# Thermally Induced Cleavage Reactions of Aziridinyl Esters

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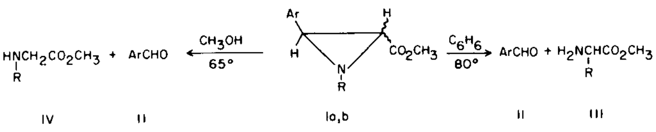
*Sir:*

Reactions of substituted aziridines which proceed *via* a 1,3-dipole and/or a 1,3-diradical intermediate arising from thermally induced C-C bond scission of the aziridine ring have been reported (2-6). Either intermediate can undergo recombination, rearrangement or be trapped by a suitably activated olefinic substrate. In all cases reported to date, temperatures of 100 to 225° were required to achieve C-C bond cleavage of the aziridine ring.

*Cis*- and *trans*-1-cyclohexyl-2-*p*-biphenyl-3-carbomethoxyaziridine (Ia,b) were prepared by the reaction of methyl-α-bromo-*p*-phenylcinnamate and a ten fold excess of cyclohexylamine in benzene (7). The isomeric aziridinyl esters were found to undergo rather facile thermally induced C-C bond scission of the aziridine ring at 65-80° with the mode of rearrangement being solvent dependent.

Thus, both Ia and Ib yielded products II and III when heated at the reflux temperature of benzene. The structure of II was assigned as *p*-phenylbenzladehyde (II) while reaction product III was converted to its hydrochloride salt and identified as methyl α-aminocyclohexylacetate (III).



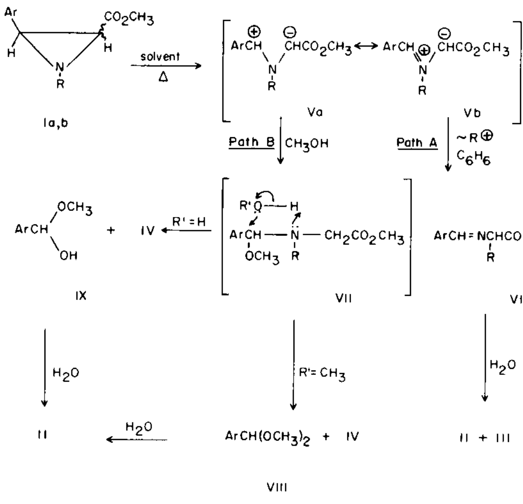
In refluxing methanol, II was again obtained. A second product IV was characterized as its hydrobromide salt and found to be *N*-cyclohexylglycine methyl ester (IV). Structural assignment of all reaction products was made on the basis of ir, nmr, mass spectrometry and independent synthesis.

The proposed mechanism is believed to involve a 1,3-dipole intermediate (V) (Scheme I) (8).

In benzene (Path A), it is proposed that a 1,2-shift of the *N*-alkyl substituent gives rise to Schiff base (VI) which is subsequently hydrolyzed to II and III (9).

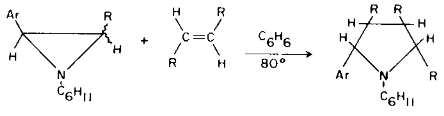
The reaction course followed in methanol (Path B) probably involves immediate reaction of Va with solvent to yield VII (10). Reaction product IV can then arise from reaction of VII with methanol or water to form either VIII or IX, both of which are then hydrolyzed to II.

Scheme I



The 1,3-dipole (V) can be trapped by suitable dipolarophiles to form five-membered heterocyclic rings. Equimolar quantities of Ia (or Ib) and dimethyl fumurate in refluxing benzene yielded a single adduct X in 75% and 65% yields, respectively. The adduct was assigned the structure trimethyl-1-cyclohexyl-5-(*p*-biphenyl)pyrollidine-2,3,4-tricarboxylate (X) on the basis of ir, nmr, mass spectrometry and elemental analysis.

Adduct X does not form a hydrohalide salt and is recovered unchanged when subjected to chloranil in boiling xylene.



