

## Structure of (1*S*,4*R*,6*S*)-5-Acetyl-6-hydroxy-8,8-dimethyl-2-phenylacetyl-7-thia-2,5-diazabicyclo[2.2.2]octan-3-one

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### Abstract

$C_{17}H_{20}N_2O_4S$ ,  $M_r = 348.43$ , crystallizes in the space group  $P2_12_12_1$  with  $a = 28.546$  (8),  $b = 9.063$  (3),  $c = 6.543$  (2) Å,  $Z = 4$ ,  $U = 1692.8$  Å<sup>3</sup>,  $D_c = 1.367$  Mg m<sup>-3</sup>,  $\mu(Cu K\alpha) = 7.656$  mm<sup>-1</sup>. Final  $R = 0.036$  for 1483 observed reflexions [ $I > 2\sigma(I)$ ]. The conformation of the diazabicyclo[2.2.2]octane ring is boat–boat–boat. Molecules are connected in an infinite chain by hydrogen bonds between acetyl and hydroxy groups: O(22)–H(22)···O(21), 2.732 (4) Å.

### Introduction

An X-ray structure determination of D- $\alpha$ -benzylpenilloic acid (I) (Kojić-Prodić & Ružić-Toroš, 1978) enabled us to determine the configurations of the epimers of 3,8-diacyl derivatives of 7,7-dimethyl-6-

thia-3,8-diazabicyclo[3.2.1]octan-2-one (II) (Herak, Kovačević, Lukić & Gašpert, 1979). Treatment of (II) with phosphorus pentachloride gave a halogen compound, isolated in high yield and purity, which reacted rapidly with water yielding a hydroxy compound. Four possible structures (III–VI) could be assigned to the stereoisomer obtained on the basis of elemental analysis, IR and <sup>1</sup>H NMR spectral data.

The fact that the present X-ray analysis established structure (VI) requires special comment on the formation of this compound. Rearrangement of the 6-thia-3,8-diazabicyclo[3.2.1]octan-2-one ring to the 7-thia-2,5-diazabicyclo[2.2.2]octan-3-one system occurred. This rearrangement was coupled with the stereospecific introduction of a hydroxy group, since only one stereoisomer has been found in the reaction product.

### Experimental

The space group was determined from Weissenberg photographs recorded with Cu  $K\alpha$  radiation. The diffraction symmetry and extinctions determined  $P2_12_12_1$  uniquely.

The intensities were collected with a needle-shaped crystal, 0.055 × 0.095 × 0.435 mm, on a Philips PW 1100 computer-controlled four-circle diffractometer in the  $\omega$ - $2\theta$  scan mode [scan width = 1.20°( $\theta$ ), scan speed = 0.030°( $\theta$ )s<sup>-1</sup>] with graphite-monochromated Cu  $K\alpha$  radiation. 1483 independent reflexions [ $I > 2\sigma(I)$ ] in the range  $3 < \theta < 70^\circ$  were recorded and used in the calculations. Three standard reflexions were measured every 2 h. The data were corrected for background, Lorentz and polarization effects but not for absorption.

### Structure determination and refinement

Overall temperature ( $B = 2.96$  Å<sup>2</sup>) and scale factors were determined (Wilson, 1942) and used to compute

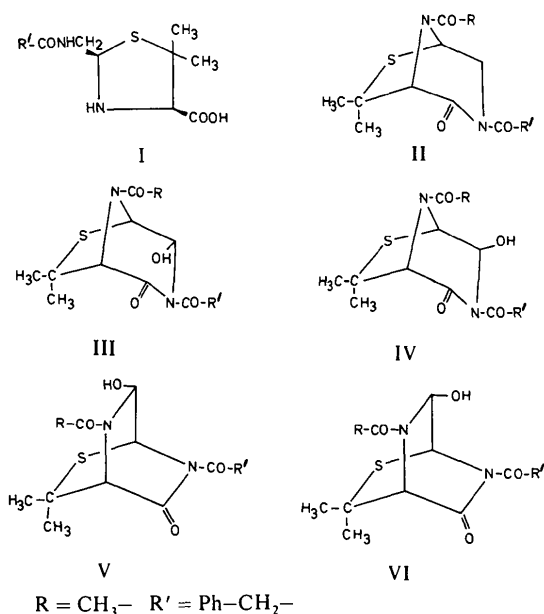


Table 1. Final atomic coordinates ( $\times 10^4$ ) and isotropic thermal parameters ( $\times 10^2$ ) for non-hydrogen atoms

