Application of the Bucherer Hydantoin Synthesis to Diacetyl Mono-oxime. The Mechanism of the Bucherer Reaction, and the Constitution of the Hypothetical 'Dimethylbishydantoin' of Bucherer and Lieb

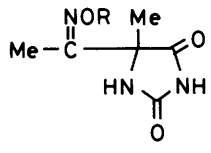
W. Gary Bowness, Ralph Howe,* and Balbir S. Rao
Imperial Chemical Industries PLC, Pharmaceuticals Division, Alderley Park, Macclesfield, Cheshire SK10 4TG

The major product obtained when the Bucherer conditions for hydantoin synthesis were applied to diacetyl mono-oxime was (3a*RS*,6a*SR*)-6-amino-1,3,3a,6a-tetrahydro-1-hydroxy-3a,6a-dimethylpyrrolo-[3,4-*d*]imidazole-2,4-dione (3). Two minor products (7) and (9) are related to (3) but a third, the imidazole 1-oxide (10), is not. Compound (10) was obtained from diacetyl mono-oxime and ammonium carbonate in the absence of cyanide. It is proposed that 4,4-disubstituted 5-imino-oxazolidin-2-ones (18), postulated by Bucherer and Steiner to be intermediates in hydantoin syntheses, rearrange to hydantoins by a base catalysed $E1_{cB}$ mechanism. It is further proposed that (3) is the hypothetical dimethylbishydantoin' (35) reported by Bucherer and Lieb in 1934.

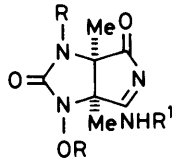
When diacetyl mono-oxime [(*E*)-3-hydroxyiminobutan-2-one][1] was treated with potassium cyanide and ammonium carbonate under Bucherer conditions several products were formed, but the expected hydantoin (imidazolidine-2,4-dione) (1) was not amongst them. The major product was the new pyrrolo[3,4-*d*]imidazole derivative (3). Compounds (7), (9), and (10) were minor products and they were accompanied by a trace of diacetyl dioxime. Compound (7) was readily obtained from compound (3) by acid hydrolysis. Chemical evidence detailed below, physical evidence given in the Experimental section, and reaction pathway considerations (Scheme 1) led to the correct assignment of structure to (7) and to an initial working structure (6) for compound (3).

Structure (6) gained support from the following colour tests. Compound (7) produced an intense blue colour with neutral $FeCl_3$ solution, characteristic of an *N*-hydroxyurea,[2] whereas the supposed compound (6) gave no colour. *O*-Carbamoylhydroxylamine, the acyclic analogue of (6), gives but a fleeting rose colour with $FeCl_3$.[3] The *O*-acetyl derivative of (7), compound (8), did not give a colour with $FeCl_3$. After structures (3) and (7) had been confirmed by *X*-ray crystallography studies,[4] the amino group of (3) was acetylated. The product (4) gave a blue colour with $FeCl_3$, showing that the free amino group of (3) had interfered with the colour test for the *N*-hydroxy cyclic urea. With excess of acetic anhydride, compound (3) gave a triacetyl derivative (5).

The empirical formula of compound (3) ($C_7H_{10}N_4O_3$) was that of (1) ($C_6H_9N_3O_3$) plus HCN, suggesting that two molecules of cyanide had reacted with each molecule of diacetyl mono-oxime. No product could be isolated when diacetyl itself was used as the substrate in the Bucherer reaction, implying that the hydroxyimino group was essential for the production of (3). Further, when 3-methoxyiminobutan-2-one was used as substrate, the expected hydantoin (2) was obtained, suggesting that the hydroxy group of the oxime was involved in the formation of (3). The structure of the hydantoin (2) was in accord with the physical data. In addition, it formed a 3-morpholinomethyl derivative, and with hot 2M-hydrochloric acid it was converted into 5-methylhydantoin, presumably by sequential formation and then fission of 5-acetyl-5-methylhydantoin. The involvement of two molecules of cyanide and, it seemed, of the hydroxy group of the oxime, together with the initial $FeCl_3$ colour experiments, led to consideration of a reaction pathway leading to (6) and then (7) (shown in Scheme 1). The oxazolidine (11) is the intermediate expected in the formation of the hydantoin (1; R = H),[5] and the events depicted in structure (12) are advantageous in that they produce an amide group required for the next cyclisation step, shown in structure (13).

