Degradation of Cobaloximes to Derivatives of Imidazo[1,2-*a*]pyridine

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Acetic anhydride in pyridine degrades several alkylcobaloximes to 2-[(*E*)-1-acetoxyiminoethyl]-3-acetylimidazo-[1,2-*a*]pyridine (5), the structure of which is established by direct *X*-ray crystallographic analysis of 3-acetyl-2-[(*E*)-1-hydroxyiminoethyl]imidazo[1,2-*a*]pyridine (6) derived from compound (5) by mild hydrolysis. Treatment of compound (6) with nitric acid gives 3-acetyl-2-(1,1-dinitroethyl)imidazo[1,2-*a*]pyridine (11). Spectroscopic properties of compounds (5), (6), and (11) confirm the assigned structures. Experiments concerning the mechanism of formation of compound (5) are reported, and the generality of the described degradation is indicated.

Compound (6) is orthorhombic, space group *Pbca*, with $a = 16{\cdot}402(10)$, $b = 13{\cdot}463(10)$, $c = 9{\cdot}735(10)$ Å, $Z = 8$. The structure was solved by direct methods and refined to R 0·089 for 520 observed reflections measured by diffractometer.

FOR our studies[1] of the solvolytic chemistry of 2-acetoxyalkylcobaloximes,† compounds (1) and (2) were initially prepared by acetylation of the 2-hydroxyalkylcobaloximes (3) and (4), respectively, with an excess of acetic anhydride in pyridine. This gave a high yield (>90%) of (2) from (4) after 13 h at room temperature. However, after 9 days at room temperature (or 2 days at 60°) (2) had vanished, and a new compound had accumulated [30% yield based on (4)]. Preliminary analytical and spectral studies indicated that the new substance was a cobalt-free, heteroaromatic compound. Since it was likely that a major structural change of mechanistic interest had occurred, we have rigorously identified the new compound as 2-[(*E*)-1-acetoxyiminoethyl]-3-acetylimidazo[1,2-*a*]pyridine (5). The identification rests on a spectroscopic examination of (5) and its degradation products and on an *X*-ray crystallographic study of the oxime (6), formed by mild alkaline hydrolysis of (5).[3] Treatment of the alkyl-(γ-picoline)cobaloxime (7) with acetic anhydride in γ-picoline gives a homologue (8), pointing to the generality of the described degradation for appropriate pyridine derivatives of cobaloximes.

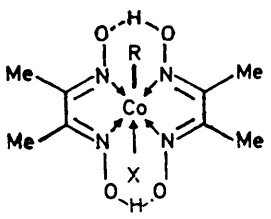
† Alkyl(base)cobaloximes are bis(dimethylglyoximato)cobalt complexes with an alkyl group and a Lewis base as axial ligands (for reviews of their chemistry see ref. 2).

[1] B. T. Golding, H. L. Holland, U. Horn, and S. Sakrikar, *Angew. Chem. Internat. Edn.*, 1970, **9**, 959; B. T. Golding and S. Sakrikar, *J.C.S. Chem. Comm.*, 1972, 1183.

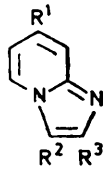
[2] See *e.g.* G. N. Schrauzer, *Accounts Chem. Res.*, 1968, **1**, 97; D. Dodd and M. D. Johnson, *J. Organometallic Chem.*, 1973, **52**, 1.

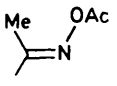
[3] Preliminary report, N. W. Alcock, B. T. Golding, D. R. Hall, and U. Horn, *J. Amer. Chem. Soc.*, 1972, **94**, 8610.

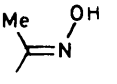
Evidence bearing on the mechanism of formation of (5) is presented and discussed.

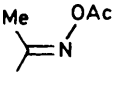


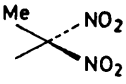
	R	X
(1)	$CH_2{\cdot}CH_2{\cdot}OAc$	pyridine
(2)	$CH_2{\cdot}CHMe{\cdot}OAc$	pyridine
(3)	$CH_2{\cdot}CH_2{\cdot}OH$	pyridine
(4)	$CH_2{\cdot}CHMe{\cdot}OH$	pyridine
(7)	$CH_2{\cdot}CHMe{\cdot}OH$	γ-picoline
(14)	Br	pyridine
(15)	Me	pyridine
(17)	•	pyridine

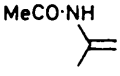


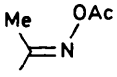
(5) R^1 = H, R^2 = COMe, R^3 = 

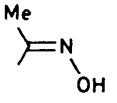
(6) R^1 = H, R^2 = COMe, R^3 = 

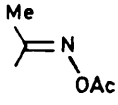
(8) R^1 = Me, R^2 = COMe, R^3 = 

(11) R^1 = H, R^2 = COMe, R^3 = 

(16) R^1 = H, R^2 = COMe, R^3 = 

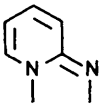
(18) R^1 = H, R^2 = H, R^3 = 

(19) R^1 = H, R^2 = H, R^3 = 

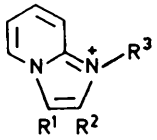
(20) R^1 = H, R^2 = H, R^3 = 

RESULTS AND DISCUSSION

Spectroscopic Examination of Compound (5) *and its Degradation Products.*—The n.m.r. spectrum of (5) (Figure 1) shows a total of 13 protons, consistent with the analytical data ($C_{13}H_{13}N_3O_3$). The three high-field singlets are from methyl groups [COMe (δ 2·64), MeC=N (δ 2·57), and $MeCO_2$ (δ 2·27)]. A first-order analysis of the 4 low-field protons is included in Figure 1 and points to the presence of a pyridinimine system (9). This conclusion was verified by comparison with literature data [4] and with a readily available [5] model compound (10). Although there is a close correspondence between the coupling constants of the ring protons of (5) and (10), the chemical shifts of these protons are different (see Experimental section). In particular H-5 in (10) resonates at δ 8·40 (an unexceptional position for an α-proton on a pyridine ring), yet H-5 in (5) resonates at much lower field (δ 9·69). This effect is also seen in (6), but not in the degradation product (11) [from treating (6) with nitric acid], which shows the H-5 signal at δ 8·91. The deshielding effect of a *peri*-carbonyl group is well documented.[6] Hence, the unusual chemical shift of H-5 in (5) and (6) could be due to the proximity of a carbonyl function, a conclusion supported by comparison with the model compounds (12) and (13).[7] These compounds



(9)



(10) R^1 = O⁻, R^2 = COMe, R^3 = $PhCH_2$

(12) R^1 = $ClCH_2CO$, R^2 = O⁻, R^3 = $PhCH_2$

(13) R^1 = $ClCH_2CO$, R^2 = O⁻, R^3 = Me

both show an H-5 signal at δ *ca.* 9·98. The presence of a carbonyl function in (5) and (6) was indicated by C=O stretching absorptions at *ca.* 1640 cm^{-1}, n.m.r. spectra [see above for (5), below for (6)], a positive iodoform test with (6), and an exchange experiment. Thus, on dissolution in NaOD–D_2O the three-proton signal at δ 2·55 in the n.m.r. spectrum of (6) disappeared ($t_{\frac{1}{2}}$ 1·3 min at 37°) while the other signals (except that due to OH) were unchanged. Selective exchange of the acetyl protons in butane-2,3-dione mono-oxime has been reported [8] and under our conditions proceeds with $t_{\frac{1}{2}}$ 3 min.