Isotropic  $U$  is derived from the anisotropic thermal parameters by  $U = \frac{1}{3} \sum_i \sum_j U_{ij} a_i^* a_j^* a_i \cdot a_j$ .

|       | $x$       | $y$      | $z$       | $U (\text{Å}^2)$ |
|-------|-----------|----------|-----------|------------------|
| C(1)  | 9110 (1)  | 2276 (3) | -1369 (4) | 3.80             |
| N(2)  | 8924 (0)  | 1593 (3) | 515 (4)   | 3.46             |
| C(3)  | 9065 (1)  | 2315 (3) | 2286 (5)  | 3.55             |
| C(4)  | 9344 (1)  | 3690 (3) | 1804 (5)  | 3.59             |
| N(5)  | 9749 (0)  | 3278 (3) | 546 (4)   | 3.55             |
| C(6)  | 9638 (1)  | 2365 (3) | -1244 (4) | 3.52             |
| S(7)  | 8854 (0)  | 4092 (1) | -1731 (1) | 5.05             |
| C(8)  | 9038 (1)  | 4863 (4) | 767 (5)   | 4.32             |
| C(9)  | 8616 (1)  | 375 (4)  | 321 (6)   | 4.55             |
| O(10) | 8589 (1)  | -246 (3) | -1301 (4) | 7.09             |
| C(11) | 8308 (1)  | -11 (4)  | 2116 (6)  | 5.00             |
| C(12) | 7950 (1)  | 1198 (4) | 2473 (6)  | 4.67             |
| C(13) | 7894 (1)  | 1827 (4) | 4387 (6)  | 5.56             |
| C(14) | 7573 (1)  | 2946 (5) | 4683 (7)  | 7.11             |
| C(15) | 7305 (1)  | 3455 (5) | 3078 (8)  | 8.16             |
| C(16) | 7354 (1)  | 2827 (6) | 1179 (8)  | 7.90             |
| C(17) | 7674 (1)  | 1692 (5) | 871 (6)   | 5.95             |
| O(18) | 8971 (0)  | 1909 (2) | 4004 (3)  | 4.65             |
| C(19) | 10183 (1) | 3790 (4) | 974 (5)   | 4.23             |
| C(20) | 10572 (1) | 3420 (4) | -477 (6)  | 4.97             |
| O(21) | 10256 (0) | 4544 (3) | 2509 (4)  | 5.89             |
| O(22) | 9848 (0)  | 966 (2)  | -1162 (3) | 4.34             |
| C(23) | 9314 (1)  | 6273 (4) | 391 (7)   | 6.00             |
| C(24) | 8602 (1)  | 5181 (4) | 2089 (6)  | 5.50             |

