

phénoxy)méthyl comme le montrent les valeurs des angles de torsion C(1)—C(7)—O(8)—C(9) = 179 (1), C(7)—O(8)—C(9)—C(14) = 173 (1), C(9)—C(14)—O(15)—C(16) = -176(1) et C(14)—O(15)—C(16)—C(17) = -179 (1)°. Le plan ainsi défini fait un angle de 33 (1)° avec le plan moyen de la morpholine. Si l'on considère les deux groupements méthoxy et éthoxy portés par le cycle phényl, ils correspondent au conformère *anti-anti* [la conformation *anti-syn* trouvée par mécanique moléculaire en utilisant le programme MM2 (Liljefors & Allinger, 1985) ne diffère de cette dernière que par 4 kJ].

L'azote protoné N(3) ne s'écarte que peu du plan du cycle phényl [0,177 (2) Å]. Il est distant de 5,99 (1) Å du milieu des atomes O(8) et O(15). Cet arrangement topographique d'un azote protoné et d'un nuage électronique π (représenté ici par les paires libres des oxygènes) se retrouve dans la plupart des drogues agissant sur le système nerveux central (Andrews, Lloyd, Martin & Munro, 1986; Lloyd & Andrews, 1986).

La cohésion cristalline est assurée par une liaison hydrogène N(3)⁺...Cl(18)⁻ (2-x, $\frac{1}{2}+y$, $\frac{1}{2}-z$) = 3,112 (3), H(203)...Cl(18)⁻ = 2,20 (5) Å, N(3)⁺—H(203)...Cl(18)⁻ = 154 (4)° et par de nombreux con-

tacts de van der Waals. Une vue de la maille est représentée sur la Fig. 2.

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Références

- ANDREWS, P. R., LLOYD, E. J., MARTIN, J. L. & MUNRO, S. L. A. (1986). *J. Mol. Graphics*, **4**, 41–45.
 BOSCH, J.-J., FORFAR, I., JARRY, C., OUHABI, J., LÉGER, J.-M. & CARPY, A. (1990). *Arch. Pharm. (Weinheim)*. Sous presse.
International Tables for X-ray Crystallography (1974). Vol. IV, pp. 201–209. Birmingham: Kynoch Press. (Distributeur actuel Kluwer Academic Publishers, Dordrecht.)
 JARRY, C., BOSCH, J.-J., OUHABI, J. & CARPY, A. (1990). *Arch. Pharm. (Weinheim)*, **323**, 157–161.
 LILJEFORS, T. & ALLINGER, N. L. (1985). *J. Comput. Chem.* **6**, 478–483.
 LLOYD, E. J. & ANDREWS, P. R. (1986). *J. Med. Chem.* **29**, 453–462.
 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*. Univ. de York, Angleterre, et de Louvain, Belgique.
 STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

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Structures of Two Isomers of C₁₈H₁₈N₂OS

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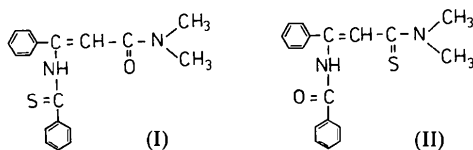
Abstract. *N,N*-Dimethyl- β -(thiobenzoylamino)-cinnamamide (I), C₁₈H₁₈N₂OS, M_r = 310.4, orthorhombic, $P2_12_12_1$, a = 9.901 (1), b = 17.762 (2), c = 9.319 (1) Å, V = 1638.8 (3) Å³, Z = 4, D_m = 1.26, D_x = 1.23 g cm⁻³, $\lambda(\text{Cu } K\alpha)$ = 1.54178 Å, μ = 17.4 cm⁻¹, $F(000)$ = 656, T = 291 K, R = 0.048 for 1110 observed reflections. β -(Benzoylamino)-*N,N*-dimethylthiocinnamamide (II), C₁₈H₁₈N₂O₂S, M_r = 310.4, orthorhombic, $Pna2_1$, a = 14.982 (2), b = 19.250 (3), c = 5.655 (1) Å, V = 1630.8 (4) Å³, Z = 4, D_m = 1.26, D_x = 1.26 g cm⁻³, $\lambda(\text{Cu } K\alpha)$ =

1.54178 Å, μ = 17.4 cm⁻¹, $F(000)$ = 656, T = 291 K, R = 0.055 for 986 observed reflections. The constitutional isomers (I) and (II) are very similar in their structures, with slight conformational differences. Intramolecular hydrogen bonds of the type N—H...O and N—H...S, respectively, are formed.

