

Fig. 1. Vue en perspective de la molécule et numérotation atomique.

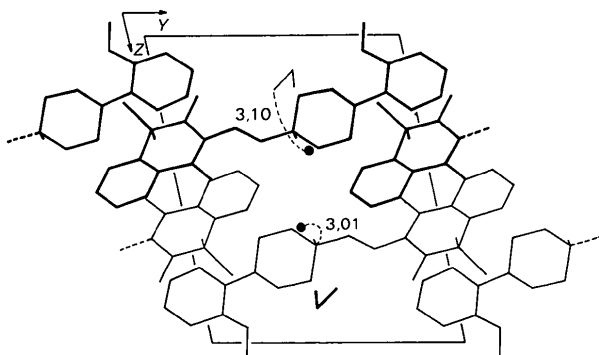


Fig. 2. Projection sur (100) suivant  $O_x$ .

L'azote protoné et les groupements aromatiques sont impliqués dans le mode de fixation des ligands adrénergiques sur leurs récepteurs spécifiques (Easson & Steadman, 1933; Pullman, Coubeils, Courrière &

Gervois, 1972). La distance  $N(17)-\pi_1$  [ $\pi_1$  milieu de  $C(4)-C(9)$ ] est égale à 6,18 (2) Å quant à  $N(17)-\pi_2$  ( $\pi_2$  centre du noyau phényle), elle vaut 5,67 (2) Å. Les distances  $N(17)$ -plan I et  $N(17)$ -plan III sont respectivement égales à 1,13 (1) et 0,43 (1) Å. C'est ainsi que la position de  $N(17)$  par rapport au groupement méthoxyphényle est très voisine de celle trouvée pour les pôles équivalents dans le WB-4101, autre antagoniste  $\alpha_1$  spécifique (Carpy, Colleter & Léger, 1981).

Le cristal est caractérisé par un empilement moléculaire sensiblement parallèle à l'axe (010) (Fig. 2). La cohésion cristalline est étayée par la liaison hydrogène  $N(17)\cdots Cl(31)$  ( $\bar{x}, 1-y, 1-z$ ) = 3,01 (1) Å,  $N(17)-H(170)$  = 1,0 (1) Å,  $H(170)\cdots Cl(31)$  = 2,0 (1) Å,  $N-H\cdots Cl$  = 174 (1)°. L'hydroxyle de l'éthanol est lié par liaison hydrogène à l'ion  $Cl^-$ :  $O(32)\cdots Cl(31)$  ( $x, y, 1+z$ ) = 3,10 (2) Å.

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#### Références

- CARPY, A., COLLETER, J.-C. & LÉGER, J. M. (1981). *Cryst. Struct. Commun.* **10**, 1391-1395.  
 EASSON, L. H. & STEADMAN, E. (1933). *Biochem. J.* **27**, 1257-1268.  
*International Tables for X-ray Crystallography* (1974). Tome IV. Birmingham: Kynoch Press.  
 MAIN, P., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERQ, J.-P. & WOOLFSON, M. M. (1978). *MULTAN78. A system of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. de York, Angleterre, et Louvain, Belgique.  
 PULLMAN, B., COUBEILS, J.-L., COURRIÈRE, PH. & GERVOIS, J.-P. (1972). *J. Med. Chem.* **15**, 17-23.  
 STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175-3187.

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## Benzotriazole 1-Oxide and 1-Hydroxybenzotriazole, $C_6H_5N_3O$ : Structures of Both Tautomeric Forms\*

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**Abstract.** (I)  $C_6H_5N_3O.H_2O$ ,  $M_r = 153.14$ , monoclinic,  $P2_1/c$ ,  $a = 10.343$  (3),  $b = 9.514$  (2),  $c = 7.094$  (2) Å,  $\beta = 98.81$  (2)°,  $V = 689.7$  (1) Å<sup>3</sup>,  $D_x = 1.475$  Mg m<sup>-3</sup>,  $Z = 4$ ,  $\lambda(Mo K\alpha) = 0.7107$  Å,  $\mu(Mo K\alpha) = 0.048$  mm<sup>-1</sup>,  $F(000) = 264$ , room temperature. (II)

