Pyrrole Studies. Part 26.[1] A Novel Thermochromic and Photochromic Pyrrole System

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2-Dichloromethyl-3,5-bisethoxycarbonyl-4-methylpyrrole (3) yields a thermally labile 5,10-methylenedioxy-5*H*,10*H*-dipyrrolo[1,2-*a*;1',2'-*d*]pyrazine (1) when heated with 6% aqueous potassium hydroxide. Upon being heated at 160 °C the colourless dipyrrolopyrazine is converted into a red bis-(1-azafulvene) system, which can be reconverted photochromically into the dipyrrolopyrazine *via* a [6π + 6π] cycloaddition reaction.

It has been reported [2] that during the hydrolysis of 3,5-bisethoxycarbonyl-2-formyl-4-methylpyrrole, which had been prepared according to the procedure described by Corwin *et al.*,[3] a light-sensitive [4] orange-red compound (*ca.* 1%) was formed, in addition to the expected dicarboxylic acid. Re-examination [5] of this reaction has shown that the coloured product results not from the aldehyde but from a base-catalysed reaction of 2-dichloromethyl-3,5-bisethoxycarbonyl-4-methylpyrrole, which is a precursor of the aldehyde and with which it has a similar melting point.[5,6] Treatment of a pure sample of the dichloromethylpyrrole with potassium hydroxide under the conditions described in the literature [2] or, preferably, under phase-transfer catalysed conditions, results in the formation of the coloured compound as the major product (65%), whereas hydrolysis of the pure formylpyrrole yields only the dicarboxylic acid.[5]

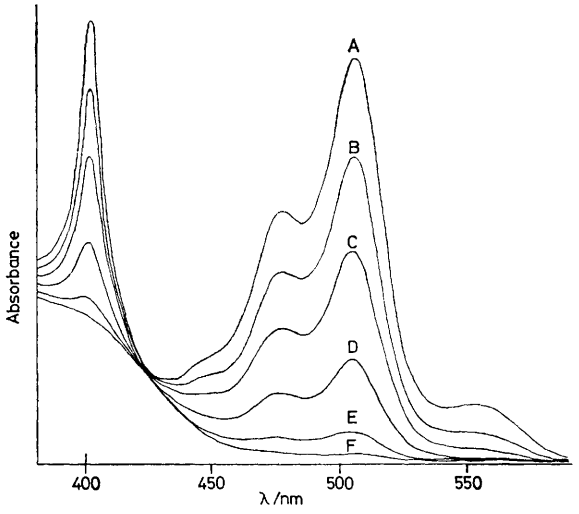


FIGURE 1 Visible spectrum of compound (7) (10^{-3} M in $CHCl_3$) upon irradiation at 400 nm after (A) 0, (B) 300, (C) 660, (D) 1 560, (E) 2 160, and (F) 3 060 s

Upon being heated, the orange-red compound acquired a deeper red colour at *ca.* 160 °C and melted at 217 °C. Solutions of the red compound exhibited a strong yellow-green fluorescence and irradiation of the solid compound, or its solutions in chloroform, at 400 nm caused rapid decolouration. Kinetic measurements of the photochromic process showed it to be unimolecular with a first-order rate constant of *ca.* 10^{-3} s^{-1} (Figure 1). The thermochromic and photochromic changes are reversible and the orange-red product, obtained from the hydrolysis reaction, proved to be a mixture of the red and colourless components.

The ^1H n.m.r. spectral data for the colourless compound showed that it has a lower degree of symmetry than was indicated by the originally reported measurements.[2] In particular, the spectrum showed three non-equivalent aryl-methyl groups (δ 2.50, 2.60, and 2.66), implying that the system has three non-equivalent pyrrole rings. The high resolution spectrum also showed signals at low field (δ 5.85, 8.65, and 8.71) each equivalent to one proton, which were not reported in the earlier publication. The ^{13}C n.m.r. spectrum confirms the presence of three non-equivalent pyrrole rings but shows that two of the rings have closely similar environments. The majority of the ^{13}C resonance signals are readily assigned to ethoxycarbonyl and methyl groups and to the pyrrole-ring carbon atoms, but three signals, which appear as doublets in the proton-coupled spectrum, at 75.4, 75.9 and 90.3 p.p.m. are consistent with –CH(X)Y groups, where X and Y are electronegative elements. The electronic spectrum is compatible with that expected of a polysubstituted pyrrole [7] and the infrared spectral data confirm the presence of α- and β-carboxylic esters but only a low intensity band attributable to a ν(NH) vibration was observed, which showed the expected frequency shift upon H–D exchange with deuterium oxide. The originally reported molecular weight, obtained by the Rast method, is at variance with that expected for a system having three pyrrole rings. It is noteworthy that the base peak of the electron-impact mass spectrum appeared at *m/e* 472.185, which corresponds to the originally proposed formula $C_{24}H_{28}N_2O_8$. A molecular ion compatible with the system having three pyrrole rings was not observed in the electron-impact spectrum, but the chemical-ionization spectrum established the molecular weight to be 741.264.

The structure of the colourless isomer (1) was established unequivocally by *X*-ray crystallographic measurements (Figure 2). Such a structure having three chiral centres, two of which are fixed by the rigid structure, accounts for the non-equivalence of the ^1H and ^{13}C n.m.r. signals, respectively at δ 8.65 and 8.71 and at 75.4 and 75.9 p.p.m., due to the –O–CH–N– group, and also, the general overall non-equivalence of the pyrrole rings and

substituents of the dipyrrolopyrazine system. The absence of the molecular ion under electron impact and the appearance of a high intensity peak at *m/e* 472 in the electron-impact mass spectrum of (1) is readily explicable

