Table I. Methoxycarbonylation of Organic Halides

$$RHal \xrightarrow[CH_3OH,\ CH_3O^-]{Ni(CO)_4} RCOOCH_3$$

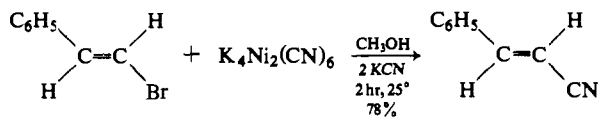
RX	Reaction time, hr, and temp, °C	Methyl ester, % yield
trans-1-Bromo-2-phenylethylene	2, 25[a]	*trans*-Cinnamate, 95
cis-1-Bromo-2-phenylethylene	1, 45[b]	*cis*-Cinnamate, 96;[c] *trans*-cinnamate, 4[c]
1-Bromo-2,2-diphenylethylene	12, 25[a]	β-Phenylcinnamate, 84
1-Bromocyclohexene	70, 25[a]	1-Cyclohexenecarboxylate, 65
1-Bromo-4-*t*-butylcyclohexene	6, 60[a]	4-*t*-Butyl-1-cyclohexenecarboxylate, 71
cis-1-Bromo-2-ethoxyethylene	1.6, 45[b]	β-Ethoxyacrylate, 62[d]
Iodobenzene	24, 25[a]	Benzoate, 88

[a] Molar ratio halide:nickel carbonyl:methoxide 1:6:3. [b] Molar ratio halide:nickel carbonyl:methoxide 1:6:1. [c] Based on reacted bromide; longer reaction time caused increasing isomerization of *cis* ester to *trans*. [d] Based on reacted bromide; longer reaction time led to formation of methyl β-ethoxy-β-methoxypropionate.

Table II. *t*-Butoxycarbonylation of Organic Halides

$$RHal \xrightarrow[t\text{-BuOH},\ t\text{-BuO}^-]{Ni(CO)_4} RCOO\text{-}t\text{-Bu}$$

RX	Ratio RX : $Ni(CO)_4$: *t*-BuO^-	Reaction time, hr, and temp, °C	*t*-Butyl ester, % yield
trans-1-Bromo-2-phenylethylene	1:3:1	2, 25	*trans*-Cinnamate, 60
trans-1-Chloro-2-phenylethylene	1:6:1.5	60, 60	*trans*-Cinnamate, 50
1-Chlorocyclohexene	1:6:3	48, 60	1-Cyclohexenecarboxylate, 64
1-Bromo-4-*t*-butylcyclohexene	1:6:3	16, 60	4-*t*-Butyl-1-cyclohexenecarboxylate, 76
1-Iodoheptane	1:6:2	24, 50	Octanoate, 66
1,6-Diiodohexane	1:6:3	40, 60	Octane-1,8-dioate, 61



The experimental execution of the alkoxycarbonylation reaction is illustrated by the procedure for the synthesis of methyl 4-*t*-butyl-1-cyclohexenecarboxylate. (*All operations involving nickel carbonyl were performed in a well-ventilated hood.*) To a solution of sodium methoxide (3.0 mmol, 0.16 g) in 5 ml of dry methanol under argon in a 25-ml flask fitted with side arm and reflux condenser was added nickel carbonyl (*danger, toxic*) (6.0 mmol, 0.8 ml) followed by 1-bromo-4-*t*-butylcyclohexene (1.0 mmol, 0.22 g). The mixture was heated to 60° and held there for 6 hr, during which time a deep red color developed. After cooling to 25°, carbon monoxide was bubbled through the mixture for 0.5 hr to dispel any remaining nickel carbonyl and to decompose nickel-containing side products which interfere with isolation. The exit gas stream was passed through a trap containing concentrated nitric acid to decompose the volatile nickel complexes. The resulting green solution was poured into 50 ml of 0.1 *N* HCl and 50 ml of ether in a separatory funnel and thoroughly shaken. The ether phase was washed with two 50-ml portions of distilled water, dried over anhydrous magnesium sulfate, concentrated, and distilled to give 0.14 g (71%) of methyl 4-*t*-butyl-1-cyclohexenecarboxylate as a colorless liquid having identical infrared and nmr spectra with a pure sample and homogeneous by vapor phase and thin layer chromatographic analysis.[10-12]

(9) For preparation of the cyanonickel(I) reagent see W. M. Burgess and J. W. Eastes, *Inorg. Syn.*, **5**, 197 (1957).

