

acetate (25 ml). The aqueous layer was treated with aqueous KHSO_4 (2.5 g in 20 ml H_2O) and extracted with ethyl acetate (2×30 ml). After the usual workup and recrystallization, 2.44 g (75%) of (I) was isolated. 2.3 g of (I) in 200 ml of glacial acetic acid was chlorinated for 0.5 h at 278 K. Without purification, the sulfonyl chloride obtained was added in portions, under inert atmosphere, to about 50 ml of freshly condensed liquid ammonia. Excess ammonia was removed under reduced pressure to give 2.1 g [75% referred to (I)] of crude *N*-BOC derivative (II). Trifluoroacetic acid (TFA) (35 mol) in CH_2Cl_2 (10 ml) was added to a solution of (II) (2.1 g, 7.5 mol) in CH_2Cl_2 (10 ml) at room temperature. After the solution was stirred for 2 h, the solvent evaporated and aqueous 3 M NaOH (30 ml) and CH_2Cl_2 (30 ml) were added. The organic layer was worked up to give 1.2 g (89%) of (III) after recrystallization from water.

Profile analysis was performed on all reflections (Lehmann & Larsen, 1974; Grant & Gabe, 1978); a semi-empirical absorption correction was applied, using ψ scans (North, Phillips & Mathews, 1968). The structure was solved by direct methods using *SHELXS86* (Sheldrick, 1985) and Fourier synthesis. Isotropic least-squares refinement was carried out using *SHELX76* (Sheldrick, 1976). Empirical absorption correction was applied using *DIFABS* (Walker & Stuart, 1983). Geometrical calculations were made with *PARST* (Nardelli, 1983). All calculations were performed on a MicroVAX 3400 at the Scientific Computer Center of the University of Oviedo, Spain.

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Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and complete geometry have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55610 (18 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: LI1011]

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Structures of Pyrazole Derivatives. I. A Potential Bioisoster of Thromboxane Synthetase Inhibitors

I. CARACELLI

Centro Nacional de Recursos Genéticos e Biotecnologia, EMBRAPA, Caixa Postal 10372, 70770 Brasília, DF, Brazil

J. ZUKERMAN-SCHPECTOR*

Instituto de Física e Química de São Carlos, Universidade de São Paulo, Caixa Postal 369, 13560 São Carlos, SP, Brazil

ELIEZER J. BARREIRO AND ANTONIO C. C. FREITAS

Departamento de Tecnologia Farmaceutica, Faculdade de Farmacia, Universidade Federal de Rio de Janeiro, 21941 Rio de Janeiro, RJ, Brazil

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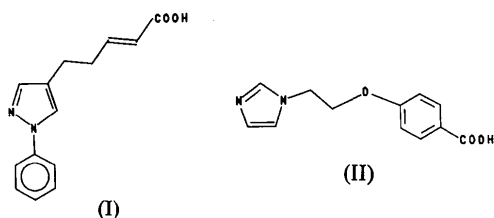
Abstract

In (*E*)-5-(1-phenyl-4-pyrazolylium)-2-pentenoate, the $\text{N}\cdots\text{O}$ distances lie in the range 8.557 (5)-8.812 (5) Å. The phenyl and pyrazole rings are planar making a dihedral angle of 14.1 (5)°. The molecular packing involves $\text{C}-\text{H}\cdots\text{O}$ contacts.

Comment

Thromboxane A_2 synthetase inhibitors (TXSi) have therapeutic utility in several conditions where platelets are believed to play a role in the pathogenesis of the disease process, e.g. ischemia, arrhythmias, pulmonary hypertension and thromboembolic disorders [for a recent review see Collington & Finch (1989)]. Among the great variety of heterocyclic substances

described as TXSi, 1-substituted imidazole derivatives such as compound (II) are found (Martinez *et al.*, 1989, and references therein). Structure-activity relationship studies have shown that some structural features are related to an effective TXSi activity, for example the presence of a sterically hindered nitrogen-containing heterocyclic ring and a carboxylic acid terminus located 8–10 Å from the heterocyclic N atoms (Cross & Dickinson, 1987). Considering the close bioisosteric relationship between the imidazole and pyrazole ring, compound (I) was synthesized and a three-dimensional crystal structure determination was undertaken in order to verify its overall conformation and the distance between the two functional moieties.