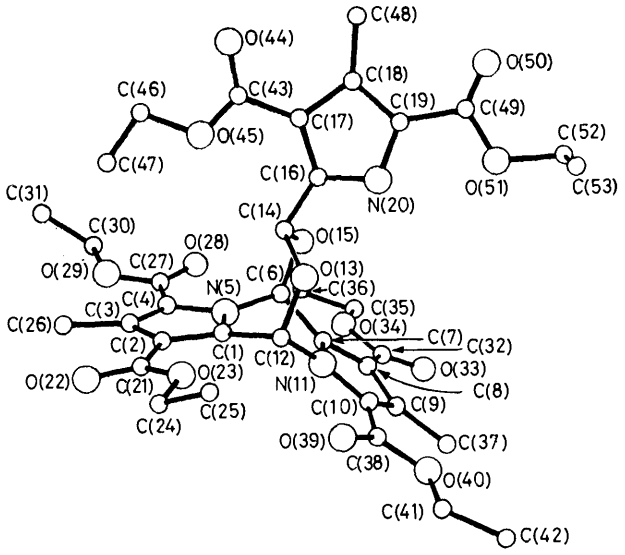
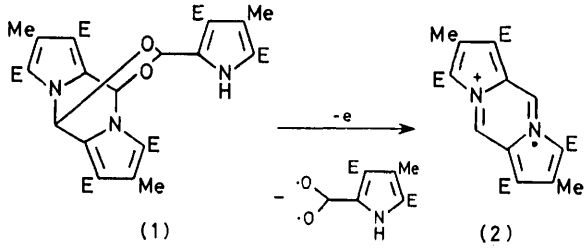


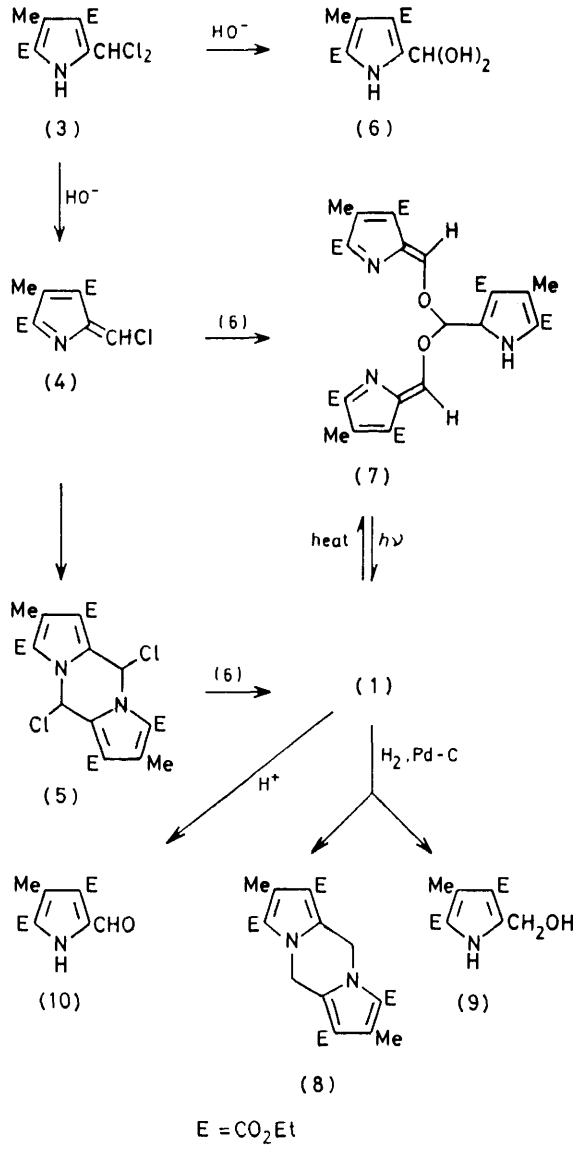
FIGURE 2 Computer-drawn molecular structure of the acetal (1) from *X*-ray data

in terms of the formation of the highly stable dipyrrolo-[1,2-*a*;1′,2′-*d*]pyrazinium radical cation (2) through the cleavage of the acetal group; *cf.* the formation of a similar stable radical cation in the mass spectrum of the 5,10-bis(dialkylamino)dipyrrolo[1,2-*a*;1′,2′-*d*]pyrazines.[8]



The formation of the unusual and novel pyrrolyl acetal structure may be rationalised in terms of the initial formation of the 2-chloromethylene-2*H*-pyrrole (4), through the base-catalysed elimination of HCl from the 2-dichloromethylpyrrole (3). The spontaneous dimerisation of (4) to give the 5,10-dichloro-5*H*,10*H*-dipyrrolo[1,2-*a*;1′,2′-*d*]pyrazine (5) (*cf.* the dimerisation of 6-dimethylamino-1-azafulvene [6,8]) and its subsequent reaction with the hydrate of the aldehyde (6) or, alternatively, the reaction of the 2-chloromethylene-2*H*-pyrrole with the hydrate (6) to give the bis-(1-azafulvene) system (7) and subsequent ring closure, gives the 5,10-methylenedioxy-5*H*,10*H*-dipyrrolo[1,2-*a*;1′,2′-*d*]pyrazine (1). Predictably, 2-dichloromethyl-3,5-bisethoxycarbonyl-1,4-dimethylpyrrole failed to produce an analogue of the bis-(1-azafulvene) system under basic conditions, owing to its inability to form the 2-chloromethylene-2*H*-pyrrole, but readily underwent solvolysis to give the 2-formylpyrrole.

The thermal instability of 5*H*,10*H*-dipyrrolo[1,2-*a*;1′,2′-*d*]pyrazines to give 1-azafulvenes is well established [4,9] and the electronic spectrum of the red isomer, obtained upon heating (1) at *ca.* 160 °C for several minutes, is compatible with that expected of the bis-(1-



azafulvene) system (7). The ^1H and ^{13}C n.m.r. spectra are also fully consistent with the structure proposed for the red isomer, showing signals, not only characteristic of the ethoxycarbonyl and methyl groups, but also a sharp ^1H singlet at δ 10.31 and a ^{13}C signal at 182.6 p.p.m., which appears as a doublet in the proton-coupled ^{13}C spectrum. These signals are closely similar to those produced by the *meso*-CH group of 3,3′,5,5′-tetrakis-ethoxycarbonyl-4,4′-dimethyldipyrrolylmethane. On this evidence it is proposed that the reversible thermo-

chromic–photochromic process involves ring–chain isomerism of the type (1) ⇌ (7).

