

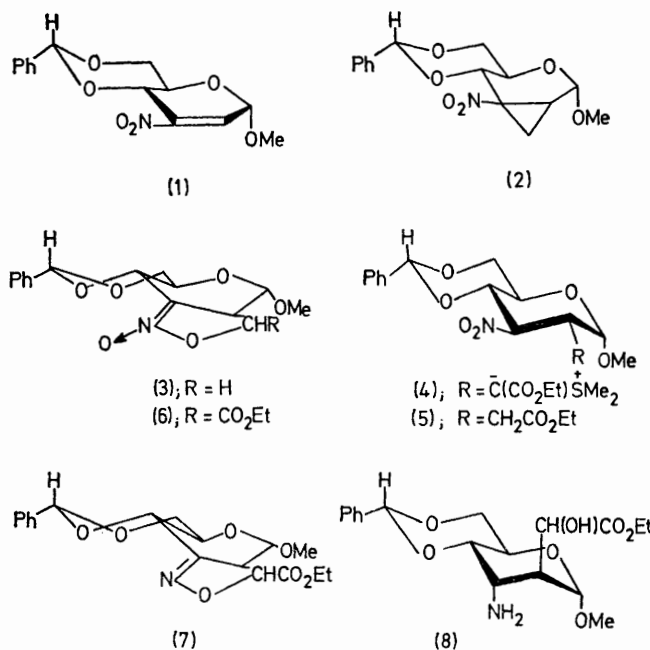
Preparation of Isoxazoline *N*-Oxide Derivatives from a Nitro-sugar and *S*-Ylides

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Summary Axial attack predominates over equatorial attack in the addition of dimethylsulphoxonium methylide and ethyl dimethylsulphuranylideneacetate to the nitro-sugar (**1**); axial attack selectively gave the 1,4-addition products (**3**) and (**6**), whereas equatorial attack afforded the 1,2-addition products (**2**) and (**4**), respectively.

VERY few examples are known of reactions between nitro-olefins and *S*-ylides,¹ where the product is a cyclopropane^{2,3} or stabilized *S*-ylide derivatives.³ We report preparations of the isoxazoline *N*-oxides (3) and (6) from the nitro-sugar (1)⁴ and *S*-ylides which are the first examples of 1,4-addition between a nitro-olefin and *S*-ylides.



Treatment of (1) with dimethylsulphoxonium methylide in Me₂SO at 0 °C gave a mixture of the cyclopropane (2) (16.5%), m.p. 131–132 °C, $[\alpha]_D^{20} + 35.0^\circ$ (*c* 1, CHCl₃), ν_{\max} (KBr) 1550 (NO₂) cm⁻¹, and the isoxazoline *N*-oxide (3) (56.2%), m.p. 178.5–179.5 °C; $[\alpha]_D^{20} - 139.2^\circ$ (*c* 1, CHCl₃), ν_{\max} (KBr) 1640 (C=N) cm⁻¹, which were separated by column chromatography on silica gel. Elemental analyses of both compounds corresponded to C₁₅H₁₇NO₆. The cyclopropane structure of (2) was determined from its i.r. (the presence of NO₂ absorption band) and n.m.r. (the presence of cyclopropane ring protons at δ 2.61, 2.18, and 1.98)

† Satisfactory elemental analysis has not yet been obtained for (4).

¹ B. M. Trost and L. S. Melvin, Jr. in 'Sulfur Ylides, Emerging Synthetic Intermediates.' Academic Press, New York, 1975.

² J. Asunkis and H. Shechter, *J. Org. Chem.*, 1968, **33**, 1164.

³ T. Sakakibara, T. Takamoto, R. Sudoh, and T. Nakagawa, *Chem. Letters*, 1972, 1219.

⁴ H. H. Baer and F. Kienzle, *Canad. J. Chem.*, 1967, **45**, 983.

⁵ B. Radatus and B. Fraser-Reid, *Canad. J. Chem.*, 1972, **50**, 2909.

⁶ P. M. Collins, D. Gardiner, S. Kumar, and W. G. Overend, *J.C.S. Perkin I*, 1972, 2611.

spectra. The *allo*-configuration of (2) was assigned on the basis of the value of $J_{1,2}$ (6.3 Hz)⁵ and that of long range coupling (1.0 Hz) between the *exo*-proton of the cyclopropane ring and H-4. The structure of (3) was deduced from a comparison of its i.r. and n.m.r. spectra with those of (6) described below.

Reaction of (1) with ethyl (dimethylsulphuranylidene)-acetate in tetrahydrofuran (THF) at 0 °C gave a mixture of the stabilized *S*-ylide (4)† (*ca.* 22%, as syrup) and the isoxazoline *N*-oxide (6) (54.9%), m.p. 151.5–152.0 °C (decomp.), $[\alpha]_D^{20} - 121^\circ$ (*c* 1, CHCl₃), which were separated by preparative t.l.c. The former, having the characteristic absorption band of the ester carbonyl group of the ylide species at 1630 cm⁻¹ in its i.r. spectrum and two methyl signals (SMe₂) in its n.m.r. spectrum, was characterized as the reduced compound (5), m.p. 91.5–92.0 °C, $[\alpha]_D^{20} + 72^\circ$ (*c* 1, CHCl₃), ν_{\max} (KBr) 1720 (CO₂Et) and 1550 (NO₂) cm⁻¹, $J_{1,2}$ 3.1 and $J_{2,3} = J_{3,4} = 11.1$ Hz, obtained by catalytic hydrogenation of (4) over 10% palladium on charcoal.

The structure of (6) was determined on the basis of its elemental analysis (molecular formula C₁₈H₂₁NO₆) and i.r. [KBr, ν (NO₂), ν (C=N) 1645 and ν (CO₂Et) 1720 cm⁻¹] and n.m.r. (CO₂Et, and $J_{1,2}$ 6.0 Hz) spectroscopy. This was supported by the fact that treatment of (6) with Ph₃P in boiling benzene for 15 h afforded the isoxazoline (7) (91%), m.p. 159–160 °C, $[\alpha]_D^{20} - 120^\circ$ (*c* 0.5, CHCl₃). The *arabino*-configuration of (6) was assigned chemically. Reduction of (6) with Raney nickel afforded a mixture of at least two products as identified by n.m.r. spectroscopy, from which crystals of the *all-endo*-pyranoside (8) were isolated in 35% yield, m.p. 167–168 °C, $[\alpha]_D^{20} + 64.2^\circ$ (*c* 1, CHCl₃), ν_{\max} (KBr) 3380 (OH), 3310 (NH), and 1718 and 1700 (CO₂Et) cm⁻¹, $J_{1,2}$ 0, $J_{2,3}$ 1.3, and $J_{3,4}$ 3.8 Hz.

No other product was formed in either reaction, as shown by n.m.r. spectroscopy, suggesting that the 1,4-addition occurred selectively when the *S*-ylides approached C-2 axially, whereas 1,2-addition took place when the *S*-ylides approached equatorially. It is noteworthy that similar nucleophilic addition of dimethylsulphoxonium methylide to the 3-arylaazo-derivatives of (1) gave only the 1,4-adducts regardless of the direction of approach of the nucleophile.⁶

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