Introduction. The two isomeric cinnamamides *N,N*-dimethyl- β -(thiobenzoylamino)cinnamamide (I) and β -(benzoylamino)thiocinnam-*N,N*-dimethylamide (II) were first synthesized by Schroth (1989) during systematic investigations of the 1,3-thiazine system. The X-ray analyses served to identify both com-

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pounds in order to elucidate the reactions involved in their formation. Furthermore, we were interested in obtaining accurate information about the molecular structures of (I) and (II) and their intramolecular hydrogen bonds.



Experimental. Compounds (I) and (II) prepared as described by Schroth (1989). (I): red crystals by recrystallization from acetonitrile, m.p. 434–437 K, (II): yellow crystals from ethanol, m.p. 447–449 K. Density measured by flotation in aqueous KI solution. X-ray measurements performed on a Syntex P_2 diffractometer using graphite-monochromatized Cu $K\alpha$ radiation. Lattice parameters by least-squares refinement from the setting angles of 15 reflections $20 < 2\theta < 26^\circ$ (I) and $19 < 2\theta < 25^\circ$ (II), respectively; intensity data measurement: $\theta/2\theta$ scan, bisecting mode, corrections for Lorentz and polarization effects, no absorption correction; other details given in Table 1. Structures solved by Patterson and Fourier methods, full-matrix least-squares refinement on F with anisotropic displacement parameters for non-H atoms, H atoms at calculated positions (with the exception of H1 inferred from $\Delta\rho$ maps in each case) and 'riding' on their carrier atoms, weighting scheme $w = 1/\sigma^2(F_o)$ with $\sigma(F_o)$ based on counting statistics, empirical secondary-extinction correction $F_{\text{corr}} = F_c(1 - 10^{-6}\chi F^2/\sin\theta)$ where χ refined to 2.0 (1) and 2.1 (2), respectively, two reflections with large $\Delta F/\sigma(F)$ omitted [only for (II)]. Final R values given in Table 1 correspond with the atomic parameters of Table 2 and all other results derived from them. For both structures parallel refinement of the inverted models was performed giving the following results: (I) $R^- = 0.055$, $wR^- = 0.055$, (II) $R^- = 0.056$, $wR^- = 0.051$. Application of the \mathcal{R} test (Hamilton, 1965) (I) $R_w^-/R_w^+ = 1.119$, \mathcal{R} (1, 904, 0.001) = 1.0059; (II) $R_w^-/R_w^+ = 1.025$, \mathcal{R} (1, 781, 0.001) = 1.0068 formally indicated that the first enantiomorphs should be corrected at a significance level lower than 0.001. But the conclusion that they represent the true absolute structures is justified only for (I) showing an appreciable difference in R values but not for (II).

All calculations performed on IBM compatible PCs of the Halle and Poznań Universities using program packages *PRARA* (Jaskólski, 1981), *SHELX76* (Sheldrick, 1976), *SHELXS86* (Sheldrick, 1986), and *CRYSRULER* (Rizzoli, Sangermano, Calestani & Andreotti, 1987).

Table 1. *Details of data collection and structure refinement*

Crystal dimensions (mm)	0.20 × 0.21 × 0.28	0.15 × 0.15 × 0.43
$\sin\theta/\lambda$ (\AA^{-1})	0.546	0.546
h,k,l range	0/10, 0/19, 0/10	0/16, 0/21, 0/6
Standard reflections	112, $\bar{2}21$	211 , $2\bar{1}1$
Variation (%)	4.4, 1.9	5.6, 4.8
Measured unique reflections,	1260	1186
Observed reflections [$I \geq 1.96\sigma(I)$]	1110	986
Reflections/parameter	5.39	4.81
$(\Delta/\sigma)_{\text{max}}$ in final LS cycle	0.056	0.002
Heights in final $\Delta\rho$ map ($e \text{\AA}^{-3}$)		
max.	0.208	0.354
min.	-0.224	-0.347
R (wR)	0.048 (0.048)	0.055 (0.049)

