ORGANIC COMPOUNDS

Acta Cryst. (1998). C**54**, 57–60

Conformational Polymorphs of Acetone Tosylhydrazone

CHARLES R. OJALA,[a] WILLIAM H. OJALA,[b] SHANIEKA Y. PENNAMON[c] AND WILLIAM B. GLEASON[d]

[a]*Department of Chemistry, Normandale Community College, Bloomington, MN 55431, USA,* [b]*Department of Chemistry, University of St. Thomas, St. Paul, MN 55105, USA,* [c]*Minnesota Supercomputer Institute, University of Minnesota, Minneapolis, MN 55455, USA, and* [d]*Department of Laboratory Medicine & Pathology, Biomedical Engineering Center, University of Minnesota, Minneapolis, MN 55455, USA. E-mail: bgleason@maroon.tc.umn.edu*

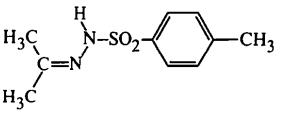
(*Received 2 January 1997; accepted 1 September 1997*)

Abstract

Two polymorphs of 2-isopropylidene-1-(*p*-toluenesulfono)hydrazide (acetone tosylhydrazone, $C_{10}H_{14}N_2O_2S$) are described. Both forms, one triclinic and the other monoclinic, are obtained upon crystallization from the same solvent. These are conformational polymorphs; the aryl ring eclipses one of the S—O bonds in the triclinic structure [O1—S1—C4—C5 = −0.9 (2)°] but not in the monoclinic structure [O1—S1—C4—C5 = −14.2 (2)°]. In spite of the conformational difference, molecules of the two polymorphs engage in similar intermolecular hydrogen-bonding contacts. Calculations using *Cerius*[2] [Molecular Simulations (1996). *Cerius*[2] *Program*. MS, 9685 Scranton Road, San Diego, CA 92121–3752, USA] indicate that the triclinic form is more stable than the monoclinic form by approximately 1 kcal. Subtle conformational differences of the type described here may be expected to present a challenge to the successful prediction of crystal structures.

Comment

As part of our investigation of protein/carbohydrate interactions, we have been examining the structures of the derivatives formed by the reaction of phenylhydrazine, and related compounds, with monosaccharides. These reactions yield cyclic products (*N*-glycosides) or acyclic products (true hydrazones), the product type varying with the sugar. In an attempt to obtain spectroscopic data that might be diagnostic for the acyclic form, we performed the derivatization reaction on several compounds which should unquestionably yield hydrazones under these reaction conditions. Although tosylhydrazone derivatives of the cyclic ketones cyclopentanone and cyclohexanone were prepared and characterized crystallographically and spectroscopically in a straightforward manner, a similar attempt with the simplest ketone, acetone, resulted in the isolation of four different crystalline materials. We describe here the molecular and crystal structure of acetone tosylhydrazone as found in two polymorphic forms, one of them triclinic, compound (1), and the other monoclinic, compound (2). Two crystalline by-products are described in the following report (Ojala, Ojala & Gleason, 1998). We also present here the results of lattice-energy minimization calculations for the polymorphic pair.



(1)/(2)

The conformation and the atom-numbering scheme for acetone tosylhydrazone are shown in Fig. 1 for the triclinic polymorph and in Fig. 2 for the monoclinic polymorph. There are no major discrepancies in bond lengths and angles between the two structures; however, the molecules do differ in conformation, notably in the orientation of the aryl ring with respect to the sulfonyl group. The ring eclipses one of the S—O bonds in the triclinic form [O1—S1—C4—C5 = −0.9 (2)°], but it is twisted substantially out of this position in the monoclinic form [O1—S1—C4—C5 = −14.2 (2)°]. We report here the low temperature (173 K) structures of these materials. We have also determined the crystal structures of both polymorphs at room temperature (298 K) and find, apart from the expected larger anisotropic displacement parameters, no significant difference in torsional parameters between the high and low temperature structures. These structures serve as yet another example of conformational polymorphism (Bernstein & Hagler, 1978).

