trans- and *cis*-2,5-Dimethoxy-3,6-diphenyl-3,6-dihydropyrazine

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Abstract

The title compounds, *trans*-$C_{18}H_{18}N_2O_2$, (I), and *cis*-$C_{18}H_{18}N_2O_2$, (II), both have an essentially planar central bis-lactim ether ring. Compound (I) is exactly centrosymmetric with the *trans*-phenyl substituents nearly perpendicular to the ring [dihedral angle 86.0 (1)°]. In compound (II), the phenyl substituents lie on the same side of the ring, forming dihedral angles of 86.6 (1) and 72.3 (1)° with it in order to minimize repulsive interactions. The methoxy groups lie in the plane of the central ring in each case.

Comment

Biological activity is usually displayed by only one enantiomer of a compound (the other one might even be toxic), so it is desirable to synthesize enantiomerically pure compounds. This is especially true for amino acids which are used in large quantities by the pharmaceutical industry and in medical science and biochemistry, *e.g.* as building blocks for peptides (Schöllkopf, 1983*a*). Over recent years, Schöllkopf and co-workers have developed a generally applicable stereospecific synthesis of amino acids *via* metallated bis-lactim ethers of 2,5-diketopiperazines (Schöllkopf, 1983*b*). In order to understand the reasons for the observed stereospecificity, we have performed a series of structural investigations (Bolte, Benecke & Egert, 1996) and report here the crystal structures of two intermediate products, *trans*-(I) and *cis*-2,5-dimethoxy-3,6-diphenyl-3,6-dihydropyrazine (II).
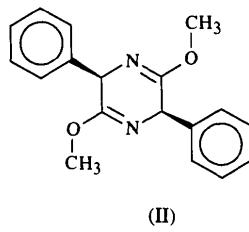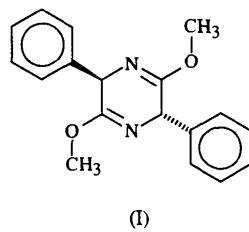
Compound (I) lies on a crystallographic centre of symmetry with the two phenyl substituents in *trans* positions, as expected, nearly perpendicular [86.0 (1)°]

to the heterocycle (Fig. 1). In a similar structure (Schöllkopf, Grüttner, Anderskewitz, Egert & Dyrbusch, 1987), the phenyl/heterocycle angles were 86.9 and 90.6° for the two molecules in the asymmetric unit.
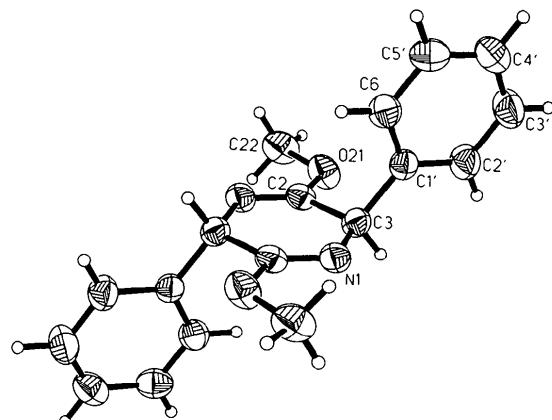

Fig. 1. Perspective view of (I) with the atom-numbering scheme and displacement ellipsoids at the 50% probability level.

Compound (II), a diastereomer of (I), carries the two phenyl groups on the same side of the bis-lactim ether ring (Fig. 2). Repulsive interactions are minimized such that the orientation of one phenyl group (C1''–C6'') remains essentially unchanged [phenyl/heterocycle angle 86.6 (1)°], while the other one (C1'–C6') forms an angle of 72.3 (1)° with the heterocycle.
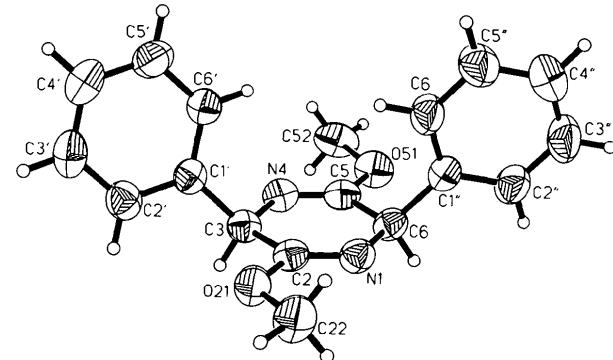

Fig. 2. Perspective view of (II) with the atom-numbering scheme and displacement ellipsoids at the 50% probability level.

