Synthesis of 5-Iminopyrrol-2-one Derivatives from 1,3-Oxazines. Ring Transformations *via* Attack on the 2- or 6-Position of 1,3-Oxazines[1]

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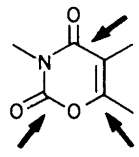
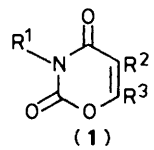
Reaction of the 2*H*-1,3-oxazine-2,4(3*H*)-dione derivatives (**1**) with potassium cyanide resulted in a ring contraction to give the corresponding 5-imino-1,5-dihydro-2*H*-pyrrol-2-ones (**2**), together with the 3-acetyl-4-amino-1*H*-pyrrole-2,5-diones (**3**) or the (*E*)-3-cyanoacrylamides (**5**). Irradiation of the (*E*)-3-cyanomethacrylamide (**5b**) in the presence of a catalytic amount of potassium cyanide also afforded the cyclized 5-iminopyrrol-2-one (**2d**). Further treatment of the iminopyrroles (**2a—c**) and (**2e**) with hydrochloric acid furnished the corresponding 1*H*-pyrrole-2,5-dione derivatives (**4a—d**). A mechanism involving initial attack on the 2- or 6-position of 1,3-oxazines is proposed for the ring transformations. This is the first example of ring transformation *via* attack on the 6-position.

Ring transformations of heterocyclic compounds have been widely utilized in the synthesis of new heterocyclic ring systems or of heterocycles possessing special functional groups, and many reports have appeared in the literature.[2] It is known that 2*H*-1,3-oxazine-2,4(3*H*)-diones undergo ring transformations into pyrimidines,[3-5] pyrazoles,[4] or pyridines[4a,b] on reaction with ammonia, primary aliphatic amines, hydroxylamine, hydrazine, hydroxide anion, or a carbanion. Although the 1,3-oxazine-2,4-dione ring system has three sites for a nucleophilic attack, as shown in structure (I), all these ring transformations



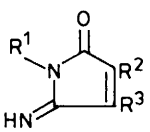
(I)

are initiated by a nucleophilic attack on the 2-position. To the best of our knowledge, no ring transformations resulting from initial attack on the 4- and 6-positions have been reported in the literature. Using the concepts of hard and soft acids and bases, the 6-position is the softest of the three sites and, therefore, the most susceptible to attack by soft nucleophiles.[6] We therefore investigated the reaction of 1,3-oxazine-2,4-diones (**1**) with potassium cyanide, cyanide anion being a soft nucleophile, and found that a novel ring transformation of 1,3-oxazine into pyrrole took place *via* nucleophilic attack on the 6-position; this transformation is applicable to the synthesis of 5-iminopyrrol-2-one derivatives.



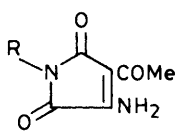
(**1**)

a; $R^1 = R^3 = Me$, $R^2 = H$
b; $R^1 = CH_2Ph$, $R^2 = H$, $R^3 = Me$
c; $R^1 = R^3 = Me$, $R^2 = Br$
d; $R^1 = Me$, $R^2 = R^3 = H$
e; $R^1 = R^2 = Me$, $R^3 = H$
f; $R^1 = Me$, $R^2 = Cy$, $R^3 = H$
g; $R^1 = R^3 = H$, $R^2 = Rf$
h; $R^1 = R^2 = H$, $R^3 = Me$



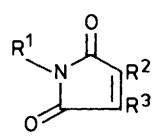
(**2**)

a; $R^1 = R^3 = Me$, $R^2 = H$
b; $R^1 = CH_2Ph$, $R^2 = H$, $R^3 = Me$
c; $R^1 = R^3 = Me$, $R^2 = Br$
d; $R^1 = R^2 = Me$, $R^3 = H$
e; $R^1 = Me$, $R^2 = Cy$, $R^3 = H$



(**3**)

a; R = Me
b; $R = CH_2Ph$



(**4**)

a; $R^1 = R^3 = Me$, $R^2 = H$
b; $R^1 = CH_2Ph$, $R^2 = H$, $R^3 = Me$
c; $R^1 = R^3 = Me$, $R^2 = Br$
d; $R^1 = Me$, $R^2 = Cy$, $R^3 = H$
e; $R^1 = R^3 = H$, $R^2 = Rf$

Cy = cyclohexyl
Rf = β-D-ribofuranosyl

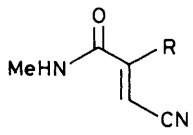
Results and Discussion

Treatment of 3,6-dimethyl-2*H*-1,3-oxazine-2,4(3*H*)-dione (**1a**) with an aqueous solution of potassium cyanide (1.2 mol equiv.) in dimethylformamide (DMF) at room temperature afforded 5-imino-1,4-dimethyl-1,5-dihydro-2*H*-pyrrol-2-one (**2a**) along with 3-acetyl-4-amino-1-methyl-1*H*-pyrrole-2,5-dione (**3a**) in 50 and 15% yield, respectively. The ^1H n.m.r. spectrum of the major pyrrole (**2a**) showed the presence of an imino proton (δ 7.30), a vinyl proton (δ 6.19), and two methyl groups (δ 3.09 and 2.11), and the ^{13}C n.m.r. spectrum revealed the appearance of an imine carbon (δ 164.3) and the loss of one carbon from the starting oxazine (**1a**).[4a] The i.r. spectrum also supported the presence of an imine moiety ($\nu_{max.}$ 3 310 and 1 640 cm^{-1}).

