256. *Some Unsymmetrical Azo-nitriles.*

By (the late) M. C. FORD and R. A. RUST.

OXIDATION with bromine of hydrazo-nitriles $R \cdot NH \cdot NH \cdot CMe_2 \cdot CN$ ($R = Ar$ or CO_2Me), obtained by adaption of standard methods,[1,2] gave the corresponding azo-nitriles, $R \cdot N \vdots N \cdot CMe_2 \cdot CN$, in good yield. It was thought that these would decompose at moderate temperatures to yield 1-cyano-1-methylethyl (2-cyano-2-propyl) radicals together with aryl or methoxycarbonyl radicals:

$$R \cdot N \vdots N \cdot CMe_2 \cdot CN \longrightarrow R \cdot + N_2 + \cdot CMe_2 \cdot CN$$

However, they proved too stable for an investigation of their decomposition in organic solvents to be profitable.

When α-(phenylazo)*iso*butyronitrile, $Ph \cdot N \vdots N \cdot CMe_2 \cdot CN$, was heated in the presence of iodine small quantities of iodobenzene and α-iodo*iso*butyronitrile were formed, indicating that homolysis of the azo-nitrile occurred to some extent. Pyrolysis of the azo-nitrile gave very low yields of simple products: these were tetramethylsuccinonitrile (the typical dimer of 2-cyano-2-propyl radicals [3]), benzene, α-methylacrylonitrile, and an oil which was probably a mixture of α- and β-phenyl*iso*butyronitrile.

Pyrolysis of α-(methoxycarbonylazo)*iso*butyronitrile, $MeO_2C \cdot N \vdots N \cdot CMe_2 \cdot CN$, gave methyl α-cyano*iso*butyrate, in small yield. No tetramethylsuccinonitrile was isolated, and, in the presence of iodine, no iodo-nitrile was formed, suggesting that the decomposition probably occurred by an intramolecular process not involving free radicals.

Experimental.—*Hydrazino-nitriles.* A mixture of phenylhydrazine (50 ml., 0·5 mole), acetone cyanohydrin (45 ml., 0·5 mole), and ether (13 ml.) was set aside in a pressure-bottle at room temperature for 8 days: α-phenylhydrazino*iso*butyronitrile gradually crystallised; air-dried and recrystallised from ether–light petroleum (b. p. 80—90°) it gave prisms (66 g., 75%), m. p. 69° (lit.,[2] 70°) (Found: C, 68·9; H, 7·5; N, 23·7. Calc. for $C_{10}H_{13}N_3$: C, 68·5; H, 7·5; N, 24·0%).

α-m-*Tolyl*-, prisms, m. p. 86·5—87° (Found: C, 69·9; H, 8·1; N, 22·3. $C_{11}H_{15}N_3$ requires C, 69·8; H, 8·0; N, 22·2%), and α-p-*tolyl-hydrazino*iso*butyronitrile*, needles, m. p. 94·5—96·5° (Found: C, 69·7; H, 8·0; N, 22·0%) (both from ether–light petroleum), were prepared similarly, 100% excess of the cyanohydrin being used in the preparation of the latter.

Methyl hydrazinoformate [4] (18 g., 0·2 mole) and acetone cyanohydrin (45 ml.) were heated together in a pressure-bottle at 100° for $7\frac{1}{2}$ hr. Concentration under reduced pressure and recrystallisation of the residue from benzene–light petroleum gave α-N'-*methoxycarbonyl-hydrazino*iso*butyronitrile* (20 g., 65%) as needles, m. p. 99—101° (Found: C, 46·0; H, 7·2; N, 26·9. $C_6H_{11}O_2N_3$ requires C, 45·8; H, 7·05; N, 26·7%).

Azo-nitriles. A saturated solution of bromine in 15% aqueous potassium bromide was added in portions, with shaking, to one of phenyl hydrazino-nitrile (50 g.) in chloroform (140 ml.), the temperature being maintained at *ca.* 0° by addition of ice. When the aqueous layer was permanently yellow the chloroform layer was separated, shaken in turn with aqueous sodium sulphite, 2N-sodium carbonate, and water, and dried ($MgSO_4$). Removal of the solvent left an orange liquid, which yielded α-*(phenylazo)*iso*butyronitrile* (40 g., 82%) as a yellow oil, b. p. 64°/0·05 mm., d_D^{19} 1·011, n_D^{19} 1·5284, with a penetrating odour (Found: C, 69·6; H, 6·6; N, 24·4. $C_{10}H_{11}N_3$ requires C, 69·3; H, 6·4; N, 24·3%). The light absorption, λ_{max} 270 mμ and 390 mμ (log ε 3·81 and 2·30 respectively), resembled that of phenylazomethane.[5] A solution in concentrated sulphuric acid, set aside for 12 hr. and then poured on ice, gave α-*(phenylazo)*iso*butyramide, yellow needles, m. p. 65·5—67°, from light petroleum (b. p. 40—60°) (Found: C, 62·8; H, 7·0; N, 22·3. $C_{10}H_{13}ON_3$ requires C, 62·8; H, 6·85; N, 22·0%).

[1] Reissert, *Ber.*, 1884, **17**, 1458.
[2] Bucherer and Grolée, *Ber.*, 1906, **39**, 1005.
[3] Bickel and Waters, *Rec. Trav. chim.*, 1950, **69**, 1490.
[4] Diels, *Ber.*, 1914, **47**, 2187.
[5] Burawoy, *J.*, 1937, 1865.

Pyrolysis of the azo-nitrile (50 g.) at *ca.* 180°, in five portions, gave benzene (1·7 g.) (*m*-dinitrobenzene, m. p. 89°), a little α-methylacrylonitrile, tetramethylsuccinonitrile (1·2 g.), m. p. and mixed m. p. 166—168°, and an oil (3 g.), b. p. 90—96°/10 mm. (Found: C, 82·2; H, 7·7; N, 9·8%), probably a mixture of α- and β-phenyl*iso*butyronitrile (Calc. for $C_{10}H_{11}N$: C, 82·7; H, 7·6; N, 9·6%), which could not be separated by means of solid derivatives. Much intractable material of higher molecular weight was also formed.

Gradual addition of the azo-nitrile (4·3 g.) to iodine (6·3 g.) in boiling toluene (10 ml.), followed by 2 hours' refluxing, gave α-iodo*iso*butyronitrile (0·3 g.) (α-iodo*iso*butyramide,[6] m. p. 181—182°) and iodobenzene (0·3 g.) (*p*-iodonitrobenzene, m. p. 169—170°).

α-(m-*Tolylazo*)*iso*butyronitrile, an orange-yellow oil, b. p. 68·5°/0·04 mm., n_D^{25} 1·5245 (Found: C, 70·3; H, 6·9; N, 22·4. $C_{11}H_{13}N_3$ requires C, 70·6; H, 7·0; N, 22·4%) [α-(m-*tolylazo*)*iso*butyramide, yellow needles, m. p. 82·5—83·5° (Found: C, 64·6; H, 7·3; N, 20·2. $C_{11}H_{15}ON_3$ requires C, 64·4; H, 7·4; N, 20·5%)], and α-(p-*tolylazo*)*iso*butyronitrile, pale yellow needles, m. p. 55·5—58° (Found: C, 70·4; H, 6·9; N, 22·2%), were prepared similarly.

α-(*Methoxycarbonylazo*)*iso*butyronitrile. The hydrazino-compound (10 g.) in chloroform (50 ml.) was oxidised as above. The purified chloroform extracts from five such oxidations were combined, and yielded the *azo-compound* (31 g., 65%) as a pleasant-smelling lemon-yellow oil, b. p. 54°/0·01 mm., d_D^{19} 1·064, n_D^{25} 1·4266 (Found: C, 46·7; H, 5·7; N, 26·8. $C_6H_9O_2N_3$ requires C, 46·4; H, 5·85; N, 27·1%). Oxidation in larger batches led to poor yields. Cautious pyrolysis of the azo-compound (23 g.) at *ca.* 170°, in ten portions, gave methyl α-cyano*iso*butyrate (2·5 g.), b. p. 70—72°/17 mm. (lit.,[7] 76—78°/20 mm.), characterised by conversion[7] into dimethylmalonic acid, m. p. and mixed m. p. 189—191°.

