

The Reaction of 2,3-Disubstituted 1,2-Thiazetidine 1,1-Dioxides with Butyl-lithium

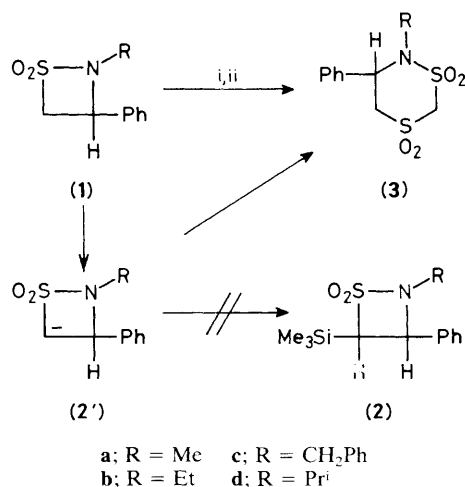
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When treated with butyl-lithium the title compounds are shown to undergo dimerisation and rearrangement yielding a new type of six-membered heterocycle.

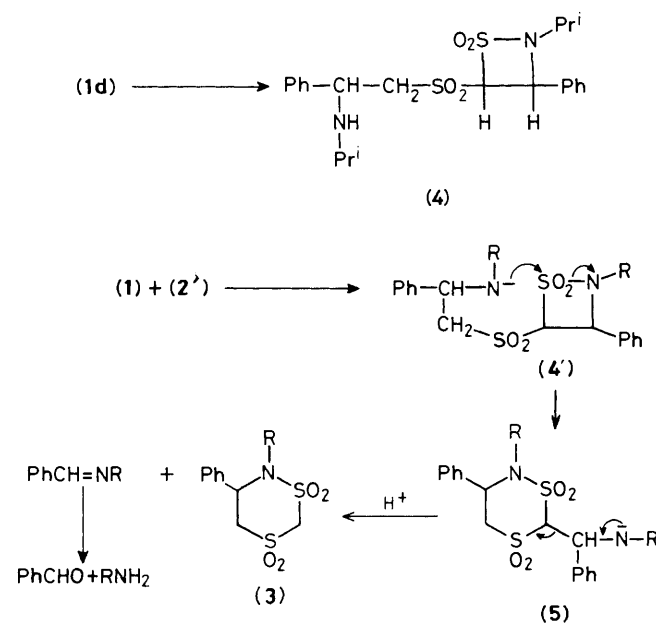
It is generally assumed that the antibacterial activity of β -lactam antibiotics depends on the stability and reactivity of the four-membered ring. Replacement of the carbonyl group in β -lactams by the sulphonyl group results in 1,2-thiazetidine 1,1-dioxides, β -sultams, which are more reactive than the corresponding β -lactams. Furthermore these β -sultams are valuable intermediates for synthesis of other heterocycles¹ and provide novel entries into a variety of systems including biologically interesting bicyclic systems.^{2,3} We have recently reported effective methods for the synthesis of monocyclic⁴ and bicyclic systems.² In this communication we report an unusual reaction of 2,3-disubstituted β -sultams with deprotonating reagents, e.g. butyl-lithium or lithium diisopropylamide.

When compound (1a) was dissolved in tetrahydrofuran (THF) and *n*-butyl-lithium was added at -78°C deprotonation occurred fairly rapidly, but the addition of Me_3SiCl did not result in formation of the expected substitution product (2) as is known to occur with β -lactams. After hydrolytic work-up we isolated a product, $\text{C}_{10}\text{H}_{13}\text{NO}_4\text{S}_2$, m.p. $213\text{--}215^\circ\text{C}$, which



Scheme 1. Reagents: i, $\text{Bu}^\bullet\text{Li}$, -78°C , THF; ii, HCl, H_2O .

contains two sulphonyl groups. Its ^1H n.m.r. spectrum ($[\text{D}_6\text{H}_6]$ acetone, 250 MHz) shows signals due to one *N*-methyl group (δ 2.64, s, 3H), one CH_2 -group (δ 4.92, dd, 1H, 3-H; δ 5.05 m, 1H, 3'-H), and one AMX system (δ 3.72, m, 1H, 5'-H; δ 4.05, dd, 1H, 5-H; δ 5.46, dd, 1H, 6-H). Its ^{13}C n.m.r. spectrum ($[\text{D}_6\text{H}_6]$ acetone, 20.15 MHz) shows corresponding signals [δ 29.67 (s, *N*-Me), 47.07 (s, 5-C), 55.89 (s, 6-C), 64.41 (s, 3-C), and 127.44—134.56 (6s, Ar-C)], and together with its i.r. (KBr, 1360, 1320, 1170, and 1140 cm^{-1}) and mass spectra (m/z 275, M^+) established structure (3a).[†] Analogous products (3b)[†] and (3c)[†] were isolated starting from (1b) and (1c), respectively. However, (1d) did not yield (3d), but



Scheme 2

[†] All new compounds gave satisfactory spectral data and elemental analyses: yields: (3a) 87%; (3b) 80%; (3c) 83%; (4) 49%.

instead a crystalline compound having the structure (4)⁺ was isolated. Chlorotrimethylsilane is not incorporated into any of these products (Scheme 1).

For an explanation of this surprising reaction we postulate the sequence in Scheme 2. The deprotonated sultam (2') reacts with another molecule of (1) forming the 'dimeric' anion (4'). Intramolecular rearrangement yields the anion of an unstable Mannich base (5), which on acidification decomposes yielding (3). In the case of (1d) (R = Prⁱ), the dimeric product is stable; the rearrangement is probably sterically hindered by the bulky isopropyl group. Me₃SiCl is not involved but yields on hydrolysis HCl which is used for the hydrolytic fragmentation of (5). This was proved by reactions in the absence of Me₃SiCl; the reaction proceeds in the same way if a trace of HCl is added to the NaCl solution which is used for hydrolytic workup.

To the best of our knowledge a similar reaction has not been described previously for four-membered rings. Furthermore it provides a simple synthesis of the hitherto unknown 2,4,1-dithiazine 2,2,4,4-tetroxides,⁵ which show some other

interesting reactions, on which we shall report in a forthcoming paper.

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References

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- 4 E. Meyle and H. H. Otto, *Arch. Pharm. (Weinheim, Ger.)*, 1983, **316**, 281.
- 5 According to 'Revision of the extended Hantzsch-Widman System of Nomenclature for Heteromonocycles,' *Pure Appl. Chem.*, 1979, **51**, 1995, the system is numbered without regard to priority beginning at N as this gives the lowest set of numbers.