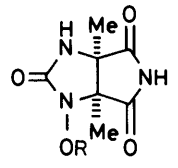


(1) R = H
(2) R = Me

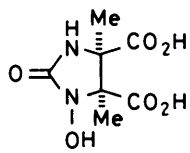


(3) R = R^1 = H
(4) R = H, R^1 = COMe
(5) R = R^1 = COMe

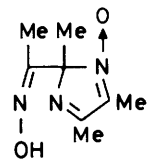
(6)



(7) R = H
(8) R = COMe



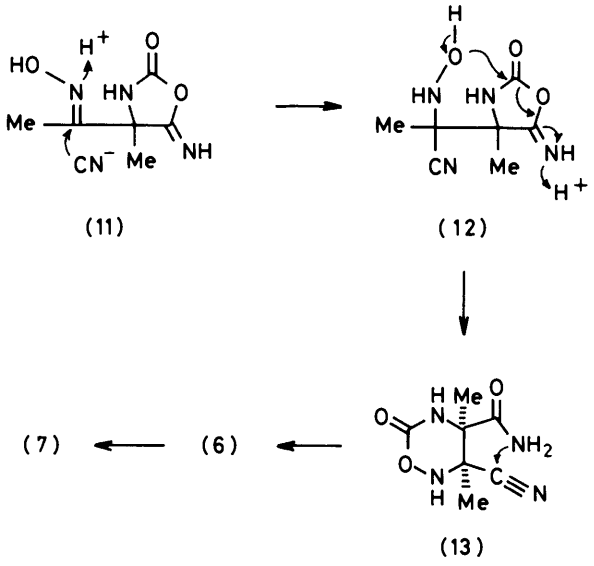
(9)



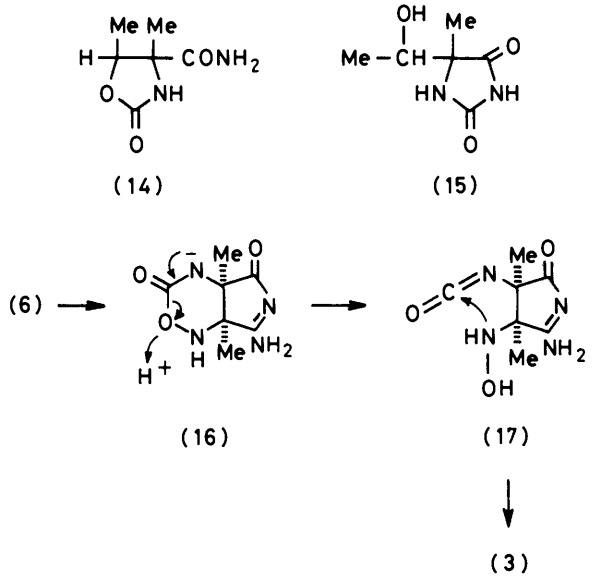
(10)

We considered that there may be some precedent for events similar to those shown in (12) in that under Bucherer conditions the α-ketol, acetoin, gave the oxazolidin-2-one (14) rather than the hydantoin (15).[6] The authors did not suggest a reaction pathway. They noted that α-ketol methyl ethers react in the expected manner with potassium cyanide and ammonium carbonate to give hydantoins.

In support of Scheme 1, cyanide adds readily to oximes,[7] and β-cyanoamides cyclise to iminopyrrolidinones [8] which can be hydrolysed to succinimides.[9] Addition of cyanide to the oxime from the less hindered side, remote from the methyl group attached to the ring, would lead to the observed *cis*-disposition of methyl groups in the product.

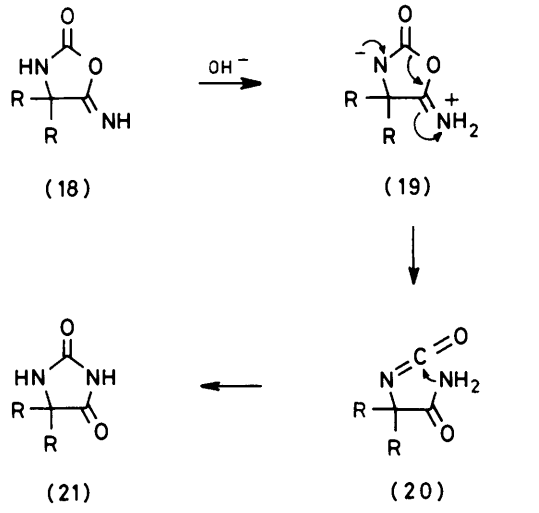


Scheme 1.

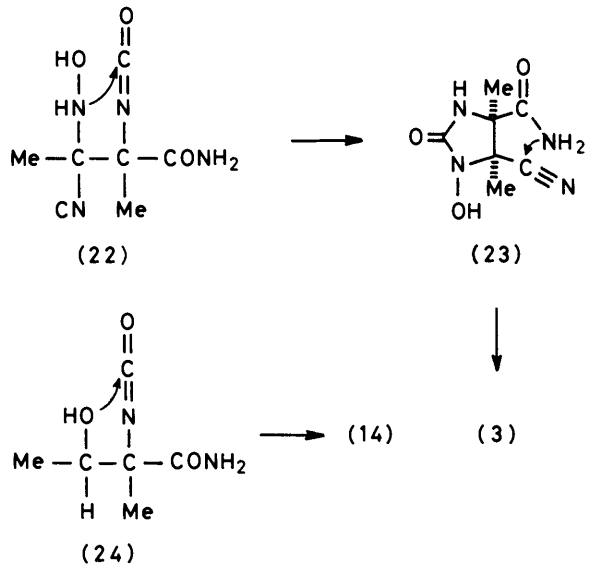


Scheme 2.