[6] Ford and Waters, *J.*, 1951, 1851.
[7] Hesse, *Amer. Chem. J.*, 1896, **18**, 743.

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257. *The Effect of Urea on the Streaming Birefringence and Viscosity of Sodium Deoxyribonucleate.*

By A. R. MATHIESON and M. R. PORTER.

THE effect of urea on aqueous solutions of sodium deoxyribonucleate (DNA) was studied by Butler and Conway[1] who found that, after removal of the urea by dialysis, there is a reduction in the viscosity and the extent of hysteresis in the titration curves, together with an increase in the sedimentation and diffusion constants. They ascribed these changes to the effect on the DNA molecule of the breaking of hydrogen bonds by the urea.

We have studied the effect of urea at 25° in presence of 0·2M-sodium chloride on the viscosity and streaming birefringence of DNA. The sample of DNA employed was extracted from calf-thymus glands and has been fully described elsewhere.[2] Measurements were made on solutions of DNA in 0·2M-sodium chloride solution after the urea had been removed by dialysis. The effects of the time of contact with urea, and of the urea concentration are shown in Fig. 1 for solutions of DNA for which χ° (orientation angle) is independent of DNA concentration. A 1·0M-urea solution has no detectable effect during 22 hours, but a 5·0M-urea solution has a small but significant influence on χ during 2—48 hours. The values of the rotary-diffusion constant (θ), calculated from these results by considering the DNA molecule to be a prolate ellipsoid of revolution, and by using Peterlin

[1] Butler and Conway, *J.*, 1952, 3075.
[2] Jordan, Mathieson, and Matty, *J.*, 1956, 154.

and Stuart's [3] equations, are $\theta = 10$ sec.$^{-1}$ for untreated solutions and for solutions treated with 1M-urea, and $\theta = 16$ sec.$^{-1}$ for solutions treated with 5M-urea. A 0·022% solution of DNA in 5M-urea and 0·2M-sodium chloride has pH 8·4. No alkaline denaturation should have occurred under these conditions [4] but as a check the value of θ was measured for DNA in 0·2M-sodium chloride at pH 8·9; $\theta = 9·0$ sec.$^{-1}$ was found. The intrinsic viscosity at zero shear ($[\eta]$) was measured for DNA in 0·2M-sodium chloride solution. For DNA which

FIG. 1. *Effect of urea on the birefringence of nucleic acid in presence of* 0·2M-*sodium chloride (nucleic acid concn.*: 0·026%).

× *Untreated.*
○ 1M-*Urea for* 75 *min.*
+ 1M-*Urea for* 22 *hr.*
● 5M-*Urea for* 105 min.
△ 5M-*Urea for* 20 *hr.*
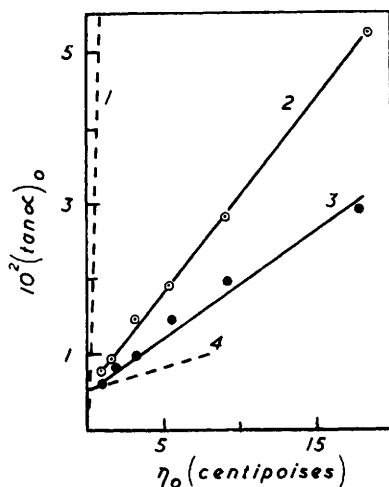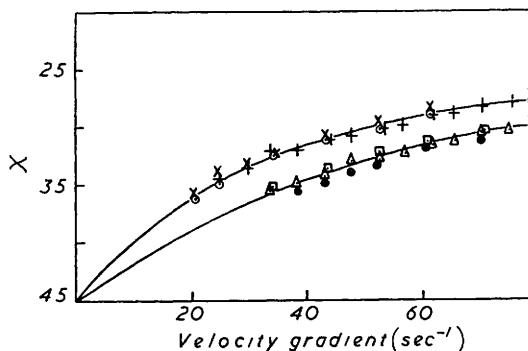⊡ 5M-*Urea for* 48 *hr.*

FIG. 2. *Effect of solvent viscosity on* (tan $\alpha)_0$.

1, *Tobacco-mosaic virus.*
2, *Nucleic acid.*
3, *Nucleic acid in presence of* 5M-*urea.*
4, *Polystyrene.*

had been treated with a 5M-urea solution $[\eta] = 40·7$ (c in %) and for untreated DNA $[\eta] = 52·5$.

The increase in θ and decrease in $[\eta]$ brought about by 5M-solutions indicate either that the DNA molecules have been degraded or that they have lost some of their rigidity with a decrease in their extreme assymmetry. There are reasons based on experiment for preferring the second alternative. Solutions of DNA in 0·2M-sodium chloride in water–glycerol (with up to 50% of glycerol) were examined by using DNA which had been treated with 5M-urea solution in the presence of 0·2M-sodium chloride, and untreated DNA. Fig. 2 shows the variation of (tan $\alpha)_0$ [initial slope of plots of χ against velocity gradient (G) in the concentration-independent region of χ] with solvent viscosity η_0. Comparison of the results with Cerf's predictions [5] and the results he quotes for tobacco-mosaic virus (a rigid

[3] Peterlin and Stuart, *Z. Physik*, 1939, **112**, 1, 129.
[4] Jordan, Mathieson, and Matty, *J.*, 1956, 158.
[5] Cerf, *Compt. rend.*, 1950, **230**, 81.

molecule) and polystyrene (a flexible molecule), also shown in Fig. 2, suggests that treatment with urea makes DNA molecules less rigid.

Calculations based on Peterlin's theory [6] for concentrated solutions, which is obeyed [7] by DNA, also suggest a decrease in molecular rigidity after treatment with urea. The value of $(\tan \Lambda)_0$ [the initial slope of the plot of χ against $(\eta - \eta_0)G/c$] for untreated DNA is $1 \cdot 66 \times 10^{-4}$ and for DNA treated with 5M-urea solution $(\tan \Lambda)_0 = 1 \cdot 16 \times 10^{-4}$. If the value of $(\tan \Lambda)_0$ is interpreted on a coiled model and a " stiffness factor," β, lying between 1 for a stiff coil and 3 for a soft coil, is defined as the ratio of the true molecular weight to that calculated on the assumption of complete rigidity,[7] then the decrease of $(\tan \Lambda)_0$ observed after treatment with urea requires an increase in β and so a less rigid molecule.

Doty and Rice [8] maintained that treatment with urea has little or no effect on the molecular weight of DNA. Butler and Conway [1] suggested that urea causes a change in shape of DNA molecules by rupture of hydrogen bonds. Stacey and Alexander [9] reported that electron microscopy of herring-sperm DNA treated with urea revealed globular instead of fibrous particles, although their results on herring-sperm DNA imply that its behaviour towards urea is different from that of calf-thymus DNA.

The results of the measurements of streaming birefringence suggest that urea makes the DNA molecules more flexible and less asymmetrical. Some of the chain-linking hydrogen bonds may be broken by 5M-urea solution, leading to partial collapse of the molecule in spite of the overall charge reduction by sodium gegenions, from sodium chloride, which stabilises the intramolecular hydrogen bonds by reducing the repulsion of charged amino-groups. 1M-Urea solution cannot do this.

Experimental.—Viscosities were measured in a Couette-type apparatus.[10] Streaming birefringence was measured by adapting the viscometer as recommended by Ogston and Stanier.[11] The cylinders were of ebonite, the inner having a diameter of $1 \cdot 097$ cm. and the outer, $1 \cdot 408$ cm. The optical path length through the solution was $9 \cdot 5$ cm. and very low velocity gradients were used. Polaroids were used in place of Nicol prisms.

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BRITISH NYLON SPINNERS LTD., PONTYPOOL, MON.