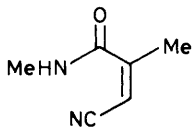
Table. ^{13}C N.m.r. chemical shifts for the 5-imino-1,5-dihydro-2*H*-pyrrol-2-ones (**2**) and 1*H*-pyrrole-2,5-diones (**4**)[a]

Compound	C-2	C-3	C-4	C-5	NMe	3-Me	4-Me	Other
(**2a**)	170.4	125.5	144.4	164.3	24.2		11.2	
(**2b**)	170.2	125.5	142.5	164.7			11.2	137.0 (s, Ph), 128.6, 127.8, and 127.5 (d, Ph), 41.7 (t, CH_2)
(**2c**)	165.2	122.9	138.6	162.8	25.2		10.8	
(**2d**)	171.5	141.5	127.5	163.0	24.2	10.8		
(**2e**)	170.9	150.4	124.9	163.0	24.0			34.8 (d, CH), 31.5 and 26.0 [t, $(CH_2)_5$]
(**4a**)	171.9[b]	145.8	127.6	170.8[b]	23.6	10.9		
(**4b**)	171.3[b]	145.6	127.3	170.3[b]		10.8		136.5 (s, Ph), 128.5, 128.2, and 127.6 (d, Ph), 41.4 (t, CH_2)
(**4c**)	165.5[b]	124.8	142.3	169.4[b]	24.6	10.6		
(**4d**)	170.9[b]	154.7	124.7	171.3[b]	23.5			35.1 (d, CH), 31.4 and 26.0 [t, $(CH_2)_5$]

[a] Chemical shifts in p.p.m. from internal Me_4Si; recorded for solutions in $CDCl_3$. [b] Assignments may be interchanged.



(**5**)



(**6**)

a; R = H
b; R = Me
c; R = cyclohexyl

Furthermore, the pyrrole-2,5-dione (**4a**) obtained by hydrolysis of the 5-iminopyrrol-2-one (**2a**) (*vide infra*) was identical in every respect with an authentic sample.[7] The structure of the minor pyrrole (**3a**) was deduced from the analytical and spectral data, and confirmed by direct comparison with an authentic sample prepared by condensation of *N*-methylacetoacetamide with ethyl cyanoformate.[8] Carrying the reaction out at lower temperature or use of a more dilute aqueous solution of potassium cyanide resulted in a decrease in the yields of compounds (**2a**) and (**3a**).

Analogous treatment of the 3-benzyl-6-methyloxazine (**1b**) and the 5-bromo-3,6-dimethyloxazine (**1c**) [the latter of which was prepared by bromination of the oxazine (**1a**) in the presence of a catalytic amount of anhydrous iron(III)chloride] with potassium cyanide gave the corresponding iminopyrroles (**2b**) and (**2c**) in good yields, together with the 3-acetyl-4-aminopyrrole-2,5-diones (**3b**) and (**3a**),* respectively. Hydrolysis of the iminopyrroles (**2a**—**c**) with 3M-hydrochloric acid in methanol at room temperature easily gave the corresponding pyrrole-2,5-diones (**4a**—**c**). The bromopyrrole-2,5-dione (**4c**) could also be prepared by bromination of the pyrrole (**4a**).

When the 6-unsubstituted 3-methyl-1,3-oxazine-2,4-dione (**1d**) was similarly allowed to react with potassium cyanide, no 5-iminopyrrol-2-one derivative was isolated; instead (*E*)-3-cyano-*N*-methylacrylamide (**5a**) was obtained as the sole product in 18% yield. The ^{13}C n.m.r. spectrum of the acrylamide (**5a**) showed a signal at δ 116.1 due to a cyano carbon and the loss of one carbonyl carbon from the starting oxazine (**1d**). The i.r. spectrum also showed an absorption band characteristic of a cyano group at 2 210 cm^{-1}. In the ^1H n.m.r. spectrum, the *N*-methyl signal appeared as a doublet at δ 2.91, changing to a singlet on the addition of deuterium oxide. The acrylamide (**5a**) was shown to adopt the *E*-configuration on the basis of the coupling constant (*J* 16 Hz) of the AB-type doublet signals at δ 6.72 and 6.44 due to 2-H and 3-H.

On the other hand, the analogous reaction of the 6-unsubstituted 3,5-dimethyloxazine (**1e**) afforded the expected 5-iminopyrrol-2-one (**2d**) in 13% yield, together with 3-cyano-*N*-methylmethacrylamide (**5b**) as the major product (73%); the latter compound was subjected to photoisomerisation in order to elucidate its configuration.

