Tetrahedron Letters, Vol.31, No.26, pp 3685-3686, 1990
Printed in Great Britain

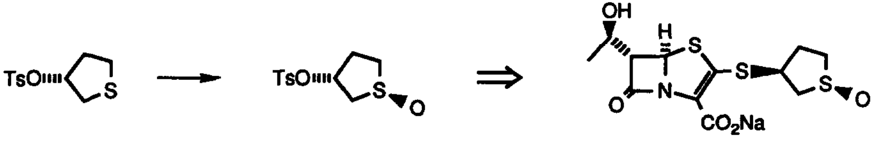
0040-4039/90 $3.00 + .00
Pergamon Press plc

DIASTEREOSELECTIVE OXIDATION OF SULFIDES TO SULFOXIDES WITH POTASSIUM PEROXYMONOSULFATE

George J.Quallich* and J.William Lackey
Pfizer Central Research
Process Research and Development
Groton, Connecticut 06340

Summary: Potassium peroxymonosulfate oxidation of sulfides to sulfoxides occurs with high diastereoselectivity.

In seeking a preparative process for the side chain of antibacterial CP-70,429, penem 1, we prepared the sulfoxide side chain 3 as a 4:1 mixture of trans and cis sulfoxides by oxidation of the sulfide 2 with m-chloroperoxybenzoic acid.[1] Chromatography was required to obtain the desired trans sulfoxide 3. Significant improvement in the diastereoselectivity of the oxidation was sought to improve the yield and eliminate the chromatography.



2 3 1

We were aware of the pioneering work of Johnson, who studied the oxidation stereochemistry of four, five, and six membered ring sulfides to the sulfoxides with a number of reagents.[2] Trost and Curran employed potassium persulfate in methanol as a convenient method to convert sulfides into sulfones. In their paper, one example of sulfide oxidation to the sulfoxide was reported without comment on stereochemistry.[3] During our research directed toward the development of an efficient synthesis of 1, two reports on the chemoselective oxidation of sufides to sulfoxides with potassium persulfate under phase transfer conditions and via catalytic use of N-sulfonyloxaziridines appeared, as did a review article.[4] Herein we report that these additives are not necessary to obtain good yields of sulfoxides in potassium persulfate oxidations, and high diastereoselectivity can also be obtained.

We discovered that diastereoselective oxidation of 2 into 3 was attained with potassium persulfate in aqueous acetone. Curci postulated a dioxirane intermediate as the oxidant in the epoxidations of olefins performed with potassium persulfate in aqueous acetone.[5] To evaluate whether this intermediate might account for the high diastereoselective oxidation, effect of solvents on the oxidation of 2 was investigated. All the results are tabulated in Table 1. This data demonstrate that good diastereoselective sulfide oxidation was obtained in all the solvents screened, and we believe that sulfide oxidation occurs faster than formation of the dioxirane intermediate. While all the solvents screened produced 3 with at least 10:1 selectivity, the manner in which the oxidation was conducted was found to affect the selectivity of the oxidation. To achieve high stereoselectivity, it was important to charge potassium persulfate all at once to the reaction, otherwise more sulfone and poor diastereoselectivity were obtained.[6]

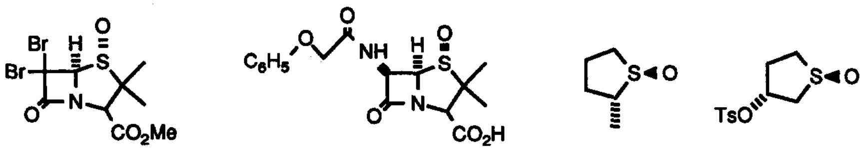
Examples of the diasteroselective oxidation obtained with potassium persulfate are depicted in Table 2. It is known that sulfide oxidation of penicillins with coordinating groups at the 6-position oxidize syn to that group. Oxidation of penicillin V afforded the syn sulfoxide, conforming to this tenet.[7] Penicillins without coordinating groups at the 6-position yield predominately the anti product.[8] Methyl dibromopenicillanate afforded the anti sulfoxide on reaction with potassium persulfate.[9] Finally, the oxidation of 2-methyltetrahydrothiophene yielded a modest increase in selectivity over m-chloroperoxybenzoic acid (70:30).[3c]

