STERICALLY CROWDED HETEROCYCLES. VI. RELATIVE CONFIGURATION OF DIASTEREOISOMERIC (*Z*)-1,3-DIPHENYL-3- (5-METHYL-2-PHENYLIMIDAZO[1,2-*a*]PYRIDIN-3-YL)PROP-2-EN-1-OLS

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Dedicated to Professor Jaroslav Podlaha on the occasion of his 60th birthday.

Relative configuration of the titled racemic compounds **1a** and **1b** has been elucidated on the basis of a complete X-ray structure determined for the higher melting diastereoisomer. The compound **1a** crystallizes in the orthorhombic space group $P2_12_12$, a = 15.610(3) Å, b = 18.634(4) Å, c = 7.5672(7) Å, V = 2 201.1(6) Å^3, Z = 4. Preparative separation of both diastereoisomers is reported.

Key words: X-Ray analysis; Diastereoisomerism; Imidazo[1,2-*a*]pyridines.

It has been reported recently[1] that a separable mixture of diastereoisomeric alcohols **1a**, **1b** can be obtained by borohydride reduction of chiral sterically crowded ketone **2**. Although the diastereoisomerism of the products was undoubtedly recognized, no configurational assignments could be made by spectroscopic means. In this communication we attempted to clear up the configuration relationship between compounds **1a** and **1b**.

Diastereoisomers **1a**, **1b** are found to be easily separable using their different solubility in diethyl ether. The less soluble and higher melting substance has been observed to form crystals suitable for X-ray structure analysis. The result of the analysis is given in Fig. 1. The crucial problem for the configurational assignment is undoubtedly a correct bond recognition in the O1–C11–C10–C3 linkage. From the detailed picture given in Fig. 2 it is obvious that the observed molecular structure agrees with the formula **1a** which belongs to one of the possible enantiomers of the higher melting racemic sub-

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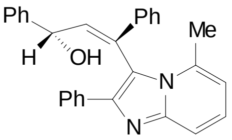
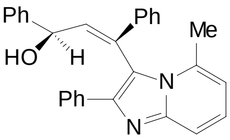
stance. Because the investigated crystal exhibits the non-centrosymmetric $P2_12_12$ space group, only one enantiomer can be seen in the crystal packing given (Fig. 3).

Hence, the compound exists in enantiomeric crystals at least under experimental conditions used.

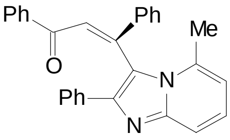
The above mentioned findings enable conclusion that relative space configuration of the higher melting diastereoisomer can be depicted by the formula **1a** while the alternative formula **1b** is attributed of lower melting diastereoisomer. Related absolute configuration investigations based on resolution experiments are intended in future.



1a



1b



2

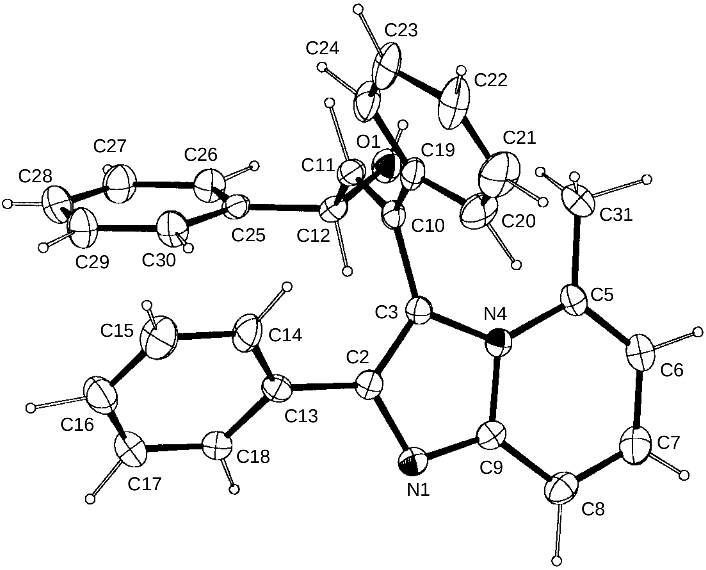


Fig. 1
Molecular structure of heterocyclic alcohol **1a**

EXPERIMENTAL

The temperature data are uncorrected. Melting points were determined on a Boetius block.

