Oxidation of Glycerol by Periodate in Alkaline Solution.

By L. HARTMAN.

[Reprint Order No. 5379.]

WHEN oxidizing glycerol with periodate in N-sodium hydroxide at 30° Fleury and Fatome (*J. Pharm. Chim.*, 1935, **21**, 247) observed an apparent regeneration of periodate, its consumption amounting to 32% of the theoretical value after ½ hr., 16% after 4 hr., and 90% after 48 hr. Lundblad (*Arkiv Kemi, Min. Geol.*, 1947, **24**, *A*, No. 25) attributed this regeneration to the method used by Fleury and Fatome for estimating the excess of the oxidizing reagent, *viz.*, reduction of periodate to iodate with standard arsenite solution and potassium iodide in a sodium hydrogen carbonate buffer, and titration of the excess of arsenite with iodine solution (Fleury and Lange, *J. Pharm. Chim.*, 1933, **17**, 107). According to Lundblad, di- and tri-sodium paraperiodates which were formed and partly settled out under the condition of the experiment did not react with arsenite, and thus escaped determination. Furthermore, " blanks " varied with time, and over-oxidation was observed after 15 hr. However, if the excess of periodate was determined by the addition of potassium iodide and sulphuric acid the oxidation proceeded normally and was complete in 48 hr.

Lundblad's results, amongst others, imply that the reaction between arsenite and periodate is not quantitative. This could not be confirmed in the present work, and no definite " regeneration " of periodate was observed whether the excess of reagent was estimated by the arsenite or by the potassium iodide–sulphuric acid method. The reproducibility of periodate estimation in " samples " was admittedly poor, but " blanks " were constant.

It is suggested that the conflicting results, summarized in Table 1, are due, at least in part, to the complex mechanism of oxidation by periodates in alkaline solution. This

TABLE 1. *Oxidation of glycerol with sodium periodate at* pH 13, *at* 30°.

	Consumption of $NaIO_4$ (mol./mol. of glycerol) (Theor. 2 mols./mol.)				
				Present work	
	Fleury & Fatome	Lundblad		Results from various batches of periodates	
Time (hr.)	Arsenite	Arsenite	KI–H_2SO_4	Arsenite	KI–H_2SO_4
(5 min.)	—	0·34	—	0—0·21	0
(8 min.)	0·39	—	0·17	0—0·15	0
0·25	1·26	0·30	0·21	0·08—0·15	0·15—0·24
0·5	1·29	0·45	0·24	0·14—0·32	0·22—0·35
1	1·07	0·51	0·29	0·18—0·33	0·30—0·35
2	—	0·27	0·40	0·21—0·49	0·37—0·67
4	0·65	0·61	0·53	0·35—0·41	0·45—0·71
8	—	0·83	—	0·40—0·56	0·49—0·88
15	1·41	2·20	0·88	0·53—1·06	0·92—1·39
22	—	2·04	—	0·57—1·03	0·99—1·40
36	—	—	1·66	1·31—1·58	1·65—1·91
48	1·78	2·79	2·03	1·50—2·02	1·82—2·34

complexity, established, for instance, for cellulose (Davidson, *J. Text. Inst.*, 1941, **32**, T 109; Head, *ibid.*, 1947, **38**, T 389), seems to apply also to the oxidation of glycerol. Already at a comparatively early stage of the reaction the occurrence of secondary reactions was observed. These consist, amongst others, in the oxidation of one of the primary reaction products, formaldehyde, to formic acid. On the basis of the overall consumption of periodate the oxidation of glycerol is apparently complete in about 48 hr. (cf. Table 1) but, if secondary reactions are considered, seems to extend over a period of about 7 days (cf. Table 2). Photosensitivity (Head and Hughes, *J.*, 1952, 2046) might be also responsible for the differing results shown in Table 1. Photochemical interference was avoided in the present work by the use of amber-glass reaction bottles, but possibly previous investigators did not take this precaution.

In view of the difficulty of studying the kinetics of glycerol oxidation in strongly alkaline solutions, the study of this reaction in a sodium hydrogen carbonate buffer appears more convenient. No over-oxidation was noted under these conditions and the agreement between the results obtained by Fleury and Fatome (*loc. cit.*) and in the present work was quite satisfactory (cf. Table 3).

TABLE 2. *Consumption of periodate by glycerol and by secondary reactions.*

	Consumption of $NaIO_4$ (mol./mol. of glycerol)			
	Observed		Calculated	
Time (hr.)	After stopping reaction with KI–H_2SO_4	After oxidizing residual glycerol	For glycerol	For secondary reactions
1	0·30	2·03	0·27	0·03
2	0·37	2·12	0·25	0·12
4	0·71	2·17	0·54	0·17
6	0·78	2·17	0·61	0·17
12	1·02	2·18	0·84	0·18
(days)				
1	1·51	2·44	1·07	0·44
2	2·34	2·69	1·65	0·69
3	2·54	2·94	1·60	0·94
4	2·90	3·09	1·81	1·09
5	3·14	3·27	1·87	1·27
6	3·31	3·45	1·86	1·45
7	3·55	3·59	1·96	1·59

TABLE 3. *Consumption of* $NaIO_4$ *(mol./mol.) on oxidation of glycerol at* pH 8·5 *and* 30°.

Time (min.)	5	10	15	30	45	60	90	150	180
Fleury & Fatome [a]	1·04	1·36	1·62	1·84	1·88	1·92	1·95	1·98	2·0
Present work [b] ...	0·83	1·27	1·68	1·86 *	1·91	1·94 *	1·98	1·99	1·99 *†

[a] Arsenite. [b] KI–H_2SO_4.
* No consumption in secondary reactions. † After 24 hr., 1·99.

Experimental.—The experiments were carried out at 30°, the quantity of reactants being as specified by Fleury and Fatome, *i.e.*, 0·01M-glycerol 10 ml., 2N-sodium hydroxide 15 ml., and 0·1M-periodic acid 5 ml. The reaction was stopped with sodium arsenite and potassium iodide or with potassium iodide and sulphuric acid severally.

The consumption of periodate by glycerol and by secondary reactions was assessed as follows: Sets of 2 "samples" and 1 "blank" were held at 30° for various periods. At appropriate intervals one sample of each set was acidified with N-sulphuric acid and left for 15 min. in order to oxidize the residual glycerol. Potassium iodide solution (2 ml. of 30%) and an excess of sulphuric acid were then added and the mixture was titrated with sodium thiosulphate. In the second sample the reaction was stopped with potassium iodide and sulphuric acid, titration being with sodium thiosulphate. The amount of periodate consumed by glycerol and by secondary reactions was then calculated (cf. Table 2) by assuming that the reduction of periodate which took place after the acidification of the first sample was caused solely by the residual glycerol. Some indication of the nature of the secondary reactions was obtained by determining the concentration of formaldehyde by dimedone (Reeves, *J. Amer. Chem. Soc.*, 1941, **63**, 1476) in samples kept at 30° for 24 hr. or more. This concentration was always lower than expected from the amount of glycerol consumed, but was not reproducible. Other changes such as oxidation of formic acid to carbon dioxide and water probably occurred simultaneously.

Results shown in Table 3 were obtained by proceeding as in the main set of experiments except that 15 ml. of M-sodium hydrogen carbonate solution were used instead of sodium hydroxide.

The quantitative character of the reaction between periodate and arsenate was confirmed by testing a number of commercial samples of periodic acid and its sodium salts under various conditions (with and without previous addition of sodium hydroxide, without delay and after several days' storage at 30°). Most samples contained appreciable amounts of iodate, but in each case there was close agreement between the estimation of the actual periodate content by the arsenite and by the potassium iodide and sulphuric acid methods.

FATS RESEARCH LABORATORY, DEPARTMENT OF SCIENTIFIC AND INDUSTRIAL RESEARCH,
WELLINGTON, NEW ZEALAND. [*Received, May 11th*, 1954.]

Reactions of Metallic Salts of Acids. Part V. Synthesis of Fluoro-dienes from Fluoro-dicarboxylic Acids.*

By R. N. HASZELDINE.

[Reprint Order No. 5382.]

MANY fluoro-dicarboxylic acids of general formula $[CF_2]_n(CO_2H)_2$ (see Haszeldine and Sharpe, " Fluorine and its Compounds," Methuen, 1951) are available for use in synthetic fluorine chemistry. The present communication describes methods for the conversion of these into fluoroalkadienes, and in particular describes the conversion of the compound where $n = 4$ into hexafluorobutadiene.

Pyrolysis of anhydrous disodium octafluoroadipate at 100—350° yields two major volatile fractions and a residue of sodium fluoride and carbon. The more volatile fraction contains carbon dioxide, carbonyl fluoride, hexafluorobutadiene, and, probably, acyl fluorides formed by breakdown of the carbon chain. The formation of hexafluorobutadiene can be visualised as follows :

$$NaO_2C\cdot[CF_2]_4\cdot CO_2Na \longrightarrow {}^-O_2C\cdot CF_2\cdot CF_2\cdot CF_2\cdot CF_2\cdot CO_2^- \xrightarrow{-CO_2} {}^-CF_2\cdot CF_2\cdot CF_2\cdot CF_2^-$$

$$^-CF_2\text{–}CF\text{–}CF\text{–}CF_2^- \longrightarrow CF_2{:}CF\cdot CF{:}CF_2 + 2F^-$$

i.e., formation of a fluorocarbanion followed by elimination of fluoride. A similar mechanism has been proposed for the formation of perfluoroalk-1-enes by the pyrolysis of sodium salts of perfluoro-monocarboxylic acids (Haszeldine, *J.*, 1952, 4259, 3423; *Nature*, 1951, **168**, 1028, where other evidence for fluorocarbanion instability is summarised; see also Hals, Reid, and Smith, *J. Amer. Chem. Soc.*, 1951, **73**, 4054). The yields of conjugated fluoroalkadienes prepared in this way (*ca.* 30%) are less than those of the perfluoroalk-1-enes (*ca.* 80%). Alternative routes to hexafluorobutadiene have been described in another series (*J.*, 1952, 4423).