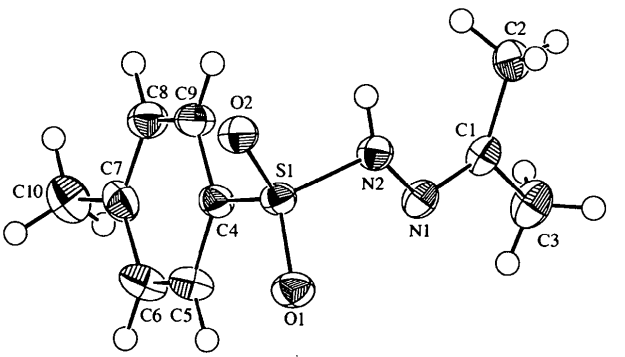


Fig. 1. *ORTEP*II (Johnson, 1976) view of the triclinic polymorph (1) showing the atom numbering. For non-H atoms, 50% probability ellipsoids are shown. The aromatic ring assumes an eclipsed orientation with respect to the S1—O1 bond.

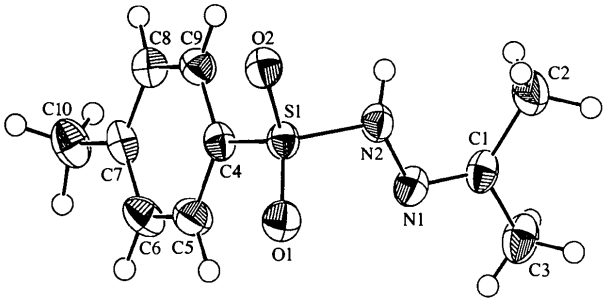


Fig. 2. *ORTEP*II (Johnson, 1976) view of the monoclinic polymorph (2) showing the atom numbering. For non-H atoms, 50% probability ellipsoids are shown. The aromatic ring is twisted away from both S—O bonds.

The torsional freedom shown by the sulfonyl group in these structures is similar to that shown by the sulfonate group in the crystal structures of sulfonated azo dyes we have examined previously. In these structures, both staggered and eclipsed orientations of sulfonate groups with respect to the adjacent aromatic ring can be found (Ojala *et al.*, 1994, 1996).

Views of the molecular packing are presented in Fig. 3 for the triclinic polymorph and in Fig. 4 for the monoclinic polymorph. In spite of the difference in molecular conformation, molecules in the two structures engage in the same intermolecular interaction, a hydrogen bond between the NH group and sulfonyl O2 atom that links molecules into pairs about crystallographic inversion centers.

We are interested in the use of lattice-energy minimization techniques for applications in pharmaceutical chemistry and so used the *Cerius*^{2} program (Molecular Simulations, 1996) for lattice-energy calculations. Since typical energy differences between polymorphs are on the order of a few kilocalories (Kitaigorodsky, 1973), such systems are useful for evaluating computational approaches, since they should compute energy differences of this magnitude. The triclinic polymorph is calculated to be 0.719 kcal more stable than the monoclinic when default values for the charges are used. These calculations were performed allowing the cell constants to vary. For the monoclinic polymorph, the percent change was: a +5.6%, b −0.9%, c −4.8%, β +6.1%. For the triclinic form, the change in the cell constants was on the order of 1% or less, except for γ which changed by 2.6%. Changes of these magnitudes in cell constants are typical for lattice-energy minimization calculations of this type; see, for example, the work of Ellern *et al.* (1994). The calculated greater stability for the triclinic polymorph seems not to depend a great deal on the actual charges assigned, since scaling the atomic charges to half the initially used value results in the triclinic polymorph again being calculated to be more stable, in this case by 0.907 kcal. The general trend in polymorphic systems seems to be that the more dense form is the more stable (Burger & Ramburger, 1979). In this case, the triclinic form is slightly more dense than the monoclinic, in accord with the calculated lower energy. On the other hand, the monoclinic form had the higher melting point, perhaps indicating greater stability. As discussed in the experimental section, however, we do not report these melting points with the greatest confidence.