Inspection of models suggested that a similar pathway leading directly to compound (3) by attack of the hydroxylamine nitrogen atom of (12) on the carbonyl group was unlikely because the distance between the groups is too large. This view was confirmed by computer based molecular graphics, which gave better control of bond lengths and bond angles. At the optimum distance the nitrogen atom is still too far away (3.3 Å) to attack the carbonyl group, whereas the oxygen atom in (12) is within bonding distance (2.1 Å) and the angle of attack is virtually tetrahedral (108°) as required. It is possible that the reaction proceeds *via* (12), (13), and (6) and that the last of these rearranges to (3) *via* (16) and (17) (Scheme 2) by a base catalysed $E1_{cB}$ mechanism of the type reported by Williams.[10] However, an explanation would still be required for the formation of (14) from acetoin, because in that case the hydroxy group is too far (3.4 Å) from the carbonyl group in the appropriate oxazolidin-2-one.



Scheme 3.

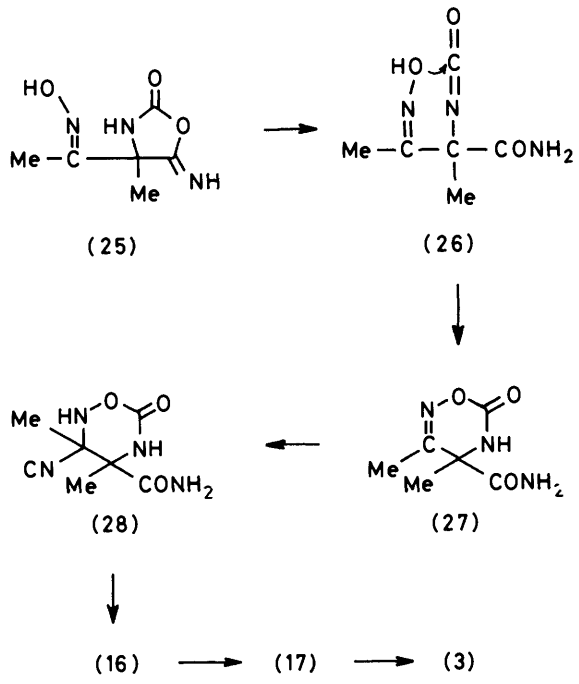


Scheme 4.

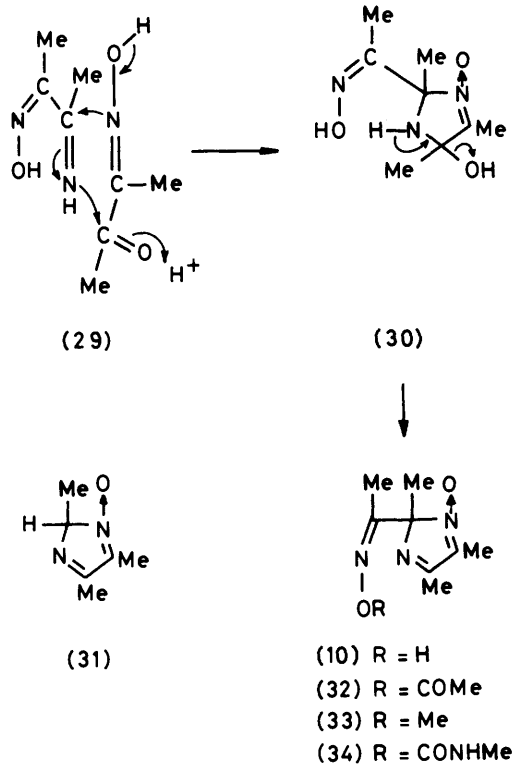
So far as we are aware, it has not been made clear in the literature how the intermediate 4,4-disubstituted 5-iminooxazolidin-2-one (18) postulated [11] in the Bucherer synthesis actually rearranges to the hydantoin (21). We propose that it is *via* the $E1_{cB}$ route [10] shown in Scheme 3.

The intermediate (20) is that postulated in hydantoin formation by the action of alkaline hypochlorite on a cyanoacetamide or a malondiamide.[12,13] Carboxamides are known to react readily with alkyl isocyanates to give acylureas.[14] If this pathway is accepted then the formation of compounds (3) and (14) can be explained readily by preferential intramolecular attack on an intermediate isocyanate (22) or (24) of type (20) by an available and better nucleophile than the amide amino group, *viz* NH (22) ⟶ (23) and OH (24) ⟶ (14) (Scheme 4).

