The Reaction of 2-Aroylaziridines with Aldehydes to form Oxazolidines

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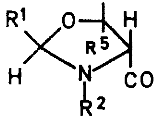
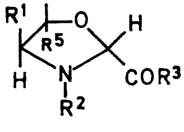
Summary 2-Aroylaziridines undergo thermal 1,3-dipolar addition *via* azomethine ylides to aromatic aldehydes and to chloral to give exclusively 4-aroyloxazolidines.

ADDITION reactions of substituted aziridines involving cleavage of the 2,3 bond to an azomethine ylide intermediate and subsequent [2+3] cycloaddition to carbon–carbon and heteromultiple bonds are useful synthetic routes to pyrroles,[1–4] pyrrolines, [1,4] pyrrolidines [3,4] thiazolines,[5] and imidazolidines.[6] We report the analogous addition to the C=O bond of aldehydes to form oxazolidines, together with unambiguous proof of the structure and orientation of the 1,3-dipolar addition and stereochemistry. 2-Benzoyl-1-isopropyl-3-(3-nitrophenyl)aziridine[7] reacted with 1 equiv. of 2,4-dinitrobenzaldehyde in refluxing benzene to give the oxazolidine [I; $R^1 = m\text{-}NO_2\cdot C_6H_4$, $R^2 = Me_2CH$, $R^3 = Ph$, $R^4 = H$, $R^5 = 2,4\text{-}(NO_2)_2\cdot C_6H_3$], (65%) m.p. 134—136°: ν_{max} ($CHCl_3$) 1678 (C=O), 1528 cm^{-1} (NO_2)[8]; δ ($CDCl_3$, Me_4Si as standard) 0·85 (d, 3H, *J* 6·5 Hz), 1·12 [d, 3H, *J* 6·5 Hz, $(CH_3)_2CH$], 3·18—3·6 [m, 1H, $(CH_3)_2CH$], 6·42 (s, 1H, H^2), 6·22 and 6·04 (AB quartet, 2H, *J* 5·7 Hz, *cis*, $H^{4,5}$), 7·17—8·88 (12H, ArH): mass spectrum; 196·0216 ($C_7H_4N_2O_5$; $M - C_{18}H_{18}N_2O_3$) calc. 196·0213; 310·1317 ($C_{18}H_{18}N_2O_3$; $M - C_7H_4N_2O_5$) calc. 310·1319. A series of similar oxazolidines synthesised from aryl aldehydes and chloral with the appropriate 2-aroylaziridine were assigned structures corresponding to *cis*- or *trans*-(I) (see Table). The alternative structures (II) and (III) were discounted by the following experiments using specific deuterium labelling. Reaction of 2-benzoyl-1-isopropyl-3-(3-nitrophenyl)aziridine with PhCDO† gave a mixture of *cis*-(IV) and *trans*-(IV) in the ratio of 67:33.


(I)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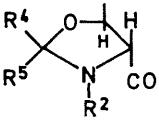
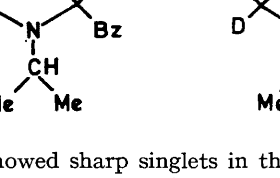
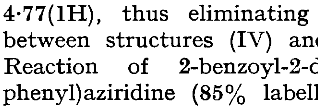
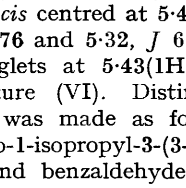

(III)


(IV)


(V)


(VI)

Both products showed sharp singlets in the n.m.r. at 6·20 (1H, *cis*) and 6·10 (1H, *trans*) (H^2) and the original AB quartets in the protium analogues (*cis* centred at 5·42 and 5·61, *J* 5·7 Hz; *trans* centred at 4·76 and 5·32, *J* 6·4 Hz) were simplified to two sharp singlets at 5·43(1H) and 4·77(1H), thus eliminating structure (VI). Distinction between structures (IV) and (V) was made as follows. Reaction of 2-benzoyl-2-deuterio-1-isopropyl-3-(3-nitrophenyl)aziridine (85% labelled)[9] and benzaldehyde gave the mixture of *cis*- and *trans*-oxazolidines (IV) where the deuterium is located unambiguously at the 4-position. The n.m.r. spectrum showed sharp singlets at 6·23(1H, *cis*) and 6·09(1H, *trans*) (H^2) and the original AB quartets

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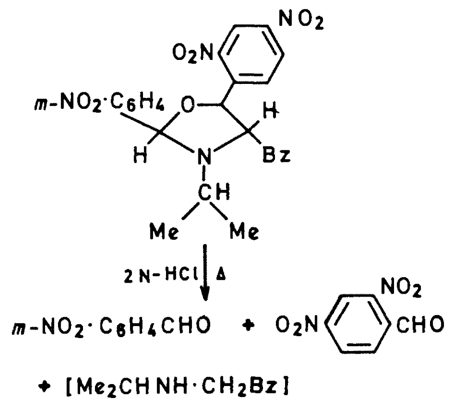
† PhCDO (99·5%) was used because of its commercial availability (Merck, Sharp and Dohme, Montreal, Quebec).

