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Stereoisomerism in Partial Bile Pigment Structures. The Crystal Structures of the *Z* and *E* isomers of 5′-Ethoxycarbonyl-3,4-dihydro-3′,4′-dimethyl-5(1*H*)-2,2′-pyrromethenone and Their Reaction Products with $Et_3O^+BF_4^-$

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The configuration at the exocyclic double bond of the two stereoisomers of 5′-ethoxycarbonyl-3,4-dihydro-3′,4′-dimethyl-5(1*H*)-2,2′-pyrromethenone has been established by X-ray analysis. The *Z* isomer (I) crystallizes in the space group $P2_1/c$, with $a = 12{\cdot}705$ (3), $b = 7{\cdot}425$ (2), $c = 15{\cdot}356$ (4) Å, $\beta = 102{\cdot}82$ (2)°, $Z = 4$; the *E* isomer (II) also crystallizes in $P2_1/c$, with $a = 6{\cdot}275$ (2), $b = 8{\cdot}068$ (2), $c = 26{\cdot}651$ (8) Å, $\beta = 94{\cdot}72$ (2)°, $Z = 4$. Treatment of (I) with $Et_3O^+BF_4^-$ in CH_2Cl_2 yields the corresponding *Z*-lactim ether (III), whereas (II) is converted under the same conditions without isomerization into the *N*-alkylated derivative (IV). (III) crystallizes in the space group *Cc*, with $a = 11{\cdot}297$ (3), $b = 13{\cdot}265$ (2), $c = 10{\cdot}973$ (2) Å, $\beta = 101{\cdot}34$ (1)°, $Z = 4$, and (IV) in $P2_1/c$, with $a = 8{\cdot}068$ (3), $b = 12{\cdot}464$ (3), $c = 15{\cdot}775$ (5) Å, $\beta = 91{\cdot}51$ (4)°, $Z = 4$. The structures were solved by direct methods and refined to $R = 0{\cdot}077$, 0·078, 0·037 and 0·070 for 1346, 1366, 1477 and 1632 reflexions for (I)–(IV) respectively. Interplanar angles of 131·5, −176·6, −0·3 and 150·9°, corresponding to twisted *anti-Z*, *anti-E*, *syn-Z* and twisted *anti-E* conformations, are observed between the two rings in (I)–(IV) respectively. (I), (II) and (IV) are linked into chains through linear N–H···O hydrogen bonds involving the lactam O atom; for (I) and (IV) these bridges are to the N of the pyrrole ring, for (II) to that of the pyrrolidinone ring.

Introduction

5(1*H*)-Pyrromethenones are known as essential partial structures of the natural series of bile pigments. As such they play a significant role, not only as starting materials in the synthesis of bile pigments (Hudson & Smith, 1976), but also as model systems for the study of the thermal and photochemical isomerization of the tetrapyrrole chromophore. A correlation of their configuration and conformation with light-absorption properties is essential to an understanding of the biological function and properties of the bile pigments. It has, for instance, been postulated, on the basis of simple Hückel MO calculations (Burke, Pratt & Moscowitz, 1972), that the spectral shift between the 'red' and 'far-red' forms of the chromophore of the plant photomorphogenic pigment, phytochrome, which is probably a bile pigment of the rhodin type (Grambein, Rüdiger & Zimmermann, 1975), may be accounted for in terms of geometrical isomerization at the methine bridge. However, although the occurrence of such *Z*,*E* isomerization at the exocyclic double bond of some α-vinyl pyrroles is well documented (Herz, 1949; Jones & Lindner, 1965; Jones, Pojarlieva & Head, 1968; Gossauer, Miehe & Inhoffen, 1970; Flitsch & Neumann, 1971), no known example of such isomers has been established for the bile pigments. The X-ray analyses of bilirubin and biliverdin dimethyl ester have demonstrated that these occur respectively as *syn-Z*, *syn-Z′* (Bonnett, Davies & Hursthouse, 1976) and all *syn-Z* isomers (Sheldrick, 1976) in the crystalline state (Fig. 1). As a result of the flexibility of the central methylene bridge, bilirubin is capable of taking up a 'ridge-tile' conformation, which enables it to gain maximum stabilization through six intramolecular hydrogen bonds. In contrast, biliverdin dimethyl ester crystallizes as an extended helical dimer with intermolecular N–H···O hydrogen bonds between symmetry-equivalent pyrrolone rings.

Falk, Grubmayr, Herzig & Hofer (1975) have achieved the photochemical transformation (Fig. 2) of a *Z*-5(1*H*)-pyrromethenone (V) into the thermodynamically less stable *E* isomer (VI), which they could isolate by preparative TLC. They were able to assign the configurations on the basis of nuclear Overhauser and lanthanide-shift measurements, the latter yielding a most probable interplanar angle between the two rings for (V) of about −40° [viewed down C(5)–C(4), as

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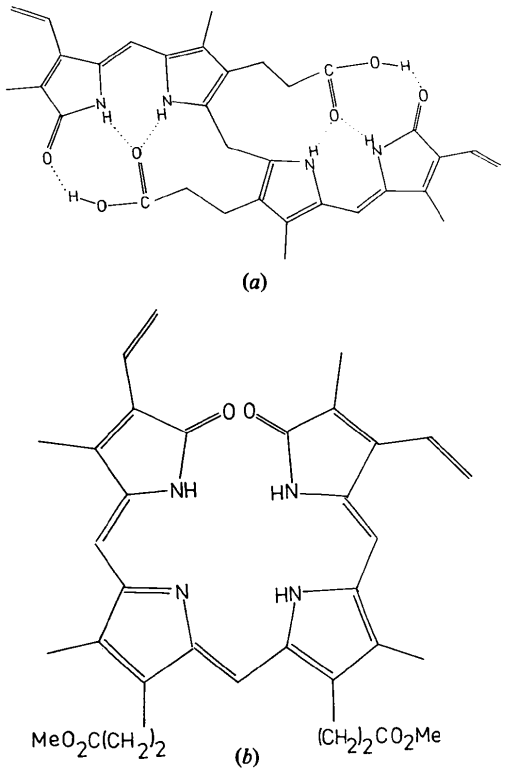


Fig. 1. Structures of (*a*) bilirubin and (*b*) biliverdin dimethyl ester (the latter was studied as a 1:1 mixture of the 22*H* and 23*H* isomers).

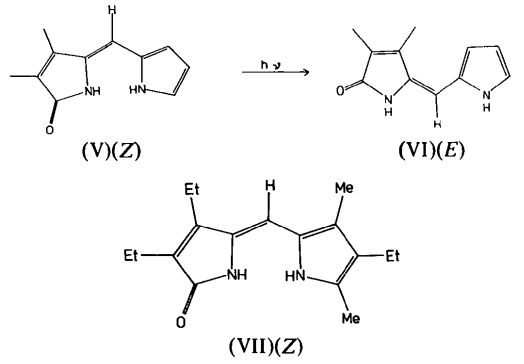


Fig. 2. Derivatives V, VI and VII.

numbered in Fig. 4], corresponding to a twisted *syn* conformation. Because of its thermal instability in aprotic solvents, the lanthanide-shift measurements for the *E* isomer (VI) could not be performed with sufficient accuracy to enable a conformational analysis. A planar *syn-Z* form in the solid state has also been established for another 5(1*H*)-pyrromethenone (VII) (Cullen, Black, Meyer, Lightner, Quistad & Pak, 1977). As delocalization of the *p*-electron pair at the pyrrolic N atom into the lactam C=O group and hence a decrease of the double-bond character of the exocyclic

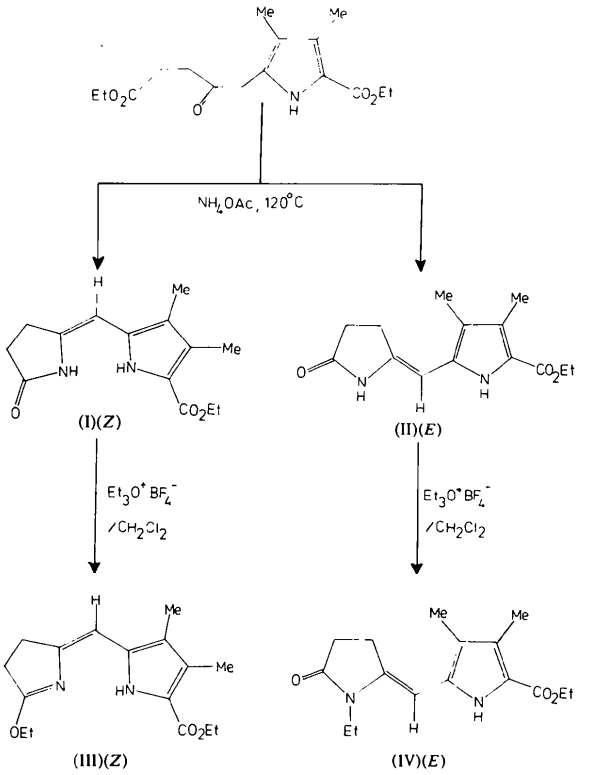


Fig. 3. Preparation of derivatives I–IV.

