solution was diluted with water (370 ml.), filtered, and made alkaline. The *product* (3·8 g., 67·5%) had m. p. 137° (from aqueous ethanol) (Found: C, 68·6; H, 6·5. $C_{11}H_{13}FN_2$ requires C, 68·6; H, 6·8%).

Diethyl α-acetamido-6-fluoroskatylmalonate. In a current of nitrogen, a mixture of 6-fluorogramine (7·1 g.), diethyl acetamidomalonate (8 g.), sodium hydroxide (0·6 g.), and toluene (75 ml.) was refluxed until the evolution of dimethylamine had ceased. The glistening *crystals* (9 g., 67%) had m. p. 201° (from propan-2-ol) (Found: C, 59·3; H, 5·9. $C_{18}H_{21}FN_2O_5$ requires C, 59·3; H, 6·0%).

[1] Sharon and Lipmann, *Arch. Biochem. Biophys.*, 1957, **69**, 219; Canal, Clementi, and Pecile, *Giorn. Ital. Chemioter.*, 1958, **5**, 15; Barbieri and Pecile, *Atti Soc. lombarda sci. med. biol.*, 1959, **14**, 130 (*Chem. Abs.*, 1960, **54**, 9036); Moyed and Friedman, *Science*, 1959, **129**, 968; Frieden, Westmark, and Schor, *Arch. Biochem. Biophys.*, 1961, **92**, 176.

[2] See the preceding paper.

[3] Harvey and Robson, *J.*, 1938, **97**.

[4] Marchant and Harvey, *J.*, 1951, 1808.

[5] Cf. Moe and Warner, *J. Amer. Chem. Soc.*, 1948, **70**, 2763.

N-*Acetyl*-6-*fluorotryptophan*. The ester (9 g.) was hydrolysed with boiling 10% sodium hydroxide solution (70 ml.) for 4 hr. Acidification of the filtered solution with dilute hydrochloric acid gave α-*acetamido*-6-*fluoroskatylmalonic acid* (7 g., 92%), m. p. 158°. It was decarboxylated by boiling water (120 ml.) for 2 hr. The *product* (5·4 g., 92%) crystallised from the solution as glistening crystals, m. p. 178—179° (Found: C, 59·0; H, 5·2. $C_{13}H_{13}FN_2O_3$ requires C, 59·1; H, 5·0%).

Diethyl α-*formamido*-6-*fluoroskatylmalonate*. From 6-fluorogramine (1·85 g.), diethyl formamidomalonate (2·22 g.), sodium hydroxide (0·1 g.), and toluene (10 ml.), which were refluxed for 1 hr. in a current of nitrogen, a solid (3·3 g., 98%) was obtained which was filtered off and recrystallised from aqueous alcohol (1 : 1). It melted at 159° (Found: C, 58·3; H, 5·6. $C_{17}H_{19}FN_2O_5$ requires C, 58·3; H, 5·4%).

6-*Fluorotryptophan*. (*a*) A solution of the foregoing substance (1·7 g.) and sodium hydroxide (0·97 g.) in water (10 ml.) was refluxed for 6 hr. and, after acidification with glacial acetic acid (1·75 ml.), for a further 2 hr. After 12 hr. at room temperature, the *product* (1 g., 93%) was filtered off and dried; it had m. p. 255°.

(*b*) In a silver flask, *N*-acetyl-6-fluorotryptophan (5·4 g.) was refluxed for 26 hr. with a 10% sodium hydroxide solution (60 ml.). After treatment with charcoal and neutralisation of the solution, the *product* (4 g., 88%), m. p. 255°, crystallised as voluminous crystals (Found: C, 59·4; H, 4·6. $C_{11}H_{11}FN_2O_2$ requires C, 59·4; H, 5·0%).

6-*Methoxygramine*. A mixture of dimethylamine (0·8 g.), glacial acetic acid (1·4 g.), and formaldehyde (0·75 g.) was added to 6-methoxyindole [6] (1·2 g.) which dissolved with an exothermic reaction. After 12 hr. the solution was made alkaline and the product recrystallised from cyclohexane. The *gramine derivative* (1 g., 59%) melted at 85° (Found: C, 70·8; H, 8·0. $C_{12}H_{16}N_2O$ requires C, 70·6; H, 7·8%).

Diethyl α-*acetamido*-6-*methoxyskatylmalonate*. A mixture of 6-methoxygramine (2·5 g.), diethyl acetamidomalonate (2·5 g.), sodium hydroxide (0·05 g.), and toluene (60 ml.) was refluxed for 5 hr. and the filtered solution cooled at 0°. The *product* (3 g., 68%) melted at 146—147° (Found: C, 60·3; H, 6·4. $C_{19}H_{24}N_2O_6$ requires C, 60·6; H, 6·4%).

