Acta Cryst. (1977). B**33**, 2165–2169

The Crystal and Molecular Structure of 1,4:3,6-Bis(thioanhydro)-2,5-*O*-acetyl-D-iditol (*R*,*R*)-Disulphoxide. Analysis of the Rotational Freedom of the Ester Group by means of Potential-Energy Calculations

By K. Börje Lindberg and Anna Wägner

Department of Structural Chemistry, Arrhenius Laboratory, University of Stockholm, S-104 05 Stockholm, Sweden

(*Received* 22 *November* 1976; *accepted* 10 *January* 1977)

The crystal structure of the title compound was determined from three-dimensional X-ray diffractometer data. It was solved by the heavy-atom method and refined to $R = 0{\cdot}054$. Crystals of $C_{10}H_{14}O_6S_2$ are monoclinic, space group $C2$, with $a = 18{\cdot}714\ (3)$, $b = 4{\cdot}9317\ (10)$, $c = 15{\cdot}101\ (3)$ Å, $\beta = 109{\cdot}72\ (3)°$, and $Z = 4$. There are two crystallographically independent sets of molecules, *A* and *B*, in the structure; angles, interatomic distances and ring conformations are almost identical for the two sets, however. The molecules have twofold symmetry, a crystallographic axis passing through the centre of each, and the rings possess a 'near envelope' conformation. The 'semi-torsion angles' H(2)–C(2)···C(4)–O(3) between the carbonyl bond in the ester group and the nearest C–H bond in the ring are ~40° instead of 0°, *i.e.* the ideal eclipsed conformation value. Potential-energy calculations show that the deviation is caused mainly by intramolecular interactions; therefore the molecules probably retain this conformation also in solution.

Introduction

The structure determination was undertaken as part of our series of investigations on acetylated carbohydrates. The title compound (Fig. 1) has also been studied by Kuszmann & Sohár (1972); the crystals used in our investigation were kindly supplied by Dr Kuszmann.

Structure determination

The cell dimensions were obtained from a powder photograph taken at 25 °C in a Guinier–Hägg focusing camera with monochromatized Cu $K\alpha_1$ radiation and with KCl ($a = 6{\cdot}29300$ Å) as an internal standard. The optical density curve of the Guinier photograph was measured with a SAAB filmscanner connected to an IBM 1800 computer and was evaluated by means of the program *PILT* (Malmros & Werner, 1973) on the same computer. The three-dimensional X-ray data were collected on a Philips PW1100 diffractometer, with graphite-monochromatized Cu $K\alpha$ radiation. The prismatic specimen crystal ($0{\cdot}03 \times 0{\cdot}18 \times 0{\cdot}05$ mm in the **a**, **b** and **c** directions respectively) was mounted with its *b* axis approximately aligned with the goniometer axis. Intensities were measured for all the 1389 reciprocal lattice points with $\theta < 78°$, with θ–2θ scans of 1·5° width; background intensities were measured at both ends of the scan intervals. 1305 intensities with $\sigma(I_{\rm net})/I_{\rm net} < 0{\cdot}5$ were considered to be observable, and were used in the structure determination. The calculations of $\sigma(I_{\rm net})$ were based on conventional counter statistics. Lorentz–polarization factors were applied, but not corrections for absorption. Both independent S atoms were located by a Patterson synthesis. The remaining atom positions were found on Fourier difference maps. Anomalous-dispersion corrections and successive cycles of anisotropic full-matrix least-squares refinement gave a final *R* value of 0·052 for the 1305 included data, and 0·054 for the 1389 measured data.* The positional parameters of the H atoms were

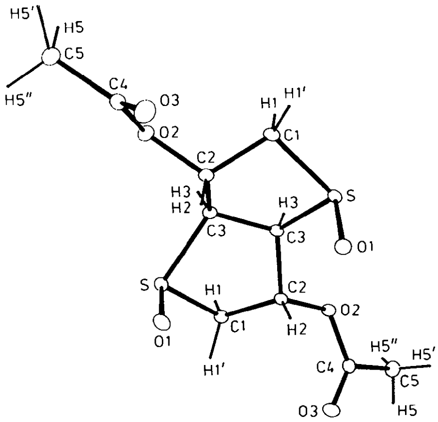

Fig. 1. Thermal-ellipsoid plot, with atom labels, of 1,4:3,6-bis(thioanhydro)-2,5-*O*-acetyl-D-iditol (*R*,*R*)-disulphoxide.