The course of the reaction of the 2-dichloromethylpyrrole (3) with aqueous potassium hydroxide was extremely sensitive to the concentration of the base. The optimum yield of the dipyrrolopyrazine was attained using 6% aqueous potassium hydroxide. Below this concentration the formylpyrrole dicarboxylic acid was formed in preference to the dipyrrolopyrazine whilst, above this concentration, the formation of an intractable tar increased. Substitution of aqueous sodium hydroxide for potassium hydroxide resulted in the solvolysis of the dichloromethylpyrrole without the formation of the dipyrrolopyrazine. Although the acetal (1) is stable under the moderately basic conditions required for its formation, acid-catalysed hydrolysis promoted the rapid cleavage of the acetal function with the formation of 3,5-bisethoxycarbonyl-2-formyl-4-methylpyrrole.

The spectral data originally reported [2] for the product obtained from the catalytic hydrogenation of (1) can be interpreted in terms of the hydrogenolysis of the acetal function to give 1,3,6,8-tetrakisethoxycarbonyl-2,7-dimethyl-5*H*,10*H*-dipyrrolo[1,2-*a*;1′,2′-*d*]pyrazine (8), together with 3,5-bisethoxycarbonyl-2-hydroxymethyl-4-methylpyrrole. The dipyrrolopyrazine (8) could also be obtained from the base-catalysed elimination of HCl from 2-chloromethyl-3,5-bisethoxycarbonyl-4-methylpyrrole and the subsequent dimerisation of the intermediate 2-methylene-2*H*-pyrrole, in addition to the more usual reaction leading to the 2,2′-dipyrrolylmethane.[7b]

Attempts to extend the base-catalysed reaction to the preparation of other methylenedioxydipyrrolopyrazines with different ester groups have been singularly unsuccessful. A dipyrrolopyrazine, analogous to (6), was obtained in low yield from the reaction of potassium hydroxide with 2-dichloromethyl-5-ethoxycarbonyl-3-methoxycarbonyl-4-methylpyrrole, but the corresponding reactions with the analogous dimethyl ester gave only 2-formyl-4-methylpyrrole-3,5-dicarboxylic acid, probably as a result of the more facile hydrolysis of the α-methoxycarbonyl group. Attempts to prepare the t-butyl and benzyl ester analogues failed on account of the facile alkyl–O-cleavage of the esters under the reaction conditions required for the preparation of the dichloromethylpyrroles. The base-catalysed conversion of 3-acetyl-2-dichloromethyl-5-ethoxycarbonyl-4-methylpyrrole into the dipyrrolopyrazine system was also unsuccessful. In this case it is probable that there is an enhancement in the rate of solvolysis of the dichloromethyl group, caused by the substitution of the adjacent ester group by the more electron-withdrawing acetal group.

EXPERIMENTAL

Infrared spectra for all compounds were measured for Nujol mulls using a Perkin-Elmer 297 spectrophotometer and electronic spectra were measured for the solvolysis products as *ca.* 10^{-5} M solutions in chloroform using a Unicam SP 700 spectrophotometer. ^{1}H N.m.r. spectra of *ca.* 40% solutions in $CDCl_3$ were recorded at 60 MHz on a Perkin-Elmer R12 spectrometer and at 100 MHz using a Varian HA-100 spectrometer. All chemical shifts are reported downfield from the internal standard (Me_4Si). ^{13}C N.m.r. spectra were recorded for solutions in $CDCl_3$, which also acted as a lock signal, using a JEOL FX100 spectrometer under conditions which gave a digital resolution of 0.05 p.p.m. All chemical shifts are reported downfield from Me_4Si. Low-resolution electron-impact and chemical-ionization mass spectra were obtained using a Kratos MS25 spectrometer. Accurate mass measurements were recorded by the Food Research Institute Mass Spectrometry Unit, Norwich, using an AEI MS902 spectrometer.

2-Dichloromethyl-3,5-bisethoxycarbonyl-4-methylpyrrole (3).—Sulphuryl chloride (14.1 ml, 0.174 mol) in dry glacial acetic acid (28 ml) was added with stirring to 3,5-bisethoxycarbonyl-2,4-dimethylpyrrole (20 g, 0.084 mol) in dry glacial acetic acid (100 ml) at such a rate that the temperature was maintained at 50 °C. The reaction mixture was kept at *ca.* 50 °C for 30 min after the addition of the sulphuryl chloride and then cooled to 20 °C. The dichloromethyl derivative (3) (17.1 g, 67%), m.p. 125—126 °C (lit.,[3] 124—125 °C), which precipitated from the cooled solution, was washed with hexane and recrystallised from toluene (Found: C, 47.0; H, 5.0; N 4.3. Calc. for $C_{12}H_{15}Cl_2NO_4$: C, 46.8; H, 4.9; N, 4.5%); δ($CDCl_3$) 1.40 (6 H, t), 2.55 (3 H, s), 4.35 (2 H, q,), 4.41 (2 H, q,), and 7.62 (1 H, s).

3,5-Bisethoxycarbonyl-2-formyl-4-methylpyrrole (10).—2-Dichloromethyl-3,5-bisethoxycarbonyl-4-methylpyrrole (15 g, 0.06 mol) in aqueous ethanol (40%; 100 ml) was refluxed for 3 h. The solution was cooled to 20 °C and the precipitated formyl derivative (10) was recrystallised from aqueous ethanol (11.8 g, 95%), m.p. 125—126 °C (lit.,[3] 124—125 °C) (Found: C, 56.9; H, 6.0; N, 5.4. Calc. for $C_{12}H_{15}NO_5$: C, 56.9; H, 6.0; N, 5.5%); δ($CDCl_3$) 1.40 (6 H, t), 2.51 (3 H, s), 3.49 (4 H, q,) and 10.28 (1 H, s).

