7.—Amounts of the bromide (1.1–4.84 g) were dissolved in thiophene-free, dry benzene to make solutions of molarities given in Table II. Freshly distilled tri-*n*-butyltin hydride (1.1 equiv relative to the amount of **7** used) was then added and the solutions were sealed in pressure bottles under nitrogen. The reaction mixtures were placed in sand baths for 42 hr at 145° and 24 hr at 155 and 150°. The vessels were cooled and opened and the contents were reduced in volume to about 5 ml by distillation of the benzene solvent. In each case the material was then chromatographed on alumina using hexane as the eluting solvent. Hydrocarbon **23** eluted first with the rearranged product **24** afterward. On occasion the elutions were speeded by use of 25–50% benzene–hexane mixtures as the eluting agent. Identification of products was by mixture melting point and spectral (ir, nmr, and mass) comparison with authentic material. Yields were calculated from the weights of isolated product.

Bromide 8.—The procedure here was similar to the above, except that all reactions were conducted at 145° for 44 hr and all the benzene was removed after the heating period. The chromatographic eluting agents employed were Skellysolve B, followed by a 1:1 mixture of Skellysolve B with benzene. Gas–liquid partition chromatography (4 ft SE-30 column at 170°) was then used on this column-chromatographed material to separate products **25** (retention time 5.79 min) and **26** (retention time 9.27 min). Identification of products was by coinjection of and spectral comparison with knowns. Compositions were calculated by electronic integration of the glpc peaks and yields by weight of column chromatographed product.

Bromides 5 and 6.—Approximately 0.1 *M* solutions of these bromides (0.4 g scale) in benzene were reduced with tri-*n*-butyltin hydride as described for **7** at 150° for 20–24 hr. Chromatography on alumina afforded only unrearranged product. Runs conducted at 78° (refluxing benzene) gave identical results.[35]

Bromide 4.—Amounts of **4** (0.27–1.00 g) were dissolved in benzene to give the molarities shown in Table III. Reduction with tri-*n*-butyltin hydride was carried out in sealed ampoules under nitrogen and the reaction material was chromatographed on alumina as described above for **7**. Analysis by glpc (4 ft polypropylene glycol succinate column at 190°) gave the composition data. Yields were obtained from the weight of the column chromatographed product. Identification of **29** and **30** was by coninjection of and spectral comparison with known samples. No evidence was found for the known[36] rearrangement possibility, 1,2-diphenylcyclopropane.

Registry No.—**4**, 32812-52-5; **5**, 32812-53-6; **6**, 32812-54-7; **7**, 32812-55-8; **8**, 32812-56-9; **14**, 32812-57-0; **14** 2,4-DNP, 32812-58-1; **15**, 32812-59-2; **16**, 24771-20-8; **17**, 32812-61-6; **19**, 807-24-9; **21**, 32812-63-8; **22**, 32812-64-9; **25**, 32812-65-0; *cis*-**26**, 32819-58-2; *trans*-**26**, 32819-59-3; **27**, 32812-66-1; **28**, 32812-67-2; **30**, 778-66-5; 1-benzyl-4-phenylcyclohexanol, 32812-69-4; 1-benzyl-4-phenylcyclohexene, 32812-70-7; 4-phenyl-1-benzylidenecyclohexane, 32812-71-8.

(35) A referee has objected that rearrangement in these cases is not precluded because no comparison was made of these reduction products with the appropriate 1,3-diphenylcycloalkane. While no such comparison was made, detailed examination by spectral and chromatographic methods of the reduction products (the interested reader may see ref 1a) showed *only* unrearranged product. Within the certainty that such results possess we claim that no rearrangement occurred under the conditions studied.

(36) C. G. Overberger, R. E. Zangaro, and J.-P. Anselme, *J. Org. Chem.*, **31**, 2046 (1966), and references therein.