[6] Peterlin, *J. Polymer Sci.*, 1954, **12**, 45.
[7] Mathieson and Porter, *Biochim. Biophys. Acta*, 1954, **14**, 288.
[8] Doty and Rice, *ibid.*, 1955, **16**, 446.
[9] Stacey and Alexander, *Trans. Faraday Soc.*, 1957, **53**, 251.
[10] Mathieson and Matty, *J. Polymer Sci.*, 1957, **23**, 747.
[11] Ogston and Stanier, *Biochem. J.*, 1953, **53**, 4.

258. *Fractional Precipitation of Nucleic Acids by Ethanol.*

By A. R. MATHIESON and M. R. PORTER.

FRACTIONAL precipitation by hydrochloric acid of deoxyribonucleic acids (DNA) from various sources, followed by turbidity titration, has been described.[1] It has now been found possible to obtain stable suspensions by using ethanol as precipitant; the results are then different in some respects from those for precipitation with hydrochloric acid.

The following samples of nucleic acids were studied: three samples of DNA of high molecular weight ($\sim 6 \times 10^6$) prepared from calf-thymus by Gulland, Jordan, and Threlfall's method,[2] designated (i) S (supplied by Professor R. Signer) (ii) Al (prepared by Dr. S. Matty) and (iii) Gl(1) (prepared by the late R. H. Garner); (iv) a degraded sample of calf-thymus DNA obtained from B.D.H. Ltd. prepared by a method involving treatment with strong alkali; (v) herring-sperm DNA obtained from Glaxo Ltd.; (vi) DNA prepared from commercial wheat germ (" Froment ") by M. R. Porter by Daly, Allfrey, and Mirsky's method [3] and deproteinised by Sevag, Lackmann, and Smolens's method; [4] (vii) yeast rebonucleic acid (RNA) of low molecular weight prepared by Dr. A. S. Anderson.

Some results for the different samples of nucleic acids are illustrated, expressed as a percentage of the final turbidity. The curves fall into two sharply defined groups: (*a*) a set of very steep curves for the samples of high molecular weight and (*b*) much shallower curves for the others. In the presence of 0·2M-sodium chloride (as illustrated) less alcohol is required for precipitation than for aqueous solutions, *i.e.*, as for precipitations by hydrochloric acid.[1] The effect of previous thermal degradation (0·2M-sodium chloride solutions at 100° for times up to 1 hr.) of the samples of high molecular weight on precipitation by ethanol is complicated. When precipitation was carried out shortly after degradation the curves for the degraded materials were of the same shape as those for undegraded DNA and more alcohol was required, but the amount did not increase with increasing degradation. A mixture of degraded and undegraded DNA required even more alcohol. These results were unexpected but it was observed at the same time that addition of sodium chloride to a solution of thermally degraded DNA caused the viscosity to increase slowly, after its initial fall, becoming constant only after 48 hr. In view of this instability, which may be due to a slow dispersion of aggregates, precipitations by alcohol were carried out on degraded samples 48 hr. after degradation. Under these conditions the curves for thermally degraded DNA resembled those of group (*b*) in the Figure, the DNA being precipitated over a greater range of alcohol concentration than before degradation. More alcohol was required the greater the extent of degradation, and the curve for a mixture fell between the curves for undegraded and degraded DNA, being roughly the average of the two.

In precipitation by ethanol material of high molecular weight is precipitated first, and degraded material is precipitated over a wider range of alcohol concentration, the normal results for the precipitation of polymers, whereas hydrochloric acid first precipitates material of low molecular weight and degraded samples are precipitated over a narrower range of hydrochloric acid concentration. Salt facilitates precipitation in both cases. The mechanisms of the two precipitations are clearly different. With hydrochloric acid it is likely to be due to reduction of the overall charge of the nucleate ions by titration, and it seems that the overall molecular charge density must be greater the greater the size of the molecules. The greater range of ethanol concentration which will precipitate

[1] Mathieson and Porter, *Nature*, 1954, **173**, 1190.
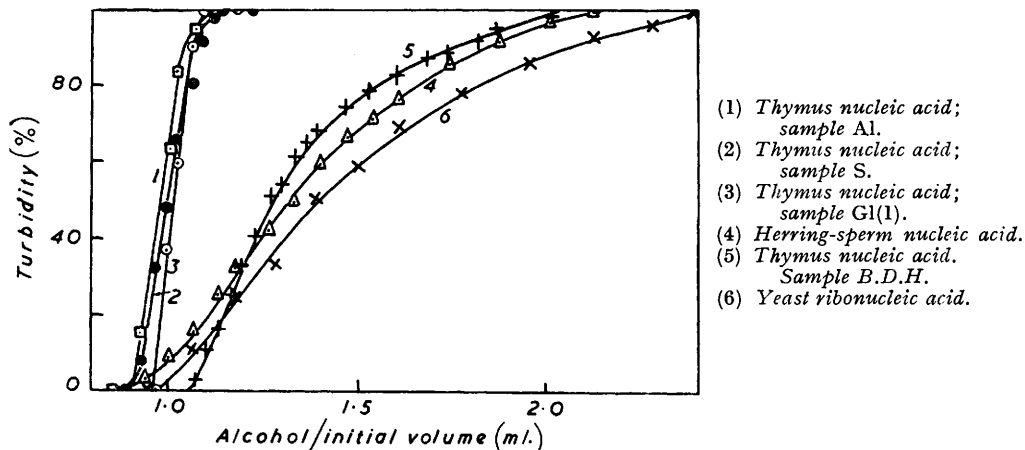[2] Gulland, Jordan, and Threlfall, *J.*, 1947, 1129.
[3] Daly, Allfrey, and Mirsky, *J. Gen. Physiol.*, 1950, **33**, 497.
[4] Sevag, Lackmann, and Smolens, *J. Biol. Chem.*, 1938, **124**, 425.

degraded DNA suggests that degraded is more polymolecular than undegraded DNA. It is hoped to learn more about the mechanism by precipitating synthetic polyelectrolytes under these conditions.

Experimental.—A Spekker photoelectric absorptiometer with a blue filter was used for measuring the optical density of the solutions. Two kinds of cell were used, both permitting titration directly in the cell. The first, used for precipitation by hydrochloric acid, was

Precipitation of different samples of nucleic acid by ethanol in 0·2M-sodium chloride. Concentration 0·072% in 0·2M-sodium chloride.

(1) *Thymus nucleic acid;*
    sample Al.
(2) *Thymus nucleic acid;*
    sample S.
(3) *Thymus nucleic acid;*
    sample Gl(1).
(4) *Herring-sperm nucleic acid.*
(5) *Thymus nucleic acid.*
    Sample B.D.H.
(6) *Yeast ribonucleic acid.*

rectangular, of Perspex. The second, employed for precipitations with alcohol, was cylindrical and was thermostatted at 19°. In all cases precipitant was added dropwise from a micro-burette while the solution was stirred mechanically. It is most important to determine whether the turbid suspensions are stable (*i.e.*, have constant optical density) over a reasonable length of time. An individual experiment took 15—20 min., and reproducibility was attained when the optical density did not alter by more than 25% in 12 hr. Attempts to separate useful quantities of the turbid suspensions from these very dilute solutions (and they flocculate rapidly at higher concentrations) were not successful.

259. *The Electrolytic Determination of Indium.*

By (the late) H. TERREY and J. THABIT.

THIEL[1] used silver electrodes in the quantitative electrodeposition of indium, because platinum was attacked. Kellock and Smith[2] recommended solutions containing Rochelle salt as giving the best results. Dennis and Geer[3] deposited indium from a solution containing pyridine, hydroxylamine, or formic acid; they also stated that no platinum black remained on the cathode after the metal was dissolved. We had determined indium by electrolysis in slightly acid solution, the platinum electrode being protected by prior deposition of copper.

Experimental.—It was found that in almost all cases the platinum cathode was attacked on dissolution of the deposited metal and we could not verify the statement[3] that the use of larger quantities of formic acid avoided the formation of platinum black.