6-*Methoxytryptophan*. The foregoing ester (3 g.) was refluxed for 1·5 hr. with 10% sodium hydroxide solution (20 ml.), and the free α-*acetamido*-6-*methoxyskatylmalonic acid*, m. p. 159—160°, was isolated by acidification with hydrochloric acid. It was refluxed with water (20 ml.) until a clear solution resulted, from which, after cooling and addition of a little acid, N-*acetyl*-6-*methoxytryptophan*, m. p. 199°, crystallised. This acid was heated for 18 hr. with 10% sodium hydroxide solution (20 ml.) in a silver flask and the filtered solution almost neutralised with acetic acid. Some brown material which separated was discarded and the solution was neutralised, whereupon the amino-acid crystallised. After re-precipitation from dilute hydrochloric acid by ammonia, the *product* (0·5 g., 27%) melted at 265° (lit.,[3] m. p. 263—268°).

o-*Methoxyphenylhydrazine*.[7] This was obtained from diazotised *o*-anisidine (30·7 g.) and stannous chloride as described for *p*-toluidine [8] as yellowish crystals (25 g., 34%), m. p. 43°.

γ-*Acetamido*-γγ-*diethoxycarbonylbutyraldehyde* 2-*methoxyphenylhydrazone*. Acraldehyde (4·2 g.) was added to a solution of sodium (0·02 g.) and diethyl acetamidomalonate (11·4 g.) in ethanol (27 ml.), and to the clear solution glacial acetic acid (2 ml.) and *o*-methoxyphenylhydrazine (7·5 g.) were added. The mixture was heated until the hydrazine derivative dissolved and, after a further 15 min., brought to dryness *in vacuo*. The non-crystallisable crude product (21 g.) was used for the next step.

Diethyl α-*acetamido*-7-*methoxyskatylmalonate*. (*a*) The crude product (21 g.) was refluxed, with agitation, with Amberlite IR-120 (60 g.) and water (60 ml.) for 6 hr., and the resin was filtered off and extracted with ethanol. From the concentrated extract, the *product* (1·5 g., 8%) precipitated upon prolonged cooling; it had m. p. 150° (from dilute alcohol).

(*b*) The crude product (53 g.) was refluxed for 6 hr. with water (300 ml.) and sulphuric acid (13 ml.). The solid was extracted thoroughly with ether, and the ether residue (5 g., 10%) was recrystallised from alcohol; it had m. p. 151° (Found: C, 60·4; H, 7·0. $C_{19}H_{24}N_2O_6$ requires C, 60·6; H, 6·4%).

N-*Acetyl*-7-*methoxytryptophan*. The foregoing ester (10 g.) was refluxed for 4 hr. with 10%

[6] Kermack, Perkin, and Robinson, *J.*, 1921, **119**, 1602. See also Kralt, Asma, Haeck, and Moed, *Rec. Trav. chim.*, 1961, **80**, 313.
[7] Reisenegger, *Annalen*, 1883, **221**, 314; Charrier and Casale, *Gazzetta*, 1914, **44**, I, 607.
[8] Robson, *J. Biol. Chem.*, 1924, **62**, 495.

sodium hydroxide solution (70 ml.), and the filtered solution was cooled and neutralised, the oily precipitate discarded, and the solution acidified. The *acetamido-7-methoxyskatylmalonic acid*, m. p. 148°, was heated with water (170 ml.) for 20 min. and the filtered solution was cooled and slightly acidified. The *product* (5 g., 68%) melted at 192°.

7-Methoxytryptophan. *N*-Acetyl-7-methoxytryptophan (5 g.) was refluxed for 20 hr. with 10% sodium hydroxide solution (50 ml.), and the solution was filtered, treated with charcoal, and acidified with glacial acetic acid. The *amino-acid* (3 g., 71%) slowly crystallised at 0°; it had m. p. 266° (decomp.) (Found: C, 61·1; H, 6·0. $C_{12}H_{14}N_2O_3$ requires C, 61·5; H, 6·0%).

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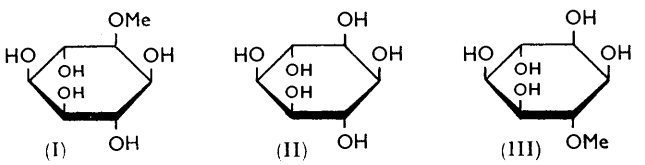
550. *Cyclitols from the Heartwood of* Phyllocladus trichomanoides.

By S. K. ADHIKARI, R. A. BELL, and W. E. HARVEY.

THE wood of *Phyllocladus trichomanoides* (Maori name "Tanekaha;" family Podocarpaceae, order Coniferales) a tree endemic to New Zealand, is valued for its strength and durability. Briggs and Sutherland [1] investigated the leaf oil from the tree, and the bark has also been studied,[2] but no chemical investigation of the wood has been undertaken.