Mass Spectra of Trimethylsilyl Derivatives of Pyrimidine and Purine Bases

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Trimethylsilyl derivatives of pyrimidine and purine bases were prepared by reaction with *N,O*-bis(trimethylsilyl)acetamide or *N,O*-bis(trimethylsilyl)trifluoroacetamide, and their mass spectra studied in detail using high-resolution and deuterium-labeling techniques. The position of thiation or methylation (C-5 *vs.* C-6) in pyrimidines can be established from a major ion species composed of C-4,5 and their attached groups, which is derived from the abundant M − Me ion. A similar process is followed in the decomposition of O^2,N^4-bis(trimethylsilyl)-cytosine following migration of trimethylsilyl to N^4 to produce *m/e* 170. Bases containing methylated amino functions characteristically eliminate methylene imine in parallel to the behavior of free bases and nucleosides. Mass spectra of bases which bear more than one trimethylsilyl group often exhibit intense peaks associated with the doubly charged species $(M - 2Me)^{2+}$, which was found by deuterium labeling to have different mechanistic origins in different bases.

Basic electron impact induced fragmentation reactions of the common pyrimidine and purine bases from ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) have been studied in some detail[1] and are clearly useful for the characterization of such compounds.[2] However, since the isolation of small quantities of biologically modified bases as single components from RNA or DNA hydrolysates for mass spectrometry is often not feasible, we have examined the mass spectra of the more volatile trimethylsilyl derivatives, which are suitable for gas chromatography–mass spectrometry. Although these derivatives[3] have been used for a number of years in synthetic procedures, the work of Sasaki and Hashizume[4] first drew our attention to their gas chromatographic properties.[5]

The present report is based on a detailed study of the mass spectra of trimethylsilyl derivatives of 33 bases, with emphasis on those compounds which are derived from RNA and DNA.[6]

(1) (a) J. M. Rice, G. O. Dudek, and M. Barber, *J. Amer. Chem. Soc.*, **87**, 4569 (1965); (b) K. C. Smith and R. T. Aplin, *Biochemistry*, **5**, 2125 (1966); (c) J. M. Rice and G. O. Dudek, *J. Amer. Chem. Soc.*, **89**, 2719 (1967); (d) J. L. Occolowitz, *Chem. Commun.*, 1226 (1968); (e) J. Ulrich, R. Teoule, R. Massot, and A. Cornu, *Org. Mass Spectrom.*, **2**, 1183 (1969); (f) E. G. Brown and B. S. Mangat, *Biochim. Biophys. Acta*, **177**, 427 (1969); (g) S. M. Hecht, A. S. Gupta, and N. J. Leonard, *ibid.*, **182**, 444 (1969).

(2) For additional references to the mass spectrometry of modified pyrimidine and purine bases, see (a) J. A. McCloskey in "Basic Principles in Nucleic Acid Chemistry," P. O. P. Ts'o, Ed., Academic Press, New York, N. Y., in press; (b) J. Deutsch, Z. Neiman, and F. Bergmann, *Org. Mass Spectrom.*, **3**, 1219 (1970).

(3) For example, (a) E. Wittenburg, *Chem. Ber.*, **99**, 2380 (1966); (b) B. Shimizu, M. Asai, and T. Nishimura, *Chem. Pharm. Bull.*, **15**, 1847 (1967); (c) T. Nishimura and I. Iwai, *ibid.*, **12**, 352 (1964); (d) T. Nishimura, B. Shimizu, and I. Iwai, *ibid.*, **11**, 1470 (1963); (e) T. Nishimura and I. Iwai, *ibid.*, **12**, 357 (1964); (f) E. Wittenburg, *Collect. Czech. Chem. Commun.*, **36**, 246 (1970).

(4) Y. Sasaki and T. Hashizume, *Anal. Biochem.*, **16**, 1 (1966).

