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AN UNUSUAL β-LACTAM RING EXPANSION REACTION

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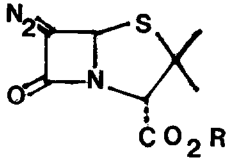
Summary Trichloroethyl 6-diazopenicillanate reacts with dithienium perchlorate to afford an unusual β-lactam ring expanded product.

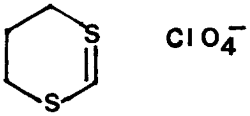
As part of a programme aimed at synthesising new penicillins possessing novel side-chains with potential anti-microbial and/or β-lactamase inhibitory activity, we have investigated the reaction of trichloroethyl 6-diazopenicillanate (1)[1] with dithiocarbenium species and now report an unusual rearrangement.

It was anticipated that reaction of (1) with dithienium perchlorate (2)[2] would yield the interesting structure (3). In the event conducting the reaction in anhydrous acetonitrile at temperatures ranging from -50° to $+80^{\circ}$ produced a complex reaction mixture from which a crystalline compound was obtained in ≈20% yield. The majority of the spectroscopic properties[3] of the product, including a ν max (KBr) at 1770 cm^{-1}, accorded with the structure (3). However minor inconsistencies led us to undertake an X-ray crystallographic analysis.

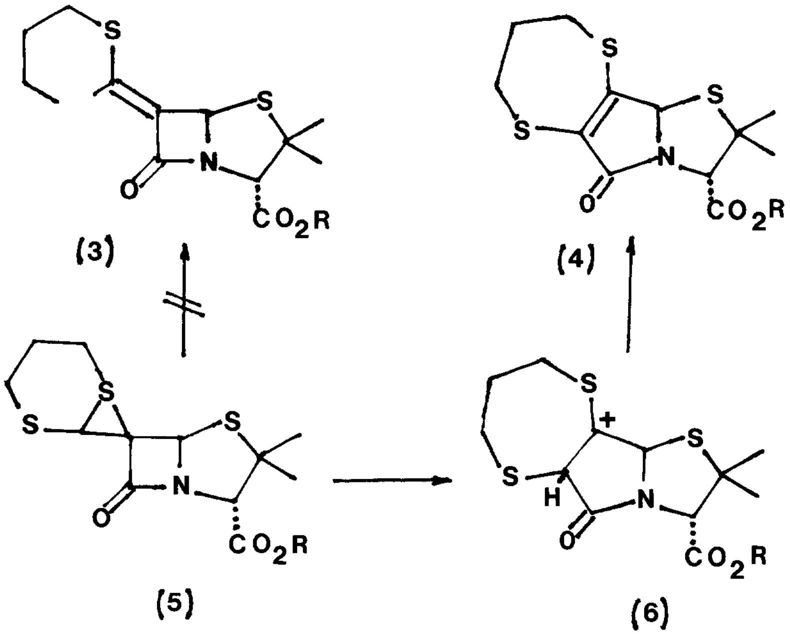


(1)

$R = CH_2CCl_3$



(2)



The crystals from isopropanol/water are orthorhombic, space group $P2_12_12_1$ with a = 6.093 (1), b = 27.830 (3), and c = 11.272(1)A^{o}. The structure was solved using MULTAN and refined using the 1553 reflection with $I>3\sigma(I)$ (Mo-K_α radiation, θ(max) 25°, graphite monochromator). The structure (4) thus revealed showed disorder in the seven membered ring which was modelled by using two positions for each of the carbon atoms next-but-one to the seven ring sulphur atoms. (Figure) The conformers were present in the approximate proportions 65:35, with refinement of non hydrogen atoms treated isotropically and hydrogens placed in calculated positions, the final R was 0.051.