Reaction of 2-Dichloromethyl-3,5-bisethoxycarbonyl-4-methylpyrrole (3) *with Aqueous Potassium Hydroxide.*—*Method* (a). 2-Dichloromethyl-3,5-bisethoxycarbonyl-4-methylpyrrole (10 g, 0.032 mol) was added to aqueous potassium hydroxide (6%, 250 ml) at *ca.* 100 °C under nitrogen and the mixture was heated under reflux for 2 h. The reaction mixture was cooled to 20 °C and the dark solution was separated from the tar (3.8 g) by filtration. The filtrate was treated with decolourising charcoal and acidified to pH 4 to give 2-formyl-4-methylpyrrole-3,5-dicarboxylic acid (5.0 g, 64%), m.p. >300 °C (lit.,[2] >300 °C). The tar was heated under reflux in aqueous potassium hydroxide (3%; 150 ml) for 4 h. The mixture was cooled to 20 °C and the insoluble material was collected and extracted with methanol. The red solid, which was insoluble in methanol, was collected and recrystallised from chloroform–methanol to give bright orange-red needles (2.1 g, 26%), m.p. 216—217 °C, (lit.,[2] 218 °C).

Method (b). 2-Dichloromethyl-3,5-bisethoxycarbonyl-4-methylpyrrole (1.54 g, 0.005 mol) in chloroform (10 ml) was added dropwise over a period of 1 h with stirring to tetrabutylammonium bromide (1.61 g, 0.005 mol) in aqueous potassium hydroxide (30%; 30 ml) at 20 °C. The organic phase was separated, washed with water (5 × 40 ml), dried, and evaporated to give the orange-red product (0.8 g, 64.8%), m.p. 216—217 °C.

Irradiation of the Orange-red Reaction Product.—Irradiation of the orange-red by-product (0.8 g), from the reaction of the 2-dichloromethylpyrrole with aqueous potassium

hydroxide, in chloroform (10 ml) with a tungsten lamp for 3 h (or ultraviolet light at 400 nm for 10 min) gave 5,10-(3,5-*bisethoxycarbonyl*-4-*methylpyrrol*-2-*ylmethylenedioxy*)-1,3,6,8-*tetrakisethoxycarbonyl*-2,7-*dimethyl*-5H,10H-*dipyrrolo*[1,2-a;1′,2′-d]*pyrazine* (1), which was recrystallised from chloroform–methanol to give white needles (0.78 g, 97.5%), m.p. 216—217 °C with a colour transition temperature of *ca.* 160 °C (Found: C, 58.0; H, 5.9; N, 5.4. M^+ 741.264. $C_{36}H_{43}N_3O_{14}$ requires C, 58.3; H, 5.8; N, 5.7%. M^+ 741.276); δ($CDCl_3$) 1.45 (18 H, t), 2.50 (3 H, s), 2.60 (3 H, s), 2.66 (3 H, s), 4.40 (12 H, q), 5.85 (1 H, s), 8.65 (1 H, s), and 8.71 (1 H, s); δ_C 11.4 (CCH_3), 12.0 (CCH_3), 14.2 (OCH_2CH_3), 14.3 (OCH_2CH_3), 59.7 (OCH_2CH_3), 60.7 (OCH_2CH_3), 60.9 (OCH_2CH_3), 61.1 (OCH_2CH_3), 75.4 (C-5 or C-10), 75.9 (C-10 or C-5), 90.3 (O–CH–O), 113.7 (C-6 or C-1), 113.8 (C-1 or C-6), 114.1 (C-5′), 120.3 (C-3′), 120.6(1) (C-3 or C-8), 120.6(3) (C-8 or C-3), 130.4 (C-7 or C-2), 130.9 (C-2 or C-7), 131.6 (C-4′), 133.0 (C-5a or C-10a), 134.9 (C-10a or C-5a), 137.9 (C-2′), 160.9 (C-5′–*C*O), 161.2(3) (C-3–*C*O or C-8–*C*O), 161.2(5) (C-8–*C*O or C-3–*C*O), 163.2 (C-3′–*C*O), 163.4(9) (C-1–*C*O or C-6–*C*O), and 163.5(0) (C-6–*C*O or C-1–*C*O); $\nu_{max.}$ 3 490 (NH) and 1 700 cm^{-1} (C=O); $\lambda_{max.}$ 270 nm (log ε 4.51).

Effect of Heat on the Orange-red Reaction Product.—The orange-red product from the base-catalysed reaction of 2-dichloromethyl-3,5-bisethoxycarbonyl-4-methylpyrrole-3,5-dicarboxylate was heated in the solid state at 240 °C for 1 min to give, in quantitative yield, (3,5-*bisethoxycarbonyl*-4-*methylpyrrol*-2-*yl*)*bis*-(3,5-*bisethoxycarbonyl*-4-*methyl*-2H-*pyrrol*-2-*ylidenemethyleneoxy*)*methane* (7) as a red amorphous solid, m.p. 217 °C (Found: C, 59.0; H, 5.8; N, 5.5. $C_{36}H_{43}N_3O_{14}$ requires C, 58.3; H, 5.8; N, 5.7%); δ($CDCl_3$) 1.30 (3 H, t), 1.43 (9 H, t), 1.46 (6 H, t), 2.53 (3 H, s), 2.62 (6 H, s), 4.41 (13 H, m), and 10.31 (2 H, s); δ_C * ($CDCl_3$) 11.3 (AF-CH_3), 11.9 (Py-CH_3), 14.4 ($CO_2CH_2CH_3$), 60.2 (Py-$CO_2CH_2CH_3$), 60.4 (Py-$CO_2CH_2CH_3$), 60.8 (AF-$CO_2CH_2CH_3$), 61.3 (AF-$CO_2CH_2CH_3$), 111.8 (Py C-5), 120.2 (AF C-5), 120.8 (Py C-3), 120.8 (O–CH–O), 123.9 (AF C-3), 130.4 (Py C-4), 131.0 (AF C-4), 133.5 (AF C-2), 139.2 (Py C-2), 160.5 (AF α-$CO_2CH_2CH_3$), 160.8 (Py α-$CO_2CH_2CH_3$), 163.3 (Py β-$CO_2CH_2CH_3$), 163.6 (AF β-$CO_2CH_2CH_3$), and 182.6 (AF =CH–O); $\nu_{max.}$ 3 265 (NH, H-bonded), and 1 695 and 1 664 cm^{-1} (C=O); $\lambda_{max.}$ ($CHCl_3$) 381 (log ε 3.74), 401 (4.34), 450sh (3.67), 480 (4.13), 508 (4.34), and 560 nm (3.62); fluorescence maximum (excitation at 400 nm) 561 nm.