$C_6H_5N_3O$ ,  $M_r = 135.13$ , monoclinic,  $C2/c$ ,  $a = 12.233$  (3),  $b = 7.937$  (5),  $c = 13.164$  (2) Å,  $\beta = 104.75$  (1)°,  $V = 1236.0$  (1) Å<sup>3</sup>,  $D_x = 1.452$  (1) Mg m<sup>-3</sup>,  $Z = 8$ ,  $\mu(Mo K\alpha) = 0.066$  mm<sup>-1</sup>,  $F(000) = 560$ , room temperature.  $R = 0.037$  (I) and 0.042 (II) for, respectively, 1070 and 1045 observed reflexions. The *N*-oxide tautomer (I) crystallizes from aqueous methanolic solutions as a hydrate and the *N*-hydroxy tautomer (II) from anhydrous ethanol/ether mixtures.

\* Dedicated to Professor Dr Rolf Geiger on the occasion of his 60th birthday.

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Stabilization of tautomer (I) is favoured by water molecules. In comparison to previously reported benzotriazole geometries, the difference between N—N bond lengths is smaller in (I) and zero in (II).

**Introduction.** König & Geiger (1970*a*) introduced 1-hydroxybenzotriazole for improving peptide couplings using the dicyclohexylcarbodiimide method. They found it to be superior to the well-known *N*-hydroxysuccinimide (Wünsch & Drees, 1966). 3-Hydroxy-1,2,3-benzotriazin-4(3*H*)-one has even better racemization-suppressing properties than 1-hydroxybenzotriazole (König & Geiger, 1970*b,c*). Obviously both tautomers are involved in the activation of the carboxy component, because König & Geiger (1970*a*) isolated the reactive *N*-acylamino acid 1-hydroxybenzotriazole esters and *N*-acylated benzotriazole *N*-oxides rearranging to esters in solution. 1-Hydroxybenzotriazole improves also the aminolysis of activated esters by bifunctional catalysis (König & Geiger, 1973). A nucleophilic catalysis was suggested by Horiki & Murakami (1980). Studies on the racemization of *N*-methylamino acids during coupling in the presence of 1-hydroxybenzotriazole were reported (Davies & Mohammed, 1981). Therefore the prototropic tautomerism of 1-hydroxybenzotriazole (I) with benzotriazole 1-oxide (II) (Fig. 1) and the bifunctional reactivity of this reagent are of major interest, in particular for mechanistic studies.

1-Hydroxybenzotriazole was described as 'azimidol' (Nietzki & Braunschweig, 1894) and 'benzazimidol' (Zincke & Schwarz, 1900) with the *N*-hydroxy formula without crystal water. '1-Hydroxy-1:2:3-benzotriazole' releases one mole of water on drying and gives *N*- and *O*-methyl derivatives (Brady & Reynolds, 1928). The tautomerism was studied by UV firstly by Macbeth & Price (1936). Boyle & Jones (1973) reported 84% *N*-oxide (I) in water and 78% *N*-hydroxy form (II) in ethanol. Tautomers were described for 1-hydroxyimidazoles (Volkamer & Zimmermann, 1969; Volkamer 1969), and for 1-hydroxybenzimidazole and benzimidazole 1-oxide (Chua, Cook & Katritzky, 1971). Multistep complex photoreactions of 1-hydroxybenzotriazole in acetonitrile were analysed by Lüddecke, Mauser & Polster (1976).

The *N*-oxide (I) is favoured in polar solvents, while the *N*-hydroxy tautomer (II) predominates in less-polar solvents (Boyle & Jones, 1973). Consequently we

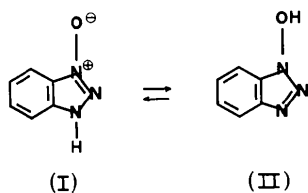


Fig. 1. The tautomerism of benzotriazole 1-oxide (I) with 1-hydroxybenzotriazole (II).

obtained tautomer (I) as the monohydrate from methanol/water as large colourless needles. Tautomer (II) was obtained as colourless needles *via* recrystallization of the dried compound (over  $P_2O_5$  *in vacuo* at 323 K) from water-free ethanol/diethyl ether.