A difference Fourier synthesis showed unambiguously an H atom bonded to N(2) so the pyrazole moiety is positively charged and the molecule as a whole is in a zwitterionic form. As can be seen in Table 2, the internal and external angles of the pyrazole ring follow the set of empirical rules given by Bonati & Bovio (1990), *i.e.* (a) N(1)—N(2)—C(3) is smaller than N(2)—N(1)—C(5); (b) N(2)—C(3)—C(4) is larger than N(1)—N(2)—C(3), C(3)—C(4)—C(5) and C(4)—C(5)—N(1); (c) C(3)—C(4)—C(5) is not the largest internal angle; (e) C(11)—N(1)—N(2) is smaller than C(11)—N(1)—C(5); (f) N(2)—C(3)—H(C3) [119.1 (4)°] is smaller than H(C3)—C(3)—

C(4) [128.0 (4)°]; and (g) C(3)—C(4)—C(6) and C(6)—C(4)—C(5) are nearly the same.

The pyrazole (1) and phenyl (2) rings and the C(8)—C(9)—COO⁻ moiety (3) are planar to within experimental accuracy, σ_{av} [defined as $(\sum d_i^2 / N - 3)^{1/2}$] being 0.004, 0.004 and 0.005 Å, respectively; the dihedral angles between (1) and (2), (1) and (3) and (2) and (3) are 14.1 (5), 6.2 (9) and 8.1 (9)°, respectively.

The N...O distances are N(1)—O(1) 8.766 (5), N(1)—O(2) 8.812 (5), N(2)—O(1) 8.846 (5) and N(2)—O(2) 8.557 (5) Å.

The molecular packing involves intermolecular C—H...O interactions as listed in Table 2.

Experimental

Crystal data

C₁₄H₁₄N₂O₂
M_r = 242.28
 Monoclinic
 P2₁/n
a = 5.6478 (6) Å
b = 5.232 (2) Å
c = 41.641 (6) Å
 β = 93.98 (2)°
V = 1227.6 (8) Å³
Z = 4
D_x = 1.311 Mg m⁻³

Mo K α radiation
 λ = 0.70926 Å
 Cell parameters from 25 reflections
 θ = 10–25°
 μ = 0.083 mm⁻¹
T = 293 K
 Irregular
 0.45 × 0.30 × 0.25 mm
 Pale yellow
 Crystal source: from ethanol

Data collection

Enraf-Nonius CAD-4 diffractometer
 $\omega/2\theta$ scans
 1432 measured reflections
 1408 independent reflections
 1105 observed reflections
 [*I* > 3 σ (*I*)]
R_{int} = 0.040

θ_{max} = 23°
h = -6 → 6
k = 0 → 5
l = 0 → 45
 2 standard reflections
 frequency: 30 min
 intensity variation: ±0.3%

Refinement

Refinement on *F*
 Final *R* = 0.054
wR = 0.062
S = 2.24
 1105 reflections
 164 parameters
 $w = [\sigma^2(|F_o| + 0.0007|F_o|)]^{-1}$

(Δ/σ)_{max} = 0.001
 $\Delta\rho_{max}$ = 0.17 e Å⁻³
 $\Delta\rho_{min}$ = -0.24 e Å⁻³
 Atomic scattering factors from SHELX76 (Sheldrick, 1976)

Table 1. Fractional atomic coordinates and equivalent isotropic thermal parameters (Å²)