normalized structure amplitudes by the *NORMAL* routine included in *MULTAN* 78 (Main, Hull, Lesinger, Germain, Declercq & Woolfson, 1978). The solution, using *MULTAN* 78, was based on 250 reflexions having  $|E| \geq 1.3$ . The  $E$  map corresponding to the solution with the best figure of merit (ABS FOM = 1.525, PSI ZERO = 2.030, RESID = 26.66) revealed the whole molecule. Refinement was by least squares minimizing  $\sum w |F_o| - |F_c|^2$ . A weighting scheme of type 3 from XRAY (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976) was used. The weights were assigned as  $w = w_1 w_2$ , where  $w_1 = 1$  for  $|F_o| \leq 25$  and  $w_1 = 25/|F_o|$  for  $|F_o| > 25$ ;  $w_2 = 1$  for  $\sin \theta \geq 0.30$  and  $w_2 = (\sin \theta)/0.3$  for  $\sin \theta < 0.30$ . Anisotropic refinement and a subsequent weighted difference synthesis located the H atoms. A scale factor, atomic coordinates of all the atoms and anisotropic thermal parameters of non-hydrogen atoms (277 variables in all) were refined. For the H atoms the isotropic thermal parameters were those of the bonded atoms plus one. Anisotropic thermal parameters are in the usual range: maximum values of  $U_{33}$  for C(15) and  $U_{22}$  for C(16) of 0.108 (4) and 0.097 (4) Å<sup>2</sup> were obtained, respectively. The final  $R = 0.036$  and  $R_w = 0.035$  for 1483 observed reflexions with  $I > 2\sigma(I)$ . An  $R = 0.047$  for the (1*R*, 4*S*, 6*R*) enantiomer was obtained. The absolute configuration was assigned as (1*S*, 4*R*, 6*S*) on the basis of the  $R$ -factor difference although the Bijvoet pairs were not measured.

Table 2. Positional parameters ( $\times 10^3$ ) for the H atoms

|        | $x$      | $y$     | $z$      |
|--------|----------|---------|----------|
| H(1)   | 905 (1)  | 166 (4) | -253 (5) |
| H(4)   | 946 (1)  | 407 (4) | 321 (5)  |
| H(6)   | 976 (1)  | 288 (3) | -256 (5) |
| H(11)1 | 816 (1)  | -95 (4) | 173 (6)  |
| H(11)2 | 850 (1)  | -11 (4) | 339 (6)  |
| H(13)  | 810 (1)  | 150 (4) | 567 (6)  |
| H(14)  | 753 (1)  | 344 (5) | 602 (6)  |
| H(15)  | 704 (1)  | 430 (5) | 332 (7)  |
| H(16)  | 715 (1)  | 311 (5) | -7 (7)   |
| H(17)  | 771 (1)  | 122 (4) | -50 (6)  |
| H(20)1 | 1061 (1) | 231 (4) | -67 (6)  |
| H(20)2 | 1051 (1) | 383 (4) | -175 (6) |
| H(20)3 | 1086 (1) | 376 (4) | 5 (6)    |
| H(22)  | 977 (1)  | 56 (4)  | 5 (5)    |
| H(23)1 | 912 (1)  | 699 (4) | -36 (6)  |
| H(23)2 | 943 (1)  | 662 (4) | 175 (6)  |
| H(23)3 | 963 (1)  | 604 (4) | -58 (6)  |
| H(24)1 | 841 (1)  | 599 (4) | 147 (6)  |
| H(24)2 | 839 (1)  | 433 (4) | 231 (6)  |
| H(24)3 | 871 (1)  | 553 (4) | 353 (6)  |

Scattering factors given by Cromer & Mann (1968) and (for H) Stewart, Davidson & Simpson (1965) were used. An anomalous-dispersion correction was included for S (Cromer & Liberman, 1970).

The calculations were carried out on a Univac 1110 computer at the University Computing Centre in Zagreb with the XRAY system (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976). Atom coordinates are listed in Tables 1 and 2.\*

### Description and discussion of the structure

The structural formula with the atom numbering and interatomic distances is given in Fig. 1. Bond angles are listed in Table 3. The conformation of the molecule is defined by the torsion angles listed in Table 4. The molecular packing is illustrated in Fig. 2.

\* Lists of structure factors, anisotropic thermal parameters and isotropic thermal parameters for H atoms have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35688 (15 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

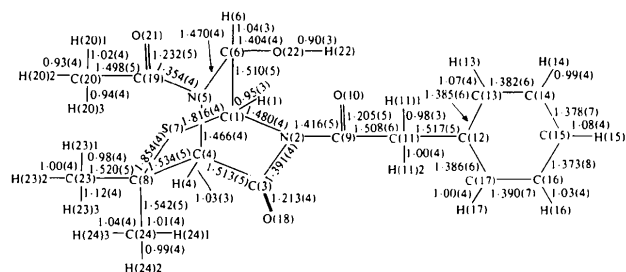


Fig. 1. The atom numbering and intramolecular distances (Å).

