

INVESTIGATION ON ALKALINE CLEAVAGE OF N-NITROSO-N-CARBOMETHOXY AMINO ACID ESTERS

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Abstract. Alkaline cleavage of L (+) N-nitroso-N-carbomethoxy-alanine methyl ester and N-nitroso-N-carbomethoxy-1-phenyl-2, 2, 2-trifluoroethylamine methyl ester yielded substitution and denitrosation products. A reaction mechanism has been proposed.

Reaction of aliphatic amines with nitrous acid is known to involve diazotisation followed by deamination¹ to give rise to varying products depending on substrate and reaction conditions. Investigations have been carried out to establish the nature of the intermediate diazoalkanes and their mode of decomposition.³ N-Alkyl nitrosoamides and N-carbamates on basic hydrolysis give products which were attributed to diazonium ions and were shown to be dependent on the nature of the solvent, base and alkyl groups.^{3,4} Solvolysis of methyl-(S)-N-nitroso (phenethyl) N-carbamate methyl ester in methanol yields 1-methoxy-1-phenylethane with partial inversion of configuration and 1-phenyl-ethanol with predominant retention of configuration.⁵ It was not clear whether the intermediate diazonium ion had decomposed by a concerted process or whether ion-pairs were involved in such reactions leading to partial racemisation of products. For such an investigation, substitution by suitable groups capable of exerting an electron attracting effect should make the resulting diazonium ion susceptible to alkaline cleavage and provide an answer to the preceding question. Thus, replacing a methyl group with a trifluoromethyl group which is approximately the same size, but exerting the opposite inductive effect on substitution of carbomethoxy group for the phenyl group in methyl-N-nitroso-(1-phenethyl)-N-carbamate methyl ester should render a strong impact in this respect. Hence L(+)-N-nitroso-N-carbomethoxyalanine methyl ester and N-nitroso-N-carbomethoxy-1-phenyl-2, 2, 2-trifluoroethylamine methyl ester were selected as models to observe the effect of carboxymethyl group or a CF₃ group on the stability of the resulting diazonium ion and the effect this has upon the substitution products arising thereafter.

Results and Discussion

The results have shown that diazoesters were formed under the reaction conditions (Table 1). The stability of these esters was considered to be due to the carboxymethyl or trifluoromethyl substituent groups whose negative inductive-effects increase the C-N₂ bond strength. Since deamination reaction did not proceed appreciably, as a result the products were formed in low yield and were difficult to collect pure in sufficient amounts for recording

of optical rotation. Hence, the stereochemical consequences of the reaction are unknown. However, most of the products produced in low yields were collected by preparative GLC and compared with authentic samples by GLC. These fractions were also used for recording of IR, NMR, or mass spectra for structure elucidation. The following general scheme accounts for the products produced in these reactions (Scheme I).

TABLE 1

SUBSTRATE	ALKALI	PRODUCT	PERCENT
$\begin{array}{c} \text{CO}_2\text{Me} \\ \\ \text{CH}_3-\text{CH}-\text{N}-\text{CO}_2\text{Me} \\ \\ \text{N}=\text{O} \end{array}$	NaOMe/MeOH or NaOH/MeOH	$\begin{array}{c} \text{CO}_2\text{Me} \\ \\ \text{CH}_3-\text{CH}-\text{OCH}_3 \\ \\ \text{CO}_2\text{Me} \end{array}$	3.0
		$\begin{array}{c} \text{CO}_2\text{Me} \\ \\ \text{CH}_3-\text{C}=\text{N}_2 \\ \\ \text{CO}_2\text{Me} \end{array}$	16.85
		$\begin{array}{c} \text{CO}_2\text{Me} \\ \\ \text{CH}_3-\text{CH}-\text{N}-\text{CO}_2\text{Me} \\ \\ \text{H} \end{array}$	76.44
$\begin{array}{c} \text{CF}_3 \\ \\ \text{C}_6\text{H}_5-\text{CH}-\text{N}-\text{CO}_2\text{Me} \\ \\ \text{N}=\text{O} \end{array}$	NaOMe/MeOH or NaOH/MeOH	$\begin{array}{c} \text{O} \\ \\ \text{C}_6\text{H}_5-\text{C}-\text{CF}_3 \end{array}$	13.6
		$\text{C}_6\text{H}_5-\text{CHOH}-\text{CF}_3$	15.7
		$\begin{array}{c} \text{CF}_3 \\ \\ \text{C}_6\text{H}_5-\text{C}=\text{N}_2 \end{array}$	43.17
		$\begin{array}{c} \text{CF}_3 \\ \\ \text{C}_6\text{H}_5-\text{CH}-\text{N}-\text{CO}_2\text{Me} \\ \\ \text{H} \end{array}$	14.15
		$\begin{array}{c} \text{CF}_3 \\ \\ \text{C}_6\text{H}_5-\text{CH}-\text{OCO}_2\text{Me} \\ \\ \text{CF}_3 \end{array}$	1.01
		$\text{C}_6\text{H}_5-\text{CH}-\text{ONO}_2$	2.8