(5) (a) Y. Mizuno, N. Ikekawa, T. Itoh, and K. Saito, *J. Org. Chem.*, **30**, 4066 (1965); (b) C. W. Gehrke, D. L. Stalling, and C. D. Ruyle, *Biochem. Biophys. Res. Commun.*, **28**, 869 (1967); (c) T. Hashizume and Y. Sasaki, *Anal. Biochem.*, **24**, 232 (1968); (d) C. W. Gehrke and C. D. Ruyle, *J. Chromatogr.*, **38**, 473 (1968); (e) W. C. Butts, *J. Chromatogr. Sci.*, **8**, 474 (1970); (f) J. E. Mrochek, W. C. Butts, W. T. Rainey, Jr., and C. A. Burtis, *Clin. Chem.*, **17**, 72 (1971); (g) C. W. Gehrke and D. B. Lakings, *J. Chromatogr.*, **61**, 45 (1971).

(6) E. White, V, and J. A. McCloskey in "Archives of Mass Spectral Data," Vol. 2, E. Stenhagen, S. Abrahamsson, and F. W. McLafferty, Eds., Wiley-Interscience, New York, N. Y., 1971, pp 450–525.

TABLE I

SELECTED IONS FROM THE MASS SPECTRA OF TRIMETHYLSILYL DERIVATIVES OF PYRIMIDINE AND PURINE BASES

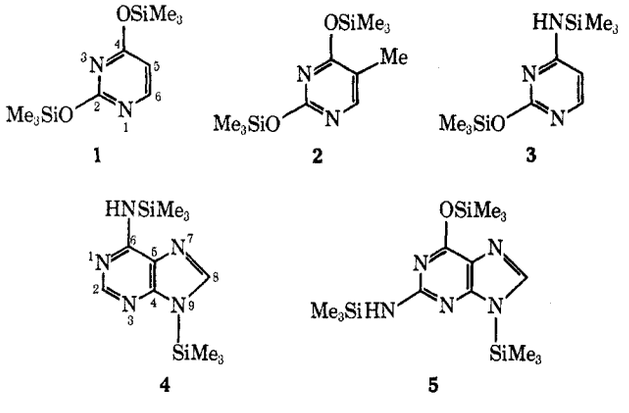
Parent base	No. of SiMe3 groups	Mass (relative abundance) M	M − H	M − Me	c	o	m/e 147	m/e 84	m/e 73	Other characteristic ions
Purine (17)	1	192 (67)	191 (3.6)	177 (100)	119 (0.0)	81 (<1)	(0.0)	(8.6)	(21)	123 (29); m, 150 (7.3)
6-Methylpurine (11)	1	206 (73)	205 (3.5)	191 (100)	133 (0.0)	88 (1.5)	(0.0)	(9.0)	(23)	123 (16); m, 164 (5.6)
3-Methyladenine (9)	1	221 (52)	220 (4.1)	206 (100)	148 (0.7)	95.5 (11)	(0.0)	(14)	(21)	176 (8.2); m, 179 (17)
N^6-Methyladenine (15)	1	221 (100)	220 (19)	206 (53)	148 (6.5)	95.5 (0.6)	(0.0)	(10)	(53)	n, 192 (28); 193 (25)[a]
6-Chloropurine (18)[b]	1	226 (96)	225 (1.1)	211 (100)	153 (0.0)	98 (<1)	(0.0)	(6.4)	(45)	m, 184 (8.0); 191 (6.0)