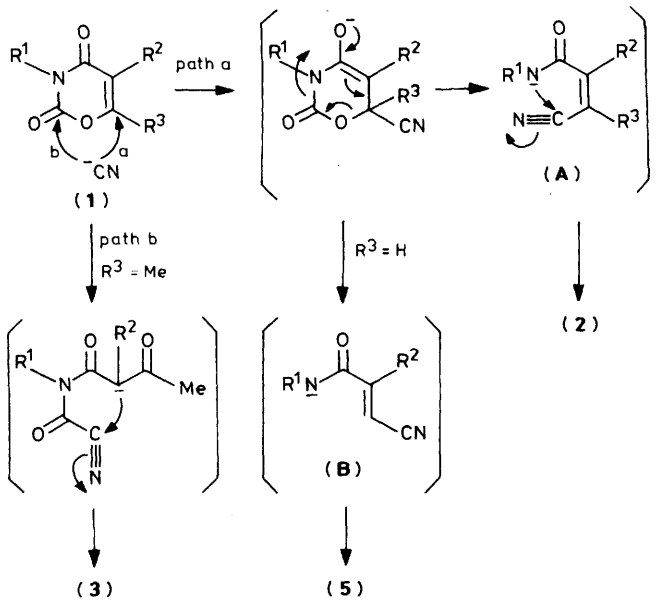
Irradiation of the methacrylamide (**5b**) in methanol for 30 h afforded a *ca.* 1:1 mixture of the (*E*)- and (*Z*)-methacrylamides, and a further, pure isomer (**6**) was also isolated on chromatographic separation. In the ^1H n.m.r. spectra, the vinyl proton signal of (**5b**) appeared at lower field (δ 6.14) than that of (**6**) (δ 5.51). This downfield shift is best explained in terms of the paramagnetic anisotropy of the amide-carbonyl group which is *cis* to the vinyl proton. In a nuclear Overhauser effect (n.O.e.) experiment on compound (**6**), an 8.4% enhancement of the vinyl proton signal occurred on irradiation of the 2-methyl protons (δ 2.16), whereas no such enhancement was observed in the case of (**5b**). On the basis of these ^1H n.m.r. spectral results and the mechanistic considerations described below, it was confirmed that compounds (**5b**) and (**6**) adopt the (*E*)- and (*Z*)-configurations, respectively.

The above photoisomerisation results prompted us to investigate the photocyclisation of compound (**5b**) to the cyclic isomer (**2d**). Thus, irradiation of (**5b**) in the presence of a catalytic amount of potassium cyanide in methanol resulted in the formation of the corresponding 5-iminopyrrol-2-one (**2d**), as expected, in 30% yield.

The analogous reaction of the 5-cyclohexyloxazine (**1f**), which is structurally similar to the nucleoside antibiotic oxazinomycin (**1g**),[9] led to the formation of the 3-cyclohexyl-5-iminopyrrol-2-one (**2e**) in a better yield (57%) than that obtained from the 5-methyloxazine (**1e**), accompanied by the (*E*)-acrylamide (**5c**). The pyrrole (**2e**) was easily hydrolysed to give the corresponding pyrrole-2,5-dione (**4d**), the structure of which is closely similar to the nucleoside antibiotic showdomycin (**4e**).[10]

The proposed mechanism for the formation of the iminopyrrole (**2**), the acetylaminopyrrole (**3**), and the (*E*)-acrylamide (**5**) is depicted in the Scheme. The initial nucleophilic attack by the soft cyanide anion occurs mostly at the soft 6-position rather than at the hard 2-position of the 1,3-oxazine-2,4-diones (**1**) to give the (*Z*)- and (*E*)-3-cyanoacrylamide intermediates (**A**) and (**B**). The intermediate (**A**) can undergo intramolecular cyclisation to give the 5-iminopyrrol-2-one (**2**), while protonation of the anion (**B**) produces the (*E*)-acrylamide (**5**) (path a in the Scheme). The product distribution of the (*Z*)- and (*E*)-intermediates (**A**) and (**B**) seems to depend upon the bulkiness of the 5- and 6-substituents of the starting oxazines; that is to say, the greater the bulk of the 5-substituent (H < Me < cyclohexyl), the greater the yield (0⟶13⟶57%) of

* A reason for the formation of the debrominated product (**3a**) from the 5-bromo-oxazine (**1c**) remains equivocal.



Scheme.

the 5-iminopyrrol-2-one (**2**). The presence of the 6-methyl group prevents the formation of the corresponding (*E*)-crotonamide.

The formation of the minor pyrrole (**3**) can also be explained in terms of conventional initial nucleophilic attack of the cyanide anion on the 2-position [3-5] (path b in the Scheme). The attack of the soft nucleophile on the hard 2-position is accounted for by the steric hindrance of the 6-position due to the 6-methyl group. This consideration accommodates the fact that the 6-unsubstituted 1,3-oxazine-2,4-diones (**1d—f**) give no product resulting from attack on the 2-position. The photocyclisation of the (*E*)-acrylamide (**5b**) is explained in terms of an initial photoisomerisation to give the corresponding (*Z*)-acrylamide intermediate (**A**) which cyclizes to give the pyrrole (**2d**).

The ring transformation described here represents a useful synthetic method for the preparation of the 5-imino-1,5-dihydro-2*H*-pyrrol-2-one derivatives because of the ready accessibility of the starting compounds,[4a,c5a] and is of interest in connection with the possible transformation of oxazinomycin (**1g**) into showdomycin (**4e**). However, the reaction of the oxazine (**1h**), which contains an acidic NH proton, with potassium cyanide did not take place. Therefore, the protection of the NH group of oxazinomycin (**1g**) is requisite for the transformation into showdomycin (**4e**).

Experimental

M.p.s were determined on a Yanagimoto hot-stage apparatus and are uncorrected. Low-pressure column chromatography was carried out with 230—400 mesh silica gel 60 (Nakarai) and a Kiriyama ILC-135-10 low-pressure pump system with a typical flow pressure of 3 kg cm^{-2}. Centrifugal thin layer chromatography (c.t.l.c.) was carried out on a Harrison centrifugal thin layer chromatotron model 7924 with kieselgel 60 GF_{254} (Merck). T.l.c. was performed using silica gel 60 F_{254} precoated glass plates (Merck). Mass spectra were measured with a Hitachi M-52 spectrometer and i.r. spectra were obtained on a JASCO IRA-1 spectrophotometer. U.v. spectra were recorded for solutions in methanol on a JASCO UVIDEC-1 double-beam spectrophotometer. ^1H N.m.r. spectra were recorded on a JEOL JNM-PS-100 nuclear magnetic resonance spectrometer or a JEOL JNM-FX-100 Fourier transform spectrometer, and ^{13}C n.m.r. spectra on the latter spectrometer operating at 25.00 MHz, with tetramethylsilane as an internal standard. The assignments of all the ^{13}C resonances were confirmed by off-resonance decoupling and single-frequency selective proton-decoupling experiments, and by comparison of the chemical shifts of different compounds taking into consideration the known substituent effects.[11]