The presence of the grouping MeC=N–OAc in (5) was inferred from i.r. data (acetyl C=O stretch at 1775 cm^{-1}), n.m.r. data (see above), mass spectral data (loss of OAc from molecular ion), and its ready hydrolysis. The last caused difficulties in the isolation and purification of (5) and it was found easier to examine (6), the product from hydrolysis of (5) with methanolic sodium methoxide. The spectral properties of (6) are similar to those of (5) except that, as expected, it lacks *O*-acetyl absorptions and possesses hydroxy-absorptions. The presence of the function MeC=N–OH was also suggested by its mass spectrum (prominent loss of OH from molecular ion) and the selective conversion in high yield of this grouping into a geminal dinitro-function [in compound (11)] by treatment with nitric acid.[9]

From the information described so far structure (5) could be derived. But several other structures were conceivable. U.v. data and extensive mass spectral data for compounds (5), (6), and (11) were of little help and even misleading (the u.v. absorptions were quite unlike those for imidazo[1,2-*a*]pyridine [10]). As noted above, H-5 in (11) in contrast to H-5 in (5) resonates at δ 8·91, and we felt at the time that this observation was inconsistent with structures such as (5). We were attracted to

[4] W. W. Paudler and H. L. Blewitt, *Tetrahedron*, 1965. **21**, 353.
[5] A. Lawson and D. H. Miles, *J. Chem. Soc.*, 1959, 2865.
[6] R. M. Acheson and D. A. Robinson, *J. Chem. Soc.* (*C*), 1968, 1633.
[7] W. K. Anderson and A. E. Friedman, *Canad. J. Chem.*, 1971, **49**, 668.
[8] R. L. Beach, *Tetrahedron Letters*, 1972, 1913.
[9] *Cf.* J. R. Bull, Sir E. R. H. Jones, and G. D. Meakins, *J. Chem. Soc.*, 1965, 2601.
[10] J. G. Lombardino, *J. Org. Chem.*, 1965, **30**, 2403.

structures in which the hydroxyimino-grouping could be near H-5, thus causing the observed deshielding. It was argued that the conversion (6) ⟶ (11), involving a gross structural change in the vicinity of H-5, would be expected to alter its chemical shift appreciably. The solution to this dilemma was only apparent after an *X*-ray crystallographic study of (6).

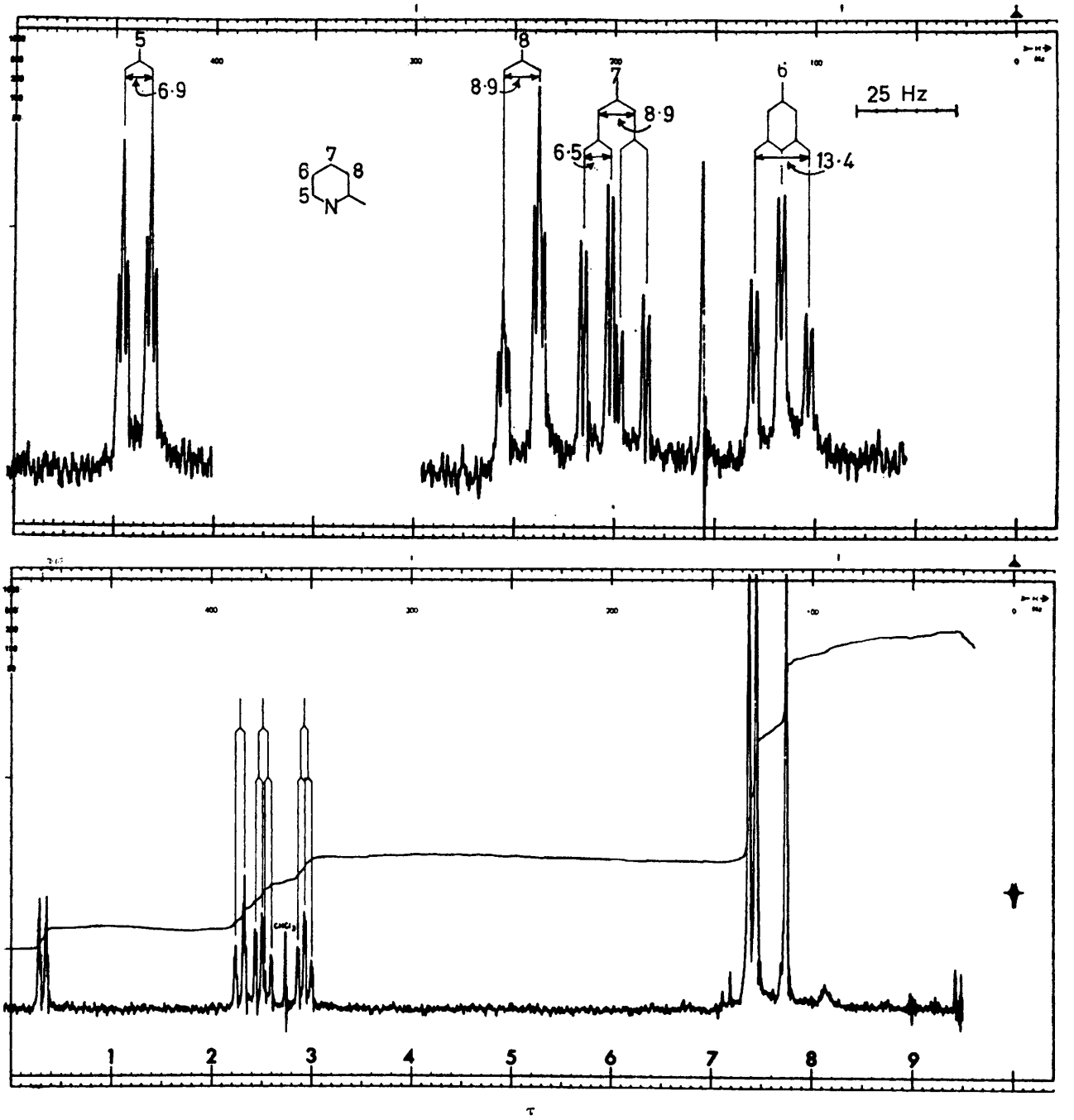


FIGURE 1 N.m.r. spectrum of compound (5)

Crystal Structure of Compound (6).—An *X*-ray crystallographic study shows (6) to be 3-acetyl-2-[(*E*)-(1-hydroxyiminoethyl)imidazo[1,2-*a*]pyridine and the structures of (5) and (11) follow from consideration of the chemical data (see previous section). Figure 2 gives a view of the structure of (6) along the *b* axis; Figure 3 includes bond angles and bond lengths and Figure 4 shows the packing of molecules within one unit cell. The planar heteroaromatic rings are arranged in stacks parallel to the *a* axis, with molecules of adjacent stacks situated in head-to-tail ' herring-bone ' fashion. The main intermolecular interactions are between ring hydrogen atoms, although the oxime proton and N(1) of

the ring of adjacent molecules are sufficiently close for hydrogen bonding to occur.