6-Methylthiopurine (19)	1	238 (100)	237 (9.0)	223 (17)	165 (17)[a]	104 (0.0)	(0.0)	(6.9)	(83)	164 (4.4); 192 (8.9)
5-Methylcytosine	2	269 (37)	268 (2.8)	254 (100)	196 (2.4)	119.5 (17)	(12)	(3.7)[a]	(39)	1, 112 (13); 184 (6.0)
Hypoxanthine	2	280 (48)	279 (2.5)	265 (100)	207 (3.7)[a]	125 (5.5)	(3.9)	(4.2)	(47)	d, 206 (6.8); m, 238 (1.6)
1-Methyladenine[c]	2	293 (8.1)	292 (0.7)	278 (100)	220 (1.1)	131.5 (0.3)	(0.0)	(3.4)	(48)	206 (8.6); 221 (4.6)
2-Methyladenine	2	293 (32)	292 (2.4)	278 (100)	220 (3.0)	131.5 (1.5)	(0.0)	(5.6)	(40)	237 (1.7); 206 (10)
7-Methyladenine (12)	2	293 (37)	292 (24)	278 (100)	220 (2.9)	131.5 (2.4)	(0.0)	(26)	(57)	125 (17); 179 (16)
7-Methylguanine	2	309 (22)	308 (2.9)	294 (100)	236 (2.8)	139.5 (2.6)	(3.0)	(14)	(51)	k, 99 (10); f, 180 (17)
7-Methylxanthine	2	310 (50)	309 (11)	295 (100)	237 (1.9)	140 (6.6)	(18)	(8.8)	(42)	k, 100 (5.2); f, 180 (8.0)
5-Hydroxyuracil	3	344 (41)	343 (20)	329 (100)	271 (1)	157 (0.5)	(10)	(1.4)	(84)	255 (7.8); 270 (6.6)
6-Hydroxyuracil	3	344 (75)	343 (52)	329 (100)	271 (1)	157 (1.3)	(38)	(0.0)	(62)	241 (4.1); 270 (7.0)
5-Hydroxymethylcytosine (14)	3	357 (100)	356 (5.1)	342 (42)	284 (6.5)	163.5 (0.0)	(27)	(6.1)[a]	(92)	254 (11); 268 (5.2)
5-Hydroxymethyluracil (13)	3	358 (60)	357 (5.0)	343 (29)	285 (3.1)	164 (0.0)	(17)	(3.6)[a]	(100)	k, 100 (16); 255 (7.8)[a]
Xanthine	3	368 (72)	367 (3.7)	353 (100)	295 (8.5)[a]	169 (0.8)	(26)	(2.5)	(80)	f, 238 (2.5); 279 (12)
Orotic acid	3	372 (7.0)	371 (3.6)	357 (52)	299 (0.0)	171 (0.0)	(21)	(0.9)	(94)	254 (100); 329 (2.6)
Uric acid	4	456 (78)	455 (4.0)	441 (57)	383 (6.9)[a]	213 (0.5)	(18)	(1.6)	(100)	367 (5.1); 382 (16)