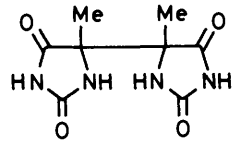
The formation of the hydantoin (2) as expected from 3-methoxyiminobutan-2-one appeared to give some support for the involvement of the hydroxy group of the oxime in the formation of (3). The straightforward production of (2) may be because nucleophiles, *e.g.* cyanide add less readily to *O*-



Scheme 5.



Scheme 6.



alkyl oximes than to free oximes.[7] However, an attractive alternative explanation, which we favour, is that formation of (3) actually proceeds through the species (25), (26), (27), (28), (16), and (17) (Scheme 5). The attraction is that species (27) should be much more susceptible to attack by nitrile than any previous species because of the electron-withdrawing effect of the carbonyl group next to what was the hydroxylamine oxygen. No species corresponding to (27) can be formed from 3-methoxyiminobutan-2-one. Compound (27) is not in the literature and we have been unable to locate any related 2*H*-1,2,5-oxadiazin-6-ones. Models show that cyanide will add to the C=N bond from the face opposite to the 4-methyl group. This explanation requires an *E* to *Z* oxime isomerisation, a process which can readily occur.[15]

The minor product (9) was isolated serendipitously on only one occasion from mother-liquors which had been set aside. It has not been seen again despite several attempted repeats. Although it can be formally derived by hydrolysis of (3) or (7) we have not found conditions for bringing that reaction about. With methanol–thionyl chloride, compound (9) formed a monomethyl ester.

The n.m.r. spectrum of the minor product (10) ($C_8H_{13}N_3O_2$) showed four different methyl signals and a low-field proton signal. The presence of four methyl groups suggested that the carbon skeleton was derived from two molecules of diacetyl mono-oxime ($2\ C_4H_7NO_2 + NH_3 - 2\ H_2O = C_8H_{13}N_3O_2$), and that cyanide had not entered into the reaction. Compound (10) was obtained in moderate yield by heating diacetyl mono-oxime with ammonium carbonate in aqueous ethanol. The ammonium carbonate was necessary. Following Wright,[16] the proposed reaction pathway is *via* (29) and (30) (Scheme 6).

The structure of (10) is in accord with the spectral data. In the mass spectrum a peak was noted at *m/z* 126 which is consistent with loss of the side chain from (10) with hydrogen transfer to give the species (31). In support of the structure, compound (10) formed an acetyl derivative (32) with acetic anhydride in pyridine, a monomethyl derivative (33) with dimethyl sulphate, and an *N*-methylurethane (34) with methyl isocyanate. Reduction with sodium dithionite gave 2,4,5-trimethylimidazole.

The Bucherer reaction on diacetyl mono-oxime was capricious in that under what were meant to be identical conditions the yield of the major product (3) ranged from *ca.* 15—35% on various scales up to two molar. The product (9) was obtained on only one occasion and the minor products were not always obtained. The differences are attributed to variations in the rate at which the reaction mixture could be raised to 70 °C without fear of local overheating. The reaction is very sensitive to conditions, the yield of (3) being lower if a temperature of 70 °C and a heating time of 4 h are exceeded. The relatively low yield of product (3) and its variability made it difficult to demonstrate with any certainty that two molecules of cyanide reacted with each molecule of diacetyl mono-oxime. On an 0.1 molar scale, increasing the mole ratio of KCN from 1.2 to 2.4 increased the yield of (3) from 18 to 37%, but on a molar scale a similar change did not improve the yield of (3).

We propose that compound (3), m.p. 270 °C (decomp.) is the hypothetical ' dimethylbishydantoin ' (35), m.p. 265—270 °C (decomp.) obtained from diacetyl or diacetyl mono-oxime by Bucherer and Lieb.[17] Their diacetyl was prepared from methyl ethyl ketone *via* diacetyl mono-oxime and must have been contaminated with the latter compound. Also, their analytical figures fit better for (3) ($C_7H_{10}N_4O_3$) than for ' dimethylbishydantoin ' (35) ($C_8H_{10}N_4O_4$).

Experimental

I.r. spectra were determined for Nujol mulls. N.m.r. spectra were measured at 100 MHz with Me_4Si as internal standard. Mass measurements were made on a Kratos (AEI) MS 902 instrument. Ether refers to diethyl ether.

Reaction of 3-Hydroxyiminobutan-2-one with Potassium Cyanide and Ammonium Carbonate.—A solution of 3-hydroxyiminobutan-2-one (100 g, 0.99 mol), potassium cyanide (78 g, 1.2 mol), and ammonium carbonate (320 g, 3.33 mol) in ethanol (1 l) and water (1 l) was heated at 70 °C for 4 h, after which time a substantial amount of solid had separated. The mixture was cooled and filtered to give solid A (21.6 g). The filtrate was evaporated to *ca.* 400 ml, cooled, and filtered to give more solid A (49.0 g). The filtrate was extracted with ethyl acetate. The extract gave an oil B (18 g). The aqueous layer was acidified with hydrochloric acid and then extracted with ethyl acetate. The extract gave a solid C (1.0 g). The acidic aqueous solution was concentrated to 50 ml and after 1 week solid D separated as chunky crystals (7.3 g).