The bicyclic ring system in (6) is planar with the 3-acetyl group almost in this plane (ϕ 12·4°), but the 2-[(*E*)-1-hydroxyiminoethyl] substituent is twisted 60·0° out of this plane. The deshielding of H-5 in the n.m.r. spectra of (5) and (6) (see previous section) must be due to the *peri*-carbonyl group. The rotamer observed in the crystalline state is presumably not the exclusive conformation in $CDCl_3$, but there will be restricted rotation about the MeCO–C bond due to conjugation with the 10-electron heteroaromatic system, and the rotamer shown may be favoured over the alternative planar rotamer on steric grounds.

The reason for reduced deshielding of H-5 in the dinitro-derivative (11) is not so immediately apparent, and this was a misleading factor in our initial attempts at structural elucidation. However, the greater bulk of the

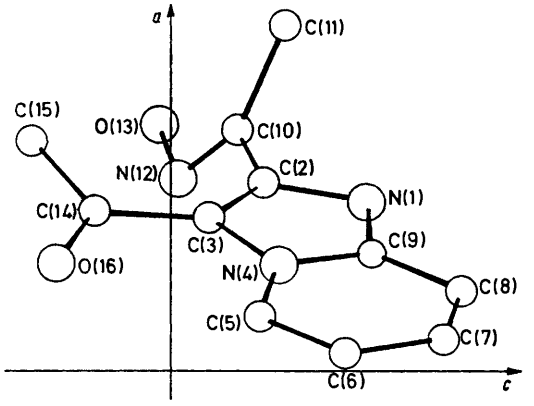


FIGURE 2 Compound (6) viewed along the *b* axis, showing the atom numbering system used in the crystallographic analysis

2-(1,1-dinitroethyl) substituent in (11) could make the planar orientation of the 3-acetyl group much less favourable than in (5) or (6), and this is corroborated by the higher frequency of the carbonyl stretching frequency in (11) (1656 cm^{-1}) relative to (5) and (6) (1640 cm^{-1}), indicating less conjugation of the carbonyl group with the aromatic system in (11).

The crystal structure determination of (6) is the first exact structural analysis of an imidazo[1,2-*a*]pyridine. The structural parameters are consistent with those expected from such a 10 π-electron system with bond lengths mostly intermediate between standard values for C–C and C–N *versus* C=C and C=N. The shortness of C(5)–C(6) and N(1)–C(9) compared with N–C(5) and C(8)–C(9) may indicate some bond localisation [represented in the extreme by a non-delocalised pyridin-imine structure (9)].

Studies on the Mechanism of Formation of Compound (5). —The likely precursors of (5) (pyridine, dimethylglyoxime, and acetic anhydride) can be clearly recognised in its structure in unrearranged form, an oxidation having occurred at one of the methyl groups of dimethylglyoxime. The formation of (5) from cobaloxime (4) is not influenced by oxygen as shown by assaying parallel

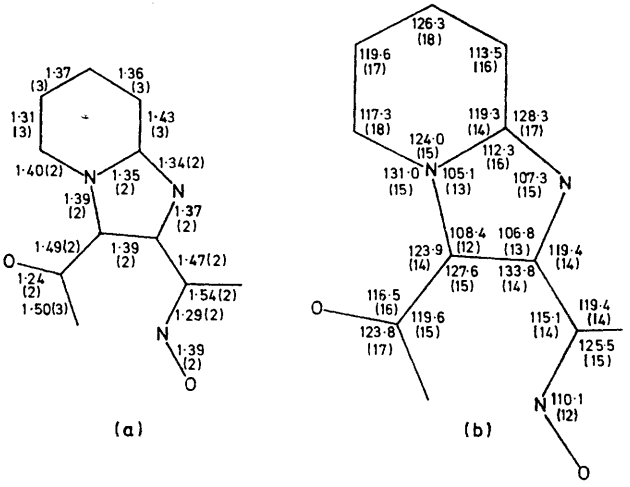


FIGURE 3 (a) Bond lengths and (b) angles in compound (6) with standard deviations in parentheses

oxygenated and degassed runs. Yields of (5) were consistently about 0·27 mol. equiv., and this product was accompanied by 0·7—1·0 mol. equiv. of dimethylglyoxime di-*O*-acetate. The cobalt atom of (4) is therefore likely to be the oxidant. However, bromo(pyridine)-cobaloxime (14) gives no imidazopyridine (5) under the usual reaction conditions, indicating that oxidation state Co^{III} is inactive. Since (5) is formed irrespective of the nature of the alkyl group in several cobaloximes [(3), (4), and (15)],* a possible first step is homolysis of the Co–C

