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CYCLOADDITIONS OF AN AZIRIDINE VIA AZOMETHINE YLIDE TO HETEROMULTIPLE BONDS

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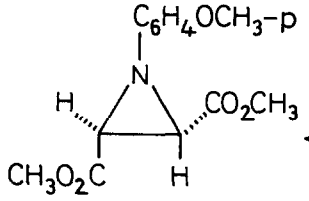
Recent reports on the cycloadditions of aziridines to heteromultiple bonds to form 5-membered heterocycles (1-5) make it desirable to publish briefly our experimental results which go back several years. 2,3-Diphenyl-1-(p-methoxy-phenyl)aziridine (1) has served as model substance to establish the steric course and the kinetics of the electrocyclic ring opening to azomethine ylides (6,7). The same model was used in a preliminary investigation to examine the range of applicable dipolarophiles which contain heteromultiple bonds.

On heating 1 with 10 equiv. of benzaldehyde for 48 hrs. at 120°, three diastereomeric oxazolidines were formed and separated by thick-layer chromatography (t.l.c.). N.m.r. analysis showed that the original mixture consisted of 57% of 4 (b.p. 170-180°/0.001 Torr), 25% of 5 (m.p. 90-92°) and 16% of 6 (m.p.



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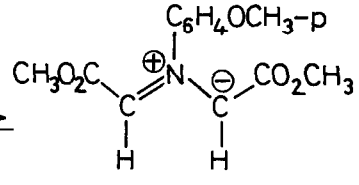

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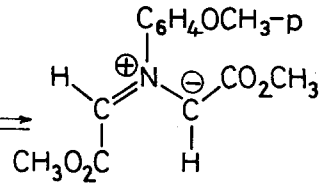

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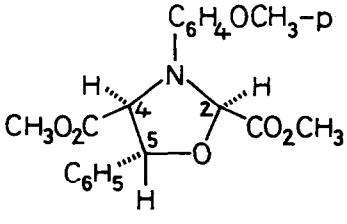

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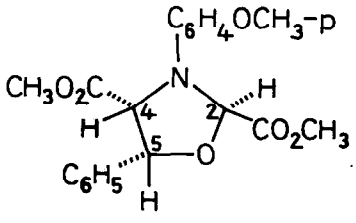

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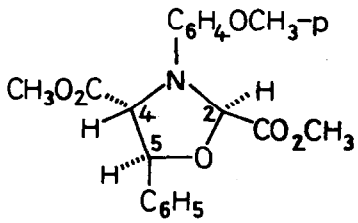

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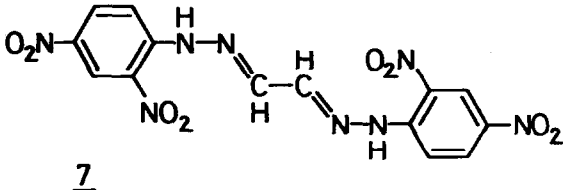
116-117°) (8). N.m.r. spectra allowed a configurational assignment by using the following principles: a. A cis-located ester group in 2-position deshields 4-5-H more efficiently than trans-CO_2CH_3 does; b. 4-H is shielded by cis-5-C_6H_5, but deshielded by trans-C_6H_5; c. the τ-value of 4-CO_2CH_3 is shifted to higher field by cis-5-C_6H_5. $J_{4,5}$ is without diagnostic value; it is 7.0, 6.5, 6.5 Hz for 4-6.

Thus, 57% of the cis-azomethine ylide 2 reacted with benzaldehyde to give 4; 41% isomerised to 3 prior to cycloaddition. As shown earlier (9), 3 is a more active 1,3-dipole than 2. The oxazolidines 4-6 with their O,N-acetal group are stable to 2,4-dinitrophenylhydrazine in ethanolic sulphuric acid. However, after $LiAlH_4$ reduction of the two ester functions, glycolaldehyde was liberated by acid hydrolysis; 46% of the osazone 7 was isolated.

Diethyl mesoxalate reacted with 1 to form 75% of a 93:7 mixture of the oxazolidine 8 (m.p. 82-83°) and 9 (m.p. 75-76°) which were again separated by t.l.c. on silicagel. The two ester ethyl groups are non-equivalent. The ring protons 2-H and 4-H appear in the main product 8 at τ 4.35 and 4.81 (10); as expected, the τ values are lower in the trans-2,4-diester 9 (2-H 4.22, 4-H 4.51). Also



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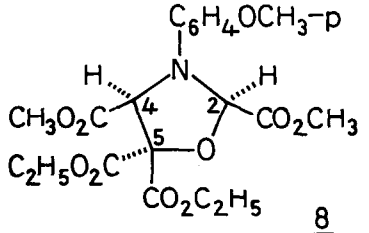