Hydrogenation of the Acetal (1).—The acetal (1) (0.25 g, 0.0003 mol) in acetic acid (20 ml) was hydrogenated at atmospheric pressure over palladium–carbon (10%; 0.01 g) at room temperature for 36 h. The catalyst was removed by filtration and washed with acetic acid (5 ml). The filtrate and the washings were poured into water (100 ml) and the aqueous solution was extracted with dichloromethane (20 ml). The organic extract was washed with saturated aqueous sodium hydrogencarbonate (50 ml) and water (50 ml), dried ($MgSO_4$), and evaporated. Preparative t.l.c. (silica; CH_2Cl_2) of the crude product gave 3,5-bisethoxycarbonyl-2-hydroxymethyl-4-methylpyrrole (9) (0.076 g, 89%), m.p. 121—122 °C (lit.,[3] 123 °C); δ($CDCl_3$) 1.45 (6 H, t), 2.50 (3 H, s), 4.33 (2 H, q), 4.50 (2 H, q), and 4.73 (2 H, s); δ_C ($CDCl_3$) 11.8 (CCH_3), 14.4 (OCH_2CH_3), 58.4 (CH_2OH), 60.1 (OCH_2CH_3), 60.5 (OCH_2CH_3), 112.7 (C-5), 118.5 (C-3), 130.9 (C-4), 141.7 (C-2), 161.6 (CO), and 165.8 (CO); and 1,3,6,8-*tetrakisethoxycarbonyl*-2,7-*dimethyl*-5H,10H-*dipyrrolo*[1,2-a;1′,2′-d]*pyrazine* (8) (0.073 g, 46%), m.p. 225—226 °C (Found: C, 60.6; H, 6.2; N, 5.6. $C_{24}H_{30}N_2O_8$ requires C, 60.8; H, 6.4; N, 5.9%); δ($CDCl_3$) 1.47 (12 H, t), 2.60 (6 H, s), 4.45 (4 H, q), 4.57 (4 H, q), and 5.75 (4 H, s); δ_C 12.3 (CCH_3), 14.4 (OCH_2CH_3), 44.6 (C-5 and C-10), 60.0 (OCH_2CH_3), 60.3 (OCH_2CH_3), 110.9 (C-1 and C-6), 120.2 (C-3 and C-8), 132.6 (C-2 and C-7), 133.6 (C-5a and C-10a), 161.5 (CO), and 164.4 (CO); M^+ 474. Extraction of the catalyst with chloroform (3 × 20 ml) yielded a further sample (0.049 g, 31%) of the pyrrolopyrazine, m.p. 224—226 °C.

Reaction of 2-*Chloromethyl*-3,5-*diethoxycarbonyl*-4-*methylpyrrole with Aqueous Potassium Hydroxide.*—2-Chloromethyl-3,5-bisethoxycarbonyl-4-methylpyrrole [3] (10.7 g, 0.04 mol) was added with stirring to aqueous potassium hydroxide (10%; 250 ml) at *ca.* 100 °C and the mixture heated under reflux for 3 h. A brown insoluble solid was removed by filtration and the filtrate was refluxed with decolourising charcoal for 15 min. After removal of the charcoal, the filtrate was acidified to pH 4 with concentrated hydrochloric acid to give 3,3′-bisethoxycarbonyl-4,4′-dimethyl-2,2′-dipyrrolylmethane-5,5′-dicarboxylic acid (4.1 g, 39%), m.p. 255—256 °C (lit.,[10] 254 °C). The brown insoluble solid was taken up in hot ethanol (30 ml) and heated under reflux with decolourising charcoal for 15 min. After removal of the charcoal, the filtrate was poured into water (200 ml), and the aqueous solution was extracted with dichloromethane (3 × 30 ml). The organic extracts were washed with water (2 × 50 ml), dried ($MgSO_4$), and evaporated. Preparative t.l.c. (silica; CH_2Cl_2) of the crude product gave 1,3,6,8-tetrakisethoxycarbonyl-2,7-dimethyl-5*H*,10*H*-dipyrrolo[1,2-*a*;1′,2′-*d*]pyrazine (8) (0.19 g, 21%), m.p. 222—223 °C.

Acid-catalysed Hydrolysis of the Acetal (1).—The acetal (0.74 g, 0.001 mol) and toluene-*p*-sulphonic acid (0.05 g) in aqueous acetic acid (1 : 10 v/v; 10 ml) were heated under reflux for 2 h and then poured into water (100 ml) with vigorous stirring. The mixture was allowed to stand at room temperature for 2 h and the precipitated product was then collected, washed with water (10 ml), and recrystallised from aqueous ethanol to give 3,5-bisethoxycarbonyl-2-formyl-4-methylpyrrole (10) (0.68 g, 91%), m.p. 124—125 °C (lit.,[3] 124—125 °C).

2-*Dichloromethyl*-5-*ethoxycarbonyl*-3-*methoxycarbonyl*-4-*methylpyrrole.*—5-Ethoxycarbonyl-3-methoxycarbonyl-2,4-dimethylpyrrole [11] was converted into the 2-*dichloromethylpyrrole* (76%), m.p. 128 °C (Found: C, 44.8; H, 4.7; N, 4.6. $C_{11}H_{13}Cl_2NO_4$ requires C, 44.9; H, 4.5; N, 4.8%); δ($CDCl_3$) 1.38 (3 H, t), 2.54 (3 H, s), 3.85 (3 H, s), 4.36 (2 H, q), and 7.58 (1 H, s), using a procedure analogous to that described for the corresponding diethyl ester.