Separation of Diastereoisomers **1a** and **1b**

A mixture of compounds **1a** and **1b** (3 g, m.p. 223–227 °C) obtained by borohydride reduction[2] of ketone **2** was treated with ether (60 ml) at room temperature and filtered. The insoluble solid was

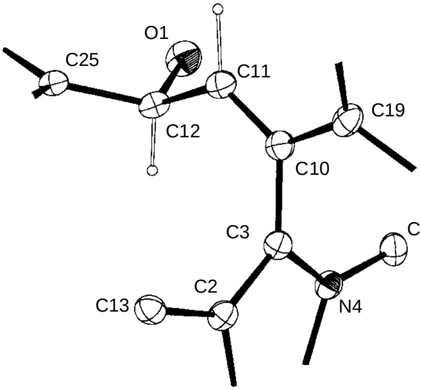


FIG. 2
A detailed view on relative configuration of the chain at the ring position 3 in molecule **1a**

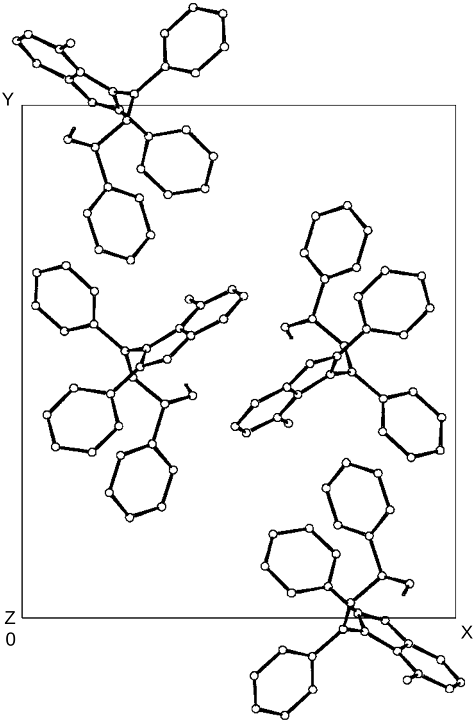


FIG. 3
Crystal packing of heterocyclic alcohol **1a**

repeatedly crystallized from ether–chloroform giving 1.5 g (50%) of compound **1a**, white crystals, m.p. 245–247 °C. For $C_{29}H_{24}N_2O$ (416.5) calculated: 83.63% C, 5.81% H, 6.73% N; found: 83.83% C, 5.90% H, 6.72% N. The filtrate was evaporated, the residue was dissolved in ether (15 ml) and allowed to free crystallization. It was obtained 0.9 g (30%) of compound **1b**, white crystals, m.p. 174–176 °C. For $C_{29}H_{24}N_2O$ (416.5) calculated: 83.63% C, 5.81% H, 6.73% N; found: 83.79% C, 5.84% H, 6.73% N. Complete assignments of ^{1}H NMR and ^{13}C NMR spectra of the both samples are given in ref.[2].

X-Ray Analysis of Compound **1a**

Diastereoisomer **1a**, orthorhombic space group $P2_12_12$ (No. 18), a = 15.610(3) Å, b = 18.634(4) Å, c = 7.5672(7) Å, V = 2 201.1(6) Å, Z = 4, D_{calc} = 1.257 g cm^{-3}, μ(CuKα) = 0.06 mm^{-1}, F(000) = 880.

The structure was solved by direct methods and subsequent Fourier techniques. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares based on F values. The hydrogen atoms were placed in positions found from ideal geometry with $U_{iso} = U_{eq}$ of the attached partners

TABLE I
Data collection and structure refinement parameters

Crystal dimensions	0.35 × 0.42 × 0.74 mm
Diffractometer and radiation used	Enraf–Nonius CAD4, λ(CuKα_1) = 1.54056 Å
Scan technique	ω/2θ
Temperature	293 K
No. and θ range of reflections for lattice parameter refinement	20; 35–40°
Range of h, k and l	$0\rightarrow17$, $0\rightarrow20$, $-8\rightarrow8$
Standard reflections monitored in interval; intensity fluctuation	60 min; –1.5%
Total number of reflections measured; 2θ range	3 179; 7–120°
No. of observed reflections	3 141
Criterion for observed reflections	$I \geq 1.96\sigma(I)$
Function minimized	$\sum w\,(\lvert F_o\rvert - \lvert F_c\rvert)^2$
Weighting scheme	$w = 1/\sigma[(F_o^2) - (F_c^2)]$
Parameters refined	292
Value of R, wR and S	0.0584, 0.0800, 1.03
Ratio of max. least-squares shift to e.s.d. in the last cycle	<0.0001
Max. and min. heights in final Δρ map	0.242, –0.306 e Å^{-3}
Source of atomic scattering factors	International Tables for X-Ray Crystallography (ref.[3])
Programs used	CRYSTALS (ref.[4]), PARST91 (ref.[5]), SIR92 (ref.[6])