C(4)–C(5) is only possible in 5(1*H*)-pyrromethenone derivatives [with a C(2)=C(3) double bond], a relatively greater stability of both the *Z* and *E* stereoisomers would be expected in the 3,4-dihydro-5(1*H*)-pyrromethenone series, which are also of considerable synthetic significance as they may easily be converted into bile pigments of the rhodin type (Gossauer & Miehe, 1974; Gossauer & Kühne, 1977), to which, as mentioned previously, the chromophore of phytochrome probably belongs. We have briefly reported the synthesis and structural characterization of the *Z* and *E* stereoisomers of 5′-ethoxycarbonyl-3,4-dihydro-3′,4′-dimethyl-5(1*H*)-2,2′-pyrromethenone (I) and (II) (Gossauer, Blacha & Sheldrick, 1977). We commented that the treatment of (I) with $Et_3O^+BF_4^-$ in CH_2Cl_2 yielded the corresponding lactim ether (III), whereas under the same conditions (II) was converted without isomerization into the *N*-alkylated derivative (IV) (Fig. 3). We now report the synthesis and structure analyses of (I)–(IV) in full.

Preparation

δ-(5-Ethoxycarbonyl-3,4-dimethylpyrrol-2-yl)laevulinic ethyl ester (VIII)

A solution of ethyl *δ*-diazolaevulinate (Ratuský & Šorm, 1958) in 5 ml of absolute benzene was dropped

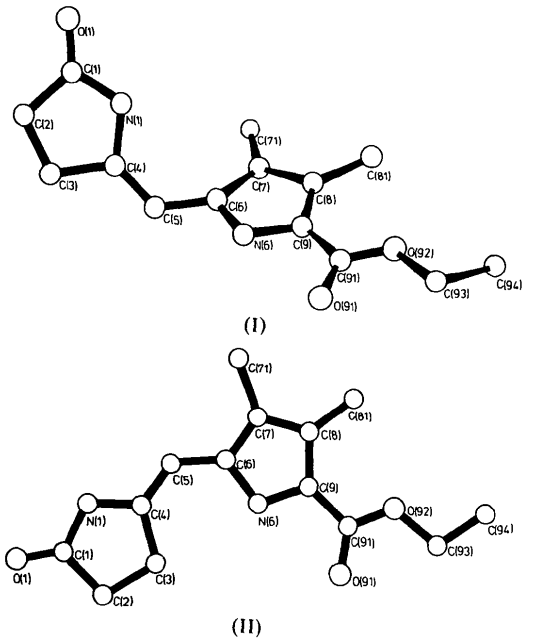


Fig. 4. Derivatives I and II in perspective with atom numbering.

slowly into a vigorously stirred suspension of 0·5 g Cu powder and 4·2 g fused ethyl 3,4-dimethylpyrrole-2-carboxylate (IX) (Badger, Jones & Laslett, 1964). The reaction mixture was subsequently held at 80–90 °C for 30 min, then cooled to room temperature and taken up in CH_2Cl_2. The Cu powder was filtered out and the solvent evaporated. (VIII) was separated from the residual pyrrole (IX) by preparative TLC with diethyl ether/petroleum spirit (7:3), and recrystallized from the same solvent as long white needles (yield 47%): m.p. 92 °C; *m/e* (70 eV), 309 (M^+, 8%); IR (KBr), $\tilde{\nu}_{max}$ = 3350, 3230(NH), 2900(CH), 1720, 1655(C=O) cm^{-1}; 90 MHz, ^1H NMR ($CDCl_3$), δ = 1·22 and 1·33 (each *t*, each J = 7 Hz, ethoxy-CH_3), 1·92 (*s*, 3-pyrrole-CH_3), 2·25 (*s*, 4-pyrrole-CH_3), 2·5–2·8 (*m*, 4H, laevulinic acid α- and β-CH_2), 3·71 (*s*, 2H, δ-CH_2), 4·12–4·29 (each *q*, each J = 7 Hz, ethoxy-CH_2), 9·36 ppm (broad NH).

Z- and E-5'-ethoxycarbonyl-3,4-dihydro-3',4'-dimethyl-5(1H)-2,2'-pyrromethenone (I) *and* (II)

A mixture of 620 mg of (VIII) and 8·6 g ammonium acetate was held at 120 °C for 30 min and then allowed to cool to 80 °C. The melt was taken up in 21·5 ml 25% NH_3 solution, cooled to room temperature and extracted repeatedly with CH_2Cl_2. The extracts were combined, dried with Na_2SO_4 and the solvent evaporated. Two isomers were separated by repeated preparative TLC with CH_2Cl_2/2% CH_3OH. 234 mg of the slow-running isomer (m.p. 202 °C) were obtained upon recrystallization from CH_2Cl_2/petroleum spirit. The product is only moderately soluble in CH_2Cl_2 and $CHCl_3$, whereas the fast-running isomer, of which 106 mg were obtained, is highly soluble in these solvents (total yield of both isomers = 65%). It was observed for the m.p. measurement of the latter product that a structural transition occurs at 160 °C – presumably a transformation to the other isomer – and that the final m.p. is 202 °C. The fast-running *Z* isomer (I) as characterized by X-ray analysis: *m/e* (70 eV), 262 (M^+, 100%); IR (KBr), $\tilde{\nu}_{max}$ = 3400, 3310(NH), 2980, 2920, 2860(CH), 1715, 1675(C=O), 1440, 1280 cm^{-1}, *etc.*; 90 MHz, ^1H NMR (DMSO-d_6), δ = 1·31 (*t*, J = 7 Hz, ethoxy-CH_3), 1·93 (*s*, 3'-pyrrole-CH_3), 2·24 (*s*, 4'-pyrrole-CH_3), 2·4–2·7 and 2·8–3·0 (each *m*, 4H, 3- and 4-pyrrolidinone-H), 4·23 (*q*, J = 7 Hz, ethoxy-CH_2), 5·31 (*dd*, $J_1 = J_2$ = 2 Hz, methine-H), 8·89 and 9·22 ppm (each broad *s*, NH). Crystals suitable for X-ray analysis were grown by slow cooling of a saturated methanol solution. The slow-running *E* isomer (II) as characterized by X-ray analysis: *m/e* (70 eV), 262 (M^+, 100%); IR (KBr), $\tilde{\nu}_{max}$ = 3480, 3140(NH), 2990, 2920, 2860(CH), 1700, 1655(C=O), 1445, 1320, 1250, 1145 cm^{-1}, *etc.*; 90 MHz, ^1H NMR (DMSO-d_6), δ = 1·27 (*t*, J = 7 Hz, ethoxy-CH_3), 1·84 (*s*, 3'-pyrrole-CH_3), 2·17 (*s*, 4'-pyrrole-CH_3), 2·20–2·53 (*m*, partially hidden by DMSO signals) and 2·7–3·0 (*m*, 3- and 4-pyrrolidinone-H), 4·19 (*q*, J = 7 Hz, ethoxy-CH_2), 5·59 (*dd*, $J_1 = J_2$ = 2 Hz, methine-H), 10·10 and 10·27 ppm (each broad *s*, NH). Crystals suitable for X-ray analysis were grown by slow diffusion of diethyl ether into a saturated methanol solution.