(10) 1-Bromo-4-*t*-butylcyclohexene[4] was prepared by a new method from 4-*t*-butylcyclohexanone (E. J. Corey and L. S. Hegedus, in preparation).

(11) A modified procedure was used for work-up when potassium *t*-butoxide was used as base, since treatment with carbon monoxide failed to free the reaction mixture of volatile nickel complexes. In these instances the reaction mixture was subjected directly to ether–water extraction, and the ether layer was evaporated to dryness under aspirator vacuum using a liquid nitrogen trap. The nonvolatile residue was then subjected to the standard isolation procedure.

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Migrations of the Trimethylsilyl Group upon Electron Impact in Steroids

Sir:

Trimethylsilylation is used extensively by the chemist and biochemist in the gas–liquid partition chromatographic separation and mass spectrometric identification of a wide range of biologically important substances.[1] In the course of studies on the metabolism of C_{19} steroids in rat liver microsomes,[2] an intense and unexplained peak at *m/e* 191 was encountered frequently in the mass spectra of various dihydroxy and trihydroxy steroid trimethylsilyl (TMS) ethers. Because of both the key role that such TMS derivatives play in analytical mass spectrometry and

(1) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day Inc., San Francisco, Calif., 1967, pp. 471–476.

(2) J.-Å. Gustafsson, B. P. Lisboa, and J. Sjövall, *Eur. J. Biochem.*, **5**, 437 (1968).

Table I. Mass Shift Data[a,b]

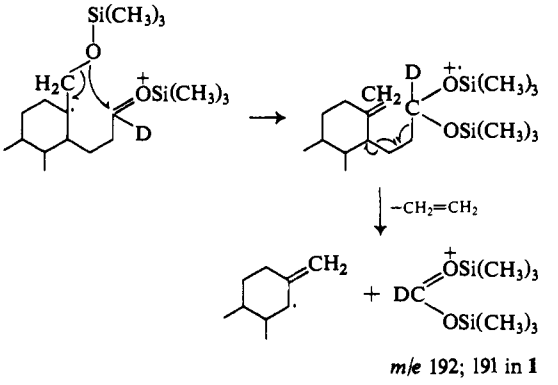
Compound	*m/e*	*m/e* upon C_{17} deuteration[c]	*m/e* upon formation of CD_3SiO-[d]
1	129 (76)		138 (68)
	191 (36)		209 (35)
	217 (29)		235 (31)
3α,17β,18-Triol	129 (59)	130 (51)	
2	191 (49)	192 (46)	
	217 (100)	217 (100)	
15α-Hydroxytestosterone bis(trimethylsilyl ether)	191 (24)		209 (23)
	217 (100)		235 (100)
3β,15α,17β-Triol	191 (44)	191, 192 (29:26)	
4	217 (100)	218 (100)	
5	191 (62)		209 (53)
	205 (27)		223 (25)
	218 (23)		236 (21)
3β,16α,17β-Triol	191 (100)	191 (100)	
	205 (23)	205, 206 (20:16)	
	218 (18)	219 (18)	

[a] Compounds **1**, **3**, and **5** were prepared by standard trimethylsilylation procedures. Compounds **2**, **4**, and 6 were prepared by sodium borohydride reduction of the corresponding 17-ketosteroid followed by trimethylsilylation. [b] The base peak for **1** and **5** is at *m/e* 358 (M − 90). Values in parentheses refer to per cent abundance. [c] These derivatives were prepared by sodium borodeuteride reduction of the ketone to yield C_{17} β-ols. [d] Prepared with 100 μl of perdeuteriotrimethylsilyl chloride–pyridine, 10:1 (v/v), room temperature, overnight.

the potential theoretical implications and diagnostic value associated with the occurrence of this peak, we undertook a mechanistic study aimed at elucidating the structure and origin of this *m/e* 191 fragment.

