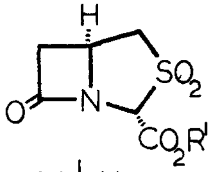
Tetrahedron Letters,Vol.24,No.43,pp 4731-4732,1983   0040-4039/83 $3.00 + .00
Printed in Great Britain

AN EFFICIENT SYTHESIS OF (±) 7-OXO-3-THIA-1-AZABICYCLO[3.2.0]HEPTANE-2-CARBOXYLATE-3,3-DIOXIDE

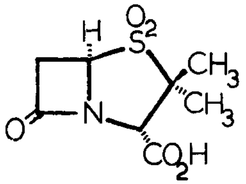
John Brennan* and Ivan L. Pinto,
Department of Chemistry, UMIST, P.O. Box 88, Manchester, M60 1QD

Abstract: The title compound was prepared in good yield *via* intramolecular insertion of an α-alkoxycarbonyl, α-sulphonyl carbene into the N-H bond of an azetidinone.

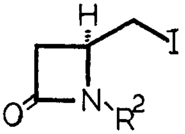
Esters of (±) 7-oxo-3-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate-3,3-dioxide, 1, are potentially useful intermediates in the synthesis of novel β-lactam compounds and are closely related in structure to penicillanic acid sulphone, 2, a powerful β-lactamase inhibitor.[1]



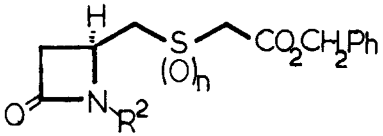
1 R^1=H
8 R^1=CH_2Ph



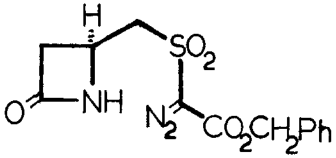
2



3 R^2=H
4 R^2=TBDMS



5 R^2=TBDMS n=0
6 R^2=H n=2



7

Only one synthesis of 1 has been reported and this was effected by oxidation of a bicyclic sulphide precursor,[2] several derivatives of which are known; these have all been prepared by insertion of sulphur or sulphide into the suitably activated C(2) and C(4) positions of the target bicyclic system.[3] The novel method described here is analogous to a route used in carbapenem synthesis and proceeds by N(1), C(2) bond closure;[4] in this case the high C-H acidity of monocyclic β-sulphonyl ester 6 facilitated diazo transfer to yield 7 which was catalytically decomposed to give 8 in good yield by an insertion of a carbenoid intermediate into the azetidinone N-H bond.

Thus 4-iodomethylazetidinone 3[5] was N-protected with the t-butyldimethylsilyl (TBDMS) group (TBDMS-Cl,Et$_3$N,DMF,0°) to yield 4 (97%); reaction of 4 with benzyl mercaptoacetate (NaH,THF,0°-20°) yielded sulphide 5[6] (78%); this was simultaneously oxidised and deprotected ("Oxone"[7],MeOH, H$_2$O) to yield sulphone 6 (90%). Diazo transfer (p-carboxybenzenesulphonyl azide, Et$_3$N,CH$_3$CN) gave diazoester 7 (83%) which cyclised upon decomposition (rhodium(II) acetate, benzene, 80°) to yield 8[8] (95%, 54% overall from 3) which was assigned the stereochemistry shown at C (2), presumed to be the thermodynamically more stable.

Hydrogenolysis of ester 8 (H$_2$,Pd-C, H$_2$O, EtOH, EtOAc, 1 equiv NaHCO$_3$) yielded the sodium salt of 1 (63%) as an amorphous solid.

References and Notes.

(1) A.R. English, J.A. Retsema, A.E. Girard, J.E. Lynch and W.E. Barth, Antimicrob Agents and Chemother., 1978, 14, 414.

(2) C.M. Pant and R.J. Stoodley, J. Chem. Soc., Chem. Commun., 1980, 928

(3) (a) W.F. Huffman, R.F. Hall, J.A. Grant and K.G. Holden, J. Med. Chem. 1978, 21, 413.
(b) G.H. Hakimelahi and A. Ugolini, Tetrahedron Lett., 1982, 913.
(c) K. Hirai, Y. Iwano and K. Fujimoto, Tetrahedron Lett., 1982, 4025.

(4) D.G. Melillio, I. Shinkai, T. Liu, K. Ryan and M. Sletzinger, Tetrahedron Lett., 1980, 2783.

(5) T. Tanaka and T. Miyadera, Heterocycles, 1982, 19, 1497;use of freshly distilled allyl iodide and addition of Na$_2$CO$_3$ to the reaction mixture gave 3 in yields of 55 - 60% (reported 37%).

(6) All compounds are racemic mixtures of which one isomer is shown; all new compounds exhibited satisfactory microanalytical and/or spectroscopic properties.

(7) B.M. Trost and D.P. Curran, Tetrahedron Lett., 1981, 1287.

(8) Compound 8 m.p. 102-103°; ir (nujol), 1790, 1760 cm^{-1}; nmr (CDCl$_3$), δ, 3.05-3.20 (2H,m,C-4 and C-6), 3.50 (1H,dd, J=7.3 Hz, 13.4 Hz, C-4), 3.64 (1H,dd, J=4.9Hz, 15.9Hz, C-6), 4.35 (1H,m,C-5), 5.25 (2H,2s, ester CH$_2$), 3.35 (1H, s, C-2), 7.39 (5H,s, ester Ph)

(Received in UK 18 August 1983)