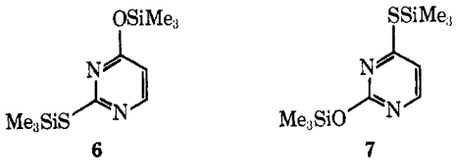
[a] Doublet; intensity uncorrected. [b] Masses and abundances of chlorine containing ions correspond to ^{35}Cl species. [c] Contaminated by an isomeric derivative; see Experimental Section.

Results and Discussion

As reported in a preliminary communication,[7] the mass spectra of trimethylsilylated bases exhibit far fewer fragment ions than the corresponding nucleosides because of the exceptional stabilization afforded by the aromatic nucleus. However, the certainty of identification and of structure correlations for fragment ions of low abundance is maintained largely through the use of gas chromatography–mass spectrometry, which precludes most ions otherwise present which could arise from artifacts and impurities. In addition, the complementary use of d_9-trimethylsilyl derivatives[8] [*e.g.*, $-Si(CD_3)_3$] and of high-resolution techniques constitutes a highly useful means for identification of minor ions.

General Fragmentation Reactions.—Mass spectra of trimethylsilyl derivatives of the five major bases from RNA and DNA (**1**–**5**) are shown in Figure 1. Molecular ion (M) abundances are generally high, reflecting their aromatic character. As shown in Table I, greatest molecular ion stability is shown by derivatives in which the charge can be localized on an exocyclic heteroatom not bearing a trimethylsilyl group, such as 6-methylthiopurine and N^6-methyladenine. Also of interest are the lower molecular ion stabilities exhibited by derivatives of 2- and 4-thiouracil (**6** and **7**) compared with that of uracil (**1**), in contrast to the opposite behavior usually shown by sulfur analogs.[9] Similar effects were found in the spectra of *O,S*-bis(trimethylsilyl) derivatives of 5- and 6-methyl-2-thiouracil, and 6-propyl-2-thiouracil, and are in all cases attributed to the enhanced stability of the M − CH_3 fragment ion, discussed below.





As indicated in Figure 1 and Table I, loss of hydrogen or methyl radicals from M constitute major fragmentation pathways. The spectra of a number of d_9-trimethylsilyl derivatives, including the representative examples shown in Table II, reveal that hydrogen lost

TABLE II

HYDROGEN RANDOMIZATION IN THE FORMATION OF M − HYDROGEN AND M − METHYL IONS IN THE MASS SPECTRA OF d_9-Trimethylsilyl Derivatives

Compd	(M − H)/(M − D)[a]	(M − CD_2H)/(M − CD_3)
O^2,O^4-Bis(d_9-trimethylsilyl)uracil	2.1	0.02
O^2,O^4-Bis(d_9-trimethylsilyl)-6-methyluracil	1.6	0.05
O^2,O^4-Bis(d_9-trimethylsilyl)-5,6-dihydrouracil	6.2	0.04
O^2,N^4-Bis(d_9-trimethylsilyl)-cytosine	1.8	0.05
d_9-Trimethylsilyl O^2,O^4-bis(d_9-trimethylsilyl)orotate	1.7	0.01
$1,N^6$-Bis(d_9-trimethylsilyl)-7-methyladenine	2.1	0.09
6-Methyl-9-(d_9-trimethylsilyl)-purine	2.0	0.22

[a] Corrected for naturally occurring heavy isotopes.

(7) J. A. McCloskey, A. M. Lawson, K. Tsuboyama, P. M. Krueger, and R. N. Stillwell, *J. Amer. Chem. Soc.*, **90**, 4182 (1968).

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

(9) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967, Chapter 7.