Solvent-extraction of the heartwood yielded wax, terpenoid and phenolic substances, and water-soluble material (2·5%) from which sequoyitol was readily isolated by fractional crystallisation. Concentration of the methanolic mother-liquors gave further crystalline material and finally a syrup. By chromatography of the solid material on cellulose, sequoyitol, pinitol, and myoinositol were isolated: the syrup on chromatography yielded sequoyitol, myoinositol, and (+)-inositol, together with another fraction which was eluted at approximately the same rate as pinitol but did not crystallise. This material, which gave a positive test for pentoses, was resolved by preparative ionophoresis in borate buffer into three components: the fastest-moving of these crystallised and was identified as arabinose by mixed m. p., colour reactions, and chromatography with four solvent systems; a component with M_G 0·6 also crystallised and was identified as pinitol; and the third component, a gum, was shown to be 1-*O*-methylmucoinositol (I).



Analyses of the compound and its acetyl derivative (also gummy) were consistent with its formulation as an inositol monomethyl ether, and demethylation gave mucoinositol (II). Mucoinositol can form only two monomethyl ethers, (I) and (III), and since the ionophoretic mobility of the ether (M_G in 0·05M-sodium tetraborate, 0·3) is very much lower than that of the parent inositol [3] (M_G, 0·96), it is very probable that only one *cis*-1,2-diol system is present in the ether, which is therefore 1-*O*-methylmucoinositol (I).

At this stage of the work we learned from Professor S. J. Angyal, to whom we express our thanks, that he and Dr. R. Hoskinson had synthesised 1-*O*-methylmucoinositol, and

[1] Briggs and Sutherland, *J. Org. Chem.*, 1948, **13**, 1.
[2] White, *Bull. Imp. Inst.*, 1930, **28**, 450.
[3] Angyal and McHugh, *J.*, 1957, 1423; Frahn and Mills, *Austral. J. Chem.*, 1959, **12**, 65.

comparison of the chromatographic behaviour of the natural and the synthetic compounds and of the infrared spectra of the amorphous pentabenzoates established their identity. 1-*O*-Methylmucoinositol is unusual in that it, the penta-acetate, and the pentabenzoate all failed to crystallise.

This is, to our knowledge, the first occasion on which a derivative of mucoinositol has been found in Nature.

Experimental.—Paper chromatography was carried out with the solvent systems and detecting reagents described by Angyal *et al.*[4]

Extraction. Finely ground wood (10 kg.) was extracted (Soxhlet) with light petroleum and then with acetone. The acetone extract was concentrated and poured, with stirring, into a large volume of ether. The voluminous precipitate which separated was boiled with water (2 l.), and the aqueous extract was evaporated under reduced pressure to give a brown solid (250 g.).

Sequoyitol. The brown solid (15 g.) was triturated with two 50-ml. portions of warm methanol (see below), and the residue (8 g.) was recrystallised repeatedly from aqueous methanol and then sublimed at 220°/0·1 mm., giving chromatographically pure sequoyitol, m. p. 237—238° (Found: C, 43·5; H, 7·2; OMe, 16·1. Calc. for $C_6H_{11}O_5$·OMe: C, 43·3; H, 7·3; OMe, 15·9%). The penta-acetate melted at 199—200° (lit.,[5] 200—202°).

Pinitol and myoinositol. The methanol mother-liquor (above), on concentration, deposited crystals (5·5 g.). A sample (1 g.) was chromatographed on a column (50 × 3 cm.) of cellulose powder (Whatman, standard grade) with acetone–water (4 : 1 v/v) as solvent and Methyl Orange to mark the solvent front, as described by Angyal *et al.*;[6] 10-ml. fractions were collected. Fractions 10—20 gave a mixture of crystals and gum. Crystallisation from aqueous alcohol, followed by sublimation in a high vacuum at 180°, gave chromatographically pure pinitol, m. p. 187°, $[\alpha]_D$ +67° (*c* 4 in H_2O) (Found: C, 43·5; H, 7·2; OMe, 15·9. Calc. for $C_6H_{11}O_5$·OMe: C, 43·3; H, 7·3; OMe, 15·9%). The di-isopropylidene derivative was sublimed at 90°/0·1 mm. and had m. p. 102—103° [lit.,[7] 104—106° (corr.)]. Fractions 30—40 yielded sequoyitol. Fractions 90—100 were evaporated and the residue was sublimed at 210°/0·1 mm., giving myoinositol, m. p. 223°, identical (chromatographic behaviour, mixed m. p., *X*-ray powder pattern) with an authentic sample.