Bond lengths, angles and torsion angles of the bis-lactim ether ring are nearly identical (Table 3) in the two molecules. They are in excellent agreement with those of the five previously published structures of bis-lactim ethers (Schöllkopf, Grüttner, Anderskewitz, Egert & Dyrbusch, 1987; Schöllkopf, Hupfeld, Küper, Egert & Dyrbusch, 1988; Schöllkopf, Kühnle, Egert & Dyrbusch, 1987; Schöllkopf, Pettig, Busse, Egert & Dyrbusch, 1986; Schöllkopf, Pettig, Schulze, Klinge, Egert, Benecke & Noltemeyer, 1988) found in the

Cambridge Structural Database (version 5.10, October 1995; Allen & Kennard, 1993) and with those of the lactim ether moiety of dihydrooxazinones (Bolte, 1995). The heterocycles of both structures can be regarded as planar [(I): Q = 0.0 Å, φ = 0.0, θ = 0.0°; (II): Q = 0.0 Å, φ = 277.0, θ = 89.6° (Cremer & Pople, 1975)]. The methoxy groups lie in the plane of the heterocycle with the C(2)—O(21) and C(5)—O(51) bonds in the *cis* conformation and one methyl H atom *trans* with respect to the C(2) and C(5) atoms, respectively.

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters ($\mathring{A}^2$) for (I)*

$$U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij}a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	U_{eq}
N1	0.79474 (8)	0.5620 (3)	0.49479 (10)	0.0393 (4)
C2	0.67111 (9)	0.7583 (3)	0.44457 (12)	0.0358 (4)
C3	0.70771 (9)	0.5527 (3)	0.42692 (11)	0.0366 (4)
O21	0.59113 (6)	0.7299 (2)	0.38262 (9)	0.0480 (4)
C22	0.54685 (10)	0.9118 (4)	0.38904 (14)	0.0540 (5)
C1'	0.67400 (9)	0.5494 (3)	0.31318 (12)	0.0352 (4)
C2'	0.62366 (10)	0.3659 (3)	0.24673 (13)	0.0469 (5)
C3'	0.59333 (11)	0.3655 (4)	0.14362 (15)	0.0564 (6)
C4'	0.61297 (11)	0.5473 (4)	0.10616 (14)	0.0530 (5)
C5'	0.66271 (11)	0.7308 (4)	0.17132 (14)	0.0502 (5)
C6'	0.69309 (10)	0.7319 (3)	0.27455 (13)	0.0443 (5)

Experimental

Both compounds were recrystallized from ether–cyclohexane solution.

Compound (I)

Crystal data

$C_{18}H_{18}N_2O_2$	Mo $K\alpha$ radiation
M_r = 294.34	λ = 0.71069 Å
Monoclinic	Cell parameters from 62
$C2/c$	reflections
a = 21.519 (3) Å	θ = 10.0–12.5°
b = 5.5068 (4) Å	μ = 0.085 mm^{-1}
c = 16.422 (2) Å	T = 293 (2) K
β = 128.692 (12)°	Block
V = 1519.0 (4) Å^3	0.50 × 0.30 × 0.10 mm
Z = 4	Colourless
D_x = 1.287 Mg m^{-3}	
D_m not measured	

Data collection

Stoe–Siemens–AED four-circle diffractometer	R_{int} = 0.0249
$2\theta/\omega$ scans with on-line profile fitting (Clegg, 1981)	θ_{max} = 25.0°
	h = −25 → 19
	k = −6 → 1
	l = 0 → 19
Absorption correction: none	3 standard reflections
1978 measured reflections	monitored every 100
1336 independent reflections	reflections
1028 observed reflections	intensity decay: none
[$I > 2\sigma(I)$]	