---

* Lists of observed and calculated structure factors and non-hydrogen anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32429 (4 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

refined with each H given the isotropic temperature factor of the atom to which it is bonded. Hughes's (1941) weighting scheme was used ($F_{\min} = 4·0$). Atomic coordinates and H isotropic thermal parameters are in Tables 1 and 2. Table 3 shows bond distances and angles, and Table 4 torsion angles.

Table 1. *Fractional atomic coordinates of the non-hydrogen atoms*

The estimated standard deviations are given in parentheses.

	x	*y*	*z*
Molecule *A*			
S	0·41138 (7)	0*	0·37286 (8)
O(1)	0·4132 (2)	−0·300 (1)	0·3876 (3)
O(2)	0·6328 (2)	0·096 (1)	0·4299 (2)
O(3)	0·6384 (3)	−0·266 (1)	0·3465 (3)
C(1)	0·4954 (3)	0·071 (1)	0·3435 (4)
C(2)	0·5606 (3)	0·008 (1)	0·4324 (3)
C(3)	0·5430 (3)	0·154 (1)	0·5103 (3)
C(4)	0·6663 (3)	−0·056 (2)	0·3828 (3)
C(5)	0·7400 (4)	0·057 (2)	0·3842 (6)
Molecule *B*			
S	0·48292 (6)	0·4520 (4)	0·12797 (7)
O(1)	0·4774 (2)	0·755 (1)	0·1143 (3)
O(2)	0·6707 (2)	0·330 (1)	0·0682 (2)
O(3)	0·7291 (3)	0·669 (2)	0·1605 (4)
C(1)	0·5825 (3)	0·367 (1)	0·1562 (3)
C(2)	0·5989 (3)	0·434 (1)	0·0670 (3)
C(3)	0·5369 (3)	0·294 (1)	−0·0115 (3)
C(4)	0·7330 (3)	0·474 (2)	0·1196 (4)
C(5)	0·8030 (4)	0·337 (4)	0·1166 (6)

* Assigned value.

Table 2. *Hydrogen fractional atomic coordinates and assigned isotropic temperature factors*

The estimated standard deviations are given in parentheses.

	x	*y*	*z*	*B*
Molecule *A*				
H(1)	0·489 (3)	−0·02 (2)	0·285 (3)	4·70
H(1′)	0·490 (3)	0·21 (2)	0·333 (4)	4·70
H(2)	0·565 (3)	−0·16 (2)	0·445 (4)	4·24
H(3)	0·443 (3)	0·31 (2)	0·485 (4)	4·21
H(5)	0·755 (3)	0·03 (2)	0·328 (5)	6·72
H(5′)	0·777 (3)	−0·02 (2)	0·436 (4)	6·72
H(5″)	0·740 (4)	0·20 (2)	0·363 (5)	6·72
Molecule *B*				
H(1)	0·610 (3)	0·47 (2)	0·207 (4)	4·74
H(1′)	0·582 (3)	0·16 (1)	0·165 (4)	4·74
H(2)	0·599 (3)	0·62 (1)	0·059 (4)	4·34
H(3)	0·450 (3)	0·10 (2)	0·013 (4)	4·40
H(5)	0·807 (4)	0·31 (2)	0·059 (5)	7·78
H(5′)	0·812 (4)	0·12 (2)	0·157 (5)	7·78
H(5″)	0·843 (4)	0·38 (2)	0·140 (5)	7·78

Potential-energy calculations

The interaction energies were calculated from the Lennard–Jones potential

$$\sum_{i>j}\sum -A_{ij}r_{ij}^{-6} + B_{ij}r_{ij}^{-12}$$

Table 3. *Intramolecular non-hydrogen bond distances and angles*

Estimated standard deviations are given in parentheses.