(+)-*Inositol, arabinose, and* 1-O-*methylmucoinositol.* The mother-liquors from which the crude pinitol and myoinositol had separated gave, on evaporation, a gum which was chromatographed on cellulose powder as before. Appropriate fractions gave sequoyitol and myoinositol and also (+)-inositol, m. p. 247—248°, identified by comparison (mixed m. p., *X*-ray powder pattern) with an authentic sample prepared by demethylation of pinitol. Fractions from the column expected to contain pinitol yielded a syrup which gave a positive test for pentose with aniline hydrogen phthalate. Ionophoresis on Whatman No. 3 paper with 0·05M-sodium tetraborate buffer[3] and a voltage gradient of 10 v/cm. for 15 hr. resolved the syrup into three components (M_G values, 0·28, 0·60, 0·90) detected by a permanganate–periodate spray reagent.[8] The ionophoretograms were cut into strips, the compounds were eluted with water, and the resulting solutions were passed through a short column of Amberlite IR-100 (H-form), then evaporated repeatedly with methanol to remove boric acid. The fastest-moving component was identified as arabinose by colour reactions and by its chromatographic behaviour in four solvent systems. The component with M_G 0·6 was isolated and identified as pinitol. The slowest-moving component, 1-O-*methylmucoinositol*, obtained as a gum, was distilled in a high vacuum at 210° (bath), giving a hygroscopic glass (Found: C, 42·8; H, 7·0; OMe, 14·7. $C_6H_{11}O_5$·OMe requires C, 43·3; H, 7·3; OMe, 15·9%). In acetone–water (4 : 1 v/v) it moved with R_F 0·47, in phenol–water (4 : 1 w/w) with R_F 0·48. The *penta*-O-*acetate*, prepared by treatment with acetic anhydride and a trace of perchloric acid, was a gum which distilled in high vacuum at *ca.* 200° (Found: C, 50·4; H, 5·7; OMe, 8·0. $C_{16}H_{21}O_{10}$·OMe requires C, 50·5; H, 6·0; OMe, 7·7%). The penta-*O*-benzoate, prepared by treatment with benzoyl chloride and pyridine in the usual way, separated from methanol as an amorphous powder, m. p. *ca.* 95—

[4] Angyal, McHugh, and Gilham, *J.*, 1957, 1432.
[5] Ballou and Anderson, *J. Amer. Chem. Soc.*, 1953, **75**, 648.
[6] Angyal, Gilham, and MacDonald, *J.*, 1957, 1417.
[7] Anderson, MacDonald, and Fischer, *J. Amer. Chem. Soc.*, 1952, **74**, 1479.
[8] Lemieux and Bauer, *Analyt. Chem.*, 1954, **26**, 920.

100°. The infrared spectrum was identical with that of penta-*O*-benzoyl-1-*O*-methylmucoinositol prepared [9] *via* acetic acid solvolysis of 2-*O*-methyl-5-*O*-tosyl-(−)-inositol.

Mucoinositol. The methyl ether was treated with constant-boiling hydriodic acid under reflux for 1 hr. Sublimation of the product at 200°/0·1 mm. gave mucoinositol, m. p. 322—325°, identical (chromatographic behaviour, *X*-ray powder pattern) with an authentic sample (Found: C, 39·8; H, 7·1. Calc. for $C_6H_{12}O_6$: C, 40·0; H, 6·7%).

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[*Received, January 23rd*, 1962.]

[9] Angyal and Hoskinson, personal communication.

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551. *Oxidation of 5-Acetyl-2-methylpyridine.*

By F. BINNS and G. A. SWAN.

WE were investigating possible methods for the synthesis of nicotinic acid labelled in the ring with isotopic carbon, for studies of the biogenesis of nicotine, when a paper by Dawson *et al.*[1] appeared. As these workers demonstrated the incorporation of the labelled nicotinic acid into nicotine, we discontinued our work; but we report some results.

5-Acetyl-2-methylpyridine can be obtained from hydroxymethyleneacetone [2] so we investigated methods for converting it into nicotinic acid. We confirmed an earlier finding [2] that oxidation with nitric acid at 100° yields 6-methylpyridine-3-carboxylic acid nitrate and found the same product also resulted at 170°. However, oxidation with aqueous permanganate gave a low yield of pyridine-2,5-dicarboxylic acid, which could be decarboxylated to nicotinic acid in 50% yield. We thought that 5-acetyl-2-styrylpyridine might undergo smoother oxidation, so we investigated the condensation of 5-acetyl-2-methylpyridine with benzaldehyde. Condensation of the ketone with benzaldehyde (2 mol.) in refluxing acetic anhydride yielded 5-acetyl-2-styrylpyridine, together with a small amount of 5-cinnamoyl-2-styrylpyridine. Engler and Engler [3] prepared 2-cinnamoylpyridine by condensation of 2-acetylpyridine with benzaldehyde in the presence of cold, dilute sodium hydroxide solution. We prepared 3-cinnamoylpyridine similarly from 3-acetylpyridine and showed that under the same conditions 5-acetyl-2-methylpyridine yields 5-cinnamoyl-2-methylpyridine. The structures allotted to the two isomeric monostyryl compounds derived from 5-acetyl-2-methylpyridine were confirmed spectroscopically. 5-Cinnamoyl-2-methylpyridine and 3-cinnamoylpyridine had absorption maxima at 312·5 mμ (log ε 4·38 and 4·30, respectively), whereas cinnamoylbenzene has a maximum at 310 mμ (log ε 4·30).[4] 5-Ethyl-2-styrylpyridine [5] also shows a maximum at 312 mμ (log ε 4·48), but the substitution of an acetyl group for the ethyl group (5-acetyl-2-styrylpyridine) produces a shift to 335 mμ (log ε 4·72).