Reaction of 2-*Dichloromethyl*-5-*ethoxycarbonyl*-3-*methoxycarbonyl*-4-*methylpyrrole with Aqueous Potassium Hydroxide.*—The 2-dichloromethylpyrrole (5 g, 0.02 mol) was added to refluxing aqueous potassium hydroxide (6%; 75 ml) and the mixture was heated for a further 30 min. Filtration of the cooled solution and treatment of the clear orange filtrate with decolourising charcoal and acidification to pH 4.0 gave 2-formyl-4-methylpyrrole-3,5-dicarboxylic acid (2.7 g, 81%), m.p. >300 °C (lit.,[2] >300 °C). The residual orange-brown tar (0.8 g) from the filtration was heated with aqueous potassium hydroxide (2%; 25 ml) for 2 h and the insoluble residue was extracted with methanol to give an orange-red solid which, upon heating for 5 min at 200 °C, gave (5-*ethoxycarbonyl*-3-*methoxycarbonyl*-4-*methylpyrrol*-2-*yl*)*bis*-(5-*ethoxycarbonyl*-3-*methoxycarbonyl*-4-*methyl*-2H-*pyrrol*-2-*ylidene*-

* AF and Py refer to azafulvene and pyrrole rings respectively.

methyleneoxy)methane (0.1 g, 2.5%), which crystallised from $CHCl_3$–methanol as a red amorphous solid, m.p. 237—238 °C (Found: C, 56.7; H, 5.2; N, 6.4. $C_{33}H_{37}N_3O_{14}$ requires C, 56.65; H, 5.3; N, 6.3%); $\lambda_{max.}$ ($CHCl_3$) 508, 480, 450, 401, and 380 nm; $\nu_{max.}$ 3 150 (NH, H-bonded), and 1 695 and 1 665 cm^{-1} (C=O); δ 1.27 (3 H, t), 1.40 (6 H, t), 2.83 (9 H, s), 3.85 (6 H, s), 3.91 (3 H, s), 4.38 (7 H, m), and 9.48 (2 H, s).

2-Dichloromethyl-3,5-dimethoxycarbonyl-4-methylpyrrole.—3,5-Dimethoxycarbonyl-2,4-dimethylpyrrole [12] was converted into the corresponding *2-dichloromethylpyrrole* (55%), m.p. 191 °C (Found: C, 42.9; H, 4.1; N, 5.3. $C_{10}H_{11}Cl_2NO_4$ requires C, 42.9; H, 4.0; N, 5.3%); δ($CDCl_3$) 2.55 (3 H, s), 3.87 (3 H, s), 3.94 (3 H, s), and 7.63 (1 H, s), using a procedure analogous to that described for the corresponding diethyl ester.

Solvolysis of the 2-dichloromethylpyrrole in refluxing aqueous potassium hydroxide following the procedure used for the corresponding diethyl ester gave 2-formyl-4-methylpyrrole-3,5-dicarboxylic acid (86%), m.p. >300 °C (lit.,[2] >300 °C), which was contaminated by a red by-product (<1%); $\lambda_{max.}$ 381sh, 401, 450sh, 480, and 508 nm.

TABLE 1

Atomic co-ordinates for C, N, and O

	x/a	*y/b*	*z/c*
C(1)	0.966(1)	0.337(1)	0.606 6(9)
C(2)	0.962(1)	0.312(1)	0.504 2(9)
C(3)	0.883(1)	0.385(1)	0.447(1)
C(4)	0.838(1)	0.450(1)	0.514 6(9)
N(5)	0.891 7(9)	0.421 2(9)	0.613 4(8)
C(6)	0.870(1)	0.455(1)	0.716 1(9)
C(7)	0.990(1)	0.464(1)	0.794 6(9)
C(8)	1.043(1)	0.535(1)	0.881 5(9)
C(9)	1.156(1)	0.492(1)	0.926(1)
C(10)	1.166(1)	0.395(1)	0.866 9(9)
N(11)	1.063 6(9)	0.379 3(8)	0.785 5(7)
C(12)	1.021(1)	0.286(1)	0.703 2(9)
O(13)	0.933 0(7)	0.225 8(7)	0.735 1(6)
C(14)	0.814(1)	0.258(1)	0.703 0(9)
O(15)	0.798 4(7)	0.370 6(7)	0.740 4(6)
C(16)	0.741(1)	0.190(1)	0.752 6(9)
C(17)	0.630(1)	0.136(1)	0.714 2(9)
C(18)	0.606(1)	0.086(1)	0.797 2(9)
C(19)	0.703(1)	0.108(1)	0.879(1)
N(20)	0.786 4(9)	0.169 0(9)	0.851 3(8)
C(21)	1.035(1)	0.228(1)	0.464(1)
O(22)	1.038(1)	0.214(1)	0.374(1)
O(23)	1.092 1(9)	0.166 9(9)	0.533 2(8)
C(24)	1.169(2)	0.078(2)	0.499(2)
C(25)	1.188(2)	0.000(2)	0.574(2)
C(26)	0.853(1)	0.386(1)	0.329(1)
C(27)	0.751(1)	0.534(1)	0.499(1)
O(28)	0.710(1)	0.583(1)	0.566(1)
O(29)	0.704(1)	0.544(1)	0.400 7(9)
C(30)	0.604(2)	0.618(2)	0.373(2)
C(31)	0.521(2)	0.575(2)	0.278(2)
C(32)	0.991(1)	0.634(1)	0.918(1)
O(33)	1.030 9(8)	0.686 9(8)	1.003 8(7)
O(34)	0.895 4(8)	0.663 8(8)	0.850 9(7)
C(35)	0.837(1)	0.763(1)	0.879(1)
C(36)	0.755(2)	0.794(2)	0.786(2)
C(37)	1.245(1)	0.544(1)	1.025(1)
C(38)	1.261(1)	0.320(1)	0.874(1)
O(39)	1.265 0(9)	0.243 4(9)	0.807 9(8)
O(40)	1.347 3(8)	0.336 4(8)	0.961 0(7)
C(41)	1.446(1)	0.260(1)	0.974(1)
C(42)	1.527(2)	0.295(2)	1.080(1)
C(43)	0.551(1)	0.137(1)	0.610 5(9)
O(44)	0.455 0(9)	0.089 7(8)	0.583 2(8)
O(45)	0.589 8(8)	0.194 3(7)	0.547 9(7)
C(46)	0.516(1)	0.195(1)	0.443(1)
C(47)	0.575(2)	0.267(2)	0.389(1)
C(48)	0.495(1)	0.023(1)	0.795(1)
C(49)	0.729(1)	0.073(1)	0.982(1)
O(50)	0.663(1)	0.016(1)	1.011(1)
O(51)	0.829(1)	0.114(1)	1.042 6(9)
C(52)	0.867(2)	0.088(2)	1.151(1)
C(53)	0.934(2)	−0.014(2)	1.152(2)