5-Ethoxy-5'-ethoxycarbonyl-3,4-dihydro-3',4'-dimethyl-2,2'-pyrromethene (III) *and* *1-ethyl-5'-ethoxycarbonyl-3,4-dihydro-3',4'-dimethyl-5(1H)-2,2'-pyrromethenone* (IV)

1 ml of diisopropylethylamine and 1·5 g of triethyloxonium tetrafluoroborate were added to 100 mg of (I) [or (II) respectively] dissolved in 60 ml of dry CH_2Cl_2. The mixture was allowed to stand under nitrogen for 2 h at room temperature, then washed with water, dried with Na_2SO_4 and the solvent removed. (III) [or (IV)] was separated from the residue by preparative TLC with CH_2Cl_2/1% CH_3OH. (III): yield 66 mg (60%); m.p. 130 °C; *m/e* (70 eV), 290 (M^+, 100%); IR (KBr), $\tilde{\nu}_{max}$ = 3440, 3340(NH), 2980, 2923, 2860(CH), 1680(C=O), 1585(C=C or C=N), 1372, 1261, 1240, 1070 cm^{-1}, *etc.*; 90 MHz, ^1H NMR ($CDCl_3$), δ = 1·31 and 1·42 (each *t*, each J = 7 Hz, ethoxy-CH_3, lactim ether-CH_3), 1·98 (*s*, 3'-pyrrole-CH_3), 2·27 (*s*, 4'-pyrrole-CH_3), 2·5–2·7 and 2·8–3·0 (each *m*, 4H, 3- and 4-pyrrolinene-H), 4·26 and 4·46 (each *q*, each J = 7 Hz, ethoxy-CH_2 and lactim ether-CH_2), 5·64 (*dd*, $J_1 = J_2$ = 2 Hz, methine-H), 10·88 ppm (broad *s*, NH). Crystals suitable for X-ray analysis were grown by slow evaporation from diethyl ether. (IV): yield 68 mg (62%); m.p. 112 °C; *m/e* (70 eV), 290 (M^+, 85%); IR

Table 1. *Crystal and refinement data*

Compound	(I)	(II)	(III)	(IV)
Stoichiometry	$C_{14}H_{18}N_2O_3$	$C_{14}H_{18}N_2O_3$	$C_{16}H_{21}N_2O_3$	$C_{16}H_{21}N_2O_3$
Configuration	*Z*	*E*	*Z*	*E*
Space group	$P2_1/c$	$P2_1/c$	*Cc*	$P2_1/c$
a (Å)	12·705 (3)	6·275 (2)	11·297 (3)	8·068 (3)
b (Å)	7·425 (2)	8·068 (2)	13·265 (2)	12·464 (3)
c (Å)	15·356 (4)	26·651 (8)	10·973 (2)	15·775 (5)
β (°)	102·82 (2)	94·72 (2)	101·34 (1)	91·51 (4)
U (Å^3)	1342·5 (6)	1344·6 (6)	1612·3 (5)	1585·8 (9)
Z	4	4	4	4
M_r	262·3	262·3	289·4	289·4
D_c (g cm^{-3})	1·30	1·30	1·19	1·21
Radiation	Mo $K\alpha$	Mo $K\alpha$	Cu $K\alpha$	Mo $K\alpha$
μ (cm^{-1})	0·55	0·55	5·94	0·50
2θ range (°)	3·0–50·0	3·0–50·0	3·0–135·0	3·0–50·0
F rejection criterion	$<3{\cdot}0\sigma(F)$	$<3{\cdot}0\sigma(F)$	$<3{\cdot}0\sigma(F)$	$<3{\cdot}0\sigma(F)$
Number of reflexions	1346	1366	1477	1632
R	0·077	0·078	0·037	0·070
$R_w = (\Sigma w^{1/2}\Delta/\Sigma w^{1/2}F_o)$	0·059	0·068	0·043	0·059
$R_G = (\Sigma w\Delta^2/\Sigma wF_o^2)^{1/2}$	0·058	0·073	0·053	0·062
k	2·1541	1·9987	1·0	2·0208
g	0·000293	0·001020	0·001586	0·000612
Largest shift/e.s.d.*	0·037	0·207	−0·168	0·088
Highest difference Fourier peak (e Å^{-3})*	0·33	0·33	0·12	0·25

* Refers to the last refinement cycle.

(KBr), $\tilde{\nu}_{max}$ = 3450(NH), 2993, 2940, 2883(CH), 1700, 1680(C=O), 1640(C=C), 1440, 1340, 1270, 1135 cm^{-1}, *etc.*; 90 MHz, ^{1}H NMR ($CDCl_3$), δ = 1·20 (*t*, *J* = 7 Hz, *N*-ethyl-CH_3), 1·36 (*t*, *J* = 7 Hz, ethoxy-CH_3), 1·98 (*s*, 3′-pyrrole-CH_3), 2·27 (*s*, 4′-pyrrole-CH_3), 2·5–2·7 and 2·9–3·1 (each *m*, 4H, 3- and 4-pyrrolidinone-H), 3·66 (*q*, *J* = 7 Hz, *N*-ethyl-CH_2), 4·30 (*q*, *J* = 7 Hz, ethoxy-CH_2), 5·60 (*dd*, $J_1 = J_2 = 2$ Hz, methine-H), 8·52 ppm (broad *s*, NH). Crystals suitable for X-ray analysis were obtained by slow cooling of a saturated diethyl ether solution.

Experimental

Crystal and refinement data for (I)–(IV) are summarized in Table 1. Cell parameters were determined by a least-squares fit to the settings for 15 reflexions ($\pm hkl$) on a Syntex $P2_1$ four-circle diffractometer [(I), (II) and (IV) with Mo $K\alpha$, λ = 0·71069 Å, (III) with Cu $K\alpha$, λ = 1·54178 Å]. Intensities were collected with graphite-monochromated radiation. Measurements were carried out in the θ–2θ mode for one quarter of reciprocal space at scan speeds varying linearly between 2·93° min^{-1} (150 c.p.s. and below) and 29·30° min^{-1} (5000 c.p.s. and above). The angular 2θ range traversed was from 1·2° below the $K\alpha_1$ reflexion to 1·2° above the $K\alpha_2$ reflexion. The net intensity of each reflexion (scaled to counts per minute) was assigned a standard deviation, based on the counting statistics, of $\sigma(I) = t(N_s + N_b)^{1/2}$, where *t* is the scan rate, N_s the gross count and N_b the total background count. Lorentz and polarization corrections (but no absorption correction) were applied. Only those reflexions with $F \geq 3{\cdot}0\sigma(F)$ were retained in the refinements.

Structure solution and refinement

All reflexions were included in the direct-methods structure solutions, those with $I \geq 1{\cdot}0\sigma(I)$ being assigned a value of $0{\cdot}25\sigma(I)$. The structures of (I), (II) and (IV), which are centrosymmetric, were solved by an automatic multisolution technique (*SHELX*-76, G. M. Sheldrick) in which 2^{20} sign permutations were expanded by the Σ_2 formula. That of (III) was solved by multisolution tangent refinement with four reflexions with high estimated α values being allocated starting phases of 45, 135, 225 and 315°. The solution and subsequent refinement of the structures was performed with *SHELX*-76.