Oxidation of 5-acetyl-2-styrylpyridine with nitric acid or with permanganate in acetone

[1] Dawson, Christman, Anderson, Solt, D'Adamo, and Weiss, *J. Amer. Chem. Soc.*, 1956, **78**, 2645.
[2] Benary and Psille, *Ber.*, 1924, **57**, 828.
[3] Engler and Engler, *Ber.*, 1902, **35**, 4061.
[4] Braude, *Ann. Reports*, 1945, **42**, 127.
[5] Anderson, Clemo, and Swan, *J.*, 1954, 2962.

yielded pyridine-2,5-dicarboxylic acid; but the yield was again low, although somewhat higher with the latter reagent.

Experimental.—Absorption measurements were carried out in ethanol, a Hilger Uvispec spectrophotometer being used.

Oxidation of 5-acetyl-2-methylpyridine with permanganate. A solution of potassium permanganate (5 g.) in water (50 ml.) was added gradually to a stirred mixture of 5-acetyl-2-methylpyridine (1 g.), potassium permanganate (5 g.), and water (50 ml.) at 50°, which was kept for 24 hr. at 50° and then filtered. The filtrate was treated with sulphur dioxide, concentrated (water-bath/reduced pressure), acidified with acetic acid, and treated with silver nitrate solution. The silver salt was collected, washed with water, suspended in boiling water, and decomposed with hydrogen sulphide. The precipitate was removed and the filtrate was evaporated to dryness (water-bath/reduced pressure). The residue was recrystallised from water, giving pyridine-2,5-dicarboxylic acid (0·27 g.), m. p. 225°. We were unable to increase the yield by varying the amount of permanganate or the time or temperature of reaction. The product (217 mg.) when heated with powdered glass at 250—260° yielded a sublimate (80 mg.) of nicotinic acid, m. p. 233° alone or mixed with an authentic sample.

Condensation of 5-acetyl-2-methylpyridine with benzaldehyde. (*a*) A mixture of 5-acetyl-2-methylpyridine (5 g.), benzaldehyde (8 g.), and acetic anhydride (7·5 g.) was refluxed for 48 hr., then poured into water (100 ml.) and acidified with hydrochloric acid. The excess of benzaldehyde was removed by steam distillation and yellow crystals of *5-cinnamoyl-2-styrylpyridinium chloride* (0·17 g.), m. p. 219—220°, were filtered off (Found: C, 76·2; H, 5·6. $C_{22}H_{18}ClNO$ requires C, 76·0; H, 5·2%); the *base* (from acetone) had m. p. 152—153° (Found: C, 82·8; H, 6·2. $C_{22}H_{17}NO,0{\cdot}5C_3H_6O$ requires C, 82·9; H, 5·9%). The filtrate was basified with sodium hydroxide solution; *5-acetyl-2-styrylpyridine* then separated and after recrystallisation from aqueous methanol formed yellowish crystals (3 g.), m. p. 118—119° (Found: C, 80·65; H, 6·4. $C_{15}H_{13}NO$ requires C, 80·7; H, 5·8%).

(*b*) A mixture 5-acetyl-2-methylpyridine (0·14 g.), benzaldehyde (0·14 g.), water (7 ml.), and 10% sodium hydroxide solution (0·35 ml.) was shaken for 1 hr., then boiled to remove excess of benzaldehyde. The solid, which separated on cooling, was recrystallised from aqueous methanol affording *5-cinnamoyl-2-methylpyridine* (0·13 g.) as plates, m. p. 72—74° (Found: C, 80·65; H, 6·0. $C_{15}H_{13}NO$ requires C, 80·7; H, 5·8%).

3-Cinnamoylpyridine. As (*b*) above, 3-acetylpyridine (2 g.), benzaldehyde (1·9 g.), water (100 ml.), and 10% sodium hydroxide solution (5 ml.) yielded the *product* (2·3 g.) as crystals, m. p. 80°, from aqueous ethanol (Found: C, 80·65; H, 5·55. $C_{14}H_{11}NO$ requires C, 80·4; H, 5·25%).