	$B_{eq} = (4/3)\sum_i \sum_j \beta_{ij} a_i \cdot a_j$			
	<i>x</i>	<i>y</i>	<i>z</i>	<i>B_{eq}</i>
N(1)	-0.1053 (5)	0.1326 (5)	0.3468 (1)	3.92 (9)
N(2)	-0.3070 (5)	0.1733 (7)	0.3614 (1)	5.9 (1)
O(1)	0.5861 (5)	1.3180 (6)	0.4690 (1)	7.2 (1)
O(2)	0.2509 (5)	1.3169 (6)	0.4927 (1)	7.4 (1)
C(3)	-0.2495 (7)	0.3519 (9)	0.3835 (1)	5.8 (2)
C(4)	-0.0139 (6)	0.4288 (7)	0.3831 (1)	4.2 (1)
C(5)	0.0732 (6)	0.2861 (7)	0.3594 (1)	4.2 (1)
C(6)	0.1156 (6)	0.6300 (7)	0.4037 (1)	4.7 (1)

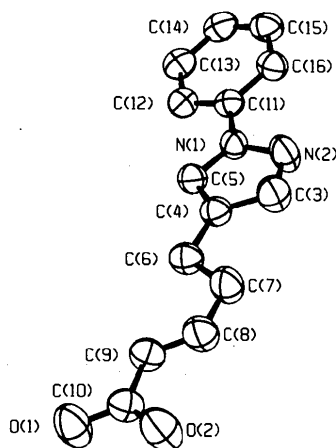


Fig. 1. The molecular structure of C₁₄H₁₄N₂O₂ showing the atom labelling. 50% thermal ellipsoids are shown.

C(7)	-0.0360 (7)	0.7383 (9)	0.4285 (1)	6.1 (2)
C(8)	0.0787 (7)	0.9407 (8)	0.4499 (1)	5.8 (2)
C(9)	0.2904 (6)	1.0298 (8)	0.4498 (1)	4.8 (1)
C(10)	0.3817 (7)	1.2307 (7)	0.4717 (1)	4.7 (1)
C(11)	-0.0988 (5)	-0.0536 (6)	0.3222 (1)	3.9 (1)
C(12)	0.0884 (6)	-0.0577 (7)	0.3027 (1)	4.8 (1)
C(13)	0.0932 (6)	-0.2424 (7)	0.2787 (1)	5.3 (1)
C(14)	-0.0871 (6)	-0.4182 (7)	0.2742 (1)	5.1 (1)
C(15)	-0.2739 (6)	-0.4109 (7)	0.2936 (1)	5.1 (1)
C(16)	-0.2826 (6)	-0.2283 (7)	0.3181 (1)	4.6 (1)

Table 2. Bond lengths (Å), valence angles (°) and geometrical parameters of selected intermolecular interactions (Å, °)

