*The S_N Mechanism in Aromatic Compounds. Part VIII.**

By G. Peter Briner and Joseph Miller.

[Reprint Order No. 5446.]

The Hughes–Ingold theory of solvent action (*J.*, 1940, 956; *Trans. Faraday Soc.*, 1941, **37**, 657) as applied to aromatic S_N reactions has been discussed briefly (Miller, *Rev. Pure and Appl. Chem.*, 1951, **1**, 171) and a preliminary test also reported (Miller, *Chem. and Ind.*, 1953, 40). For attack by an anion on an electrically neutral reactant, the theory predicts that solvent effects are small, and that more ionising solvents retard reaction. The present work was designed to test this, by using solvents in which ion-pair formation would not be expected to play an important part, and in which polarity and dielectric constant might be expected to run parallel.

The reactions investigated were: (*a*) sodium 4-chloro-3 : 5-dinitrobenzoate with hydroxyl ions in water, and with methoxyl ions in methanol; (*b*) 1-chloro-2 : 4-dinitrobenzene with methoxyl ions in methanol, and in methanol–methyl acetate (1 : 1 v/v).

Sodium 4-chloro-3 : 5-dinitrobenzoate, though ionic, has no formal charge at the point of attack, and in both a mononitro- and a dinitro-series has been shown to fit smoothly into a group differing only in the nature of carbonyl substituents, all other members of the group being uncharged (Miller, *J. Amer. Chem. Soc.*, 1954, **76**, 448; and to be published).

Leahy and Miller (*Chem. and Ind.*, 1953, 40), reporting on reagents in aromatic S_N reactions, showed that the rates of attack by hydroxyl and methoxyl ions in methanol may be taken as equal, and therefore the two pairs of reactions may be compared as a series. The experimental results are given in the Table.

Reaction	Compound	Solvent	ε *	10^5k_2 (l. mole^{-1} sec.$^{-1}$), at temp. in parentheses				
1.	Sodium 4-chloro-3 : 5-dinitrobenzoate	H_2O	81·0	73·3 (25·0)	127 (30·2)	201 (35·2)	500 (45·3)	—
2.	Sodium 4-chloro-3 : 5-dinitrobenzoate	MeOH	33·7	57·0 (0)	686 (26·1)	970 (30·2)	—	—
3.	1-Chloro-2 : 4-dinitrobenzene	MeOH	33·7	200 (0)	1060 (15·0)	2190 (22·0)	2960 (25·0)	—
4.	1-Chloro-2 : 4-dinitrobenzene	MeOH–MeOAc (1 : 1 v/v)	25·0 †	688 (0)	1208 (5·6)	1460 (7·6)	1855 (10·5)	3080 (16·4)

Reaction	10^5k_2, calc. at		k_2-ratio (MeOH = 1)			
	0°	50°	0°	50°	*E* (cal.) ‡	$\log_{10} B$
1.	5·17	751	0·0907	0·159	17,450 ± 250	$9\cdot7 \pm 0\cdot2$
2.	57·0	4720	1	1	15,500 ± 50	$9\cdot1_5 \pm 0\cdot0_5$
3.	200	28,750	1	1	17,450 ± 50	$11\cdot2_5 \pm 0\cdot0_5$
4.	688	40,800	3·44	1·42	14,250 ± 150	$9\cdot2_5 \pm 0\cdot1_5$

* Dielectric constant of the solvent, taken from " International Critical Tables."

† A linear relation between dielectric constant and mole fractions of methyl acetate and methanol being assumed.

‡ The probable errors are obtained by the method of least squares, from all runs, and are intended to indicate the fit of the $\log_{10}k_2$ against $1/T$ plot to a straight line.

The relation between dielectric constant and rate constant is as predicted by theory. The results show also that the increase in solvating power is associated with an increase in activation energy, accompanied, however, by an increase in the frequency factor.

In forming the transition state in a more ionising (solvating) medium, there is a relatively larger decrease in solvation, and in comparison therefore the activation energy is greater. The greater solvation loss appears to be associated also with an increase of entropy.

Experimental.—Methyl acetate was dried over anhydrous sodium sulphate; the fraction, b. p. 56—57°, being used. The preparation of other materials and the procedure were

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* Part VII, *J.*, 1954, 1265.

described in Part II (Miller, *J.*, 1952, 3550). Two runs were made at each temperature and k_2 was found by a graphical method.

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An Examination of the Ericaceae of Hong Kong. The Occurrence of Ursolic Acid.

By H. R. Arthur and (Miss) W. H. Hui.

[Reprint Order No. 5494.]

The seven indigenous species of Ericaceae of the Colony of Hong Kong are confined to two genera, *Rhododendron* and *Enkianthus.* The former genus contains the six species *Rhododendron championae,* Hook., *R. farrerae,* Tate (*Azalea squamata,* Lindl.), *R. simiarum,* Hance (*R. fordii,* Hemsl.), *R. simsii,* Planch. (*R. calleryi,* Planch., *R. balfouria,* Leveille, *R. indicum* var. *simsii,* Maxim., *Azalea indica,* Sims non Linn.), *R. westlandii,* Hemsl., and *R. mucronatum,* Don. (*R. ledifolium,* Don., *Azalea mucronata,* Bl.). The latter genus is represented by only one species, *Enkianthus quinqueflorus,* Lour. (*E. reticulatus,* Lindl., *E. uniflora,* Benth., *Melidora pellucida,* Noron.).

We reported earlier (*J.*, 1954, 2782) that ursolic acid is present in the leaves of *R. simsii.* With the exception of *R. mucronatum,* leaves of which we have been unable to obtain, the leaves of all the other indigenous species of Ericaceae have now been found to contain ursolic acid as the only triterpenoid compound.

Ursolic acid has been reported before in Ericaceous genera (for a discussion of its occurrence in the genus *Rhododendron* see *loc. cit.*). Its isolation from *Enkianthus quinqueflorus* is the first report of it from this genus; no chemical work, in fact, appears to have been carried out on *Enkianthus* spp.

Ursolic acid, which has now been reported from nine different species of *Rhododendron* and seems to be the only triterpene acid present therein, appears to be characteristic of that genus, and probably of the family as a whole.

Experimental.—Fresh or dried leaves of all species were extracted by the method given by us (*loc. cit.*) for *R. simsii.* The crude crystalline ursolic acid was recrystallised to constant m. p. and then converted into derivatives by the usual methods. Acidification of the alkaline extracts produced negligible amounts of crude ursolic acid. All triterpenoid compounds have been characterised by mixed m. p. determinations. M. p.s are corrected. Samples were analysed by Dr. Zimmermann, Melbourne. Rotations are in 1 : 1 MeOH–$CHCl_3$ at 23°.

Plant	Yield (%) (leaves)	M. p. of acid	M. p. of acetate	M. p. of Me ester	M. p. of Me ester acetate	$[\alpha]_D$
E. quinqueflorus	Fresh 0·30 Dry 0·85	290—292°	294—296°	168—169°	245—246°	+67·0°
R. championae ...	Dry 0·56	288—291	—	168—169	246—247	+66·0
R. farrerae	Fresh 0·13 Dry 0·40	290—292	—	168—170	246—247	+65·5
R. simiarum	Fresh 0·60	289—290	294—296	168—170	246—247	+66·0
R. westlandii	Fresh 0·30	291—292	—	168—169	245—246	—

Samples of the acid from all plants gave a red → violet → blue → green colour in the Liebermann–Burchardt test. A sample of ursolic acid from *E. quinqueflorus* was analysed (Found : C, 78·8; H, 10·6. Calc. for $C_{30}H_{48}O_3$: C, 78·9; H, 10·6%). This was characterised as acetate (Found : C, 77·0; H, 10·0. Calc. for $C_{32}H_{50}O_4$: C, 77·0; H, 10·1%), methyl ester (Found : C, 79·0; H, 10·6. Calc. for $C_{31}H_{50}O_3$: C, 79·1; H, 10·7%), and methyl ester acetate. Other experimental results are summarised in the Table.

The authors thank Professor J. E. Driver for his interest and Mr. H. C. Tang (Government Herbarium, Hong Kong) for the identification of plant material.

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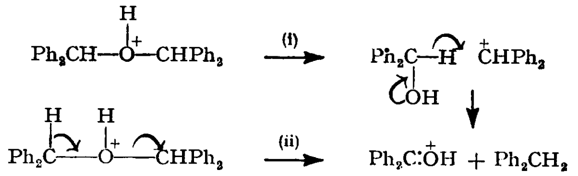
[*Received, June 26th,* 1954.]

The Dismutation of Bisdiphenylmethyl Ether by Deuterium Perchlorate.

By G. BADDELEY and P. G. NIELD.

[Reprint Order No. 5528.]

IN a previous communication (*J.*, 1953, 3726) it was suggested that dismutation of the ether in benzene by perchloric acid might involve transfer of hydride ion. It was recognised that since this mechanism (i), in contrast to the alternative (ii), requires the hydrogen atoms of the methylene group in the resulting diphenylmethane to be those which were initially attached to the carbon atoms of the $>CH{\cdot}O{\cdot}CH<$ group, evidence of mechanism might be obtained by application of isotopically marked hydrogen atoms. This evidence has now been obtained and is compatible with (i).



The dismutation of the ether as described by Burton and Cheeseman (*J.*, 1953, 986) was repeated by using as catalyst a solution (80%) of deuterium perchlorate in deuterium oxide. The catalyst was prepared by protracted interaction of deuterium oxide and a solution of chlorine heptoxide in carbon tetrachloride (Meyer and Kessler, *Ber.*, 1921, **54**, 566, but reading 82 g. as 8·2 g. of 70% perchloric acid) and volatilising the organic solvent. A mixture of the ether (0·05 mole), deuterium perchlorate (0·05 mole), and benzene (50 c.c.) was gently refluxed for 5 hr. and gave diphenylmethane which, by infra-red analysis, did not contain deuterium.

This result would have little significance should the catalyst exchange hydrogen with the solvent benzene at a rate comparable with that of the dismutation. This possibility was excluded by demonstrating that the catalyst was rich in deuterium at the end of the experiment.

We are indebted to Dr. Meakins for the infra-red analyses.

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The Heat of Solution of Aluminium Iodide. A Correction.

By D. J. A. DEAR and D. D. ELEY.

[Reprint Order No. 5534.]

ELEY and WATTS recently (*J.*, 1954, 1319) published a value $Q_s = 135 \pm 0{\cdot}8$ kcal. mole^{-1} for the heat of solution of AlI_3(c) in 2N-hydrochloric acid or water. This was very much larger than the two previous values of 89·0 and 89·9, but since analysis had established that the sample of aluminium iodide used was *ca.* 99·5% pure, and there were adequate checks on the accuracy of the calorimeter, the result was accepted and published. In the meantime Professor J. D. Corbett, of Iowa State College (personal communication), pointed out that this value for Q_s, combined with his own recent value for $\Delta G_f°$ for AlI_3(c) (Corbett and Gregory, *J. Amer. Chem. Soc.*, 1954, **76**, 1446), leads to a value of 193 cal. deg.$^{-1}$ mole^{-1} for the standard entropy, which seems impossibly high. We have accordingly carried out a further five calorimetric runs at 25°, using three new samples prepared from the elements by Mr. J. D. Coombes of this laboratory. The runs were carried out in water, and the result and calculated probable error was $Q_s = 91{\cdot}4 \pm 1{\cdot}5$ kcal. mole^{-1} (25°).

Comparing this with Berthelot's value of 89·0 at 9° (Landolt–Börnstein, " Tabellen," Vol. II, p. 1554) we find a difference of 2·4 kcal. It is possible to estimate that the difference in temperature might give rise to a difference of 2·2 kcal. by using values of $\bar{C}_p^\circ = -20$ cal. deg.$^{-1}$ mole^{-1} for Al^{+++}(aq.) (estimated), $\bar{C}_p^\circ = -31{\cdot}0$ cal. deg.$^{-1}$ mole^{-1} for I^-(aq.) (Selected Values of Chemical Thermodynamic Properties, National Bureau of Standards, Circular 500), and $C_p^\circ = 23{\cdot}9$ cal. deg.$^{-1}$ mole^{-1} for AlI_3 (Fischer, *Z. anorg. Chem.*, 1931, **200**, 332).

The new result is therefore in satisfactory agreement with earlier values. Seeking an explanation of Eley and Watts's value, we conclude that by an accident a storage ampoule of aluminium bromide had been taken for one of the iodide. A consideration of the seven values of the heats of solution (H. Watts, Thesis, Bristol, 1952) shows that these lie on exactly the same straight line (heat *vs.* wt.) as do those for the bromide. However, a check has established that the aluminium iodide–*N*-base complexes were not confused with bromides, so that taking the Q_s values of Eley and Watts for these complexes, together with the above value of 91·4 for the iodide, we derive values for the dissociation energy of the complex in the condensed phase, D_c, kcal. mole^{-1} :

$$C_5H_5N,AlI_3,\ D_c = 31{\cdot}5. \qquad Me_3N,AlI_3,\ D_c = 33{\cdot}1.$$

For NH_3,AlI_3 we revert to the D_c value of 32 given by Klemm, Clausen, and Jacobi (*Z. anorg. Chem.*, 1931, **200**, 367). The corrected value for C_5H_5N,AlI_3 should also be inserted in Eley and Watts's paper, p. 23 in " Cationic Polymerisation and Related Complexes " (ed. P. H. Plesch, Heffer, Cambridge, 1953).