The production of hexafluorobutadiene does not necessarily involve the simultaneous formation of both double bonds in the molecule, since fluoride elimination could occur first from a carbanion at one end of the chain and then from a carbanion at the other end of the chain :

$$^-O_2C\cdot[CF_2]_4\cdot CO_2^- \xrightarrow{-CO_2} {}^-O_2C\cdot[CF_2]_3\cdot CF_2^- \longrightarrow {}^-O_2C\cdot[CF_2]_2\cdot CF{:}CF_2 \xrightarrow{-CO_2}$$

$$^-CF_2\cdot CF_2\cdot CF{:}CF_2 \longrightarrow C_4F_6$$

Some support for this is given by the isolation of 2 : 2 : 3 : 3 : 4 : 5 : 5-heptafluoropent-4-en-1-oic acid (I) by hydrolysis of the less-volatile products from the pyrolysis of sodium octafluoroadipate; that these products contain an acyl fluoride with a $\cdot CF{:}CF_2$ group

$$[CF_2]_4(CO_2Na)_2 \longrightarrow CF_2{:}CF\cdot CF_2\cdot CF_2\cdot COF \longrightarrow \underset{\text{(I)}}{CF_2{:}CF\cdot CF_2\cdot CF_2\cdot CO_2H}$$

is shown by spectroscopic detection of the C:O and C:C vibrations. The formation of acyl fluorides is not unexpected, since Swarts (*Bull. Acad. roy. Belg.*, 1922, **8**, 343) showed that trifluoroacetyl fluoride is a product of the pyrolysis of sodium trifluoroacetate.

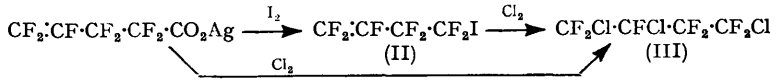
Unsaturated fluoro-carboxylic acids can also by converted into fluoro-dienes in good yield by the sodium-salt reaction, *e.g.*;

$$CF_2{:}CF\cdot CF_2\cdot CF_2\cdot CO_2Na \longrightarrow CF_2{:}CF\cdot CF{:}CF_2$$

This reaction, and the fact that the acid (I) or the crude acyl fluoride yields perfluorosuccinic acid when oxidised, establish the constitution of the heptafluoropentenoic acid. Comments on the m. p. of perfluorosuccinic acid are made on p. 4027.

* Parts I, III, and IV, *J.*, 1951, 584; 1952, 4259; 1953, 4172.

The unsaturated acid (I) readily yields a silver salt which, on reaction with iodine (cf. Parts I and III *) gives heptafluoro-4-iodobut-1-ene (II), and on reaction with an excess of chlorine yields 1 : 2 : 4-trichloroheptafluorobutane (III); chlorination of the iodo-compound also yields (III).



Perfluoroadipic acid can thus be used as a convenient source of substituted butanes, butenes, and butadienes, and the extension of the above reactions to other polycarboxylic fluoro-acids will be described later.

Experimental

Pyrolysis of sodium octafluoroadipate. Octafluoroadipic acid, prepared by oxidation of perfluoro*cyclo*hexene with permanganate (Tatlow and Worthington, *J.*, 1952, 1251; Haszeldine, *Nature*, 1951, **168**, 1028), was converted into the disodium salt by neutralisation with aqueous sodium hydroxide. The salt, isolated by evaporation of the aqueous solution to dryness *in vacuo*, was ground in a mortar and thoroughly dried at 120° *in vacuo*. Sodium octafluoroadipate (5·0 g., 0·015 mole) was spread in a thin layer in a horizontal open cylinder of platinum foil which was then inserted into a horizontal nickel furnace tube 1″ in diameter and sealed at one end. The tube was evacuated to 10^{-2} mm. and then heated stepwise (2·5 hr.) to 450°. Two glass traps connected in series between the furnace tube and the pump were examined periodically; appreciable reaction occurred below 300°; there was little sign of further reaction at temperatures above 370°. The solid residue from the pyrolysis contained sodium fluoride, carbon, and carbonaceous material.

The combined volatile products were transferred to a vacuum system where they were arbitrarily separated into fractions boiling above or below 10°. Infra-red spectroscopic examination of the more volatile fraction showed it to contain hexafluorobuta-1 : 3-diene, contaminated by carbon dioxide, carbonyl fluoride, and by material (probably acyl fluorides) which showed carbonyl absorption at 5·3 μ. The fraction was washed with 2N-sodium hydroxide and refractionated *in vacuo* to give hexafluorobutadiene (0·73 g., 30%), b. p. 5·7° (Found: C, 29·7%; *M*, 162. Calc. for C_4F_6: C, 29·6%; *M*, 162). The b. p. and infra-red spectrum of the purified material were identical with those reported by the author (*J.*, 1952, 4423). In other experiments the yields of hexafluorobutadiene were 32, 37, and 25%. The diene did not contain perfluoro*cyclo*butene.

Infra-red spectroscopic examination of the less volatile fraction (*M*, 240; cf. CF_2:$CF{\cdot}CF_2{\cdot}CF_2{\cdot}COF$, *M*, 228) showed it to contain the $-CF_2{\cdot}COF$ group (C:O absorption at 5·31 μ; cf. $CF_3{\cdot}COF$ 5·25 μ; $C_2F_5{\cdot}COF$ 5·29 μ, $C_3F_7{\cdot}COF$ 5·3 μ) and the $-CF{:}CF_2$ group (C:C absorption at 5·6 μ; cf. $CF_3{\cdot}CF{:}CF_2$ 5·56 μ, $C_2F_5{\cdot}CF{:}CF_2$ 5·56 μ; *J.*, 1952, 4423, 4259). The fraction was shaken with water (5 ml.) in a sealed tube (20 min.), to leave only a small unidentified fraction (0·05 g.), b. p. 60° (isoteniscope) (Found: *M*, 275). The main bulk of the fraction had dissolved, with liberation of fluoride ion; the aqueous solution was extracted with ether (10 × 3 ml.). The ethereal solution was dried (Na_2SO_4), and after removal of the ether the residual liquid was distilled from a small amount of phosphoric anhydride through a short column to give 2 : 2 : 3 : 3 : 4 : 5 : 5-*heptafluoropent-4-en-1-oic acid* (0·69 g., 21% based on sodium octafluoroadipate), b. p. 75—76°/59 mm. (Found: C, 26·4; H, 0·5%; equiv., 226. $C_5HO_2F_7$ requires C, 26·6; H, 0·4%; equiv., 226), and unidentified material of higher b. p. The infra-red spectrum of the acid showed a band at 5·62 μ revealing the presence of the carboxyl group; the C:C stretching absorption is combined with this band.

Oxidation of the pentenoic acid (0·2 g.) by potassium permanganate, as for the oxidation of compounds which contain the $\cdot CF{:}CF_2$ group (*J.*, 1952, 4259), gave perfluorosuccinic acid (53%), m. p. 116°, identified by comparison of its infra-red spectrum with that of an authentic specimen. The same acid was obtained (58%) (Found: C, 25·0; H, 1·0%; equiv., 95. Calc. for $C_4H_2O_4F_4$: C, 25·3; H, 1·1%; equiv., 95) by oxidation of a specimen (0·4 g.) of the original crude acyl fluoride of the heptafluoropentenoic acid. Perfluorosuccinic acid shows carbonyl absorption in the infra-red at 5·65 μ (cf. $CF_3{\cdot}CO_2H$ 5·60, $C_2F_5{\cdot}CO_2H$ 5·64, $C_3F_7{\cdot}CO_2H$ 5·61, $C_9F_{19}{\cdot}CO_2H$ 5·68 μ). Henne and Zemmerschied (*J. Amer. Chem. Soc.*, 1947, **69**, 281) reported m. p. 86·4—87·4° for an acid which had apparently the correct equivalent for perfluorosuccinic acid, but Padbury and Kropa (U.S.P. 2,502,478) reported m. p. 116—119°.

Buxton, Ingram, Smith, Stacey, and Tatlow (*J.*, 1952, 3830) confirmed Padbury and Kropa's results, but stated that intensive drying was essential to obtain a m. p. of 116°. In our experience intensive drying is not essential if the acid is distilled *in vacuo* from a small amount of phosphoric anhydride (*ca.* 5% of that theoretically required to form the cyclic anhydride); the m. p. drops to that of the hydrate (86°) only after exposure to moist air for several hours.

Preparation of hexafluorobutadiene from heptafluoropentenoic acid. Heptafluoropentenoic acid (1·02 g.) was neutralised with 5N-sodium hydroxide, and the anhydrous sodium salt was obtained by evaporation of the aqueous solution *in vacuo*. The salt was powdered, re-dried at 120°/10^{-2} mm., placed in the platinum cylinder as described above, and pyrolysed by raising the temperature from 160° to 450° (4·5 hr.) at 10^{-2} mm. The residual sodium fluoride contained only a small amount of carbon. The volatile products were shaken in a sealed tube with 2N-sodium hydroxide, then fractionated *in vacuo* to give hexafluorobuta-1 : 3-diene (61%), identified by means of its infra-red spectrum.

The hexafluorobutadiene prepared by the methods described above was mixed with a slight excess of chlorine and exposed to ultra-violet light (1 hr.) to give, by absorption of two molecular equivalents of chlorine, 1 : 2 : 3 : 4-tetrachlorohexafluorobutane (91%), b. p. 131—133°, spectroscopically identical with the compound previously described (*J.*, 1952, 4423).

Heptafluoro-4-iodobut-1-ene. Heptafluoropentenoic acid (1·2 g.), prepared as described above, was treated with a slight excess of freshly prepared silver carbonate. Evaporation of the aqueous solution to dryness *in vacuo* yielded *silver* 2 : 2 : 3 : 3 : 4 : 5 : 5-*heptafluoropent-4-en-1-oate* (97%) (Found: Ag, 32·2. $C_5O_2F_7Ag$ requires Ag, 32·4%) as a white crystalline solid. The silver salt (1·5 g.) was mixed with a 300% excess of powdered dry iodine in a silica flask connected *via* pressure tubing to two traps cooled by liquid oxygen. The pressure was maintained at 300 mm., and the solid was heated by a small flame. The gases evolved by the smooth reaction were pumped into the traps, and the combined volatile material was washed with 2N-sodium hydroxide in a sealed tube. The residual organic material was distilled *in vacuo* to give *heptafluoro-4-iodobut-1-ene* (72%), b. p. (isoteniscope) 20°/65 mm., *ca.* 70°/760 mm. (Found: C, 15·4%; *M*, 309. C_4IF_7 requires C, 15·6%; *M*, 308). At higher temperatures there was some reaction with the mercury of the isoteniscope, and the b. p. at 760 mm. is subject to error. The compound shows a band at 5·6 μ in the infra-red.