**Experimental.** Crystallographic data: Enraf-Nonius CAD-4 automated diffractometer, Mo  $K\alpha$  radiation (graphite monochromator). (I) Intensity measurement: single crystal  $0.4 \times 0.35 \times 0.3$  mm, 3158 reflexions with  $3 \leq \theta \leq 27^\circ$ ,  $\omega/\theta$  scan,  $h,k,l$  up to 9,12,13, 1074 unique reflexions with  $I \geq 2\sigma(I)$ ,  $R_{int} = 0.018$ . Structure analysis: direct methods (MULTAN80; Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980); refinement on  $F$  with SHELX76 (Sheldrick, 1976),  $R = 0.12$  (isotropic); nonhydrogen atoms anisotropic, H atoms (from  $\Delta F$  synthesis) isotropic, exclusion of four strong low-angle reflexions (extinction effects), final  $R$  values 0.0370 ( $R_G = 0.0393$ , unit weights), no electron density  $> \pm 0.2 e \text{ \AA}^{-3}$  in last difference Fourier synthesis, maximum least-squares shift to error = 0.01.

(II) Intensity measurement: single crystal  $0.8 \times 0.5 \times 0.3$  mm, 1991 reflexions,  $3 \leq \theta \leq 30^\circ$ ,  $\omega$  scan,  $h,k,l$  up to 17,11,18, 1048 unique reflexions with  $I > 2\sigma(I)$ ,  $R_{int} = 0.022$ . Structure analysis: MULTAN80, SHELX76,  $R = 0.18$  (isotropic); nonhydrogen atoms anisotropic, H atoms (from  $\Delta F$  synthesis) isotropic, exclusion of three strong low-angle reflexions (extinction effects), final  $R$  values 0.0417 ( $R_G = 0.0366$ , unit weights), no electron density  $> \pm 0.07 e \text{ \AA}^{-3}$  in last difference Fourier synthesis, maximum least-squares shift to error = 0.01.\* Scattering factors were from Cromer & Mann (1968). The values of  $f'$  and  $f''$  were those of Cromer & Liberman (1970). The coordinates of (I) and (II) are shown in Table 1. In Fig. 2 bond lengths and angles of both tautomeric forms are shown together with the numbering scheme. Stereoscopic views of the crystal packing and hydrogen bonding of (I) and (II) are illustrated in Fig. 4.

**Discussion.** As shown in Fig. 2, the title compound crystallizes from aqueous polar solvents as the *N*-oxide hydrate tautomer (I) and from nonaqueous less-polar solvents as the *N*-hydroxy tautomer (II), in accordance with the UV-spectroscopic measurements of the equilibrium (I)  $\rightleftharpoons$  (II) (Boyle & Jones, 1973). In both cases, the benzotriazole ring systems are essentially planar. Deviations from the least-squares planes through the ring moieties in (I) and (II) are about 0.01–0.02 Å (e.s.d.'s for the distances  $\sim 0.003$  Å).

\* Lists of structure factors, anisotropic thermal parameters, H-atom coordinates, least-squares planes and [for (II)] intermolecular distances have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38522 (18 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Atomic coordinates and equivalent isotropic thermal parameters of (I) and (II) with e.s.d.'s in parentheses

$$U_{eq} = (U_{11} \times U_{22} \times U_{33})^{1/3} \times 10^2 (\text{\AA}^2).$$