5-Bromo-3,6-dimethyl-2H-1,3-oxazine-2,4(3H)-dione (**1c**) *and 5-Bromo-6-dibromomethyl-3-methyl-2H-1,3-oxazine-2,4-(3H)-dione*.—To a mixture of the oxazine (**1a**) (560 mg, 4 mmol), anhydrous iron(III) chloride (50 mg), and 1,2-dichloroethane (10 ml) was added a solution of bromine (1 400 mg, 8.75 mmol) in 1,2-dichloroethane (5 ml) and the whole mixture was refluxed for 15 h. After it had been cooled, triethylamine (1 ml) was added, the mixture was washed successively with aqueous sodium thiosulphate and water, and dried ($MgSO_4$), and the solvent was then evaporated. The residue was chromatographed under low pressure with benzene. From the earlier fractions was isolated the *dibromomethyloxazine*, which was recrystallized from hexane to give colourless needles (20 mg, 1%), m.p. 110—111 °C (Found: C, 19.3; H, 1.05; N, 3.7. $C_6H_4Br_3NO_3$ requires C, 19.05; H, 1.05; N, 3.7%); *m/z* 381 ($M^+ + 6$), 379 ($M^+ + 4$), 377 ($M^+ + 2$), and 375 (M^+); $\delta_H(CDCl_3)$ 6.72 (1 H, s, 5-H) and 3.46 (3 H, s, NMe); $\delta_C(CDCl_3)$ 157.1 (s), 156.6 (s), 146.4 (s), 96.1 (s, C-5), 30.4 (q, NMe), and 28.8 p.p.m. (d, CH).

The *5-bromo-oxazine* (**1c**) was obtained from the later fractions with the same solvent and recrystallized from hexane to afford colourless plates (730 mg, 83%), m.p. 92—93 °C (Found: C, 32.55; H, 2.7; N, 6.3. $C_6H_6BrNO_3$ requires C, 32.75; H, 2.75; N, 6.35%); *m/z* 221 ($M^+ + 2$) and 219 (M^+); $\delta_H(CDCl_3)$ 3.39 (3 H, s, NMe) and 2.42 (3 H, s, CMe); $\delta_C(CDCl_3)$ 161.9 (s), 157.9 (s), 147.7 (s), 99.2 (s, C-5), 29.7 (q, NMe), and 19.7 p.p.m. (q, 6-Me).

3-Methyl-2H-1,3-oxazine-2,4(3H)-dione (**1d**).—The oxazine (**1d**) was prepared according to the procedure described previously [5a] and its ^{13}C n.m.r. spectrum was measured; $\delta_C[(CD_3)_2SO]$ 161.2 (s), 154.7 (d, C-6), 148.9 (s), 103.7 (d, C-5), and 27.9 p.p.m. (q, NMe).

5-Cyclohexyl-3-methyl-2H-1,3-oxazine-2,4(3H)-dione (**1f**).—A mixture of cyclohexylmalonyl dichloride (33.5 g, 0.15 mol) and methyl isocyanate (8.6 g, 0.15 mol) was heated at 140 °C for 5 h and at 180—200 °C for 2 h. The crude oil was distilled under reduced pressure to give *6-chloro-5-cyclohexyl-3-methyl-2H-1,3-oxazine-2,4(3H)-dione* as a colourless viscous oil (22.0 g, 60%), b.p. 138 °C at 1.8 mmHg (Found: C, 54.25; H, 6.0; N, 5.7. $C_{11}H_{14}ClNO_3$ requires C, 54.2; H, 5.8; N, 5.75%); *m/z* 245 ($M^+ + 2$) and 243 (M^+); $\delta_H(CDCl_3)$ 3.27 (3 H, s, NMe), 2.92—2.52 (1 H, m, CH), and 2.20—1.04 [10 H, m, $(CH_2)_5$].

A mixture of the above-obtained 6-chloro-oxazine (1 200 mg, 5 mmol) and ethanol (30 ml) was hydrogenated in the presence of 5% palladium on barium sulphate (120 mg) under atmospheric pressure and at room temperature. A usual treatment of the reaction mixture and recrystallisation from hexane gave *colourless plates* (**1f**) (810 mg, 79%), m.p. 96—97 °C (Found: C, 63.05; H, 7.4; N, 6.6. $C_{11}H_{15}NO_3$ requires C, 63.15; H, 7.25; N, 6.7%); *m/z* 209 (M^+); $\delta_H(CDCl_3)$ 7.13 (1 H, s, 6-H), 3.30 (3 H, s, NMe), 2.68—2.28 (1 H, m, CH), and 2.04—0.80 [10 H, m, $(CH_2)_5$].