Refinement

Refinement on F^2	$\Delta\rho_{max}$ = 0.179 e Å^{-3}
$R(F)$ = 0.0416	$\Delta\rho_{min}$ = −0.182 e Å^{-3}
$wR(F^2)$ = 0.1366	Extinction correction:
S = 1.110	SHELXL93 (Sheldrick,
1335 reflections	1993)
102 parameters	Extinction coefficient:
H atoms riding	0.050 (4)
$w = 1/[\sigma^2(F_o^2) + (0.0633P)^2 + 0.3436P]$	Atomic scattering factors from *International Tables*
where $P = (F_o^2 + 2F_c^2)/3$	*for Crystallography* (1992,
$(\Delta/\sigma)_{max} < 0.001$	Vol. C, Tables 4.2.6.8 and 6.1.1.4)

Compound (II)

Crystal data

$C_{18}H_{18}N_2O_2$	Cu $K\alpha$ radiation
M_r = 294.34	λ = 1.5418 Å
Orthorhombic	Cell parameters from 62
$Pbca$	reflections
a = 15.7468 (4) Å	θ = 23–32°
b = 17.3677 (5) Å	μ = 0.655 mm^{-1}
c = 11.5306 (4) Å	T = 293 (2) K
V = 3153.7 (4) Å^3	Block
Z = 8	0.80 × 0.30 × 0.30 mm
D_x = 1.240 Mg m^{-3}	Colourless
D_m not measured	

Data collection

Stoe–Siemens–AED four-circle diffractometer	R_{int} = 0.0402
$2\theta/\omega$ scans with on-line profile fitting (Clegg, 1981)	θ_{max} = 69.90°
	h = −19 → 19
	k = −18 → 19
	l = −14 → 13
Absorption correction: none	3 standard reflections monitored every 100
15 587 measured reflections	reflections
2860 independent reflections	intensity decay: none
2691 observed reflections	
[$I > 2\sigma(I)$]	

Refinement

Refinement on F^2	$\Delta\rho_{max}$ = 0.199 e Å^{-3}
$R(F)$ = 0.0387	$\Delta\rho_{min}$ = −0.115 e Å^{-3}
$wR(F^2)$ = 0.1055	Extinction correction:
S = 1.079	SHELXL93 (Sheldrick,
2859 reflections	1993)
202 parameters	Extinction coefficient:
H atoms riding	0.0032 (2)
$w = 1/[\sigma^2(F_o^2) + (0.0418P)^2 + 0.7339P]$	Atomic scattering factors from *International Tables*
where $P = (F_o^2 + 2F_c^2)/3$	*for Crystallography* (1992,
$(\Delta/\sigma)_{max} < 0.001$	Vol. C, Tables 4.2.6.8 and 6.1.1.4)

Table 2. *Fractional atomic coordinates and equivalent isotropic displacement parameters* $(Å^2)$ *for (II)*