Table 2. *Fractional coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) with e.s.d.'s in parentheses*

$$U_{\text{eq}} = (1/3)\sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j$$

	x	y	z	U_{eq}
(I)				
C1	5575 (5)	8115 (3)	6886 (6)	49 (2)
C2	6770 (5)	8158 (3)	7615 (6)	49 (2)
C3	7578 (6)	7495 (3)	8008 (6)	54 (2)
C4	3845 (6)	7136 (3)	6324 (6)	52 (2)
C5	9119 (7)	8301 (4)	9448 (8)	83 (3)
C6	9471 (7)	6933 (4)	9229 (8)	79 (3)
C7	4826 (6)	8792 (3)	6425 (6)	51 (2)
C8	4261 (6)	8813 (4)	5052 (7)	59 (2)
C9	3628 (6)	9470 (4)	4570 (8)	73 (3)
C10	3556 (7)	10094 (4)	5447 (9)	75 (3)
C11	4133 (6)	10084 (4)	6804 (8)	72 (3)
C12	4755 (6)	9430 (4)	7285 (7)	64 (2)
C13	3789 (6)	6402 (3)	5566 (7)	55 (2)
C14	4818 (7)	6156 (4)	4671 (7)	74 (3)
C15	4718 (8)	5456 (4)	3965 (9)	92 (3)
C16	3594 (10)	5011 (4)	4169 (10)	97 (4)
C17	2579 (9)	5255 (4)	5032 (10)	89 (3)
C18	2670 (7)	5937 (4)	5746 (8)	73 (3)
N1	5128 (4)	7407 (3)	6431 (5)	57 (2)
N2	8671 (5)	7589 (3)	8838 (5)	62 (2)
O	7269 (4)	6849 (2)	7582 (5)	72 (2)
S	2500 (2)	7564 (1)	6966 (2)	77 (1)
(II)				
C1	7715 (5)	7504 (3)	9303 (15)	44 (3)
C2	8484 (4)	7722 (3)	8269 (16)	43 (3)
C3	8849 (4)	8432 (3)	8131 (17)	43 (2)
C4	6225 (4)	7937 (4)	9510 (16)	46 (3)
C5	9707 (5)	7997 (4)	4664 (17)	60 (3)
C6	9975 (6)	9181 (4)	6296 (21)	77 (4)
C7	7490 (5)	6753 (3)	9395 (16)	43 (3)
C8	7074 (5)	6473 (4)	11366 (17)	51 (3)
C9	6920 (5)	5766 (4)	11531 (17)	55 (3)
C10	7176 (5)	5330 (4)	9700 (18)	56 (3)
C11	7593 (5)	5593 (4)	7738 (17)	57 (3)
C12	7739 (5)	6308 (4)	7566 (16)	52 (3)
C13	5796 (5)	8450 (3)	12160 (16)	45 (3)
C14	6233 (5)	8714 (4)	14137 (16)	49 (3)
C15	5782 (5)	9158 (4)	15702 (17)	60 (3)
C16	4911 (5)	9344 (4)	15167 (21)	64 (3)
C17	4470 (5)	9084 (4)	13204 (18)	53 (3)
C18	4915 (4)	8639 (3)	11701 (17)	47 (3)
N1	7140 (4)	7959 (3)	10484 (13)	48 (2)
N2	9460 (4)	8522 (3)	6446 (13)	49 (2)
O	5794 (3)	7539 (2)	9297 (12)	62 (2)
S	8556 (1)	9078 (1)	10000 (0)	60 (1)

Discussion. Final atomic parameters are listed in Table 2.* The molecular structures including atomic numbering are shown in Figs. 1 and 2. Selected bond lengths and angles and relevant torsion angles are given in Table 3.

The investigated compounds are constitutional isomers very similar in their molecular structures; the only difference between them is the exchange of the O and S atomic positions. The molecules deviate

* Lists of structure factors, anisotropic thermal parameters, bond lengths, bond angles, torsion angles and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53019 (32 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

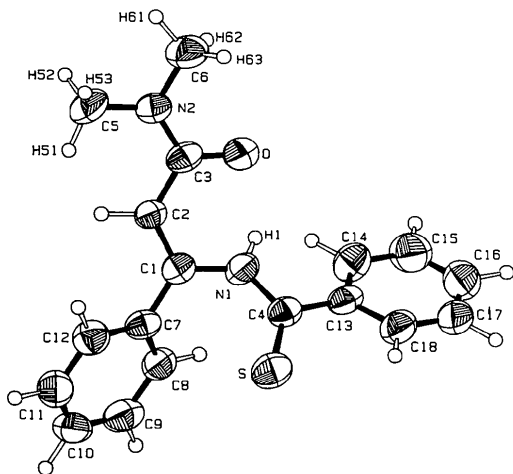


Fig. 1. ORTEP plot (Johnson, 1976) of the molecular structure of (I) (thermal ellipsoids at the 50% probability level, H atoms drawn at arbitrary size).