5-Imino-1,4-dimethyl-1,5-dihydro-2H-pyrrol-2-one (**2a**) *and 3-Acetyl-4-amino-1-methyl-1H-pyrrole-2,5-dione* (**3a**).—To a stirred solution of the oxazine (**1a**) (1 410 mg, 10 mmol) in DMF (20 ml) was added a solution of potassium cyanide (780 mg, 12 mmol) in water (2 ml) dropwise at room temperature. After being stirred for 2 h, the reaction mixture was diluted with water

(20 ml) and the mixture was extracted with chloroform. The extract was washed with water and dried ($MgSO_4$), and the solvent was evaporated off under reduced pressure. Hexane was added to the resulting residue and the insoluble *pale yellow solid* (**3a**) was filtered off. The hexane solution was evaporated off and the residue was chromatographed under low pressure with hexane–ethyl acetate (3:2, v/v). From the earlier fractions, further crops of the pale yellow solid was obtained. The combined pale yellow solid was recrystallized from acetone to give pale yellow prisms (250 mg, 15%), m.p. 241—243 °C (decomp.) (Found: C, 49.9; H, 4.8; N, 16.55. $C_7H_8N_2O_3$ requires C, 50.0; H, 4.8; N, 16.65%); *m/z* 168 (M^+); $\nu_{max.}$(KBr) 3 300 and 3 100 (NH_2), 1 710, 1 660, and 1 640 cm^{-1} (C=O); $\lambda_{max.}$ 247sh, 252, and 360 nm (log ε 4.23, 4.24, and 3.51); δ_H[$(CD_3)_2SO$] 9.16 (2 H, br s, NH_2, exchanged in D_2O), 2.87 (3 H, s, NMe), and 2.31 (3 H, s, COMe); δ_C[$(CD_3)_2SO$] 191.9 (s, *C*OMe), 169.4 (s, 2-CO), 164.1 (s, 5-CO), 155.1 (s, C-4), 97.3 (s, C-3), 28.0 (q, CO*Me*), and 23.2 p.p.m. (q, NMe). The acetylaminopyrrole (**3a**) was identical with an authentic sample prepared by a modified version of the patent method[7] as follows. To a stirred mixture of anhydrous zinc chloride (3 270 mg, 24 mmol) (dried at 100 °C *in vacuo* for 1 h), *N*-methylacetoacetamide (2 020 mg, 18 mmol), and dry dichloromethane (20 ml) was added a solution of triethylamine (2 020 mg, 20 mmol) in dry dichloromethane (10 ml) and the whole mixture was stirred at room temperature for 2 h. After addition of a solution of ethyl cyanoformate (1 980 mg, 20 mmol) in dry dichloromethane (20 ml), the mixture was stirred for 24 h. To the reaction mixture was added 2M-hydrochloric acid (10 ml) and water (20 ml), and the mixture was stirred for a further 1 h. The resulting precipitate was collected by filtration, washed with a small amount of water, dried, and recrystallized from acetone to give pale yellow prisms (1 990 mg, 67%), m.p. 243—245 °C (decomp.).

From the later fractions, was isolated the *iminopyrrole* (**2a**), which was recrystallized from hexane to give colourless sticks (620 mg, 50%), m.p. 90—91 °C (Found: C, 58.0; H, 6.55; N, 22.45. $C_6H_8N_2O$ requires C, 58.05; H, 6.5; N, 22.6%); *m/z* 124 (M^+); $\nu_{max.}$($CHCl_3$) 3 310 and 1 640 (C=NH), and 1 720 cm^{-1} (C=O); $\lambda_{max.}$ 235 and 294 nm (log ε 4.21 and 3.20); δ_H($CDCl_3$) 7.30 (1 H, br, NH, exchanged in D_2O), 6.19 (1 H, q, *J* 2 Hz, 3-H), 3.09 (3 H, s, NMe), and 2.11 (3 H, d, *J* 2 Hz, 4-Me).

1-*Benzyl*-5-*imino*-4-*methyl*-1,5-*dihydro*-2H-*pyrrol*-2-*one* (**2b**) *and* 3-*Acetyl*-4-*amino*-1-*benzyl*-1H-*pyrrole* -2,5-*dione* (**3b**).—A mixture of the oxazine (**1b**) (1 090 mg, 5 mmol) and DMF (10 ml) was treated with a solution of potassium cyanide (390 mg, 6 mmol) in water (1 ml) for 1 h and the reaction mixture was treated as described above for the preparation of the iminopyrrol-2-one (**2a**) and the pyrrole-2,5-dione (**3a**). To the resulting residue was added chloroform and the insoluble solid was filtered off and recrystallized from acetone to give *pale yellow needles* (**3b**) (250 mg, 20%), m.p. 236—238 °C (decomp.) (Found: C, 63.9; H, 4.9; N, 11.45. $C_{13}H_{12}N_2O_3$ requires C, 63.9; H, 4.95; N, 11.5%); *m/z* 244 (M^+); $\nu_{max.}$(KBr) 3 300 and 3 140 (NH_2), 1 710 and 1 670 cm^{-1} (C=O); $\lambda_{max.}$ 210, 242, and 360 nm (log ε 4.04, 4.26, and 3.52); δ_H[$(CD_3)_2SO$] 9.32 (2 H, br, NH_2, exchanged in D_2O), 7.26 (5 H, s, Ph), 4.62 (2 H, s, CH_2), and 2.35 (3 H, s, COMe); δ_C[$(CD_3)_2SO$ + $CDCl_3$] 192.2 (s, *C*OMe), 168.9 (s, 2-CO), 163.8 (s, 5-CO), 154.9 (s, C-4), 136.5 (s, Ph), 128.4 and 127.2 (d, Ph), 97.2 (s, C-3), 40.4 (t, CH_2), and 28.0 (q, CO*Me*).