Solid A (70.6 g crude) was crystallised from water (3 l) containing a few drops of ammonium hydroxide (*d* 0.88) to give (3aRS,6aSR)-6-*amino*-1,3,3a,6a-*tetrahydro*-1-*hydroxy*-3a,6a-*dimethylpyrrolo*[3,4-d]*imidazole*-2,4-*dione* (3) (53 g, 26.5%), as needles m.p. 270 °C (decomp.) (Found: C, 42.4; H, 5.1; N, 28.0. $C_7H_{10}N_4O_3$ requires C, 42.4; H, 5.1; N, 28.3%); $\nu_{max.}$ 3 300 (OH), 3 300—3 100 (NH_2), 3 100—2 500 (br, H bonding), 1 715 (4 C=O), 1 685 (2 C=O), and 1 580 cm^{-1} (C=N); deuteriated sample 2 480 (OD), 2 420 (ND), 2 360 and 2 220 (ND_2), and 1 580 (C=N), enhanced; δ_H[$(CD_3)_2SO$] 1.12 (s, 3 H, Me), 1.32 (s, 3 H, Me), 7.71 (s, OH), 8.25 (s, NH), and 9.2 (br, NH_2); *m/z* 198 (M^+).

The hydrochloride of (3) was prepared as follows. A suspension of (3) (0.2 g) in methanol (10 ml) was stirred and a slight excess of ethereal hydrogen chloride was added to form a solution. After 5 min ether was added to precipitate the *hydrochloride* of (3) which was crystallised at room temperature by dissolving in methanol (2 ml) and adding ethyl acetate (*ca.* 10 ml), prisms, m.p. 243—245 °C (0.12 g) (Found: C, 35.5; H, 4.8; N, 23.5. $C_7H_{11}ClN_4O_3$ requires C, 35.8; H, 4.7; N, 23.9%).

Oil B (18 g) was stirred with ethyl acetate (50 ml) and the solid which separated (0.39 g) was isolated. It was shown by i.r. to consist of the imidazole 1-oxide (10) (see below) contaminated with 2,3-bis(hydroxyimino)butane. The second crop (0.07 g) consisted of 2,3-bis(hydroxyimino)butane, needles, m.p. and mixed m.p. 240—241 °C. The remainder of oil B was essentially 3-hydroxyiminobutan-2-one.

Solid C (1.0 g) was recrystallised from methanol to give the product (10) (see below) as stout prisms (0.5 g), m.p. and mixed m.p. 208 °C from ethyl acetate. Note: on the one occasion that the reaction was carried out on this scale compound (7) (0.4 g) (see below), m.p. and mixed m.p. 246—247 °C, was isolated here and not compound (10).

Solid D (7.3 g) was recrystallised from water to give 1-*hydroxytetrahydro*-4,5-*dimethyl*-2-*oxoimidazole*-4,5-*dicarboxylic acid* (9) *dihydrate* (7.0 g, 3%) as rhombs, m.p. 150 °C (decomp.) (Found: C, 33.8; H, 5.5; N, 11.0; H_2O, 14.6. $C_7H_{10}N_2O_6{\cdot}2H_2O$ requires C, 33.5; H, 5.5; N, 11.0; H_2O, 14.2%); δ_H [$(CD_3)_2SO$] 1.28 (s, 3 H, Me), 1.32 (s, 3 H, Me), 6.7 (br, 7 H, 2 CO_2H, 2 H_2O, NH or OH), and 7.3 (s, 1 H, NH or OH). A monomethyl ester of (9) was prepared as follows. Thionyl chloride (2 ml) was added dropwise with stirring to methanol (20 ml) at −25 °C and then (9) (1.0 g) was added. After 20 min the solution was allowed to warm to room temperature. After 18 h the solvent was evaporated. The residual gum was triturated with ethyl acetate to give a solid which gave a *monomethyl ether of* (9) as prisms, m.p. 134—135 °C (from methanol–ethyl acetate) (Found: C, 38.5; H, 5.7; N, 11.0; H_2O, 7.5. $C_8H_{12}N_2O_6{\cdot}H_2O$ requires C, 38.4; H, 5.6; N, 11.2; H_2O, 7.2%); δ_H [$(CD_3)_2SO$] 1.58 and 1.60 (2 s, 6 H, 2 Me), 4.28 (s, 3 H, OMe), and 8.93 (s, 1 H).