Since the heat of mixing of AlI_3(c) with excess of pyridine is 70·1, we must now conclude that in mixing, more than one molecule of pyridine is co-ordinated to aluminium iodide.

For consistency we calculated changes in derived quantities using other data as used by Eley and Watts on the pages of their paper indicated in parentheses : Q_f, 75·0 kcal. mole^{-1} (p. 1321) ; * bond energy E(Al–I), 61 kcal. mole^{-1} (p. 1323) ; reorganisation energy K(Al–I) (planar ⟶ tetrahedral), 49·7 (p. 1324). With these values we now correct values in Table 2 (p. 1323). D_{cg} is the dissociation energy of the solid complex into gaseous components, L_1 the sublimation energy of the solid complex, and D(N→Al) the dissociation energy of the gaseous complex giving AlI_3 in the *tetrahedral* state, all values being in kcal. mole^{-1} :

Complex	D_{cg}	D(N→Al) + L_1
C_5H_5N,AlI_3	63·4	113
Me_3N,AlI_3	62·2	112
NH_3,AlI_3	55·4	105

It is now no longer possible to conclude that the energy quantity in the last column remains constant ; there seems to be a decrease over the series $C_5H_5N > Me_3N > NH_3$. Referring to the other data in Eley and Watts's paper, there appears to be an even more marked decrease, for a given *N*-base, over the series $AlCl_3 > AlBr_3 > AlI_3$. A probable lower limit for D(N→Al) for the complexes examined is nearer 80 than 90 kcal. as given previously.

We thank Professor Corbett for his communication and Mr. Coombes for his help in this work.

CHEMISTRY DEPARTMENT, UNIVERSITY OF BRISTOL. [*Received, July 7th,* 1954.]

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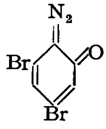
* If we use the Q_f for Al^{+++}(aq.) (given in the Selected Table of Chemical Thermodynamic Properties, Nat. Bur. Stand., Circular 500) we obtain $Q_f = 74{\cdot}1$ kcal. mole^{-1} for AlI_3(c).

Infra-red Spectra of Certain Quinone Diazides.

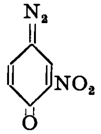
By R. J. W. LE FÈVRE, J. B. SOUSA, and R. L. WERNER.

[Reprint Order No. 5549.]

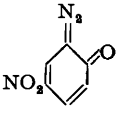
ANDERSON, LE FÈVRE, AND WILSON (*J.*, 1949, 2082) considered the dipole moments of a number of so-called diazophenols and diazonaphthols to be consistent with their being resonance hybrids, *e.g.*, $\overset{-}{O}\text{–}C_6H_4\text{–}\overset{+}{N}{\equiv}N \longleftrightarrow O{=}C_6H_4{=}\overset{+}{N}{=}\overset{-}{N}$. Further evidence is now available from the infra-red absorption spectra (recorded in paraffin mulls with rock-salt optics on a Perkin–Elmer 12C Spectrometer) of the seven representative compounds (I)—(VII).



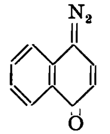
(I)
2110 cm.$^{-1}$
1582 cm.$^{-1}$



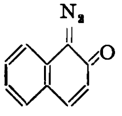
(II)
2173 cm.$^{-1}$
1618 cm.$^{-1}$



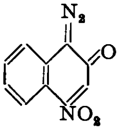
(III)
2157 cm.$^{-1}$
1562 cm.$^{-1}$



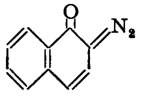
(IV)
2014 cm.$^{-1}$
1618 cm.$^{-1}$



(V)
2017 cm.$^{-1}$
1622 cm.$^{-1}$



(VI)
2015 cm.$^{-1}$
1642 cm.$^{-1}$



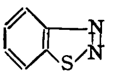
(VII)
2148 cm.$^{-1}$
1610 cm.$^{-1}$
1618 cm.$^{-1}$

Of the bands observed only those relevant to the present question are noted beneath the formulæ; all are " strong " except those at 1610 and 1618 cm.$^{-1}$ for (VII). For comparison (VIII) and (IX) have also been examined.

The occurrence throughout (I) to (VIII) of absorption, suggestive of triple bonds, in the 4-μ region, supports the rejection of cyclic formulations [based on (IX) with O for S] for the " *ortho* "-derivatives (I), (III), (V), (VI), and (VII); in contrast benzo-1-thia-2 : 3-diazole, being transparent around 2000 cm.$^{-1}$, is probably correctly represented by (IX).

(VIII) $[C_6H_5\cdot N_2^+]BF_4^-$

2296 cm.$^{-1}$ (medium-strong)



(IX)

1542 cm.$^{-1}$ (medium)

The feature at 2296 cm.$^{-1}$ in the diazonium borofluoride (VIII) shows what may be expected for the $-^{+}N{\equiv}N$ group; previous work (Le Fèvre, O'Dwyer, and Werner, *Austral. J. Chem.*, 1953, **6**, 341) indicates that –N=N–, if it displays itself in the infra-red at all, does so at much lower frequencies. Analogous results have been reported for diazomethane ($CH_2{=}N^{+}{=}N^{-} \longleftrightarrow {}^{-}CH_2\text{–}N^{+}{\equiv}N$) where N–N stretching has been recognised at 2101 cm.$^{-1}$ (Ramsay, *J. Chem. Phys.*, 1949, **17**, 666; Crawford, Fletcher, and Ramsay, *ibid.*, 1951, **19**, 406) and for sundry azides ($R\text{–}N{=}N^{+}{=}N^{-} \longleftrightarrow R\text{–}N^{-}\text{–}N^{+}{\equiv}N$) where absorption is listed as: HN_3, 2141 cm.$^{-1}$; MeN_3, 2141 cm.$^{-1}$; DN_3, 2105 cm.$^{-1}$; by Randall, Fowler, Fuson, and Dangl (" Infra-red Determination of Organic Structures," van Nostrand and Co. Inc., New York, 1949). Methyl azide gives a Raman displacement of 2104 cm.$^{-1}$ (Otting, " Der Raman-Effekt," Springer, Berlin, 1952, p. 44).

The lower frequencies written beneath formulæ (I)—(VII) are of the order of those due to ketonic groups in the simpler tropolones (Koch, *J.*, 1951, 512; Haworth and Hobson, *ibid.*, p. 561; Scott and Tarbell, *J. Amer. Chem. Soc.*, 1950, **72**, 240) or in the " conjugated chelates " of Rasmussen *et al.* (*J. Amer. Chem. Soc.*, 1949, **71**, 1068). The four " parent " quinones to substances (I)—(VII) are known to have bands within the limits 1667 and 1678 cm.$^{-1}$ (Josien, Fuson, Lebas, and Gregory, *J. Chem. Physics*, 1953, **21**, 331; cf. also Flett, *J.*, 1948, 1441), but the effects of resonance between the N_2 and the ring, and of the contribution of fully dipolar forms should both operate to reduce the ν_{CO} in the quinone diazides. The former cause (conjugation) is well documented: the influence of the latter may be inferred from the facts that the introduction of *o*-amino-groups into benzoic or naphthoic acids diminishes the ketonic frequency by 15—25 cm.$^{-1}$ (Flett, *J.*, 1951, 962) and that metal carboxylates and zwitterionic amino-acids absorb at 1613—1575 cm.$^{-1}$ and 1613—1562 cm.$^{-1}$ respectively (Randall *et al.*, *op. cit.*, p. 4). Consistently with this, " azibenzil " ($C_6H_5{\cdot}CO{\cdot}CN_2{\cdot}C_6H_5$) exhibits strong bands at 2073 and 1619 cm.$^{-1}$.

We conclude, therefore, that, in the diazophenols and diazonaphthols, (*a*) the linkage between the two nitrogen atoms is of between double and triple bond type and (*b*) the CO group is modified in the sense $C\overset{\curvearrowright}{=}O$. These views are in harmony with those of Anderson, Le Fèvre, and Wilson (*loc. cit.*).

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[*Received, July* 12*th*, 1954.]

The Gray and Cruickshank Method of Calculating Diamagnetic Susceptibility of Organic Molecules.

By C. M. French and D. Harrison.

[Reprint Order No. 5554.]

The method devised by Gray and Cruickshank (*Trans. Faraday Soc.*, 1935, **31**, 1491) differs from Pascal's purely empirical one (*Bull. Soc. chim.*, 1911, **9**, 6 and subsequent papers) in employing certain " theoretically " calculated quantities, *i.e.*, ionic susceptibilities and residual charges. Certain defects in this method were indicated by Angus (*Ann. Reports*, 1941, **38**, 39) and by Sugden (*J.*, 1943, 328). More recently, Pacault (*Rev. Sci.*, 1948, **86**, 38) stated that whatever values are taken for the ionic susceptibilities and residual charges, the same value is obtained for the susceptibility of an unknown compound, provided that the bond depressions are suitably adjusted. Pacault does not mention one important fact which would result if this were strictly true, namely, that as a particular case, all the ionic susceptibilities could be taken as zero. The original Gray and Cruickshank method would then become simply an involved way of obtaining the results of a system of additive bond susceptibilities, built up with the same reference compounds. It is well established that such a system is inadequate to deal with even quite simple organic structures, apart from having no theoretical justification.

We have investigated this matter in detail for the cases of normal organic compounds whose formulæ do not involve ionic or co-ordinate linkages, and have reached the following conclusions: (*a*) Pacault's statement is true only in a limited number of cases, determined by a close structural relation between the compound studied and the reference compounds used in determining the particular bond depressions needed. Suppose, for instance, that the C=O, C–O, and O–H bond depressions are obtained from acetone, dimethyl ether, and methyl alcohol respectively. Then Pacault's statement is true for all aliphatic ketones, and all *n*-alcohols, but not for any aldehydes or carboxylic acids. (*b*) Where the susceptibility does depend on the values taken for the charges and ionic susceptibilities, the differences produced by reasonable changes in these values are very small. For instance, in the case of acetic acid, taking all the ionic susceptibilities as zero instead of the Pauling values produces a change of less than 1% in the calculated molecularsu sceptibility. (*c*) The Gray and Cruickshank method does not predict the differences in the susceptibilities of certain types of isomers, well established experimentally by the work of Angus and Hill (*Trans. Faraday Soc.*, 1943, **39**, 197), Trew (*Trans. Faraday Soc.*, 1953, **49**, 604), and many other workers. The particular types of isomers concerned are branched-chain hydrocarbons and aliphatic alcohols. In such cases, alteration of the values of the ionic susceptibilities or charges will not rectify this inadequacy. The same is true of the application of the method to aromatic compounds, polymethylene rings, etc. This applies particularly to the modified form of the method studied by Anantakrishnan (*Proc. Indian Acad. Sci.*, 1945, **21**, *A*, 114) whose numerical calculations, however, we are unable to reproduce.

It is concluded that for the purpose of obtaining a reliable value of the susceptibility of an organic molecule, for use in structural studies, the Gray and Cruickshank method (or any simple modification of it) has no advantage over the Pascal system, and in several respects is definitely inferior to it.

Whilst it is undoubtedly desirable to take account of the polarity of the various linkages in a molecule, the Gray and Cruickshank method of calculation is not a satisfactory way of doing this, and its further use in structural investigations appears of very doubtful value.

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[*Received, July* 15*th*, 1954.]

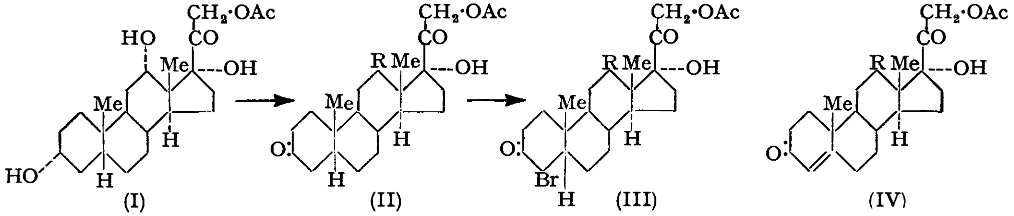
12-*Oxygenated Pregnane Derivatives. Part IV.**

21-*Acetoxy*-17α-*hydroxypregn*-4-*ene*-3 : 12 : 20-*trione.*

By (Mrs.) W. J. Adams, D. K. Patel, and V. Petrow.

[Reprint Order No. 5559.]

In Part II (Adams, Kirk, Patel, Petrow, and Stuart-Webb, *J.*, 1954, 2209) an attempt to prepare 21-acetoxy-17α-hydroxypregn-4-ene-3 : 12 : 20-trione (IV; R = O) from hecogenin was recorded. No difficulty was experienced in transforming the genin into 21-acetoxy-17α-hydroxy*allo*pregnane-3 : 12 : 20-trione, but conversion of the latter into the 4 : 5-ene by conventional bromination–dehydrobromination procedures proved impossible. A partial synthesis of the required compound from 21-acetoxy-3α : 12α : 17α-trihydroxypregnan-20-one (I), previously obtained from deoxycholic acid (Part I, Adams, Patel, Petrow, and Stuart-Webb, *J.*, 1954, 1825), is now reported.