The chloroform solution was concentrated to a small volume and purified by c.t.l.c. using chloroform as eluant, and then recrystallized from hexane to give *pale yellow plates* (**2b**) (730 mg, 73%), m.p. 71.5—72.5 °C (Found: C, 71.9; H, 5.95; N, 13.95. $C_{12}H_{12}N_2O$ requires C, 72.0; H, 6.0; N, 14.0%); *m/z* 200 (M^+); $\nu_{max.}$($CHCl_3$) 3 300 and 1 635 (C=NH), and 1 715 cm^{-1} (C=O); $\lambda_{max.}$ 212, 235, and 294 nm (log ε 4.04, 4.19, and 3.19); δ_H($CDCl_3$) 8.24 (1 H, br, NH, exchanged in D_2O), 7.26 (5 H, s, Ph), 6.19 (1 H, q, *J* 2 Hz, 3-H), 4.78 (2 H, s, CH_2), and 2.09 (3 H, d, *J* 2 Hz, 4-Me).

3-*Bromo*-5-*imino*-4-*methyl*-1,5-*dihydro*-2H-*pyrrol*-2-*one* (**2c**) *and the Acetylaminopyrrole*-2,5-*dione* (**3a**).—A mixture of the oxazine (**1c**) (1 100 mg, 5 mmol) and DMF (10 ml) was treated with a solution of potassium cyanide (390 mg, 6 mmol) in water (1 ml) for 2 h and the reaction mixture was treated as described above for the preparation of the iminopyrrol-2-one (**2a**) and the pyrrole-2,5-dione (**3a**). The resulting residue was chromatographed under low pressure with chloroform. From the earlier fractions was isolated the *iminopyrrol*-2-*one* (**2c**), which was recrystallized from ethyl acetate to give colourless prisms (720 mg, 71%), m.p. 150—151 °C (decomp.) (Found: C, 35.55; H, 3.5; N, 13.8. $C_6H_7BrN_2O$ requires C, 35.5; H, 3.5; N, 13.8%); *m/z* 204 (M^+ + 2) and 202 (M^+); $\nu_{max.}$($CHCl_3$) 3 310 and 1 645 (C=NH), and 1 735 cm^{-1} (C=O); $\lambda_{max.}$ 249 nm (log ε 4.29); δ_H($CDCl_3$) 8.32 (1 H, br, NH, exchanged in D_2O), 3.15 (3 H, s, NMe), and 2.11 (3 H, s, 4-Me).

From the later fractions was isolated the acetylaminopyrrole-2,5-dione (**3a**) (80 mg, 10%), which was identical in every respect with an authentic sample prepared above.

1H-*Pyrrole*-2,5-*diones* (**4a—d**).—*General procedure.* To a solution of the iminopyrrol-2-ones (**2a—c**) and (**2e**) (1 mmol) in methanol (20 ml) was added 3M-hydrochloric acid (1 ml) and the mixture was stirred at room temperature for appropriate times. The progress of the reaction was followed by t.l.c. The solvent was evaporated under reduced pressure and chloroform was added to the residue. The chloroform solution was washed successively with aqueous sodium hydrogen carbonate and water, and dried ($MgSO_4$). Chloroform was evaporated under reduced pressure and the residue was distilled under reduced pressure or recrystallized from hexane.

1,3-Dimethyl-1*H*-pyrrole-2,5-dione (**4a**) (60%)* had b.p. 113—115 °C (bath) at 18 mmHg (lit.,[7] 84.5—85 °C at 10 mmHg) and n_D^{26} 1.4970 (lit.,[7] 1.4943) (Found: C, 57.4; H, 5.7; N, 11.05. Calc. for $C_6H_7NO_2$: C, 57.6; H, 5.65; N, 11.2%); *m/z* 125 (M^+); $\nu_{max.}$($CHCl_3$) 1 690 cm^{-1} (C=O); $\lambda_{max.}$ 222 nm (log ε 4.18); δ_H($CDCl_3$) 6.32 (1 H, q, *J* 2 Hz, 4-H), 3.00 (3 H, s, NMe), and 2.09 (3 H, d, *J* 2 Hz, 3-Me); 1-benzyl-3-methyl-1*H*-pyrrole-2,5-dione (**4b**) (90%) had b.p. 160—162 °C (bath) at 4 mmHg (lit.,[12] 189—190 °C at 26 mmHg) (Found: C, 50.1; H, 4.85; N, 16.65. Calc. for $C_{12}H_{11}NO_2$: C, 50.0; H, 4.8; N, 16.65%); *m/z* 201 (M^+); $\nu_{max.}$($CHCl_3$) 1 705 cm^{-1} (C=O); $\lambda_{max.}$ 215 and 222sh nm (log ε 4.16 and 4.14); δ_H($CDCl_3$) 7.30—7.14 (5 H, m, Ph), 6.22 (1 H, q, *J* 2 Hz, 4-H), 4.56 (2 H, s, CH_2), and 1.95 (3 H, d, *J* 2 Hz, 3-Me); 3-*bromo*-1,4-*dimethyl*-1H-*pyrrole*-2,5-*dione* (**4c**) (94%) had m.p. 50—51 °C (Found: C, 35.2; H, 3.0; N, 6.85. $C_6H_6BrNO_2$ requires C, 35.3; H, 2.95; N, 6.85%); *m/z* 205 (M^+ + 2) and 203 (M^+); $\nu_{max.}$($CHCl_3$) 1 715 cm^{-1} (C=O); $\lambda_{max.}$ 238 nm (log ε 4.21); δ_H($CDCl_3$) 3.06 (3 H, s, NMe) and 2.06 (3 H, s, 4-Me). Compound (**4c**) was identical with an authentic sample prepared as follows. A mixture of the pyrrole-2,5-dione (**4a**) (1 000 mg, 8 mmol), bromine (1 300 mg, 8 mmol), and carbon tetrachloride (20 ml) was gently refluxed for 30 min. Triethylamine (900 mg, 8.9 mmol) was added to the cooled reaction mixture and the mixture was washed with water, dried ($MgSO_4$), and evaporated under reduced pressure. The resulting residue was recrystallized from hexane to give colourless sticks (1 380 mg, 85%), m.p. 51—52 °C; 3-*cyclohexyl*-1-*methyl*-1H-*pyrrole*-2,5-*dione* (**4d**) (99%) had m.p. 94—95 °C (Found: C, 68.1; H, 8.0; N, 7.1. $C_{11}H_{15}NO_2$ requires C, 68.35; H,