TABLE II
Final atomic parameters with e.s.d.'s in parentheses. The isotropic equivalent parameter is defined as $U_{eq} = 1/3\sum_i\sum_j U_{ij}a_i^*a_j^*\boldsymbol{a}_i\boldsymbol{a}_j$

Atom	x	y	z	U_{eq}, Å^2
O1	–0.1074(3)	0.0660(2)	–0.0765(6)	0.041(2)
N1	–0.1643(3)	–0.0053(2)	–0.7632(6)	0.033(1)
C2	–0.2270(4)	0.0094(3)	–0.6397(7)	0.030(2)
C3	–0.2119(3)	–0.0261(3)	–0.4832(8)	0.029(2)
N4	–0.1361(3)	–0.0651(2)	–0.5102(6)	0.029(1)
C5	–0.0881(4)	–0.1096(3)	–0.4011(8)	0.032(2)
C6	–0.0160(4)	–0.1392(3)	–0.4711(9)	0.041(2)
C7	0.0101(4)	–0.1267(3)	–0.645(1)	0.045(2)
C8	–0.0361(4)	–0.0822(3)	–0.7528(9)	0.040(2)
C9	–0.1107(3)	–0.0504(3)	–0.6841(8)	0.032(2)
C10	–0.2612(3)	–0.0214(3)	–0.3157(8)	0.029(2)
C11	–0.2438(4)	0.0296(3)	–0.1974(8)	0.032(2)
C12	–0.1705(4)	0.0816(3)	–0.2086(8)	0.032(2)
C13	–0.2950(4)	0.0614(3)	–0.6793(8)	0.033(2)
C14	–0.3814(4)	0.0498(3)	–0.696(1)	0.047(2)
C15	–0.4423(4)	0.1010(4)	–0.662(1)	0.061(3)
C16	–0.4223(5)	0.1637(4)	–0.751(1)	0.057(3)
C17	–0.3394(5)	0.1745(3)	–0.804(1)	0.054(3)
C18	–0.2762(4)	0.1246(3)	–0.7680(8)	0.040(2)
C19	–0.3335(4)	–0.0741(3)	–0.2939(8)	0.035(2)
C20	–0.3318(5)	–0.1381(3)	–0.391(1)	0.053(2)
C21	–0.3975(5)	–0.1884(4)	–0.375(1)	0.069(3)
C22	–0.4659(5)	–0.1749(4)	–0.263(1)	0.068(3)
C23	–0.4687(4)	–0.1116(4)	–0.169(1)	0.071(3)
C24	–0.4025(4)	–0.0609(3)	–0.182(1)	0.051(2)
C25	–0.2000(3)	0.1594(3)	–0.2001(8)	0.030(2)
C26	–0.1519(4)	0.2098(3)	–0.1067(9)	0.041(2)
C27	–0.1792(4)	0.2811(3)	–0.100(1)	0.050(2)
C28	–0.2523(4)	0.3018(3)	–0.188(1)	0.050(2)
C29	–0.2988(4)	0.2531(3)	–0.285(1)	0.052(2)
C30	–0.2724(4)	0.1812(3)	–0.2906(9)	0.042(2)
C31	–0.1141(4)	–0.1214(4)	–0.2127(9)	0.047(2)

(except (H501), which was obtained from the Δρ–map and fixed in position). Data collection and structure refinement parameters are listed in Table I. Final coordinates and thermal parameters are given in Table II. Table III shows a summary of selected bond distances and angles for the non-hydrogen atoms. One intermolecular hydrogen bond was found between the atoms O(1) and N(1) (x, y, z + 1) with the O(1)...N(1) separation value of 2.859(5) Å and the angle O(1)–H...N(1) = 173(7)°. Figs 1 and 2 show drawings of molecular structure and corresponding molecular packing is given in Fig. 3.

TABLE III
Selected bond distances (Å) and angles (°) with e.s.d's in parentheses

Atoms	Distances	Atoms	Angles
O1–C12	1.433(7)	C3–C10–C11	120.6(5)
C3–C10	1.486(8)	C3–C10–C19	116.4(5)
C10–C11	1.334(7)	C11–C10–C19	123.0(5)
C10–C19	1.505(7)	C10–C11–C12	125.2(5)
C11–C12	1.501(7)	O1–C12–C11	110.7(5)
C12–C25	1.524(7)	O1–C12–C25	111.8(5)

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