(3aRS,6aSR)-1,3,3a,6a-*Tetrahydro*-1-*hydroxy*-3a,6a-*dimethyl*-5H-*pyrrolo*[3,4-d]*imidazole*-2,4,6-*trione* (7).—Compound (3) (1.0 g) was heated under reflux with 2M-hydrochloric acid (10 ml) for 2 min and then the solution was cooled. (3aRS,6aSR)-1,3,3a,6a-*Tetrahydro*-1-*hydroxy*-3a,6a-*dimethyl*-5H-*pyrrolo*[3,4-d]*imidazole*-2,4,6-*trione* (7) (0.82 g, 82%) separated as prisms, m.p. 246—247 °C (Found: C, 42.2; H, 4.5; N, 20.8. $C_7H_9N_3O_4$ requires C, 42.2; H, 4.6; N, 21.1%); $\nu_{max.}$ 1 792 (4 or 6 C=O) and 1 715 cm^{-1} (br, C=O); δ_H (TFA) 1.68 (s, 3 H, Me), 1.70 (s, 3 H, Me), 7.20 (s, 1 H, 3NH), and 9.83 (s, 1 H, 5 NH); *m/z* 199 (M^+).

(3aRS,6aSR)-1-*Acetoxy*-1,3,3a,6a-*tetrahydro*-3a,6a-*dimethyl*-5H-*pyrrolo*[3,4-d]*imidazole*-2,4,6-*trione* (8).—A solution of (7) (1.0 g, 0.005 mol) and acetic anhydride (0.65 g, 0.0064 mol) in pyridine (5 ml) was kept at room temperature for 18 h and then the solvent was evaporated. The residual gum was triturated with ethyl acetate and the solid thus obtained gave (3aRS,6aSR)-1-*acetoxy*-1,3,3a,6a-*tetrahydro*-3a,6a-*dimethyl*-5H-*pyrrolo*[3,4-d]*imidazole*-2,4,6-*trione* (8) (0.7 g, 58%) as prisms, m.p. 225—227 °C (from ethanol) (Found: C, 44.5; H, 4.6; N, 17.3. $C_9H_{11}N_3O_5$ requires C, 44.8; H, 4.6; N, 17.4%); δ_H [$(CD_3)_2SO$] 1.31 (s, 3 H, Me), 1.36 (s, 3 H, Me), 2.11 (s, 3 H, COMe), 8.67 (s, 1 H, urea NH), and 11.4 (br, 1 H, imide NH).

(3aRS,6aSR)-6-*Acetylamino*-1,3,3a,6a-*tetrahydro*-1-*hydroxy*-3a,6a-*dimethylpyrrolo*[3,4-d]*imidazole*-2,4-*dione* (4).—A solution of (3) (1.0 g, 0.005 mol) and acetic anhydride (1.03 g, 0.01 mol) in pyridine (70 ml) was heated at 100 °C for 5 h and then the solvent was evaporated. The residual gum was triturated with ethyl acetate to give a solid which gave (3aRS,6aSR)-6-*acetylamino*-1,3,3a,6a-*tetrahydro*-1-*hydroxy*-3a,6a-*dimethylpyrrolo*[3,4-d]*imidazole*-2,4-*dione* (4) (0.36 g, 34%) as prisms, m.p. 245 °C (decomp.) (from ethanol) (Found: C, 44.9; H, 5.1; N, 23.4. $C_9H_{12}N_4O_4$ requires C, 45.0; H, 5.0; N, 23.3%); δ_H [$(CD_3)_2SO$] 1.21 (s, 3 H, Me), 1.40 (s, 3 H, Me), 2.13 (s, 3 H, COMe), 8.4 (s, 2 H), and 9.0 (s, 1 H).

(3aRS,6aSR)-1-*Acetoxy*-3-*acetyl*-6-*acetylamino*-1,3,3a,6a-*tetrahydro*-3a,6a-*dimethylpyrrolo*[3,4-d]*imidazole*-2,4-*dione* (5).—Compound (3) (1 g, 0.005 mol), acetic anhydride (2.17 g, 0.0215 mol), and pyridine (75 ml) were heated at 100 °C for 3½ h and then the solvent was evaporated. The residual gum was triturated with ethyl acetate to give a solid (250 mg) which was crystallised by quickly dissolving it in the minimum amount of methanol and adding ethyl acetate to give (3aRS,6aSR)-1-*acetoxy*-3-*acetyl*-6-*acetylamino*-1,3,3a,6a-*tetrahydro*-3a,6a-*dimethylpyrrolo*[3,4-d]*imidazole*-2,4-*dione* (5) as prisms, m.p. 167—168 °C (poor recovery) (Found: C, 47.9; H, 5.0; N, 17.0. $C_{13}H_{16}N_4O_6$ requires C, 48.2; H, 5.0; N, 17.3%); δ_H [$(CD_3)_2SO$] 1.47 (s, 3 H, Me), 1.79 (s, 3 H, Me or OAc), 1.86 (s, 3 H, OAc or Me), 2.26 (s, 3 H, NAc), and 2.42 (s, 3 H, NAc). The ethyl acetate solution from the above trituration yielded (3a*RS*,6a*SR*)-1-acetoxy-1,3,3a,6a-tetrahydro-3a,6a-dimethyl-5*H*-pyrrolo[3.4-*d*]imidazole-2,4,6-trione (8) m.p. and mixed m.p. 225—227 °C.