Table I presents the pertinent mass spectral data derived from mass shifts between trimethylsilylation and perdeuteriotrimethylsilylation for the 18-, 15α-, and 16α-hydroxytestosterone bis(trimethylsilyl ethers) **1**, **3**, and **5**, and substitution of deuterium at the 17α position of the analogous derivatives **2**, **4**, and **6**. Accurate mass measurement (high-resolution spectra were obtained with an Atlas SM-1 spectrometer) for *m/e* 191 determined for the three hydroxytestosterone bis(trimethylsilyl ether) derivatives **1**, **3**, and **5** fixes the composition as $C_7H_{19}Si_2O_2$. The mass shift of 18 mass units upon formation of the $(CD_3)_3$-SiO derivative for **1**, **3**, and **5** indicates the presence of six CD_3 groups and, therefore, two TMS groups in the fragment *m/e* 191. These data are accommodated by the structures $(CH_3)_3SiO^+{=}CHOSi(CH_3)_3$ and $(CD_3)_3Si$-$O^+{=}CHOSi(CD_3)_3$ (*m/e* 191 + 18), respectively. Generation of this ion requires a remarkable degree of mobility for the TMS group since it must undergo 1,2 and 1,3 migration in order to arrive at the geminal arrangement present in the above ions. Furthermore the mass shift upon deuteration at C_{17} for the analogous androstane derivatives **2**, **4**, and **6** indicates a further complexity, namely, an ion of *m/e* 191, depending upon the steroid, may form with loss or retention of deuterium at C_{17} (*cf.* Table I).

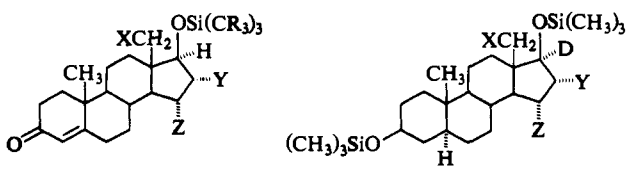
The following tentative mechanisms may be written to account for the formation of ion *m/e* 191 for **1** and the retention of the $C_{17\alpha}$ deuterium for **2** in *m/e* 192.



m/e 192; 191 in **1**

Formation of ion *m/e* 191 without incorporation of deuterium for **5** and **6** is shown in Scheme I. Formation of ion *m/e* 191 with and without incorporation of deuterium for **3** and **4** is shown in Scheme II.

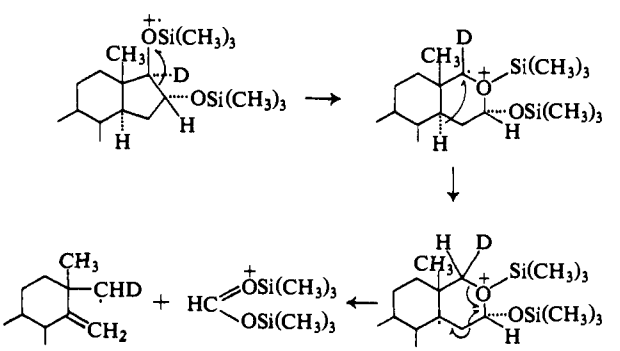
Other peaks of interest, such as *m/e* 129, may be assigned to $(CH_3)_3SiO^+{=}CHCH{=}CH_2$ on the basis of the data in Table I and the fact that this peak has been noted before in the mass spectra of TMS derivatives of 3β-hydroxy Δ^5-steroids and C_{19} steroids with a 17β-



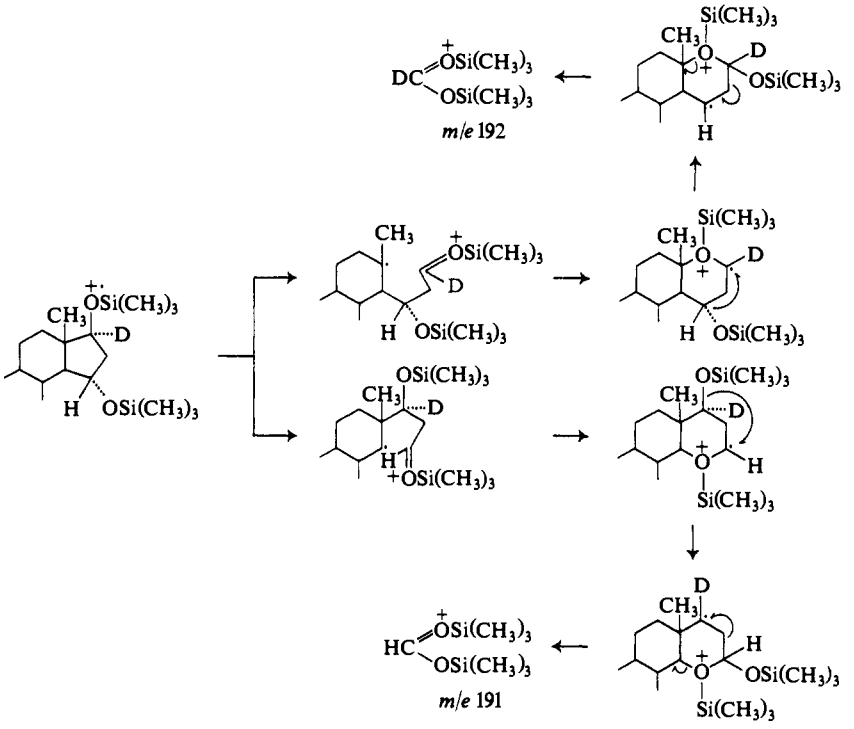
1, X = $OSi(CR_3)_3$; Y, Z = H
3, Z = $OSi(CR_3)_3$; X, Y = H
5, Y = $OSi(CR_3)_3$; X, Z = H