N(1)—N(2)	1.345 (5)	N(1)—C(5)	1.365 (5)	
N(1)—C(11)	1.416 (5)	N(2)—C(3)	1.336 (6)	
O(1)—C(10)	1.254 (5)	O(2)—C(10)	1.266 (5)	
C(3)—C(4)	1.391 (5)	C(4)—C(5)	1.357 (6)	
C(4)—C(6)	1.514 (5)	C(6)—C(7)	1.498 (6)	
C(7)—C(8)	1.502 (6)	C(8)—C(9)	1.284 (5)	
C(9)—C(10)	1.462 (6)	C(11)—C(12)	1.377 (5)	
C(11)—C(16)	1.385 (5)	C(12)—C(13)	1.392 (6)	
C(13)—C(14)	1.375 (5)	C(14)—C(15)	1.373 (5)	
C(15)—C(16)	1.401 (6)			
N(2)—N(1)—C(5)	111.1 (3)	C(8)—C(9)—C(10)	123.2 (4)	
N(2)—N(1)—C(11)	120.1 (3)	O(1)—C(10)—O(2)	121.1 (4)	
C(5)—N(1)—C(11)	128.8 (3)	O(1)—C(10)—C(9)	119.5 (4)	
N(1)—N(2)—C(3)	104.4 (3)	O(2)—C(10)—C(9)	119.3 (4)	
N(2)—C(3)—C(4)	112.4 (4)	N(1)—C(11)—C(12)	119.8 (3)	
C(3)—C(4)—C(5)	104.2 (3)	N(1)—C(11)—C(16)	119.1 (3)	
C(3)—C(4)—C(6)	128.3 (4)	C(12)—C(11)—C(16)	121.1 (3)	
C(5)—C(4)—C(6)	127.5 (3)	C(11)—C(12)—C(13)	119.2 (3)	
N(1)—C(5)—C(4)	107.9 (3)	C(12)—C(13)—C(14)	120.7 (3)	
C(4)—C(6)—C(7)	112.1 (3)	C(13)—C(14)—C(15)	119.5 (3)	
C(6)—C(7)—C(8)	115.6 (3)	C(14)—C(15)—C(16)	121.0 (3)	
C(7)—C(8)—C(9)	128.2 (4)	C(11)—C(16)—C(15)	118.4 (3)	
D—H...A	D...A	D—H	H...A	D—H...A
C(7)—H(C7)...O(1) ⁱ	3.569 (5)	1.13 (1)	2.469 (5)	164.3 (4)
C(9)—H(C9)...O(2) ⁱⁱ	3.547 (5)	1.07 (1)	2.484 (5)	170.3 (4)

Symmetry codes: (i) $x - 1, y - 1, z$; (ii) $x - 1, y, z$.

Data were corrected for Lorentz and polarization effects. The structure was solved by direct methods. The H atoms were found in a difference synthesis and included as fixed contributors with an overall isotropic thermal parameter [$U = 0.109(4) \text{ \AA}^2$]. The programs used were *SHELXS86* (Sheldrick, 1985), *SHELX76* and *ORTEP* (Johnson, 1965). The refinement was by full-matrix least-squares methods. Most of the calculations were performed on a VAX 6420 computer at the Instituto de Física e Química de São Carlos.

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Lists of structure factors, anisotropic thermal parameters and H-atom coordinates have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55420 (11 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: LI1023]

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Structures of Three Alicyclic α -Dioximes with a Ring Size of Six to Eight

NATALY R. STRELTSOVA AND VITALY K. BEL'SKY

Karpov Physico-Chemical Institute, Obukha St. 10, 103064, Moscow, Russia

YAN Z. VOLOSHIN

Institute of General and Inorganic Chemistry, 252680, Kiev 142, Ukraine

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Abstract

The structures of (I) 1,2-cyclohexanedione dioxime, (II) 1,2-cycloheptanedione dioxime and (III) 1,2-cyclooctanedione dioxime have been studied by X-ray diffraction. In (I) the cyclohexane fragment has a twist conformation. The cycloheptane ring in (II) exhibits a distorted chair conformation. The cyclooctane moiety in (III) has a boat-chair conformation. In structures (I)–(III), molecules form layered structures through a hydrogen-bonding system. There are two types of hydrogen bond (OH...O and OH...N) in (I) and (III) but only one type (OH...N) in (II). The bond lengths in the dioxime fragments correspond to the statistical averages obtained from an analysis of data held on the Cambridge Structural Database [Allen, Kennard, Watson, Brammer, Orpen & Taylor (1987). *J. Chem. Soc. Perkin Trans.* **2**, pp. S1–S19]. In the α -dioxime (II), which has the most strained seven-membered ring, the N—N intramolecular distance and the torsion angle between dioxime groups [2.731 (4) Å and 47.2°] are substantially larger than those in (I) and (III) [2.683 (3) and 2.667 (3) Å, and 26.2 and 26.6°, respectively]. These structural features are also retained in solution,