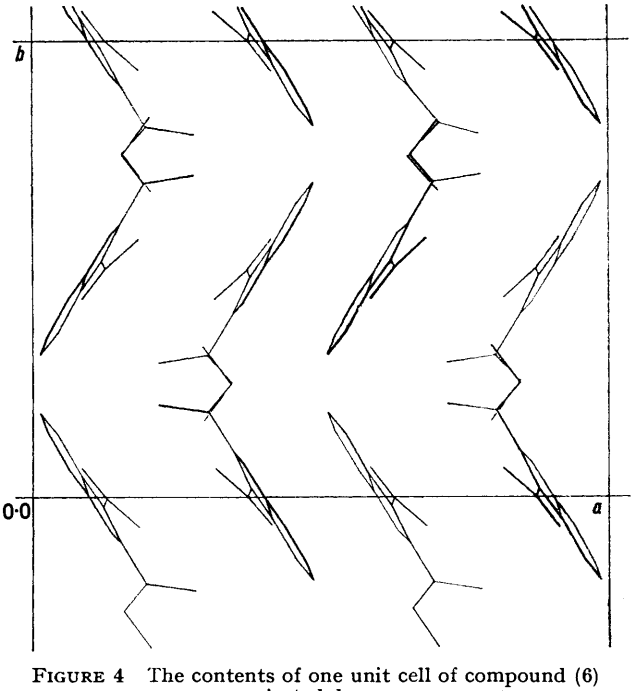
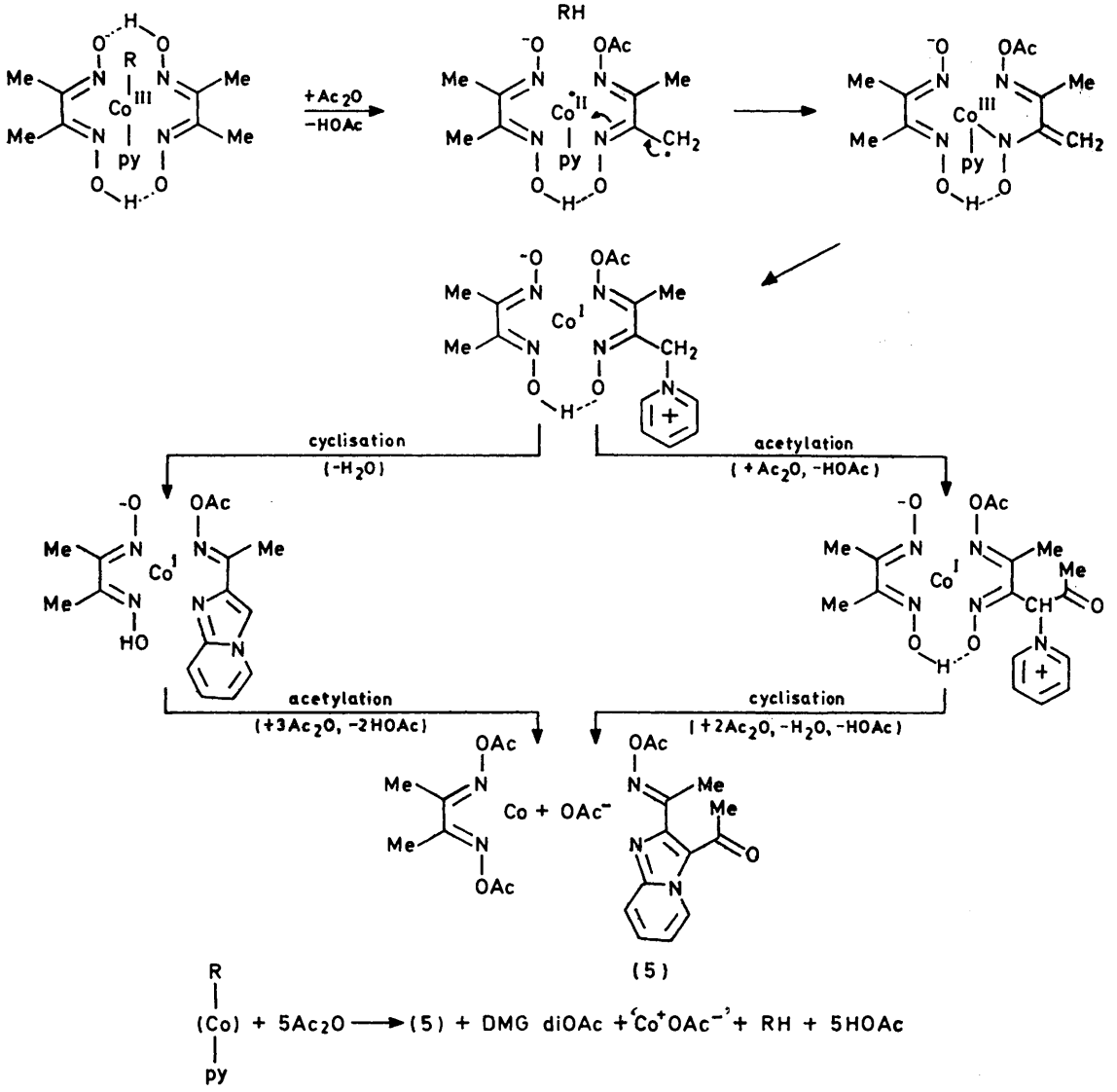


FIGURE 4 The contents of one unit cell of compound (6) projected down *c*

bond [2] to produce an alkyl radical and (pyridine)-cobaloxime(II) (17). Formation of (5) could then take

* Compound (16) (probable structure) was isolated as a by-product in the degradations starting from (3) and (15).

place as shown in the Scheme. The imidazo[1,2-*a*]-pyridine (18) is an attractive intermediate since such compounds undergo electrophilic substitution at position 3.[11] Accordingly, the isomer (19) was synthesised by condensing 2-aminopyridine with 1-bromo-3-hydroxyiminobutan-2-one.[12] The derivation of the latter compound from 3-hydroxyiminobutan-2-one, prepared by nitrosation of butanone, probably means that the methyl group and oxime hydroxy-group are *anti* [*cf. syn* in (18)], *i.e.* (19) is 2-[(*Z*)-1-hydroxyiminoethyl]imidazo[1,2-*a*]-pyridine. However, (19) suffered only *O*-acetylation [to (20)] on treatment with acetic anhydride in pyridine. Although some other observations are not fully consistent with the Scheme, none excludes it given the complexity of the reactions involved. Thus, (pyridine)cobaloxime(II) (17) also yields (5) (3—4%) on treatment with acetic anhydride in pyridine. Increased light did not improve the yield of (5) from (4), although photolysis is known to induce homolysis of Co–C bonds.[2] Perhaps our conditions (daylight) were insufficient for competition with concomitant thermolysis to be effective.



SCHEME

Treatment of (4) with benzoic anhydride in pyridine did not produce an analogue of (5). This may be due to the lower susceptibility of a benzoyl carbonyl group to nucleophilic attack (as compared with an acetyl carbonyl), causing a critical step to be inhibited.

EXPERIMENTAL

T.l.c. analyses were carried out on silica gel G/UV_{254} (Machery, Nagel and Co.). M.p.s were determined in open capillary tubes. ^1H N.m.r. spectra were taken for *ca.* 10%

[11] W. C. Mosby, in 'The Chemistry of Heterocyclic Compounds,' ed. A. Weissberger, Interscience, New York, 1961, vol. 15, part 1, p. 460.

[12] O. Diels and M. Farkas, *Ber.*, 1910, **43**, 1959.

solutions in $CDCl_3$ (60 MHz; Perkin-Elmer R12) or *ca.* 5% solutions in $CDCl_3$ (100 MHz; Varian HA100) with tetramethylsilane as internal standard. U.v. spectra were taken for solutions in methanol.