It was found that all the suggested method required rather a long time (a few hours in some cases) to deposit 0·1 g. of indium, and there was no way of checking the end-point of electro-deposition.

To avoid attack of the platinum cathode and achieve conditions under which a few tenths of a gram of indium could be deposited quantitatively in a reasonable time, the following procedure was found satisfactory.

In + Cu found (g.)	Cu added (g.)	In found (g.)	Mean value found	In calc. (g.)	In + Cu found (g.)	Cu added (g.)	In found (g.)	Mean value found	In calc. (g.)
0·0396	0·0148	0·0248			0·1613	0·0372	0·1241		
0·0394	0·0148	0·0246	0·0247	0·0248	0·1610	0·0372	0·1238	0·1239	0·1242
0·0396	0·0148	0·0248			0·1611	0·0372	0·1239		
0·0767	0·0148	0·0619			0·2230	0·0372	0·1858		
0·0767	0·0148	0·0619	0·0619	0·0621	0·2228	0·0372	0·1859	0·1858	0·1863
0·0766	0·0148	0·0618			0·2231	0·0372	0·1859		

A known volume of standard copper sulphate (the copper content of which has been determined electrolytically) is added to indium sulphate solution. As little as 15 mg. of copper in 10 ml. of copper sulphate solution suffices to protect the platinum cathode. The solution is made basic with sodium hydroxide or ammonia, then just enough formic acid is added to make the solution acidic, discharge the blue colour, and redissolve the gelatinous precipitate.

By applying a potential of about 2 v, copper is deposited first; after all the copper has been deposited, the potential is increased to allow a current of 4—5 amp. to carry the indium on to the cathode.

Completion of deposition of indium can be detected by exposing a fresh area of the copper-plated cathode to the solution.

Finally the electrodes are washed repeatedly with distilled water, then with absolute alcohol without interruption of the current. Then the cathode is dried in an electric oven at 110—120°, allowed to cool, and weighed.

Dilute nitric acid is a good solvent for the deposit. If the potential is increased before all the copper has been deposited, a rather dark deposit is obtained, otherwise the deposit is silver-white.

Some typical results are tabulated.

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[1] Thiel, *Z. anorg. Chem.*, 1904, **39**, 119.
[2] Kellock and Smith, *J. Amer. Chem. Soc.*, 1910, **32**, 1248.
[3] Dennis and Geer, *ibid.*, 1904, **26**, 438.

260. *Hydroxyl Stretching Frequencies of Some Analogues of
8-Hydroxyquinoline.*

By F. J. C. ROSSOTTI and HAZEL S. ROSSOTTI.

RUNDLE and PARASOL[1] have found that the hydroxyl fundamental stretching frequency, ν,
of a number of hydrogen-bonded compounds decreases with decreasing length of the
O–H–O bonds. A similar correlation between ν and the estimated O–H–O and O–H–N
distances in several organic reagents for metal ions has been reported by Dyrssen.[2] The
hydroxyl stretching frequency of 8-hydroxyquinoline and a number of its aza-analogues
and related compounds have now been measured in carbon tetrachloride solution. The
results are shown in the Table, together with values of the O–H force constant, k, calculated
by using Hooke's relation for a simple harmonic oscillator.

No.	Reagent, HA	ν (cm.$^{-1}$) (in CCl_4)	$10^{-5}k$ (dyne cm.$^{-1}$)	pK_{OH} * (50% dioxan)	pK_{NH} *
1	8-Hydroxyquinoline (I)	3419	6·59	10·80	4·48
2	8-Hydroxy-2-methylquinoline	3415	6·57	11·01	5·01
3	8-Hydroxycinnoline (II)	3433	6·64	8·84	1·77
4	8-Hydroxy-4-methylcinnoline	3423	6·60	9·00	2·59
5	8-Hydroxyquinazoline (III)	3454	6·57	9·59	3·30
6	8-Hydroxy-2 : 4-dimethylquinazoline	3426	6·61	10·14	3·15
7	8-Hydroxy-4-methyl-2-phenylquinazoline	3435	6·65	10·33	<1
8	5-Hydroxyquinoxaline (IV)	3465	6·77	9·29	<1
9	8-Hydroxy-1 : 6-naphthyridine (V)	3455	6·72	9·16	3·86

* Stoicheiometric values valid for 50% v/v aqueous dioxan containing 0·3M-sodium perchlorate
at 20°. The values for reagent 9 are taken from ref. 4 and those for other reagents from ref. 3.

Although the dimensions of the heterocyclic skeleton are the same for all the reagents
studied, the O–H stretching frequencies vary by as much as 50 cm.$^{-1}$, corresponding to a
difference in force constant of $0·2 \times 10^5$ dynes cm.$^{-1}$. The values of ν, and hence of k,
may be affected (i) by electromeric or inductive effects produced by the ring-nitrogen
atoms or by methyl or phenyl substituents (cf. ref. 5), or (ii) by hydrogen-bonding through
the hydroxyl group, or by a combination of these factors. If the former effects were

(I)   (II)   (III)   (IV)   (V)
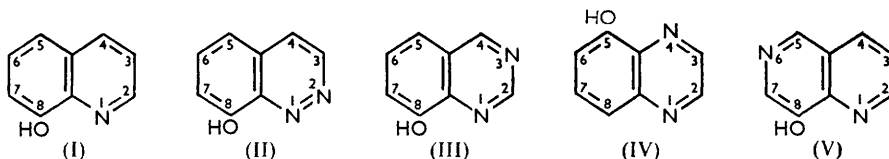
predominant, it might be expected that an increase in ν would be accompanied by an
increase in the value of pK_{OH} ($= \log [HA]/[H^+][A^-]$). However, no such correlation
with pK_{OH} is observed (see Table), and it may be assumed that the influence of electro-
meric and inductive effects on the hydroxyl stretching frequency is obscured by the
formation of hydrogen bonds. Moreover, since the values of ν refer to dilute solution
and are unaffected by changes in concentration, the differences presumably reflect the
differing tendencies of the reagents to form intramolecular O–H–N bonds. Some measure
of the affinity between nitrogen and hydrogen atoms in the various reagents is afforded

[1] Rundle and Parasol, *J. Chem. Phys.*, 1952, **20**, 1487.
[2] D. Dyrssen, *Rec. Trav. chim.*, 1956, **75**, 753.
[3] Irving and H. S. Rossotti, *J.*, 1954, 2910.
[4] H. S. Rossotti, D.Phil. Thesis, Oxford, 1954.
[5] Osborn, Schofield, and Short, *J.*, 1956, 4191.

by the values of pK_{NH} ($= \log [H_2A^+]/[HA][H^+]$) in 50% aqueous dioxan, which are given in the Table. However, exact correlation of the O–H stretching frequency with pK_{NH} could not be expected; not only do these quantities refer to different media, but the former value depends on the force between the hydroxylic-hydrogen atom and the adjacent nitrogen atom, while the latter describes the tendency of a solvated proton to react with the more basic of the two nitrogen atoms, regardless of its position in the ring.