5-(1-*Methoxyiminoethyl*)5-*methylimidazolidine*-2,4-*dione* (2).—A solution of 3-methoxyiminobutan-2-one (1.15 g, 0.01 mol), potassium cyanide (0.78 g, 0.012 mol), and ammonium carbonate (3.2 g, 0.033 mol) in ethanol (10 ml) and water (10 ml) was heated at 70 °C for 20 h and then the solvent was

evaporated. The residue was extracted with hot ethanol (60 ml) and then the ethanol soluble fraction was extracted with hot light petroleum (b.p. 60—80 °C; 100 ml). The petroleum soluble fraction was chromatographed on silica (30 g). Elution with ethyl acetate gave 5-(1-*methoxyimino-ethyl*)-5-*methylimidazolidine*-2,4-*dione* (2) (0.5 g, 27%) as prisms, m.p. 162 °C (from ethyl acetate) (Found: C, 45.6; H, 6.0; N, 22.5. $C_7H_{11}N_3O_3$ requires C, 45.4; H, 6.0; N, 22.7%); δ_H [$(CD_3)_2SO$] 1.31 (s, 3 H, 5-Me), 1.57 (s, 3 H, Me), 3.66 (s, 3 H, OMe), and 8.04 (s, 1 H, NH); *m/z* 185 (M^+).

5-(1-*Methoxyiminoethyl*)-5-*methyl*-3-*morpholinomethyl-imidazolidine*-2,4-*dione*.—Morpholine (0.09 g, 0.001 mol) and then formaldehyde (0.075 ml; 37% solution; 0.93 mmol) were added to a solution of (2) (0.185 g, 0.001 mol) in methanol (10 ml) and then the mixture was allowed to stand overnight. Evaporation of the solvent gave 5-(1-*methoxyiminoethyl*)-5-*methyl*-3-*morpholinomethylimidazolidine*-2,4-*dione* (0.105 g, 37%) as prisms, m.p. 130—131 °C (from ether) (Found: C, 50.6; H, 7.1; N, 19.3. $C_{12}H_{20}N_4O_4$ requires C, 50.7; H, 7.1; N, 19.7%); δ_H [$(CD_3)_2SO$] 1.7 (s, 3 H, 5 Me), 2.0 (s, 3 H, Me), 2.7 (m, 4 H, CH_2O), 3.8 (m, 4 H, CH_2N), 3.95 (s, 3 H, OMe), 4.55 (s, 2 H, NCH_2N), and 7.3 (s, 1 H, NH).

Acid Hydrolysis of Compound (2).—A solution of (2) (1.0 g) in 2M-hydrochloric acid (20 ml) was heated at 100 °C for 20 h and then evaporated to dryness. The residue, which smelled of acetic acid, gave recovered (2) as a solid (0.17 g) when stirred with water (5 ml). The aqueous mother-liquors were evaporated to dryness and the residue was fractionally crystallised from ethanol–ethyl acetate to give hydroxylamine hydrochloride (0.225 g, 73%) as plates, m.p. and mixed m.p. 150—151 °C and 5-methylimidazolidine-2,4-dione (0.185 g, 37%) as prisms, m.p. and mixed m.p. 147—148 °C (Found: C, 42.0; H, 5.2; N, 24.5. Calc. for $C_4H_6N_2O_2$: C, 42.1; H, 5.3; N, 24.6%).

2-(1-*Hydroxyiminoethyl*)-2,4,5-*trimethyl*-2H-*imidazole* 1-*Oxide* (10).—A solution of 3-hydroxyiminobutan-2-one (50 g, 0.5 mol) and ammonium carbonate (320 g, 3.3 mol) in ethanol (500 ml) and water (500 ml) was heated under reflux for 3 days and then the ethanol was allowed to evaporate. On cooling, the aqueous solution deposited 2,3-bis(hydroxyimino)butane (9.0 g) which formed needles, m.p. and mixed m.p. 240—241 °C from ethanol. The aqueous mother-liquors were adjusted to pH 7, saturated with salt, and then extracted with ethyl acetate. The extract gave 2-(1-*hydroxyiminoethyl*)-2,4,5-*trimethyl*-2H-*imidazole* 1-*oxide* (10) (31.7 g, 35%) as stout prisms, m.p. 208 °C (from methanol) (Found: C, 52.1; H, 7.1; N, 22.7. $C_8H_{13}N_3O_2$ requires C, 52.4; H, 7.2; N, 22.9%); δ_H [$(CD_3)_2SO$] 1.24 (s, 3 H, Me), 1.47 (s, 3 H, Me), 2.00 (s, 3 H, Me), 2.15 (s, 3 H, Me), and 11.29 (s, 1 H, OH); *m/z* 183.1006 ($C_8H_{13}N_3O_2$ requires 183.1007), 126.0788 ($C_6H_{10}N_2O$ requires 126.0793).