Isolation of 2-[(E)-1-*Acetoxyiminoethyl*]-3-*acetylimidazo*-[1,2-a]*pyridine* (5) *and Factors influencing its Formation.*—2-Hydroxypropyl(pyridine)cobaloxime [13] (158 mg, 0·37 mmol) was dissolved with warming in dry pyridine (1·4 ml) and redistilled acetic anhydride (0·4 ml) was added. The mixture was heated at 60° for 48 h, then evaporated under high vacuum at room temperature or below. The residue was dissolved in chloroform (containing 2% ethanol) (25 ml) and shaken with silica gel N (for t.l.c.) (1 g); the mixture was then filtered to give a pale brown filtrate. The black residue was washed with more chloroform (total *ca.* 60 ml). The chloroform washings were combined and evaporated to an oily solid (118 mg) which was chromatographed on silica gel N (4 g) under suction. Elution with dichloromethane gave dimethylglyoxime di-*O*-acetate (81 mg, 0·41 mmol), then elution with 25 and 50% chloroform–dichloromethane gave (5) (25 mg, 0·097 mmol) as coloured crystals, pure on t.l.c. (R_F 0·4 in 5% MeOH–$CHCl_3$; R_F 0·3 in EtOAc–PhH, 1 : 1). This material could be sublimed (100° and 0·001 mmHg) to obtain white crystals. Carrying out this procedure on gram scale gave a *sublimate* of (5) which was recrystallised (CS_2); m.p. 112°, δ 2·27 (3H, s, OAc), 2·57 (3H, s, MeC=N), 2·64 (3H, s, CAc), 7·08 (1H, dd, $J_{5,6} + J_{6,7}$ 13·5 Hz, H-6), 7·49 (1H, dd, $J_{6,7}$ 6·5, $J_{7,8}$ 8·9 Hz, H-7), 8·73 (1H, d, $J_{7,8}$ 8·9 Hz, H-8), and 9·69 (1H, d, $J_{5,6}$ 6·9 Hz, H-5), $\nu_{max.}$ ($CHCl_3$) 1775s and 1640s cm^{-1}, *m/e* 259 (11%, M^+, $C_{13}H_{13}N_3O_3$), 217 (26, $C_{11}H_{11}N_3O_2$), 200 (100, $C_{11}H_{10}N_3O$, 217 − OH*), 186 (19, $C_{10}H_8N_3O$), 185 (17, $C_{10}H_7N_3O$), 170 (32, $C_9H_4N_3O$), 105 (47, $C_6H_5N_2$), 78 (62, 105 − 27*), and 51 (15, 78 − 27*) (Found: C, 60·05; H, 4·85; N, 16·55. $C_{13}H_{13}N_3O_3$ requires C, 60·2; H, 5·05; N, 16·2%).

The above procedure was used to determine the effects on the reaction of: (*a*) the presence or absence of oxygen; (*b*) the nature of the cobaloxime; (*c*) the effect of light. Representative results are summarised in Table 1.

TABLE 1

Experiments to determine the effect on the cobaloxime degradation of (*a*) the presence or absence of oxygen; (*b*) the nature of the cobaloxime component

	Temp. (°C)	Time (h)	Mol % DMG di-OAc*	Mol % (5)
(i) 2-Hydroxypropyl(pyridine) cobaloxime				
O_2 bubbled through, in daylight	60	48	70	29
degassed in a sealed vial, in daylight	60	48	108	27
sealed in air, irradiated by a flood lamp	60	48	93	12
(ii) 2-Hydroxyethyl(pyridine) cobaloxime				
sealed in air, in daylight	60	114	74	16
(iii) Methyl(pyridine) cobaloxime				
sealed in air, in daylight	60	144	16	14
(iv) Bromo(pyridine)-cobaloxime	60	144	60	0
(v) 2-Hydroxypropyl(4-methylpyridine)-cobaloxime	60	48	77	16 †
(vi) (Pyridine)cobaloxime (II)				
sealed in air	60	48	111	3
degassed with argon and sealed	60	48	115	4

* DMG di-OAc = dimethylglyoxime di-*O*-acetate. † Product (8).

In a further experiment to assess the effect of light on the degradation, 2-hydroxypropyl(pyridine)cobaloxime (0·427 g, 1 mmol) was dissolved with warming in pyridine (4 ml) in a stoppered test tube, and acetic anhydride (1 ml) was added. The mixture was kept at room temperature in daylight or wrapped in foil, and at intervals samples (0·5 ml) were withdrawn and evaporated under high vacuum at room temperature. The residue was dissolved in dichloromethane and filtered through Celite. The filtrate was evaporated and the residue dissolved in $CDCl_3$ (0·4 ml), and the n.m.r. spectrum was taken. Ratios of starting material, product (5), and dimethylglyoxime di-*O*-acetate were estimated by integration. There were no significant differences in yields for these products under the two sets of conditions.

Large-scale Preparation of 3-*Acetyl*-2-[(E)-1-*Hydroxyiminoethyl*]*imidazo*[1,2-a]*pyridine* (6).—2-Hydroxypropyl(pyridine)cobaloxime (3·63 g, 8·5 mmol) was dissolved with warming in dry pyridine (30 ml) and redistilled acetic anhydride (9 ml, 90 mmol) was added. The mixture was stirred at room temperature with exclusion of moisture, and the reaction monitored by withdrawing samples (0·5 ml) at intervals, evaporating, and examining their n.m.r. spectra ($CDCl_3$). Formation of 2-acetoxypropyl(pyridine)cobaloxime (2) was 90% complete after 13 h. After 9 days, the mixture [less six samples (10%)] was evaporated (0·05 mmHg), and the residue dissolved in ethyl acetate, and the evaporation repeated. The final residue was dissolved in dichloromethane and filtered through silica gel, and the total dichloromethane washings were evaporated to give a mixture (1·28 g) of (5) and dimethylglyoxime di-*O*-acetate. Washing the residue with ethyl acetate gave a dark oil (0·080 g) containing a little (5), which could not be purified further. No alkylcobaloxime was present. The oily dichloromethane eluate was sublimed (100° and 0·001 mmHg) to give white crystals (0·825 g). This material was added to a solution of sodium (0·23 g, 10 mmol) in methanol (20 ml). T.l.c. (5% MeOH–$CHCl_3$) showed immediate conversion of (5) (R_F 0·4) into (6) (R_F 0·2). Next day the solution was evaporated, and water and M-HCl were added until the mixture was neutral. Compound (6) was extracted into dichloromethane (3 × 30 ml); dimethylglyoxime was insoluble in water and in dichloromethane. The extracts, dried and evaporated, gave white crystals (0·50 g, 2·3 mmol). Recrystallisation from ethyl acetate gave (6) as colourless *plates* (0·30 g), m.p. 190°, n.m.r. data similar to those of (5) except for absence of a signal at δ 2·27 and the gain of a signal at δ 9·30br (1H, OH); $\nu_{max.}$ 3585m, 3320m,br, and 1640s cm^{-1}, $\lambda_{max.}$ 227 (ε 17,350), 252 (25,000), 311br (7510), 219sh (16,800), and 299sh nm (7230), *m/e* 217 (100%, M^+, $C_{11}H_{11}N_3O_2$) and 200 (90, 217 − 17*), *M* (osmometric; $CHCl_3$) 221. A second crop (0·10 g) from the recrystallisation had m.p. 189°.

3-([$^2H_3$]*Acetyl*)-2-{(E)-1-[$^2H_1$]*hydroxyiminoethyl*}*imidazo*-[1,2-a]*pyridine*.—Compound (6) (40 mg, 0·18 mmol) was dissolved in 1·94 M-NaOD (1 ml) (10 min), neutralised with DCl in D_2O, and extracted into dichloromethane. The extracts, dried and evaporated, gave crystalline material (40 mg), m.p. 190°, n.m.r. data identical with those of (6) except for absence of signals at δ 2·55 and 9·30; *m/e* 221 (M^+).