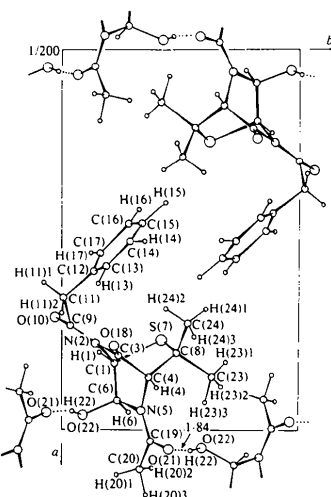


Fig. 2. A view of the crystal structure along *c*. Molecules are connected in an infinite chain by hydrogen bonds acting between acetyl and hydroxy groups: O(22)—H(22)···O(21), 2.732 (4) Å; ∠O(22)—H(22)—O(21), 168 (3)°.

Table 3. Bond angles (°)

|                 |           |                     |           |
|-----------------|-----------|---------------------|-----------|
| H(1)—C(1)—N(2)  | 110 (2)   | C(23)—C(8)—C(24)    | 110.5 (3) |
| H(1)—C(1)—C(6)  | 105 (2)   | N(2)—C(9)—O(10)     | 118.9 (3) |
| H(1)—C(1)—S(7)  | 110 (2)   | N(2)—C(9)—C(11)     | 118.2 (3) |
| N(2)—C(1)—C(6)  | 109.7 (2) | O(10)—C(9)—C(11)    | 122.7 (3) |
| N(2)—C(1)—S(7)  | 110.0 (2) | C(9)—C(11)—H(11)1   | 104 (2)   |
| C(6)—C(1)—S(7)  | 111.1 (2) | C(9)—C(11)—H(11)2   | 111 (2)   |
| C(1)—N(2)—C(3)  | 113.1 (3) | C(9)—C(11)—C(12)    | 110.1 (3) |
| C(1)—N(2)—C(9)  | 118.4 (3) | H(11)1—C(11)—H(11)2 | 112 (3)   |
| C(3)—N(2)—C(9)  | 128.4 (3) | H(11)1—C(11)—C(12)  | 112 (2)   |
| N(2)—C(3)—C(4)  | 111.5 (3) | H(11)2—C(11)—C(12)  | 107 (2)   |
| N(2)—C(3)—O(18) | 124.4 (3) | C(11)—C(12)—C(13)   | 120.9 (3) |
| C(4)—C(3)—O(18) | 124.0 (3) | C(11)—C(12)—C(17)   | 120.0 (4) |
| C(3)—C(4)—H(4)  | 105 (2)   | C(13)—C(12)—C(17)   | 119.1 (4) |
| C(3)—C(4)—N(5)  | 108.8 (3) | C(12)—C(13)—H(13)   | 122 (2)   |
| C(3)—C(4)—C(8)  | 111.2 (3) | C(12)—C(13)—C(14)   | 120.3 (4) |
| N(5)—C(4)—H(4)  | 110 (2)   | H(13)—C(13)—C(14)   | 117 (2)   |
| C(8)—C(4)—H(4)  | 110 (2)   | C(13)—C(14)—H(14)   | 122 (2)   |
| C(8)—C(4)—N(5)  | 112.1 (3) | C(13)—C(14)—C(15)   | 120.4 (5) |
| C(4)—N(5)—C(6)  | 114.9 (2) | H(14)—C(14)—C(15)   | 117 (2)   |
| C(4)—N(5)—C(19) | 121.2 (3) | C(14)—C(15)—H(15)   | 120 (2)   |
| C(6)—N(5)—C(19) | 123.7 (3) | C(14)—C(15)—C(16)   | 119.6 (5) |
| C(1)—C(6)—N(5)  | 106.7 (2) | H(15)—C(15)—C(16)   | 120 (2)   |
| C(1)—C(6)—O(22) | 112.3 (3) | C(15)—C(16)—H(16)   | 124 (2)   |
| N(5)—C(6)—O(22) | 112.7 (3) | C(15)—C(16)—C(17)   | 120.3 (5) |
| C(1)—C(6)—H(6)  | 109 (2)   | H(16)—C(16)—C(17)   | 116 (2)   |
| N(5)—C(6)—H(6)  | 109 (2)   | C(12)—C(17)—C(16)   | 120.2 (4) |
| O(22)—C(6)—H(6) | 107 (2)   | C(16)—C(17)—H(17)   | 121 (2)   |
| C(1)—S(7)—C(8)  | 96.5 (1)  | H(17)—C(17)—C(12)   | 119 (2)   |
| C(4)—C(8)—S(7)  | 106.8 (2) | N(5)—C(19)—C(20)    | 118.1 (3) |
| C(4)—C(8)—C(23) | 111.0 (3) | N(5)—C(19)—O(21)    | 120.8 (3) |
| C(4)—C(8)—C(24) | 109.9 (3) | C(20)—C(19)—O(21)   | 121.1 (3) |
| S(7)—C(8)—C(23) | 108.7 (3) | C(6)—O(22)—H(22)    | 107 (2)   |
| S(7)—C(8)—C(24) | 109.7 (2) |                     |           |

