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

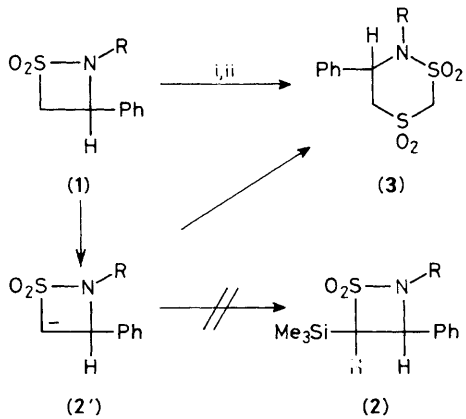
Eberhard Meyle and Hans-Hartwig Otto*

Department of Chemistry and Pharmacy, University of Freiburg, Hermann-Herderstrasse 9,D-7800 Freiburg, Germany

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

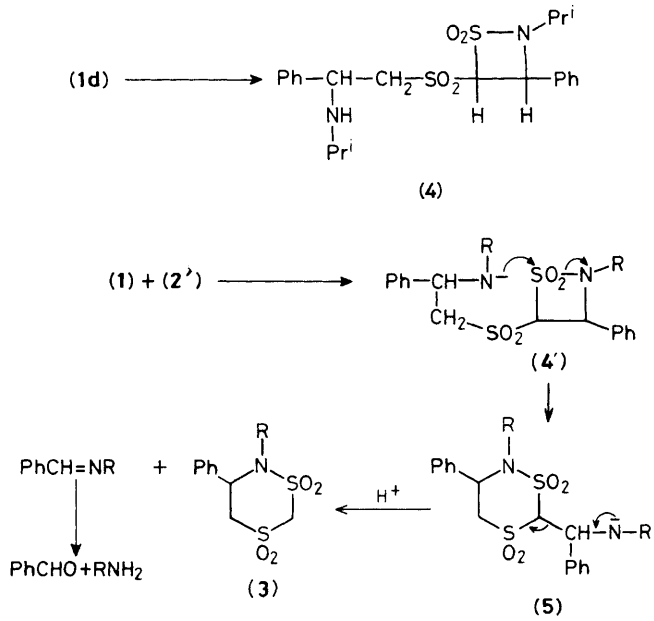
It is generally assumed that the antibacterial activity of β-lactam antibiotics depends on the stability and reactivity of the four-membered ring. Replacement of the carbonyl group in β-lactams by the sulphonyl group results in 1,2-thiazetidine 1,1-dioxides, β-sultams, which are more reactive than the corresponding β-lactams. Furthermore these β-sultams are valuable intermediates for synthesis of other heterocycles[1] 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 monocyclic[4] 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 di-isopropylamide.

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, $C_{10}H_{13}NO_4S_2$, m.p. 213—215 °C, which contains two sulphonyl groups. Its ^1H n.m.r. spectrum ([$^2H_6$]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 ([$^2H_6$]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



a; R = Me **c**; R = CH_2Ph
b; R = Et **d**; R = Pr^i

Scheme 1. *Reagents:* i, Bu^nLi, −78 °C, THF; ii, HCl, H_2O.



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 = Pr^i), the dimeric product is stable; the rearrangement is probably sterically hindered by the bulky isopropyl group. Me_3SiCl 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 Me_3SiCl; 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.

Support of this work by a grant from the Deutsche Forschungsgemeinschaft is gratefully acknowledged.

Received, 14th May 1984; Com. 673

References

1 E. Meyle, Thesis, Freiburg, 1983.
2 H. H. Otto and P. Schwenkkraus, *Tetrahedron Lett.*, 1982, **23**, 5389.
3 F. Cavagna, W. Koller, A. Linkies, H. Rehling, and D. Reuschling, *Angew. Chem.*, 1982, **94**, 549.
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.