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Structure and Conformation of *N*-(Morpholinomethyl)-*m*-bromophenylsuccinimide

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Abstract. $C_{15}H_{17}BrN_2O_3$, $M_r = 353.22$, monoclinic, $P2_1/c$, $a = 12.369$ (2), $b = 5.564$ (1), $c = 23.044$ (4) Å, $\beta = 100.49$ (2)°, $V = 1559.4$ (5) Å^3, $Z = 4$, $D_x = 1.504$ Mg m^{-3}, λ(Cu $K\alpha$) = 1.54178 Å, $\mu = 3.71$ mm^{-1}, $F(000) = 720$, room temperature, final $R = 0.069$ for 2987 observed reflections with $I > 3\sigma(I)$ (of 3241 unique data). The morpholine ring has a chair conformation. The conformational analysis (obtained by a molecular-mechanics calculation) indicates that there are three orientations of the morpholine ring in the molecule with similar energies. One of them agrees with the molecule found crystallographically.

Introduction. The present investigation was undertaken as part of our systematic studies on the conformation and structure of phenylsuccinimides with potential anticonvulsant properties to determine structure–activity relationships. All 27 compounds considered have been subjected to pharmacological screening (Łucka-Sobstal, Zejc & Obniska, 1977; Lange, Rump, Ilczuk, Łapiszewicz, Rabsztyn & Walczyna, 1977; Lange, Rump, Gałecka, Ilczuk, Lechowska-Postek, Rabsztyn, Szymańska & Walczyna, 1977; Łapiszewicz, Lange, Rump & Walczyna, 1978; Chmielewska, 1983, 1984; Zejc & Obniska, 1984; Zejc, Obniska, Chojnacka-Wójcik, Tatarczyńska & Wiczyńska, 1987; Zejc, Obniska, Wilimowski, Rutkowska, Witkowska, Barczyńska, Kędzierska-Goździk, Wojewódzki, Orzechowska-Juzwenko, Pławiak, Duś, Gryska & Gliniak, 1990), of which 12 reveal pharmacological activity against maximal electrical shock. We have solved the structures of eight derivatives (Kwiatkowski, Karolak-Wojciechowska, Obniska & Zejc, 1990; Kwiatkowski & Karolak-Wojciechowska, 1990, 1991, 1992*a*,*b*) and intend to calculate the conformations of the remaining derivatives on the basis of the generated models of the molecules and energy minimization. However, even though the morpholinomethyl group has two degrees of freedom, the (active) molecule under discussion may be represented by more than one local minimum-energy conformation. For this reason we decided to solve the structure.

Experimental. The title compound (Lange & Łapszewicz, 1978) was recrystallized from ethanol and gave colorless thin needles. Crystal dimensions 0.25 × 0.10 × 0.15 mm. CAD-4 diffractometer; final lattice parameters from least-squares refinement of 25 reflections ($25 < \theta < 50°$); no absorption correction applied; $\theta < 80°$; h − 15/15, k 0/7, l 0/28; ω–2θ scan technique; Cu $K\alpha$ radiation at room temperature; intensity of three standard reflections monitored every 70 reflections showed no significant fluctuations; 3241 unique reflections measured, of which 2987 satisfied the criterion $I > 3\sigma(I)$.

The structure was solved by the *SHELXS*86 program (Sheldrick, 1986) and the E map provided positions of all non-H atoms. All H atoms were located from a $\Delta\rho$ map and refined in the riding model with a common thermal parameter. Refinement by full-matrix least squares on F values with anisotropic temperature factors for all non-H atoms converged to $R = 0.069$ and $wR = 0.109$ with $w = 1/[\sigma^2(F) + 0.0047F^2]$ for 2987 reflections and 192 refined parameters; extinction correction coefficient $g = 0.008$; changes in all parameters $\Delta/\sigma < 0.05$; $S = 2.22$; the minimum and maximum peaks in the final $\Delta\rho$ map were −1.3 and 1.4 e Å^{-3} and the extremes on the $\Delta\rho$ map were located around the Br-atom position; atomic scattering factors as given in *SHELX*. The refinement was performed using *SHELXTL-PC* (Sheldrick, 1989) and the *CSU* program (Vicković, 1988).

Discussion. A general view of the molecule together with its atom-numbering system is shown in Fig. 1. The atomic coordinates are given in Table 1.† All bond lengths and angles in the molecule are normal (see Table 2).