The positions of the basic centres of the hydroxydiazines are uncertain. The suggestion [3] (based on the relative values of pK_{NH} of 8-hydroxycinnoline and its 4-methyl derivative, and on the similarity between the ultraviolet absorption spectra of the

Hydroxyl stretching frequencies in carbon tetra-chloride of analogues of 8-hydroxyquinoline as a function of pK_{NH} *in 50% aqueous dioxan. The numbers of the reagents are those given in the Table.* (X = pK_{NH} < 1.)
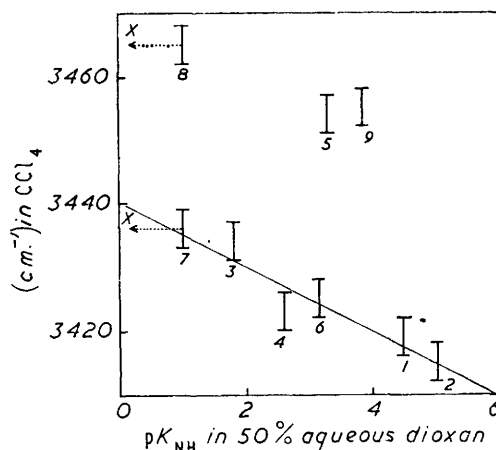
8-hydroxycinnolinium and the 8-hydroxyquinolinium ion) that $N_{(1)}$ is the more basic centre in 8-hydroxycinnoline has recently been questioned.[6] It is probable [5] that the 8-hydroxy-quinazolinium ion is hydrated in aqueous solution, and that the reaction of 8-hydroxy-quinazoline with dilute acid involves addition of hydrogen to both $N_{(1)}$ and $N_{(3)}$. Methyl-ation occurs at $N_{(3)}$ in 8-hydroxyquinazoline,[7] but at $N_{(1)}$ in some 4-substituted quinazol-

(III) + H⁺aq ⇌

ines,[8] and spectrophotometric measurements [3] are compatible with the assignment of $N_{(1)}$ as the more basic centre in 8-hydroxy-2 : 4-dimethyl- and 8-hydroxy-4-methyl-2-phenyl-quinazoline. Results of both methylation [7] and spectrophotometric work [4] suggest that $N_{(6)}$ is the more basic nitrogen atom in 8-hydroxy-1 : 6-naphthyridine. Methylation occurs at $N_{(1)}$ in 5-hydroxyquinoxaline,[7] although the ultraviolet absorption spectra [3] of the 5-hydroxyquinoxalinium and the 8-hydroxyquinolinium ion are very similar.

The relation between hydroxyl stretching frequency and pK_{NH} is shown in the Figure. The reagents fall into two groups, comprising (i) compounds 1, 2, 3, 4, 6, and 7 for which ν lies between 3415 and 3435 cm.⁻¹, and increases almost linearly with decreasing pK_{NH} and (ii) compounds 5, 8, and 9, for which ν lies between 3454 and 3565 cm.⁻¹. Since the

[6] Osborn and Schofield, *J.,* 1956, 4207.
[7] Albert and Hampton, *J.,* 1954, 505.
[8] Morley and Simpson, *J.,* 1948, 360; 1949, 1354.

first group includes 8-hydroxyquinoline and its 2-methyl derivative, the observed correlation between ν and pK_{NH} suggests that the latter value refers to the nitrogen atom adjacent to the hydroxyl group, *i.e.*, that $N_{(1)}$ is the more basic centre in 8-hydroxycinnoline, 8-hydroxy-4-methylcinnoline, and 8-hydroxy-2 : 4-dimethyl- and 8-hydroxy-4-methyl-2-phenyl-quinazoline. The values of ν for the second group of reagents lie about 30 cm.$^{-1}$ above the line through the first set of points indicating that weaker intramolecular O–H–N bonds occur in these compounds. These results are compatible with the observation [7] that methylation of 8-hydroxyquinazoline, 5-hydroxyquinoxaline, and 8-hydroxy-1 : 6-naphthyridine occurs at $N_{(3)}$, $N_{(1)}$, and $N_{(6)}$ respectively, and suggest that the nitrogen atoms adjacent to the hydroxyl groups are not the more basic centres in these reagents.

Experimental.—Commercial samples of 8-hydroxy- and 8-hydroxy-2-methyl-quinoline were recrystallised from ethanol. Pure specimens of reagents 3, 4, 5, 8, and 9 were kindly supplied by Dr. A. Hampton, and of reagents 6 and 7 by Dr. K. Schofield. Commercial carbon tetrachloride was purified as described by Hicks, Hooley, and Stephenson.[9]

Hydroxyl stretching frequencies in carbon tetrachloride solution were measured to ± 3 cm.$^{-1}$ on a Hilger H800 spectrophotometer, with a lithium fluoride prism. The frequency scale was calibrated by using ammonia and carbon dioxide. Each reagent was studied for at least two concentrations in the range 0·01—0·001M, and the values of ν were reproducible within the experimental error. Samples of 8-hydroxy-1 : 5- and 8-hydroxy-1 : 7-naphthyridine (supplied by Dr. Hampton) were too insoluble in carbon tetrachloride to be investigated. The absorption spectra of Nujol mulls of the solid reagents were also measured in the range 1750—650 cm.$^{-1}$, a sodium chloride prism being used and a frequency scale calibrated against carefully fractionated " AnalaR " pyridine.

We are most grateful to Dr. A. Hampton and Dr. K. Schofield for gifts of hydroxydiazines, and to Dr. D. M. W. Anderson for calibrating the spectrophotometer.

[9] Hicks, Hooley, and Stephenson, *J. Amer. Chem. Soc.*, 1944, **66**, 1064.

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261. *A Common Precursor of Conhydrine and* pseudo*Conhydrine.*

By T. R. GOVINDACHARI and S. RAJAPPA.

ROBINSON [1] has pointed out that the formation in Nature of conhydrine and *pseudo*-conhydrine which are derivatives of coniine carrying a hydroxyl group at a β-position to the nitrogen, suggests a kind of oriented oxidation. It appeared likely that a laboratory analogy could be furnished by the rearrangement of 2-*n*-propylpyridine 1-oxide, since it has been reported by Berson and Cohen [2] that 4-picoline 1-oxide on rearrangement yields a mixture of 4-pyridylmethanol and 3-hydroxy-4-picoline. It has now been found that rearrangement of 2-*n*-propylpyridine 1-oxide yields a mixture containing 2-1'-hydroxy-propylpyridine (49%) and 5-hydroxy-2-propylpyridine (2·5%). The structure of the former product was proved by reduction to ($\pm$)-conhydrine and comparison with an authentic sample.[3] The structure of the latter rests on positive colour reactions with ferric chloride and Folin–Denis reagent, the ultraviolet absorption spectrum exhibiting characteristic shifts in the maxima in neutral, acidic, and alkaline media expected for β-hydroxypyridines,[4] non-identity with 3-hydroxy-2-propylpyridine,[5] and agreement in

[1] Sir Robert Robinson, " The Structural Relations of Natural Products," Oxford, 1955, p. 64.
[2] Berson and Cohen, *J. Amer. Chem. Soc.*, 1955, **77**, 1281.
[3] Galinovsky and Mulley, *Monatsh.*, 1948, **79**, 426.
[4] Specker and Gawrosch, *Ber.*, 1942, **75**, 1338; Govindachari and Narasimhan, *J.*, 1953, 2635.
[5] Gruber, *Canad. J. Chem.*, 1953, **31**, 564.

melting point with 5-hydroxy-2-propylpyridine prepared by other methods.[6] Since the last compound has been reduced [6] to *pseudo*conhydrine, the present work constitutes yet another synthesis of the alkaloid.

Experimental.—2-*Propylpyridine* 1-*oxide.* 2-Propylpyridine [7] (5 g.) in acetic acid (25 ml.) containing 30% hydrogen peroxide (5 ml.) was heated at 70° for 3 hr. More hydrogen peroxide (3 ml.) was added and the mixture left at 70° for a further 12 hr. The solution was evaporated *in vacuo* with repeated additions of water to remove the last traces of acetic acid and hydrogen peroxide. The residual liquid in chloroform was treated with an aqueous paste of potassium carbonate. Filtration after 16 hr. and evaporation of the solvent, followed by vacuum-distillation of the residual oil, gave 2-*propylpyridine* 1-*oxide* (4 g.), b. p. 102°/2 mm. (Found: C, 69·8; H, 7·8. $C_8H_{11}ON$ requires C, 70·1; H, 8·0%).