[13] G. N. Schrauzer and R. J. Windgassen, *J. Amer. Chem. Soc.*, 1967, **89**, 143.

2-(1-*Acetamidovinyl*)-3-*acetylimidazo*[1,2-a]*pyridine* (16).—After reactions of 2-hydroxyethyl(pyridine)cobaloxime (3) and of methyl(pyridine)cobaloxime (15) with acetic anhydride in pyridine, for 7 days at 60°, and isolation of dimethylglyoxime di-*O*-acetate and (5) as described above, further elution of the column with chloroform gave *ca.* 5% of (16). On t.l.c. (EtOAc–PhH, 1 : 1) (16) had the same R_F value as (6) (0·2), but in 5% MeOH–$CHCl_3$ had a slightly lower R_F value. The sample of (16) for mass spectral analysis was purified by p.l.c. (developed 4 times in 5% MeOH–$CHCl_3$); m.p. 184°, δ 2·14 (3H, s, NHAc), 2·65 (3H, s, CAc), 5·02 (1H, d, *J* 1·0 Hz, $=CH_A$) (collapses to singlet on irradiation at δ 7·95 or shaking with D_2O), 6·39 (1H, s, $=CH_B$), 7·00 (1H, t, $J_{5,6} + J_{6,7}$ 14·0 Hz, H-6), 7·55 (2H, m, H-7 and 8), 7·95br (1H, NH) (disappears on addition of D_2O and shaking for 10 min), and 9·53 (1H, d, $J_{5,6}$ 6·7 Hz, H-5), $\nu_{max.}$ (CH_2Cl_2) 3420m, 1690s, 1638s, and 1485s cm^{-1}, *m/e* 243 (69%, M^+, $C_{13}H_{13}N_3O_2$), 228 (20), 200 (100, 243 − 43*), and 186 (20, 228 − 42*).

3-*Acetyl*-2-(1,1-*dinitroethyl*)*imidazo*[1,2-a]*pyridine* (11).—Compound (6) (43 mg, 0·2 mmol) was added to concentrated nitric acid (2 ml) and dissolved with evolution of brown fumes. After 10 min at room temperature, water (5 ml) was added, and the pale yellow solid (31 mg) filtered off. This was homogenous on t.l.c. (R_F 0·6 in 5% MeOH–$CHCl_3$); a further 10 mg of slightly less pure material was extracted from the acidic solution into dichloromethane. Recrystallisation from ether, then water, gave (11) as *needles*, m.p. 177°, δ 2·65 (3H, s, Me), 2·70 (3H, s, Me), 7·31 (1H, dd, $J_{7,8}$ 11·3, $J_{6,7}$ 7·0 Hz, H-7), 7·71 (1H, d, $J_{7,8}$ 11·3 Hz, H-8), 7·83 (1H, t, $J_{5,6} + J_{6,7}$ 14·0 Hz, H-6), and 8·91 (1H, d, $J_{5,6}$ 6·7 Hz, H-5), $\nu_{max.}$ (CH_2Cl_2) 1656s and 1580vs cm^{-1}, $\lambda_{max.}$ 218·5 (ε 21,600), 248 (12,030), 318 (5710), 254sh (10,190), 302sh (5560), and 330sh nm (5090), *m/e* 278 (5%, M^+, $C_{11}H_{10}N_4O_5$), 232 (7), 186 (100, $C_{11}H_{10}N_2O$) (Found: C, 47·55; H, 3·85; N, 19·8. $C_{11}H_{10}N_4O_5$ requires C, 47·5; H, 3·6; N, 20·15%).

Synthesis of Possible Intermediates (19) *and* (20).—2-(1-*Hydroxyiminoethyl*)*imidazo*[1,2-a]*pyridine* (19). 1-Bromo-3-hydroxyiminobutan-2-one [12] (0·90 g, 5 mmol) in dry dioxan (5 ml) was mixed with a solution of 2-aminopyridine (0·47 g, 5 mmol) in dioxan (5 ml), and sodium hydrogen carbonate (0·42 g, 5 mmol) in dioxan (2 ml) was added. The mixture was heated at 100° until evolution of carbon dioxide ceased (*ca.* 1·5 h). Black insoluble matter was filtered off, and the filtrate evaporated. The residue was dissolved in chloroform (250 ml) and washed with several small portions of water. The aqueous washings were extracted once with chloroform, and the combined chloroform extracts were dried and evaporated to give an off-white solid (0·50 g), m.p. 213°. Two recrystallisations from ethyl acetate gave colourless *crystals* of (19) (0·30 g, 35%), m.p. 215°, δ (NaOD) 2·22 (3H, s, Me), 6·70 (1H, t, $J_{5,6} + J_{6,7}$ 13·0 Hz, H-6), 7·20 (2H, m, H-7 and 8), 7·64 (1H, s, H-3), 8·02 (1H, d, $J_{5,6}$ 6·0 Hz, H-5), $\nu_{max.}$ (Nujol) 3400—2300m and 1630w cm^{-1}, $\lambda_{max.}$ 234 (ε 30,850), 315 (5580), 278sh (4000), 288sh (4270), 306sh (5240), and 328sh nm (4090), *m/e* 175 (100%, M^+) (Found: C, 61·0; H, 5·15; N, 24·0. $C_9H_9N_3O$ requires C, 61·7; H, 5·2; N, 24·0%).

2-(1-*Acetoxyiminoethyl*)*imidazo*[1,2-a]*pyridine* (20). To (19) (70 mg, 0·4 mmol) in dry pyridine (1·6 ml) was added redistilled acetic anhydride (0·4 ml, 4 mmol). After 3 h at room temperature the mixture was evaporated under high vacuum to give crystalline (20) (83 mg). Three recrystallisations from benzene–petroleum gave a *sample* of m.p. 131°, δ 2·25, (3H, s, Ac), 2·53 (3H, s, Me), 6·80 (1H, t, $J_{5,6} + J_{6,7}$ 12·9 Hz, H-6), 7·18 (1H, dd, $J_{6,7}$ 6·3, $J_{7,8}$ 9·0 Hz, H-7), 7·60 (1H, d, $J_{7,8}$ 9·0 Hz, H-8), 8·09 (1H, d, $J_{5,6}$ 6·6 Hz, H-5), and 8·09 (1H, s, H-3), $\nu_{max.}$ (CH_2Cl_2) 1763s, 1635w, and 1611w cm^{-1}, *m/e* 217 (33%, M^+) (Found: C, 60·9; H, 5·1; N, 19·35. $C_{11}H_{11}N_3O_2$ requires C, 60·8; H, 5·1; N, 19·35%).