Of the three rings in the molecule the phenyl ring is the only planar one. The five-membered ring has an open-envelope conformation with C1 out of the plane passing through the remaining four atoms by

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† Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 54604 (11 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: AL0472]

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Table 1. *Non*-H *fractional atomic coordinates* (Br × 10^5; C, N, O × 10^4) *and equivalent temperature factors* (Å^2 × 10^3) *with e.s.d.'s in parentheses*

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

	x	y	z	U_{eq}
N1	−268 (2)	2438 (4)	6497 (1)	38 (1)
C4	636 (3)	1372 (6)	6325 (1)	42 (1)
C1	1629 (2)	2953 (6)	6517 (1)	41 (1)
C2	1253 (3)	4588 (5)	6972 (2)	50 (1)
C3	36 (3)	4307 (6)	6879 (2)	44 (1)
O1	−621 (3)	5474 (5)	7100 (2)	64 (1)
O2	595 (2)	−512 (6)	6068 (2)	65 (1)
C11	2671 (2)	1536 (5)	6717 (1)	39 (1)
C12	3503 (3)	1616 (6)	6393 (1)	45 (1)
C13	4413 (3)	192 (7)	6553 (2)	49 (1)
C14	4529 (3)	−1360 (8)	7027 (2)	64 (1)
C15	3674 (3)	−1349 (8)	7354 (2)	61 (1)
C16	2760 (3)	46 (6)	7203 (2)	49 (1)
Br1	55872 (4)	4192 (14)	61183 (2)	81 (1)
C5	−1392 (3)	1460 (5)	6344 (1)	41 (1)
N2	−2047 (2)	2344 (4)	5809 (1)	40 (1)
C6	−1612 (3)	1785 (7)	5276 (2)	52 (1)
C7	−2449 (4)	2522 (9)	4743 (2)	62 (1)
O3	−2685 (4)	4962 (7)	4760 (1)	74 (1)
C8	−3112 (4)	5531 (7)	5273 (2)	64 (1)
C9	−2313 (4)	4862 (6)	5822 (2)	51 (1)

Table 2. *Bond lengths* (Å) *and bond angles* (°) *with e.s.d.'s in parentheses*

N1—C4	1.386 (4)	C13—C14	1.379 (6)
N1—C3	1.370 (4)	C13—Br1	1.913 (4)
N1—C5	1.475 (4)	C14—C15	1.406 (6)
C4—C1	1.510 (4)	C15—C16	1.363 (5)
C4—O2	1.201 (5)	C5—N2	1.433 (3)
C1—C2	1.523 (5)	N2—C6	1.461 (5)
C1—C11	1.510 (4)	N2—C9	1.441 (4)
C2—C3	1.490 (5)	C6—C7	1.512 (6)
C3—O1	1.221 (6)	C7—O3	1.391 (6)
C11—C12	1.378 (4)	O3—C8	1.416 (6)
C11—C16	1.382 (5)	C8—C9	1.504 (6)
C12—C13	1.371 (5)		

C4—N1—C3	111.5 (3)	C11—C12—C13	119.6 (3)
C4—N1—C5	123.3 (2)	C12—C13—C14	122.5 (4)
C3—N1—C5	124.8 (3)	C12—C13—Br1	119.0 (3)
N1—C4—C1	108.8 (3)	C14—C13—Br1	118.5 (3)
N1—C4—O2	123.4 (3)	C13—C14—C15	116.2 (4)
C1—C4—O2	127.8 (3)	C14—C15—C16	122.4 (4)
C4—C1—C2	102.5 (2)	C11—C16—C15	119.2 (4)
C4—C1—C1	112.9 (2)	N1—C5—N2	116.1 (2)
C2—C1—C11	116.9 (2)	C5—N2—C6	114.4 (3)
C1—C2—C3	105.4 (3)	C5—N2—C9	114.3 (3)
N1—C3—C2	108.9 (3)	C6—N2—C9	110.2 (3)
N1—C3—O1	123.1 (4)	N2—C6—C7	108.8 (3)
C2—C3—O1	128.0 (4)	C6—C7—O3	111.0 (4)
C1—C11—C12	119.9 (2)	C7—O3—C8	110.7 (4)
C1—C11—C16	119.9 (3)	O3—C8—C9	111.1 (4)
C12—C11—C16	120.1 (3)	N2—C9—C8	109.9 (3)

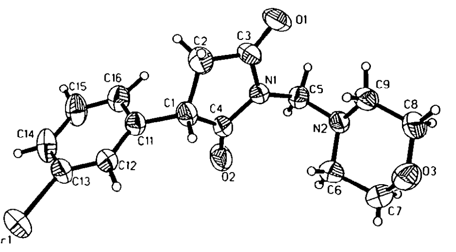

Fig. 1. The molecular structure and atom-numbering system of *N*-(morpholinomethyl)-*m*-bromophenylsuccinimide.