TABLE 2

Bond lengths (Å) (standard deviations in parentheses)

C(1)–C(2)	1.37(2)	C(30)–C(31)	1.43(2)
C(1)–N(5)	1.36(2)	C(32)–O(33)	1.24(1)
C(1)–C(12)	1.49(2)	C(32)–O(34)	1.32(2)
C(2)–C(3)	1.41(2)	O(34)–C(35)	1.46(2)
C(2)–C(21)	1.48(2)	C(35)–C(36)	1.45(2)
C(3)–C(4)	1.36(2)	C(38)–O(39)	1.23(2)
C(3)–C(26)	1.54(2)	C(38)–O(40)	1.33(2)
C(4)–N(5)	1.40(2)	O(40)–C(41)	1.46(2)
C(4)–C(27)	1.44(2)	C(41)–C(42)	1.51(2)
N(5)–C(6)	1.49(2)	O(15)–C(14)	1.44(1)
C(6)–C(7)	1.51(2)	O(13)–C(14)	1.42(1)
C(5)–O(15)	1.45(2)	C(14)–C(16)	1.51(2)
C(7)–N(11)	1.36(2)	C(16)–C(17)	1.40(2)
C(7)–C(8)	1.39(2)	C(17)–C(18)	1.42(2)
C(8)–C(9)	1.43(2)	C(18)–C(19)	1.36(2)
C(8)–C(32)	1.44(2)	C(19)–N(20)	1.38(2)
C(9)–C(37)	1.53(2)	N(20)–C(16)	1.35(2)
C(9)–C(10)	1.37(2)	C(17)–C(43)	1.46(2)
C(10)–N(11)	1.39(1)	C(43)–O(44)	1.20(1)
C(10)–C(38)	1.44(2)	C(43)–O(45)	1.32(1)
N(11)–C(12)	1.48(2)	O(45)–C(46)	1.45(2)
C(12)–O(13)	1.44(1)	C(46)–C(47)	1.48(2)
C(21)–O(22)	1.23(2)	C(18)–C(48)	1.49(2)
C(21)–O(23)	1.30(2)	C(19)–C(49)	1.44(2)
O(23)–C(24)	1.52(2)	C(49)–O(50)	1.21(2)
C(24)–C(25)	1.43(3)	C(49)–O(51)	1.30(17)
C(27)–O(28)	1.23(2)	O(51)–C(52)	1.49(2)
C(27)–O(29)	1.32(2)	C(52)–C(53)	1.47(3)
O(29)–C(30)	1.47(2)		

2-Dichloromethyl-3,5-bisethoxycarbonyl-1,4-dimethylpyrrole.—Sulphuryl chloride (7 ml, 0.08 mol) in dry glacial acetic acid (10 ml) was added with stirring to 3,5-bisethoxycarbonyl-1,2,4-trimethylpyrrole [3] (10 g, 0.04 mol) in dry glacial acetic acid (30 ml) at 50 °C. The reaction mixture was stirred at 50 °C for 30 min and then cooled to 4 °C to precipitate the *2-dichloromethylpyrrole* (7.8 g, 61%), m.p. 109 °C (Found: C, 48.3; H, 5.4; N, 4.4. $C_{13}H_{17}Cl_2NO_4$ requires C, 48.5; H, 5.3; N, 4.4%); δ 2.38 (6 H, t), 2.50 (3 H, s), 4.18 (3 H, s), 4.36 (q, 4 H), and 8.26 (1 H, s).

Solvolysis of the dichloromethyl compound in refluxing aqueous potassium hydroxide under the conditions described for the preparation of the dipyrrolo[1,2-*a*;1′,2′-*d*]-pyrazine (1) gave 2-formyl-1,4-dimethylpyrrole-3,5-dicarboxylic acid (83%), m.p. >300 °C.

Solvolysis of the 2-dichloromethyl compound in refluxing aqueous sodium acetate (30%) for 8 h gave 3,5-bisethoxycarbonyl-2-formyl-1,4-dimethylpyrrole (78%), m.p. 92—93 °C (lit.,[13] 93 °C).

3-Acetyl-2-dichloromethyl-5-ethoxycarbonyl-4-methylpyrrole.—3-Acetyl-5-ethoxycarbonyl-2,4-dimethylpyrrole was converted into the 2-dichloromethyl derivative (72%), m.p. 157—158 °C (lit.,[13] 158 °C), according to the procedure described in the literature; [14] δ($CDCl_3$) 1.41 (3 H, t), 2.51 (3 H, s), 2.62 (3 H, s), 2.62 (3 H, s), 2.62 (3 H, s), 4.40 (2 H, q), and 7.58 (1 H, s).

Recrystallisation of the dichloromethylpyrrole from aqueous ethanol converted it into 3-acetyl-5-ethoxycarbonyl-2-formyl-4-methylpyrrole, m.p. 103 °C (lit.,[14] 103 °C).

Solvolysis of the dichloromethylpyrrole in refluxing aqueous potassium hydroxide (6%) for 4 h and neutralisation of the solution to pH 4.0 gave 3-acetyl-2-formyl-4-methylpyrrole-2-carboxylic acid (79%), m.p. >300 °C (lit.,[15] >300 °C).