Rearrangement of the N-*oxide.* The oxide (3·9 g.) was refluxed for 1 hr. with acetic anhydride (20 ml.). The acetic anhydride was then distilled off *in vacuo*, and the residue transferred to a Vigreux flask and distilled at 2 mm., all the distillable liquid (3·9 g.) being collected. The total distillate was heated on a steam-bath for ½ hr. with potassium hydroxide (5 g.) in water (60 ml.) and alcohol (40 ml.) and left overnight at 30°. Next morning the alcohol was removed *in vacuo*, and the aqueous alkaline solution repeatedly extracted with chloroform. Evaporation of the dried (Na_2SO_4) extract and distillation gave the non-phenolic material (1·9 g.), b. p. 114°/15 mm. The residual aqueous alkaline solution was just acidified with concentrated hydrochloric acid, basified with ammonia, and thoroughly extracted with chloroform. Evaporation of the dried (Na_2SO_4) extract left the phenolic portion (150 mg.) as an oil.

(*a*) The phenolic portion: Sublimation at 150°/2 mm., followed by crystallisation from ether–light petroleum (b. p. 40—60°), gave 5-hydroxy-2-propylpyridine (100 mg.), m. p. 92—93° (Found: C, 70·2; H, 7·7. Calc. for $C_8H_{11}ON$: C, 70·1; H, 8·0%), $\lambda_{max.}$ (in EtOH), 285 mμ (log ε 3·41); (in EtOH–HCl), 295 mμ (log ε 3·60); (in EtOH–KOH), 310 mμ (log ε 3·42).

(*b*) The non-phenolic portion: This (1·9 g.) in N-hydrochloric acid (20 ml.) was hydro-genated at 55 lb. per sq. in., after addition of Adams catalyst (0·2 g.). The solution was then filtered, concentrated to a small volume (5 ml.), basified with sodium hydroxide solution, and repeatedly extracted with ether. The dried (Na_2SO_4) extract was distilled, the fraction boiling at 120°/20 mm. being collected. Recrystallisation from ether afforded ($\pm$)-conhydrine (0·8 g.), m. p. and mixed m. p. 99—100° (Found: C, 67·4; H, 11·6. Calc. for $C_8H_{17}ON$: C, 67·1; H, 11·9%).

We are grateful to Mr. S. Selvavinayakam for the analyses and to the Government of India for the award of a senior research scholarship (to S. R.).

Presidency College, Madras, India.

[6] Gruber and Schlögl, *Monatsh.*, 1949, **80**, 499; Marion and Cockburn, *J. Amer. Chem. Soc.*, 1949, **71**, 3402.

[7] Brown and Murphey, *ibid.*, 1951, **73**, 3308.

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262. *Ring Expansion. Part III.*[1] *The Isomerisation of Dibenzylidene Derivatives of* cyclo*Hexanones.*
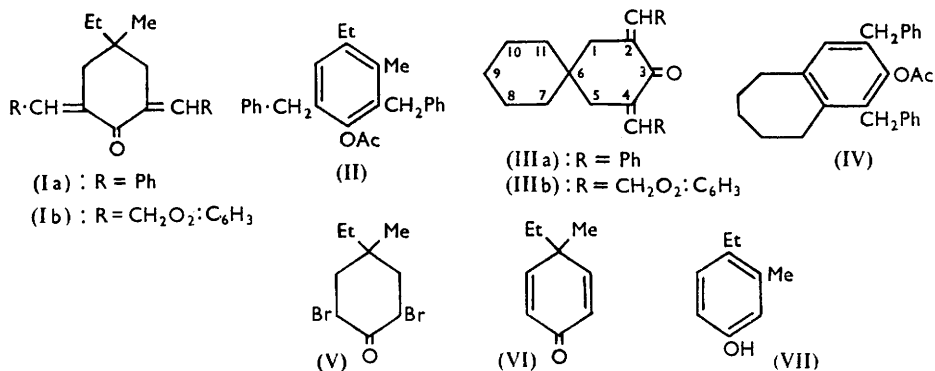
By R. H. Burnell.

The aromatisation of the dibenzylidene derivatives of *cyclo*hexanones was extended by Leonard and Robinson [2] to *cyclo*heptane-1 : 2-dione. Since this reaction appears to be related to the dienone–phenol isomerisation it was of interest to test its applicability to 4 : 4-disubstituted *cyclo*hexanone derivatives since aromatisation in such cases would

[1] Part II, *J.*, 1957, 3307.

[2] Leonard and Robinson, *J. Amer. Chem. Soc.*, 1952, **74**, 2143.

necessitate migration of one of the substituents. The benzylidene derivatives of 4-ethyl-4-methyl*cyclo*hexanone (Ia) and *spiro*[5 : 5]undecan-3-one (IIIa) were prepared and, on subjection to the reaction conditions employed by Leonard and Robinson,[2] gave products which from their infrared and ultraviolet spectra were aryl acetates. In the case of the *spiro*-compound (IIIa) there could be no ambiguity as to the structure of the product (IV), which was characterised by hydrolysis to the phenol and the preparation of a 3 : 5-dinitrobenzoate. The dibenzylidene derivative of 4-ethyl-4-methyl*cyclo*hexanone (Ia) on the other hand may have given a 3-ethyl-4-methylphenyl acetate rather than the isomer (II).

Arnold and Buckley[3] presented some evidence favouring a mechanism of pinacol–pinacone type for the dienone–phenol rearrangement but in the example cited (1 : 4-dihydro-4-methyl-1-oxo-4-phenylnaphthalene ⟶ 4-methyl-3-phenyl-1-naphthol) steric effects cannot be ignored. A simple case of the reaction was investigated, to compare the migratory aptitudes of methyl and ethyl groups in the dienone–phenol transformation. Dehydrobromination of the dibromo-ketone (V) afforded 4-ethyl-4-methyl*cyclo*hexa-

(Ia) : R = Ph
(Ib) : R = CH$_2$O$_2$:C$_6$H$_3$

(II)

(IIIa) : R = Ph
(IIIb) : R = CH$_2$O$_2$:C$_6$H$_3$

(IV)

(V)

(VI)

(VII)

2 : 5-dienone (VI) which was aromatised in acetic anhydride containing sulphuric acid. The hydrolysed product from the rearrangement was shown by analysis and spectral evidence to be a phenol isomeric with the ketone (VI). A sample of 3-ethyl-4-methyl-phenol was prepared from *m*-cresol acetate by low-temperature Fries rearrangement[4] and subsequent Clemmensen reduction:[5] comparison of it with the phenol obtained from the rearrangement of (VI) left no doubt as to their identity. The 3 : 5-dinitrobenzoates melted sharply at 130° alone or on admixture.

By analogy it can be assumed that the product obtained from the aromatisation of the ketone (Ia) is 2 : 6-dibenzyl-4-ethyl-3-methylphenyl acetate (II).

Dipiperonylidene*cyclo*hexanones were also prepared from *cyclo*hexanone, 4-ethyl-4-methyl*cyclo*hexanone and *spiro*[5 : 5]undecan-3-one. Under the conditions efficacious with the dibenzylidene derivatives, the first-mentioned dipiperonylidene derivative gave a low yield of an aryl acetate but in the other two cases only starting material was isolated, even when more vigorous conditions were employed.[6]

Experimental.—Ultraviolet spectra are for EtOH solutions unless otherwise stated.

Diarylidenes. The preparation is exemplified by the following: *spiro*[5 : 5]Undecan-3-one [7] (4·2 g.), piperonaldehyde (15 g.), and piperidine (5 c.c.) were refluxed for 6 hr. in absolute

[3] Arnold and Buckley, *J. Amer. Chem. Soc.*, 1949, **71**, 1781.
[4] Rosenmund and Schnurr, *Annalen*, 1928, **460**, 56.
[5] von Auwers and Mauss, *ibid.*, p. 240.
[6] Weiss and Ebert, *Monatsh.*, 1935, **65**, 399.
[7] Burnell and Taylor, *J.*, 1954, 3486.

ethanol (50 c.c.). Cooling and dilution with water gave yellow needles, m. p. 203° (from ethanol). Yields were usually high (*ca.* 80%) (see Table).