2, X = $OSi(CH_3)_3$; Y, Z = H
4, Z = $OSi(CH_3)_3$; Y, X = H
6, Y = $OSi(CH_3)_3$; X, Z = H

Scheme I

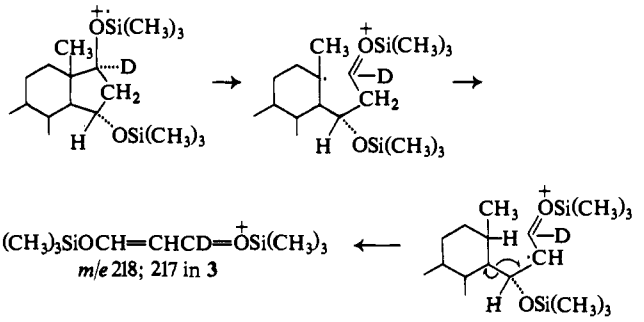


Scheme II



hydroxy group in an otherwise unsubstituted D ring.[3]

The base peak in **3** and **4** appearing at *m/e* 217 may be found in the following way.



This peak of *m/e* 217 has been observed in long-chain compounds.[4]

These mechanisms involve α cleavage and H migration, both of which are well-documented processes for the TMS group.[5] The neutral products are often allylic and homoallylic radicals. Migrations of the TMS group as proposed are novel for steroids, and cyclic structures such as those drawn above may offer a lower energy pathway for their occurrence. Migration of the TMS group upon electron impact has been observed in the case of fatty acid esters and for long-chain compounds.

The driving force for most of the fragmentations is the production of highly stable ions containing the Si-O^+=CHR group where R = O or allyl. The above mechanisms agree with the experimental data presented in Table I. They are reasonable in terms of known decompositions of related ions, but clearly other pathways may be written.

Two important points which emerge from these findings with steroids are (a) we concur with McCloskey's opinion that the TMS group has a high migratory ability similar to that of hydrogen,[6] and (b) as a corollary, element mapping with TMS derivatives is inevitably subject to uncertainties.

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(3) (a) P. Eneroth, K. Hellstrom, and R. Ryhage, *J. Lipid Res.*, **5**, 245 (1964); (b) J. Sjovall and R. Vihko, *Steroids*, **7**, 447 (1966); (c) J. Diekman and C. Djerassi, *J. Org. Chem.*, **32**, 1005 (1967).

(4) P. Capella and C. M. Zorgut, *ibid.*, **40**, 1459 (1968). (a) In the mass spectra of 1,10-decanediol bis(trimethylsilyl) ether and 1,22-docosanediol bis(trimethylsilyl) ether[5] an ion of *m/e* 177 appears which has been assigned to structure $(CH_3)_2Si{=}O^+CH_2OSi(CH_3)_3$. Formation of this ion apparently requires a close proximity of the termini of these long molecules. (b) W. J. Richter and A. L. Burlingame, *Chem. Commun.*, 1158 (1968).

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

(6) G. H. Draffan, R. N. Stillwell, and J. A. McCloskey, 16th Annual Conference on Mass Spectroscopy and Allied Topics, Pittsburgh, Pa., May 1968.

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