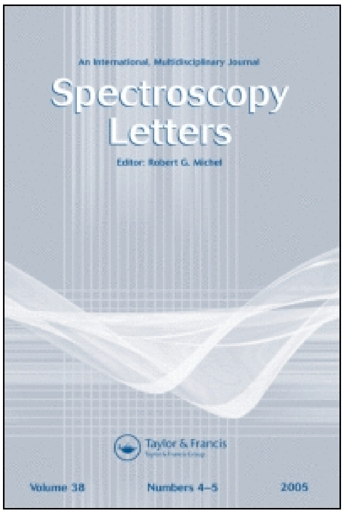
This article was downloaded by:
On: *30 January 2011*
Access details: *Access Details: Free Access*
Publisher *Taylor & Francis*
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Spectroscopy Letters
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597299

Some Aspects of Intra- and Inter-Molecular Reactions of Siliconium Ions in the Vapor Phase

Paul Vouros[a]; D. J. Harvey[a]; T. J. Odiorne[a]
[a] Institute for Lipid Research Baylor College of Medicine Houston, Texas

To cite this Article Vouros, Paul , Harvey, D. J. and Odiorne, T. J.(1973) 'Some Aspects of Intra- and Inter-Molecular Reactions of Siliconium Ions in the Vapor Phase', Spectroscopy Letters, 6: 10, 603 — 615

To link to this Article: DOI: 10.1080/00387017308060850

URL: http://dx.doi.org/10.1080/00387017308060850

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

SPECTROSCOPY LETTERS, 6(10), 603-615 (1973)

SOME ASPECTS OF INTRA- AND INTER-MOLECULAR REACTIONS OF SILICONIUM IONS IN THE VAPOR PHASE

Paul Vouros, D. J. Harvey and T. J Odiorne

Institute for Lipid Research
Baylor College of Medicine
Houston, Texas 77025

Downloaded At: 04:29 30 January 2011

ABSTRACT

Intramolecular rearrangement processes in the mass spectra of trimethylsilyl derivatives of hydroxy steroids are discussed in terms of the reaction of a siliconium center and a heteroatom. The reaction is shown to be stereospecific. The reactivity of siliconium cations also results in the occurrence of intermolecular reactions under electron impact ionization conditions. Tetramethylsilane is used as a precursor for the production of siliconium ions and examples of chemical ionization mass spectra employing this reagent are shown.

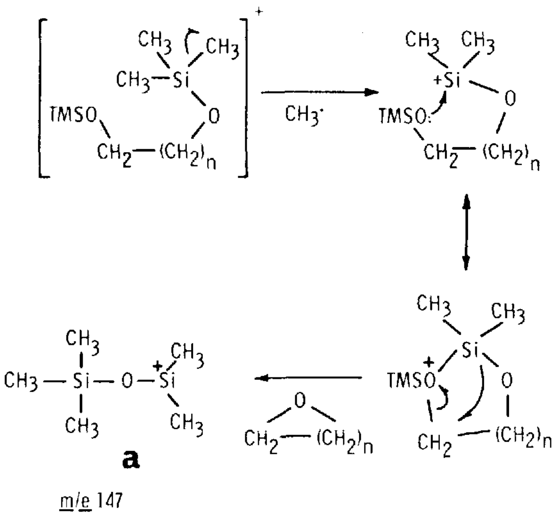
INTRODUCTION

The study of many compounds of biological interest by vapor phase analytical methods requires their conversion into volatile derivatives. Trimethylsilylation is a commonly used procedure for the preparation of volatile derivatives of natural products in order to study them by gas chromatography and/or mass spectrometry. In recent years trimethylsilyl (TMS) derivatives have been employed extensively in the separation and identification of various types of biological compounds.

Copyright © 1973 by Marcel Dekker, Inc. All Rights Reserved. Neither this work nor any part may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, microfilming, and recording, or by any information storage and retrieval system, without permission in writing from the publisher.