	Molecule *A*	Molecule *B*
S–O(1)	1·495 (5) Å	1·505 (5) Å
S–C(1)	1·807 (6)	1·816 (5)
S–C(3)	1·845 (5)	1·844 (5)
C(1)–C(2)	1·511 (7)	1·516 (7)
C(3)–C(3)	1·534 (10)	1·534 (9)
C(2)–C(3)	1·509 (7)	1·515 (7)
C(2)–O(2)	1·434 (6)	1·432 (6)
C(4)–O(2)	1·329 (7)	1·362 (9)
C(4)–O(3)	1·205 (10)	1·161 (13)
C(4)–C(5)	1·482 (10)	1·487 (12)
O(1)–S–C(1)	104·5 (3)°	106·2 (3)°
O(1)–S–C(3)	106·7 (2)	107·8 (2)
C(1)–S–C(3)	89·7 (2)	89·2 (2)
S–C(3)–C(2)	104·5 (4)	103·9 (3)
C(1)–C(2)–C(3)	105·7 (4)	105·4 (4)
S–C(1)–C(3)	108·1 (4)	108·0 (4)
C(2)–C(3)–C(3)	109·3 (5)	109·5 (4)
C(1)–C(2)–O(2)	113·5 (4)	112·4 (4)
C(3)–C(2)–O(2)	109·2 (4)	108·3 (4)
S–C(3)–C(2)	113·3 (4)	114·1 (4)
C(2)–O(2)–C(4)	117·4 (5)	116·0 (5)
O(2)–C(4)–O(3)	121·4 (5)	122·8 (6)
O(2)–C(4)–C(5)	112·6 (7)	109·8 (9)
O(3)–C(4)–C(5)	126·1 (6)	127·3 (8)

Table 4. *Torsion angles*

The estimated standard deviations are given in parentheses.

	Molecule *A*	Molecule *B*
C(3)–S–C(1)–C(2)	40·4 (4)°	42·4 (4)°
S–C(1)–C(2)–C(3)	−49·7 (5)	−50·4 (4)
C(1)–C(2)–C(3)–C(3)	34·6 (6)	33·6 (5)
C(2)–C(3)–C(3)–S	−4·8 (5)	−2·4 (5)
C(3)–C(3)–S–C(1)	−20·7 (4)	−23·1 (4)
O(1)–S–C(1)–C(2)	−66·7 (4)	−66·0 (4)
O(1)–S–C(3)–C(3)	84·4 (4)	83·7 (4)
O(1)–S–C(3)–C(2)	−36·8 (4)	−38·3 (4)
C(1)–S–C(3)–C(2)	−141·9 (4)	−145·1 (4)
C(4)–O(2)–C(2)–C(1)	−78·8 (6)	−78·2 (6)
C(4)–O(2)–C(2)–C(3)	163·5 (7)	165·6 (6)
C(2)–O(2)–C(4)–O(3)	−2·7 (9)	0·0 (11)
C(2)–O(2)–C(4)–C(5)	179·3 (8)	178·3 (9)
S–C(1)–C(2)–O(2)	−169·4 (6)	−168·2 (5)
O(2)–C(2)–C(3)–S	−82·4 (5)	−84·8 (4)
O(2)–C(2)–C(3)–C(3)	157·1 (6)	154·1 (5)
C(1)–C(2)–C(3)–S	155·2 (5)	154·7 (5)
C(2)–C(3)–C(3)–C(2)	118·8 (6)	122·3 (5)
S–C(3)–C(3)–S	−128·5 (4)	−127·2 (4)

Table 5. *Parameters used in the potential-energy calculations*

	$\alpha \times 10^{24}$ (cm^3)	N_i	R_i (Å)	q_i (e)	
				σ	π
S	0·50	14·80	1·80	−0·26	+0·30
O(1)	0·84	7·00	1·52	−0·03	−0·30
O(2)	0·59	7·00	1·52	−0·29	+0·10
O(3)	0·84	7·00	1·52	−0·14	−0·30
C(1)	0·93	5·20	1·70	−0·02	
C(2)	0·93	5·20	1·70	+0·13	
C(3)	0·93	5·20	1·70	+0·06	
C(4)	1·51	5·20	1·70	+0·30	+0·19
C(5)H$_3$	2·19	7·75	1·95	+0·01	+0·01
H(1)	0·42	0·85	1·20	+0·07	
H(2)	0·42	0·85	1·20	+0·05	
H(3)	0·42	0·85	1·20	+0·07	

and the 'monopole' approximation

$$\sum_{i>j}\sum q_i q_j \epsilon^{-1} r_{ij}^{-1} \text{ (with } \epsilon = 1).$$

The A_{ij} values were found from the Slater–Kirkwood equation:

$$A_{ij} = \tfrac{3}{2} e\hbar m^{-1/2} \alpha_i \alpha_j [(\alpha_i/N_i)^{1/2} + (\alpha_j/N_j)^{1/2}]^{-1}.$$

The values of α_i (the atomic polarizabilities) and N_i (the effective valence electron numbers) were taken from Scheraga (1968). The atomic polarizabilities for the atoms in the S=O and C=O bonds were increased owing to the double bonds. The B_{ij} values were derived from the minimum condition for the Lennard–Jones potential at the van der Waals distances ($R_i + R_j$). The σ charges were calculated using the Del Re (1958) method and the π charges were estimated from CNDO results on model compounds. All the parameters used are listed in Table 5.