* Compound (**4a**) is volatile even at room temperature and atmospheric pressure; when allowed to stand for 30 min at 23.5 °C and 753.6 mmHg, 1 mg of the compound (**4a**) reduced in weight by 158 × 10^{-3} mg.

7.8; N, 7.25%); *m/z* 193 (M^+); $\nu_{max.}$($CHCl_3$) 1 705 cm^{-1} (CO); $\lambda_{max.}$ 227 nm (log ε 4.19); δ_H($CDCl_3$) 6.21 (1 H, d, *J* 2 Hz, 4-H), 2.96 (3 H, s, NMe), 2.68—2.28 (1 H, m, CH), and 2.32—0.96 [10 H, m, $(CH_2)_5$].

(E)-3-*Cyano*-N-*methylacrylamide* (**5a**).—A mixture of the oxazine (**1d**) (1 270 mg, 10 mmol) and DMF (20 ml) was treated with a solution of potassium cyanide (780 mg, 12 mmol) in water (2 ml) for 1 h and the reaction mixture was treated as described above for the preparation of the iminopyrrol-2-one (**2a**) and the pyrrole-2,5-dione (**3a**). The resulting residue was recrystallized from ethyl acetate to give *colourless leaves* (**5a**) (200 mg, 18%), m.p. 142—143 °C (Found: C, 54.4; H, 5.5; N, 25.25. $C_5H_6N_2O$ requires C, 54.55; H, 5.5; N, 25.45%); *m/z* 110 (M^+); $\nu_{max.}$($CHCl_3$) 2 210 (CN) and 1 665 cm^{-1} (CO); $\lambda_{max.}$ 218, 231sh, and 252 nm (log ε 4.16, 3.99, and 3.68); δ_H($CDCl_3$) 6.72 (1 H, d, *J* 16 Hz, 2-H), 6.44 (1 H, d, *J* 16 Hz, 3-H), 6.08 (1 H, br, NH, exchanged in D_2O), and 2.91 (3 H, d, *J* 5 Hz, changed to s in D_2O, NMe); δ_C($CDCl_3$) 162.4 (s, CO), 141.9 (d, C-2), 116.1 (s, CN), 109.8 (d, C-3), and 26.8 p.p.m. (q, NMe).

5-*Imino*-1,3-*dimethyl*-1,5-*dihydro*-2H-*pyrrol*-2-*one* (**2d**) *and* (E)-3-*Cyano*-N-*methylmethacrylamide* (**5b**).—A mixture of the oxazine (**1e**) (2 820 mg, 20 mmol) and DMF (40 ml) was treated with a solution of potassium cyanide (1 560 mg, 24 mmol) in water (4 ml) for 2 h and the reaction mixture was treated as described above for the preparation of the iminopyrrol-2-one (**2a**) and the pyrrole-2,5-dione (**3a**). The resulting residue was subjected to c.t.l.c. using chloroform–methanol (20:1, v/v) as eluant. From the earlier fractions was isolated the 5-*iminopyrrol*-2-*one* (**2d**), which was recrystallized from hexane to give colourless plates (320 mg, 13%), m.p. 58—59 °C (Found: C, 57.95; H, 6.5; N, 22.55. $C_6H_8N_2O$ requires C, 58.05; H, 6.5; N, 22.55%); *m/z* 124 (M^+); $\nu_{max.}$($CHCl_3$) 3 320 and 1 650 (C=NH), and 1 720 cm^{-1} (CO); $\lambda_{max.}$ 236 and 295 nm (log ε 4.17 and 3.17); δ_H($CDCl_3$) 7.52 (1 H, br, NH, exchanged in D_2O), 6.41 (1 H, q, *J* 2 Hz, 4-H), 3.11 (3 H, s, NMe), and 2.03 (3 H, d, *J* 2 Hz, 3-Me).

From the later fractions, was isolated the (E)-*methacrylamide* (**5b**), which was recrystallized from benzene to give colourless prisms (1 820 mg, 73%), m.p. 76—77 °C (Found: C, 58.0; H, 6.55; N, 22.4. $C_6H_8N_2O$ requires C, 58.05; H, 6.5; N, 22.55%); *m/z* 124 (M^+); $\nu_{max.}$($CHCl_3$) 2 220 (CN) and 1 670 cm^{-1}(CO); $\lambda_{max.}$ 223 nm (log ε 4.13); δ_H($CDCl_3$) 7.36 (1 H, br, NH, exchanged in D_2O), 6.14 (1 H, q, *J* 1 Hz, 3-H), 2.86 (3 H, d, *J* 5 Hz, changed to s in D_2O, NMe), and 2.27 (3 H, d, *J* 1 Hz, 2-Me); δ_C($CDCl_3$) 165.9 (s, CO), 153.7 (s, C-2), 116.1 (s, CN), 103.4 (d, C-3), 26.9 (q, NMe), and 17.3 p.p.m. (q, 2-Me).