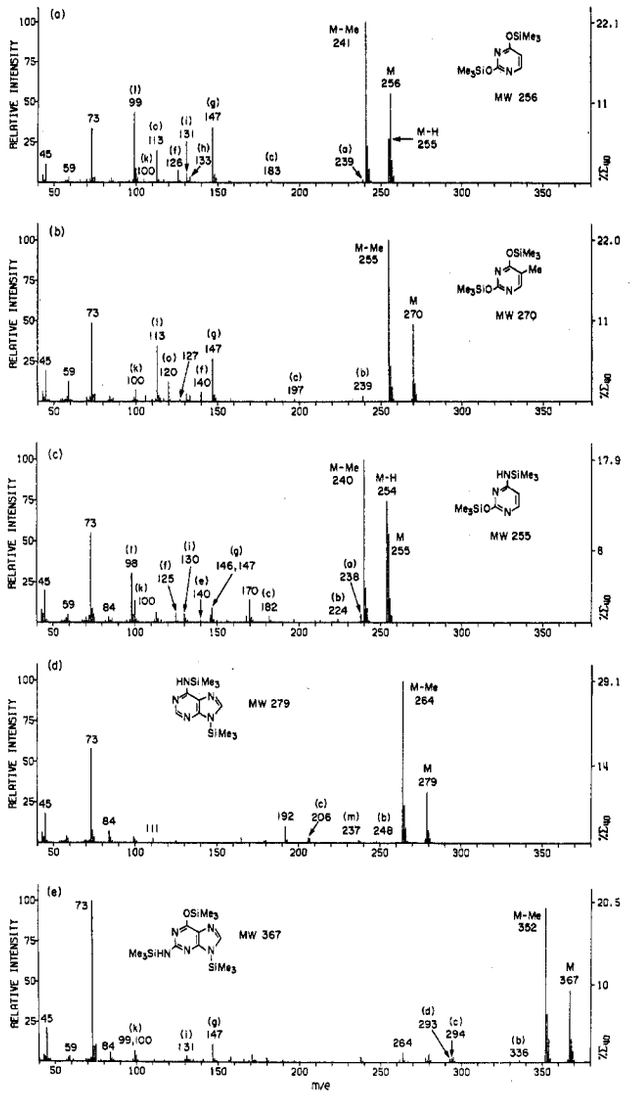


Figure 1.—Mass spectra of (a) O^2,O^4-bis(trimethylsilyl)uracil (**1**), (b) O^2,O^4-bis(trimethylsilyl)thymine (**2**), (c) O^2,N^4-bis(trimethylsilyl)cytosine (**3**), (d) N^6,9-bis(trimethylsilyl) adenine (**4**), (e) N^2,O^6, 9-tris(trimethylsilyl)guanine (**5**).

in the formation of M − H originates both from trimethylsilyl functions and the base. An intense M − H peak is also found in the spectrum of free 7-methyladenine,[2] where it is derived mainly by loss of hydrogen from N^6.[2a] Although scrambling of trimethylsilyl hydrogens with other hydrogens during fragmentation has been reported,[10] simple loss of a hydrogen radical from the trimethylsilyl group has not to our knowledge been previously observed. It is therefore worthwhile to examine the ubiquitous loss of a methyl radical from the molecular ion, in the spectra of d_9-trimethylsilyl derivatives as shown in Table II. The ratio (M − 14)/(M − 15) from spectra of unlabeled derivatives can be measured with an accuracy of ~0.01. With the exception of the dihydrouracil derivative, the values of (M − CD_2H)/(M − CD_3) show that hydrogen randomization before loss of a methyl radical occurs to a slight to moderate extent in the compounds examined. Since the effect was greatest in the case of 6-methyl-9-(d_9-trimethylsilyl)purine, the ratio of (M − CD_2H)/(M − CD_3) in that compound was examined as a function of ionizing electron energy. The results, shown in Figure 2, show that hydrogen interchange between methyl functions and the base increases substantially at low voltage values. This behavior is attributed to increased molecular ion lifetimes in the low-energy region,[11] and therefore increased opportunity for interchange. Comparison of data from both columns in Table II indicates that the higher values of (M − H)/(M − D) relative to (M − CD_2H)/(M − CD_3) cannot be attributed primarily to hydrogen scrambling in the molecular ion, although it is undoubtedly a contributing factor.

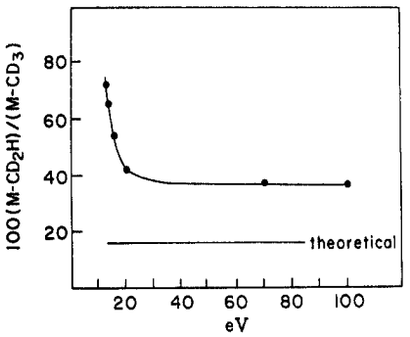
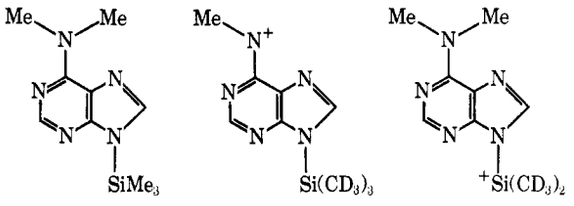


Figure 2.—Variation of the ratio (M − CD_2H)/(M − CD_3) as a function of ionizing electron energy in the mass spectrum of 6-methyl-9-(d_9-trimethylsilyl)purine.