Preparation of Model Compounds.—1-*Benzyl*-2-*acetylimidazo*[1,2-a]*pyridinium*-3-*olate* (10). This compound, prepared as described,[5] gave yellow needles from benzene, m.p. 176—178° (lit.,[5] 170—171°), δ 2·65 (3H, s, Me), 5·90 (2H, s, CH_2), 6·91 (1H, t, $J_{5,6} + J_{6,7}$ 13·2 Hz), 7·1—7·4 (6H, m, H-8 + Ph), 7·53 (1H, dd, $J_{6,7}$ 6·5, $J_{7,8}$ 9·2 Hz, H-7), and 8·40 (1H, d, $J_{5,6}$ 6·7 Hz, H-5), $\nu_{max.}$ (CH_2Cl_2) 1675s, 1635w, 1605s, and 1535m cm^{-1}, $\lambda_{max.}$ 262 (ε 14,100), 271 (11,810), and 394 nm (10,820), *m/e* 266 (32%, M^+) (Found: C, 72·45; H, 5·4; N, 10·4. Calc. for $C_{16}H_{14}N_2O_2$: C, 72·15; H, 5·3; N, 10·5%).

1-*Benzyl*-3-*chloroacetylimidazo*[1,2-a]*pyridinium*-2-*olate* (12). A mixture of 2-(benzylamino)pyridine (1·84 g, 10 mmol) in dry, peroxide-free dioxan (25 ml) with chloroacetic anhydride (5·13 g, 30 mmol) and chloroacetic acid (1·89 g, 20 mmol) was refluxed for 2·5 h, then evaporated. 10% Sodium hydroxide was added until the mixture was basic. Extraction with dichloromethane (3 × 40 ml) and evaporation of the dried extracts gave a brown oil (3·4 g). This was purified on a short silica gel column (40 g) under suction, with chloroform as eluant, to give material (2·6 g, 87%) which was recrystallised from benzene. The pink crystals of (12) obtained turned brown on exposure to light; m.p. 157° (lit.,[7] 154—155°) (Found: C, 64·05; H, 4·55; N, 9·25. Calc. for $C_{16}H_{13}ClN_2O_2$: C, 63·9; H, 4·35; N, 9·3%).

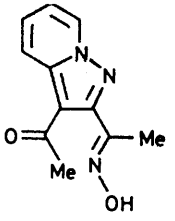
3-*Chloroacetyl*-1-*methylimidazo*[1,2-a]*pyridinium*-2-*olate* (13). 2-(Methylamino)pyridine was refluxed with chloroacetic anhydride (3 mol. equiv.) and chloroacetic acid (2 mol. equiv.) for 2 h [*cf.* procedure for (12)]. The crude product was recrystallised from acetone twice giving green crystals of (13), m.p. 245° (decomp.) (lit.,[7] 234°), δ 3·48 (3H, s, Me), 4·77 (2H, s, CH_2), 7·11 (1H, d, $J_{7,8}$ 8·0 Hz, H-8), 7·15 (1H, m, H-6), 7·62 (1H, t, $J_{6,7} + J_{7,8}$ 15·7 Hz, H-7), and 9·98 (1H, d, $J_{5,6}$ 6·5 Hz, H-5), $\nu_{max.}$ (CH_2Cl_2) 1665s, 1635w, 1593s, and 1520m cm^{-1}.

Crystal Structure Determination.—Crystals were chosen from the first crop from ethyl acetate obtained as described in the preparation of (6). The crystals were laths with *c* along their length and *b* across them.

Crystal data. $C_{11}H_{11}N_3O_2$, $M = 217·1$. Orthorhombic, $a = 16·402(10)$, $b = 13·463(10)$, $c = 9·735(10)$ Å, $U = 2149·7$ Å^3, $D_m = 1·332$ g cm^{-3}, $Z = 8$, $D_c = 1·346$ g cm^{-3}, $F(000) = 912$, Space group *Pbca* from systematic absences: $0kl$ for $k \neq 2n$, $h0l$ for $l \neq 2n$, and $hk0$ for $h \neq 2n$. Mo-K_α radiation for intensity measurement and unit-cell parameters, $\lambda = 0·7107$ Å, with graphite monochromator.

Data were collected on a Stoe–Weissenberg two-circle diffractometer, by ω-scan technique. Unit-cell parameters were obtained from the reflecting positions of high-angle reflections, with standard deviations estimated from the agreement of observed and calculated values. 1865 Reflections were measured in 11 layers of the primary axis (*c*), and 439 reflections in 3 layers of the crossing axis (*b*), with check reflections measured every 30 reflections. Lorentz and polarisation corrections were applied, and the intensities merged to give 1903 independent reflections of which 546 having $I < 0·1\sigma(I)$, were taken to have the limiting values of $0·1\sigma(I)$. The intensities were converted to normalised structure factors and placed on an absolute scale. The program PHASER was used for the solution of the structure

by direct methods.[14] In this procedure, as applied here, all the Σ_2 relationships were generated between the 366 reflections with $E > 1.3$, and sorted in order of descending probability. The 60 strongest reflections ($E > 2.045$) were used as generators, with three origin-specifying reflections: 8,5,0 E 3·471; 3,11,5 E 3·264; and 1,9,6 E 2·761. The remaining 57 phases were determined from the first-encountered relationships. Five cycles to remove discrepant relationships resulted in 23 phases being changed from the values initially assigned. Further application of the Σ_2 relationships starting from these 60 generator phases allowed 247 new phases to be determined. An E map based on these phases showed 16 peaks corresponding to the 16 non-hydrogen atoms. This molecular framework does not distinguish between the two alternative interpretations (6) and (21). Further considerations show (6) to be the correct



(21)

structure: (i) the peak on the E-map due to the atom N-4 is the most intense on the entire map; and (ii) structure (21)

TABLE 2

Atomic co-ordinates, with standard deviations in parentheses. Here, and in subsequent Tables, the atom numbering system is that used in the crystallographic analysis and shown in Figure 2

	x/a	y/b	z/c
C(2)	0·1511(10)	−0·0968(12)	0·1238(17)
C(3)	0·1205(10)	−0·0174(12)	0·0475(13)
C(5)	0·0431(10)	0·1385(12)	0·1124(20)
C(6)	0·0134(11)	0·1857(12)	0·2193(25)
C(7)	0·0247(12)	0·1473(15)	0·3485(21)
C(8)	0·0633(11)	0·0607(13)	0·3802(17)
C(9)	0·0934(8)	0·0089(11)	0·2630(20)
C(10)	0·1951(10)	−0·1878(12)	0·0880(15)
C(11)	0·2811(9)	−0·2053(12)	0·1470(16)
C(14)	0·1266(10)	−0·0017(14)	−0·1035(19)
C(15)	0·1839(12)	−0·0643(15)	−0·1863(20)
N(1)	0·1353(7)	−0·0762(9)	0·2592(16)
N(4)	0·0833(8)	0·0489(10)	0·1370(15)
N(12)	0·1564(7)	−0·2477(12)	0·0084(17)
O(13)	0·2039(7)	−0·3313(7)	−0·0186(12)
O(16)	0·0848(8)	0·0663(11)	0·1522(14)
H(5)	0·0221	0·1401	−0·0016
H(6)	−0·0229	0·2413	0·2403
H(7)	0·0143	0·1830	0·4380
H(8)	0·0679	0·0184	0·4821
H(111)	0·3167	−0·2000	−0·0500
H(112)	0·2500	−0·1800	0·2250
H(113)	0·3000	−0·2800	0·2250
H(13)	0·1706	−0·3634	−0·1097
H(151)	0·1667	−0·1200	−0·2000
H(152)	0·2333	−0·0600	−0·2000
H(153)	0·1750	−0·0200	−0·2500

would provide no explanation for the deshielding of the α-pyridine proton observed in the n.m.r. spectrum; in structure (6), H-5 would be deshielded by the *peri*-carbonyl group of the 3-acetyl substituent.