Irradiation of the (E)-*Methacrylamide* (**5b**).—Preparative irradiations were carried out in a flask equipped with a Pyrex-jacketted immersion lamp. The light source was a Riko-UVL 400W high-pressure mercury arc lamp.

Photoisomerisation of the (E)-*Methacrylamide* (**5b**) *to the* (Z)-*Methacrylamide* (**6**).—A solution of the (*E*)-methacrylamide (**5b**) (200 mg, 1.6 mmol) in methanol (100 ml) was irradiated for 30 h. After evaporation of the solvent, the residue was subjected to c.t.l.c. using chloroform–menthanol (20:1, v/v) as eluant. From the earlier fractions was recovered the starting material (**5b**) (86 mg). From the later fractions, was obtained the (Z)-*isomer* (**6**), which was recrystallized from benzene to give colourless sticks {94 mg, 47% [82% based on the consumed (**5b**)]}, m.p. 80—81 °C (Found: C, 58.05; H, 6.65; N, 22.5. $C_6H_8N_2O$ requires C, 58.05; H, 6.5; N, 22.55%); *m/z* 124 (M^+); $\nu_{max.}$($CHCl_3$) 2 220 (CN) and 1 660 cm^{-1} (CO); $\lambda_{max.}$ 217 nm (log ε 4.00); δ_H($CDCl_3$) 7.36 (1 H, br, NH, exchanged in D_2O), 5.51 (1 H, q, *J* 2 Hz, 3-H), 2.96 (3 H, d, *J* 5 Hz, changed to s in D_2O, NMe), and 2.15 (3 H, d, *J* 2 Hz, 2-Me); δ_C($CDCl_3$) 165.9 (s, CO), 155.9 (s, C-2), 115.6 (s, CN), 99.7 (d, C-3), 26.6 (q, NMe), and 20.7 p.p.m. (q, 2-Me).

Photocyclisation of the (E)-*Methacrylamide* (**5b**).—To a solution of the (*E*)-methacrylamide (**5b**) (200 mg, 1.6 mmol) in methanol (100 ml), was added a solution of potassium cyanide (30 mg, 0.5 mmol) in water (0.5 ml), and the mixture was irradiated for 30 h. After evaporation of the solvent and addition of water, the mixture was extracted with chloroform. The extract was washed with water and dried ($MgSO_4$), and the solvent was evaporated under reduced pressure. The residue was recrystallized from hexane to give the 5-iminopyrrol-2-one (**2d**) (60 mg, 30%), which was identical in every respect with the sample prepared above by the reaction of the oxazine (**1e**) with potassium cyanide.

3-*Cyclohexyl*-5-*imino*-1-*methyl*-1,5-*dihydro*-2H-*pyrrol*-2-*one* (**2e**) *and* (E)-3-*Cyano*-2-*cyclohexyl*-N-*methylacrylamide* (**5c**).—A mixture of the oxazine (**1f**) (1 050 mg, 5 mmol) and DMF (10 ml) was treated with a solution of potassium cyanide (390 mg, 6 mmol) in water (1 ml) for 1 h and the reaction mixture was treated as described above for the preparation of the iminopyrrol-2-one (**2a**) and the pyrrole-2,5-dione (**3a**). The resulting residue was subjected to c.t.l.c. using chloroform as eluant. From the earlier fractions, the 5-*iminopyrrol*-2-*one* (**2e**) was isolated and recrystallized from hexane to give colourless prisms (550 mg, 57%), m.p. 68—70 °C (Found: C, 68.65; H, 8.65; N, 14.6. $C_{11}H_{16}N_2O$ requires C, 68.7; H, 8.4; N, 14.55%); *m/z* 192 (M^+); $\nu_{max.}$($CHCl_3$) 3 300 and 1 635 (C=NH), and 1 720 cm^{-1} (CO); $\lambda_{max.}$ 240 and 290 nm (log ε 4.28 and 3.21); δ_H($CDCl_3$) 7.94 (1 H, br, NH, exchanged in D_2O), 6.37 (1 H, d, *J* 2 Hz, 4-H), 3.09 (3 H, s, NMe), 2.68—2.28 (1 H, m, CH), and 2.12—0.96 [10 H, m, $(CH_2)_5$].

The (E)-*acrylamide* (**5c**) was isolated from the later fractions and recrystallized from hexane–ethyl acetate to give colourless needles (400 mg, 41%), m.p. 122—124 °C (Found: C, 68.75; H, 8.7; N, 14.65. $C_{11}H_{16}N_2O$ requires C, 68.7; H, 8.4; N, 14.55%); *m/z* 192 (M^+); $\nu_{max.}$($CHCl_3$) 2 210 (CN) and 1 655 cm^{-1} (CO); $\lambda_{max.}$ 220 nm (log ε 4.08); δ_H($CDCl_3$) 6.66 (1 H, br, NH, exchanged in D_2O), 5.50 (1 H, s, 3-H), 2.82 (3 H, d, *J* 5 Hz, changed to s in D_2O, NMe), 2.92—2.48 (1 H, m, CH), and 2.08—0.96 [10 H, m, $(CH_2)_5$]; δ_C($CDCl_3$) 167.3 (s, CO), 165.9 (s, C-2), 115.5 (s, CN), 98.5 (d, C-3), 43.0 (d, CH), 30.8, 26.1, and 25.4 [t, $(CH_2)_5$], and 26.1 p.p.m. (q, NMe).

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