There are considerable precedences to support the proposal that the spiro sulphenium ion (5) is initially formed from the reaction of (1) with (2). Presumably (5) does not collapse to the expected product (3) due to the substantial non-bonding interactions which would be imposed by its rigid geometry. Alternatively (5) can undergo either a 6,7 or 5,6 bond migration to the intermediate (6) which can then readily deprotonate to afford the observed product (4). In this particular case, it is not possible to distinguish which bond has migrated but in a recent communication a similar ring expansion was described which specifically involved the shift of the carbonyl group of the β-lactam ring.[5]

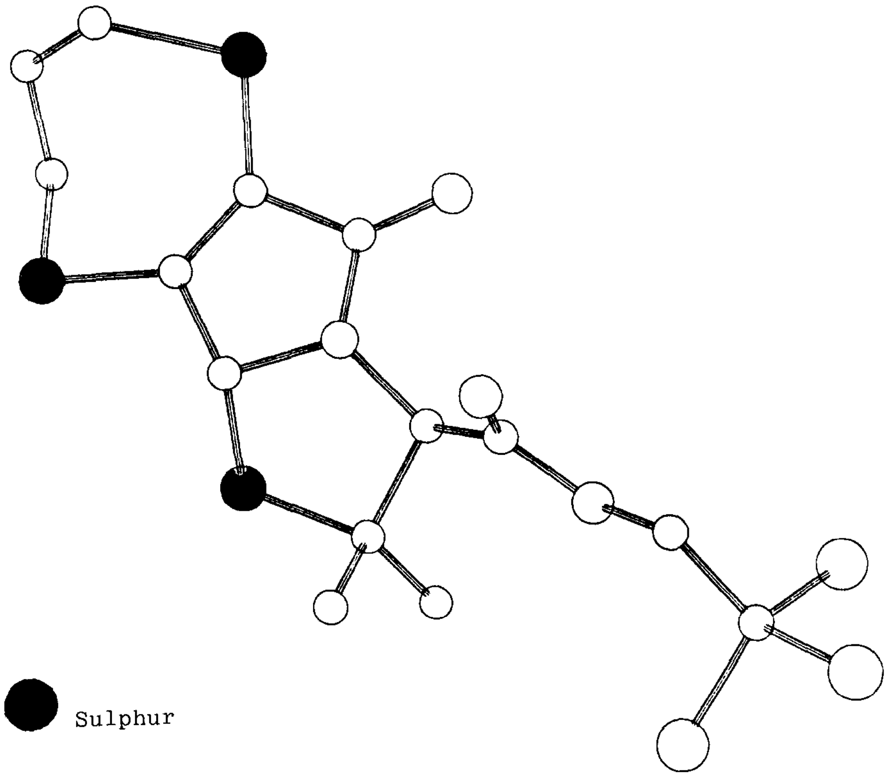


Figure. X-ray crystallographic structure of (4) showing major conformer of the seven-membered ring.

References

1. J.C. Sheehan, Y.S. Lo, J. Löliger and C.C. Podeswell, J.Org.Chem., 1974, 39, 14444.

2. Dithienium perchlorate was prepared from trityl perchlorate and excess 1,3-dithiane in anhydrous acetonitrile. A similar reaction product mixture yielding (4) was obtained with dithienium fluoroborate cf. E.J. Corey and S. Walinsky, J.Amer.Chem.Soc., 1972, 94, 8932.

3. This ester m.p. 163-164° exhibited the following spectroscopic properties: Found M^+ 446.9352; $C_{14}H_{16}Cl_3^{35}NO_3S_3$ requires 446.9358; $\lambda_{max}(CH_3CN)$ 237, 328nm. $^1H\delta(CDCl_3)$ 1.58 (3H,s,Me), 1.60 (3H,s,Me), 2.28-2,38 (2H,m,$-SCH_2-C\underline{H}_2-CH_2S-$), 3.33-3.87 (4H,m,$-S-C\underline{H}_2-CH_2-C\underline{H}_2-S$), 4.68 (1H,s,H-3), 4.72, 4.92 (2H,ABq,$-C\underline{H}_2Cl_3$), 5.66 (1H,S,H-5).

4. J.C. Sheehan, E. Chacko, Y.S. Lo, R. Ponzi and E. Sato, J.Org.Chem., 1978, 43, 4856; L. Chan and S.A. Matlin, Tetrahedron Letters, 1981, 4025 and references cited therein.

5. A.A. Jaxa-Chamiec, W.S. McDonald, P.G. Sammes, and R.R. Talekar, Tetrahedron Letters, 1982, 2813.

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