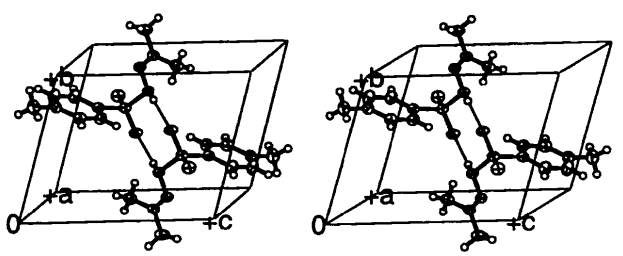


Fig. 3. Centrosymmetric hydrogen bonding in the unit cell of the triclinic polymorph.

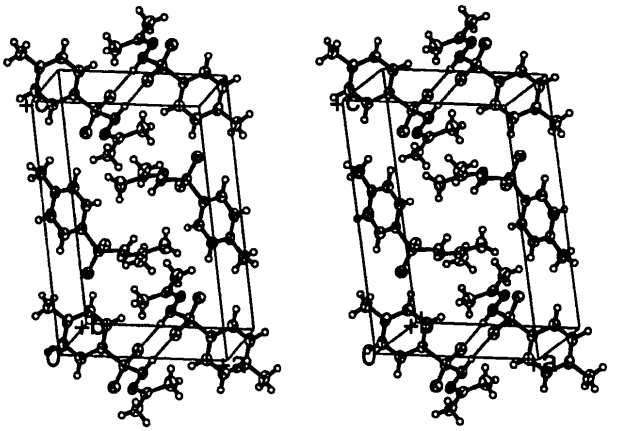


Fig. 4. View of the packing in the monoclinic polymorph. Centrosymmetric hydrogen bonding occurs between the pairs of molecules at the top and bottom faces of the cell as it is shown here.

Although prospects for *ab initio* crystal structure prediction seem dim (Gavezzotti, 1994), programs aimed at polymorph prediction are under development (Karfunkel & Gdanitz, 1992; Leusen, Docherty & Payne, 1995). Subtle conformational differences of the type reported here, in this very simple system, could present a serious complication for those engaged in crystal structure and polymorph prediction. The fact that both polymorphs can be obtained simultaneously under the same conditions of temperature and solvent also has practical implications for areas where consistent production of a specific polymorph is desirable, such as in pharmaceutical science.

Experimental

The compound was prepared using literature procedures (Borsche & Frank, 1926). Both polymorphs could be obtained by crystallization from anhydrous ethanol, sometimes with both polymorphs appearing within the same flask. The triclinic

form crystallized as thick plates and as thick masses of block-shaped crystals. The monoclinic form crystallized as rectangular prisms. When the solvent was allowed to evaporate slowly at room temperature, the quality of the monoclinic prisms kept under solvent appeared to decline and the solid residue which formed upon complete evaporation contained only the triclinic plates and no monoclinic prisms. We have not explored this phenomenon in sufficient depth to know if this is a general trend, nor have we attempted to develop a crystallization scheme which reproducibly yields one polymorph in preference to the other. In our laboratory, the melting points (Fisher–Johns melting point apparatus, uncorrected readings) of the polymorphs were found to be 411–416 K for the triclinic form and 415–421 K for the monoclinic form, significantly lower than values such as 432–433 K (Borsche & Frank, 1926) or 426 K (Bamford & Stevens, 1952) reported in the literature without mention of the polymorphism. It is possible that decomposition of the sample during heating caused lowering and broadening of the melting point range.