Table 1 Potassium persulfate oxidation of 2 in aqueous organic solvents (1:1)

Solvent	% Trans	%Cis	Trans/Cis Ratio
Methanol	58	2	29:1*
Isopropanol	94	6	16:1
t-Butanol	82	8	10:1*
Acetone	94	6	15:1
Acetic Acid	91	9	10:1
Acetonitrile	92	8	11:1
Tetrahydrofuran	95	5	19:1

* The remainder of the material was starting sulfide 2.

Table 2 Major product of potassium persulfate oxidation (ratio of diastereomers/%yield)



20:1/91% >20:1/85% 4:1/83% >10:1/90%

In summary, potassium persulfate has been found to be an inexpensive and useful oxidant in the diastereoselective conversion of sulfides into sulfoxides. It should be a practical addition to the reagents developed to date for the replacement of m-chloroperoxybenzoic acid as suppliers discontinue its sale.[10]

References and Notes

[1] E. Hamanaka, US 4,619,924 (1986); R. A. Volkmann, D. L. Lindner US 4,794,179.

[2] a) C.R.Johnson, and D.McCants, J. Am. Chem. Soc., 87, 1109 (1965). b) C.R.Johnson, J.J.Rigau, and C.C.Bacon, J. Org. Chem., 35, 3655 (1970). c) C.R.Johnson, and W.O.Siegl, ibid. 35, 3657 (1970).

[3] B.M.Trost, and D.P.Curran, Tetrahedron Letters, 22, 1287 (1981).

[4] F.A.Davis, and S.G.Lal, J. Org. Chem., 53, 5004 (1988), T.L.Evans, M.M.Grade Syn Comm. 1207 (1986), M. Madesclaire, Tetrahedron 42, 5459 (1986).

[5] R. W. Murray, R. Jeyaraman, J. Org. Chem., 50, 2847, (1985) and references cited within.

[6] The following experimental is representative of the oxidation procedure. At 0°C, a solution of potassium peroxymonosulfate (2.8g, 9.12mmole, 1.2eq.) in 40ml of water was added in one portion to a solution of sulfide 2 (2.0g, 7.75mmole, 1.0eq) in 40 ml of acetone with stirring. After stirring for 40 min, without external cooling, aqueous sodium bisulfite was added to the cloudy reaction mixture. The resulting clear solution was extracted with dichloromethane, dried with magnesium sulfate and evaporated under vacuum. The crude product 2.1g (99%) contained 90% of 3, 5% of the cis isomer and 5% of other impurities by HPLC. The crude product was crystallized from toluene to give 1.08g (51%) which was 98% pure and had a trans to cis ratio of 44:1. A second crop, 0.51g (24%) which was 88% pure had a trans to cis ratio of 10:1 was also recovered. Oxidation of thioanisole and tetrahydrothiopyran afforded crude sulfoxides with no sulfide and <2% and <4% sulfone respectively. Chromatography gave the sulfoxides in 91% and 85% yield respectively.

[7] E. Guddal, P. Morch, L. Tybring, Tetrahedron Letters 381, (1962). M. Davis, W. Wu, Aust. J. Chem. 39,1165, (1986).

[8] R. D. Cooper, P. V. DeMarco, J. C. Cheng, N. D. Jones, J. Am. Chem. Soc. 91, 1408 (1969). D. H. R. Barton, F. Comer, P. G. Sammes, J. Am. Chem. Soc., 91, 1528 (1969).

[9] R. A. Volkmann, B. B. Brown Tetrahedron Letters, 1545, (1986) and reference 11 cited within.

[10] See rear cover advertisement on J. Org. Chem., 55, No. 3, (1990).

(Received in USA 5 February 1990)