Discussion

The structure determination shows that the unit cell contains two crystallographically independent sets of molecules, *A* and *B*. The two molecules within each set are related by the *C* centring translation; the twofold rotation symmetry, however, rotates two halves of each molecule. An interesting feature of the packing is that *A* is in closer contact with *A*, and *B* in closer contact with *B* than *A* is with *B*. This can be seen in Fig. 2 or inferred from Table 6.

The intermolecular distances indicate (Table 7) possible weak hydrogen bonding between the sulphoxide O atom in one molecule and a ring H atom in another molecule of the same set. There also seems to be an interaction between the carbonyl O atom of the ester group in set *A*, with a ring H atom in set *B*.

The conformations are almost identical for the *A* and *B* sets of molecules (Table 4) despite the differences in crystal field. This indicates that the conformation is determined principally by intramolecular interactions

Table 6. *Intermolecular contacts shorter than* 3·7 Å *involving non-hydrogen atoms*

Between *A* molecules		Between *B* molecules	
O(1)–C(3)	3·071 (7) Å	O(1)–C(3)	3·045 (7) Å
O(1)–C(5)	3·300 (9)	O(1)–C(5)	3·301 (8)
O(2)–O(3)	3·401 (8)	S–O(1)	3·446 (5)
S–O(1)	3·458 (5)	O(1)–C(1)	3·542 (7)
O(1)–C(1)	3·622 (8)	O(2)–O(3)	3·556 (9)
O(1)–C(3)	3·680 (7)	O(1)–C(3)	3·653 (7)

Between *A* and *B* molecules	
O(3)$_A$–C(1)$_B$	3·256 (8) Å

Table 7. *Possible hydrogen bonds*

Between *A* molecules in the **b** direction	
O(1)–H(3)	2·39 (7) Å
O(1)–C(3)	3·071 (7)
O(1)···H(3)–C(3)	146 (5)°
Between *B* molecules in the **b** direction	
O(1)–H(3)	2·23 (6) Å
O(1)–C(3)	3·045 (7)
O(1)···H(3)–C(3)	139 (4)°
Between *A* and *B* molecules in the **c** direction	
O(3)$_A$–H(1)$_B$	2·39 (6) Å
O(3)$_A$–C(1)$_B$	3·256 (8)
O(3)$_A$···H(1)$_B$–C(1)$_B$	159 (4)°

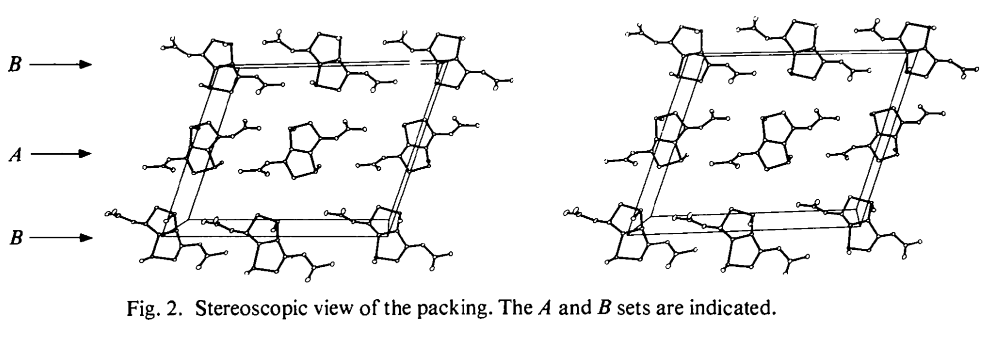

Fig. 2. Stereoscopic view of the packing. The *A* and *B* sets are indicated.