Downloaded At: 04:29 30 January 2011

In the mass spectra of most TMS derivatives the trimethylsilyl group tends to direct the fragmentation of the parent nucleus resulting in a high abundance of ions containing the trimethylsilyl moiety.[1] Electron impact ionization has also been known to readily induce the formation of rearrangement ions involving the TMS group. Perhaps most notable among them is the ion of m/e 147 (a) (Scheme 1) which has been observed in the mass spectra of compounds containing two or more trimethylsilyloxy (TMSO) substituents.[2] It has been proposed that formation of a



SCHEME 1

involves reaction of a positively charged siliconium center with the oxygen of another TMSO group, the oxygen atom providing the nucleophilic center as shown in Scheme 1.[2a,3] Analogous ions are formed in cases where one of the TMSO groups has been substituted by a methoxyl or phenyl function.[4]

Ion a is quite prominent even in the mass spectra of the TMS derivatives of long chain diols where the trimethylsilyloxy groups may be separated by twenty or more methylene groups.[5] In fact analogous interactions have been observed in straight chain bis-trimethylsilyl ethers in which as many as forty-six methylene groups separated the interacting functionalities.[6] Recognition of the silyl content of these rearrangement ions has been greatly facilitated following the introduction of perdeutero-trimethylsilylating reagents by McCloskey and coworkers.[7]

The present manuscript summarizes the results of investigations which evaluate some of the conditions under which ionic reactions of silicon can occur in the vapor phase. The first section deals with stereochemical requirements for intramolecular siliconium reactions, the second section discusses intermolecular siliconium reactions observed under electron impact conditions, and the final part enters into some applications of siliconium ion reactivity in chemical ionization mass spectrometry.

Downloaded At: 04:29 30 January 2011

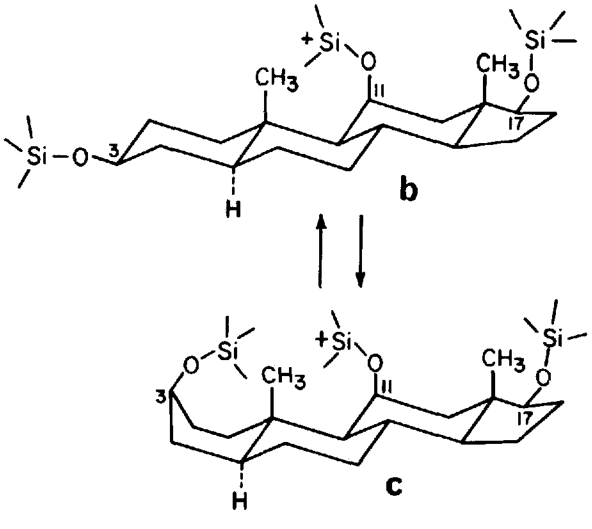
RESULTS AND DISCUSSION

(i) Intramolecular Siliconium Reactions

The interaction of TMSO groups occupying the two ends of a straight chain diether has been interpreted in terms of a macrocylic transition state which can occur because of the conformational mobility of the system. We sought to determine whether restriction of this conformational mobility could influence the formation of these rearrangement ions. Variation of the relative abundance of specific rearrangement ions in a predictable fashion in molecules of fixed conformation should obviously be of some help in structural identifications. The rigid structure of the steroid system offers an excellent means for evaluating this hypothesis. Moreover, our choice of the steroid system was motivated by the potential applicability of the results of our study since trimethylsilyl derivatives of steroids are being studied extensively by gas chromatography-mass spectrometry.[8]

The mass spectra of more than fifty <u>bis</u> or <u>poly</u>-trimethylsilyl steroidal ethers have been examined[9] and the occurrence and/or relative abundance of ion <u>a</u> has been determined. As a representative example we present here the results obtained with a series of steroids containing an 11α- or β-trimethylsilyloxy group and substituents in the 3- and/or 17-positions. Table 1 summarizes the variation of the relative abundance of ion <u>a</u> in terms of both % Σ_{40} and % base peak. It is clear from the data in Table 1 and the structural formulae in Scheme 2 that in the 5α-epimeric androstanes, interaction between the 3β, 11β and 17β groups

Downloaded At: 04:29 30 January 2011



SCHEME 2

(structures <u>b</u> and <u>c</u>, Scheme 2) is inhibited by the angular methyl groups and, in the case of the 3, 17-diols, strongly hindered because of the separation of the TMSO functions. When the A-ring assumes the boat conformation as in structure c (Scheme 2) the 3β- and 11β-TMSO groups are actually almost within bonding distance, but the 19-angular methyl group is apparently responsible for the low intensity of m/e 147. It might be noted that charge localization is depicted here on the 11-TMSO silicon atom only for the sake of convenience. In the case of the triol (V) selective labeling on the 11β-position with TMS-$\underline{d}_9$[10] revealed that the bulk of $[M-15]^+$ is actually formed by loss of a methyl group from either the 3β- or 17β-TMS groups.[11] In either case, however, the resulting transition states would be equivalent to those shown in Schemes 2 and 3.