Heptafluoro-4-iodobut-1-ene (0·7 g.) and a 10% excess of chlorine in a sealed silica tube exposed to ultra-violet light (2 days) gave iodine trichloride and 1 : 2 : 4-*trichloroheptafluorobutane* (83%), b. p. 96—97° (micro) (Found: C, 16·8%; *M*, 285. $C_4Cl_3F_7$ requires C, 16·7%; *M*, 287·5). The same compound was obtained (66%) by reaction of an excess of dry chlorine with silver heptafluoropentenoate (1·1 g.) in a sealed tube at 100° for 4 hr.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, May 13th*, 1954.]

The Esterifying Acids of Lycoctonine Alkaloids.

By R. C. COOKSON, J. E. PAGE, and M. E. TREVETT.

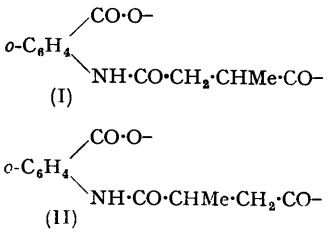
[Reprint Order No. 5419.]

BY hydrolysis with acid to lycoctonine and acetic and anthranilic acid, and with alkali to lycoctonine and *N*-acetylanthranilic acid (Goodson, *J.*, 1944, 108) ajacine was shown to be a *N*-acetylanthranilic ester of the trihydroxy-alkamine, lycoctonine. Methyl-lycaconitine, similarly, yields lycoctonine and (−)-methylsuccinic and anthranilic acid on acid hydrolysis, and lycoctonine and (−)-methylsuccinylanthranilic acid on alkaline hydrolysis (Goodson, *J.*, 1943, 139).

Methyl-lycaconitine seems to have been tacitly assumed to be a diester-amide (I or II), but we have now obtained decisive evidence in favour of the alternative monoester-imide structure (III).

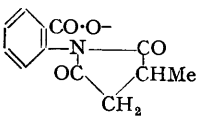
Ajacine and methyl-lycaconitine both react with periodic acid at about the same rate as lycoctonine (although reaction does not cease after consumption of 1 mol.), so that the α-glycol group of the alkamine (Edwards and Marion, *Canad. J. Chem.*, 1954, **32**, 195) must be free in both ester alkaloids, in which therefore only the primary alcohol group (*idem, ibid.*, 1952, **30**, 627) can be esterified. The presence of the monoester-imide grouping (III) in methyl-lycaconitine is confirmed by spectroscopic evidence. The ultra-

violet absorption spectrum of the alkaloid (max. at 230 and 273 mμ; ε 15,300 and 3500 respectively) differs markedly from that of ajacine (max. at 223, 252, 310 mμ; ε 28,400, 16,600, and 5400 respectively), which is identical with that of methyl *N*-acetylanthranilate. The shift of absorption to shorter wave-lengths than that shown by the two known



(I)

(II)



(III)

acetylanthranilic esters is in line with structure (III). Conclusive evidence was provided by the infra-red spectra (see Table). That of methyl-lycaconitine lacks the low-frequency

Infra-red absorption frequencies (*cm.*$^{-1}$, *in* CS_2).

Compound	NH	Amide	Imide	Ester
Methyl *N*-acetylanthranilate	3310 (m)	1692 (s)	—	1712 (s), 1262 (s)
Ajacine dihydrate	3320 (m)	1690 (s)	—	1710 (s), 1256 (s)
N-Phenylsuccinimide	—	—	1725 (s), 1786 (w)	—
Methyl-lycaconitine	—	—	1722 (s), 1787 (w)	1722 (s), 1256 (s)
,, ...	—	—	1720 (s), 1785 (w) *	1720 (s), 1265 (s) *

* In Nujol. s = Strong, m = medium, w = weak; — denotes absence of an absorption peak.

amide-carbonyl stretching band (*ca.* 1690 cm.$^{-1}$) shown by *N*-acylanthranilates; instead, a very strong absorption peak, due to the superimposed C=O stretching frequencies of the amide and the ester group, appears at *ca.* 1720 cm.$^{-1}$. The characteristic, though relatively weak, high-frequency imide band (*ca.* 1785 cm.$^{-1}$) also occurs in the spectrum of methyl-lycaconitine. The absence of CO·NH in methyl-lycaconitine is revealed by the transparency of the alkaloid near 3320 cm.$^{-1}$, where the N–H stretching frequency of ajacine occurs, and (in Nujol) near 1560 cm.$^{-1}$, where the C–N stretching peak of secondary amides is found (Letaw and Gropp, *J. Chem. Phys.*, 1953, **21**, 1621, and earlier papers listed there). Lycoctonine hydrate does not, of course, absorb in the C=O stretching region.

Experimental.—Measurements of ultra-violet absorption were made in absolute ethanol with a Unicam SP 500 Spectrophotometer and of infra-red absorption with a Model 21 Perkin-Elmer double-beam spectrophotometer.

Lycoctonine hydrate and ajacine dihydrate were pure recrystallised samples. Methyl-lycaconitine was isolated from its crystalline hydriodide by treatment with sodium hydrogen carbonate solution and extraction with chloroform. Evaporation of the washed chloroform extract at reduced pressure left the free base as a colourless froth, which was dried at 50° *in vacuo*.

Periodic acid titrations. The alkaloid (*ca.* 25 mg.) was dissolved in freshly prepared periodic acid solution (5 ml.: *ca.* 0·54M), and the mixture, made up to 10 ml. with water, was stored in the dark. At daily intervals, 1-ml. portions were pipetted into water (5 ml.) and 0·10N-sodium arsenite (1 ml.) containing potassium iodide (*ca.* 50 mg.). After 15 min. the mixture was titrated with 0·020N-iodine (starch indicator). The spontaneous deterioration of a blank solution of periodic acid was followed at the same time (cf. Jackson, *Org. Reactions*, 1944, **2**, 341). Up-takes of periodic acid (mols.) at daily intervals were:

Lycoctonine	0·82	0·96	1·11	1·33	1·40	1·74
Ajacine	0·42	0·57	0·81	1·00	1·23	1·44
Methyl-lycaconitine	0·44	0·49	0·65	0·70	0·98	1·12

We are indebted to the Central Research Fund of London University for a grant for purchase of *Delphinium* seed.

Birkbeck College, London, W.C.1.
Glaxo Laboratories Ltd., Greenford, Middlesex.

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Naphthyridines. Part II. The Attempted Cyclisation of Schiff's Bases.*

By E. P. Hart.

[Reprint Order No. 5441.]

During attempts to prepare unknown naphthyridine bases, attention was directed to the possibility of cyclisation of the Schiff's bases prepared from pyridine-aldehydes and aminoacetal (2 : 2-diethoxyethylamine), following the general procedure of the Pomeranz–Fritsch reaction. This reaction has proved of considerable value in *iso*quinoline syntheses, the cyclisation being carried out with sulphuric acid, alone or in the presence of phosphoric oxide or phosphoryl chloride.

In the present work aminoacetal was heated with the pyridine-aldehydes and with quinoline-2-aldehyde, giving in high yield Schiff's bases of type (I; R = pyridyl). Attempted cyclisation of these anils in sulphuric acid, alone or in the presence of phosphoryl chloride and phosphoric oxide resulted only in the cleavage of the azomethine system. The action of boron trifluoride upon these Schiff's bases resulted in formation of dark-brown resins from which no substance was isolated. Andersag (" Medicine in its chemical aspects," I.G. Farbenind., Leverkusen, 1934, Vol. II) states that nitrobenzylideneamino-acetal (I; R = $O_2N{\cdot}C_6H_4$) does not cyclise in sulphuric acid, but gives no experimental details. We have consequently prepared the *m*- and the *p*-nitrobenzylideneamino-acetal and confirmed the statement that cyclisation does not occur. Hey and Williams (*J.*, 1951, 1528) report an abortive attempted cyclisation of the *o*-3-pyridylbenzylideneamino-acetal (I; R = *o*-3-$C_5H_4N{\cdot}C_6H_4$) by using sulphuric acid, phosphoryl chloride, or anhydrous hydrogen fluoride.

Application of the Pomeranz–Fritsch reaction to the preparation of thionaphtheno-pyridines was reported by Herz and Tsai (*J. Amer. Chem. Soc.*, 1953, **75**, 5122), who found that while the use of sulphuric acid was not successful, a mixture of polyphosphoric acid and phosphoryl chloride gave the required product. We have found in the present work that while benzylidene-aminoacetal affords *iso*quinoline with this mixture, the Schiff's bases from pyridine-aldehydes and from quinoline-2-aldehyde did not cyclise to form naphthyridines, and the nitrobenzylideneaminoacetals did not cyclise to nitro*iso*quinolines.

$R{\cdot}CH{:}N{\cdot}CH_2{\cdot}CH(OEt)_2$
(I)

Experimental.—Schiff's bases. The aldehyde (2 g.) and aminoacetal (2 ml.) were heated (water-bath) for 2 hr., during which time water separated. The residual mixture was dissolved in ethanol, dried (Na_2SO_4), and distilled *in vacuo*. The Schiff's bases obtained by this method are given in the following Table and these, with the exception of the one prepared from *p*-nitro-benzaldehyde, were pale straw-coloured oils when freshly prepared, rapidly darkening on exposure to air.

				Found (%)			Required (%)		
R in (I)	Yield (%)	B. p./mm.	Formula	C	H	N	C	H	N
2-Pyridyl	77	160°/11	$C_{12}H_{18}O_2N_2$	64·4	8·35	12·3	64·8	8·2	12·5
3-Pyridyl	75	170°/11	,,	65·0	8·25	12·3	64·8	8·2	12·5
4-Pyridyl	75	170°/14	,,	64·3	8·25	12·3	64·8	8·2	12·5
2-Quinolyl	72	235°/13	$C_{16}H_{20}O_2N_2$	69·9	7·6	10·4	70·4	7·4	10·3
m-Nitrophenyl	77	208°/14	$C_{13}H_{18}O_4N_2$	58·5	6·9	10·2	58·6	6·8	10·5
p-Nitrophenyl	60	M. p. 51—52 [a]	,,	58·5	6·8	10·2	58·6	6·8	10·5

[a] Twice recrystallised from aqueous ethanol.

iso*Quinoline.* Phosphoric oxide (6 g.) was added slowly to syrupy phosphoric acid (6 g.) followed by phosphoryl chloride (1 ml.). Benzylideneaminoacetal (2 g.) was then added and the temperature maintained at 140° for 2 hr. The viscous residue was poured into a small volume of water, and extracted with ether. The aqueous portion of this extract was basified with potassium hydroxide, and extracted with ether. Distillation of the dried extract afforded *iso*quinoline (0·6 g.), b. p. 240—241°.

* Part I, *J.*, 1954, 1879.