Partial oxidation of the alcohol (I) with *N*-bromoacetamide to the 3-oxo-derivative (II; R = α-OH), followed by monobromination, gave 21-acetoxy-4β-bromo-12α : 17α-dihydroxypregnane-3 : 20-dione (III; R = α-OH) (Part I, *loc. cit.*). Cautious oxidation of the last compound with chromic acid under conditions which leave the ketol side chain intact (Lieberman, Katzenellenbogen, Schneider, Studer, and Dobriner, *J. Biol. Chem.*, 1953, **205**, 87), however, gave 21-acetoxy-17α-hydroxypregnane-3 : 12 : 20-trione (II; R = O) as main product, together with the required 4β-bromo-ketone (III; R = O) in small amount. The unexpected loss of halogen observed during this reaction appears to be connected with the polar effect exerted by the 12-oxo-group on the 4β-bromo-3-oxo-system. Thus we find that methyl 12α-acetoxy-4β-bromo-3-oxocholanate is recovered unchanged after similar treatment with chromic acid, whilst the 12α-hydroxy-compound

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* Part III, *J.*, 1954, 2298.

passes smoothly into a mixture of diketones in which the bromine-free product again predominates.

The difficulty thus encountered was overcome in two ways. First, the compound (I) was carefully oxidised to 21-acetoxy-17α-hydroxypregnane-3 : 12 : 20-trione (II; R = O), which was converted into the 4β-bromo-derivative (III; R = O) and thence by dehydrobromination *via* the semicarbazone into 21-acetoxy-17α-hydroxypregn-4-ene-3 : 12 : 20-trione (IV; R = O). Alternatively, the compound (I) was transformed into 21-acetoxy-12α : 17α-dihydroxypregn-4-ene-3 : 20-dione (IV; R = α-OH) (Part I, *loc. cit.*), which was converted into the trione (IV; R = O) by careful oxidation. The overall yields, however, were disappointingly low.

Experimental.—Optical rotations were measured in $CHCl_3$ solution in a 1-dm. tube.

21-*Acetoxy*-17α-*hydroxypregnane*-3 : 12 : 20-*trione* (II; R = O). 21-Acetoxy-12α : 17α-dihydroxypregnane-3 : 20-dione (2 g.) in acetic acid (125 ml.) was treated with chromium trioxide (60 ml. of 1·5% solution in 95% acetic acid) for 3 hr. at room temperature. The solution was then diluted with water, and treated with sodium dithionite (hydrosulphite) solution, and the products were extracted with ether. The neutral fraction crystallised from acetone–hexane, yielding 21-*acetoxy*-17α-*hydroxypregnane*-3 : 12 : 20-*trione*, m. p. 156°, $[\alpha]_D^{25°}$ +76° (*c*, 0·4312) (Found: C, 68·0; H, 8·0. $C_{23}H_{32}O_6$ requires C, 68·3; H, 7·9%).

21-Acetoxy-4β-bromo-17α-hydroxypregnane-3 : 12 : 20-trione (III; R = O) was prepared by treating a solution of the foregoing compound (500 mg.) in acetic acid (22 ml.) with bromine (1·32 ml. of 0·986M-solution in acetic acid) portionwise during about 2 min. The decolorised solution was immediately diluted with water and extracted with ether, which was washed successively with water, sodium hydroxide solution and water, and dried. Removal of the ether furnished a crystalline bromo-derivative, m. p. *ca.* 174—176°, which was used immediately for the next stage.

21-*Acetoxy*-17α-*hydroxypregn*-4-*ene*-3 : 12 : 20-*trione* (IV; R = O). (*a*) The foregoing crude bromo-derivative in acetic acid (100 ml. of 98%) was heated at 70° under nitrogen for 2 hr. with semicarbazide hydrochloride (480 mg.) and sodium acetate (480 mg.), after which pyruvic acid (8 ml.) in water (16 ml.) was added and heating at 70° maintained for a further 2 hr. After dilution with water the product was extracted with ether, and the neutral fraction crystallised from acetone–hexane. 21-*Acetoxy*-17α-*hydroxypregn*-4-*ene*-3 : 12 : 20-*trione* formed needles, m. p. 189·5—190·5°, $[\alpha]_D^{20°}$ +125° (*c*, 0·406), $\lambda_{max.}$ 238 mμ (4·23) (Found: C, 68·2; H, 7·5. $C_{23}H_{30}O_6$ requires C, 68·7; H, 7·5%). The compound was recovered unchanged after heating with acetic anhydride.

(*b*) 21-Acetoxy-12α : 17α-dihydroxypregn-4-ene-3 : 20-dione (IV; R = α-OH) (250 mg.) in acetic acid (16 ml.) and chromium trioxide (6·7 ml. of 1·5% solution in 95% acetic acid) was left at room temperature for 3 hr., after which it was diluted with water and treated with aqueous sodium dithionite, and the product extracted with ether. The neutral fraction, on purification from acetone–hexane, furnished (IV; R = O), m. p. 189·5—190·5°, alone or in admixture with a sample prepared as under (*a*). The identity of the two materials was further confirmed by comparison of the infra-red absorption spectra, kindly determined by Dr. A. E. Kellie, Courtauld Institute of Biochemistry.

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Addition of the Amino-radical, $\cdot NH_2$, to Benzene, Toluene, and cyclo*Hexene.*

By H. Seaman, P. J. Taylor, and William A. Waters.

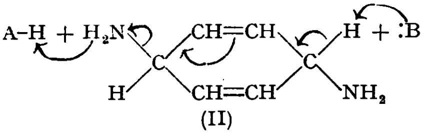
[Reprint Order No. 5568.]

Davies, Evans, and Higginson (*J.*, 1951, 2463) have shown that the free amino-radical, $\cdot NH_2$, can be produced in aqueous solution by the reduction of hydroxylamine with titanous salts. They found that this reacting mixture attacked emulsified benzene to give, in small amounts, an unstable oil which was not aniline and which when boiled with dilute acid decomposed yielding diphenyl. Consequently they suggested that $\cdot NH_2$ radicals can add to benzene to give a radical, $\cdot C_6H_6{\cdot}NH_2$, which then dimerises to a di(amino*cyclo*hexadienyl) (I).

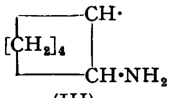
We have examined more closely the unstable product of this reaction between $\cdot NH_2$ radicals and benzene. It is a base which decomposes slowly at room temperature, and more rapidly when warmed, yielding ammonia and aniline as well as diphenyl. It is unsaturated, catalytic reduction decomposes it to ammonia, aniline, and, probably, benzene amongst other products, and from its reactions it appears to contain diamino*cyclo*hexadiene (*e.g.*, II) as well as the dimer (I). Solid derivatives, other than those of its decomposition products, could not be obtained pure and this failure can be ascribed to the fact that both acids and bases would easily convert (I) into diphenyl and (II) into aniline.

$(H_2N{\cdot}C_6H_6{-})_2$

(I)



(II)



(III)

Toluene gave traces of a similar product, and not benzylamine, indicating that the $\cdot NH_2$ radical does not dehydrogenate the methyl group but preferably attacks the aromatic nucleus.

Emulsions of *cyclo*hexene also yielded a basic oil, the most volatile fraction of which proved to be *cyclo*hexylamine. In this case therefore it seems that the initial radical adduct (III) can be further reduced by the titanous salt. Oct-1-ene and non-1-ene were too sparingly soluble in water to give isolable amounts of reaction products.

Experimental.—Reaction with benzene. To benzene (50 ml.), emulsified by rapid stirring with water (200 ml.) in a nitrogen atmosphere, were simultaneously added during 45 min. N-hydroxylamine hydrochloride (250 ml.) and *ca.* 0·9N-titanous chloride, in just sufficient amount for complete oxidation (calc. about 80% conversion into reacting NH_2 radicals). After separation of the benzene layer, which contained no other product, boric acid (30 g.) was added and then sufficient aqueous ammonia (150 ml.; *d* 0·88) to precipitate all the Ti^{4+} in a form that, after settling for ½—1 hr., could be filtered off at the pump. Without the addition of boric acid the precipitated titanic hydroxide was far too gelatinous for successful filtration. To the pale yellow filtrate, which darkened on storage, and when fresh gave a negative bleaching-powder test for aniline, sodium hydroxide solution (100 ml.; 40%) was added. Extraction with cold ether (12 × 60 ml.), and evaporation of the extract without undue heating, gave an oil (0·8 g.) having the reactions of a primary aliphatic amine (carbylamine test; N_2 with HNO_2 but no coupling). After storage for 2 weeks it smelled strongly of ammonia, contained much aniline (preparation of tribromoaniline and benzanilide), and had deposited some diphenyl (m. p. and mixed m. p. 69°). Diphenyl distilled in steam when either an acid or an alkaline solution of the original reaction product was boiled; the boiled solutions with bromine gave heavy precipitates of tribromoaniline and coupled with β-naphthol to form phenylazo-β-naphthol. The freshly prepared oil immediately decolorised cold aqueous permanganate and, in alcohol, absorbed hydrogen at room temperature and pressure in the presence of Raney nickel. The hydrogenated product contained free ammonia and aniline and gave a colour test for benzene (Lansing, *Ind. Eng. Chem. Anal.*, 1935, **7**, 184). Attempts to prepare solid derivatives of the basic oil yielded products which decomposed when warmed in solvents. The freshly prepared alkaline solution of the reaction mixture (250 ml.) gave a pale yellow precipitate (3·5 g.) when treated with a 1% solution of salicylaldehyde. This could be dried (m. p. 143—147°) [Found, C, 76·5; H, 6·1; N, 7·9. Calc. for $C_{26}H_{24}O_2N_2$, the disalicylidene derivative of (I) : C, 78·5; H, 6·1; N, 7·1. Calc. for $C_{20}H_{18}O_2N_2$, the disalicylidene derivative of (II) : C, 75·5; H, 5·7; N, 8·8%) but decomposed when warmed in alcohol. It was not salicylaldazine (m. p. 213°) and hence the free $\cdot NH_2$ radicals have not combined extensively to form hydrazine.

Reaction with toluene. This gave a similar aliphatic base (0·5 g.) from which an unstable salicylidene derivative, m. p. 174° (decomp.), was obtained. After boiling, solutions of the reaction product contained *p*-toluidine (preparation of *N*-phenyl-*N'*-*p*-tolylurea, m. p. and mixed m. p. 213°, and of benzo-*p*-toluidide).

Reaction with cyclo*hexene.* Reaction on a similar scale gave 8 g. of a reddish-brown oil which evolved nitrogen on treatment with nitrous acid, leaving a reddish residue which gave a positive Liebermann test for a nitrosamine. Reaction with benzil gave no indication of the presence of 1 : 2-diamine. Distillation gave, at 31°/13 mm. (130°/1 atm.), about 1 g. of *cyclo*hexylamine, which was identified by reaction with α-naphthyl *iso*thiocyanate, the product (m. p. 142°) being identical with that from *cyclo*hexylamine made by reduction of *cyclo*hexanone oxime (Baeyer, *Annalen*, 1894, **278**, 103) (Found, for *N*-*cyclo*hexyl-*N'*-α-naphthylthiourea : C, 71·8; H, 6·9; N, 9·7; S, 11·5. Calc. for $C_{17}H_{20}N_2S$: C, 71·8; H, 7·0; N, 9·9; S, 11·3%). At 120—130°/13 mm. a yellowish oil (1·3 g.) distilled; this contained a little *cyclo*hexylamine but also gave reactions of a secondary amine. Pure crystalline derivatives could not be obtained. The involatile residue was a brownish polymer, m. p. about 75°. It may be suggested that these less volatile materials are dimers and polymers of the radical (III).

THE DYSON PERRINS LABORATORY, OXFORD. [*Received, July 17th,* 1954.]

Ethyl 6-Acetylindane-1-carboxylate.

By V. ASKAM and W. H. LINNELL.

[Reprint Order No. 5583.]

DURING work on the preparation of analogues of cortical hormones, the Friedel–Crafts reaction of acetyl chloride on ethyl indane-1-carboxylate was investigated. A crystalline ketone separated from the product, a liquid distilling over a wide range of temperature. When oxidised with nitric acid the ketone gave trimellitic acid, indicating it to be either ethyl 5- or 6-acetylindane-1-carboxylate. Hydrolysis and Clemmensen reduction converted the ketone into an ethylindane-1-carboxylic acid, not identical with 5-ethylindane-1-carboxylic acid prepared by Clemmensen reduction of 5-ethyl-3-oxoindane-1-carboxylic acid (Askam and Linnell, *J.*, 1954, 2435). The structure ethyl 6-acetylindane-1-carboxylate was confirmed by the following method. The oxime was subjected to the Beckmann transformation, and the resulting acetamido-compound converted into the phenolic acid by hydrolysis and diazotisation. The phenolic acid and its acetate were identical with authentic specimens of 6-hydroxy- and 6-acetoxy-indane-1-carboxylic acid, prepared from 6-methoxy-3-oxoindane-1-carboxylic acid (Askam and Linnell, *loc. cit.*).

Experimental.—6-*Methoxyindane*-1-*carboxylic acid.* 6-Methoxy-3-oxoindane-1-carboxylic acid (42 g.) was reduced by the Clemmensen method, with amalgam prepared from zinc wool (100 g.) with 5% mercuric chloride solution (200 ml.), and 12% hydrochloric acid (1·5 l.). After 6 hr. the mixture was filtered. Water (700 ml.) was added to the residual amalgam, and the mixture boiled and filtered. This procedure was repeated with more water (400 + 200 ml.). When the combined filtrates were cooled, a solid (32 g.) was deposited. This crystallised from water (2300 ml.) (charcoal), to give 6-methoxyindane-1-carboxylic acid as colourless needles (30 g.), m. p. 110—111° (Found : C, 68·5; H, 6·2; MeO, 16·3. $C_{11}H_{12}O_3$ requires C, 68·7; H, 6·3; MeO, 16·1%). The p-*nitrobenzyl ester* crystallised from methanol as yellow prisms, m. p. 82·5—83·5° (Found : C, 66·0; H, 5·5; N, 4·2. $C_{18}H_{17}O_5N$ requires C, 66·1; H, 5·2; N, 4·3%).