Molecule (I)					Molecule (II)				
	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> <sub>eq</sub>		<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> <sub>eq</sub>
C(1)	0.1809 (2)	0.2567 (2)	0.3679 (3)	3.5 (1)	C(1)	0.7051 (1)	0.0705 (2)	0.5651 (1)	4.1 (1)
C(2)	0.1967 (2)	0.4024 (2)	0.3629 (3)	4.3 (1)	C(2)	0.6343 (2)	0.1884 (3)	0.5940 (1)	4.6 (1)
C(3)	0.3201 (2)	0.4481 (3)	0.3503 (3)	4.7 (1)	C(3)	0.5431 (2)	0.2548 (3)	0.5179 (2)	5.7 (1)
C(4)	0.4252 (2)	0.3564 (3)	0.3437 (3)	4.6 (1)	C(4)	0.5298 (2)	0.2023 (3)	0.4174 (2)	5.9 (1)
C(5)	0.4113 (2)	0.2141 (2)	0.3519 (3)	3.9 (1)	C(5)	0.6028 (2)	0.0829 (3)	0.3903 (2)	5.6 (1)
C(6)	0.2854 (2)	0.1668 (2)	0.3627 (3)	3.2 (1)	C(6)	0.6912 (2)	0.0164 (3)	0.4623 (2)	5.1 (1)
N(1)	0.0761 (2)	0.1727 (2)	0.3753 (3)	4.1 (1)	N(1)	0.7819 (1)	0.0373 (2)	0.6568 (1)	5.0 (1)
N(2)	0.1081 (2)	0.0365 (2)	0.3756 (3)	4.2 (1)	N(2)	0.7641 (2)	0.1232 (3)	0.7369 (1)	5.8 (1)
N(3)	0.2342 (2)	0.0345 (2)	0.3687 (2)	3.5 (1)	N(3)	0.6729 (2)	0.2156 (2)	0.6997 (1)	5.6 (1)
O(1)	0.2975 (1)	−0.0839 (1)	0.3681 (2)	4.5 (1)	O(1)	0.8723 (1)	−0.0677 (2)	0.6700 (1)	6.9 (1)
O(2)	0.1586 (2)	−0.2337 (2)	0.0721 (3)	5.8 (1)					

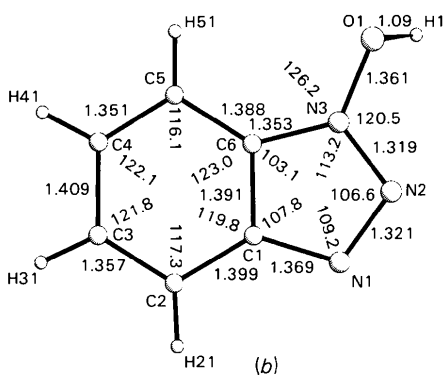
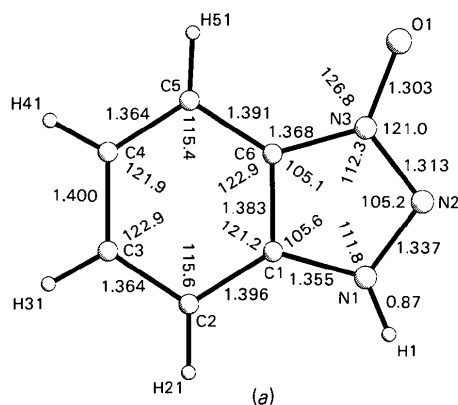


Fig. 2. (a) View of a single molecule of (I) with atomic numbering, bond lengths (Å) and angles (°). Mean e.s.d.'s: 0.002 Å and 0.3°. (b) View of a single molecule of (II) with atomic numbering, bond lengths (Å) and angles (°). Mean e.s.d.'s: 0.002 Å and 0.3°.

For a direct comparison of the bond lengths in both tautomers, the bond orders in the benzotriazole units have been estimated by use of a bond-length bond-order curve (Burke-Laing & Laing, 1976) in which all atoms are assumed to have  $sp^2$ -hybridization (see Fig. 3). This procedure shows that in valence-bond terms (I) is best described by the formula given in Fig. 1, whereas the identical bond lengths between the N atoms in (II) are

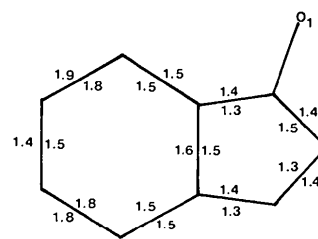


Fig. 3. Bond orders in the benzotriazole ring systems; numbers inside the rings [left for the central C(1)–C(6) bond] correspond to tautomer (I), the remaining values correspond to tautomer (II).

not satisfactorily expressed by the formula (II) in Fig. 1. However, the N(3)–O(1) bond in (I) has a much higher double-bond character as is suggested by formula (I).