The structures were refined by blocked full-matrix least squares, $\Sigma w\Delta^2$ being minimized; anisotropic temperature factors were introduced for all nonhydrogen atoms. Difference syntheses revealed the positions of the H atoms, which were included, with isotropic temperature factors [for (III) two group temperature factors], in the final cycles. The weights were given by $w = k/[\sigma^2(F_o) + gF_o^2]$; *k* was fixed at 1·0 for (III). Complex neutral-atom scattering factors (Cromer & Waber, 1965; Cromer & Liberman, 1970) were employed for the nonhydrogen atoms. The final atom coordinates are listed in Table 2 and their anisotropic

Table 2. *Atom positional parameters* ($\times 10^4$)

	x	y	z
Compound I			
N(1)	1809 (2)	9171 (4)	2501 (2)
C(1)	1704 (3)	7856 (5)	1872 (2)
C(2)	965 (4)	8567 (6)	1020 (2)
C(3)	544 (3)	384 (6)	1273 (2)
C(4)	1213 (3)	756 (5)	2216 (2)
C(5)	1240 (3)	2307 (5)	2641 (2)
N(6)	2463 (2)	4456 (4)	3598 (2)
C(6)	1919 (3)	2822 (5)	3520 (2)
C(7)	2104 (3)	2053 (5)	4379 (2)
C(8)	2800 (3)	3250 (5)	4975 (2)
C(9)	3007 (3)	4730 (5)	4483 (2)
O(1)	2163 (2)	6379 (3)	1976 (1)
C(71)	1582 (5)	325 (7)	4608 (4)
C(81)	3247 (5)	2908 (9)	5959 (3)
C(91)	3619 (3)	6420 (6)	4698 (3)
O(91)	3641 (2)	7611 (4)	4147 (2)
O(92)	4125 (2)	6556 (3)	5559 (2)
C(93)	4711 (5)	8266 (7)	5842 (3)
C(94)	5104 (6)	8204 (11)	6837 (4)
Compound III			
N(1)	9308 (1)	9517 (1)	7810 (1)
C(1)	9645 (2)	8659 (1)	7462 (2)
C(2)	10505 (2)	8659 (1)	6575 (2)
C(3)	10654 (2)	9875 (1)	6383 (2)
C(4)	9880 (1)	260 (1)	7214 (2)
C(5)	9744 (2)	1265 (1)	7371 (2)
N(6)	8336 (1)	1163 (1)	8835 (2)
C(6)	8993 (2)	1710 (1)	8164 (2)
C(7)	8781 (2)	2727 (1)	8368 (2)
C(8)	7985 (2)	2782 (1)	9208 (2)
C(9)	7715 (2)	1797 (1)	9481 (2)
O(11)	9298 (2)	7776 (1)	7837 (2)
C(12)	8487 (3)	7788 (2)	8708 (3)
C(13)	8160 (4)	6735 (3)	8921 (4)
C(71)	9279 (2)	3609 (1)	7765 (3)
C(81)	7535 (2)	3707 (1)	9724 (3)
C(91)	6934 (1)	1420 (1)	10270 (2)
O(91)	6383 (1)	1931 (1)	10894 (2)
O(92)	6884 (1)	398 (1)	10263 (2)
C(93)	6193 (2)	9961 (2)	11107 (3)
C(94)	6274 (3)	8846 (2)	11000 (3)

	x	y	z
Compound II			
N(1)	3222 (5)	2799 (4)	2817 (1)
C(1)	4070 (7)	1301 (6)	2735 (1)
C(2)	2744 (8)	11 (6)	2965 (1)
C(3)	885 (7)	956 (5)	3168 (1)
C(4)	1378 (6)	2755 (5)	3090 (1)
C(5)	412 (7)	4109 (5)	3236 (1)
N(6)	7515 (5)	2911 (4)	3704 (1)
C(6)	8574 (7)	4230 (5)	3526 (1)
C(7)	7541 (7)	5645 (5)	3683 (1)
C(8)	5856 (6)	5152 (5)	3970 (1)
C(9)	5863 (7)	3444 (5)	3978 (1)
O(1)	5707 (5)	1059 (4)	2514 (1)
C(71)	8210 (8)	7404 (6)	3576 (1)
C(81)	4329 (7)	6290 (5)	4216 (2)
C(91)	4633 (7)	2190 (6)	4213 (1)
O(91)	4918 (5)	697 (4)	4170 (1)
O(92)	3112 (4)	2822 (3)	4480 (1)
C(93)	1803 (8)	1653 (6)	4736 (1)
C(94)	191 (8)	2660 (6)	4990 (2)
Compound IV			
N(1)	4527 (3)	2818 (2)	1261 (1)
C(1)	4419 (5)	3395 (3)	1991 (2)
C(2)	3598 (6)	2711 (3)	2634 (2)
C(3)	3441 (5)	1596 (3)	2233 (2)
C(4)	3884 (4)	1761 (2)	1325 (2)
C(5)	3707 (4)	1094 (2)	668 (2)
N(6)	2841 (3)	9349 (2)	1317 (1)
C(6)	2957 (4)	36 (2)	649 (2)
C(7)	2199 (4)	9546 (2)	9950 (2)
C(8)	1604 (4)	8536 (2)	200 (2)
C(9)	2035 (4)	8417 (2)	1054 (2)
C(11)	5196 (5)	3272 (2)	490 (2)
C(12)	3858 (6)	3747 (3)	9906 (2)
O(1)	4888 (3)	4323 (2)	2078 (1)
C(71)	2035 (5)	19 (3)	9070 (2)
C(81)	650 (5)	7770 (3)	9629 (2)
C(91)	1836 (5)	7565 (2)	1663 (2)
O(91)	2276 (4)	7604 (2)	2402 (1)
O(92)	1096 (3)	6687 (1)	1324 (1)
C(93)	960 (7)	5756 (3)	1874 (3)
C(94)	9901 (10)	4953 (4)	1424 (4)

temperature factor components in Table 3.* H atom positional parameters and isotropic temperature factors are presented in Table 4, and bond lengths and bond angles for the nonhydrogen atoms in Tables 5 and 6. Figs. 4–7 and Fig. 9, which show the molecules in perspective and projections of the unit-cell contents, were drawn by *MIRAGE* (W. S. Sheldrick and D. N. Lincoln). For clarity, the 5(1*H*)-pyrromethenone skeleton has been allocated a continuous numbering system in this work (Figs. 4 and 5) and not as recommended by systematic nomenclature (Jackson & Smith, 1973; Bonnett, 1977).

* Lists of structure factors and Table 3 have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32750 (41 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Discussion

The analyses confirm the *Z* and *E* configurations for (I) and (II) respectively and demonstrate that their conversion to the lactim ether (III) and the *N*-alkylated derivative (IV) respectively, on treatment with $Et_3O^+BF_4^-$ in CH_2Cl_2, takes place without isomerization. As displayed in Fig. 8, both 5(1*H*)-pyrromethenone derivatives, (I) and (II), may be represented by two planar conformations, which are denominated as the *syn* and *anti* forms respectively. The observation of a particular conformation in the crystalline state, which does, of course, provide only limited information about possible conformational preferences in solution, will be the result of an interplay of four major contributing factors: (1) The electronic stabilization which may be achieved by an extension of $p\pi$

Table 4. *Hydrogen-atom positional parameters* ($\times 10^3$) *and isotropic temperature factors* ($Å^2 \times 10^3$)