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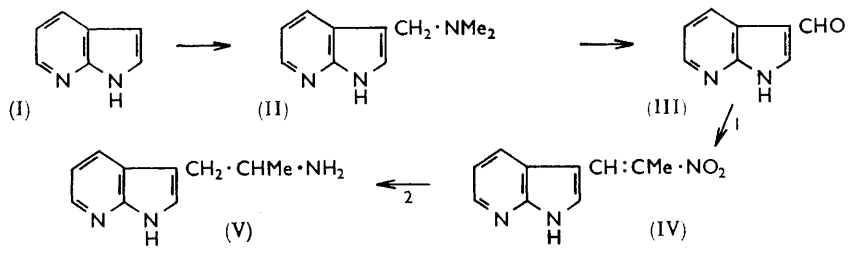
552. *Synthesis of* 3-2′-*Aminopropyl*-1H-*pyrrolo*[2,3-b]*pyridine.*

By W. R. N. Williamson.

Recent interest [1] in the pharmacological properties of α-alkyltryptamines prompted the preparation of 3-2′-aminopropyl-1*H*-pyrrolo[2,3-*b*]pyridine (V). The scheme of synthesis outlined in the chart followed that of Young [2] for the corresponding indoles. Compounds I—III are already known [3] but improvements in their preparation were made.



1 $EtNO_2$ + $Me{\cdot}CO_2NH_4$.
2 $LiAlH_4$.

Experimental.—3-*Dimethylaminomethyl*-1H-*pyrrolo*[2,3-b]*pyridine* (II). 1*H*-Pyrrolo[2,3-*b*]-pyridine (23·6 g.) (I) (prepared in 34·7% yield from 82 g. of 2-formamido-3-picoline; cf. ref. 3), dimethylammonium chloride (17·6 g.), and paraformaldehyde (6·6 g.) were stirred and refluxed in butanol (800 g.) for ½ hr. The solution was evaporated to dryness and treated with water (200 ml.) and concentrated hydrochloric acid (20 ml.). It was extracted with ether (3 × 70 ml.), and the aqueous phase freed from ether by passing air through it. It was then treated with potassium carbonate solution until the pH was *ca.* 10 and an oil separated. Addition of ether (*ca.* 100 ml.) and stirring initiated crystallisation. The dimethylamino-compound (25·85 g.), m. p. 147—152°, was filtered off, washed with ether, and dried. The filtrate, after being kept for 2 days, yielded a further 8·42 g., m. p. 146—152° (99% yield). The formyl compound, m. p. 207—210°, was obtained in 53% yield from 14·8 g. of the dimethylamino-compound (cf. ref. 3) by the method of Robison and Robison. Attempted preparation of the formyl compound by Smith's method [4] resulted in an 18·6% recovery of the starting compound (I).

3-2′-*Nitropropenyl*-1H-*pyrrolo*[2,3-b]*pyridine* (IV). 3-Formyl-1*H*-pyrrolo[2,3-*b*]pyridine (III) (10 g.), nitroethane (40 ml.), and ammonium acetate (4 g.) were stirred at 100° for ¾ hr. The mixture was cooled and the bright yellow solid (12·33 g.), m. p. 254—257° (decomp.), filtered off. Crystallisation of material (0·53 g.) from methanol (300 ml.) gave the *nitro-compound* (0·375 g.) as yellow needles, m. p. 266—267° (decomp.) (Found: C, 59·3; H, 4·9; N, 20·7. $C_{10}H_9N_3O_2$ requires C, 59·1; H, 4·5; H, 20·7%).

3-2′-*Aminopropyl*-1H-*pyrrolo*[2,3-b]*pyridine* (V). Lithium aluminium hydride (10 g.) was stirred in refluxing dry tetrahydrofuran (330 ml.) and treated dropwise with a hot solution of the above nitro-compound (12·7 g.) in tetrahydrofuran (1·7 l.) during ¾ hr. The mixture was refluxed 6 hr., stored at room temperature overnight, cooled, and treated cautiously with water (50 ml.). The aqueous mixture was stirred for 1½ hr., "Supercel" added and filtered off, and the filter cake washed with ether and tetrahydrofuran (100 ml.). Evaporation left an oil (10·28 g.) which on distillation gave the *amino-compound*, b. p. 168—172°/0·5 mm., a colourless, hygroscopic, waxy solid (5·93 g.), m. p. 58—60° (Found: C, 68·5; H, 7·5. $C_{10}H_{13}N_3$ requires C, 68·1; H, 8·0%); ν 3190 (NH_2, NH) and 1605, 1579, 1533, 1490 $cm.^{-1}$ (aromatic system).

Analyses were by Mr. F. H. Oliver and the spectrum was determined and interpreted by Miss E. M. Tanner. Thanks are due to Dr. R. E. Bowman for helpful discussions.

Parke, Davis and Company, Hounslow, Middlesex. [*Received, February 6th,* 1962.]