Compound	M. p.	Calc. (%)			Found (%)			$\lambda_{max.}$ ‡ (ε)	ν(C=O) (cm.$^{-1}$)
		C	H	O	C	H	O		
(Ia)	108°	87·3	7·7	5·1	86·7	7·7	5·1	233 (14,010), 324 (23,700)	1668 †
(IIIa)	183	87·7	7·7	4·7	87·8	7·7	4·6	233 (15,700), 322 (22,300)	1668 †

Dipiperonylidene derivatives:

From *cyclo*hexanone	189	72·9	5·0	22·1	72·7	5·0	22·0	261 (15,700), 371 (31,000) *	1665 †
(Ib)	184	74·2	6·0	19·8	74·0	6·0	19·9	261 (15,400), 370 (24,900) *	1666 †
(IIIb)	203	75·5	6·1	18·6	75·5	6·3	18·7	257 (15,500), 370 (24,800) *	1664 †

　　　　* Measured in CHCl₃.　　　　† KBr mull.　　　　‡ In mµ.

Aryl acetates. The method was essentially that of Leonard and Robinson,[2] *e.g.*: the dibenzylidene derivative (Ia) (1·0 g.), acetic anhydride (3 c.c.), and acetic acid saturated with dry hydrogen bromide (5 c.c.) were mixed and kept at 65° for 15 hr. After cooling, the mixture was diluted with water and extracted with ether. The ethereal solution was washed free from acid, evaporated, and dried (Na₂SO₄), giving a dark yellow residue (0·91 g.) which was purified by evaporative distillation. The product, b. p. 248° (0·70 g.), had $\lambda_{max.}$ 307 mµ (ε 8000) and ν(C=O) 1760 cm.$^{-1}$ (and 1195 cm.$^{-1}$) (Found: C, 83·4; H, 7·5. C₂₅H₂₆O₂ requires C, 83·8; H, 7·3%).

1′ : 3′-Dibenzyl-2′-hydroxybenzocyclohephene (IV; R = H). The isomerisation product from the spiran (IIIa) was refluxed in 5% ethanolic potassium hydroxide (50 c.c.) for 4 hr. Dilution with water and ether-extraction furnished an oil, b. p. 285°, $\lambda_{max.}$ 288 mµ (ε 4610) and OH stretching band at 3470 cm.$^{-1}$ (no carbonyl absorption). Its 3 : 5-*dinitrobenzoate*, prepared in pyridine, had m. p. 158° (from ethanol) (Found: C, 71·6; H, 5·3. C₃₂H₂₈O₆N₂ requires C, 71·6; H, 5·3%).

2 : 6-Dibromo-4-ethyl-4-methylcyclohexanone (V). To a cooled solution of 4-ethyl-4-methyl-*cyclo*hexanone (2·8 g.) in acetic acid (15 c.c.) was added bromine (6·4 g.) in acetic acid (15 c.c.). Hydrobromic acid (3 c.c.) was added and the solution set aside for 4 hr. Dilution with water and ether-extraction gave a yellow oil (5·51 g.) which crystallised (m. p. 74°) from light petroleum (Found: C, 36·7; H, 4·6; Br, 53·5. C₉H₁₄OBr₂ requires C, 36·3; H, 4·7; Br, 53·7%).

4-Ethyl-4-methylcyclohexa-2 : 5-dien-1-one (VI). The dibromo-compound (VI) (3·0 g.) was refluxed in collidine (10 c.c.) for 4 min. The usual working up afforded a brown oil (1·25 g.) which was purified by chromatography over alumina. Elution with light petroleum (b. p. 60—80°) gave the dienone as a pale oil (1·01 g.), $\lambda_{max.}$ 234 mµ (ε 10,500), characterised as the unstable dark red 2 : 4-*dinitrophenylhydrazone*, m. p. 131° (from chloroform–ethanol), $\lambda_{max.}$ 256 and 390 mµ (ε 24,000 and 49,700 respectively) (Found: N, 17·8. C₁₅H₁₆O₄N₄ requires N, 17·7%).

3-Ethyl-4-methylphenol (VII). To the dienone (0·91 g.) in acetic anhydride (10 c.c.) was added sulphuric acid (3 drops) in acetic anhydride (3 c.c.). After 12 hr. water was added and the mixture kept in the cold overnight. Ether-extraction gave a yellow oil (0·77 g.) from which the phenol was obtained by alkaline hydrolysis; it had b. p. 226—228°, $\lambda_{max.}$ 286 mµ (ε 1600), and gave a 3 : 5-*dinitrobenzoate*, m. p. 130° (from ethanol) (Found: C, 57·9; H, 4·3; N, 8·4. C₁₆H₁₄O₆N₂ requires C, 58·2; H, 4·3; N, 8·5%). Admixture with an authentic sample (see text) of 3-ethyl-4-methylphenyl 3 : 5-dinitrobenzoate (m. p. 130°) caused no depression in the m. p. and the infrared spectra of the phenols were identical.

The author is indebted to Mr. D. Taylor for technical assistance and to Mr. A. W. Sangster for the infrared spectra.

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MONA, ST. ANDREW, JAMAICA, B.W.I.　　　　[*Received, November 15th, 1957.*]

263. *A Short Synthesis of 3-Methylfuran.*

By J. W. Cornforth.

Several 3-monosubstituted furans have been recognized among natural products, but only two 3-monoalkylfurans, 3-methyl-[1] and 3-*iso*propyl-furan,[2] have been synthesized; and these always by removal of other substituents from an existing furan ring. The overall yields are uniformly bad.

3 : 4-Epoxy-3-methylbutanal diethyl acetal (I; R = Me) is now readily available[3] from the reaction of 2-methylallyl chloride with magnesium and ethyl orthoformate, followed by oxidation of the product by perphthalic acid. Boiling this epoxy-acetal with
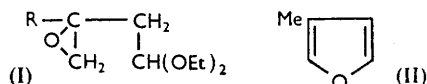
0·1N-sulphuric acid gave 3-methylfuran (II) in 57% yield. Acetic acid (0·5N) seemed to be somewhat less effective than the mineral acid. More than one mode of cyclization could be postulated, and more than one may actually operate.

2-Methylallyl chloride is exceptional among 2-substituted allyl halides in being available commercially; a useful general synthesis of 3-monosubstituted furans based on this cyclization must await general methods for preparing substances of type (I).

Experimental.—3 : 4-Epoxy-3-methylbutanal diethyl acetal (10 g.) and 0·1N-sulphuric acid (1 l.) were heated under a fractionating column for 3 hr., the *methylfuran* and ethanol being removed intermittently by distillation. The distillate was washed once with half-saturated aqueous calcium chloride (20 ml.) and twice with a little saturated aqueous ammonium chloride, dried by boiling with sodium, and redistilled, to give 3-*methylfuran* (2·7 g.), b. p. 65—65·5°/749 mm., n_D^{19} 1·4330 (Found: C, 73·2; H, 7·4. C_5H_6O requires C, 73·1; H, 7·3%). (This appears to be the first published analysis of synthetic 3-methylfuran.) The refractive index is higher than that given by Asahina[4] (n_D^{18} 1·4255). The pine-splinter test and the colours with vanillin in hydrochloric acid were as recorded.[4] With an Ehrlich's reagent made from *p*-dimethylaminobenzaldehyde (0·2 g.), acetic acid (9·5 ml.), and hydrochloric acid (0·5 ml.),[5] 3-methylfuran in acetic acid gave a pink colour slowly changing (more rapidly with excess of reagent or more hydrochloric acid) to intense green. Furan treated similarly gave, more slowly, an orange-pink colour changing to green.

National Institute for Medical Research,
London, N.W.7.

[1] Reichstein and Zschokke, *Helv. Chim. Acta*, 1931, **14**, 1270; Rinkes, *Rec. Trav. chim.*, 1931, **50**, 1127; Gilman and Burtner, *J. Amer. Chem. Soc.*, 1933, **55**, 2903.

[2] Gilman, Calloway, and Burtner, *ibid.*, 1935, **57**, 906.

[3] Cornforth and Firth, *J.*, 1091.

[4] Asahina, *Acta Phytochim.*, 1924, **2**, 1; *Chem. Zentr.*, 1924, II, 1694.