	x	*y*	*z*	*U*		*x*	*y*	*z*	*U*
Compound I					Compound II				
H(11)	225 (3)	906 (4)	294 (2)	29 (10)	H(11)	372 (7)	387 (6)	268 (2)	97 (16)
H(21)	32 (3)	768 (5)	71 (2)	64 (13)	H(21)	372 (6)	947 (5)	324 (1)	67 (13)
H(22)	135 (3)	868 (5)	46 (2)	66 (14)	H(22)	231 (6)	921 (4)	277 (1)	44 (10)
H(31)	59 (3)	135 (5)	76 (2)	66 (13)	H(31)	942 (6)	58 (5)	298 (2)	73 (13)
H(32)	975 (3)	47 (5)	125 (2)	60 (12)	H(32)	90 (5)	69 (4)	352 (1)	42 (10)
H(51)	82 (3)	329 (4)	231 (2)	32 (10)	H(51)	87 (5)	512 (4)	315 (1)	31 (9)
H(61)	233 (5)	529 (7)	300 (4)	137 (21)	H(61)	779 (4)	186 (4)	367 (1)	21 (9)
H(711)	119 (3)	46 (6)	512 (3)	51 (14)	H(711)	767 (7)	805 (6)	377 (2)	79 (15)
H(712)	84 (5)	2 (7)	420 (3)	94 (21)	H(712)	968 (10)	758 (8)	359 (2)	165 (25)
H(713)	207 (4)	936 (7)	476 (3)	92 (20)	H(713)	724 (9)	775 (7)	329 (2)	118 (19)
H(811)	399 (4)	260 (7)	611 (3)	69 (18)	H(811)	284 (8)	595 (6)	408 (2)	99 (17)
H(812)	270 (7)	169 (13)	611 (6)	268 (48)	H(812)	442 (9)	610 (7)	452 (2)	120 (20)
H(813)	317 (5)	387 (8)	629 (4)	117 (27)	H(813)	447 (8)	747 (7)	412 (2)	108 (18)
H(931)	535 (4)	827 (7)	549 (3)	82 (19)	H(931)	126 (6)	87 (5)	451 (2)	71 (14)
H(932)	407 (5)	929 (8)	556 (3)	114 (21)	H(932)	274 (7)	108 (5)	496 (2)	78 (14)
H(941)	556 (5)	946 (8)	712 (3)	106 (20)	H(941)	93 (7)	335 (5)	524 (2)	74 (14)
H(942)	441 (5)	817 (7)	717 (4)	104 (22)	H(942)	−82 (7)	192 (5)	514 (2)	73 (14)
H(943)	555 (5)	711 (8)	712 (4)	110 (24)	H(943)	−56 (8)	327 (6)	474 (2)	95 (16)
Compound III					Compound IV				
H(21)	629 (3)	671 (3)	1195 (3)	87 (3)	H(111)	593 (5)	274 (3)	22 (2)	76 (12)
H(22)	1011 (3)	829 (3)	577 (3)	87 (3)	H(112)	596 (4)	385 (3)	65 (2)	59 (11)
H(31)	1041 (3)	2 (3)	550 (3)	87 (3)	H(121)	296 (5)	322 (3)	973 (3)	100 (14)
H(32)	1157 (3)	2 (3)	670 (3)	87 (3)	H(122)	328 (5)	438 (4)	25 (3)	118 (16)
H(51)	1021 (3)	173 (3)	686 (3)	87 (3)	H(123)	439 (4)	404 (3)	944 (2)	64 (11)
H(61)	823 (3)	48 (2)	882 (3)	87 (3)	H(21)	418 (5)	272 (3)	317 (2)	78 (12)
H(121)	885 (4)	816 (3)	943 (4)	118 (3)	H(22)	248 (5)	295 (3)	275 (3)	102 (15)
H(122)	771 (4)	817 (4)	840 (4)	118 (3)	H(31)	428 (5)	110 (3)	251 (3)	93 (14)
H(131)	783 (4)	645 (3)	805 (4)	118 (3)	H(32)	241 (6)	134 (4)	226 (3)	113 (16)
H(132)	782 (4)	666 (4)	950 (4)	118 (3)	H(51)	411 (3)	135 (2)	14 (2)	31 (8)
H(133)	896 (4)	635 (3)	903 (4)	118 (3)	H(61)	335 (4)	937 (3)	181 (2)	55 (10)
H(711)	854 (4)	395 (3)	717 (4)	118 (3)	H(711)	263 (7)	966 (4)	867 (3)	139 (19)
H(712)	458 (5)	162 (4)	1190 (5)	118 (3)	H(712)	93 (7)	997 (4)	885 (3)	134 (18)
H(713)	1020 (4)	353 (4)	770 (5)	118 (3)	H(713)	226 (6)	76 (4)	905 (3)	134 (18)
H(811)	670 (4)	363 (4)	960 (4)	118 (3)	H(811)	102 (6)	775 (3)	910 (3)	105 (15)
H(812)	729 (4)	421 (3)	911 (4)	118 (3)	H(812)	59 (6)	706 (4)	987 (3)	105 (15)
H(813)	774 (4)	379 (3)	1054 (4)	118 (3)	H(813)	952 (7)	799 (5)	955 (3)	146 (20)
H(931)	539 (5)	16 (4)	1089 (5)	118 (3)	H(931)	50 (5)	603 (3)	239 (3)	75 (16)
H(932)	653 (4)	15 (3)	1193 (5)	118 (3)	H(932)	214 (6)	549 (4)	203 (3)	92 (16)
H(941)	597 (4)	863 (3)	1011 (5)	118 (3)	H(941)	975 (5)	443 (4)	178 (3)	78 (16)
H(942)	586 (4)	848 (4)	1177 (4)	118 (3)	H(942)	879 (7)	522 (4)	123 (4)	132 (25)
H(943)	713 (4)	856 (4)	1114 (4)	118 (3)	H(943)	46 (6)	469 (4)	90 (4)	112 (21)

delocalization of the lactam group of the pyrrolidinone system into the carbonyl group substituent at the pyrrole ring. (2) The minimization of intramolecular steric repulsions between the two ring systems. Fig. 8 indicates that the *syn* conformation should be preferred for the *Z* isomer, and the *anti* conformation for the *E* isomer (assuming the planar representations), in the absence of intermolecular interactions. Steric contacts between one of the *β*-methyl substituents of the pyrrole ring and the pyrrolidinone system in the *anti-Z* and *syn-E* forms would be expected to force these to adopt a twisted conformation. (3) Potential intermolecular N—H···O hydrogen bonding. Owing to the higher acidity of the pyrrolic N—H (Yagil, 1967) compared with that of the pyrrolidinones (Caillet, Bauer, Froyer & Sekiguchi, 1973), such bonding would be expected *a priori* to take place preferentially with the pyrrole ring as proton donor. The presence of such bonding would be predicted to lead to a twisted conformation for the *syn-Z* or *anti-E* isomers, in order to reduce non-bonded intermolecular contacts. An N(1)—H···O hydrogen bond should, however, be compatible with a *planar* [see (2) above] *anti* conformation for the *E* isomer. Crystal-packing effects could also lead to the observation of preferential hydrogen bonding to the pyrrolidinone N—H proton. (4) Non-bonded intermolecular interactions. Such contacts will be of importance in determining the exact interplanar angle for a twisted conformation. Furthermore, dispersion forces would be expected to enhance the stability of planar 5(1*H*)-pyrromethenone systems with extended π delocalization, which are capable of stacking parallel to

one another at a van der Waals distance of 3·4–4·0 Å between molecule sheets, as is regularly observed for other aromatic systems (*e.g.* nucleobases, porphyrins).

The conformations of (I)–(IV) in the crystalline state will now be discussed in terms of these factors. Intermolecular hydrogen bonding (Table 7) is observed for all derivatives except (III), but N(1) is involved, rather than N(6), for derivative (II). Presumably as a result of hydrogen bonding, twisted conformations are observed for (I) and (IV). The respective interplanar angles of 131·5 and 150·9° between the two rings correspond to the *anti* conformation in both cases. The atoms were assigned weights equal to their atomic numbers in the least-squares-plane calculations and C(5) was included. For (II), however, for which N(1) is capable of taking part in hydrogen bonding without leading to other short intermolecular contacts, a planar *anti-E* conformation is observed (interplanar angle −176·6°). Planarity over the two ring systems is likewise observed for (III), which takes up a *syn-Z* conformation (interplanar angle −0·3°). The planar system of (III) is also stabilized by intramolecular hydrogen bonding between the pyrrole N(6)–H and the lactim ether N(1) (Table 7). The further enhancement of the electronic stability of the planar skeleton for (II) and (III) through dispersion forces between neighbouring parallel aromatic systems is illustrated by their stacking patterns in Fig. 9.