2-(1-*Acetoxyiminoethyl*)-2,4,5-*trimethyl*-2H-*imidazole* 1-*Oxide* (32).—A solution of (10) (0.915 g, 0.005 mol) and acetic anhydride (0.77 g, 0.0075 mol) in dry pyridine (10 ml) was kept overnight during which time 2-(1-*acetoxyiminoethyl*)-2,4,5-*trimethyl*-2H-*imidazole* 1-*oxide* (32) (0.9 g, 80%) separated as chunky prisms, m.p. 179—180 °C (from ethyl acetate) (Found: C, 53.3; H, 6.7; N, 18.7. $C_{10}H_{15}N_3O_3$ requires C, 53.3; H, 6.7; N, 18.7%); δ_H [$(CD_3)_2SO$; 353 K] 1.52 (s, 3 H, Me), 1.60 (s, 3 H, Me), 2.06 (s, 3 H, Me), 2.18 (s, 3 H, Me), and 2.30 (s, 3 H, Me); *m/z* 225 (M^+).

2-(1-*Methoxyiminoethyl*)-2,4,5-*trimethyl*-2H-*imidazole* 1-*Oxide* (33).—A solution of (10) (0.915 g, 0.005 mol) in water (15 ml) containing sodium hydroxide (0.35 g, 0.0088 mol) was shaken with dimethyl sulphate (0.945 g, 0.0075 mol) until a homogeneous solution was obtained. Extraction with ethyl acetate gave an oil which on distillation gave 2-(1-*methoxy-iminoethyl*)2,4,5-*trimethyl*-2H-*imidazole* 1-*oxide* (33) (0.8 g, 81%), b.p. 100 °C/4.5 mmHg, which formed needles, m.p. 58—59 °C (from ethyl acetate) (Found: C, 54.5; H, 7.9; N, 21.5. $C_9H_{15}N_3O_2$ requires C, 54.8; H, 7.7; N, 21.3%); δ_H (60 MHz; $CDCl_3$) 1.50 (s, 3 H, Me), 1.76 (s, 3 H, Me), 2.22 (s, 3 H, Me), 2.43 (s, 3 H, Me), and 4.0 (s, 3 H, OMe).

2-(1-*Methylaminocarbonyloxyiminoethyl*)-2,4,5-*trimethyl*-2H-*imidazole* 1-*Oxide* (34).—Methyl isocyanate (0.57 g, 0.01 mol) was added to a solution of (10) (1.83 g, 0.01 mol) and triethylamine (1.01 g, 0.01 mol) in dry dimethylformamide (30 ml) and the mixture was stirred for 18 h at room temperature. The solvent was removed and the residual solid recrystallised from ethyl acetate to give 2-(1-*methylamino-carbonyloxyiminoethyl*)-2,4,5-*trimethyl*-2H-*imidazole* 1-*oxide* (34) as prisms, m.p. 143—144 °C (Found: C, 49.7; N, 6.9; N, 23.4. $C_{10}H_{16}N_4O_3$ requires C, 50.0; H, 6.7; N, 23.3%); δ_H ($CDCl_3$) 1.69 (s, 3 H, Me), 1.72 (s, 3 H, Me), 2.15 (s, 3 H, Me), 2.35 (s, 3 H, Me), 2.88 (d, 3 H, NHMe), and 6.17 (br, NH).

Reduction of Compound (10) *with Sodium Dithionite*.—A suspension of (10) (2.62 g, 0.0143 mol) and sodium dithionite (7.1 g, 0.037 mol) in water (50 ml) was heated under reflux for 3 h, cooled, saturated with potassium carbonate, and then extracted with ether. The ether extract gave 2,4,5-trimethylimidazole as an oil (0.766 g, 49%) which formed a hydrochloride as prisms, m.p. 318—320 °C (from methanol–ethyl acetate) (lit.,[16] m.p. 315 °C) (Found: C, 49.0; H, 7.7; Cl, 24.0; N, 18.9. Calc. for $C_6H_{11}ClN_2$: C, 49.1; H, 7.5; Cl, 24.2; N, 19.1%); δ_H (CD_3OD) 2.15 (s, 6 H, 4 Me, and 5 Me), and 2.59 (s, 3 H, 2 Me); *m/z* 110 (M^+).

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