The Oxoazetidinesulphenic Acid Anion: *S*- *vs.* *O*-Alkylation

By G. A. KOPPEL* and S. KUKOLJA

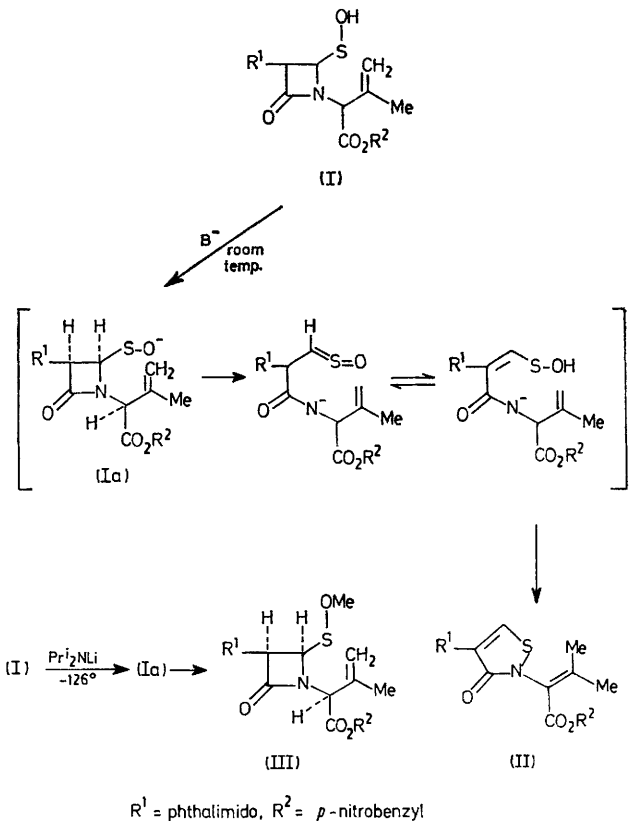
(*The Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, Indiana* 46206)

Summary The anionic intermediate (Ia) derived by treatment of the oxoazetidinesulphenic acid (I) with lithium di-isopropylamide in tetrahydrofuran at −126° undergoes exclusive *O*-alkylation to give the sulphenate (III).

THE intermediacy of the azetidinesulphenic acid (I), which has recently been isolated, has been proposed in the rearrangement of penicillin sulphoxide into the cephem and azetidinothiazoline systems,[3] and in the epimerization of penicillin (*R*)-sulphoxide into the corresponding (*S*)-sulphoxide.[4] Surprisingly the sulphenic acid (I) is quite stable in the crystalline form, whereas in solution it reverts to starting sulphoxide.[1] We have investigated the stability of the sulphenic acid anion (Ia) and its ambident nucleophilic character.

We felt that a weak base should effect deprotonation of (I) to (Ia). Thus, treatment of (I; R^1 = phthalimido, R^2 = *p*-nitrobenzyl) with 4-methylmorpholine in CH_2Cl_2 gave the isothiazolone (II) in excellent yield, m.p. 189—190°, *m/e* 479 (M^+).† The sulphur lone pair–oxygen anion interaction apparently causes formation of the unstable anion (Ia) which spontaneously fragments to relieve this electronic repulsion and then recyclizes to (II).

In attempts to suppress this fragmentation and stabilize the anion (Ia), we treated (I) with 1 equiv. of lithium di-isopropylamide in tetrahydrofuran (THF) at −78°. Subsequent quenching with methyl fluorosulphonate afforded only polymeric material. However, generation of the anion (Ia; R^1 = phthalimido, R^2 = *p*-nitrobenzyl) with lithium di-isopropylamide in THF at −126° and reaction



† When the sulphenic acid is protected as its silyl ester, no rearrangement occurs, suggesting that formation of the sulphenic acid anion is essential for this reaction. See ref. 1.

with methyl fluorosulphonate gave the sulphenate (III) after work up and preparative thick layer chromatography in 60% yield; ν_{max} 915 cm^{-1} (S–OMe); τ ($CDCl_3$) 1·9 br (s, MeC=), 4·14 (s, 3- and 4-H), 4·80—5·0 (m, $=CH_2$), and 6·47 (s, OMe); *m/e* 511 (M^+) and 479 $(M - 32)^+$; λ_{max} (EtOH) 265 nm (ϵ 1·3 × 10^3).

Sulphenic acid anions have been reported to be unstable and to undergo dimerization to thiosulphinates.[5] The fact that (Ia) rearranges much more rapidly than it dimerizes might be due to the large steric requirements of the azetidinone group and the ready rupture of the C(5)–N bond by a β-elimination mechanism. The exclusive *O*-alkylation of (Ia) is in contrast to the alkylation of phosphinic acids which gives predominant *P*-alkylation.[6]

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[6] T. S. Chou (*Tetrahedron Letters*, 1974, 725) has reported *O*-silylation of sulphenic acids; alkylation conditions which give exclusive *O*-alkylation with (Ia) yield methyl dimethyl phosphonate (60%) with the anion derived from dimethyl phosphite.