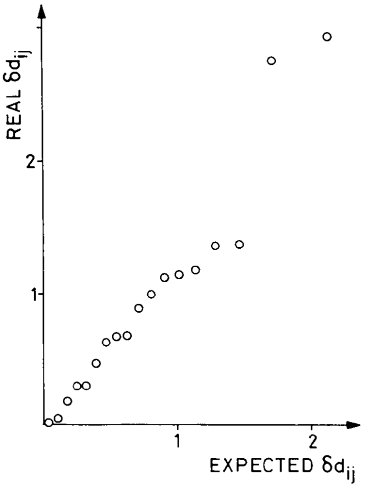

Fig. 3. Half-normal probability plot comparing the non-hydrogen intramolecular distances within the *A* molecules with those within the *B* molecules.

Table 8. *Orientation of the* OAc *group*

	A molecules	*B* molecules
H(2)–[C(2)–O(2)–C(4)]–O(3)	43 (7)°	41 (7)°
O(3)···H(2)	2·40 (6) Å	2·41 (5) Å

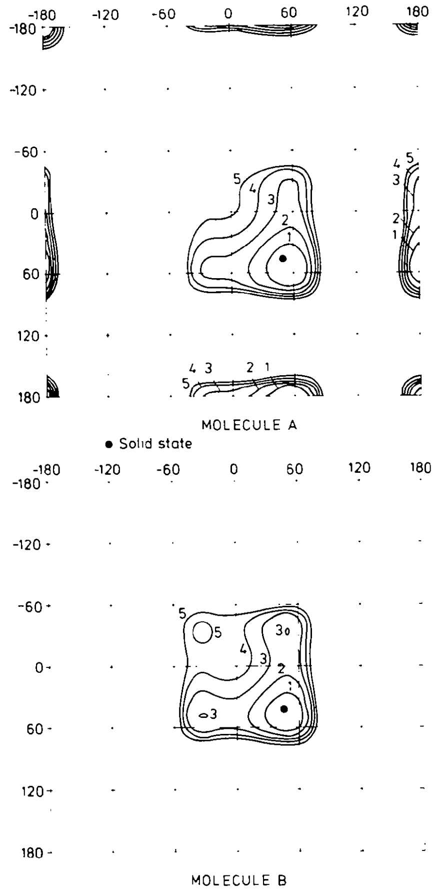

Fig. 4. Results of the potential-energy calculations in kcal mol⁻¹.

and, hence, that the solid-state conformation should be retained also in solution. NMR results show that this is the case for the ring conformations (Kuszmann, 1973).

All the molecules contain a double furanose ring, in which O is substituted by S. Each ring has the 'near envelope' ($_1E$) conformation, with C(1) displaced 0·83 Å out of the average plane in the *A* molecule, and 0·81 Å in *B*. The angles between the 'best planes' of the rings are 124 and 125° in the *A* and *B* molecules respectively.

Fig. 3 shows a comparison of intramolecular distances in the *A* molecule with the corresponding distances in the *B* molecule by means of a half-normal probability plot (Abrahams & Keve, 1970). They are seen to agree within the estimated standard deviations. The ester groups attached to the rings have, as observed earlier (Mathieson, 1965; Leung & Marchessault, 1974), a preference for the eclipsed conformation of the carbonyl O to the ring H (Table 8). However, the deviation from the ideal conformation is pronounced. The question arises whether this deviation is caused by the crystal field or by intramolecular interactions alone. The rotational freedom of the ester group *in vacuo* was therefore estimated by potential-energy calculations. The C(2)–O(2) bonds of the two acetyl groups in each molecule were rotated independently of each other, keeping all the other structural parameters fixed. Calculations were performed on both *A* and *B* molecules. The results of the calculations (Fig. 4) show minima at the observed solid-state values of the 'semi-torsion angles' and not at the expected values (0°, 0°). The result confirms the idea that the intramolecular interactions mainly determine the deviation of the ester group from the ideal eclipsed conformation. A comparison of the results from the two independent molecules also gives an estimation of the accuracy of this type of calculation. The only differences between the plots are the two extra minima (60°, 180°) and (180°, 180°) present in the result from the *A* molecule but not in that from *B*. These extra minima are probably caused by the inaccuracy of the positional parameters. The reason for this assumption is that the *antiperi* (180°) conformation has not yet been observed in all the crystal structures where an ester group (–OAc) is directly attached to a carbohydrate ring (about 110 ester groups).

We thank Dr J. Kuszmann for supplying the crystals. We also thank Professor Peder Kierkegaard for many stimulating discussions. We are indebted to Dr Sven Westman for revising the English of this article. This investigation has received financial support from the Swedish Natural Science Research Council.