As may be seen from Table 8, the carbonyl substituent of the pyrrole ring lies close to the aromatic plane in all four derivatives. All non-hydrogen atoms in (II) and (III) are approximately planar. In (III) the carbonyl group takes up an *anti* position with respect to the pyrrole ring N–H vector, whereas in the other derivatives it is *syn*. Both conformations have previously been observed for 2-ethoxycarbonylpyrroles

Table 5. *Bond lengths* (Å)

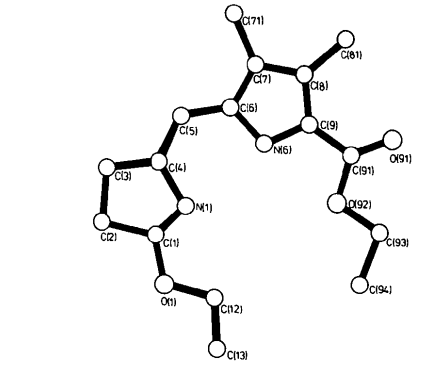
	(I)	(II)	(III)	(IV)
C(1)–N(1)	1·359 (5)	1·346 (6)	1·282 (3)	1·363 (5)
C(4)–N(1)	1·398 (5)	1·417 (6)	1·409 (3)	1·420 (4)
C(2)–C(1)	1·506 (5)	1·495 (7)	1·504 (4)	1·493 (6)
O(1)–C(1)	1·223 (5)	1·241 (6)	1·326 (3)	1·223 (5)
C(3)–C(2)	1·522 (6)	1·529 (7)	1·523 (3)	1·530 (5)
C(4)–C(3)	1·519 (5)	1·502 (7)	1·519 (4)	1·500 (5)
C(5)–C(4)	1·321 (6)	1·324 (7)	1·356 (3)	1·333 (5)
C(6)–C(5)	1·466 (5)	1·444 (7)	1·454 (4)	1·450 (5)
C(6)–N(6)	1·373 (5)	1·360 (6)	1·355 (3)	1·363 (4)
C(9)–N(6)	1·386 (5)	1·385 (6)	1·378 (3)	1·389 (4)
C(7)–C(6)	1·409 (6)	1·394 (7)	1·396 (3)	1·388 (5)
C(8)–C(7)	1·412 (5)	1·411 (6)	1·410 (4)	1·407 (5)
C(71)–C(7)	1·505 (7)	1·515 (7)	1·507 (4)	1·511 (5)
C(9)–C(8)	1·387 (6)	1·378 (7)	1·387 (3)	1·390 (5)
C(81)–C(8)	1·509 (6)	1·515 (7)	1·483 (4)	1·510 (5)
C(91)–C(9)	1·457 (6)	1·445 (7)	1·442 (4)	1·445 (5)
O(91)–C(91)	1·229 (6)	1·224 (6)	1·219 (3)	1·210 (5)
O(92)–C(91)	1·331 (5)	1·338 (6)	1·357 (3)	1·350 (4)
C(93)–O(92)	1·471 (6)	1·457 (6)	1·444 (4)	1·454 (5)
C(94)–C(93)	1·498 (8)	1·502 (8)	1·487 (4)	1·484 (8)
C(12)–O(1)	–	–	1·448 (5)	–
C(13)–C(12)	–	–	1·475 (5)	–
C(11)–N(1)	–	–	–	1·458 (5)
C(12)–C(11)	–	–	–	1·521 (6)

Table 6. *Bond angles* (°)

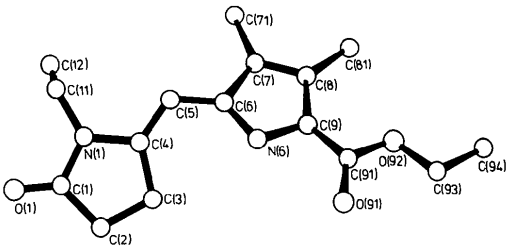
	(I)	(II)	(III)	(IV)
C(4)–N(1)–C(1)	115·0 (3)	114·3 (4)	107·0 (2)	113·4 (2)
C(2)–C(1)–N(1)	108·0 (3)	108·5 (4)	117·4 (2)	108·2 (3)
O(1)–C(1)–N(1)	125·7 (3)	124·9 (4)	124·6 (2)	124·5 (4)
O(1)–C(1)–C(2)	126·2 (4)	126·5 (4)	118·0 (2)	127·3 (4)
C(3)–C(2)–C(1)	104·8 (3)	105·3 (4)	101·1 (2)	105·7 (3)
C(4)–C(3)–C(2)	105·5 (3)	105·1 (4)	103·4 (2)	104·6 (3)
C(3)–C(4)–N(1)	105·8 (3)	106·3 (4)	111·1 (2)	107·0 (3)
C(5)–C(4)–N(1)	128·7 (3)	123·0 (4)	123·7 (2)	123·7 (3)
C(5)–C(4)–C(3)	125·4 (4)	130·7 (4)	125·3 (2)	129·3 (3)
C(6)–C(5)–C(4)	129·0 (4)	128·3 (4)	124·7 (2)	128·3 (3)
C(9)–N(6)–C(6)	109·2 (3)	110·5 (4)	110·0 (2)	109·6 (3)
N(6)–C(6)–C(5)	118·0 (3)	124·6 (4)	123·7 (2)	126·3 (3)
C(7)–C(6)–C(5)	134·2 (4)	128·9 (4)	128·9 (2)	126·3 (3)
C(7)–C(6)–N(6)	107·6 (3)	106·5 (4)	107·5 (2)	107·4 (3)
C(8)–C(7)–C(6)	107·4 (4)	108·6 (4)	107·9 (2)	108·5 (3)
C(71)–C(7)–C(6)	125·2 (4)	124·6 (4)	126·1 (3)	125·7 (3)
C(71)–C(7)–C(8)	127·3 (4)	126·8 (4)	126·0 (2)	125·8 (3)
C(9)–C(8)–C(7)	107·4 (3)	106·8 (4)	106·7 (2)	106·8 (3)
C(81)–C(8)–C(7)	124·9 (4)	126·3 (4)	127·1 (2)	124·8 (3)
C(81)–C(8)–C(9)	127·7 (4)	126·9 (4)	126·2 (3)	128·5 (3)
C(8)–C(9)–N(6)	108·3 (3)	107·7 (4)	108·0 (2)	107·7 (3)
C(91)–C(9)–N(6)	117·1 (4)	117·4 (4)	122·0 (2)	118·4 (3)
C(91)–C(9)–C(8)	134·6 (4)	134·9 (4)	130·0 (2)	133·9 (3)
O(91)–C(91)–C(9)	123·5 (4)	124·1 (5)	125·8 (2)	125·2 (3)
O(92)–C(91)–C(9)	112·9 (4)	113·2 (4)	111·9 (2)	112·8 (3)
O(92)–C(91)–O(91)	123·6 (4)	122·7 (4)	122·2 (2)	122·0 (3)
C(93)–O(92)–C(91)	116·3 (4)	117·2 (4)	115·2 (2)	116·7 (3)
C(94)–C(93)–O(92)	107·2 (5)	106·7 (4)	107·4 (3)	107·7 (4)
C(12)–O(1)–C(1)	–	–	117·4 (2)	–
C(13)–C(12)–O(1)	–	–	107·8 (3)	–
C(11)–N(1)–C(1)	–	–	–	122·2 (3)
C(11)–N(1)–C(4)	–	–	–	124·3 (3)
C(12)–C(11)–N(1)	–	–	–	112·6 (3)

Table 7. *Hydrogen bonding of the type* N–H···*X* (*X* = N, O)

	(I)	(II)	(III)	(IV)
	N(6)–H···O(1) (intermolecular)	N(1)–H···O(1) (intermolecular)	N(6)–H···N(1) (intramolecular)	N(6)–H···O(1) (intermolecular)
N···*X* (Å)	2·82	2·87	2·78	3·09
H···*X* (Å)	1·74	1·88	2·21	2·23
N–H (Å)	1·09 (5)	1·00 (5)	0·91 (3)	0·87 (3)
Symmetry transformation	1·0 + *x*, 1·0 + *y*, 1·0 + *z*	−*x*, 0·5 + *y*, 0·5 − *z*	*x*,*y*,*z*	−*x*, 0·5 + *y*, 0·5 − *z*
Interplanar angle (°)	131·5	−176·6	−0·3	150·9
Conformation	*anti-Z*	*anti-E*	*syn-Z*	*anti-E*



(III)



(IV)

Fig. 5. Derivatives III and IV in perspective with atom numbering.