$$U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij}a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	*y*	*z*	U_{eq}
N1	0.35661 (7)	0.43268 (6)	0.13688 (10)	0.0462 (3)
C2	0.32267 (8)	0.49537 (8)	0.10684 (11)	0.0436 (3)
C3	0.36508 (8)	0.57259 (8)	0.08945 (11)	0.0440 (3)
N4	0.45564 (7)	0.57210 (7)	0.11698 (10)	0.0473 (3)
C5	0.48912 (8)	0.50968 (8)	0.14906 (11)	0.0450 (3)
C6	0.44772 (8)	0.43169 (8)	0.16126 (11)	0.0448 (3)
O21	0.23921 (6)	0.49959 (5)	0.08198 (9)	0.0550 (3)
C22	0.19135 (10)	0.42947 (9)	0.0962 (2)	0.0670 (5)
O51	0.57249 (6)	0.50568 (6)	0.17541 (9)	0.0587 (3)
C52	0.61902 (10)	0.57731 (11)	0.17297 (14)	0.0692 (5)
C1'	0.32039 (8)	0.63625 (7)	0.15598 (11)	0.0431 (3)
C2'	0.25669 (9)	0.67887 (8)	0.10408 (13)	0.0534 (4)
C3'	0.21616 (10)	0.73733 (9)	0.1638 (2)	0.0647 (4)
C4'	0.23830 (10)	0.75341 (9)	0.2765 (2)	0.0673 (4)
C5'	0.30127 (11)	0.71126 (9)	0.32934 (14)	0.0633 (4)
C6'	0.34231 (9)	0.65298 (8)	0.26967 (12)	0.0523 (3)
C1''	0.46220 (7)	0.39571 (8)	0.27945 (11)	0.0441 (3)
C2''	0.50493 (10)	0.32704 (9)	0.29123 (15)	0.0619 (4)
C3''	0.51408 (12)	0.29264 (11)	0.3988 (2)	0.0768 (5)
C4''	0.48210 (11)	0.32742 (11)	0.4955 (2)	0.0695 (5)
C5''	0.44001 (11)	0.39596 (11)	0.48541 (14)	0.0695 (5)
C6''	0.42981 (10)	0.42958 (9)	0.37787 (13)	0.0594 (4)

Table 3. *Selected geometric parameters* $(Å, °)$

Compound (I)		Compound (II)	
N1—C2^i	1.263 (2)	N1—C2	1.261 (2)
		N4—C5	1.261 (2)
N1—C3	1.464 (2)	N1—C6	1.462 (2)
		N4—C3	1.461 (2)
C2—C3	1.508 (2)	C2—C3	1.512 (2)
		C5—C6	1.510 (2)
C2—O21	1.354 (2)	C2—O21	1.347 (2)
		C5—O51	1.349 (2)
O21—C22	1.431 (2)	O21—C22	1.442 (2)
		O51—C52	1.444 (2)
C2^i—N1—C6	117.69 (13)	C2—N1—C6	118.61 (11)
		C5—N4—C3	118.49 (11)
N1^i—C2—C3	128.58 (14)	N1—C2—C3	127.95 (12)
		N4—C5—C6	128.17 (12)
N1—C3—C2	113.63 (12)	N4—C3—C2	113.41 (11)
		N1—C6—C5	113.28 (11)
N1^i—C2—O21	121.52 (14)	N1—C2—O21	121.25 (12)
		N4—C5—O51	121.14 (12)
O21—C2—C3	109.90 (13)	O21—C2—C3	110.77 (11)
		O51—C5—C6	110.67 (12)
C2—O21—C22	117.13 (13)	C2—O21—C22	116.11 (11)
		C5—O51—C52	116.42 (12)
N1^i—C2—O21—C22	−0.3 (2)	N1—C2—O21—C22	2.3 (2)
		N4—C5—O51—C52	4.4 (2)

Symmetry code: (i) $\frac{3}{2} - x, \frac{3}{2} - y, 1 - z$.

H atoms, revealed in a difference synthesis, were re-fined with fixed individual displacement parameters [U(H) = 1.5U_{eq}(C$_{methyl}$) or 1.2U_{eq}(C$_{other}$)] using a riding model with aromatic C—H = 0.93, tertiary C—H = 0.98 and methyl C—H = 0.96 Å. The methyl groups were also allowed to rotate about their local threefold axes.

For both compounds, data collection: *DIF*4 (Stoe & Cie, 1988*a*); cell refinement: *DIF*4; data reduction: *REDU*4 (Stoe & Cie, 1988*b*); program(s) used to solve structures: *SHELXS*86 (Sheldrick, 1985); program(s) used to refine structures: *SHELXL*93 (Sheldrick, 1993); molecular graphics: *SHELXTL-Plus* (Sheldrick, 1991).

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2,2'-Bi(1*H*-imidazolium) Dichloride

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Abstract

The basic structural unit in the title compound, 2,2'-bi(1*H*-imidazol-3-ium) dichloride, $C_6H_8N_4^{2+}.2Cl^-$, consists of a planar diprotonated biimidazole moiety and two Cl^- ions each connected to the dication *via* a pair of