Bases which contain methyl groups other than those in the trimethylsilyl moiety, as in N^6,N^6-dimethyl-9-(trimethylsilyl)adenine (**8**), can in principle lose methyl radicals from two sources. Several such examples have been examined as the d_9-trimethylsilyl derivatives in order to determine the extent to which nontrimethylsilyl methyls participate in the reaction. In the case of **8a**, approximately 77% of the methyl groups lost were



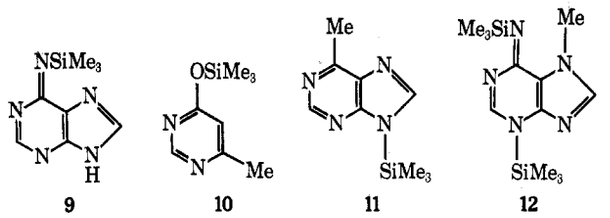
8 **8a**

found to be from N^6 (M − CH_3) as opposed to the remaining 23% (M − CD_3) from the trimethylsilyl group. Loss of methyl from N^6 is energetically favorable since the charge can be delocalized into the purine nucleus, as also shown by the analogous reaction which occurs with the free base.[12] Similarly, a substantial fraction (34%) of nontrimethylsilyl methyl is lost from the derivative of 3-methyladenine, **9**. However when the methyl group is bound to the aromatic nucleus its loss is suppressed in favor of fragmentation in the trimethylsilyl moiety, as shown by derivatives of 6-methyluracil (**10**) (loss <3%) and 6-methylpurine (**11**) (loss <2%). Of the labeled derivatives which were examined, the sole exception was the 7-methyladenine derivative **12**, in

(10) G. H. Draffan, R. N. Stillwell, and J. A. McCloskey, *Org. Mass Spectrom.*, **1**, 669 (1968).

(11) A. N. H. Yeo, R. G. Cooks, and D. H. Williams, *Chem. Commun.*, 1269 (1968).

(12) Y. Rahamim, J. Sharvit, A. Mandelbaum, and M. Sprecher, *J. Org. Chem.*, **32**, 3856 (1967).



9 10 11 12

which only 4% of total methyl groups lost were from N-7, in spite of the well-stabilized ion which would be formed. From these limited data it is apparent that by use of deuterium-labeled silylating reagents, the presence of methyl groups can be recognized in some but not all cases, by examination of the M − methyl ion.

In numerous instances loss of either a hydrogen or a methyl radical from the molecular ion is followed by expulsion of methane involving methyl from the trimethylsilyl moiety (*e.g.*, ions a and b, in Figure 1). The origin of additional hydrogen lost in forming ion a as shown by the d_9-trimethylsilyl derivatives is difficult to determine because of minor isotopic impurities associated with the M − CD_3 peak, although net losses of both CD_3H_2 and CD_4H were found to occur. In the case of ion b the fourth hydrogen in methane was determined to originate both from trimethylsilyl functions and from the ring and its substituents.

Most mass spectra examined showed the formation of ions 72, 73, or 74 mass units below the molecular ion. The ion corresponding in mass to M − 72, which was observed most often in spectra of purines, was determined by measurement of exact mass to differ from the molecular ion by C_3H_8Si. Deuterium labeling in the trimethylsilyl moiety resulted in a shift to 81 mass units below M, in support of an elemental composition equivalent to M − $Si(CD_3)_3$ + H, but not M − $CD_2Si(CD_3)_2$. From this we conclude that, even though the samples are introduced by gas chromatograph and are generally homogeneous, some molecules which contain one fewer trimethylsilyl group than the principal species are present or are formed by exchange in the ion source, giving rise to a molecular ion 72 mass units below M. By contrast, the prominent peak at *m/e* 192 in the spectrum of the adenine derivative (Figure 1d) was determined to be derived by loss of Me_3SiCH_2 from *m/e* 264 (M − Me). Appropriate metastable peaks were observed in the mass spectra of **4** (139.6 calcd, 139.8 found) and its d_{18}-trimethylsilyl analog (141.9 calcd, 141.9 found), and was confirmed by metastable defocussing for **4**. The peak shifted seven mass units upon labeling in the trimethylsilyl moiety, clearly showing retention of a silyl hydrogen from the neutral species which is lost.