[1] Vane, *Brit. J. Pharmacol.*, 1959, **14**, 87, and refs. therein.
[2] Young, *J.*, 1958, 3493.
[3] Robison and Robison, *J. Amer. Chem. Soc.*, 1955, **77**, 457.
[4] Smith, *J.*, 1954, 3842.

553. 3-*Prop*-2′-*ynylindole*.

By W. R. N. Williamson.

Brown, Henbest, and Jones [1] reported their failure to prepare 3-prop-2′-ynylindole by treating 3-indolylmagnesium bromide with prop-2-ynyl bromide, "chiefly because the Grignard reagent reacted first with the active acetylenic hydrogen atom to regenerate indole." They do not report the solvent used, but it was presumably diethyl ether. According to Majima and Kotake [2] anisole is a superior solvent for the preparation and subsequent reaction with carbonyl compounds of indolyl Grignard reagents. This apparently cannot be attributed to the higher boiling point of anisole, since in this solvent ethylmagnesium iodide evolves ethane on treatment with indole in the cold, while in ether no gas is evolved at room temperature and heat is required. When we used anisole in the preparation of 3-indolylmagnesium iodide from ethylmagnesium iodide, with subsequent reaction with prop-2-ynyl bromide, a 39·5% yield of 3-prop-2′-ynylindole was obtained. The compound, which was a pale yellow oil slowly becoming darker, was characterised by conversion into 3-indolylacetone [2] by heating it with acidic mercuric sulphate.

Experimental.—3-*Prop*-2′-*ynylindole*. Ethylmagnesium iodide [from magnesium (4·8 g.) and ethyl iodide (32 g.)] in dry anisole (20 ml.) was cooled in ice, and indole (15·6 g.) in anisole (20 ml.) was added dropwise. After being stirred (½ hr.) at 20° it was treated at 0° with prop-2-ynyl bromide (20 ml.) in anisole (10 ml.) during 15—20 min., stirring continued at 0° for 1¼ hr., and the mixture then stored at 20° overnight. It was cooled to 0° and treated with ether (100 ml.), water (200 ml.), acetic acid (12 ml.), and more water (100 ml.), and then extracted with ether (5 × 25 ml.). The extract was washed with sodium bicarbonate solution and water and dried ($MgSO_4$ and charcoal), the solvents were removed under reduced pressure, and the 3-*prop*-2′-*ynylindole* (8·17 g.) was distilled as a pale yellow oil, b. p. 143—145°/2 mm., which solidified when cooled below 20° (Found: C, 84·4; H, 5·9; N, 8·85. $C_{11}H_9N$ requires C, 85·1; H, 5·85; N, 9·0%); ν 3425 (NH), 3310 (C≡CH), 2130 (RC≡CH), 745 $cm.^{-1}$ (*ortho*-disubstituted benzene).

3-*Indolylacetone*. 2N-Sulphuric acid (10 ml.) was treated with mercuric sulphate (0·05 g.),[3] stirred and heated on a steam-bath, and the propynylindole (1·5 g.) in ethanol (10 ml.) added. Stirring and heating was maintained for 2 hr. Pouring the solution into water and treatment with sodium hydrogen carbonate produced a brown gum (1·42 g.), m. p. 95° (softening at 75°). Crystallisation from benzene (charcoal) gave the ketone as brownish rhombs (0·28 g.), m. p. 112—115° (Found: C, 76·0; H, 6·4; N, 7·9. Calc. for $C_{11}H_{11}NO$: C, 76·3; H, 6·4; N, 8·1%). The m. p. of a mixture with authentic 3-indolylacetone,[4] was m. p. 112—115°.

The author thanks Dr. R. E. Bowman for helpful discussions, Miss E. M. Tanner for determination of the spectrum, and Mr. F. H. Oliver for the microanalyses.

Parke, Davis and Co., Hounslow, Middlesex. [*Received, February 6th*, 1962.]

[1] Brown, Henbest, and Jones, *J.*, 1952, 3172.
[2] Majima and Kotake, *Ber.*, 1922, **55**B, 3859, 3865; cf. Kharasch and Reinmuth, "Grignard Reactions of Nonmetallic Substances," 1954, Prentice-Hall, Inc., New York, p. 81.
[3] Thomas, Campbell, and Hennion, *J. Amer. Chem. Soc.*, 1938, **60**, 718.
[4] Kindly donated by Dr. D. J. Tivey.

554. *The Infrared C=O Absorption of 2,4-Dihydroxybenzaldehyde.*

By S. Pinchas.