The C—C lengths for C in *sp*<sup>3</sup> hybridization range from 1.510 (5) to 1.542 (5) Å. Bond lengths in the phenyl ring are in the range 1.373 (8) to 1.390 (7) Å. There are two categories of C to N bonds: the C—N

Table 4. Torsion angles (°)

|                        |            |
|------------------------|------------|
| C(13)—C(12)—C(11)—C(9) | −128.2 (4) |
| C(12)—C(11)—C(9)—N(2)  | 67.1 (4)   |
| C(11)—C(9)—N(2)—C(3)   | 15.8 (5)   |
| O(18)—C(3)—N(2)—C(9)   | 6.7 (5)    |
| C(4)—C(3)—N(2)—C(1)    | 4.3 (4)    |
| N(2)—C(3)—C(4)—N(5)    | −57.1 (3)  |
| O(18)—C(3)—C(4)—N(5)   | 123.8 (3)  |
| N(2)—C(3)—C(4)—H(4)    | −174 (2)   |
| C(3)—C(4)—N(5)—C(19)   | −133.3 (3) |
| C(3)—C(4)—N(5)—C(6)    | 50.4 (3)   |
| C(4)—N(5)—C(6)—C(1)    | 6.6 (4)    |
| C(4)—N(5)—C(6)—O(22)   | −117.1 (3) |
| N(5)—C(6)—C(1)—S(7)    | 61.7 (3)   |
| H(6)—C(6)—C(1)—S(7)    | −56 (2)    |
| H(6)—C(6)—C(1)—H(1)    | 63 (3)     |
| C(3)—N(2)—C(1)—S(7)    | −67.1 (3)  |
| C(3)—C(4)—C(8)—S(7)    | −64.8 (3)  |
| C(3)—C(4)—C(8)—C(23)   | 176.9 (3)  |
| C(3)—C(4)—C(8)—C(24)   | 54.2 (4)   |
| C(1)—S(7)—C(8)—C(4)    | 5.0 (2)    |
| O(21)—C(19)—N(5)—C(4)  | 4.5 (5)    |
| C(20)—C(19)—N(5)—C(4)  | −175.1 (3) |
| H(22)—O(22)—C(6)—N(5)  | 52 (2)     |

Table 5. Displacements of atoms from least-squares planes (Å)

Atoms included in the calculations of the planes are denoted by asterisks.