The crystal structures of benzotriazole (Escande, Galigné & Lapasset, 1974) and *N*-substituted benzotriazoles (Fayos & Garcia-Blanco, 1972; Lopez de Lerma, Martinez-Carrera & Garcia-Blanco, 1973; Giordano & Zagari, 1977) known so far have all shown higher double-bond character for bonds corresponding to C(2)–C(3) and C(4)–C(5) (in Fig. 2) than for C(1)–C(2), C(3)–C(4) and C(5)–C(6). As in (I) and (II), the elongated C(2)···C(5) distances, *i.e.* the compressed C(1)–C(2)–C(3) and C(4)–C(5)–C(6) angles, have been likewise observed in the aforementioned benzotriazoles. However, there seems to exist a significant difference between the title compound and these benzotriazoles: the latter are connected with exocyclic H or C atoms at one of the N atoms, whereas in (I) and (II) there is an exocyclic N–O bond. This O(1) atom in (I) and (II) reduces the differences in N–N bond lengths, because in the other known benzotriazoles the corresponding N–N bonds differ by up to 0.06 Å. As depicted in the packing diagram of (I) (see Fig. 4), the planes of all the molecules are nearly perpendicular to [001]. One water molecule links three molecules of (I) at different heights along [001] by hydrogen bonds; a complete three-dimensional hydrogen-bond network is made possible by the fact that the acceptor atom O(1) is involved in a bifurcated hydrogen bond to two water molecules [see Fig. 4;

O(2)...O(1)' = 2.753 (3) Å, O(2)...O(1)' = 2.794 (3) Å and N(1)...O(2)' = 2.665 (3) Å; symmetry codes:  $x, y, z; x, -\frac{1}{2}-y, -\frac{1}{2}+z; -x, \frac{1}{2}+y, \frac{1}{2}-z$ .

The packing of the tautomer (II) is characterized by chains of hydrogen-bonded molecules. These chains are built up by only one type of hydrogen bond: O(1)—H(1)...N(3)' [O(1)...N(3)' = 2.586 (2) Å; symmetry code:  $1\frac{1}{2}-x, -\frac{1}{2}+y, 1\frac{1}{2}-z$ ] and the chains are themselves held together by close contacts of antiparallel, centrosymmetrically related triazole rings, suggesting some charge-transfer interactions. The contact distances of the relevant atoms lie within the range 3.4–3.7 Å (symmetry codes:  $1\frac{1}{2}-x, \frac{1}{2}-y, 1-z; 1-x, -y, 1-z$ ).\*

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\* See deposition footnote.

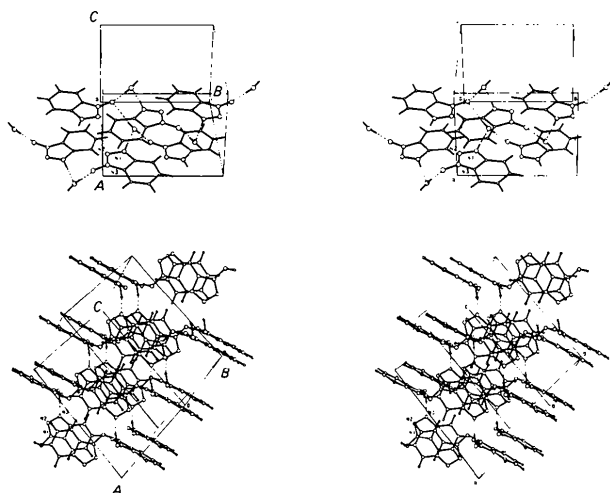


Fig. 4. (a) Crystal packing of (I). (b) Crystal packing of (II). Hydrogen bonds are illustrated with dashed lines.

