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

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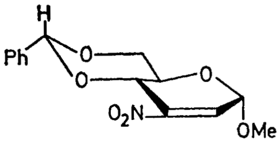
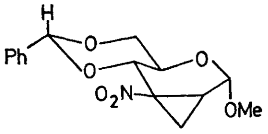
Summary Axial attack predominates over equatorial attack in the addition of dimethylsulphoxonium methylide and ethyl dimethylsulphuranylideneacetate to the nitro-sugar (**1**); axial attack selectively gave the 1,4-addition products (**3**) and (**6**), whereas equatorial attack afforded the 1,2-addition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

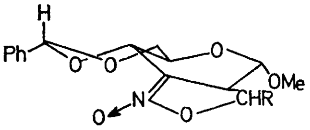
Very few examples are known of reactions between nitro-olefins and *S*-ylides,[1] where the product is a cyclopropane[2,3] or stabilized *S*-ylide derivatives.[3] We report preparations of the isoxazoline *N*-oxides (**3**) and (**6**) from the nitro-sugar (**1**)[4] and *S*-ylides which are the first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



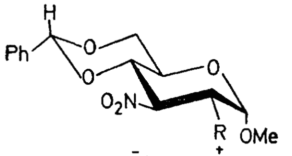
(1)



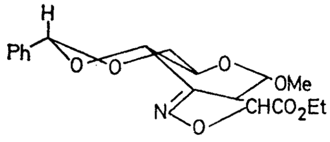
(2)



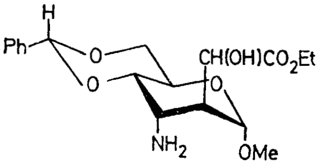
(3); R = H
(6); R = CO$_2$Et



(4); R = $\bar{C}(CO_2Et)\overset{+}{S}Me_2$
(5); R = CH$_2$CO$_2$Et



(7)



(8)

Treatment of (**1**) with dimethylsulphoxonium methylide in Me$_2$SO at 0° C gave a mixture of the cyclopropane (**2**) (16·5%), m.p. 131—132 °C, $[\alpha]_D^{20}$ +35·0° (*c* 1, CHCl$_3$), ν_{max} (KBr) 1550 (NO$_2$) cm^{-1}, and the isoxazoline *N*-oxide (**3**) (56·2%), m.p. 178·5—179·5 °C; $[\alpha]_D^{20}$ −139·2° (*c* 1, CHCl$_3$), ν_{max} (KBr) 1640 (C=N) cm^{-1}, which were separated by column chromatography on silica gel. Elemental analyses of both compounds corresponded to $C_{15}H_{17}NO_6$. The cyclopropane structure of (**2**) was determined from its i.r. (the presence of NO$_2$ absorption band) and n.m.r. (the presence of cyclopropane ring protons at δ 2·61, 2·18, and 1·98) 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° (*c* 1, CHCl$_3$), 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 (SMe$_2$) in its n.m.r. spectrum, was characterized as the reduced compound (**5**), m.p. 91·5—92·0 °C, $[\alpha]_D^{20}$ +72° (*c* 1, CHCl$_3$), ν_{max} (KBr) 1720 (CO$_2$Et) and 1550 (NO$_2$) 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 $C_{18}H_{21}NO_8$) and i.r. [KBr, no ν (NO$_2$), ν (C=N) 1645 and ν(CO$_2$Et) 1720 cm^{-1}] and n.m.r. (CO$_2$Et, and $J_{1,2}$ 6·0 Hz) spectroscopy. This was supported by the fact that treatment of (**6**) with Ph$_3$P in boiling benzene for 15 h afforded the isoxazoline (**7**) (91%), m.p. 159—160 °C, $[\alpha]_D^{20}$ −120° (*c* 0·5, CHCl$_3$). 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 *altro*-pyranoside (**8**) were isolated in 35% yield, m.p. 167—168 °C, $[\alpha]_D^{20}$ +64·2° (*c* 1, CHCl$_3$), ν_{max} (KBr) 3380 (OH), 3310 (NH), and 1718 and 1700 (CO$_2$Et) 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-arylazo-derivatives of (**1**) gave only the 1,4-adducts regardless of the direction of approach of the nucleophile.[6]

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

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