0.271 (2) Å. The asymmetry parameter for a plane going through C1 and bisecting the N1—C3 bond equals ΔC_s = 1.6°. The inclination of this ring to the phenyl ring can be defined by torsion angle C4—C1—C11—C12 = −113.2 (3)° and is close to the value observed in the structures of the other phenylsuccinimides (Kwiatkowski & Karolak-Wojciechowska, 1990, 1991, 1992*a*,*b*). The morpholine ring (with its N2 atom sp^3 hybridized) has a chair conformation with all asymmetry parameters close to 1°. Two torsion angles θ_1 = N2—C5—N1—C3 = −96.8 (4) and θ_2 = C9—N2—C5—N1 = 65.8 (3)° define the position of this ring in the molecule. All intermolecular contacts are longer than the sum of the van der Waals radii.

All the phenylsuccinimides investigated by us crystallized in centrosymmetric space groups. Therefore, an *R* relative configuration was arbitrarily chosen for the chiral center to look for structure–activity relationships. All values of torsion angles were calculated for this configuration.

The geometry of this molecule with relative configuration *R* was used as the starting point for a conformation-map calculation using a molecular-mechanics technique. The *MMX*86 program (PC version) (Burkert & Allinger, 1982) taking π overlapping into account was used. The conformational

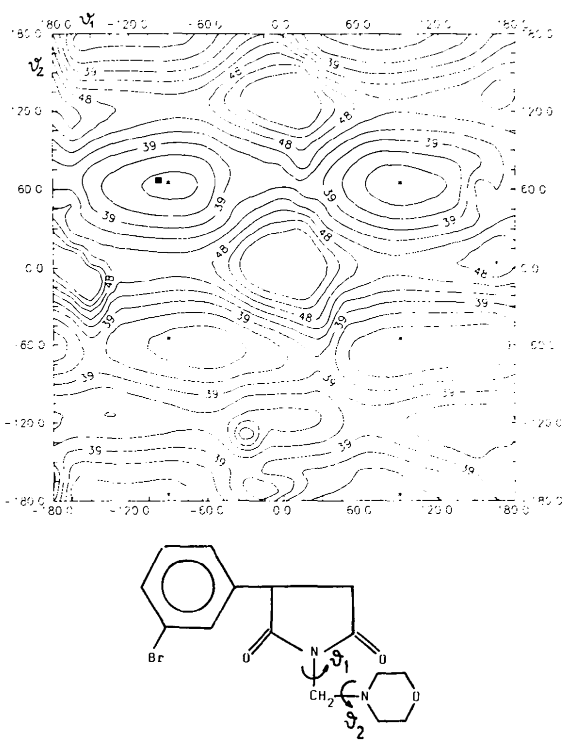

Fig. 2. The strain-energy map as a function of two angles θ_1 = N1—C5—N2—C3 and θ_2 = C9—N2—C5—N1 (the equi-energetic lines for each 3 kcal from 33 to 55 kcal).

map was calculated by the clockwise variation of two torsion angles $\theta_1 = $ N2—C5—N2—C3 and $\theta_2 = $ C9—N2—C5—N1, and energy minimization for each 15° rotation for θ_1 and θ_2 from −180 to 180°. The results of the calculation are illustrated in Fig. 2. All six conformational minima (marked on the map by the asterisks) are energetically equivalent; the differences not exceeding 1 kcal mol^{-1} (1 kcal = 4.184 kJ). In spite of the absence of a global minimum, the conformation in the local minimum with $\theta_1 = -90$ and $\theta_2 = 65°$ was accepted as most likely to exist in solution because the crystallographic conformation with the relative configuration of chiral center *R* (marked on the map by the black square) is close to the selected minimum and the energy barriers are equal to 9.2 and 14.6 kcal mol^{-1} respectively for clockwise rotation of the θ_1 and θ_2 angles.

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Strucure of 3-Hydroxyphenalenone

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Abstract. 3-Hydroxyphenalenone (enol form), $C_{13}H_8O_2$, $M_r = 196.21$, monoclinic, *Pc*, $a = 9.089$ (2), $b = 17.737$ (2), $c = 14.265$ (2) Å, $\beta = 125.65$ (2)°, $V = 1868.5$ (5) Å^3, $Z = 8$, $D_x = 1.40$ g cm^{-3}, λ(Mo $K\alpha$) = 0.71069 Å, $\mu = 0.876$ cm^{-1}, $F(000) = 816$, $T = 290$ K, $R = 0.050$ for 3182 independent reflections. The crystal structure is characterized by one-dimensional chains of hydrogen-bonded enol molecules. The intermolecular hydrogen bond in a *syn–syn* configuration has a short intermolecular oxygen distance (average 2.57 Å). All the enone

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