TABLE 1

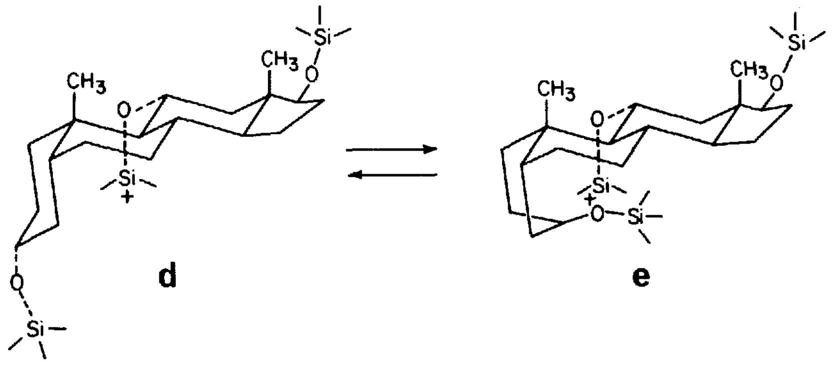
Relative Abundance of Ion a in the Mass Spectra of Some Pertrimethylsilylated Hydroxy Steroids

Parent Compound	Relative Intensity of Ion a		
	$\% \Sigma_{40}$	% Base Peak	Base Peak
5α-Androstane-3β, 17β-diol (I)	0.1	0.1	129
5β-Androstane-3α, 17β-diol (II)	0.05	0.1	129
5α-Androstane-3β, 11β-diol (III)	0.1	4	156
5α-Androstane-11β, 17β-diol (IV)	0.3	8	346
5α-Androstane-3β, 11β, 17β-triol (V)	0.4	9	434
5β-Androstane-3α, 11α, 17β-triol (VI)	0.9	26	434

When the trimethylsilyloxy groups are located in the 3α- and 11α-positions as in the isomeric triol VI, which is epimeric about C-5, a notable increase in the relative abundance of ion a was observed. Since

Downloaded At: 04:29 30 January 2011

the 11α- and 17β-TMSO groups in the derivative of VI are further apart than the 11β- and 17β-groups in the derivative of V it is expected that ion a is actually formed in the former from the interaction of the 3α- and 11α-functions. The boat conformation of ring A (structure e, Scheme 3) brings the silicon and oxygen atoms within bonding distance and hence



SCHEME 3

there is a marked increase in the abundance of ion a. These comparisons indicate that the intramolecular reactions resulting in the formation of ion a occur prior to, or independent of, ring cleavage since any cleavage of rings A or B would result in loss of conformation in the TMS derivatives of either V or VI.

(ii) Intermolecular Reactions Under Electron Impact Conditions

During a study of the mass spectra of the TMS derivatives of sugar phosphates,[12] steroidal phosphates[13] and other related compounds a series of ions was observed at mass values higher than that of the molecular ion. Prominent among them was the ion at $[M+73]^+$ corresponding to the addition of a TMS group to the molecular ion.[14] The relative abundance of the $[M+73]^+$ ion and all the other ions occurring at m/e

Downloaded At: 04:29 30 January 2011

values higher than $M^{+\cdot}$ was found to increase with sample pressure in the ion source, indicating that their formation was the result of an intermolecular reaction process. Closer examination of the mass spectrum of the TMS derivative of L-α-glycerophosphate (VII, Fig. 1) showed that most of the adduct ions observed corresponded to the combination of the molecular species with an abundant fragment ion present in the mass spectrum of the derivative. However, not all abundant fragment ions were actually observed to combine with the molecular species. Aside from m/e 73 it was only those which could be written with the general structure $R\text{-}O\text{-}{}^{+}Si(CH_3)_2$, or in other words, the ones which could be depicted with a positively charged siliconium center.[15] The implication, of course, is that siliconium ions produced during electron impact ionization of the sample react in the ion source of the spectrometer with neutral molecules which are present in large excess. From an analytical point of view it is of considerable importance to be aware of these processes since, in the interpretation of mass spectra, it is generally assumed that the peaks occurring at the highest mass are due to the molecular ion.

(iii) Siliconium Ion Reactions Under Chemical Ionization Conditions.