N-Nitroso-N-carbomethoxy methyl ester¹ on reaction in a hydroxy solvent gave either an ion-pair² or a denitrosation reaction, thus producing N-carbomethoxy derivative³ and hydroxy derivative.⁴ The former ion-pair resulted in the formation of diazoester⁵ which was one of the major products of the reaction. Ketone⁶ was produced by oxidation in air or with N₂O₄. The denitrosation reaction which has produced derivative³ further produced nitrate⁷ and carboxymethylate⁸ derivatives as secondary products of the reaction involving N-carboxymethyl-2,2, 2-trifluoroethylamine by reaction with HNO₃ or NO₃ ion produced *in situ* and ion-pair rearrangement followed by substitution respectively.¹⁵

present investigation included, α -methoxy-methyl lactate,¹¹ trifluoroacetophenone,¹² 1-phenyl-2, 2, 2-trifluoromethylethanol,¹³ 1-phenyl-2, 2, 2-trifluoromethyldiazoethane,¹⁴ 1-phenyl-2, 2, 2-trifluoroethanol methyl carbonate and 1-phenyl-2, 2, 2-trifluoroethyl nitrate.¹⁵

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References

1. J. H. Ridd, *Quart. Rev.*, **15**, 418 (1961), and R. D. Clark and G. K. Helmkamp, *J. Org. Chem.*, **29**, 1316 (1964).
2. W. H. Saunders Jr. and A. F. Cockrill, *Mechanisms of Elimination Reaction* (Wiley Interscience, N. Y., 1973), p. 280.
3. R. A. Moss, *J. Org. Chem.*, **31**, 1082 (1966).
4. W. Kirmse and G. Wächtershäuser, *Ann.*, **44**, 707 (1967) and W. Kirmse and H. A. Rinkler, *Ann.*, **57**, 707 (1967).
5. W. Kirmse and H. Arold, *Chem. Ber.*, **103**, 3722 (1970).
6. M. Goodman and W. J. McGahren, *Tetrahedron*, **23**, 2031 (1967).
7. A. L. Barker and G. S. Skinner, *J. Am. Chem. Soc.*, **46**, 403 (1924).
8. W. H. Pirkle and S. D. Beare, *J. Am. Chem. Soc.*, **91**, 5150 (1969).
9. F. Wudl and T.B.K. Lee, *J. Am. Chem. Soc.*, **93**, 271 (1971).
10. Z. A. Malik, *IU. J. Sciences*, **3**, 1-2 (1976).
11. D. Gagnaire, *Bull. Soc. Chem. France*, 1831 (1960).
12. A. Sykes, J. C. Tatlow and C. R. Thomas, *J. Chem. Soc.*, 835 (1956).
13. R. Stewart and G. G. Lee., *Can. J. Chem.*, **42**, 439 (1964).
14. R. A. Shepard and S. E. Wentworth, *J. Org. Chem.*, **32**, 3197 (1967).
15. Z. A. Malik, *IU. J. Sciences*, **3**, 1-2 (1977).