Table 1. *Selected geometric parameters (Å, °) for (1)*

S1—O1	1.428 (1)	C4—C5	1.388 (3)
S1—O2	1.444 (1)	C4—C9	1.385 (2)
S1—N2	1.644 (2)	C5—C6	1.380 (3)
S1—C4	1.755 (2)	C6—C7	1.393 (3)
N1—N2	1.411 (2)	C7—C8	1.396 (3)
N1—C1	1.277 (2)	C7—C10	1.499 (3)
C1—C2	1.490 (3)	C8—C9	1.372 (3)
C1—C3	1.494 (2)		
O1—S1—O2	119.01 (8)	S1—C4—C5	120.6 (1)
O1—S1—N2	108.82 (8)	S1—C4—C9	118.5 (1)
O1—S1—C4	108.60 (8)	C5—C4—C9	120.9 (2)
O2—S1—N2	103.42 (8)	C4—C5—C6	118.5 (2)
O2—S1—C4	109.53 (8)	C5—C6—C7	121.8 (2)
N2—S1—C4	106.75 (8)	C6—C7—C8	118.1 (2)
N2—N1—C1	115.8 (2)	C6—C7—C10	122.1 (2)
S1—N2—N1	112.1 (1)	C8—C7—C10	119.8 (2)
N1—C1—C2	125.9 (2)	C7—C8—C9	121.0 (2)
N1—C1—C3	116.2 (2)	C4—C9—C8	119.7 (2)
C2—C1—C3	117.9 (2)		
S1—N2—N1—C1	161.9 (1)	O2—S1—C4—C9	49.0 (2)
O1—S1—N2—N1	61.2 (1)	N1—N2—S1—C4	−55.8 (1)
O1—S1—C4—C5	−0.9 (2)	N2—S1—C4—C5	116.3 (2)
O1—S1—C4—C9	−179.5 (1)	N2—S1—C4—C9	−62.3 (2)
O2—S1—N2—N1	−171.3 (1)	N2—N1—C1—C2	−0.7 (3)
O2—S1—C4—C5	−132.3 (2)	N2—N1—C1—C3	179.5 (1)

Polymorph (1)

Crystal data

$C_{10}H_{14}N_2O_2S$
$M_r = 226.29$
Triclinic
$P\bar{1}$
$a = 8.115\ (1)$ Å
$b = 8.271\ (1)$ Å
$c = 10.035\ (2)$ Å
$\alpha = 76.28\ (1)°$
$\beta = 79.13\ (1)°$
$\gamma = 61.79\ (1)°$
$V = 574.3\ (3)$ Å^3
$Z = 2$
$D_x = 1.309$ Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
$\lambda = 1.5418$ Å
Cell parameters from 25 reflections
$\theta = 40.0–50.0°$
$\mu = 2.331$ mm^{-1}
$T = 173$ K
Prism
0.32 × 0.24 × 0.16 mm
Colorless

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scans (North, Phillips & Mathews, 1968)
$T_{min} = 0.569$, $T_{max} = 0.689$
2552 measured reflections
2103 independent reflections

2005 reflections with $I > 3\sigma(I)$
$R_{int} = 0.029$
$\theta_{max} = 70°$
$h = -7 \rightarrow 5$; $-9 \rightarrow 9$
$k = -7 \rightarrow 5$; $-9 \rightarrow 10$
$l = -9 \rightarrow -5$; $0 \rightarrow 12$
3 standard reflections
frequency: 60 min
intensity decay: < 1.0%

Refinement

Refinement on F
$R = 0.040$
$wR = 0.062$
$S = 3.166$
2005 reflections
140 parameters
H atoms: see below
$w = 4F_o^2/\sigma^2(F_o^2)$
$(\Delta/\sigma)_{max} = 0.001$

$\Delta\rho_{max} = 0.47$ e Å^{-3}
$\Delta\rho_{min} = -0.40$ e Å^{-3}
Extinction correction: Zachariasen (1963) type 2 Gaussian isotropic
Extinction coefficient: 0.1486×10^{-4}
Scattering factors from *International Tables for X-ray Crystallography* (Vol. IV)

Polymorph (2)

Crystal data

$C_{10}H_{14}N_2O_2S$
$M_r = 226.29$
Monoclinic
$P2_1/c$
$a = 9.7369\ (8)$ Å
$b = 8.0691\ (8)$ Å
$c = 14.776\ (1)$ Å
$\beta = 96.037\ (7)°$
$V = 1154.5\ (3)$ Å^3
$Z = 4$
$D_x = 1.302$ Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
$\lambda = 1.5418$ Å
Cell parameters from 25 reflections
$\theta = 41.0–50.0°$
$\mu = 2.319$ mm^{-1}
$T = 173$ K
Prism
0.24 × 0.16 × 0.16 mm
Colorless

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scans (North, Phillips & Mathews, 1968)
$T_{min} = 0.649$, $T_{max} = 0.690$
2466 measured reflections
2339 independent reflections