Attempted cyclisations. With the mixture of polyphosphoric acid and phosphoryl chloride prepared as in the previous experiment, and at temperatures varying between 140° and 160°, the Schiff's bases prepared in this work yielded only the corresponding aldehydes.

I am indebted to Dr. E. Tittensor for his interest and advice, and to Dr. F. L. Rose, O.B.E., Imperial Chemical Industries Limited, Dyestuffs Division, for assistance with the preparation of aminoacetal. This work was in part aided by a grant from the Research Fund of the Chemical Society.

THE TECHNICAL COLLEGE, NOTTINGHAM. [*Received, June 4th,* 1954.]

The Preparation and Structure of a Synthetic Polyglucose.

By C. R. RICKETTS.

[Reprint Order No. 5478.]

IT has long been known that the acidic hydrolysis of polysaccharides to simpler sugars is to some extent a reversible reaction and there are numerous references to the structure of the saccharides thus formed (*e.g.*, Thompson, Anno, Wolfrom, and Inatome, *J. Amer. Chem. Soc.*, 1954, **76**, 1309). Pacsu and Mora (*J. Amer. Chem. Soc.*, 1950, **72**, 1045) briefly report the isolation of saccharides containing up to 42 anhydroglucose units, but give no details. The essence of their process is to evaporate a solution of glucose in hydrochloric acid; thereby the molecules of glucose may be pictured as being brought nearer together in the presence of acid and bonds are formed between them. An alternative means of achieving the same conditions would appear to be to allow anhydrous crystalline glucose to deliquesce in an atmosphere containing water vapour and gaseous hydrogen chloride. Thereby the molecules of glucose, which in the crystalline state are as close together as they can be, slowly move apart as water penetrates the lattice and must pass through the optimum distance for bond formation under the catalytic influence of hydrochloric acid. These conditions are realised by placing a dish containing a thin layer of crystalline anhydrous glucose in a desiccator containing concentrated hydrochloric acid to which a few drops of concentrated sulphuric acid had been added to ensure copious evolution of gas. In 3—4 days there then resulted about 17% of polymeric non-dialysable material.

Experimental.—Anhydrous glucose (50 g.) in a thin layer covering a dish 16 cm. in diameter was placed in a desiccator containing concentrated hydrochloric acid to which a few drops of concentrated sulphuric acid had been added. The crystals slowly deliquesced to a pale brown syrup. After 7 days at room temperature the syrup was dissolved in crushed ice and N-sodium hydroxide, neutralised with hydrochloric acid, and dialysed. After treatment with charcoal and filtration the colourless solution was concentrated to 25 ml. Insoluble material (fraction 1) was separated on the centrifuge, and ethanol was added to the supernatant solution to precipitate the fractions shown in the Table. All fractions were obtained as powder by trituration with ethanol, washing with ether, and drying *in vacuo* over phosphoric oxide.

Serial	Ethanol (%. v/v)	Wt. (g.)	Reducing val.	$[\alpha]_D^{20}$ (*c* 0·5 in H_2O)
1	Nil	0·36	—	Insol.
2	44·4	3·21	20·0	+106°
3	45·6	1·69	19·0	+106
4	49·4	1·81	18·8	+105
5	61·1	1·25	15·3	+104
6	78·0	0·32	10·6	+ 95
7	(from supernatant soln.)	0·16	6·0	+ 74

The reciprocal of the " reducing value " is the reducing power relative to glucose (Schaffer and Hartman, *J. Biol. Chem.*, 1921, **45**, 377) : if it is assumed that there is one reducing group per molecule these figures indicate the *number* average of the glucose units in each molecule. Paper chromatography (Jeans, Wise, and Dimler, *Analyt. Chem.*, 1951, **23**, 415) showed that only fractions 5, 6, and 7 contained saccharides mobile in the solvent system butanol–pyridine–water (6 : 4 : 3 by vol.).

All the subsequent results were obtained on fraction 2. Paper chromatography of a complete hydrolysate (2N-sulphuric acid, 100°, 4 hr., sealed tube) showed the presence of glucose only. A hydrolysate from N-sulphuric acid (100°, 5 hr.) showed 95% of the theoretical reducing power. In a partial hydrolysate (N-sulphuric acid, 0·5 hr., 100°, sealed tube) a component having the R_F value of *iso*maltose was identified by chromatography of the *N*-benzylglycosylamines (Bayly and Bourne, *Nature*, 1953, **171**, 385) and by electrophoresis in borate buffer (Foster, *Chem. and Ind.*, 1952, 1050; *J. Appl. Chem.*, 1953, **3**, 19). In each case *iso*maltose prepared from dextran was used as a reference preparation.

The infra-red absorption spectrum revealed reproducible peaks at 919, 844, 834, and 767 cm.$^{-1}$, from which it is concluded (Barker, Bourne, Stacey, and Whiffen, *J.*, 1954, 171) that the polyglucose possesses predominantly 1 : 6-α-linkages since the degree of polymerisation is greater than 5. There is no indication of 1 : 3-links or of 3 : 6-anhydro-rings. The possibility of 1 : 4-α- and a small amount of β-glucosidic linkages occurring in the polymer is not excluded.

Oxidation by 0·175M-sodium metaperiodate at room temperature evolved 0·70 mole of formic acid per anhydroglucose unit. After correction for oxidation of the terminal reducing group, 0·55 mole of formic acid is evolved per anhydroglucose unit. Thus 55—70% of the linkages between glucose units are of the 1 : 6-type. Since the evolution of formic acid falls short of the theoretical 1·0 mole per glucose unit, linkages other than the 1 : 6-link must be present.

Fraction 2 had an intrinsic viscosity in water at 37° of 0·036, the optical rotation being +106° (see Table). A partially hydrolysed dextran of similar intrinsic viscosity, 0·033, had a considerably higher optical rotation, +166°. This may be taken as a further indication that linkages other than the 1 : 6-α-link are present in this polyglucose.

The investigation is being pursued with respect to conditions and mechanism of the reaction, the condensation of other sugars, and the structure of the products.

Thanks are offered to Dr. S. A. Barker of Chemistry Department, University of Birmingham, for the infra-red and electrophoresis measurements, and to Mr. C. E. Rowe of this Unit for the periodate oxidation analysis.

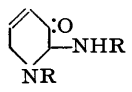
MEDICAL RESEARCH COUNCIL INDUSTRIAL INJURIES & BURNS RESEARCH UNIT,
BIRMINGHAM. [*Received, June 19th*, 1954.]

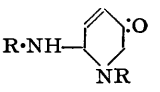
Derivatives of the Coloured Compounds formed by Condensation of Furfuraldehyde with Aromatic Amines. The Compounds of Furfuraldehyde with Two Molecules of Aromatic Amines.

By J. C. McGOWAN.

[Reprint Order No. 5486.]

McGOWAN (*J.*, 1949, 777) treated the Stenhouse dye, prepared by the condensation of aniline, aniline hydrochloride, and furfuraldehyde, with aqueous sodium hydroxide and obtained a crystalline compound $C_{17}H_{16}ON_2$ which he suggested was 2(or 6)-anilino-1 : 2 : 3 : 6-tetrahydro-3-oxo-1-phenylpyridine (I or II; R = Ph). A third possibility, (III; R = Ph), has since been suggested by Dr. J. D. Kendall (personal communication) and by Dunlop and Peters (" The Furans," Reinhold Publ. Corp., New York, 1953, p. 671). A similar compound $C_{19}H_{20}ON_2$ was obtained with the Stenhouse dye from furfuraldehyde, *p*-toluidine, and *p*-toluidine hydrochloride. Rombaut and Smets (*Bull. Soc. chim. Belg.*, 1949, **58**, 421) found that 1 mol. of furfuraldehyde combined directly with 2 mols. of a number of aromatic primary amines with the elimination of 1 mol. of water. They


(I)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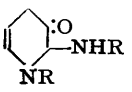
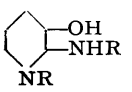

(III)


(IV)

concluded, mainly on the evidence of the ultra-violet and visible-light absorption spectra, that their compounds had formula (I) or (II) but as they used neither aniline nor *p*-toluidine

direct comparison with McGowan's compound (*loc. cit.*) was not made. It has now been found that aniline and *p*-toluidine with furfuraldehyde yield compounds identical with those prepared by McGowan (*loc. cit.*) from the corresponding Stenhouse dyes and that the new method of preparation is the more convenient.

Infra-red absorption bands in the region 1590—1800 cm.$^{-1}$ are shown in the Table for relevant compounds. Jones, Williams, Whalen, and Dobriner (*J. Amer. Chem. Soc.*, 1948, **70**, 2024) studied the infra-red absorption spectra of a large number of *cyclo*hexanones and *cyclo*hexenones. In the former there was a maximum at ~1710 cm.$^{-1}$. In the latter, which had a double bond in the αβ-position to the keto-group, this maximum was shifted by about 40 cm.$^{-1}$ to lower frequencies. The carbonyl band at 1710 cm.$^{-1}$ in the aniline and *p*-toluidine compounds, therefore, suggests that the carbonyl group and double bond are not conjugated. In the furfurylidene and benzylidene derivatives, conjugation with the ethylenic double bond has caused the carbonyl group to absorb at a frequency about 20 cm.$^{-1}$ lower. Similarly, *cyclo*hexanone gave one strong band between 1600 and 1800 cm.$^{-1}$: in pyridine, at 1724 and in chloroform at 1720 cm.$^{-1}$; benzylidene*cyclo*hexanone gave two strong bands in the same region: in pyridine at 1694 and 1611, and in chloroform at 1692 and 1611 cm.$^{-1}$. These displacements are not quite as great as those found by Jones *et al.* (*loc. cit.*) but here the conjugated ethylenic bonds are exocyclic. The bands at 1636—1642 cm.$^{-1}$ suggest the presence of an ethylenic double bond. Attempts to make dibenzylidene or difurfurylidene derivatives have failed and therefore the grouping $-CH_2\cdot CO\cdot CH_2-$ is probably absent, so that the evidence now indicates fairly conclusively the structure (III).

Infra-red absorption maxima (*cm.*$^{-1}$).