The results discussed in the preceding section indicate a high vapor phase reactivity of alkyl siliconium ions. In view of the current interest in ion molecule reactions especially in conjunction with chemical ionization mass spectrometry, we have explored possible applications in this field. Tetramethylsilane $[Si(CH_3)_4]$ provided the most suitable precursor for the generation of alkyl-siliconium ions, since it fragments readily

Downloaded At: 04:29 30 January 2011

Downloaded At: 04:29 30 January 2011

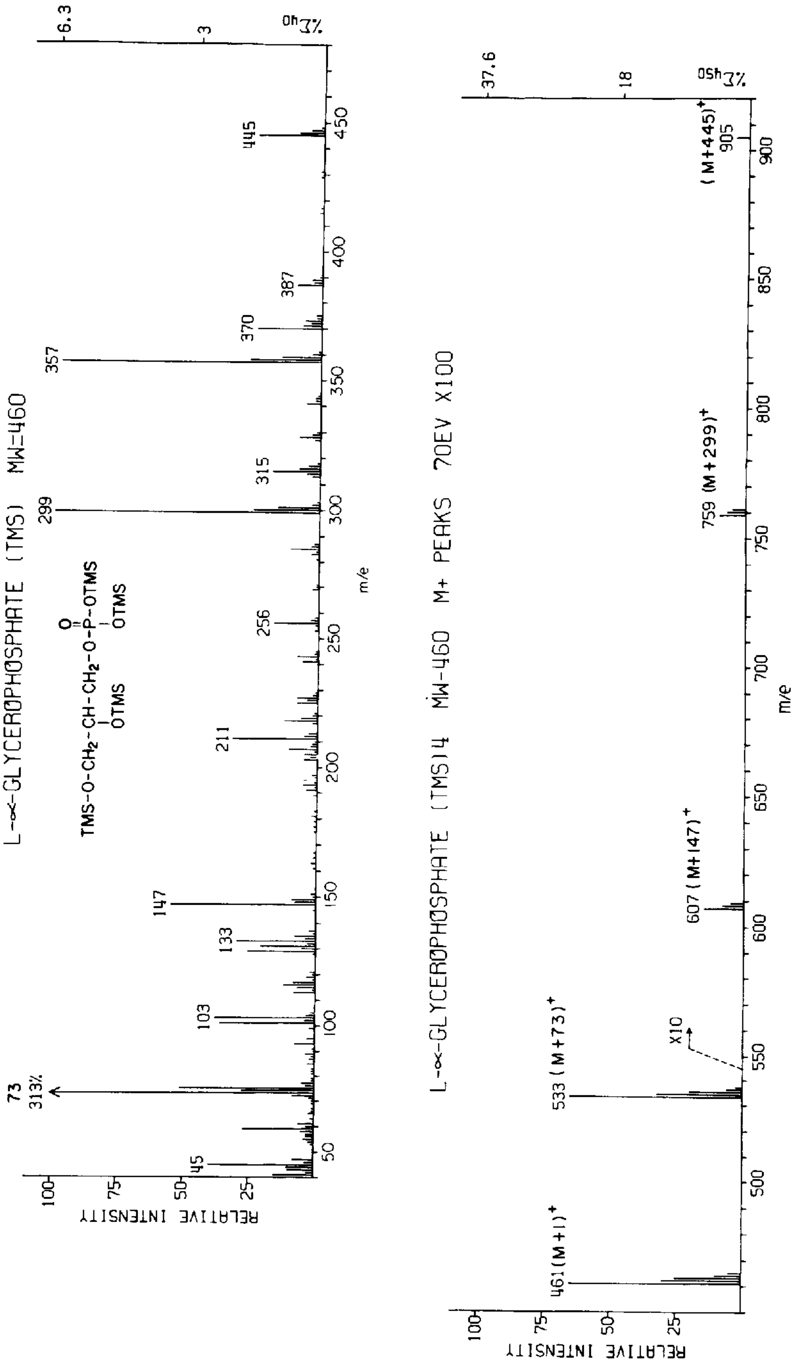


FIG. 1

(a) Mass spectrum of the TMS derivative of L-α-glycerophosphate. (b) Spectrum of L-α-glycerophosphate in the region beyond M.

upon electron impact to produce a trimethylsiliconium cation (*m/e* 73). The latter ion comprises approximately 80% of the total ion current at pressures ranging from 0.05 - 0.50 torr.[16] Major secondary ions are found at *m/e* 131 $[(CH_3)_3Si\text{-}{}^{+}Si(CH_3)_2]$ *m/e* 145 $[(CH_3)_3Si\text{-}{}^{+}Si(CH_3)_2(CH_2)]$ and *m/e* 161 $[(CH_3)_3Si\text{-}{}^{+}Si(CH_3)_4]$.