6-*Hydroxyindane*-1-*carboxylic acid.* 6-Methoxyindane-1-carboxylic acid (3·0 g.), acetic acid (10 ml.), and 48% aqueous hydrobromic acid (15 ml.) were heated under reflux for 4 hr., then cooled and filtered, and the residue was heated under reflux for 30 min. with water (20 ml.) and a little charcoal. The solution was filtered and, on cooling, gave 6-*hydroxyindane*-1-*carboxylic* acid as colourless needles, m. p. 170—171°, unchanged on crystallisation from benzene–alcohol (Found : C, 67·7; H, 5·7. $C_{10}H_{10}O_3$ requires C, 67·4; H, 5·7%). The *acetate* was prepared by Chattaway's method (*J.*, 1931, 2495), the crude product (1·0 g.) being crystallised by adding to a warm solution in 10% acetic acid sufficient glacial acetic acid to give a solution which was clear at room temperature. When this was chilled overnight, the acetate crystallised as colourless needles, m. p. 83·5—84·5° (Found : C, 65·5; H, 5·4. $C_{12}H_{12}O_4$ requires C, 65·5; H, 5·5%).

5-*Ethylindane*-1-*carboxylic acid.* The crude semicarbazone (3·25 g.) of 5-ethyl-3-oxoindane-1-carboxylic acid (Askam and Linnell, *loc. cit.*) was refluxed for 30 min. with concentrated hydrochloric acid (125 ml.). The solution was extracted with ether, and the ethereal solution dried (Na_2SO_4) and evaporated. The viscous residue was heated under reflux for 6 hr. with water (130 ml.), concentrated hydrochloric acid (65 ml.), and amalgam from 20 g. of granulated zinc with 5% mercuric chloride solution (40 ml.). The mixture was cooled and filtered, the residue dried and dissolved in ether (150 ml.), and the zinc removed by filtration. The ethereal solution was passed through charcoal, and the ether distilled off, leaving a colourless crystalline residue (1·2 g.). This crystallised from aqueous–alcohol to give 5-*ethylindane*-1-*carboxylic acid,* colourless needles, m. p. 103·5—104° (Fouud : C, 75·5; H, 7·6%; equiv., 192·6. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%; equiv., 190·2). The p-*toluidide* crystallised from aqueous–alcohol as plates, m. p. 160—161° (Found : C, 82·0; H, 7·4; N, 4·85. $C_{19}H_{21}ON$ requires C, 81·7; H, 7·6; N, 5·0%).

Ethyl indane-1-*carboxylate.* Indene-1-carboxylic acid (50 g.) was hydrogenated in absolute alcohol (700 ml.) at atmospheric pressure by use of Adams catalyst (1 g.) (uptake *ca.* 100% in 19 hr.). The catalyst was filtered off, and the filtrate heated under reflux for 3 hr. whilst a stream of dry hydrogen chloride was passed in. Approx. two-thirds of the alcohol was removed by distillation, and the residue poured into water and extracted with ether. The ethereal solution was washed with sodium hydrogen carbonate solution and with water, then dried (Na_2SO_4) and fractionally distilled to give *ethyl indane*-1-*carboxylate* (50 g.), b. p. 144°/20 mm., n_D^{25} 1·5143 (Found : C, 76·2; H, 7·6. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%).

Ethyl 6-*acetylindane*-1-*carboxylate.* Anhydrous aluminium chloride (100 g.) was added to a stirred mixture of ethyl indane-1-carboxylate (50 g.), acetyl chloride (26 g.), and carbon disulphide (500 ml.). A vigorous reaction occurred and a heavy oil separated. When the reaction had subsided, the mixture was warmed for 2 hr., with stirring, under gentle reflux. The carbon disulphide was then removed, and the residue mixed with ice and dilute sulphuric acid and then extracted with ether. The ethereal solution was dried (Na_2SO_4) and distilled. After the ether had been removed, the whole of the distillate (b. p. up to 190°/4 mm.) was collected in one fraction (50 g.) as a viscous yellow liquid. The large colourless prisms, which were deposited from the liquid when chilled overnight, were filtered off, washed with light petroleum (b. p. 40—60°), and crystallised from ether, by cooling in acetone–solid carbon dioxide to give *ethyl* 6-*acetylindane*-1-*carboxylate* as small colourless crystals, m. p. 43—44° (Found : C, 72·5; H, 7·0. $C_{14}H_{16}O_3$ requires C, 72·4; H, 6·9%). The *oxime* crystallised from ether as colourless needles, m. p. 93—94° (Found : C, 68·5; H, 6·9; N, 5·7. $C_{14}H_{17}O_3N$ requires C, 68·0; H, 6·9; N, 5·7%).

When this ester (5·3 g.) was heated under reflux with concentrated hydrochloric acid (250 ml.) for 1 hr. and the solution then chilled overnight, buff-coloured needles (3·9 g.; m. p. 93—95°) were deposited. Crystallisation from water and from benzene gave the *acid* (1·1 g.) as pale yellow needles, m. p. 94·5—95·2° (Found : C, 70·5; H, 6·2%; equiv., 204·0. $C_{12}H_{12}O_3$ requires C, 70·6; H, 5·9%; equiv., 204·2). The *oxime* crystallised from alcohol as colourless needles, m. p. 183—184·5° with softening at 181° (Found : C, 65·4; H, 5·9; N, 6·5. $C_{12}H_{13}O_3N$ requires C, 65·75; H, 6·0; N, 6·4%).

6-*Ethylindane*-1-*carboxylic acid.* 6-Acetylindane-1-carboxylic acid (1·2 g.) was reduced with concentrated hydrochloric acid (40 ml.), water (80 ml.), and amalgam from granulated zinc (10 g.) and 5% mercuric chloride solution (20 ml.) for 6 hr. The solid *acid* (1·0 g.) deposited on cooling crystallised from water (650 ml.) as colourless needles (0·45 g.), m. p. 75—76° (Found : C, 75·6; H, 7·3%; equiv., 191·5. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%; equiv., 190·2).

Oxidation of ethyl 6-*acetylindane*-1-*carboxylate.* The ketone (1·0 g.) was boiled with concentrated nitric acid (15 ml.) for 2 hr., then evaporated to half its volume, nitric acid (10 ml.) was added, and the mixture heated under reflux for a further 3 hr. When the solution was cooled, trimellitic acid (0·7 g.; equiv., 73·4) was deposited, m. p. 225—227° (decomp.) (from water).

The anhydride, prepared by Schultz's method (*Annalen*, 1908, **359**, 143), had m. p. 160—161·5° or 161·5—163° when mixed with an authentic specimen of m. p. 162—164° (Found: C, 55·8; H, 2·0. Calc. for $C_9H_4O_5$: C, 56·3; H, 2·1%).

Conversion of ethyl 6-*acetylindane*-1-*carboxylate into* 6-*hydroxyindane*-1-*carboxylic acid.* To 10 c.c. of a mixture of concentrated sulphuric acid (49 ml.) and water (10 ml.), at 100°, the oxime (2·3 g.) of ethyl 6-acetylindane-1-carboxylate was added. The temperature was raised to 140° and kept at 140—145° for 5 min. Water (6 ml.) was then added, and the mixture boiled for 6 hr., after which it was cooled in ice. A 10% solution of sodium nitrite was then slowly added, in slight excess (starch–iodide). The mixture was added, drop by drop, to copper sulphate (0·05 g.) in boiling water (10 ml.). A little charcoal was added, and the mixture boiled for 5 min. and filtered. Deep yellow needles (1·0 g.) crystallised from the filtrate. A 1% solution of this compound in ether was passed through a short column of charcoal. The ether was removed and the residue crystallised from water (5 ml.), to give 6-hydroxyindane-1-carboxylic acid as pale yellow needles, m. p. and mixed m. p. 170—171° (acetate, m. p. and mixed m. p. 82—83°).

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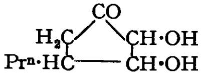
The Structure of Terrein.

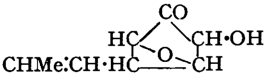
By John Frederick Grove.

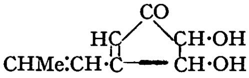
[Reprint Order No. 5591.]

The optically active cyclic ketol terrein, $C_8H_{10}O_3$, m. p. 127°, was obtained from two strains of *Aspergillus terreus* by Raistrick and Smith (*Biochem. J.*, 1935, **29**, 606). It has now been found that two strains of a species of *Penicillium* belonging to the *P. raistrickii* series also produce terrein.

The structure of terrein was substantially elucidated when Clutterbuck, Raistrick, and Reuter (*Biochem. J.*, 1937, **31**, 987) showed that tetrahydroterrein was 2 : 3-dihydroxy-4-propyl*cyclo*pentan-1-one (I) and established that the propyl side chain was present in terrein as a propenyl group. They considered all the possible structures for terrein consistent with the latter condition and resulting from the removal of 4 hydrogen atoms from (I). Of these, all were excluded except (II) and (III), and the former was preferred mainly on the grounds that oxidation of tetrahydroterrein to (+)-*n*-propylsuccinic acid was more readily explained by the presence in terrein of an asymmetric centre at $C_{(4)}$.


(I)


(II)


(III)

However, the infra-red and ultra-violet absorption spectra show the presence of a conjugated dienone grouping in terrein and are consistent only with 4 : 5-dihydroxy-3-propenyl*cyclo*pent-2-en-1-one (III). Tetrahydroterrein must therefore contain a new asymmetric centre at $C_{(4)}$ and represents one of the diastereoisomers which can be formed under the influence of the optically active RR'CH(OH) groupings in the catalytic reduction of terrein. The results of the periodate oxidation of terrein, which gave the semi-aldehyde of propenylmaleic acid, and of tetrahydroterrein, which gave the semi-aldehyde of (+)-*n*-propylsuccinic acid, are readily explicable on this hypothesis. Indeed, the former degradation can more easily be envisaged on the basis of structure (III) (for discussion see Clutterbuck *et al.*, *loc. cit.*).

Clutterbuck *et al.* cited the formation of only a mono-*p*-bromobenzoate and the failure of terrein to react when melted with maleic anhydride as additional arguments against (III). These objections are met by the observations (*a*) that the infra-red spectrum of terrein shows two hydroxyl bands (although this cannot be taken as conclusive proof of the presence of two hydroxyl groups) and (*b*) that terrein reacts with maleic anhydride in boiling benzene.

It is concluded that (III) correctly represents the structure of terrein.

Experimental.—Two strains belonging to the *P. raistrickii* series were used: culture No. 453 in our collection was received from Dr. J. H. Warcup (his No. B15b, *Trans. Brit. Mycol. Soc.*, 1951, **34**, 376) and No. 1006 was isolated from Bagshot Heath soil (Jefferys, Brian, Hemming, and Lowe, *J. Gen. Microbiol.*, 1953, **9**, 314). Conditions of fermentation and extraction (carried out by Mr. P. J. Curtis) were similar to those used by Raistrick and Ross (*Biochem. J.*, 1952, **50**, 635) for the production of dihydrogladiolic acid. Cultures No. 453 and 1006 gave yields of 190 and 300 mg./l. respectively of a neutral ketonic substance which had powerful reducing properties, was readily soluble in water, and gave a lemon-yellow colour with sodium hydroxide. It crystallised from benzene in plates, m. p. 127°, $[\alpha]_D^{19}$ +192° (*c*, 0·2035 in H_2O) (Found: C, 62·0; H, 6·8. Calc. for $C_8H_{10}O_3$: C, 62·3; H, 6·5%). The mixed m. p. with an authentic specimen of terrein kindly provided by Prof. H. Raistrick, F.R.S., showed no depression and the infra-red spectra of the two samples were identical.

The ultra-violet absorption curve of terrein showed $\lambda_{max.}$ 276 mμ (ε 25,000) in EtOH and 282·5 mμ (ε 26,500) in H_2O, due to a conjugated dienone chromophore. The infra-red spectrum of a chloroform solution (determined by Dr. L. A. Duncanson) showed bands in the double-bond stretching region at 1703 (αβ-unsaturated 5-ring ketone; Grove and Willis, *J.*, 1951, 877) and 1639 cm.$^{-1}$ (conjugated C:C); a Nujol mull showed strong bands at 3390 (OH), 3215 (bonded OH), 1697, and 1636 cm.$^{-1}$.

Terrein (1·6 mg.; 10^{-5} mol.) and maleic anhydride (5·3 mg.) in benzene (2 ml.) were heated under reflux for 2 hr., the solvent was removed, and after the addition of water (2 ml.) the residual maleic acid was estimated by titration with 0·1N-sodium hydroxide to the first end-point (0·43 ml. required) with a screened ethyl-orange indicator (Titley, Grove, and Allmand, *J. Soc. Chem. Ind.*, 1950, **69**, S23). Hence maleic anhydride consumed in the reaction = 1·0 mg. (10^{-5} mol.).

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The Heat of Formation of Auric and Thallic Fluorides.

By A. A. Woolf.

[Reprint Order No. 5592.]