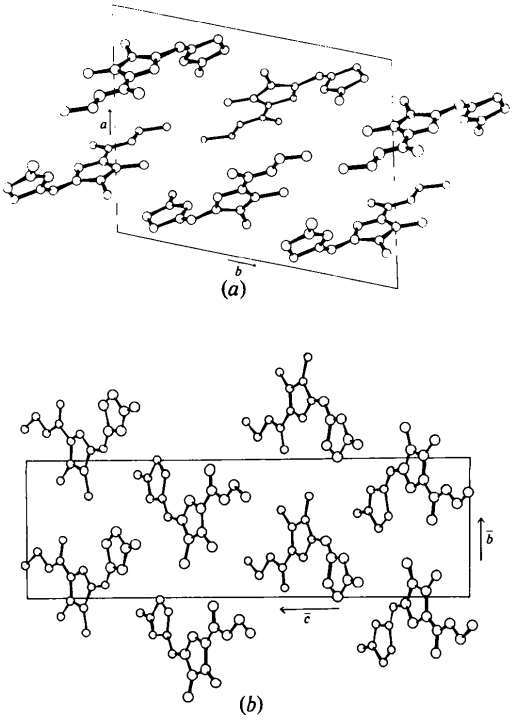


Fig. 6. Projections of the crystal structures of (*a*) compound I and (*b*) compound II.

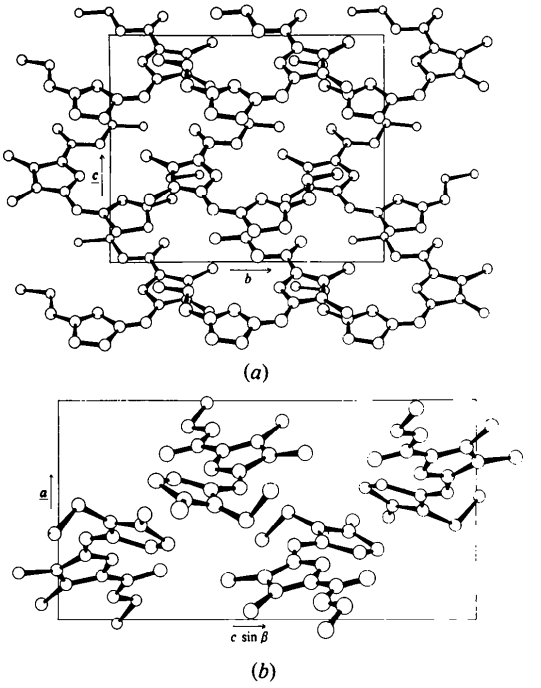


Fig. 7. Projections of the crystal structures of (*a*) compound III and (*b*) compound IV.

(Bonnett, Hursthouse & Neidle, 1972*a*,*b*). IR studies have suggested that such rotational isomers have an activation-energy barrier of about 1 kcal mol^{-1} in solution (Jones, 1970).

Equivalent bond lengths are similar in all four derivatives (Table 5). The presence of a formal N(1)–C(1) double bond in the lactim ether (III) does not lead to a significant alteration in the N(1)–C(4) length in comparison with that in the 5(1*H*)-pyrromethenones. The C(4)–C(5) length of 1·356 (3) Å in (III) is, however, significantly longer than in (I), (II) and (IV) (1·321–1·333 Å). The short N(1)–C(1), N(1)–C(4) and C(5)–C(6) distances of 1·346–1·363 [excluding (III)], 1·398–1·420 and 1·444–1·466 Å respectively in (I)–(IV) indicate that there is a considerable degree of delocalization over the conjugated system of these molecules. Bond lengths and angles in the pyrrole ring of (I)–(IV) are very similar to those established by a microwave study for pyrrole itself (Nygaard, Nielsen, Kirchheiner, Maltesen, Rastrup-Andersen & Sørensen, 1969). In contrast to the similarity of the bond-length pattern in (I) and (II) are the striking differences in the bond angles at C(4) and C(6) in these geometric isomers (Table 6). In the lactim ether (III) the C(4)–C(5)–C(6) methine bridge angle of 124·7 (2)° is smaller than in the other derivatives (128·3–129·0°), presumably as a result of the intramolecular N–H···N hydrogen bonding.

It is instructive to compare the molecular geometry of the *Z*-configurated 3,4-dihydro-5(1*H*)-pyrromethen-

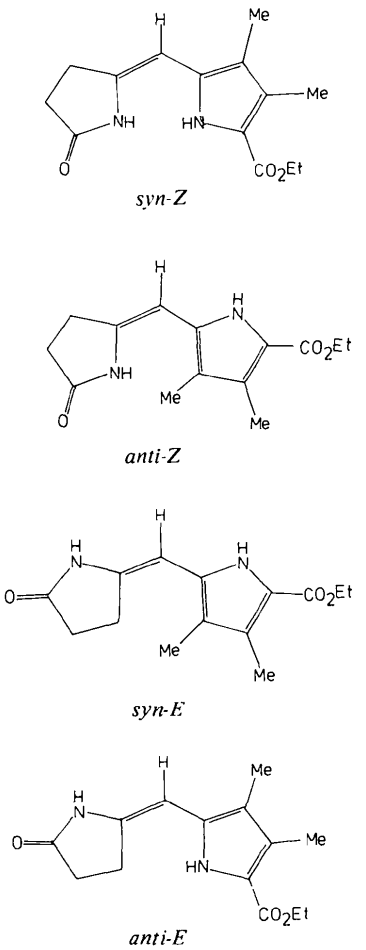


Fig. 8. The four possible planar representations of 5′-ethoxycarbonyl-3,4-dihydro-3′,4′-dimethyl-5(1*H*)-2,2′-pyrromethenone.

one (I) with that of the analogous 5(1*H*)-pyrromethenone (VII) [which contains a C(2)–C(3) double bond] and with biliverdin dimethyl ester. The *A* and *B* rings of the latter bile pigment (the right-hand pair in Fig. 10) have a formal resonance structure equivalent to that of a 5(1*H*)-pyrromethenone. The recent X-ray analysis of bilirubin has lent support to the view that it may be regarded as a 2,2′-dipyrrolylmethane (rings *B* and *C*) with conjugating α-substituents. The observed bond lengths suggested that delocalization over the local 5(1*H*)-pyrromethenone systems in bilirubin (*i.e.* rings *A* + *B* and *C* + *D*), which have planar *syn-Z* configurations, is rather limited. Thus C(4)–C(5) and C(15)–C(16) appear to be essentially double bonds (average 1·30 Å), whereas C(5)–C(6) and C(14)–C(15) resemble single bonds (average 1·48 Å). These results contrast with the observation of a considerable degree of delocalization over the conjugated systems of the model compounds (I) and (VII). However, the structure of bilirubin could not be accurately determined, on account of the limited data set (1323 observed reflexions for two independent molecules in the asymmetric unit), and it was necessary to adopt a constrained bond-length model (e.s.d.'s 0·02–0·05 Å). Thus until more accurate structural information becomes available for a bilirubin derivative, studies on pyrromethenone systems will continue to retain their valuable model character.

Delocalization is possible over all atoms of the pyrrolone ring in (VII), which leads to a shortening of C(1)–C(2) and C(3)–C(4) in comparison with (I), and is also reflected in the C(4)–C(5) and C(5)–C(6) distances. The former is longer in (VII), the latter being very significantly shorter. The C(4)–C(5)–C(6) methine bridge angle of 133·3 (9)° in (VII) is larger than those in (I)–(IV), presumably as a result of intra-

Table 8. *Distances of atoms* (Å) *from weighted least-squares planes*

The atoms were assigned weights equal to their atomic numbers. Atoms marked with an asterisk were not included in the least-squares plane calculation.