In chemical ionization mass spectrometry different types of structural information can be obtained depending on the energetics of reaction between the reagent gas ions and the sample. For example, in methane the CH_5^+ ion is highly acidic and thus there is sufficient energy released during the reaction to cause fragmentation of the predominantly formed $[M+1]^+$ ions. By contrast ammonia produces only $[M+1]^+$ of $[M+18]^+$ adduct ions which do not undergo further fragmentation.[17] Tetramethylsilane appears to be somewhere between ammonia and methane in the energy spectrum. The high reactivity of the trimethylsiliconium ion results in the formation of highly abundant $[M+73]^+$ adduct ions in compounds containing heteroatoms or sites of high electron density such as olefinic bonds.

As an example the chemical ionization spectra of 1-octadecene and 5α-androstane-17-one are summarized in Table 2. The spectra of both compounds exhibit intense $[M+73]^+$ peaks comprising more than 75% of the total ion current. Notable also are the peaks at $[M+131]^+$ and $[M+145]^+$ corresponding to the reaction of the sample molecule with two of the three principal secondary siliconium ions. The $[M+1]^+$ ions in both spectra (*m/e* 275; *m/e* 253) are probably due to protonation of M from protonated trimethylsilanol $[(CH_3)_3Si\overset{+}{O}H_2$; *m/e* 91]. The latter is

Downloaded At: 04:29 30 January 2011

formed from the reaction of the trimethylsiliconium ion $[(CH_3)_3Si^+]$ with residual water vapors present in the system.

TABLE 2

Examples of Chemical Ionization Mass Spectra Obtained in $SiMe_4$ Reagent Gas. (P=0.150 torr)

5α-Androstane-17-one		1-Octadecene	
m/e 419 (M+145)	4[a]	m/e 397 (M+145)	2
m/e 405 (M+131)	4	m/e 383 (M+131)	3
m/e 347 (M+73)	77	m/e 325 (M+73)	83
m/e 275 (M+1)	3	m/e 253 (M+1)	2
m/e 257	11		

[a] Relative abundances given in terms of % total ionization.

Finally, in a manner analogous to the methane chemical ionization spectra of 17-keto androstanes which eliminate H_2O from $[M+1]^+$, the spectrum of 5α-androstan-17-one exhibits a strong peak at m/e 257 corresponding to the elimination of $(CH_3)_3SiOH$ from $[M+73]^+$ and/or H_2O from $[M+1]^+$. Metastable peaks and ^{18}O labeling of the C-17 oxygen confirmed both processes. Metastable defocussing experiments[18] revealed additional fragmentation pathways also leading to the formation of the fragment ion m/e 257. Metastable peaks were observed for the transitions $[M+31]^+ \longrightarrow$ m/e 257, $[M+57]^+ \longrightarrow$ m/e 257 and for $[M+59]^+ \longrightarrow$ m/e 257 corresponding to elimination of H_3SiOH, $(CH_3)(CH_2)SiOH$ and $(CH_3)_2HSiOH$ respectively. The relative intensities of the latter three adduct ion peaks were less than 1% of base peak. The observed metastable transitions demonstrate the complexity of the ionization and fragmen-

Downloaded At: 04:29 30 January 2011

tation processes occurring and the reactivity of siliconium cations existing in different structural environments.

CONCLUSIONS

The data presented in the foregoing sections indicate that siliconium cations are highly reactive species in the vapor phase. This reactivity is reflected in both intramolecular and intermolecular processes, the latter type being observed even under electron impact ionization conditions. In the intramolecular reactions discussed here the steroid system provided the medium within which the ionic reactions took place. Steric and stereochemical factors were shown to influence the relative abundance of intramolecular reaction products in mass spectra and consequently this can be a useful guide in making structural assignments. The observations and conclusions drawn from electron impact ionization studies have been utilized towards the development of a chemical ionization system based on the production of positively charged siliconium ions and with potential analytical applications.