The heats of formation of a number of fluorides of elements in their highest valency states are still unknown, in some cases presumably because suitable experimental methods have yet to be devised. A few heats can be determined by solution calorimetry in water, provided that fluoro-acids are not formed or that oxygen is not liberated. For some of the latter, solution calorimetry with bromine trifluoride seems preferable to bomb calorimetry with fluorine or the halogen fluorides. The applications of solution methods to auric and thallic fluorides are described.

Both fluorides hydrolyse quantitatively [$MF_3 + 3H_2O = M(OH)_3 + 3HF$]; the heats of formation obtained from the heats of hydrolysis and the appropriate heats taken from the National Bureau of Standards Circular 500 (" Selected Values of Chemical Thermodynamic Properties," 1952) are −83·3 and −136·9 kcal./mole for solid auric and thallic fluoride, respectively, at 25°. The values for the corresponding trichlorides are respectively +55·0 and +53·0 kcal./mole greater. The mean bond energies cannot be computed unless values for the heat of sublimation of these thermally unstable fluorides are known.

The heat of formation of silver tetrafluoroaurate has also been measured as a step in the following cycle, from which the heat of formation of the complex anion could be derived:

$$\begin{tikzcd}
AgF + AuF_3 \arrow[r] & Ag_g^+ + F_g^- + AuF_{3g} \arrow[r] & Ag_g^+ + AuF_{4g}^- \arrow[r] & AgAuF_4 \arrow[lll, bend right]
\end{tikzcd}$$

The heat of formation of the fluoroaurate, −149·4 kcal./mole, leads to the value of +17·6 kcal./mole for the heat of dissociation: $AgAuF_4 \longrightarrow AgF + AuF_3$.

Experimental.—The calorimeter was similar to that described previously (Woolf, *J.*, 1951, 231), with improved electrical calibration. All measurements were made at 25°.

Auric fluoride. This was prepared immediately before use from gold and bromine trifluoride (Sharpe, *J.*, 1949, 2901) (Found, in the three specimens used: AuF_3/Au, 1·287, 1·296, and 1·290. Calc.: AuF_3/Au, 1·289). The values of the heat of hydrolysis, obtained by using 1·5—2·5 g. of fluoride in 500 ml. of water, were −39·7, −38·8, and −39·8 (mean −39·4 ± 0·4) kcal./mole.

Silver tetrafluoroaurate. This was hydrolysed similarly just after preparation. The salt was slightly impure (Found: $AgAuF_4/Au$, 1·969, 1·959, 1·965. Calc.: $AgAuF_4/Au$, 1·933) owing probably to unavoidable solvolysis. The values of the heat of hydrolysis, obtained when 2·5—3·8 g. of salt were added to 500 ml. of water, were −26·9, −27·0, −26·5 (mean −26·8 ± 0·2) kcal./mole.

Thallic fluoride. This was prepared from thallous iodate and bromine trifluoride (Emeléus and Woolf, *J.*, 1950, 164) (Found: $TlF_3/TlIO_3$, 0·690, 0·683. Calc.: $TlF_3/TlIO_3$, 0·688). The heat rise was small when 1·5—3·5 g. of fluoride were used in 500 ml. of water, and the values determined, −8·3 and −8·5 (mean −8·4) kcal./mole, are less accurate than for the gold compounds.

MANCHESTER UNIVERSITY. [*Received, July 27th,* 1954.]

A New Pyridine Complex of Selenium Tetrafluoride.

By E. E. AYNSLEY and G. HETHERINGTON.

[Reprint Order No. 5612.]

OF the complex halides of selenium, chlorides and bromides have previously been described. Thus Muthmann and Schäfer (*Ber.*, 1893, **26**, 1008) and Lenher (*J. Amer. Chem. Soc.*, 1898, **20**, 568) prepared double bromides of the type M_2SeBr_6, where M = K, Rb, Cs, or NH_4 by mixing the appropriate bromide with selenium and introducing bromine. Lenher (*loc. cit.*) showed that selenium tetrabromide unites with the hydrobromides of organic amines to form well-defined double salts of the type $(BH)_2SeBr_6$, where B is a base.

Petzold (*Z. anorg. Chem.*, 1932, **209**, 267) prepared corresponding hexachloroselenites by treating selenium or selenious acid with hydrochloric acid and the appropriate metallic or amine salt.

Fluorides of the form $M[SeF_5]$, where M = Na, K, Rb, Cs, or Tl, have been isolated by Aynsley, Peacock, and Robinson (*J.*, 1952, 1231) by dissolving the appropriate alkali fluoride in boiling selenium tetrafluoride, but no fluoride or iodide complexes with organic bases are known. A comparison of the halides of selenium and tellurium suggests that selenium might form complexes with organic bases, *e.g.*, pyridine, of the type $BSeF_4$, and salts such as $(BH)SeF_5$, $(BH)_2SeF_6$, and $(BH)_2SeI_6$ (Aynsley and Hetherington, *J.*, 1953, 2802).

When methods similar to those described for tellurium tetrafluoride are used (*idem, loc. cit.*), selenium tetrafluoride and pyridine in dry ether give a white amorphous solid which cannot be separated from ether without slight decomposition. On careful evaporation the white ether complex of pyridine–tetrafluoroselenium(IV), $(C_5H_5N)SeF_4,(C_2H_5)_2O$, is left; this readily loses ether, and breaks down into its components. Attempts to prepare hydrogen fluoride complexes from this complex or from selenium dioxide and pyridine resulted only in selenium's being deposited.

Similarly selenium oxyfluoride yields a white amorphous complex (Se : N = 1 : 1), stable under ether, but decomposes to an oily brown liquid when the ether is removed. Hydrobromic acid converts both this oily liquid and the selenium tetrafluoride–ether complex into dipyridinium hexabromoselenite, $(C_5H_5NH)_2SeBr_6$. Hydriodic acid does not give the corresponding iodide but gives instead pyridine hydrogen di-iodide, $(C_5H_5N)HI_2$ (cf. Trowbridge, *J. Amer. Chem. Soc.*, 1897, **19**, 322).

Experimental.—Pyridine–tetrafluoroselenium(IV)*–ether complex.* Selenium tetrafluoride in anhydrous ether was added to a dry ethereal solution of pyridine in a " Polythene " beaker in a dry box. Slow evaporation of the ether yielded solid white *pyridine–tetrafluoroselenium*(IV)–

ether complex on the walls of the beaker. This was collected, washed with ether, and excess of the latter was pumped off, the pumping being stopped at the first sign of decomposition. The product was dissolved in water; the selenium was determined as the element after reduction by sulphur dioxide, the fluorine as lead chlorofluoride after distillation from 50% sulphuric acid, and the nitrogen as ammonia [Found: Se, 26·0; F, 25·3; N, 4·5. $(C_5H_5N)SeF_4,(C_2H_5)_2O$ requires Se, 25·6; F, 24·7; N, 4·6%].

Reaction of the ether complex with hydrofluoric acid. The etherate solution in aqueous hydrofluoric acid evaporated (*a*) on a steam bath, (*b*) at laboratory temperatures, deposited selenium and no complex could be isolated; this behaviour is quite unlike that observed with tellurium (Aynsley and Hetherington, *loc. cit.*). Selenium was also deposited when pyridine was added to a solution of selenium dioxide in aqueous hydrofluoric acid and the solution evaporated.

Reaction between selenium oxyfluoride and pyridine. Pyridine and selenium oxyfluoride in ether gave a white complex which, after being filtered off and washed with ether, decomposed when an attempt was made to remove the latter, to an oily brown liquid (Se : N = 1 : 1).

Reactions of pyridine–tetrafluoroselenium(IV)*–ether complex* (I) *and the selenium oxyfluoride complex* (II). (i) Hydrobromic acid produced red needles of dipyridinium hexabromoselenite [Found: From (I) Se, 11·3; Br, 66·5; C, 16·9; H, 2·0; N, 3·7. From (II) Se, 11·0; Br, 66·7; C, 16·6; H, 1·9; N, 3·8. Calc. for $(C_5H_5NH)_2,SeBr_6$: Se, 11·0; Br, 66·8; C, 16·7; H, 1·7; N, 3·9%].

(ii) Hydriodic acid liberated much iodine and from the brown liquids was isolated, not the expected dipyridinium hexaiodoselenite, but brown prismatic crystals of pyridine hydrogen di-iodide [Found: From (I): C, 18·2; H, 2·0; N, 3·8; I, 75·6. From (II): C, 18·3; H, 2·1; N, 4·3; I, 75·7. Calc. for $(C_5H_5N)HI_2$: C, 18·0; H, 1·8; N, 4·2; I, 76·0%]. M. p.s were, from (I) 190—191° and from (II) 190—192°; Trowbridge (*loc. cit.*) gives 188—192°.

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Œstrogenic Activity of Certain para-*Substituted Phenols.*

By W. LAWSON.

[Reprint Order No. 5635.]

IN earlier communications (Dodds and Lawson, *Proc. Roy. Soc.*, 1938, *B*, **125**, 222; Dodds, Golberg, Lawson, and Robinson, *Nature*, 1938, **141**, 247) a number of simple *para*-substituted phenols have been described as having very low œstrogenic activity. Among these were *p*-propenylphenol (anol), *p-n*-propylphenol, *p*-propionylphenol and *p-tert.*-amylphenol. Subsequent work (Campbell, Dodds, and Lawson, *Proc. Roy. Soc.*, 1940, *B*, **128**, 253; Paulsen, Mortimore, and Heller, *J. Clin. Endocrinol.*, 1951, **11**, 892) has shown that in all except the last-mentioned the activity is wholly due to impurities, since when purified through a crystalline ester and finally sublimed at reduced pressure and crystallized they are completely inactive. It is assumed that the activity of the impure compounds is entirely due to traces of stilbœstrol-like compounds formed by dimerization involving the α-carbon atoms of two molecules. This, however, is not possible in the case of *p-tert.*-amylphenol and biological tests have been repeated at long intervals on several new preparations of this compound purified by a similar procedure. It was found that a dose of 100 mg. invariably produced œstrus in the ovariectomized rat, so that this can be regarded as the simplest molecule found to have this activity. All the other amylphenols as well as the butylphenols are completely without effect, as is also *p-neo*pentylphenol.

In view of these results it appeared of interest to prepare other *p-tert.*-alkyl-phenols. The samples used for biological tests were all very highly purified and the accompanying Table shows (nos. 1, 2, 8, 10, and 13) that increasing the length of the alkyl chains increases the activity, and that still further lengthening of the chain decreases the biological activity. When a second phenyl group is introduced (nos. 15—18) the change in activity produced by altering the aliphatic portion of the molecule is even more striking and cannot be explained by any present theory.

Œstrogenic activity of phenols, p-HO·C_6H_4·CRR′R″.

No.	R	R′	R″	Active at : mg. per rat	No.	R	R′	R″	Active at : mg. per rat
1	Me	Me	Me	(Nil at 300 mg.)	11	Et	Et	Pr^{n} [5]	25
2	Me	Me	Et	100	12	Et	Et	Bu^{n}	100
3	Me	Me	Pr^{n} [1]	100	13	Pr^{n}	Pr^{n}	Pr^{n}	25
4	Me	Me	Pr^{i} [1]	70	14	Me	Me	*cyclo*Hexyl	100
5	Me	Me	Bu^{n} [2]	(Nil at 100 mg.)	15	Me	Me	Ph [6]	100
6	Me	Me	Bu^{t} [2]	100	16	Et	Et	Ph	10
7	Me	Me	n-C_5H_{11} [3]	(Nil at 100 mg.)	17	Pr^{n}	Pr^{n}	Ph	5
8	Me	Et	Et [1]	50	18	Pr^{i}	Pr^{i}	Ph	1
9	Me	Pr^{n}	Pr^{n} [4]	100	19	Et	Ph	Ph	(Nil at 100 mg.)
10	Et	Et	Et [2]	25					

[1] Huston and Hsieh, *J. Amer. Chem. Soc.*, 1936, **58**, 439. [2] Huston and Hedrick, *ibid.*, 1937, **59**, 2001. [3] Huston and Guile, *ibid.*, 1939, **61**, 69. [4] Huston and Meloy, *ibid.*, 1942, **64**, 2655. [5] Huston, Langdon and Snyder, *ibid.*, 1948, **70**, 1474. [6] Welsh and Drake, *ibid.*, 1938, **60**, 59.

Experimental.—These phenols were prepared by the method used by Huston *et al.* (*locc. cit.*), condensation of phenol with the appropriate tertiary alcohol in presence of aluminium chloride at room temperature. They were purified by conversion into a crystalline ester (benzoate or nitrobenzoate) and recovery by hydrolysis. The following have not been previously described.

3-*Ethyl*-3-p-*hydroxyphenylheptane* (12), b. p. 171—173°/13 mm. (Found : C, 81·8; H, 11·0. $C_{15}H_{24}O$ requires C, 81·8; H, 11·0%) [p-*nitrobenzoate*, needles (from alcohol), m. p. 61—62° (Found : C, 71·9; H, 7·2. $C_{22}H_{27}O_4N$ requires C, 71·5; H, 7·4%)].

4-p-*Hydroxyphenyl*-4-n-*propyl*-n-*heptane* (13), b. p. 175—180°/15 mm. (Found : C, 81·6; H, 11·4. $C_{16}H_{26}O$ requires C, 82·0; H, 11·2%) [3 : 5-*dinitrobenzoate*, prisms (from alcohol), m. p. 67° (Found : C, 64·5; H, 6·4. $C_{23}H_{28}O_6N_2$ requires C, 64·5; H, 6·6%)].