Saturated chloroform solutions of 2,4-dihydroxybenzaldehyde show two absorption bands in the 1700—1600 cm.$^{-1}$ C=O stretching region: at 1632 (ε ~730) and at 1654 cm.$^{-1}$ (ε ~520). The 1632 cm.$^{-1}$ band, because of its higher intensity, was assigned to a C=O stretching vibration, its low frequency being explained as resulting from the assumed existence of this aldehyde as a dimer.[1] Brooks and Morman, however, have recently designated [2] the *higher* band (their value, 1657 cm.$^{-1}$) as a C=O vibration, rejecting the dimer assumption and the assignment of the main band as due to the C=O group, but not suggesting an alternative.

To clarify this matter a chloroform solution (0·1 g./l.) was measured in a 5 mm. cell. It showed the same doublet, the lower band being again the stronger. Hence, the origin of this band cannot be a dimer since this cannot be expected to persist at such a dilution.

Nevertheless the origin of the 1632 cm.$^{-1}$ band still seems to be a C=O stretching. Thus, bromoform moves this band to 1628 cm.$^{-1}$, probably as a result of stronger hydrogen-bonding between the solvent and the carbonyl group. For *N*-methylbenzamide also [3] a similar decrease of 4 cm.$^{-1}$ was observed in the carbonyl-band frequency on going from chloroform to bromoform. Also, while a solution in carbon tetrachloride shows these bands with the molecular extinction coefficients of 560 (1653 cm.$^{-1}$) and 500 (1632 cm.$^{-1}$) a similar solution containing 4% (v/v) of bromoform shows these bands with extinction coefficients of 730 (1653) and 620 (1630) units. The increase in intensity for the carbon tetrachloride–bromoform solution arises probably from formation of a hydrogen-bonded complex formation between the carbonyl group and bromoform.

The fact that two strong bands appear here in the C=O region is probably due to Fermi resonance between the C=O stretching vibration and the overtone of the *para*-disubstituted benzene C–H bending frequency at 825 (in $CHCl_3$) or 821 cm.$^{-1}$ (in $CHBr_3$). If one calculates the original interacting frequencies, by Langseth and Lord's method,[4] from the results given above for chloroform solutions, one arrives at 1645 and 1641 cm.$^{-1}$. Since the lower band is here the stronger, the 1641 cm.$^{-1}$ value must belong to the C=O stretching vibration and that of 1645 cm.$^{-1}$ to the overtone of the 825 cm.$^{-1}$ bending (= 2 × 825—anharmonicity term). In carbon tetrachloride solution the upper band is the stronger, so here the original C=O stretching is probably that of higher frequency, in agreement with the known effect of chloroform in decreasing the C=O frequencies in carbon tetrachloride solution. In bromoform both the original frequencies can be expected to be somewhat lower than in chloroform, that of the C=O group because of stronger hydrogen-bonding and the overtone frequency because the fundamental C–H bending is also observed to be lower by 3—4 cm.$^{-1}$ in bromoform. The 1628 cm.$^{-1}$ frequency observed for the main band of bromoform solutions is thus understandable.

The low value of 1641 cm.$^{-1}$ calculated for the original C=O frequency of 2,4-dihydroxybenzaldehyde in chloroform, as compared with a value of over 1660 cm.$^{-1}$ for salicylaldehyde,[1, 2] can be explained by the effect of the electron-releasing *p*-hydroxy-group (+*T* effect) on the carbonyl group.

Since this aldehyde has now been shown to be monomeric in chloroform solution one must assume that the hydrogen-bonding is here, as in salicylaldehyde itself,[1, 2] only between the carbonyl group and the *o*-hydroxy-group, leaving the formyl C–H group free. The 2747 cm.$^{-1}$ ($CHCl_3$) C–H stretching frequency of this group is however somewhat

[1] Pinchas, *Analyt. Chem.*, 1957, **29**, 334.
[2] Brooks and Morman, *J.*, 1961, 3372.
[3] Pinchas, Samuel, and Weiss-Broday, *J.*, 1961, 2666.
[4] Langseth and Lord, *Kgl. danske Videnskab. Selskab, Mat.-fys. Medd.*, 1948, **16**, 6; *Spectrochim. Acta*, 1961, **13**, 694.

higher than in most " free " benzaldehydes, which absorb at [1] 2720—2730 cm.$^{-1}$, although not as high as reported [1] previously (2765). Salicylaldehyde itself, however, also shows this band at about the same frequency (2744 cm.$^{-1}$ in CCl_4), this being attributed to the contribution of a polar chelated structure to its state.

The instrument used was mainly a Perkin–Elmer spectrophotometer, model 12 C, equipped with a sodium chloride prism. For the 2,4-dihydroxybenzaldehyde solution, at 0·1 g./l., this instrument was used with a calcium fluoride prism. The frequency values are believed to be correct to within 10 cm.$^{-1}$ in the 2800 cm.$^{-1}$ region and within 5 cm.$^{-1}$ in the 1600 cm.$^{-1}$ region.

I thank Mr. J. Goldberg for the measurements.

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