[5] Morgan and Elson, *Biochem. J.*, 1934, **28**, 988.

264. Preparation of Ketones by Cleavage of 2 : 4-Dinitrophenyl-hydrazones.

By N. M. Cullinane and B. F. R. Edwards.

2 : 4-Dinitrophenylhydrazones are frequently used for the characterization of ketones. In particular o-hydroxy-ketones, prepared, for example, by the Fries reaction, tend to be oils and can be determined quantitatively in this way.[1] Regeneration of the initial ketones is thus a matter of considerable interest, and a number of such preparations, including those of o- and p-hydroxy-ketones, have now been carried out, with very good yields.

Recent methods for the recovery of ketones include treatment of the dinitrophenyl-hydrazones with formic acid and copper carbonate,[2] and with acid stannous chloride.[3]

Experimental.—2-*Hydroxy-3-methylacetophenone.* The 2 : 4-dinitrophenylhydrazone [4] (4 g.) was boiled with acetone (500 c.c.) under reflux until a clear solution resulted. Stannous chloride dihydrate in concentrated hydrochloric acid (80 c.c.) and water (120 c.c.) was introduced at once and refluxing continued (for time see Table). The solution was then cooled and made alkaline with 2N-sodium hydroxide. The acetone was removed on a water-bath; excess of concentrated hydrochloric acid was added to the cooled product, which was then distilled with steam. The ketone was extracted from the steam-distillate with benzene and purified in the usual way; it had b. p. 107°/12 mm.[5] The quantity of stannous chloride and the duration of the reaction are seen from the Table to have a considerable influence on the yields.

Time (min.)	65	45	30	20	30	30	30	30	30
$SnCl_2,2H_2O$	10	10	10	10	4	5	6	6·5	7
Yield (%)	8·5	25	55	23	15	45	70	81	70

Benzophenone. The dinitrophenylhydrazone was not very soluble in acetone and the yields obtained in this solvent were not very good. Substituting acetic acid improved the yields. The hydrazone (4 g.) in hot glacial acetic acid (400 c.c.) was treated with stannous chloride (13 g.) in concentrated hydrochloric acid (80 c.c.) and water (120 c.c.) and boiled for 1 hr. Excess of 2N-sodium hydroxide was added to the cooled product, and the ketone driven over with steam and purified (yield, 88%). When stannous chloride (a) (20 g.) and (b) (13 g.) was used and the refluxing continued for 30 min. the yields were 19% and 23% respectively.

Acetophenone. The dinitrophenylhydrazone, m. p. 236°, was treated as was the derivative of benzophenone except that heating was for only 30 min. Distillation with steam, etc., gave a 95% yield of ketone.

o-*Hydroxybenzophenone.* The m. p. of the 2 : 4-dinitrophenylhydrazone is given as 250—251° by Johnson;[6] we obtained brick-red plates (from ethyl acetate), m. p. 260° (Found: C, 59·6; H, 3·9; N, 14·7. Calc. for $C_{19}H_{14}O_5N_4$: C, 60·3; H, 3·7; N, 14·8%); the compound was heated as just described, for 1 hr.; excess of sodium hydrogen carbonate was added to the cooled product which was then distilled with steam, giving a 73·5% yield of o-hydroxybenzo-phenone,[7] m. p. 39°.

2-*Hydroxy-5-methylacetophenone.* The dinitrophenylhydrazone [6, 8] was boiled under reflux for 30 min. with the same quantities of reactants as above (when the acetic acid was replaced by acetone the yield of ketone was considerably reduced). Addition of sodium hydrogen carbonate and distillation with steam gave an 80% yield of the hydroxy-ketone,[9] m. p. 50°.

p-*Hydroxybenzophenone.* The dinitrophenylhydrazone, brick-red needles (from aqueous alcohol [10]), m. p. 240° (Found: C, 60·1; H, 3·7; N, 14·4. Calc. for $C_{19}H_{14}O_5N_4$: C, 60·3; H,

[1] Cullinane, Evans, and Lloyd, *J.*, 1956, 2222.
[2] Robinson, *Nature*, 1954, **173**, 541.
[3] Demaecker and Martin, *Nature*, 1954, **173**, 266.
[4] Cullinane, Lloyd, and Tudball, *J.*, 1954, 3894.
[5] Anschütz and Scholl, *Annalen*, 1911, **379**, 342.
[6] Johnson, *J. Amer. Chem. Soc.*, 1951, **73**, 5888.
[7] Winkler, *Arch. Pharm.*, 1928, 48.
[8] Cullinane and Edwards, *J.*, 1957, 3018.
[9] von Auwers and Müller, *Annalen*, 1909, **364**, 147.
[10] Pallares and Garza, *Arch. Inst. Cardiol. Mexico*, 1947, **17**, 833.

3·7; N, 14·8%), was treated in the same way as the o-hydroxy-derivative, except that the product, after addition of sodium hydrogen carbonate, was extracted with benzene, and the solution shaken with 2N-sodium hydroxide. Distillation with steam removed traces of benzene, and acidification of the alkaline solution with concentrated hydrochloric acid precipitated the ketone as colourless needles (93·5%), m. p. 135°.[11]

p-*Hydroxyacetophenone.* The 2 : 4-dinitrophenylhydrazone,[12] deep red prisms (from alcohol), m. p. 269° (Found: C, 53·4; H, 3·8; N, 18·0. Calc. for $C_{14}H_{12}O_5N_4$: C, 53·1; H, 3·8; N, 17·7%), treated as described for the benzophenone derivative, gave a product from which the acetic acid was removed in steam; the residue was extracted with benzene, and the extract shaken with 2N-sodium hydroxide. Acidification of the alkaline solution with concentrated hydrochloric acid gave colourless needles (65·9%), m. p. 108°.[13]

p-*Hydroxybutyrophenone.* In the same way the 2 : 4-dinitrophenylhydrazone,[12] red prisms (from alcohol), m. p. 223° (Found: C, 56·0; H, 4·9; N, 16·2. Calc. for $C_{16}H_{16}O_5N_4$: C, 56·0; H, 4·7; N, 16·3%), gave the hydroxy-ketone,[14] colourless needles (96·8%), m. p. 91°.

Yields in the above experiments were accurately determined by reconversion of the ketones into their 2 : 4-dinitrophenylhydrazones.

One of us (B. F. R. E.) thanks the University of Wales for a Post-Graduate Studentship.

UNIVERSITY COLLEGE, CATHAYS PARK, CARDIFF.

[11] Fischer, *Ber.*, 1909, **42**, 1017.
[12] Dutton, Briggs, Brawn, and Powell, *Canad. J. Chem.*, 1953, **31**, 837.
[13] Mozingo, *Org. Synth.*, 1941, **2**, 45.
[14] Perkin, *J.*, 1889, **55**, 546.

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265. 8-*Aminoisoquinoline: A Correction.*

By K. SCHOFIELD.

RECENTLY[1] the basic strengths of *iso*quinoline (pK_a 5·40) and 8-amino*iso*quinoline (pK_a 6·06) were correctly reported, but ΔpK_a for the pair was given as 1·66 (Ref. 1, Table 2) instead of 0·66. 8-Amino*iso*quinoline would be expected to be appreciably stronger than its parent base because of the possibility of resonance in its cation involving o-quinonoid forms. In fact ΔpK_a for 8-amino*iso*quinoline is smaller than ΔpK_a (0·80)[1] for 7-amino*iso*quinoline, an isomer from which the additional possibilities for resonance are absent. The pair of isomers, 8- and 7-amino*iso*quinoline (ΔpK_a 0·66 and 0·80) is thus analogous to the pair, 5- and 6-aminoquinoline (ΔpK_a 0·52 and 0·69), and both cast doubt on the significance of o-quinonoid resonance forms. It is significant that the infrared N–H force constants are lower than expected[1] in both 8-amino*iso*quinoline and 5-aminoquinoline.

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[1] Osborn, Schofield, and Short, *J.*, 1956, 4191.