1-p-*Hydroxyphenyl*-1-*methylethyl*cyclo*hexane* (14), needles (from light petroleum), m. p. 104—105° (Found : C, 82·8; H, 10·1. $C_{15}H_{22}O$ requires C, 82·5; H, 10·15%) [*benzoate*, needles (from alcohol), m. p. 98—99° (Found : C, 82·2; H, 8·2. $C_{22}H_{26}O_2$ requires C, 82·0; H, 8·1%)].

3-p-*Hydroxyphenyl*-3-*phenyl*-n-*pentane* (16), b. p. 138—140°/0·2 mm., needles (from light petroleum), m. p. 51—52° (Found : C, 85·1; H, 8·5. $C_{17}H_{20}O$ requires C, 85·0; H, 8·4%) [*benzoate*, rectangular prisms (from alcohol), m.p. 92—93° (Found : C, 83·8; H, 6·9. $C_{24}H_{24}O_2$ requires C, 83·7; H, 7·0%)].

4-p-*Hydroxyphenyl*-4-*phenyl*-n-*heptane* (17), needles (from light petroleum), m. p. 58—59° (Found : C, 85·5; H, 9·0. $C_{19}H_{24}O$ requires C, 85·0; H, 9·0%) [*benzoate* (from alcohol), m. p. 69—70° (Found : C, 84·0; H, 7·5. $C_{26}H_{28}O_2$ requires C, 83·8; H, 7·6%)].

3-p-*Hydroxyphenyl*-2 : 4-*dimethyl*-3-*phenyl*-n-*pentane* (18), needles (from light petroleum), m. p. 64—65° (Found : C, 85·0; H, 8·7. $C_{19}H_{24}O$ requires C, 85·0; H, 8·5%) [*benzoate* (from alcohol), m. p. 114—115° (Found : C, 83·9; H, 7·3. $C_{26}H_{28}O_2$ requires C, 83·8; H, 7·6%)].

1-p-*Hydroxyphenyl*-1 : 1-*diphenylpropane* (19), prisms (from aqueous alcohol), m. p. 114—115° (Found : C, 87·8; H, 7·1. $C_{21}H_{20}O$ requires C, 87·5; H, 7·0%) [*benzoate* (from alcohol), m. p. 104—105° (Found : C, 85·9; H, 6·2. $C_{28}H_{24}O_2$ requires C, 85·7; H, 6·2%)].

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The Bromo- and Iodo-hypophosphites of Bivalent Tin.

By D. A. EVEREST.

[Reprint Order No. 5655.]

THE preparation of the two chlorohypophosphites of bivalent tin, $3Sn(H_2PO_2)_2,SnCl_2$ and $Sn(H_2PO_2)_2,SnCl_2$ (Everest, *J.*, 1951, 2903), and the subsequent discovery of the chloro-, bromo-, and iodo-hypophosphites of bivalent germanium (*idem, J.*, 1952, 1670; 1953, 4117), made it of interest to complete the bivalent tin series by studying the bromo- and iodo-hypophosphites.

Two bromohypophosphites have been isolated, $3Sn(H_2PO_2)_2,SnBr_2$ (m. p. 150°) and $Sn(H_2PO_2)_2,SnBr_2$ (m. p. 175°), depending upon the relative proportions of hydrobromic and hypophosphorous acid used. In the iodohypophosphite series only the compound $3Sn(H_2PO_2)_2,SnI_2$ (m. p. 135°) could be isolated from solutions containing excess of hypophosphorous acid; conditions expected to favour the formation of the 1 : 1 compound resulted in precipitation of stannous iodide. This closely resembled the behaviour of the germanous iodohypophosphites (*loc. cit.*). In all these preparations care was taken not to use too concentrated solutions, or to cool them too quickly, otherwise amorphous precipitates were formed.

Although no information concerning the structures of these halogenohypophosphites has been obtained, it is clear that they form a well-defined group of compounds. Eight of them have now been isolated containing either bivalent germanium or tin; they are all colourless crystalline solids with sharp melting points ranging from 124° for $Ge(H_2PO_2)_2,GeCl_2$ to 181° for the corresponding tin compound. They are all sparingly soluble in water and are only slowly hydrolysed; this being in contrast to the simple chlorides and bromides of bivalent germanium and tin which either are readily soluble in water or are easily hydrolysed. There are four possible halogenohypophosphites of bivalent germanium and tin which have not been isolated, *viz.* $3Ge(H_2PO_2)_2,GeCl_2$, $Ge(H_2PO_2)_2,GeBr_2$, $Ge(H_2PO_2)_2,GeI_2$, and $Sn(H_2PO_2)_2,SnI_2$. The failure to obtain these compounds may have resulted from inability to find the exact experimental conditions for their isolation, but it is significant that in three cases it is the 1 : 1 compound containing either bromine or iodine that is missing, so that possibly steric factors are involved.

Although no halogenohypophosphites of bivalent lead have ever been obtained it seems probable that the highly explosive double salts $Pb(H_2PO_2)_2,Pb(NO_3)_2$ (von Hertz, *Z. ges. Schiess- u. Sprengstoff.*, 1916, ii, 365; *Chem. Zentr.*, 1919, i, 271), and the one formed from equimolecular parts of lead hypophosphite and lead styphnate (McNutt and Ehrlich, U.S.P., 2,352,964), are further examples of these hypophosphite complexes. Attempts to prepare compounds of bivalent germanium and tin corresponding to those of lead have been, however, unsuccessful.

That hypophosphite complexes may be formed by metals outside the germanium group is shown by the existence of the double mercurous salt $Hg_2(H_2PO_2)_2,Hg_2(NO_3)_2$ (Hada, *J.*, 1895, **67**, 727) and by the series of complex ferric hypophosphites (Weinland and Hieber, *Z. anorg. Chem.*, 1919, **106**, 15; *Ber.*, 1919, **52**, 731). Again, however, there is no direct evidence concerning the structure of these compounds.

Experimental.—*Analytical procedures.* Halogens and tin were estimated as previously described (*J.*, 1951, 2903). The reduction equivalent was estimated iodometrically by Jones and Swift's method (*Analyt. Chem.*, 1953, **25**, 1272).

Double salt $3Sn(H_2PO_2)_2,SnBr_2$. This *salt* (m. p. 150°) was obtained when 25% hypophosphorous acid (10 ml.), saturated with stannous hypophosphite at room temperature, was treated with 23% hydrobromic acid (1 ml.) [Found : Sn, 46·5; Br, 15·8%; reduction equiv., 31·85. $3Sn(H_2PO_2)_2,SnBr_2$ requires Sn, 46·35; Br, 15·6%; reduction equiv., 32·0].

Double salt $Sn(H_2PO_2)_2,SnBr_2$. This *salt* (m. p. 175°) was formed when hypophosphorous acid was added to an excess of a hot, freshly formed hydrobromic acid solution of bivalent tin [Found : Sn, 44·8; Br, 30·65%; reduction equiv., 43·4. $Sn(H_2PO_2)_2,SnBr_2$ requires Sn, 45·0; Br, 30·3%; reduction equiv., 43·95].

Double salt $3Sn(H_2PO_2)_2,SnI_2$. This *salt* (m. p. 135°) was obtained by treating a hot 25% hypophosphorous acid solution (50 ml.), previously saturated with stannous hypophosphite at room temperature, with 15% hydriodic acid (5 ml.) with constant stirring to prevent any local excess of hydriodic acid. On cooling of the solution to *ca.* 50° crystals separated; further crystallisation was not allowed as this involved risk of contamination with stannous hypophosphite hexahydrate [Found: Sn, 42·35; I, 23·2%; reduction equiv., 35·25. $3Sn(H_2PO_2)_2,SnI_2$ requires Sn, 42·4; I, 22·7%; reduction equiv., 34·94].

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The Preparation of 1 : 4- *and* 2 : 4-*Dichloro*-9-*hydroxyfluorene*-9-*carboxylic Acids.*

By N. GREENHALGH.

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THE unequivocal preparation of 1 : 4- and 2 : 4-dichloro-9-hydroxyfluorene-9-carboxylic acids was undertaken in connection with biological work carried out in these laboratories (cf. Jones, Metcalfe, and Sexton, *J. Sci. Food Agric.*, 1954, **5**, 44). The intermediate 1 : 4- and 2 : 4-dichlorophenanthrenes were prepared by a Pschorr reaction (*Ber.*, 1896, **29**, 496) from the α-amino-α-phenylcinnamic acids derived from the dichloronitrobenzaldehydes. Iodic acid oxidation of the phenanthrenes gave the 9 : 10-quinones which on treatment with alkali gave the desired 9-hydroxyfluorene-9-carboxylic acids.

Copper in quinoline was used to effect decarboxylation of both the 1 : 4- and the 2 : 4-dichlorophenanthrene-9-carboxylic acids, which were stable to the normal method of decarboxylation by distillation at atmospheric pressure. Chromic acid oxidation of these dichlorophenanthrenes goes beyond the quinone stage, as shown by the isolation of what appears to be 4 : 6-dichlorodiphenyl-2 : 2′-dicarboxylic acid from 2 : 4-dichlorophenanthrene.

Experimental.—3 : 6-*Dichloro*-2-*nitro*-α-*phenylcinnamic acid.* 3 : 6-Dichloro-2-nitrobenzaldehyde (44 g.) (Gnehm and Bänziger, *Ber.*, 1896, **29**, 876), sodium phenylacetate (32 g.), and acetic anhydride (190 c.c.) were heated at 110° for 1 hr., then poured into water (300 c.c.) and heated on the steam-bath until the anhydride was decomposed. The product was collected and crystallised from benzene, to give the *cinnamic acid* (21 g.), m. p. 211° (Found: C, 53·4; H, 2·9; N, 4·5; Cl, 21·5. $C_{15}H_9O_4NCl_2$ requires C, 53·3; H, 2·7; N, 4·2; Cl, 21·0%).

3 : 5-*Dichloro*-2-*nitro*-α-*phenylcinnamic acid* (20 g.), m. p. 192° (Found: C, 53·4; H, 2·7; N, 4·4; Cl, 21·3%), was similarly prepared from 3 : 5-dichloro-2-nitrobenzaldehyde (22 g.) (Asinger, *Monatsh.*, 1933, **63**, 385).

2-*Amino*-3 : 6-*dichloro*-α-*phenylcinnamic acid.* A solution of 3 : 6-dichloro-2-nitro-α-phenylcinnamic acid (10 g.) in aqueous ammonia (260 c.c.; *d* 0·880; and 140 c.c. of water) at 40° was added rapidly to stirred, freshly prepared aqueous ferrous sulphate (100 g. in 250 c.c.) at 95°. This temperature was maintained for 1 hr. during which the solution was kept alkaline by the addition of aqueous ammonia. The mixture was cooled, acidified with hydrochloric acid, and extracted with ether. Evaporation of the dried extract gave a residue which crystallised from benzene to give the *amino-acid*, m. p. 162° (7·1 g.) (Found: N, 4·7. $C_{15}H_{11}O_2NCl_2$ requires N, 4·6%). 2-*Amino*-3 : 5-*dichloro*-α-*phenylcinnamic acid* (from benzene–light petroleum), m. p. 198—200° (Found: N, 4·8%), was similarly prepared.

1 : 4-*Dichlorophenanthrene*-9-*carboxylic acid.* 2-Amino-3 : 6-dichloro-α-phenylcinnamic acid (14 g.) in anhydrous alcoholic hydrogen chloride (18 g. in 75 c.c.) was diazotised (below 10°) by the addition during 1 hr. of alcoholic amyl nitrite (*ca.* 4 g. in 40 c.c.). After a further hour during which the temperature was allowed to rise to 15°, water (200 c.c.), and copper powder (2 g.) were added and the mixture was stirred for 2 hr. The precipitate which was essentially pure 1 : 4-*dichlorophenanthrene*-9-*carboxylic acid* (6 g.; m. p. 297°) was collected and dried. Crystallisation from ethyl acetate gave material of the same m. p. (Found: C, 62·1; H, 2·6; Cl, 23·7. $C_{15}H_8O_2Cl_2$ requires C, 61·9; H, 2·8; Cl, 24·4%). 2 : 4-*Dichlorophenanthrene*-9-*carboxylic acid*, m. p. 259° (Found: C, 62·1; H, 2·6; Cl, 24·1%), was similarly prepared.

1 : 4-*Dichlorophenanthrene.* 1 : 4-Dichlorophenanthrene-9-carboxylic acid (5·5 g.), redistilled quinoline (55 c.c.), and copper powder (0·4 g.) were mixed and heated under reflux for 1 hr.,

then poured into excess of dilute hydrochloric acid and extracted with ether. The extract was washed with aqueous sodium carbonate, dried, and evaporated. The residue, crystallised from aqueous methanol, gave 1 : 4-dichlorophenanthrene, m. p. 78° (2·5 g.) (Found : C, 68·1; H, 3·3; Cl, 28·1. $C_{14}H_8Cl_2$ requires C, 68·0; H, 3·2; Cl, 28·8%). 2 : 4-*Dichlorophenanthrene*, m. p. 87—88° (Found: C, 68·3; H, 3·4; Cl, 27·9%), was similarly prepared. Oxidation of 2 : 4-dichlorophenanthrene (2 g.) in acetic acid (10 c.c.) with chromic oxide (4 g.) in 70% acetic acid (12 c.c.) at 70—80° gave a product soluble in sodium hydrogen carbonate which was apparently 4 : 6-*dichlorodiphenyl*-2 : 2′-*dicarboxylic acid* (from ethyl acetate–light petroleum), m. p. 218—219° (Found: C, 54·5; H, 3·0; Cl, 23·4. $C_{14}H_8O_4Cl_2$ requires C, 54·1; H, 2·6; Cl, 22·9%).