Downloaded At: 04:29 30 January 2011

EXPERIMENTAL

5α-Androstane-3β, 11β-diol (III) and 5α-androstane-11β, 17β-diol (IV) were prepared by Wolff-Kishner reduction[19] of 5α-androstane-3β, 11β-diol-17-one and 5α-androstane-11β, 17β-diol-3-one respectively. All other samples were obtained from commercial sources. Trimethylsilyl and perdeuterotrimethylsilyl derivatives were prepared according to previously described procedures.[20,21]

Electron-impact ionization mass spectra were recorded with an LKB-9000 mass spectrometer. The electron energy was 70 eV, ion accelerating voltage 3.5 kV and ion source temperature 250°C. Samples were introduced _via_ the gas chromatographic inlet employing a 6 ft 1% SE-30 column temperature programmed at 3°/min starting at 180°C. Chemical ionization mass spectra were recorded with a modified CEC 21-110B mass spectrometer.[22] The samples were introduced _via_ the solid probe inlet.

ACKNOWLEDGMENT

Financial support from the National Institutes of Health (GM-13901, GM-02055 and GM-16216) is gratefully acknowledged.

Downloaded At: 04:29 30 January 2011

REFERENCES

1. J. Diekman and C. Djerassi, J. Org. Chem., _32_, 1005 (1967).
2. (a) J. Diekman, J. B. Thomson and C. Djerassi, J. Org. Chem., _33_, 2271 (1968); (b) _ibid_., _34_, 3147 (1969).
3. (a) H. Budzikiewicz, C. Djerassi and D. H. Williams, "Mass Spectrometry of Organic Compounds", Holden-Day, San Francisco, 1967, p. 475; (b) P. D. Woodgate, R. T. Gray and C. Djerassi, Org. Mass Spectrom., _4_, 257 (1970).
4. (a) W. P. Weber, R. A. Felix and A. K. Willard, J. Amer. Chem. Soc., _91_, 6544 (1969); (b) _ibid_., Tetrahedron Lett., 907 (1970).
5. G. H. Draffan, R. N. Stillwell and J. A. McCloskey, Org. Mass Spectrom., _1_, 669 (1968).
6. E. White, V, S. Tsuboyama and J. A. McCloskey, J. Amer. Chem. Soc., _93_, 6340 (1971).
7. J. A. McCloskey, R. N. Stillwell and A. M. Lawson, Anal. Chem., _40_, 233 (1968).
8. C. J. W. Brooks and B. S. Middleditch, "Modern Methods of Steroid Analysis", E. Heftmann, Ed., Academic Press, New York, 1973.
9. S. Sloan, D. J. Harvey and P. Vouros, Org. Mass Spectrom., _5_, 789 (1971).

10. P. Vouros and D. J. Harvey, Anal. Chem., 45, 7 (1973).

11. P. Vouros and D. J. Harvey, J. Chem. Soc., Perkin Trans. I, 727 (1973).

12. D. J. Harvey, M. G. Horning and P. Vouros, J. Chem. Soc. Perkin Trans. I, 1074 (1972).

13. D. J. Harvey, M. G. Horning and P. Vouros, Tetrahedron, 27, 4231 (1971).

14. D. J. Harvey, M. G. Horning and P. Vouros, Chem. Commun., 898 (1970).

15. D. J. Harvey, M. G. Horning and P. Vouros, Anal. Lett., 3, 489 (1970).

16. T. J Odiorne, D. J. Harvey and P. Vouros, J. Phys. Chem., 76, 3217 (1972).

17. M. S. Wilson, I. Dzidic, and J. A. McCloskey, Biochim. Biophys. Acta, 240, 623 (1971).

18. K. R. Jennings, J. Chem. Phys., 43, 4176 (1965).

19. R. C. Denney, "Named Organic Reactions", Plenum Press, New York, 1969, pp. 31-34.

20. E. M. Chambaz and E. C. Horning, Anal. Biochem., 30, 7 (1969).

21. J. A. McCloskey, R. N. Stillwell and A. M. Lawson, Anal. Chem., 40, 233 (1968).

22. (a) J. H. Futrell and L. H. Wojcik, Rev. Sci. Instrum., 42, 244 (1971); (b) I. Dzidic, D. M. Desiderio, M. S. Wilson, P. F. Crain and J. A. McCloskey, Anal. Chem., 43, 1877 (1971).

Received September 12, 1973

Accepted September 18, 1973

Downloaded At: 04:29 30 January 2011