TABLE 3

Bond angles (°) (standard deviations in parentheses)

C(1)–C(2)–C(3)	108.0(11)	C(17)–C(18)–C(19)	106.4(11)
C(1)–C(2)–C(21)	124.8(11)	C(17)–C(16)–N(20)	108.5(11)
C(21)–C(2)–C(3)	127.1(11)	C(48)–C(18)–C(19)	126.9(12)
C(2)–C(3)–C(26)	125.2(11)	C(18)–C(19)–N(20)	109.7(11)
C(2)–C(3)–C(4)	107.4(11)	C(49)–C(19)–N(20)	119.9(12)
C(26)–C(3)–C(4)	127.4(12)	C(18)–C(19)–C(49)	130.4(13)
C(3)–C(4)–N(5)	107.6(10)	C(19)–N(20)–C(16)	108.3(10)
C(3)–C(4)–C(27)	131.4(12)	C(2)–C(21)–O(22)	124.0(14)
C(27)–C(4)–N(5)	121.0(11)	C(2)–C(21)–O(23)	113.7(12)
C(4)–N(5)–C(1)	109.3(10)	O(22)–C(21)–O(23)	112.3(14)
C(4)–N(5)–C(6)	118.0(10)	C(21)–O(23)–C(24)	117.5(13)
C(6)–N(5)–C(1)	132.2(10)	O(23)–C(24)–C(25)	106.3(17)
N(5)–C(6)–C(7)	106.8(10)	C(4)–C(27)–O(28)	126.1(13)
N(5)–C(6)–O(15)	109.2(9)	C(4)–C(27)–O(29)	112.7(13)
O(15)–C(6)–C(7)	108.8(9)	O(28)–C(27)–O(29)	120.7(14)
C(6)–C(7)–N(11)	116.0(10)	C(27)–O(29)–C(30)	118.3(13)
C(6)–C(7)–C(8)	135.0(11)	O(29)–C(30)–C(31)	110.7(17)
C(8)–C(7)–N(11)	108.9(10)	C(8)–C(32)–O(33)	124.5(12)
C(7)–C(8)–C(32)	125.4(12)	C(8)–C(32)–O(34)	113.8(11)
C(7)–C(8)–C(9)	106.6(11)	O(33)–C(32)–O(34)	121.7(12)
C(32)–C(8)–C(9)	128.0(12)	C(32)–O(34)–C(35)	118.7(10)
C(8)–C(9)–C(37)	124.2(12)	O(34)–C(35)–C(36)	108.2(13)
C(8)–C(9)–C(10)	107.3(11)	C(10)–C(38)–O(39)	124.8(12)
C(37)–C(9)–C(10)	128.4(12)	C(10)–C(38)–O(40)	114.5(11)
C(9)–C(10)–C(38)	131.2(12)	O(39)–C(38)–O(40)	120.7(12)
C(9)–C(10)–N(11)	108.3(11)	C(38)–O(40)–C(41)	117.3(11)
C(38)–C(10)–N(11)	120.5(11)	O(40)–C(41)–C(42)	106.2(13)
C(10)–N(11)–C(7)	108.9(10)	C(10)–C(38)–O(39)	124.8(12)
C(10)–N(11)–C(12)	132.2(10)	C(10)–C(38)–O(40)	114.5(11)
C(7)–N(11)–C(12)	118.6(10)	O(39)–C(38)–O(40)	120.7(12)
N(11)–C(12)–C(1)	106.5(10)	O(40)–C(41)–C(42)	106.2(13)
N(11)–C(12)–O(13)	105.7(9)	C(17)–C(43)–O(44)	123.0(12)
O(13)–C(12)–C(1)	110.9(10)	C(17)–C(43)–O(45)	115.6(11)
C(12)–O(13)–C(14)	118.0(9)	O(44)–C(43)–O(45)	121.4(12)
C(6)–O(15)–C(14)	117.2(9)	C(43)–O(45)–C(46)	117.7(11)
O(13)–C(14)–O(15)	112.5(9)	O(45)–C(46)–C(47)	108.4(13)
O(13)–C(14)–C(16)	108.3(10)	C(19)–C(49)–O(50)	124.1(15)
O(15)–C(14)–C(16)	104.2(9)	C(19)–C(49)–O(51)	113.6(14)
C(14)–C(16)–C(17)	132.1(11)	O(50)–C(49)–O(51)	122.3(15)
C(14)–C(16)–N(20)	119.3(10)	C(49)–O(51)–C(52)	120.0(13)
C(16)–C(17)–C(18)	106.9(11)	O(51)–C(52)–C(53)	106.8(15)
C(16)–C(17)–C(43)	126.5(11)	C(12)–C(1)–C(2)	135.0(12)
C(43)–C(17)–C(18)	126.5(11)	N(5)–C(1)–C(12)	117.0(11)
C(17)–C(18)–C(48)	126.6(11)	N(5)–C(1)–C(2)	107.7(11)

Crystal and Molecular Structure of the Acetal (1).—*Crystal data*: $C_{36}H_{43}N_3O_{14}$, $M = 741.94$, triclinic, $a = 11.7285$, $b = 12.1309$, $c = 13.5205$ Å, $\alpha = 95.9658$, $\beta = 105.5677$, $\gamma = 90.1943°$, $D_c = 1.34$, $D_m = 1.37$ g cm^{-3}, $U = 1842.07$ Å^3, $Z = 2$, space group $P\bar{1}$.

The structure was solved by direct methods using 5401 reflections and the SHELX program, co-ordinates of 51 of the 'heavy atoms' being determined. The remaining atoms were found from an electron-difference map using the CRYSTALS package (2 343 observed reflections). The trial structure was refined using isotropic and anisotropic temperature factors to an R value of 10.64%. A Fourier difference map detected 17 of the hydrogen atoms associated with the ethyl groups and the three tertiary centres. Accordingly, all of the hydrogen atoms other than those associated with the methyl groups of the pyrrole rings were included in their calculated positions. Continued anisotropic refinement, hydrogen atoms being excluded from the calculations, led to an R value of 10.07%. A further attempt to locate the remaining methyl hydrogen atoms failed. Finally isotropic refinement, excluding the hydrogen atoms, gave an R value of 13.21%. Atomic co-ordinates, bond lengths, and bond angles are listed in Tables 1—3 respectively. Observed and calculated structure factors and thermal parameters are listed in Supplementary Publication No. SUP 23121 (24 pp.).*

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