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## 2-Benzoylcyclohexanecarboxylic Acid, C<sub>14</sub>H<sub>16</sub>O<sub>3</sub>

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**Abstract.**  $M_r = 232.28$ , monoclinic,  $C2/c$ ,  $a = 17.103$  (6),  $b = 6.758$  (2),  $c = 22.149$  (7) Å,  $\beta = 101.20$  (3)°,  $V = 2511$  (2) Å<sup>3</sup>,  $D_x = 1.22$  g cm<sup>-3</sup>,  $Z = 8$ , Mo  $K\alpha$  ( $\lambda = 0.71069$  Å),  $\mu = 1.00$  cm<sup>-1</sup>,  $F(000) =$

- References
- BOYLE, F. T. & JONES, R. A. Y. (1973). *J. Chem. Soc. Perkin Trans. 2*, pp. 160–164.
- BRADY, O. L. & REYNOLDS, C. V. (1928). *J. Chem. Soc.* pp. 193–202.
- BURKE-LAING, M. & LAING, M. (1976). *Acta Cryst.* B32, 3216–3224.
- CHUA, S. O., COOK, M. J. & KATRITZKY, A. R. (1971). *J. Chem. Soc. B*, pp. 2350–2355.
- CROMER, D. T. & LIBERMAN, D. (1970). *J. Chem. Phys.* 53, 1891–1898.
- CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst.* A24, 321–324.
- DAVIES, J. S. & MOHAMMED, A. K. (1981). *Peptides 1980*, edited by K. BRUNFELDT, pp. 165–168. Copenhagen: Scriptor.
- ESCANDE, A., GALIGNÉ, J. L. & LAPASSET, J. (1974). *Acta Cryst.* B30, 1490–1495.
- FAYOS, J. & GARCÍA-BLANCO, S. (1972). *Acta Cryst.* B28, 2863–2868.
- GIORDANO, F. & ZAGARI, A. (1977). *Acta Cryst.* B33, 1288–1290.
- HORIKI, K. & MURAKAMI, A. (1980). *Peptide Chemistry 1979*, edited by H. YONEHARA, pp. 89–94. Osaka: Protein Research Foundation.
- KÖNIG, W. & GEIGER, R. (1970a). *Chem. Ber.* 103, 788–798.
- KÖNIG, W. & GEIGER, R. (1970b). *Chem. Ber.* 103, 2024–2033.
- KÖNIG, W. & GEIGER, R. (1970c). *Chem. Ber.* 103, 2034–2040.
- KÖNIG, W. & GEIGER, R. (1973). *Chem. Ber.* 106, 3626–3635.
- LOPEZ DE LERMA, J., MARTÍNEZ-CARRERA, S. & GARCÍA-BLANCO, S. (1973). *Acta Cryst.* B29, 537–541.
- LÜDDECKE, E., MAUSER, H. & POLSTER, J. (1976). *Z. Naturforsch. Teil B*, 31, 1438–1439.
- MACBETH, A. K. & PRICE, J. R. (1936). *J. Chem. Soc.* pp. 111–119.
- MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J. P. & WOOLFSON, M. M. (1980). *MULTAN80. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.
- NIETZKI, R. BRAUNSCHWEIG, E. (1894). *Chem. Ber.* 27, 3381–3384.
- SHELDRIK, G. M. (1976). *SHELX76*. Program for crystal structure determination. Univ. of Cambridge, England.
- VOLKAMER, K. (1969). Dissertation, Univ. Freiburg i.Br.
- VOLKAMER, K. & ZIMMERMANN, H. W. (1969). *Chem. Ber.* 102, 4177–4187.
- WÜNSCH, E. & DREES, F. (1966). *Chem. Ber.* 99, 110–120.
- ZINCKE, T. & SCHWARZ, P. (1900). *Justus Liebigs Ann. Chem.* 311, 332–340.

992; 1285 independent observed reflections, measured at 298 K,  $R = 4.0\%$ . 2-Benzoylcyclohexanecarboxylic acid exists in the crystalline state as a dimer held together by two intermolecular hydrogen bonds between carboxylic acid groups. The ketone carbonyl O atom is not involved in hydrogen bonding.

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