1943 reflections with $I > 3\sigma(I)$
$R_{int} = 0.050$
$\theta_{max} = 70°$
$h = 0 \rightarrow 11$
$k = 0 \rightarrow 9$
$l = -17 \rightarrow 16$
3 standard reflections
frequency: 60 min
intensity decay: 0.45%

Refinement

Refinement on F
$R = 0.043$
$wR = 0.062$
$S = 2.835$
1943 reflections
179 parameters
H atoms: see below
$w = 4F_o^2/\sigma^2(F_o^2)$
$(\Delta/\sigma)_{max} = 0.0080$

$\Delta\rho_{max} = 0.48$ e Å^{-3}
$\Delta\rho_{min} = -0.44$ e Å^{-3}
Extinction correction: Zachariasen (1963) type 2 Gaussian isotropic
Extinction coefficient: 0.1133×10^{-5}
Scattering factors from *International Tables for X-ray Crystallography* (Vol. IV)

Table 2. *Selected geometric parameters (Å, °) for (2)*

S1—O1	1.423 (2)	C4—C5	1.380 (3)
S1—O2	1.439 (2)	C4—C9	1.392 (3)
S1—N2	1.637 (2)	C5—C6	1.391 (3)
S1—C4	1.753 (2)	C6—C7	1.382 (3)
N1—N2	1.410 (2)	C7—C8	1.394 (3)
N1—C1	1.278 (3)	C7—C10	1.500 (3)
C1—C2	1.499 (3)	C8—C9	1.375 (3)
C1—C3	1.488 (3)		
O1—S1—O2	119.63 (9)	S1—C4—C5	119.6 (2)
O1—S1—N2	108.0 (1)	S1—C4—C9	119.6 (2)
O1—S1—C4	109.02 (9)	C5—C4—C9	120.8 (2)
O2—S1—N2	103.22 (9)	C4—C5—C6	118.6 (2)
O2—S1—C4	108.33 (9)	C5—C6—C7	121.8 (2)
N2—S1—C4	108.01 (9)	C6—C7—C8	118.4 (2)
N2—N1—C1	115.8 (2)	C6—C7—C10	120.9 (2)
S1—N2—N1	114.1 (1)	C8—C7—C10	120.8 (2)
N1—C1—C2	125.6 (2)	C7—C8—C9	120.9 (2)
N1—C1—C3	116.9 (2)	C4—C9—C8	119.6 (2)
C2—C1—C3	117.5 (2)		
S1—N2—N1—C1	174.4 (2)	O2—S1—C4—C9	35.5 (2)
O1—S1—N2—N1	53.3 (2)	N1—N2—S1—C4	−64.5 (2)
O1—S1—C4—C5	−14.2 (2)	N2—S1—C4—C5	102.9 (2)
O1—S1—C4—C9	167.2 (2)	N2—S1—C4—C9	−75.7 (2)
O2—S1—N2—N1	−179.1 (1)	N2—N1—C1—C2	−1.4 (3)
O2—S1—C4—C5	−145.9 (2)	N2—N1—C1—C3	177.9 (2)

For both compounds, data collection: *CAD-4 Software* (Enraf–Nonius, 1989); cell refinement: *CAD-4 Software*; data reduction: *TEXSAN* (Molecular Structure Corporation, 1985); program(s) used to solve structures: *SHELXS86* (Sheldrick, 1985); program(s) used to refine structures: *TEXSAN*; molecular graphics: *ORTEPII* (Johnson, 1976); software used to prepare material for publication: *TEXSAN*.

Support for SYP was provided by the Undergraduate Summer Internship Program of the University of Minnesota Supercomputer Institute. We are also grateful to the Minnesota Medical Foundation and the Graduate School of the University of Minnesota for partial support of this work. We thank Professor David Grant for allowing us to use the *Cerius*^{2} software in his laboratory.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SX1030). Services for accessing these data are described at the back of the journal.