| Plane I   |            |       |            |
|-----------|------------|-------|------------|
| N(2)*     | −0.045 (4) | N(5)* | −0.043 (4) |
| C(3)*     | 0.045 (5)  | C(1)  | −0.689 (5) |
| C(6)*     | 0.042 (5)  | C(4)  | −0.639 (5) |
| Plane II  |            |       |            |
| C(3)*     | 0.005 (4)  | C(8)* | −0.004 (5) |
| N(2)*     | −0.005 (4) | C(1)  | 0.787 (4)  |
| S(7)*     | 0.004 (1)  | C(4)  | 0.744 (4)  |
| Plane III |            |       |            |
| C(6)*     | −0.059 (4) | C(8)* | −0.052 (1) |
| N(5)*     | 0.065 (3)  | C(1)  | −0.838 (4) |
| S(7)*     | 0.046 (5)  | C(4)  | −0.691 (4) |

bonds [C(1)—N(2), 1.480 (4); C(4)—N(5), 1.466 (4); C(6)—N(5), 1.470 (4) Å] and N—C=O bonds [N(2)—C(9), 1.416 (5); N(2)—C(3), 1.391 (4); N(5)—C(19), 1.354 (4) Å]. The carbonyl bonds are 1.205 (5), 1.213 (4) and 1.232 (5) Å. The C—S bonds are 1.816 (4) and 1.854 (4) Å. Bond angles are in accordance with the given atom type and hybridization (Table 3).

The diazabicyclo[2.2.2]octane ring is puckered. The angle between the least-squares planes through N(2), C(3), C(6), N(5) (plane I, Table 5) and C(3), N(2), S(7), C(8) (plane II) is 62.4 (3)°; N(2), C(3), C(6), N(5) and C(6), N(5), S(7), C(8) (plane III) 62.4 (3)°; and C(6), N(5), S(7), C(8) and C(3), N(2), S(7), C(8) 55.5 (4)°. C(1) and C(4) are both displaced on the

same side of these planes (Table 5). Thus, the conformation of the diazabicyclo[2.2.2]octane ring is boat-boat-boat. The ring conformation can also be described by the sequence of torsion angles: C(1)–S(7)–C(8)–C(4)  $5.0(2)^\circ$ , C(4)–N(5)–C(6)–C(1)  $6.6(4)^\circ$  and C(4)–C(3)–N(2)–C(1)  $4.3(4)^\circ$ . The relative orientation of H(6) to S defined by torsion angle H(6)–C(6)–C(1)–S(7),  $-56(2)^\circ$ , is *cis*; thus the hydroxy group is in the *trans* orientation. The absolute configuration appears to be (1*S*,4*R*,6*S*).

Molecules are connected in an infinite chain by hydrogen bonds O(22)–H(22)···O(21),  $2.732(4) \text{ \AA}$  [ $\angle$ O(22)–H(22)–O(21) =  $168(3)^\circ$ ] between acetyl and hydroxy groups.

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#### References

- CROMER, D. T. & LIBERMAN, D. (1970). *J. Chem. Phys.* **53**, 1891–1898.
- CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst.* **A24**, 321–324.
- HERAK, J. J., KOVAČEVIĆ, M., LUKIĆ, I. & GAŠPERT, B. (1979). *Croat. Chem. Acta.* **52**, 311–320.
- KOJIĆ-PRODIĆ, B. & RUŽIĆ-TOROŠ, Ž. (1978). *Acta Cryst.* **B34**, 1271–1275.
- MAIN, P., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J. P. & WOOLFSON, M. M. (1978). *MULTAN 78. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.
- STEWART, J. M., MACHIN, P. A., DICKINSON, C., AMMON, H. L., HECK, H. & FLACK, H. (1976). The XRAY 76 system. Tech. Rep. TR-446. Computer Science Center, Univ. of Maryland, College Park, Maryland.
- STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.
- WILSON, A. J. C. (1942). *Nature (London)*, **150**, 151–152.