	Aniline	*p*-Toluidine
Cpd. from furfuraldehyde (in $CHCl_3$)	1710, 1639, 1597	1710, 1642, 1614
Furfurylidene deriv. (in pyridine)	1685, 1636	1693, 1639
Benzylidene deriv. (in pyridine)	1698, 1642	—

A 3-hydroxy-2-*p*-toluidino-1-*p*-tolylpiperidine (IV; R = *p*-tolyl) (m. p. 133°) was previously prepared (McGowan, *loc. cit.*) by the reduction of 1 : 2 : 3 : 4-tetrahydro-3-oxo-2-*p*-toluidino-1-*p*-tolylpyridine (III; R = *p*-tolyl). This compound has no ethylene or carbonyl double bonds and shows no absorption bands between 1590 and 1800 cm.$^{-1}$. Since the molecule contains two asymmetric carbon atoms, diastereoisomers are possible and a second isomer (m. p. 149°) has now been isolated.

Experimental.—Microanalyses by Dr. A. F. Colson, Mr. C. E. O'Brien, and Mr. C. G. Scott. M. p.s are corrected.

Compound of aniline and furfuraldehyde, probably 2-*anilino*-1 : 2 : 3 : 4-*tetrahydro*-3-*oxo*-1-*phenylpyridine* (III; R = Ph). Aniline (91 c.c.), furfuraldehyde (41·4 c.c.), and methanol (200 c.c.) were boiled together under reflux for 2 hr., then cooled and filtered. The solid was made into a thick paste with acetone, filtered, washed with a little acetone, and recrystallised twice from ethyl alcohol [yield, 12 g.; m. p. 140° (decomp.); soluble in chloroform and pyridine] [Found: C, 77·3; H, 6·0; N, 10·3, 10·5%; *M*, 232 (ebullioscopic in C_6H_6). Calc. for $C_{17}H_{16}ON_2$: C, 77·2; H, 6·1; N, 10·6%; *M*, 264]. Acetylation (McGowan, *loc. cit.*) gave a monoacetate, m. p. 128° alone or mixed with material described previously (Found: C, 74·6; H, 5·8; N, 9·1. Calc. for $C_{19}H_{18}O_2N_2$: C, 74·5; H, 5·9; N, 9·15%).

Compound of p-*toluidine and furfuraldehyde, probably* 1 : 2 : 3 : 4-*tetrahydro*-3-*oxo*-2-p-*toluidino*-1-p-*tolylpyridine* (III; R = *p*-tolyl). *p*-Toluidine (107 g.), furfuraldehyde (41·4 c.c.), and methanol (200 c.c.) were refluxed for 3 hr. and then cooled. The solid was filtered off, washed with ether, and recrystallised from benzene [yield, 45·7 g.; m. p. 169° (decomp.)] [Found: C, 78·1; H, 6·6; N, 9·5%; *M*, 247 (as above). Calc. for $C_{19}H_{20}ON_2$: C, 78·0; H, 6·9; N, 9·6%; *M*, 292]. Benzoylation (McGowan, *loc. cit.*) gave a monobenzoate, m. p. and mixed m. p. 170·5° (Found: C, 78·7; H, 5·7; N, 7·2. Calc. for $C_{26}H_{24}O_2N_2$: C, 78·8; H, 6·1; N, 7·1%).

A *furfurylidene* derivative, prepared in the same way as the analogous aniline compound (McGowan, *loc. cit.*), formed yellow crystals (from 1 : 4-dioxan), m. p. 178° (decomp.) (Found: C, 78·4; H, 5·9; N, 7·2. $C_{24}H_{22}O_2N_2$ requires C, 77·8; H, 6·0; N, 7·6%).

The tetrahydro-compound was reduced as previously described (*idem, loc. cit.*). From the

mother-liquors from the recrystallisation of the compound $C_{19}H_{24}ON_2$, m. p. 133°, a small quantity of an *isomer*, m. p. 149°, was obtained (Found: C, 76·9; H, 8·1; N, 9·9%; *M*, 265. $C_{19}H_{24}ON_2$ requires C, 77·0; H, 8·2; N, 9·5%; *M*, 296). The mixed m. p. of the isomers was 120—126°.

The author thanks Mr. K. Moss for technical assistance, Mr. L. H. Cross and Mr. F. Field for infra-red spectra, and Mr. G. D. Buckley for encouragement and advice.

IMPERIAL CHEMICAL INDUSTRIES LIMITED, RESEARCH DEPARTMENT,
ALKALI DIVISION, NORTHWICH, CHESHIRE. [*Received, June 25th*, 1954.]

Miscellaneous Quinazoline Derivatives.

By K. SCHOFIELD.

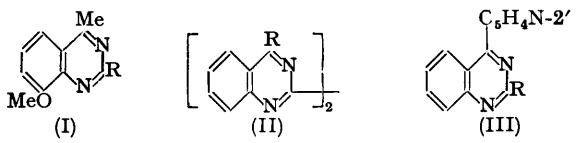
[Reprint Order No. 5488.]

THIS note describes some quinazolines of possible interest as co-ordinating reagents.

2-Acetamido- and 2-benzamido-3-methoxyacetophenone were converted by the method of Schofield, Swain, and Theobald (*J.*, 1952, 1924) into 8-methoxy-2 : 4-dimethyl- (I; R = Me) and 8-methoxy-4-methyl-2-phenyl-quinazoline (I; R = Ph), respectively. With hydriodic acid these gave the corresponding 8-hydroxyquinazolines. These compounds were inactive against *P. berghei* and *T. equiperdum*, and their bacteriostatic concentrations (mg./100 c.c. to prevent visible growth in Hedley Wright broth overnight at 37°) against three organisms are tabulated.

Quinazoline	Hæmolytic *Streptococcus*	*Staph. aureus*	*B. coli*
8-Hydroxy-2 : 4-dimethyl-	0·03	0·5	>1·0 (satd.)
8-Hydroxy-4-methyl-2-phenyl- ...	1·0	>2·0 (satd.)	>2·0 (satd.)

Oxalyl chloride reacted readily with *o*-aminoacetophenone and with *o*-amino- and 2-amino-4′-methoxy-benzophenone to give the related di-anilides, of which those from the first two amines were cyclised to give (II; R = Me) and (II; R = Ph).



2-*o*-Aminobenzoylpyridine (Ockenden and Schofield, *J.*, 1953, 3440) gave with urea 2-hydroxy-4-2′-pyridylquinazoline (III; R = OH), which was converted by phosphorus oxychloride into the chloro-compound (III; R = Cl). Unexpectedly (cf. Schofield, *J.*, 1952, 1927), catalytic reduction of the chloro-compound gave directly a poor yield of 4-2′-pyridylquinazoline (III; R = H) (unchanged by treatment with alkaline potassium ferricyanide) rather than the dihydro-derivative.

Experimental.—2-Amino-3-methoxyacetophenone (15 g.) (Alford, Irving, Marsh, and Schofield, *J.*, 1952, 3009), heated with pyridine (60 c.c.) and benzoyl chloride (15 g.) for 2 hr. at 95°, gave the anilide (22·3 g.), m. p. 108—109° (Simpson *et al.*, *J.*, 1945, 646, gave m. p. 109—110°), satisfactory for further use. Treatment of the amine (5 g.) with acetic anhydride (20 c.c.) at 95° for 2 hr., removal of the solvent at reduced pressure, and crystallisation of the residue from ethyl acetate gave *2-acetamido-3-methoxyacetophenone* (4·6 g.), m. p. 128—131°, forming glistening leaflets, m. p. 133—134° (Found: C, 63·9; H, 6·3. $C_{11}H_{13}O_3N$ requires C, 63·75; H, 6·3%), from ethyl acetate.

8-Hydroxy-2 : 4-dimethylquinazoline. The amide (10·9 g.) and fused ammonium acetate (109 g.) were kept at 165—175° and treated with a rapid stream of ammonia for 3½ hr. Dissolution soon occurred. The solution was then diluted with 1·5 volumes of water, and the solid (8·6 g.) which slowly separated was collected after 2 days. (The product was noticeably soluble in cold water, and such a solution rapidly deposited heavily hydrated crystals, with evolution of heat.) Prolonged drying gave a matte solid, m. p. 81—83°, but recrystallisation

from water, followed by drying over sulphuric acid *in vacuo* for 12 hr., gave soft felted crystals of 8-*methoxy*-2 : 4-*dimethylquinazoline dihydrate*, m. p. 62—64° (Found : C, 58·8; H, 6·8; N, 12·8. $C_{11}H_{12}ON_2,2H_2O$ requires C, 58·9; H, 7·2; N, 12·5%).

The dihydrate (2·25 g.) was refluxed for 3 hr. with hydrobromic acid (22 c.c.; *d* 1·5). Basification of the solution with aqueous ammonia gave, after some hours, a grey solid (1·2 g.), m. p. 110—115°. Recrystallisation from ethyl acetate gave fawn prisms of 8-*hydroxy*-2 : 4-*dimethylquinazoline*, m. p. 112—113° (Found : C, 68·6; H, 5·7. $C_{10}H_{10}ON_2$ requires C, 68·95; H, 4·1%). In larger-scale experiments the discoloured product was purified by passage in ethyl acetate over alumina (on which it gave a clear yellow band, but with which prolonged contact was detrimental).

8-*Hydroxy*-4-*methyl*-2-*phenylquinazoline*. 2-Benzamido-3-methoxyacetophenone (22·2 g.) and fused ammonium acetate (220 g.) were treated with ammonia for 3½ hr. at 155—160°. Dilution with water gave glistening leaflets (19·9 g.), m. p. 128—130°. 8-*Methoxy*-4-*methyl*-2-*phenylquinazoline* separated from methanol as yellow rods, m. p. 132—133° (Found : C, 76·4; H, 5·5. $C_{16}H_{14}ON_2$ requires C, 76·8; H, 5·6%).

The methoxy-compound (19·9 g.) was refluxed for 2 hr. with hydrobromic acid (190 c.c.; *d* 1·5). Basification of the solution with ammonia solution precipitated 8-*hydroxy*-4-*methyl*-2-*phenylquinazoline* (nearly 100%) which gave leaflets (from methanol), m. p. 110—111° (Found : C, 75·75; H, 5·0. $C_{15}H_{12}ON_2$ requires C, 76·2; H, 5·1%).

Oxanilides. These were obtained in theoretical yield by treating oxalyl chloride with a 100% excess of the amine in dry benzene. From acetic acid, in which they were very sparingly soluble, NN′-*di*-o-*acetylphenyl*-, m. p. 270—271° (darkening) (Found : C, 66·45; H, 4·9. $C_{18}H_{16}O_4N_2$ requires C, 66·7; H, 4·9%), NN′-*di*-(o-*benzoylphenyl*)-, m. p. 260—261° (Found : C, 75·6; H, 4·5. $C_{28}H_{20}O_4N_2$ requires C, 75·0; H, 4·5%), and NN′-*di*-(p′-*methoxybenzoylphenyl*)-*oxalodiamide*, m. p. 269—270° (Found : C, 70·2; H, 4·6. $C_{30}H_{24}O_6N_2$ requires C, 70·85; H, 4·8%), formed needles.