References

Bamford, W. R. & Stevens, T. S. (1952). *J. Chem. Soc.* pp. 4735–4740.
Bernstein, J. & Hagler, A. T. (1978). *J. Am. Chem. Soc.* **100**, 673–681.
Borsche, W. & Frank, R. (1926). *Justus Liebigs Ann. Chem.* **450**, 75–84.
Burger, A. & Ramburger, R. (1979). *Mikrochim. Acta (Wien)*, **2**, 259–271.
Ellern, A., Bernstein, J., Becker, J. Y., Zamir, S. & Shahal, L. (1994). *Chem. Mater.* **6**, 1378–1385.
Enraf-Nonius (1989). *CAD-4 Software*. Version 5.0. Enraf–Nonius, Delft, The Netherlands.
Gavezzotti, A. (1994). *Acc. Chem. Res.* **27**, 309–314.
Johnson, C. K. (1976). *ORTEPII*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
Karfunkel, H. R. & Gdanitz, R. J. (1992). *J. Comput. Chem.* **13**, 1171–1183.
Kitaigorodsky, A. (1973). In *Molecular Crystals and Molecules*, ch. 7. New York: Academic Press.
Leusen, F. J. J., Docherty, R. & Payne, R. S. (1995). 16th *Eur. Crystallogr. Meet. Abstr.* P12–04, p. 88.
Molecular Simulations (1996). *Cerius*^{2} *Program*. Molecular Simulations, 9685 Scranton Road, San Diego, CA 92121–3752, USA, and 240/250 The Quorum, Barnwell Road, Cambridge CB5 8RE, England.
Molecular Structure Corporation (1985). *TEXSAN. TEXRAY Structure Analysis Package*. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.
North, A. C. T., Phillips, D. C. & Mathews, F. S. (1968). *Acta Cryst.* A**24**, 351–359.
Ojala, W. H., Lu, L. K., Albers, K. E., Gleason, W. B., Richardson, T. I., Lovrien, R. E. & Sudbeck, E. A. (1994). *Acta Cryst.* B**50**, 684–694.
Ojala, C. R., Ojala, W. H. & Gleason, W. B. (1998). *Acta Cryst.* C**54**, 60–63.
Ojala, W. H., Sudbeck, E. A., Lu, L. K., Richardson, T. I., Lovrien, R. E. & Gleason, W. B. (1996). *J. Am. Chem. Soc.* **118**, 2131–2142.
Sheldrick, G. M. (1985). *SHELXS86. Program for the Solution of Crystal Structures*. University of Göttingen, Germany.
Zachariasen, W. H. (1963). *Acta Cryst.* **16**, 1139–1144.

Acta Cryst. (1998). C**54**, 60–63

By-products from the Preparation of Acetone Tosylhydrazone: 4,5-Dihydro-3,5,5-trimethyl-1-[(4-methylphenyl)sulfonyl]-1*H*-pyrazole and 1,2-Bis(*p*-toluenesulfono)-hydrazide

CHARLES R. OJALA,[a] WILLIAM H. OJALA[b] AND WILLIAM B. GLEASON[c]

[a]*Department of Chemistry, Normandale Community College, Bloomington, MN 55431, USA,* [b]*Department of Chemistry, University of St. Thomas, St. Paul, MN 55105, USA, and* [c]*Department of Laboratory Medicine & Pathology, Biomedical Engineering Center, University of Minnesota, Minneapolis, MN 55455, USA. E-mail: bgleason@maroon.tc.umn.edu*

(*Received 2 January 1997; accepted 1 September 1997*)

Abstract

The title compounds, 4,5-dihydro-3,5,5-trimethyl-1-[(4-methylphenyl)sulfonyl]-1*H*-pyrazole, $C_{13}H_{18}N_2O_2S$, and 1,2-bis(*p*-toluenesulfono)hydrazide, $C_{14}H_{16}N_2O_4S_2$, are both obtained as by-products in the preparation of acetone tosylhydrazone from acetone and toluenesulfonohydrazide. In the pyrazole, one of the S—O bonds is nearly eclipsed with the aryl ring [torsion angle 7.2 (2)°]. In the hydrazide, hydrogen bonding between the N—H groups and the S—O groups of the neighboring glide-related molecule [N···O distances of 2.921 (5) and 2.847 (5) Å] links the molecules into chains extending along the *c* axis.