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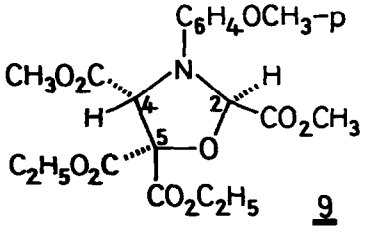

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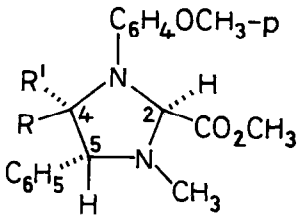
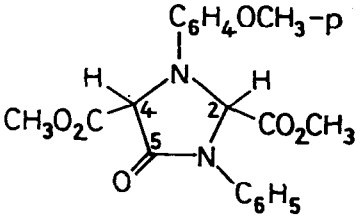
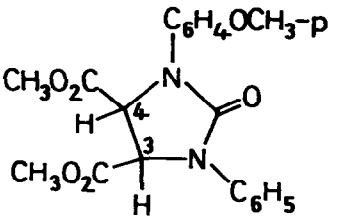
8 and 9 afforded the glyoxal derivative 7 after reduction with $LiAlH_4$ and treatment with acidic 2,4-dinitrophenylhydrazine. With 93% cis-2,4-diester 8 in the product, the stereospecificity was higher than in the case of benzaldehyde; only 7% of the azomethine ylide 2 escaped cycloaddition and isomerised to 3.

Lown et al. recently described cycloadditions of 1-alkyl-2-aryl-3-benzoyl-aziridines to chloral, 3-nitro- and 2,4-dinitrobenzaldehyde (4) as well as to imines (2).







10 R = CO_2CH_3, R' = H

11 R = H, R' = CO_2CH_3

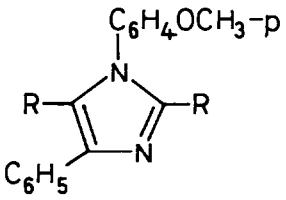
12

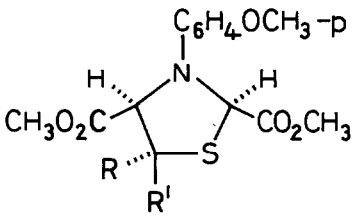
13

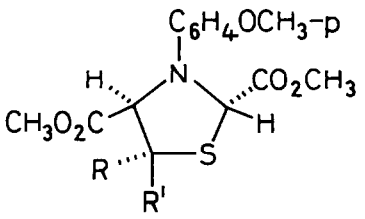
Also CN double and triple bonds are suitable dipolarophiles. N-Benzylidene-methylamine combined much more slowly with 1 than benzaldehyde did as is shown by 40% of reacted 1 after 24 hrs. at 120°; 19% of 10 (m.p. 101-102°) and 29% of 11 (16%- m.p.171°) were isolated, based on consumed 1. The structural assignment rests on n.m.r. criteria as used above. Here the major part of the azomethine ylide 2 has time to isomerise to 3 before being captured by the Schiff base.

The aziridine 1 reacted with an excess of phenylisocyanate when heated for 24 hrs. at 120° to give 73% of the adduct 12 (m.p. 148-150°). Besides the imidazolone-(4) structure 12, a cyclic urea 13 could conceivably appear as product of an electrophilic attack on the aziridine nitrogen followed by CN ring scission. 13 can be discarded because the τ-values of the ring protons differ greatly (τ 3.90 for 2-H and 4.94 for 4-H in 12). The i.r. frequency of 1717 cm^{-1} is that of a γ-lactam. Moreover, the aziridine 1 was quantitatively recovered after treatment with phenylisocyanate for 16 days at 20°. This suggests that 2 and not 1 was the reactant; $t_{1/2}$ for the process 1 ⟶ 2 amounts to 8000 days at 20° (7).

The reaction of 1 with benzonitrile (24 hrs. 120°) produced an oily mixture of products which was dehydrogenated by chloranil in boiling xylene to the imidazole derivative 14 (31%, m.p. 149-151°). Alkaline hydrolysis and thermal decarboxylation (210°, 89%) afforded 4-phenyl-1-(4-methoxyphenyl)imidazole (15, m.p. 105-106°), identical with an independently synthesised specimen.







14 R = CO_2CH_3 16 R = C_6H_5, R' = SCH_3 18

15 R = H 17 R = SCH_3, R' = C_6H_5 19

We chose methyl dithiobenzoate as an example with CS double bond. After 24 hrs. at 120° 1 was converted to a mixture of the adducts 16-19 in 63% yield; n.m.r. analysis provided the ratio 40:12:34:14. Thus, the cycloaddition furnished all four possible racemates for a thiazolidine with three asymmetric centres. All four isomers were separated by t.l.c. on silicagel. The assignment of configuration to 16-19 by n.m.r. criteria is unfortunately not without ambiguity in the present case.

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