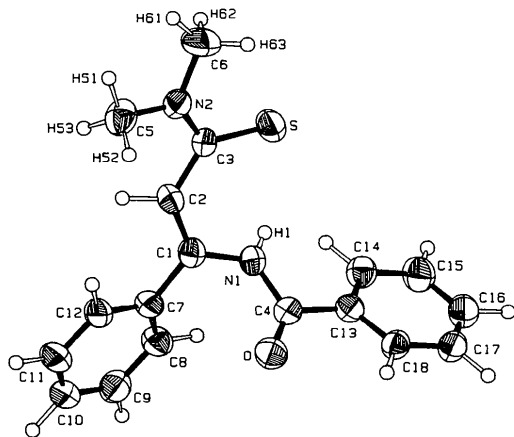


Fig. 2. Molecular structure of (II).

Table 3. Selected bond lengths (Å), bond angles (°) and torsion angles (°) in (I) and (II)

	(I)	(II)
N1—C1	1.399 (7)	1.399 (8)
N1—C4	1.363 (7)	1.371 (7)
N2—C3	1.341 (7)	1.333 (9)
N2—C5	1.457 (7)	1.474 (9)
N2—C6	1.454 (7)	1.498 (8)
S—C3		1.689 (8)
S—C4	1.645 (6)	
O—C3	1.253 (6)	
O—C4		1.208 (8)
C1—C2	1.359 (7)	1.366 (9)
C2—C3	1.469 (7)	1.474 (8)
C1—C7	1.477 (7)	1.485 (9)
C4—C13	1.483 (7)	1.510 (10)
N1—C4—S	124.4 (4)	
N1—C4—O		123.6 (7)
N1—C4—C13	112.3 (5)	114.0 (7)
O—C4—C13		122.5 (6)
S—C4—C13	123.3 (4)	
N2—C3—S		122.0 (5)
N2—C3—O	119.5 (5)	
N2—C3—C2	119.0 (5)	114.4 (7)
S—C3—C2		123.5 (6)
O—C3—C2	121.5 (5)	
C1—N1—C4	129.4 (5)	126.7 (6)
C3—N2—C5	125.3 (5)	124.9 (6)
C3—N2—C6	119.0 (5)	120.6 (7)
C5—N2—C6	115.6 (5)	114.5 (7)
C1—C2—C3	123.4 (5)	128.7 (7)
C2—C1—N1	118.3 (5)	122.2 (6)
C7—C1—N1	119.0 (5)	117.0 (6)
C2—C1—C7	122.3 (5)	120.6 (6)
C1—N1—C4—S	-10.0 (7)	-5.8 (9)
C1—N1—C4—O		173.3 (9)
C1—N1—C4—C13	170.4 (7)	142.7 (9)
C2—C1—N1—C4	145.8 (7)	-42.4 (9)
C7—C1—N1—C4	-41.1 (7)	
C5—N2—C3—O	-177.7 (7)	
C5—N2—C3—S		-176.0 (8)
C6—N2—C3—O	-0.2 (6)	
C6—N2—C3—S		6.0 (8)
C1—C2—C3—N2	-173.8 (6)	-161.0 (9)
C1—C2—C3—S		21.2 (9)
C1—C2—C3—O	6.3 (7)	
C3—C2—C1—N1	-3.1 (6)	-1.1 (10)
C3—C2—C1—C7	-176.1 (7)	-175.8 (10)

appreciably from planarity. Some of the molecular fragments, however, are largely planar. Apart from the benzene rings being exactly planar within experimental error such fragments are the acrylic acid dimethylamide [plane 1 defined by atoms C1, C2, C3, O(S), N2, C5, C6] and the acetamide moiety [plane 2, through C13, C4, S(O), N1]. Planarity of the former is better in (I) [maximum displacement from the least-squares plane 0.055 (5) Å for C2] than in (II) [0.165 (8) Å for C2]. According to experience, in cinnamic acid and its derivatives the favoured conformation for the vinylene group is (more or less) coplanar with the phenyl ring. So in a series of *p*-alkoxycinnamic acids interplanar angles have been reported that are, without exception, smaller than 5° (Bryan & Hartley, 1981); the interplanar angle of 12.3° observed in cinnamamide (Iwamoto, Kashino