1 : 4-*Dichlorophenanthrene*-9 : 10-*quinone*. 1 : 4-Dichlorophenanthrene (2 g.), iodic acid (4·8 g.), and glacial acetic acid (160 c.c.) were heated under reflux for 5 hr., then cooled. The precipitate crystallised from aqueous acetic acid, to give 1 : 4-*dichlorophenanthrene*-9 : 10-*quinone* (1 g.), m. p. 204—206° (Found : C, 60·2; H, 2·3; Cl, 26·1. $C_{14}H_6O_2Cl_2$ requires C, 60·6; H, 2·2; Cl, 25·7%). 2 : 4-*Dichlorophenanthrene*-9 : 10-*quinone*, m. p. 168—169° (Found : C, 60·1; H, 2·0; Cl, 25·3%), was similarly prepared.

1 : 4-*Dichloro*-9-*hydroxyfluorene*-9-*carboxylic acid*. 1 : 4-Dichlorophenanthrene-9 : 10-quinone (0·9 g.) and aqueous 10% sodium hydroxide (90 c.c.) were heated, with stirring, on the steam-bath for 10 min. After acidification of the cooled filtered solution with dilute sulphuric acid the product was collected and crystallised from benzene, to give 1 : 4-*dichloro*-9-*hydroxyfluorene*-9-*carboxylic acid* (0·7 g.), m. p. 176—177° (decomp.) (Found : C, 57·4; H, 2·8; Cl, 24·4. $C_{14}H_8O_3Cl_2$ requires C, 56·8; H, 2·7; Cl, 24·1%). 2 : 4-*Dichloro*-9-*hydroxyfluorene*-9-*carboxylic acid*, m. p. 195—197° (decomp.) (Found : C, 56·9; H, 2·8; Cl, 23·5%), was similarly prepared.

IMPERIAL CHEMICAL INDUSTRIES LIMITED, PHARMACEUTICALS DIVISION,
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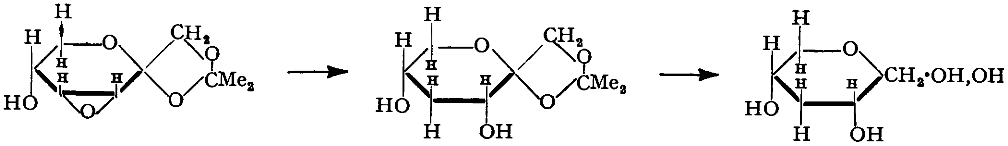
A Synthesis of 4-*Deoxy*-D-erythro*hexulose.*

By P. A. J. GORIN, L. HOUGH, and J. K. N. JONES.

[Reprint Order No. 5658.]

IN connection with some experiments on enzymes we wished to synthesize 3-deoxy-D-*erythro*hexulose. However, reduction of 3 : 4-anhydro-1 : 2-*O*-*iso*propylidene-α-D-*ribo*hexulose (I; Ohle and Just, *Ber.*, 1935, **68**, 605) with lithium aluminium hydride (Prins, *J. Amer. Chem. Soc.*, 1948, **70**, 3955) in ethereal solution gave 4-deoxy-1 : 2-*O*-*iso*propylidene-α-D-*erythro*hexulose (II), which was obtained crystalline in high yield, instead of the 3-deoxy-compound.

Chromatographic examination of the acid hydrolysis products of the crude reduction mixture (*A*) showed the presence of 4-deoxy-D-*erythro*hexulose (III) with only traces of another



(I) (II) (III)

compound [3-deoxy-D-*erythro*hexulose (?)]. (II) was not oxidised by aqueous sodium metaperiodate, thus distinguishing it from the 3-deoxy-isomer. It gave, on acid hydrolysis, syrupy 4-deoxy-D-*erythro*hexulose (III) which was converted into its crystalline phenylosazone.

Experimental.—4-*Deoxy*-1 : 2-*O*-iso*propylidene*-α-D-erythro*hexulose* (II). 3 : 4-Anhydro-1 : 2-*O*-*iso*propylidene-α-D-*ribo*hexulose [(I); 271 mg.; Ohle and Just, *loc. cit.*] in dry ether (5 c.c.) was added to an excess of lithium aluminium hydride (500 mg.) in dry ether (5 c.c.). After 10 min., ethyl acetate (10 c.c.) was added carefully to decompose the excess of reagent. Water (20 c.c.) was added, and the volatile organic liquids were evaporated. The aqueous solution was then neutralised with dilute sulphuric acid, filtered, and the filtrate extracted with chloroform. The chloroform extract was concentrated to a syrup (*A*; 245 mg.), which crystallised. Recrystallisation from benzene–light petroleum (b. p. 60—80°) gave long white *prisms* (II), m. p. 52°, $[\alpha]_D^{20}$ $-120°$ (*c*, 0·98 in H_2O) (Found : C, 52·9; H, 7·4. $C_9H_{16}O_5$ requires C, 52·9; H, 7·8%). After acid hydrolysis it gave only one spot (R_F 0·28) on the paper chromatogram.

A portion of the syrup (*A*) was hydrolysed with 0·05N-sulphuric acid at 100° for 1 hr., and the solution neutralised ($BaCO_3$), filtered, and concentrated under reduced pressure to a syrup. The syrup was examined on a paper chromatogram [solvent: butanol–ethanol–water (40 : 11 : 19 v/v)] and gave with *p*-anisidine hydrochloride two yellow-brown spots, R_F 0·28 and 0·34 respectively. The second substance (3-deoxy-D-*erythro*hexulose ?) was only present in traces.

A portion of (II) (13·38 mg.) was dissolved in 0·3N-sodium metaperiodate (5 c.c.). After 30 min. saturated sodium hydrogen carbonate solution (10 c.c.) and sodium arsenite solution (2 c.c.) were added, and the solution then titrated with 0·020N-iodine. The uptake of periodate was no greater than that of a blank solution.

4-*Deoxy*-D-erythro*hexulose* (III).—(II) (164 mg.) was hydrolysed in 0·05N-sulphuric acid (5 c.c.) at 100° for 1 hr., and the solution neutralised ($BaCO_3$), filtered, and concentrated under reduced pressure to a syrup {III; 100 mg.; $[\alpha]_D^{20}$ $+5°$ (*c*, 2·00 in EtOH)}.

A solution of the ketose (III; 90 mg.) in water (5 c.c.) containing phenylhydrazine (0·20 c.c.) and acetic acid (0·8 c.c.) was heated for 2 hr. at 50°. The resulting *osazone* was filtered off, washed with water, dried, washed with benzene, and recrystallised from aqueous ethanol. The crystals (65 mg.) had m. p. 167—169°, $[\alpha]_D^{20}$ $-114°$ (10 min.) $\longrightarrow$ $-34°$ (24 hr.; constant value) (*c*, 0·70 in C_5H_5N–EtOH; 3 : 2 v/v) (Found : C, 63·1; H, 6·5; N, 16·0. $C_{18}H_{22}O_3N_4$ requires C, 63·2; H, 6·3; N, 16·4%).

One of us (P. A. J. G.) thanks the Bristol Education Authorities for a grant.

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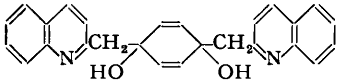
Molecular Compounds of Quinolines and Dihydric Phenols.

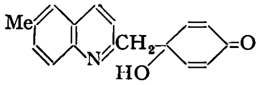
By J. F. CAVALLA.

[Reprint Order No. 5673.]

RECENTLY, Bell (*J.*, 1953, 348) described the reactions of quinaldine and 2 : 6-dimethylquinoline with benzoquinone to give compounds tentatively formulated as (I) and (II), respectively. Repetition of the work has shown, however, that the first step in the reaction is the reduction of benzoquinone to quinol which then forms a molecular compound with the base. This is similar to the formation of quinaldine complexes with monohydric phenols (Aslake and Otto, U.S.P. 2,432,064) and with phloroglucinol (Verkade and Van Leeuwen, *Rec. Trav. chim.*, 1951, **70**, 142). No work has been reported on their formation with dihydric phenols, although Wilson, Anderson, and Donohoe (*Anal. Chem.*, 1951, **23**, 1032) have described complexes with β-resorcylic acid. Besides quinol, molecular compounds were also given with catechol and resorcinol; they are of varying stability, some being decomposed in boiling benzene whilst others were easily sublimed *in vacuo*. Treatment with dry hydrogen chloride in ether resulted in precipitation of the base hydrochloride; yet on neutralising an aqueous solution of quinaldine hydrochloride and quinol the insoluble complex was obtained. In all examples examined, the base and phenol combined in simple though unpredictable proportions.

(I)





(II)

Experimental.—Light petroleum refers to the fraction, b. p. 40—60°.

Quinaldine (2)–*quinol* (1). Quinaldine (14·3 g.) was refluxed gently (bath temp. 165°) in xylene (45 ml.) with quinol (5·5 g.) for 1 hr. On cooling, the solution deposited thick green needles of the *complex* (18 g., 91%), m. p. 153—156° unchanged by repeated crystallisation from benzene or ether–light petroleum (Found : C, 79·0; H, 6·0; N, 6·9. $2C_{10}H_9N,C_6H_6O_2$ requires C, 78·8; H, 6·1; N, 7·1%). This complex was identical with that obtained by Bell (*loc. cit.*).

By use of this general method, and where necessary removal of the xylene *in vacuo* after reaction, the following complexes were obtained :

Quinaldine (2)*–resorcinol* (1), large rhombs, m. p. 129—131°, from benzene (Found : C, 78·5; H, 6·1; N, 7·0%). *Quinaldine* (1)*–catechol* (1), large rhombs, m. p. 103—105°, from benzene–light petroleum (1 : 3) (Found : C, 75·9; H, 6·0; N, 5·5. $C_{10}H_9N,C_6H_6O_2$ requires C, 75·9; H, 6·0; N, 5·5%). 2 : 6-*Dimethylquinoline* (1)*–quinol* (1), cubes, m. p. 142—144°, from ether–light petroleum (1 : 2) (Found : C, 76·3; H, 6·3; N, 4·9. $C_{11}H_{11}N,C_6H_6O_2$ requires C, 76·4; H, 6·4; N, 5·2%). This compound yielded quinol on prolonged boiling with benzene. 2 : 6-*Dimethylquinoline* (1)*–resorcinol* (1), irregular needles, m. p. 127—128°, from benzene–light petroleum (2 : 1) (Found : C, 76·6; H, 6·5; N, 5·0%). 2 : 6-*Dimethylquinoline* (1)*–catechol* (1), long thick needles, m. p. 92—94°, from benzene–light petroleum (2 : 1) (Found : C, 76·2; H, 6·3; N, 5·1%). *Quinoline* (2)*–quinol* (1), large irregular needles, m. p. 101—103°, from ether–light petroleum (1 : 1) (Found : C, 78·4; H, 5·4; N, 7·7. $2C_9H_7N,C_6H_6O_2$ requires C, 78·2; H, 5·5; N, 7·6%). This compound decomposes on prolonged boiling with benzene.

Treatment of the quinaldine–quinol complex with dry hydrogen chloride. A solution of the quinaldine–quinol compound (1·1 g.) in ether (100 ml.) was treated with a stream of dry hydrogen chloride; the precipitated solid (1·01 g., 100%; m. p. 211—214°), on crystallisation from ethanol–ether (1 : 3), gave fine needles of quinaldine hydrochloride, m. p. and mixed m. p. 222—223°. From the ethereal mother liquor quinol (0·25 g.), m. p. and mixed m. p. 168—169°, was obtained.

Precipitation of the quinaldine–quinol compound from acid solution. A solution of the quinaldine–quinol compound (1·0 g.) in dilute hydrochloric acid (20 ml.; 2N) was set aside at room temperature for 5 min. Neutralisation with excess of saturated sodium hydrogen carbonate solution precipitated starting material (0·95 g.), m. p. and mixed m. p. 153—155°. Repetition of this experiment with the quinoline–quinol compound gave a 62% recovery of the starting material.

Reaction of quinaldine hydrochloride with quinol in water. Quinaldine (1·43 g.), suspended in water (70 ml.), was treated with dilute hydrochloric acid (10 ml.; N), and the green solution added to one of quinol (0·55 g.) in water (30 ml.). The mixture was left for 1 min., then treated with excess of saturated sodium hydrogen carbonate solution. The dried precipitate (1·76 g., 89%), had m. p. 153—156° undepressed on admixture with authentic quinaldine–quinol compound.

PARKE, DAVIS & COMPANY, LIMITED, HOUNSLOW, MIDDLESEX. [*Received, August 20th,* 1954.]

The Retention of Cobalt-60 in Vitamin B_{12}.

By A. G. MADDOCK and F. PINTO COELHO.

[Reprint Order No. 5712.]