References

Abrahams, S. C. & Keve, E. T. (1970). *Acta Cryst.* A**27**, 157–165.

Del Re, G. (1958). *J. Chem. Soc.* pp. 4031–4040.

Hughes, E. W. (1941). *J. Amer. Chem. Soc.* **63**, 1737–1752.

Kuszmann, J. (1973). Personal communications.

Kuszmann, J. & Sohár, P. (1972). *Carbohydr. Res.* **21**, 19–27.

Leung, F. & Marchessault, R. H. (1974). *Canad. J. Chem.* **52**, 2516–2521.

Malmros, G. & Werner, P.-E. (1973). *Acta Chem. Scand.* **27**, 493–502.

Mathieson, A. M. (1965). *Tetrahedron Lett.* **46**, 4137–4144.

Scheraga, H. A. (1968). *Advanc. Phys. Org. Chem.* **6**, 103–184.

Acta Cryst. (1977). B**33**, 2169–2174

The Crystal and Molecular Structure of Benzylpenicillin 1′-Diethyl Carbonate Ester

By I. Csöregh and T.-B. Palm

Department of Structural Chemistry, Arrhenius Laboratory, University of Stockholm, Fack,
S-104 05 Stockholm, Sweden

(*Received* 5 *November* 1976; *accepted* 5 *January* 1977)

The crystal structure of benzylpenicillin 1′-diethyl carbonate ester, $C_{21}H_{26}N_2O_7S$, has been determined and refined from three-dimensional X-ray diffractometer data. The unit cell is monoclinic, space group $P2_1$, with $a = 13{\cdot}307\ (6)$, $b = 8{\cdot}511\ (2)$, $c = 10{\cdot}300\ (3)$ Å, $\beta = 92{\cdot}45\ (3)°$ and $Z = 2$. The refinement was carried out by the least-squares method to a final linear R value of 0·040 for the 1928 significant observed reflexions. The packing in the crystal structure gives rise to short (2·844 Å) CO···C intermolecular contacts.

Introduction

Bacampicillin {1′-(ethoxycarbonyloxy)ethyl 6-[D-α-amino(phenyl)acetamido]penicillanate} (Fig. 1) is a new, orally well absorbed ampicillin derivative (Bodin *et al.*, 1975) with a novel type of hydrolysable ester group containing a chiral centre.

Bacampicillin is prepared from potassium benzylpenicillin (natural product) and racemic α-chlorodiethyl carbonate with benzylpenicillin 1′-diethyl carbonate ester as an intermediate. The product is obtained as a mixture of diastereoisomers relative to the chiral centre in the ester group.

The X-ray analysis was undertaken in order (*a*) to

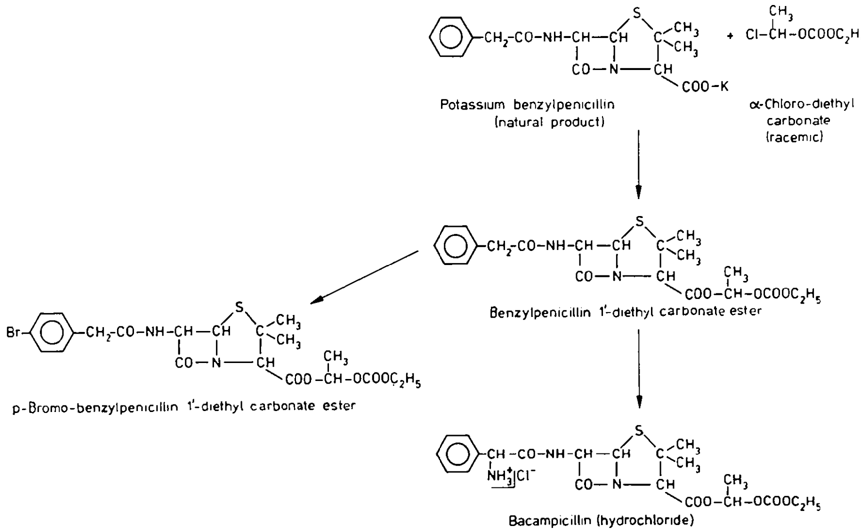

Fig. 1. Schematic figure showing the preparation of bacampicillin and *p*-bromobenzylpenicillin 1′-diethyl carbonate ester.