& Haisa, 1989) is rather large. But in (I) and (II) the plane through C7, C1, C2, C3 makes an angle of 40.0 and 35.3°, respectively, with the phenyl ring plane C7...C12. It seems that this anomaly is caused by the benzoylamino substituent in the β position. The angle between the perfect plane I and the adjacent phenyl ring in (I) (19.8°) differs only slightly from that in (II) (24.0°) and the interplanar angles 1/2 in the two isomers are practically identical (43.8 and 43.7°, respectively). Short N1...O [2.574 (6) Å in (I)] and N1...S distances [3.035 (6) Å in (II)] indicate the existence of intramolecular hydrogen bonds in both isomers. The hydrogen-bond geometries normalized following Jeffrey & Lewis (1978) (N—H distance equal to 1.030 Å) are as follows: (I) H...O 2.023 (6) Å, N1—H1...O 110.7 (5)°; (II) H...S 2.294 (6) Å, N1—H1...S 127.7 (8)°. According to the compilation given in Taylor, Kennard & Versichel (1984) the hydrogen bond in (I) is a very strong one. Corresponding bond lengths in (I) and (II) agree within 3σ and are close to standard values given in literature (Allen, Kennard, Watson, Brammer, Orpen & Taylor, 1987). Compared with the values normally observed in cinnamic acid derivatives (see e.g. Bryan & Hartley, 1981; Bryan & Forcier, 1980; Iwamoto, Kashino & Haisa, 1989) two angles in both (I) and (II) show unusual features: C7—C1—C2 is reduced and C1—C2—C3 is enlarged by about 5° in each case.

The crystal structures of (I) and (II) consist of discrete molecules with all intermolecular contacts between non-H atoms greater than the sums of the corresponding van der Waals radii given by Bondi (1964).

References

- ALLEN, F. H., KENNARD, O., WATSON, D. G., BRAMMER, L., ORPEN, A. G. & TAYLOR, R. (1987). *J. Chem. Soc. Perkin Trans. 2*, pp. S1–S19.
- BONDI, A. (1964). *J. Phys. Chem.* **68**, 441–451.
- BRYAN, R. F. & FORCIER, P. G. (1980). *Mol. Cryst. Liq. Cryst.* **60**, 157–166.
- BRYAN, R. F. & HARTLEY, P. (1981). *Mol. Cryst. Liq. Cryst.* **69**, 47–70.
- HAMILTON, W. C. (1965). *Acta Cryst.* **18**, 502–510.
- IWAMOTO, T., KASHINO, S. & HAISA, M. (1989). *Acta Cryst.* **C45**, 1110–1112.
- JASKÓLSKI, M. (1981). *PRARA*. Program for data reduction from syntex data tapes on IBM computers. Univ. of Poznań, Poland.
- JEFFREY, G. A. & LEWIS, L. (1978). *Carbohydr. Res.* **60**, 179–182.
- JOHNSON, C. K. (1976). *ORTEPII*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
- RIZZOLI, C., SANGERMANO, V., CALESTANI, G. & ANDRETTI, G. D. (1987). *J. Appl. Cryst.* **20**, 436–439.
- SCHROTH, W. (1989). Unpublished work.
- SHELDRIK, G. M. (1976). *SHELX76*. Program for crystal structure determination. Univ. of Cambridge, England.
- SHELDRIK, G. M. (1986). *SHELXS86*. Program for the solution of crystal structures. Univ. of Göttingen, Federal Republic of Germany.
- TAYLOR, R., KENNARD, O. & VERSICHEL, W. (1984). *Acta Cryst.* **B40**, 280–288.

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Structure of Chenodeoxycholic Acid in Chenodeoxycholic Acid Ethyl Acetate Solvate

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Abstract. C₂₄H₄₀O₄·C₄H₈O₂, $M_r = 480.7$, hexagonal, $P6_5$, $a = 22.169$ (6), $c = 10.226$ (4) Å, $V = 4352$ (2) Å³, $Z = 6$, $D_x = 1.10$, $D_m = 1.06$ (2) g cm⁻³, $\lambda(\text{Cu } K\alpha) = 1.54184$ Å, $\mu = 5.7$ cm⁻¹, $F(000) = 1584$, $T = 295$ K, $R = 0.071$ for 2397 unique observed diffractometer data [$I \geq 2.5\sigma(I)$]. The chenodeoxycholic acid molecules are arranged in a helical chain around

the 6_5 axis, thus forming an infinite column. The hydrophilic exteriors of these columns are stacked parallel to each other and connected by helical hydrogen-bond chains around the 2_1 axes. The mainly hydrophobic interiors of the channels, left open around the 6_5 axis, are filled with severely disordered ethyl acetate molecules. The steroid nucleus has a conformation typical for bile acids. The 17β side chain is not extended, in order to accommodate the hydrogen-bond network.

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