WHEN an atom in a molecule captures a thermal neutron the recoil, arising from the subsequent radiation of γ photons, generally ruptures the molecule. However, when a solid or a liquid substance is irradiated an appreciable fraction of the radioactive atoms produced by thermal neutron capture are found to be combined in the parent compound. The fraction of the activity found in the parent substance is called the retention. The factors determining the retention have been discussed elsewhere (McCallum and Maddock, *Trans. Faraday Soc.*, 1953, **49**, 1150). Sometimes the fragments formed recombine after losing their surplus kinetic energy by collisions with their surroundings; alternatively the radioactive atom may displace an inactive isotope in another molecule and a kind of activated exchange takes place. Green, Harbottle, and Maddock (*ibid.*, p. 1413) have shown that the retention arising in this way is influenced by the temperature and the dose of ionising radiation to which the substance is exposed. Another possibility (Green and Maddock, *J. Chim. phys.*, 1951, **48**, 207) exists : in some of the capture events the resultant recoil following emission of the photon cascade might be too small to rupture the molecule. Retention arising from this cause, referred to as the nuclear inefficiency, should be independent of the conditions of the irradiation, since it is determined by the decay processes of the compound nucleus produced by neutron capture. *A priori*, it would appear that retention because of subsequent re-formation of, or re-entry into the parent molecule would be less likely when very complex molecules are irradiated.

Existing information on the retention of cobalt-60 after irradiation of vitamin B_{12} is contradictory. Anderson and Delabarre (*J. Amer. Chem. Soc.*, 1951, **73**, 4051) report the unexpectedly high value of 80%. Lester Smith (*Biochem. J.*, 1952, **52**, 384) finds the more likely value of 5%, but two recent publications deny that the cobalt-60 is retained at all (Numerof and Kowald, *J. Amer. Chem. Soc.*, 1953, **75**, 4350; Woodbury and Rosenblum, *ibid.*, p. 4364). It was therefore decided to re-determine the retention and find out if it was dependent on the radiation dose or heat treatment of the sample.

Experimental.—Two samples (each 40 mg.) of crystalline vitamin B_{12} were irradiated *in vacuo* in silica ampoules, the first for 1 week at a pile factor of 0·1, corresponding to a neutron flux of 10^{10} neutrons cm.$^{-2}$ sec.$^{-1}$, and the second for 4 weeks at a pile factor of 1·0, corresponding to a neutron flux of 10^{11} neutrons cm.$^{-2}$ sec.$^{-1}$. In neither case did the temperature of irradiation of the sample exceed 40°, nor was any gross radiation decomposition observed. The total activity due to cobalt-60 was determined by dissolving a weighed sample of the irradiated material in 10 ml. of N-hydrochloric acid in half of a 5-cm. Petri dish and measuring the activity with the dish placed in a standard position under a NaI–Tl crystal scintillation counter. An aluminium screen interposed between the sample and the crystal absorbed the β-radiation from phosphorus-32, as well as that from the cobalt-60. The arrangement had a high sensitivity and, although requiring no processing of the samples, involved no correction for the varying composition of the solutions used.

As previous investigators have emphasized, great care must be taken in these measurements to ensure that the material is purified to constant specific activity before the retention is measured. Counter-current solvent extraction and paper chromatogrpahy have both been used previously for the purification.

Counter-current extraction was tried first. An eight-tube separation was made with equal volumes of benzyl alcohol and the aqueous solution of the vitamin. A survey of the activity in the sixteen solvent fractions thus obtained showed that most of the activity had concentrated in the two tubes at the water-soluble end of the system. The contents of these tubes, presumably the inorganic cobalt salts, were discarded and the extraction repeated for two more stages. The activity of each solution was measured. The concentration of the vitamin B_{12} in each solution was determined by measuring the absorption of the solution at 550 mμ in a 1-cm. cell with a Beckman spectrophotometer (Marsk and Kuzel, *Analyt. Chem.*, 1951, **23**, 1773). The ratio ($\times 10^3$) of the absorption to the activity is recorded for each solution. The water phase was moving towards the higher tube numbers. The vitamin content of tubes 1 and 2 was too low for accurate measurement. A repetition of the separation gave similar results. It was concluded that counter-current solvent extraction with benzyl alcohol is not an efficient method of purification of the irradiated vitamin.

No. of tube	1	2	3	4	5	6	7	8
Benzyl alcohol phase	—	—	7·8	16·3	18·8	26·7	31·9	15·8
Water phase	—	—	7·5	7·8	8·4	11·0	10·1	7·8

Paper-chromatographic separation was then tried. The method is due to Lester Smith (personal communication). To eliminate the bulk of the inorganic cobalt compounds formed by the recoil process the vitamin B_{12} was subjected to preliminary purification by solvent extraction. After equilibration of an aqueous solution containing 15 mg. of the vitamin B_{12} with an equal volume of benzyl alcohol, the alcoholic phase was separated and re-equilibrated with water. Each phase so obtained was then equilibrated with an equal volume of the opposite pure solvent. The freshly added alcoholic phase was then separated and equilibrated with the fresh aqueous phase. Finally the alcoholic phase was combined with the previous alcoholic phase. The partly purified vitamin B_{12} was recovered from the wet benzyl alcohol by the addition of a large volume of ether, whereupon the vitamin was separated in a small aqueous phase.

The mobile solvent for the paper chromatography was prepared by equilibrating 100 ml. of *sec.*-butyl alcohol with 100 ml. of water to which had been added 4 ml. of liquid hydrogen cyanide. The alcohol phase was separated and two drops of concentrated aqueous ammonia were added. The aqueous solution of the partly purified vitamin was concentrated by evaporation at room temperature and applied to a 3″-wide strip of Whatman No. 3 filter paper so as to form a narrow band across the paper near one end. After drying, the paper was suspended over a dish of the alcoholic reagent in a closed cylinder for 2 hr. The end of the paper was then allowed to dip into the alcoholic solution and the chromatogram allowed to develop upwards for 12 hr. The alcoholic cyanide converts the vitamin B_{12} into the dicyanocobalamin. The R_F value observed was 0·24.

After development and drying, the coloured band was cut out and the remainder of the strip cut into pieces 1 cm. wide, normal to the direction of development. The dicyanocobalamin was washed out of the paper and reconverted into vitamin B_{12} by a small quantity of hot water. After the solution had been made up to 10 ml. the activity and absorption at 550 mμ were measured as before. Then the chromatographic purification was repeated.

The same treatment was applied to the second sample irradiated and to a portion of that sample that had been heated *in vacuo* for 60 hr. at 100°.

Irradiation 1.	
Retention (%) after 1st chromatogram	0·74 ± 0·05
,, ,, 2nd ,,	0·70 ± 0·05

Irradiation 2. *Heated sample.*	
Retention (%) after 1st chromatogram	1·9 ± 0·1
,, ,, 2nd ,,	1·8 ± 0·1

Irradiation 2.	
Retention (%) after 1st chromatogram	1·9 ± 0·1
,, ,, 2nd ,,	1·9 ± 0·1

In each case the specific activity of the product was not significantly changed by the second chromatographic purification. The errors given combine the estimated errors in the radioactive and spectrophotometric measurements. After each separation the partitions of the activity and of the vitamin between equal volumes of benzyl alcohol and water were measured. The ratio alcohol to water was constant for both quantities at 0·79 ± 0·01.

Examination of the activity of the strips obtained from the rest of the chromatogram showed that some of the cobalt-60 is present in products of both greater and smaller R_F than the dicyanocobalamin. The presence of these products accounts for the unsatisfactory purification by counter-current solvent extraction and explains the difference in the results reported by Lester Smith and Woodbury and Rosenblum (*locc. cit.*). These results confirm Lester Smith's conclusions.

Discussion.—The retention does not appear to be changed by heat treatment of the irradiated material. On the other hand it cannot be due, to any large extent, to failure of the recoil to rupture the molecule because the retention increases with the dose of pile radiation, rising from 0·7% to 1·9% for an increase of about 40 times in the dose received.

The authors are indebted to Dr. E. Lester Smith of the Glaxo Laboratories, Greenford, for a gift of vitamin B_{12}. One of them (F. P. C.) is indebted to the Instituto de Alta Cultura and the Laboratorio Químico da Universidade de Coimbra, Portugal, for a grant.

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The Reaction of iso*Propanol with Alkali.**

By E. G. E. HAWKINS and W. E. NELSON.

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GUERBET reported (*Compt. rend.*, 1909, **149**, 129) that heating *iso*propanol with sodium *iso*propoxide at 195—200° for 24 hours, or with potassium hydroxide at 200—205° for 16 hours (*ibid.*, 1912, **154**, 222), gave 4-methylpentan-2-ol and 4 : 6-dimethylheptan-2-ol. It has been found, however, that the reaction of alkali with *iso*propanol actually yields, in addition to 4-methylpentan-2-ol, 3 : 3 : 5-trimethyl*cyclo*hexanol (instead of the dimethylheptanol) with hydrocarbons and some higher condensation products.

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* This work is the subject of B.P. 701,093, and 701,098.

The cyclic nature of the C_9-alcohol was found by Wolff–Kishner reduction of the derived ketone to 1 : 1 : 3-trimethyl*cyclo*hexane; and its structure was proved by comparison of the derivatives of the ketone with those from authentic dihydro*iso*phorone, and by pyrolysis of the acetate followed by reduction of the olefins produced to 1 : 1 : 3-trimethyl*cyclo*hexane. Ozonolysis of these olefins afforded a neutral ketonic product which, by analysis of its derivatives, was considered to be a trimethyl*cyclo*pentenealdehyde.

Experimental.—Although the temperature, time of reaction, and amount of alkali were varied, only one typical experiment is described. A solution (5 l.) of potassium hydroxide in *iso*propanol (14% w/w) was heated in an autoclave (10 l.) to 298°, the temperature being above 200° for 4½ hr. The maximum pressure reached was 142 atm., and the residual pressure left on cooling was 25 atm. The product was neutralised with acetic acid, water was added, and the unchanged *iso*propanol together with some of the methylpentanol were removed as azeotropes. The organic layer was separated from the residue and distilled under vacuum; no sharp separation into fractions was obtained but three cuts were taken, the yields, in parentheses, being based on the initial *iso*propanol, *viz.*: (i) (6·4%) 85°/15 mm. (mostly C_6 and largely methylpentanol; assignment on the basis of C_3 fragments); (ii) (10%) 85—100°/15 mm. (mostly C_9); (iii) (6·4%) >100°/15 mm. (C_9—C_{12}). Redistillation of fraction (ii) in a 5-ft. column (Fenske helices) led to a main fraction, b. p. 196—198°/742 mm., m. p. 30·5—31·5° [Found : OH (Smith and Bryant's method, *J. Amer. Chem. Soc.*, 1935, **57**, 61), 11·9. Calc. for $C_{12}H_{18}O$: OH, 12·0%]. It provided an α-naphthylurethane, m. p. 83—84°.

*Oxidation to dihydro*iso*phorone.* The C_9-alcohol (14 g.) was oxidised at 60—70° with chromium trioxide in acetic acid; distillation of the final product gave dihydro*iso*phorone (11·1 g.), b. p. *ca.* 189° (semicarbazone, m. p. and mixed m. p. 204—205°; 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 146—147°).

Reduction of the ketone. Wolff–Kishner reduction of the foregoing ketone (9·5 g.) by the Huang-Minlon modification gave a hydrocarbon (3 g.), b. p. 129°, identified as 1 : 1 : 3-trimethyl*cyclo*hexane by its infra-red spectrum.

Pyrolysis of the acetate. The C_9-alcohol was converted into its acetate by Spassow's method (*Ber.*, 1937, **70**, 1928), and the acetate (40 g.) dropped at 15 c.c./hr. through a silica tube packed with porcelain rings and heated to 500°. The crude product was washed with alkali and distilled, to give a material (12·2 g.), b. p. 128—136°. A portion of this material was hydrogenated over Adams catalyst, yielding a product containing (by infra-red analysis) 60% of 1 : 1 : 3-trimethyl*cyclo*hexane and 14% of xylenes. Evidently pyrolysis had led to cracking and dehydrogenation in addition to dehydration.

The crude olefin (6 g.) from the pyrolysis was ozonised in methylene dichloride; the neutral product (2·3 g.) had b. p. 100—110°/17 mm. and yielded a semicarbazone, m. p. 184—185° (Found: N, 21·6. Calc. for $C_{10}H_{17}ON_3$: N, 21·5%), and a 2 : 4-dinitrophenylhydrazone, m. p. 137—138° (Found: N, 17·2. Calc. for $C_{15}H_{18}O_4N_4$: 17·6%). The dinitrophenylhydrazone had an ultra-violet spectrum consistent with the presence of an αβ-unsaturated carbonyl system as in 1-formyl-3 : 5 : 5- or -3 : 3 : 5-trimethyl*cyclo*pent-1-ene.

Other products. Fraction (ii) contained, in addition to the solid (*trans*-)3 : 3 : 5-trimethyl*cyclo*hexanol, liquid products which included liquid (*cis*-)3 : 3 : 5-trimethyl*cyclo*hexanol, hydrocarbons (partly unsaturated), and ketones. Infra-red spectral analysis on one such fraction showed the presence of *trans*-3 : 3 : 5-trimethyl*cyclo*hexanol (75%), *cis*-3 : 3 : 5-trimethyl*cyclo*hexanol (11—12%), unidentified ketones (1—2%), and hydrocarbons (11—12%): 4 : 6-dimethylheptan-2-ol was not identified and could have been present only in quantities of <5%.

The authors thank Mr. A. R. Philpotts for the spectroscopic determinations, and for the identification of the cyclic hydrocarbon, and the Directors of the Distillers Company Ltd. for permission to publish this Note.

THE DISTILLERS COMPANY LIMITED, RESEARCH AND DEVELOPMENT DEPARTMENT,
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