Ia,b

X

Ar = p-$C_6H_5C_6H_4$

R = $CO_2CH_3$

The nmr spectrum of X consisted of: broad resonance signals 0.9-2.0 $\delta$ (10H, protons $\beta,\gamma$ and $\delta$ to N in cyclohexyl ring) and 2.3-3.0 $\delta$ (1H, methine proton of cyclohexyl ring); the alkoxy resonance signals appeared at 3.15, 3.22 and 3.74 $\delta$ (3H each); two doublets at 4.5 $\delta$ (1H) and 4.91 $\delta$ (1H) were assigned to the protons at $C_2$ ($\alpha$ to N, $\alpha$ to carbonyl) and $C_5$ ($\alpha$ to N, benzylic), respectively; the protons at $C_3$ and $C_4$ appeared as seven lines (2H) and were assigned chemical shifts of 3.99 and 4.19 $\delta$ (11), respectively; the aromatic protons were observed as a complex multiplet at 7.33-7.82 $\delta$ (9H). The coupling constants (Hz) are as follows: $J_{2,3}=6.5$, $J_{3,4}=11.5$ and $J_{4,5}=9.7$; no long range coupling was observed.

The ir spectrum (carbon tetrachloride) showed $\gamma$C=O 1741 cm$^{-1}$.

Most 1,3-dipolar additions are known to be concerted and hence stereospecific (13). The fact that both Ia and Ib give rise to a single adduct (X) with dimethyl fumarate indicates a two-step, nonstereospecific mechanism. However, formation of X may be the result of epimerization of an initially formed adduct arising from a concerted stereospecific addition (14). While in the absence of an activated olefin the rearrangement of Ia and Ib in benzene at reflux temperature argues against a 1,3-diradical intermediate, the reaction of Ia and Ib with dimethyl fumarate may proceed *via* a 1,3-diradical intermediate (15).

Acknowledgment.

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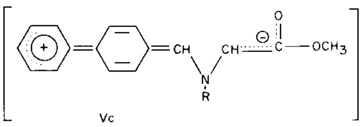
(7) Stereochemical assignments of the *cis* and *trans* isomers were made employing the usual spectroscopic methods. See A. E. Pohland, R. D. Badger and N. H. Cromwell, *Tetrahedron Letters*, 48, 4369 (1965).

(8) A third resonance form, (Vc), would be expected to contribute to the stability of the 1,3-dipole and could possibly account for the relatively low temperatures at which C-C bond scission of the aziridine ring was achieved.



Vc

(9) Schiff base VI was not isolated but when an authentic sample was subjected to identical reaction conditions only II and III were formed.

(10) The possibility of a nucleophilic attack by methanol on the $\beta$-carbon of the aziridine ring to yield VII cannot be eliminated. Attempts to hydrolyze Ia,b to the amino acid in aqueous barium hydroxide at 60° resulted in the formation of II and IV rather than hydrolysis of the ester function. Qualitatively, the rate of cleavage of the aziridine ring in aqueous base is much faster than in reagent methanol.

(11) These data were determined by deuteration studies and use of the nmr computer program of A. A. Bothner-By and A. Castellano (12). To facilitate data interpretation, a program utilizing the Cal Comp Plotter written by Dr. C. T. Watts, Department of Chemistry, University of Nebraska was used. Comparison of actual and theoretical spectra of X gave excellent agreement.

(12) A. A. Bothner-By and A. Castellano, "LAOCN 3", Program 111, Quantum Chemistry Program Exchange, Indiana University (1968).

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(14) Monitoring the reaction by TLC revealed that only X was formed. This does not eliminate the possibility of a very low concentration of an initially formed adduct. Preliminary results with Ia and Ib and dimethyl maleate in refluxing benzene indicate a two-step, nonstereospecific addition.

(15) Qualitatively, the rates of rearrangement of Ia and Ib are about the same as their respective reaction with dimethyl fumarate. In each case, Ia is more labile than Ib under these reaction conditions.

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