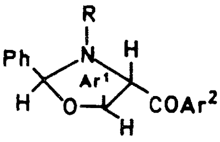
4-*Aroyloxazolidines*[a]

	R^1	R^2	R^3	R^4	R^5	M.p.	Yield (%)
(Ia)[b]	m-NO_2·C_6H_4	C_3H_7	Ph	H	2,4-$(NO_2)_2$·C_6H_3	134—136°	65
(Ib)[b]	m-NO_2·C_6H_4	C_3H_7	Ph	p-NO_2·C_6H_4	H	133—135°	71
(Ic)[b]	m-NO_2·C_6H_4	C_3H_7	Ph	H	p-NO_2·C_6H_4	116—119°	
(Id)[b]	p-NO_2·C_6H_4	C_6H_{11}	Ph	CCl_3	H	154—156°	78
(Ie)[b]	m-NO_2·C_6H_4	C_6H_{11}	Ph	CCl_3	H	128—130°	72
(If)[b]	m-NO_2·C_6H_4	C_3H_7	Ph	Ph	H	137—139°	48
(Ig)[b]	m-NO_2·C_6H_4	C_3H_7	Ph	H	Ph	124—127°[c]	
(Ih)	Ph	C_6H_{11}	Ph	p-NO_2·C_6H_4	H	oil	*ca.* 65

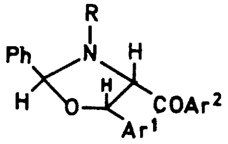
[a] Satisfactory analytical data were obtained on all new compounds.
[b] Signifies orientation of 1,3-dipolar addition confirmed by a parallel experiment with specifically 2-deuteriated aziridine.
[c] Contained some *trans*-isomer as impurity.



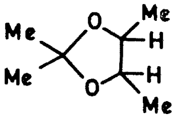
observed in the protium analogues described above were modified to 5·46(0·3H) and 5·63(1H) for the *cis*-isomer and 4·76(0·3H) and 5·30(1H) for the *trans*-isomer, thus eliminating a structure of the type (II) and confirms the orientation of the 1,3-dipolar addition of the aldehyde as represented by (I). The orientation of four other additions checked with specifically 2-deuteriated aziridines confirmed the generality of this conclusion. Chemical confirmation of the structural assignments was made by acid hydrolysis of representative oxazolidines.[10] For example, hydrolysis of oxazolidine (VII) with 2N-HCl afforded m-nitrobenzaldehyde and 2,4-dinitrobenzaldehyde identified as their 2,4-dinitrophenylhydrazones. Reaction of p-nitrobenzaldehyde with stereoisomerically pure samples of *cis*- and *trans*-2-benzoyl-1-cyclohexyl-3-phenylaziridine[11] gave the identical *trans*-4,5-oxazolidine (Ih) in approximately the same yield. Similarly, addition of chloral to *cis*- or *trans*-2-benzoyl-1-cyclohexyl-3-(3-nitrophenyl)aziridine[12] gave one stereoisomerically pure *trans*-4,5-oxazolidine (Ie). Separate control experiments with the *cis*-4,5-oxazolidine (Ia) with (i) cyclohexylamine (ii) di-isopropylethylamine, and (iii) sodium methoxide showed no evidence of epimerisation at the 4-position. We conclude that owing to the sluggish dipolarophilic activity of the C=O bond,[13] prior equilibration of the *cis*- and *trans*-azomethine ylide[14] (from conrotatory thermal opening of the *trans*- and *cis*-aziridines respectively[15]) occurs and addition takes place exclusively *via* the *trans*-azomethine ylide. The isomeric oxazolidines were accordingly assigned the following stereochemistry (VIII) and (IX). The assignment of configuration about the 4,5-positions is tentatively based on the similarity to the n.m.r. proton couplings recorded for *cis*- and *trans*-2,2,4,5-tetramethyldioxolanes.[16] The orientation of the addition of aldehydes to aziridines was exclusively in one direction [structure (I)] and is opposite to that assigned to the only previously reported example of 1,3-dipolar addition of p-nitrobenzaldehyde to 1,1a-dihydro-1-(p-nitrophenyl)-2-phenylazirino[1,2-*a*]quinoxaline.[17]



4,5-*trans*
(VIII)



4,5-*cis*
(IX)



J (*trans*) 8·35 Hz
J (*cis*) 5·85 Hz
(X)

In no case was a product corresponding to structure (III) encountered, in agreement with recent work[18] which disproved a prior claim of formation of oxazolidines by prolonged heating of ethylenimine with aldehydes.

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