Di-(4-*methyl*-2-*quinazolinyl*). The amide (3 g.) and fused ammonium acetate (90 g.) were treated with ammonia for 7 hr. at 165—175°. Addition of water precipitated the *diquinazolinyl* (2·3 g.), which formed pale yellow leaflets, m. p. 249—250° (Found : C, 75·1; H, 4·85. $C_{18}H_{14}N_4$ requires C, 75·5; H, 4·9%), from ethanol, in which it was moderately soluble.

Di-(4-*phenyl*-2-*quinazolinyl*). The anilide (0·5 g.) and fused ammonium acetate (15 g.) were treated with ammonia for 5 hr. at 160—170°. After dilution with water the product (0·39 g.; m. p. 290—291°) was collected. The *diquinazolinyl* was only very sparingly soluble in the usual solvents, and formed very pale yellow needles, m. p. 295—296° (Found : C, 81·3; H, 4·1. $C_{28}H_{18}N_4$ requires C, 81·9; H, 4·4%), from acetic acid. The insolubility of the anilide made it difficult to effect complete cyclisation on the big scale.

2-*Hydroxy*-4-2′-*pyridylquinazoline*. 2-*o*-Aminobenzoylpyridine (4·5 g.) and urea (2·25 g.) were stirred at 200—210° for 1 hr. The initial vigorous evolution of ammonia soon ended and the melt quickly solidified. The cake was pulverised and digested with alcohol, giving the product 2-*hydroxy*-4-2′-*pyridylquinazoline* (5·1 g.), which formed cream needles, m. p. 278—280° (Found : C, 69·7; H, 3·8. $C_{13}H_9ON_3$ requires C, 69·9; H, 4·0%), from ethanol.

2-*Chloro*-4-2′-*pyridylquinazoline*. The hydroxy-compound (1 g.) and phosphorus oxychloride (6 c.c.) were refluxed for 1 hr. Decomposition of the solution with ice and sodium hydroxide, followed by ether-extraction, gave substantially pure 2-*chloro*-4-2′-*pyridylquinazoline* (0·93 g.), needles (from methanol), m. p. 171—172° (Found : C, 64·6; H, 3·1. $C_{13}H_8N_3Cl$ requires C, 64·6; H, 3·3%).

4-2′-*Pyridylquinazoline*. The chloro-compound (0·5 g.) and palladium–charcoal (1·5 g., 5%) in hot methanol (50 c.c.) were shaken with hydrogen for 45 min. After removal of the catalyst and solvent the residue was treated with aqueous sodium hydroxide and extracted with ethyl acetate. The dried (Na_2SO_4) extract provided an oily solid (0·36 g.) from which was obtained with ether–light petroleum a white solid (0·15 g.), m. p. 86—87°. 4-2′-*Pyridylquinazoline* separated from ligroin (b. p. 40—60°) as very pale yellow crystals, m. p. 89—90° (Found : C, 75·4; H, 4·3. $C_{13}H_9N_3$ requires C, 75·3; H, 4·4%).

I am indebted to Dr. F. Hawking of the National Institute for Medical Research for the bacteriostatic data.

WASHINGTON SINGER LABORATORIES,
PRINCE OF WALES ROAD, EXETER.

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2 : 3-*Dihydro*-1-*methyl*-7-*phenylindole.*

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

[Reprint Order No. 5497.]

In another connection 2 : 3-dihydro-1-methyl-7-phenylindole was required. This was prepared from *N*-methyl-2-diphenylylamine by a Fisher indole synthesis, from which some points of interest emerge.

Aqueous or aqueous-ethanolic acid hydrolysed the pyruvic acid hydrazone into its components. However in acetic acid, use of zinc chloride or boron trifluoride in ether gave the indole in good reproducible yield. We were unable to prepare the dihydroindole from 1-methyl-7-phenylindole by reduction with lithium aluminium hydride in ether or tetrahydrofuran (contrast Julian and Printy, *J. Amer. Chem. Soc.*, 1949, **71**, 3206), but did so by using zinc and hydrochloric acid.

Experimental.—Ultra-violet absorption spectra were measured in 95% EtOH.

N-2-*Diphenylyl*-N-*methylhydrazine*. *N*-Methyl-2-diphenylylamine (10 g.) in concentrated hydrochloric acid (10 ml.) was added slowly to a stirred aqueous solution of sodium nitrite (4 g.) at <10°. The product (11·5 g.) was filtered off and recrystallised from aqueous methanol to yield the N-*nitroso*-compound, m. p. 65—66° (Found : C, 73·4; H, 5·6; N, 12·4. $C_{13}H_{12}ON_2$ requires C, 73·6; H, 5·7; N, 13·3%). This (10 g.) in acetic acid (13 ml.) was added during 15 min. to a stirred suspension of zinc dust (3 g.) in water (20 ml.) at 5°. After 1 hr. at room temperature the whole was heated slowly to 80°, then cooled, and the bases were extracted with ether, affording after distillation the *hydrazine*, b. p. 110—113°/0·1 mm., $\lambda_{max.}$ 232 mμ (ε 13,000) (Found : C, 78·9; H, 6·7. $C_{13}H_{14}N_2$ requires C, 78·7; H, 7·1%). Its *hydrochloride* had m. p. 217—221° (from ethanol) (Found : C, 66·2; H, 6·2; N, 11·2. $C_{13}H_{15}N_2Cl$ requires C, 66·5; H, 6·4; N, 11·9%).

1-*Methyl*-7-*phenylindole*-2-*carboxylic acid*. Pyruvic acid (5 g.) and the above hydrazine (10 g.) in aqueous methanol (30 ml.) readily gave the *hydrazone*, m. p. 72° [from chloroform–light petroleum (b. p. 40—80°)], $\lambda_{max.}$ 305 mμ (ε 9000) (Found : C, 71·6; H, 6·0; N, 10·5. $C_{16}H_{16}O_2N_2$ requires C, 71·6; H, 6·0; N, 10·4%), which dissolved in concentrated hydrochloric acid giving after a few moments a crystalline precipitate of *N*-2-diphenylyl-*N*-methylhydrazine hydrochloride, m. p. 217—221°.

The hydrazone (500 mg.) was heated in acetic acid (1 ml.) with an ethereal solution of boron trifluoride (0·5 ml.) or with zinc chloride (500 mg.) at 100° for 10 min. The product, sublimed *in vacuo*, furnished after recrystallisation from ethanol 1-*methyl*-7-*phenylindole*-2-*carboxylic acid* (180 mg.), m. p. 229—232°, $\lambda_{max.}$ 296 mμ (ε 15,000) (Found : C, 76·4; H, 5·3; N, 6·1. $C_{16}H_{13}O_2N$ requires C, 76·5; H, 5·2; N, 5·6%).

2 : 3-*Dihydro*-1-*methyl*-7-*phenylindole*. The acid (80 mg.) was heated in an evacuated tube at 240° for 30 min. The crude oily 1-methyl-7-phenylindole was characterised as its dark red *picrate*, m. p. 107—108° (from ethanol) (Found : C, 57·3; H, 3·8; N, 13·0. $C_{21}H_{16}O_7N_4$ requires C, 57·8; H, 3·7; N, 12·8%). The picrate (100 mg.) was decomposed on an alumina column, affording oily 1-methyl-7-phenylindole (54 mg.), $\lambda_{max.}$ 293 mμ (ε 6200), which was refluxed for 1 hr. with zinc (2 g.) and concentrated hydrochloric acid (10 ml.). The solution was made alkaline and extracted with ether. The extract was dried, filtered through alumina, and concentrated, and the product sublimed to give the colourless oily dihydroindole (40 mg.), $\lambda_{max.}$ 310 mμ (ε 7000), characterised as its *picrate*, m. p. 180—181° (Found : C, 57·5; H, 3·9; N, 13·2. $C_{21}H_{18}O_7N_4$ requires C, 57·5; H, 4·2; N, 12·8%).

We are indebted to the National Research Council of Canada for a grant and an N.R.C. Postdoctorate Fellowship to one of us (B. R. T.).

Chemical Laboratories,
University of New Brunswick.

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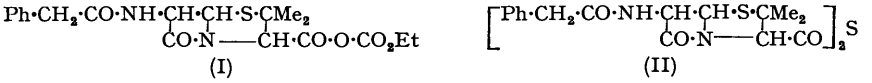
Benzylpenicillinic Thioanhydride.

By R. M. Evans and A. B. A. Jansen.

[Reprint Order No. 5502.]

The interaction of benzylpenicillinic ethoxyformic anhydride (I) with amines, alcohols, and thiols to form, respectively, amides, esters, and thioesters of penicillin has been described by Johnson (*J. Amer. Chem. Soc.*, 1953, **75**, 3636) and by Barnden, Evans, Hamlet, Hems, Jansen, Trevett, and Webb (*J.*, 1953, 3733). We have now examined the reaction of the anhydride with hydrogen sulphide. Cronyn and Jui (*J. Amer. Chem. Soc.*, 1952, **74**, 4726) and Sheehan and Johnson (*ibid.*, p. 4727) have shown that acylamino-acids may be converted into the corresponding thio-acids by treating their ethoxyformic anhydrides in methylene chloride at −20° with hydrogen sulphide in the presence of a molar proportion of triethylamine. Under these conditions (I) gave only intractable products, but benzylpenicillinic thioanhydride (II) was obtained as a crystalline solid in 69% yield when much less triethylamine was employed.



(I) (II)

For the preparation of the thioanhydride the progress of the reaction was best followed polarimetrically, the product being worked up when the rotation reached a maximum. When the reaction time was prolonged beyond this, there were formed neutral and acidic substances devoid of anti-bacterial activity and having a relatively low specific rotation. It is therefore probable that fission of the β-lactam ring had occurred. The velocity of the reaction of benzylpenicillinic ethoxyformic anhydride with hydrogen sulphide is increased markedly by increasing quantities of base and is apparently affected also by impurities, whose nature is at present unknown.