	Compound I		Compound II			Compound III			Compound IV	
O(1)	−0·055*		−0·016*		0·109	−0·003*		0·019	0·075*	
C(1)	−0·027		−0·012		0·034	−0·004		0·005	0·030	
C(2)	0·051		0·030		0·023	0·007		0·007	−0·058	
C(3)	−0·056		−0·037		−0·136	−0·009		−0·024	0·065	
C(4)	0·043		0·032		−0·064	0·007		−0·005	−0·050	
N(1)	−0·009		−0·011		−0·018	−0·002		0·000	0·012	
C(5)	0·202*	−0·060*	0·131*	0·037*	−0·026	0·024*	−0·004*	0·001	−0·215*	−0·013*
C(6)		0·008		0·007	−0·026		0·005	0·009		0·002
C(7)		−0·008		−0·006	0·014		−0·006	−0·006		0·002
C(8)		0·006		0·003	0·034		0·004	0·005		−0·006
C(9)		−0·001		0·001	−0·014		−0·001	0·005		0·007
N(6)		−0·003		−0·004	−0·058		−0·002	0·006		−0·005
C(91)		−0·033*		0·050*	0·019		−0·017*	−0·007		0·049*
O(91)		−0·107*		0·042*	−0·034		0·019*	0·027		0·037*
O(92)		−0·012*		0·089*	0·098		−0·057*	−0·043		0·112*
C(93)					0·152*			0·048*		
C(94)					0·186*			0·037*		
C(71)		−0·110*		0·022*	0·081*		−0·065*	−0·070*		0·008*
C(81)		0·057*		0·001*	0·085*		0·038*	0·035*		−0·057*

molecular repulsions between the N—H hydrogens in this derivative, which displays a virtually planar (interplanar angle 3·9°) *syn-Z* configuration. The molecules of (VII) are linked into a centrosymmetric dimer through four (C=O)···H—N intermolecular hydrogen bonds. The molecular geometry of the *A* and *B* rings of biliverdin dimethyl ester differs significantly from that in (VII). The similarity of the bond-length distribution within rings *B* and *C* indicates that there is considerable delocalization over this part of the molecule, lending support to the view that such bilatrienes may possibly be best regarded as substituted pyrromethenes. Structural data from model pyrromethenes would obviously help to further clarify the nature of the bonding in biliverdin.

The surprising regioselectivity of the reaction of both 5(1*H*)-pyrromethenone isomers (I) and (II) with $Et_3O^+BF_4^-$ may be rationalized as follows. In solution the *Z*-configurated isomer (I) is capable of developing a weak intramolecular hydrogen bond between the pyrrolic N—H and the lone electron pair at the N atom of the lactam group. Such an interaction, which represents, to some extent, a 'pre-formed' intramolecular hydrogen bond, as is present in the lactim ether (III) (Table 7), not only diminishes the nucleophilicity of the lactam N atom but also facilitates the cleavage of the proton bonded to the latter under concomitant alkylation of the O atom (Fig. 11). Since in the *E*-configurated isomer no intramolecular hydrogen bonding is possible, alkylation takes place at the N atom of the lactam ring yielding (IV). However, this behaviour of the 5(1*H*)-pyrromethenone derivative (II)

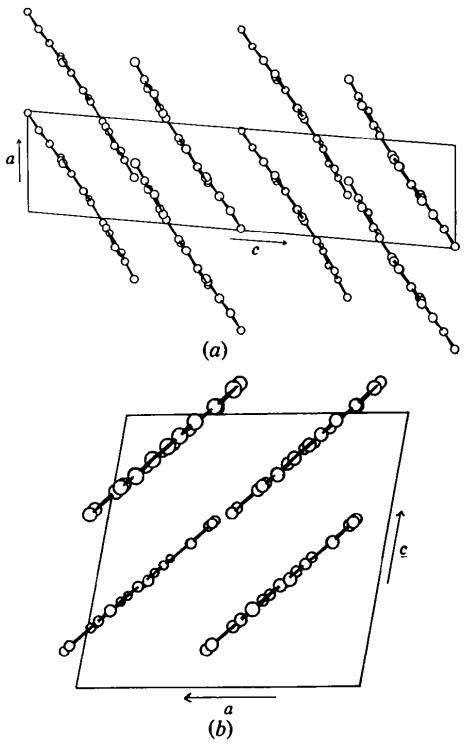


Fig. 9. Projections of the crystal structures of (*a*) compound II and (*b*) compound III showing the molecular stacking.

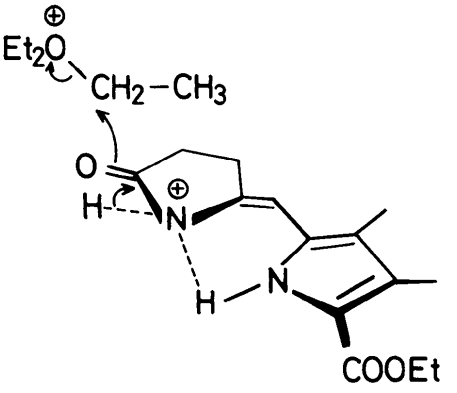


Fig. 11. Proposed mechanism for the reaction of (I) with $Et_3O^+BF_4^-$.

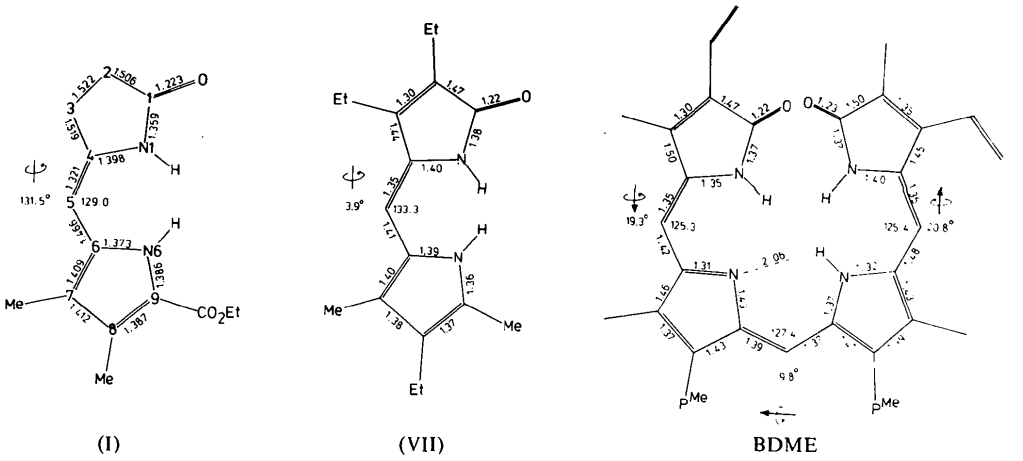


Fig. 10. Bond lengths in (I), (VII) and biliverdin dimethyl ester (BDME).

contrasts with the well documented (Glushkov & Granik, 1969) reactivity of lactams towards $Et_3O^+BF_4^-$ which regularly yield the corresponding *O*-alkylated derivatives.

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The Crystal and Molecular Structure of DL-Mannitol at −150° C

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DL-Mannitol, $C_6H_{14}O_6$, is orthorhombic, space group $Pna2_1$, with $a = 9{\cdot}048$ (7), $b = 4{\cdot}870$ (3), $c = 18{\cdot}262$ (13) Å, $Z = 4$ at −150°C. The structure was refined to $R = 0{\cdot}030$ with 956 counter reflexions collected at −150°C. In DL-mannitol the D-mannitol molecule has the same conformation as that in the B and K forms of D-mannitol. The molecule has a planar C atom chain and nearly a twofold axis of symmetry. All OH groups are involved in intermolecular hydrogen bonds. The hydrogen-bond pattern is similar to that of DL-arabinitol, but differs markedly from that in the B and K forms of D-mannitol.

Introduction

Mannitol, $C_6H_{14}O_6$, is an acyclic polyalcohol, of which the D-enantiomer is widely distributed in nature. The L and DL forms do not occur in nature. D-Mannitol is unusual in the class of alditols in that it exists in at least three crystalline polymorphs. The B form (Berman, Jeffrey & Rosenstein, 1968) and the K form (Kim,