[14] J. M. Stewart, in 'Crystallographic Computing,' ed. F. R. Ahmed, Munksgaard, Copenhagen, 1970, p. 71.

Refinement. Refinement used the 520 reflections with $I > 2.5\sigma(I)$. Two cycles reduced R to 0·130, and a difference-Fourier map at this stage enabled the positions of all the 11 hydrogen atoms to be determined. The final refinement with anisotropic temperature factors for non-hydrogen atoms brought R to 0·089. Attempts to refine the positions of the hydrogen atoms gave unacceptable bond lengths and angles, and these atoms were therefore kept at the positions shown by the difference map. All computing was with the X-Ray system [15] on the S.R.C. ATLAS computer.

Table 2 gives the co-ordinates of all the atoms, and Table 3

TABLE 3

Anisotropic temperature factors * (× 10^3) for non-hydrogen atoms, with standard deviations in parentheses. All hydrogen atoms were given isotropic temperature factors, U 2·5 × 10^{-2} Å^2

	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(2)	45(11)	36(10)	38(11)	−3(8)	26(10)	−26(9)
C(3)	31(9)	40(9)	13(8)	−6(8)	−1(7)	17(8)
C(5)	31(10)	20(10)	95(16)	−2(8)	−25(12)	22(10)
C(6)	55(14)	29(10)	115(19)	28(10)	24(14)	−9(13)
C(7)	68(15)	57(14)	68(15)	−18(11)	−19(12)	24(13)
C(8)	80(15)	32(10)	40(12)	−6(10)	−37(11)	16(10)
C(9)	−37(9)	21(8)	52(12)	−13(8)	11(10)	5(9)
C(10)	3(11)	50(11)	19(9)	−13(9)	−7(9)	15(9)
C(11)	39(11)	80(14)	38(10)	21(9)	7(9)	3(10)
C(14)	31(11)	62(13)	68(13)	−12(10)	−1(11)	19(12)
C(15)	72(14)	53(14)	88(15)	4(12)	31(13)	16(11)
N(1)	30(8)	32(8)	80(12)	15(7)	23(9)	5(9)
N(4)	39(8)	43(9)	40(9)	−13(8)	13(8)	27(8)
N(12)	55(9)	44(8)	65(11)	6(8)	6(10)	11(8)
O(13)	74(9)	37(7)	59(8)	6(6)	−17(8)	−5(7)
O(16)	60(9)	75(11)	78(10)	−2(8)	−3(9)	26(9)

* In the form: $\exp -2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^* + 2U_{13}hla^*c^* + 2U_{23}klb^*c^*)$.

TABLE 4

Details of least-squares planes. Deviations (Å) from the plane of the atoms defining the plane are given first, followed by those of other non-hydrogen atoms. σ Is the standard deviation of the defining atoms from the plane

(*a*) Deviations

Plane (1)		Plane (2)		Plane (3)	
C(2)	−0·016	C(3)	0·004	C(2)	0·000
C(3)	0·012	C(14)	−0·013	C(10)	−0·003
C(5)	0·005	C(15)	0·004	C(11)	−0·001
C(6)	−0·010	O(16)	0·005	N(12)	0·002
C(7)	0·004			O(13)	−0·001
C(8)	0·004	C(2)	−0·207		
C(9)	−0·014	C(5)	0·538	C(3)	−0·880
N(1)	0·013	C(6)	0·757	C(5)	−0·834
N(4)	0·002	C(7)	0·752	C(6)	−0·104
		C(8)	0·506	C(7)	1·060
C(10)	−0·026	C(9)	0·236	C(8)	1·586
C(11)	1·129	C(10)	−0·530	C(9)	0·802
C(14)	0·074	C(11)	0·450	C(14)	−2·186
C(15)	0·400	N(1)	−0·011	C(15)	−2·815
N(12)	−1·041	N(4)	0·274	N(1)	1·024
O(13)	−0·946	N(12)	−1·648	N(4)	−0·354
O(16)	−0·109	O(13)	0·124	O(16)	−2·710
σ	0·0106	σ	0·0087	σ	0·0020

(*b*) Equations of planes in orthogonal (Å) co-ordinates

Plane (1): $0.0865X + 0.4935Y + 0.0879Z = 1.6227$
Plane (2): $0.7397X + 0.6544Y + 0.1567Z = 1.3763$
Plane (3): $-0.3975X - 0.4579Y + 0.7952Z = 0.5698$

(*c*) Angles (deg.) between planes

(1)–(2) 60·0, (1)–(3) 12·4, (2)–(3) 62·0

[15] X-Ray System of Crystal Structure Programs, University of Maryland Technical Report TR 67 58, revised 1970.

TABLE 5

Intermolecular distances (Å) $<2\cdot5$ Å

H(8) · · · H(8^{I})	2·31	N(1) · · · H(13^{IV})	1·62
H(7) · · · H(5^{II})	2·46	H(13) · · · H(112^{V})	2·15
H(5) · · · H(7^{III})	2·46	H(13) · · · N)1^{V})	1·62
H(112) · · · H(13^{IV})	2·15		

Roman numeral superscripts refer to the following equivalent positions relative to the reference molecule at x, y, z:

I $-x, -y, 1-z$	IV $x, -\frac{1}{2}-y, \frac{1}{2}+z$
II $x, \frac{1}{2}-y, \frac{1}{2}+z$	V $x, -\frac{1}{2}-y, z-\frac{1}{2}$
III $x, \frac{1}{2}-y, z-\frac{1}{2}$	

their temperature factors. Observed and calculated structure factors are available in Supplementary Publication No. SUP 21190 (4 pp.).* Table 4 gives details of three least-squares planes defined by (1) the 9 atoms of the heteroaromatic ring system, (2) the 4 atoms of the 3-acetyl substituent, and (3) the 5 atoms of the 2-[(*E*)1-hydroxyiminoethyl] group. Table 5 lists intermolecular distances $<2\cdot5$ Å.

We thank the Royal Society for a European Exchange Scholarship (U. H.), the S.R.C. for studentships (D. R. H. and W. P. W.) and for a grant (N. W. A. with Dr. D. Russell) for the purchase of a Stoe diffractometer, P.C.M.U. Harwell for mass and 100 MHz n.m.r. spectral data, and the University of Hull service for other mass spectral spectra.

[4/1076 *Received* 3*rd June*, 1974]

* For details of Supplementary Publications see Notice to Authors, No. 7 in *J.C.S. Perkin I*, 1974, Index issue.