The thioanhydride was stable for several months in a stoppered bottle as the dry crystalline solid, but deteriorated more rapidly in solution in organic solvents or in suspension in water, and it reacted with *cyclo*hexylamine to give penicillin *cyclo*hexylamide in 42% yield. On plate bioassay against *Staphylococcus aureus* the thioanhydride showed an activity of 1500 i.u./mg. which was first thought to be due solely to sodium penicillin formed by hydrolysis of the thioanhydride in the buffer solution (quantitative hydrolysis would give 1760 i.u./mg.), but an anomalously high activity, 4000 i.u./mg., was observed when *Bacillus subtilis* was the test organism and indicated the presence of another active substance. Further examination was kindly undertaken by Dr. P. Muggleton and his staff, who found that the activity was normal against *Sarcina lutea*, *Coryne bacterium diphtheriae*, *Streptococcus* β-*haemolyticus*, and *Clostridium welchii*. Evaluation of the compound, whether administered orally or by injection, showed it to be of little use therapeutically.

Experimental.—Benzylpenicillinic thioanhydride. Ethyl chloroformate (6 c.c.) was added to a solution of triethylammonium benzylpenicillinate (26·1 g.) in chloroform (120 c.c.); after 10 min., the mixture was treated with a solution (90 c.c.; 0·7M; estimated iodometrically) of hydrogen sulphide in chloroform, together with triethylamine (8 drops). After 1 hr. at room temperature the optical roatation of the solution, observed in a 1-dm. tube, had increased from +18·7° to +28·1°. The solution was then washed successively with water, citric acid solution, disodium hydrogen phosphate solution, and water, then dried (Na_2SO_4), and evaporated *in vacuo*. The residual resin was crystallised from ethyl acetate–*iso*propyl ether, affording colourless prisms (13·75 g.), m. p. 130°, $[\alpha]_D^{20}$ + 384° (*c*, 1·0 in $CHCl_3$) (Found: C, 57·85; H, 5·45; N, 8·8; S, 13·9. $C_{32}H_{34}O_6N_4S_3$ requires C, 57·65; H, 5·1; N, 8·4; S, 14·4%).

Reaction of the thioanhydride with cyclo*hexylamine.* *cyclo*Hexylamine (0·24 c.c.) was added to a solution of the thioanhydride (0·67 g.) in chloroform (10 c.c.) and, after ½ hr., the solution was washed in turn with water, dilute hydrochloric acid, disodium hydrogen phosphate solution, and water. Evaporation of the dried solution afforded a crystalline residue (0·35 g.) which, after recrystallisation from ethyl acetate, had m. p. 197—198°, not depressed on admixture with authentic benzylpenicillin *cyclo*hexylamide.

Glaxo Laboratories, Ltd., Greenford, Middlesex. [*Received, June 29th*, 1954.]

The Oxidation of Americium to the Sexavalent State.

By M. Ward and G. A. Welch.

[Reprint Order No. 5510.]

Asprey, Stephanou, and Penneman (*J. Amer. Chem. Soc.*, 1950, **72**, 1425; 1951, **73**, 5715) state that tervalent americium is oxidised completely in 10 minutes to the sexavalent state in 0·2M-nitric acid at 85° by ammonium persulphate; also by the addition of solid argentic oxide to a dilute perchloric acid solution of americium.

Oxidation of americium in tracer amounts to its sexavalent state was achieved partially by addition of iodic acid to an americium solution in 0·2M-nitric acid (approximately 30% oxidised), and also by the passage of ozone (5% ozone at 3 ml./min.) into an americium solution in 0·2M-nitric acid for 1 hr. [20% americium(VI) obtained].

At room temperature the addition of ammonium persulphate to americium solutions, at varying acid strengths, induced no oxidation at all. At 85—90°, the reaction in 0·2M-nitric acid produced only up to 80% americium(VI), but, if a small amount of silver (as silver nitrate) was also added, almost complete (98—99%) oxidation was achieved.

Experimental.—In most of the experiments the percentage of sexavalent americium was followed by making use of the fact that, unlike tervalent americium, it is not coprecipitated on lanthanum fluoride. In a typical experiment in which 99% oxidation was obtained, the americium solution (containing 2×10^5 α d.p.m.) was pipetted into a 3-ml. centrifuge tube, and made 0·3M with respect to nitric acid, the final volume being 1 ml. One drop of 10% silver nitrate and 8 drops of 5% ammonium persulphate solution were added and the mixture was heated in boiling water for 4 min. A further 8 drops of 5% ammonium persulphate were added and the tube heated for a further 2 min. Lanthanum carrier (0·5 mg.) was added as nitrate solution and the unoxidised americium co-precipitated on lanthanum fluoride by the addition of ammonium fluoride solution. The ammonium fluoride was treated with argentic nitrate just before use to prevent any reduction of the americium by impurities in the fluoride. The lanthanum fluoride was centrifuged out, then washed twice, and its americium content determined by alpha-counting.

Thanks are offered to Dr. Milsted of A.E.R.E. for supplying the americium and to the Managing Director, Department of Atomic Energy (Industrial Group), for permission to publish this note.

Chemical Services Department, Department of Atomic Energy (Industrial Group), Windscale Works, Cumberland. [*Received, July 1st*, 1954.]

The Tuberculostatic Activity of Pyridine-acid Hydrazides.

By A. R. Katritzky.

[Reprint Order No. 5539.]

The outstanding activity, as tuberculostatic agent, of *iso*nicotinic hydrazide (Fox and Gibas, *J. Org. Chem.*, 1952, **17**, 1653) is not an isolated instance among pyridine-acid hydrazides, since picolinic hydrazide is very potent, although too toxic for clinical use (*idem, loc. cit.*). In view of the availability of the corresponding esters (in connection with another investigation), it was of interest to prepare and test biologically 4-pyridylacethydrazide, β-4-pyridylpropionhydrazide, and β-4-pyridylacrylhydrazide. Imperial Chemical Industries Limited, Dyestuffs Division, who kindly undertook the testing, report that the compounds are inactive in tubercular-infected mice. It thus appears that direct attachment of the $CO{\cdot}NH{\cdot}NH_2$ group to the pyridine nucleus is necessary for activity.

4-Pyridylacethydrazide separated from ethyl acetate with 0·22 molecule of solvent of crystallisation; β-4-pyridylpropionhydrazide from the same solvent contained 0·23 and from chloroform 0·22 molecule of solvent. These may be clathrate compounds (Powell, *J.*, 1948, 61), perhaps with an ideal solvent–solute ratio of 1 : 4.

Experimental.—*4-Pyridylacethydrazide.* Ethyl 4-pyridylacetate (3 g.) and hydrazine hydrate (100%; 1·5 c.c.) were heated on the water-bath for 2 hr. At first the *hydrazide* separated from ethyl acetate in fine needles turning to stout needles, m. p. 51—54°; in later recrystallisations fine needles turning to plates were obtained, the m. p. of which varied 50° to 120° with the rate of heating. At 120° its loss in weight was 11·4% corresponding to 0·22 mol. of solvent (Found in the residue: C, 55·6; H, 6·0. $C_7H_9ON_3$ requires C, 55·6; H, 6·0%).

β-*4-Pyridylpropionhydrazide*, prepared as above, separated from chloroform in colourless solvated needles, m. p. 55—65°. At 120° its loss in weight was 13·7% corresponding to 0·22 mol. of solvent (Found in the residue: C, 58·1; H, 6·9. $C_8H_{11}ON_3$ requires C, 58·2; H, 6·7%). The compound was also obtained in solvated needles, m. p. 64—65°, from ethyl acetate, which lost 10·9% in weight, corresponding to 0·23 mol. of solvent (Found in the residue: C, 58·3; H, 6·9%). The *benzylidene* derivative, prepared in boiling ethanol, separated from amyl alcohol in colourless prisms, m. p. 186—187° (Found: C, 71·3; H, 6·1. $C_{15}H_{15}ON_3$ requires C, 71·1; H, 5·9%).

β-4-Pyridylacrylhydrazide, prepared as above, did not crystallise. It formed an ill-defined yellow *dipicrate*, m. p. 80—90° (decomp.) (Found: C, 38·6; H, 2·8. $C_{20}H_{15}O_{15}N_9$ requires C, 38·6; H, 2·4%).

The author is indebted to Professor Sir Robert Robinson, O.M., F.R.S., for his interest. Grateful acknowledgment is also made to the Ministry of Education for an F.E.T.S. maintenance grant.

THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, July 9th,* 1954.]

The Preparation of 2 : 3-*Diaminopyridine.*

By C. L. LEESE and H. N. RYDON.

[Reprint Order No. 5555.]

THE simplest route to 2 : 3-diaminopyridine from the commercially available 2-aminopyridine, *viz.*, nitration, separation of the 3- and the 5-nitro-compound (Tschitschibabin, *J. Russ. Phys. Chem. Soc.*, 1914, **46**, 1236; Caldwell and Kornfeld, *J. Amer. Chem. Soc.*, 1942, **64**, 1695), and reduction of the former (Tschitschibabin and Kirssanov, *Ber.*, 1927, **60**, 771; Petrow and Saper, *J.*, 1948, 1389), is unsuitable for the preparation of any considerable quantity of the diamine owing to the small proportion of 3-nitro-compound formed and the large bulk of liquid which has to be handled in its separation.

The obvious alternative route involves halogenation of 2-aminopyridine in the 5-position (Tschitschibabin and Egorov, *J. Russ. Phys. Chem. Soc.*, 1928, **66**, 683; Case, *J. Amer. Chem. Soc.*, 1946, **68**, 2574), nitration in the 3-position (Petrow and Saper, *loc. cit.*; Vaughan, Krapcho, and English, *J. Amer. Chem. Soc.*, 1949, **71**, 1885), reduction of the 3-nitro-group, and removal of the 5-halogeno-group by hydrogenolysis. Ziegler (*ibid.*, p. 1891) brought about the last two stages in one operation, obtaining 2 : 3-diaminopyridine in 63% yield from 2-amino-5-chloro-3-nitropyridine by treatment with Raney nickel alloy in sodium hydroxide solution, but we were unable to obtain satisfactory yields by this method; a similar reaction with 2-amino-5-bromo-3-nitropyridine gave a 56% yield but the 2 : 3-diaminopyridine prepared in this way darkened rapidly on storage.

A satisfactory method, which has given consistent yields (18% overall from 2-aminopyridine) of material of good quality, is described below. 2-Aminopyridine is brominated by a modification of Case's method (*loc. cit.*), the product is then nitrated and reduced (cf. Petrow and Saper, *loc. cit.*), and the resulting 2 : 3-diamino-5-bromopyridine hydrogenolysed over palladised strontium carbonate in aqueous alkali.

Experimental.—*2-Amino-5-bromopyridine.* Bromine (435 g.) was added with stirring to a cooled solution of 2-aminopyridine (255 g.) in ethanol (1·5 l.). The crystalline precipitate was collected, washed with ethanol, and dissolved in water (400 ml.); basification precipitated the crude bromo-compound which was collected by filtration, washed, dried, freed from the accompanying 3 : 5-dibromo-compound by two extractions with warm light petroleum (b. p. 60—80°), and recrystallised from benzene; it had m. p. 137° (lit., m. p. 137°), the yield being 207 g. (44%).

2 : 3-*Diamino-pyridine.* (*a*) 2-Amino-5-bromopyridine was nitrated in 60% yield and the resulting 2-amino-5-bromo-3-nitropyridine reduced to 2 : 3-diamino-5-bromopyridine in 80% yield by Petrow and Saper's procedures (*loc. cit.*). The bromo-diamine (20 g.) was suspended in N-sodium hydroxide solution (100 ml.) and shaken with hydrogen in the presence of 5% palladised strontium carbonate (0·5 g.). When the uptake of hydrogen was complete, the catalyst was removed and the filtrate saturated with potassium carbonate (105 g.) and continuously extracted with ether for 12 hr. After removal of the ether from the dried extract, the residue was recrystallised (charcoal) from benzene (75 ml.). The yield of 2 : 3-diamino-pyridine, colourless needles, m. p. 116° (Tschitschibabin and Kirssanov, *loc. cit.*, give m. p. 112—113°; Petrow and Saper, *loc. cit.*, give m. p. 118·5—119·5°), was 9·9 g. (86%).

(*b*) 2-Amino-5-bromo-3-nitropyridine (3·2 g.) was suspended in 10% sodium hydroxide solution (75 ml.) and ethanol (10 ml.), and the mixture heated to 60°. Raney nickel alloy (7·5 g.) was added to the stirred mixture during 30 min., the temperature being kept at 60—65°; more ethanol (10 ml.), followed by more alloy (1 g.) was then added, the temperature being raised to 80°. The mixture was then cooled and filtered and the filtrate saturated with potassium carbonate and continuously extracted with ether for 12 hr. after addition of sodium dithionite (1 g.). Evaporation of the dried extract and crystallisation from benzene gave the diamine (0·9 g., 56%) as grey needles, m. p. 111°.

We thank the Medical Research Council for a studentship awarded to one of us (C. L. L.).

ORGANIC CHEMISTRY DEPARTMENT,
IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
LONDON, S.W.7.

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Pyrindane (2 : 3-cyclo*Pentenopyridine*) *as a Coal-tar Base.*

By P. ARNALL.

[Reprint Order No. 5611.]

NISBET and PRYDE (*Nature*, 1951, **167**, 862; 1951, **168**, 832) have reported the occurrence of 2 : 3 : 5 : 6- and 2 : 3 : 4 : 6-tetramethylpyridine in fractions of coal-tar bases boiling near 200°/760 mm. During the examination in these laboratories of crude bases extracted from the light creosote fraction of a predominantly vertical-retort tar, in addition to these two, 2 : 3-*cyclo*pentenopyridine has been isolated from a fraction of similar boiling range. This compound, though known as a constituent of shale-oil bases (Eguchi, *Bull. Chem. Soc. Japan*, 1928, **3**, 239), had not previously been identified in coal-tar bases although the corresponding hydrocarbon series (indane; Kramer and Spilker, *Ber.*, 1896, **29**, 552) and phenols (4- and 5-hydroxyindane; Kruber and Schmieden, *Ber.*, 1939, **72**, 653; Kruber and Marx, *Ber.*, 1940, **73**, 1175) are well known.

Experimental.—A bases fraction of b. p. 198—204° was dissolved in hydrochloric acid and extracted with chloroform (Perrin and Bailey, *J. Amer. Chem. Soc.*, 1933, **55**, 4136). The "aromatic" bases whose hydrochlorides were insoluble in chloroform were recovered, primary amines were removed by acetylation, and the residual bases were stirred with excess of concentrated urea solution. Milner (B.P. 584,148) and Riethoff (U.S.P. 2,295,606, 2,376,008) showed that complexes were formed between 2 : 3- and 2 : 6-lutidine and urea. This was expected also for simple pyridine homologues with 2 : 3- and 2 : 6-methyl groups. The precipitate formed was filtered off and decomposed by boiling water. Bases recovered from the filtrate and from the precipitate were each distilled through a fractionating column of approx. 70 plates efficiency. Each of these bases contained a base of high refractive index which could not be an unacetylated primary amine since these were shown to be absent. Selected fractions from each distillation were blended and treated stepwise with picric acid. The fractions from the urea-reacting bases yielded 2 : 3 : 5 : 6-tetramethylpyridine picrate, m. p. 175—176°, and a picrate of m. p. 180·5—182° in the ratio of 1 : 3½ together with a quantity of uncrystallisable syrup. Other fractions yielded 2 : 3 : 4 : 6-tetramethylpyridine picrate, m. p. 123·5—124°. The fractions from the bases which did not react with urea yielded 2 : 3 : 5 : 6-tetramethyl-pyridine picrate and a picrate of m. p. 181—182° in the ratio of 1 : 1½, and smaller amounts of unidentified picrates. The picrates of m. p. ~182° were identical (mixed m. p.) and on recrystallisation from glacial acetic acid the total product had m. p. 181—182°.

This picrate was decomposed by addition of potassium carbonate solution and distillation in steam, the distillate was dehydrated, and the base distilled (199·3—199·4°/760 mm.). Eguchi (*loc. cit.*) gives for 2 : 3-*cyclo*pentenopyridine b. p. 199·8°/761 mm., and 181° for the m. p. of the picrate. The other properties of the base, as follows, confirm the identity (in parentheses are given values by Prelog and Szpilfogel, *Helv. Chim. Acta*, 1945, **28**, 1684); d_{20}^{20} 1·0363 (d_4^{20} 1·0359), n_D^{20} 1·5444 (1·54446), styphnate m. p. 177·5° (decomp.) [(178—179° (decomp.)], picrolonate m. p. 239° (decomp.) [(235—236° (decomp.)]. A sample of the picrate synthesised by Prelog and Szpilfogel's method (*loc. cit.*) was identical (mixed m. p.) with that from our base. The infra-red spectra were also identical; they were determined by Mr. D. D. Shrewsbury using a prototype model double-beam infra-red spectrometer on loan from Messrs. Unicam Instruments Limited: the principal bands (cm.$^{-1}$) were at 722 m, 741 m, 789 s, 851 w, ~885 w, 907 w, ~943 w, ~978 w, 1000 w, 1035 m, 1090 s, 1153 m, 1186 w, 1215 m, 1263 w, 1313 m, 1389 w (shoulder), 1420 s, 1441 s, 1467 m, 1592 s, 1721 m, ~1910 w, and 1929 w (*s* = 71—100%, m = 31—70%, w = ≯30%).*

In this work 2 : 3 : 4 : 6-tetramethylpyridine was found exclusively in the urea-reacting bases as was expected; 2 : 3 : 5 : 6-tetramethylpyridine and pyrindane were found both in the urea complex and in the liquor. 2 : 3 : 4 : 6-Tetramethylpyridine forms a solid complex with urea while, contrary to expectation 2 : 3 : 5 : 6-tetramethylpyridine does not. 2 : 3-*cyclo*-Pentenopyridine forms an unstable complex and the presence of the last two compounds in both precipitate and liquor is attributed to physical distribution between the solid and the liquid phase.

The author thanks Dr. E. R. Wallsgrove for helpful discussion, Miss J. M. Moon for assistance in the experimental work, Professor H. B. Nisbet for a sample of 2 : 3 : 4 : 6-tetramethylpyridine, and the Directors of The Midland Tar Distillers Ltd. for permission to publish this note.

THE MIDLAND TAR DISTILLERS LIMITED, RESEARCH DEPARTMENT,
FOUR ASHES, NEAR WOLVERHAMPTON. [*Received, July* 31*st*, 1954.]

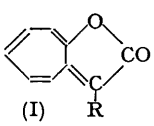
A Reaction of 2-*Chloro*cyclo*heptatrienone.*

By J. W. COOK, J. D. LOUDON, and R. K. RAZDAN.

[Reprint Order No. 5624.]

CONDENSATION of 2-chloro*cyclo*heptatrienone with ethyl acetonedicarboxylate afforded (I; R = CO·CH_2·CO_2Et) which by acid hydrolysis yielded (I; R = COMe) apparently identical with the compound (m. p. 204—205°) obtained by Nozoe, Seto, and Matsumura (*Proc. Jap. Acad.*, 1952, **28**, 483; Seto, *Sci. Rep. Tôhoku Univ.*, 1953, **37**, 367) through a similar condensation using ethyl acetoacetate.

Experimental.—2-Chloro*cyclo*heptatrienone (0·9 g.) was added to the sodio-derivative of ethyl acetonedicarboxylate—from the ester (1·44 g.) and atomised sodium (0·16 g.)—in ether (50 c.c.), and the deep-red solution, after 18 hr. at room temperature, was heated under reflux for 1 hr., cooled, washed with water and concentrated, affording *γ-ethoxycarbonyl-α-2-hydroxy*cyclo*heptatrienylidene-β-oxobutyrolactone* as yellow plates, m. p. 126° (from ethanol) (Found: C, 64·5; H, 4·5; double bonds, 3·85, by micro-hydrogenation. $C_{14}H_{12}O_5$ requires C, 64·6; H, 4·6%). Light absorption in ethanol: $\lambda_{max.}$, 4225, 2750, 2500, 2250 Å; log ε 4·40, 4·32, 4·24, 4·41. The compound gave a green-brown colour with ferric chloride in ethanol; when it (0·1 g.) was heated (2 hr.) with concentrated hydrochloric acid (5 c.c.) and water (20 c.c.), recovery in chloroform afforded α-2-hydroxy*cyclo*heptatrienylidene-β-oxobutyrolactone (I; R = CO·CH_3) as yellow needles, m. p. 210° (from ethanol) (Found: C, 70·1; H, 4·2; double bonds, 4·2, by micro-hydrogenation. Calc. for $C_{11}H_8O_3$: C, 70·2; H, 4·25%). The latter had light absorption in ethanol: $\lambda_{max.}$, 4200, 2725, 2475, 2225 Å; log ε 4·38, 4·32, 4·26, 4·42.



(I)

THE UNIVERSITY OF GLASGOW. [*Received, August* 6*th*, 1954.]

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* A copy of the spectrum has been deposited with the Chemical Society. Photocopies (price 3*s.* 0*d.* each) may be obtained from the General Secretary on application quoting C.S. no. 140.