The characteristic peak frequently observed at M − 73 (ion c; see Table I) arises from loss of a trimethylsilyl radical from the molecular ion. The peak one mass unit lower found in many spectra (ion d) involves loss of Me_2SiO from M, which was verified both by measurements of exact mass and shifts of six mass units in the mass spectra of d_9-trimethylsilyl derivatives. In the case of the thiated uracil analogs **6** and **7** the loss of Me_2SiS (*m/e* 182) but not Me_2SiO (*m/e* 198) occurs as shown in Figure 3, indicating no apparent positional specificity. However, the analogous Me_2SiNH is not lost on electron impact from **3** or any of its derivatives. Formation of ion d requires migration and retention of

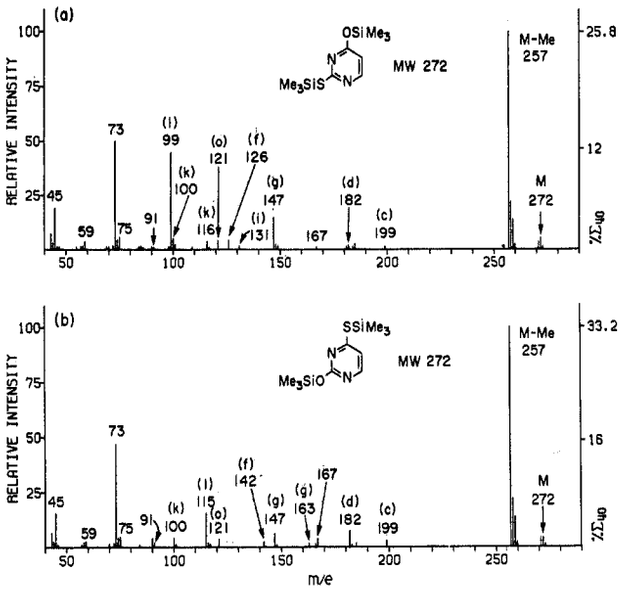
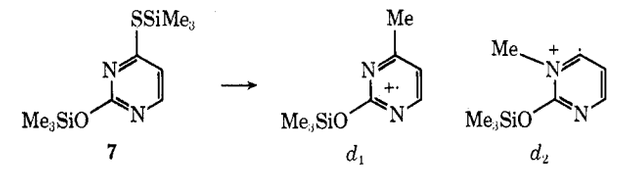


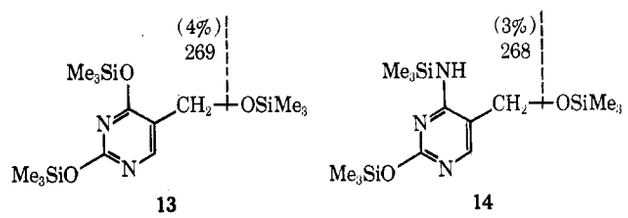
Figure 3.—Mass spectra of (a) S^2,O^4-bis(trimethylsilyl)-2-thiouracil (**6**), (b) O^2,S^4-bis(trimethylsilyl)-4-thiouracil (**7**).

a trimethylsilyl methyl group, *e.g.*, **7** → d_1 or d_2, and serves as a minor but diagnostic indicator of the presence of sulfur or oxygen in the base. Participation of nitrogen in the methyl migration either directly (d_2) or



7 d_1 d_2

indirectly seems probable since the analogous ion of mass 180 is absent from the mass spectrum of the bis(trimethylsilyl) ether of resorcinol. Similarly, loss of Me_3SiX was found to often produce a small peak at M − 89 (X = O), except in the case of **6** and **7** which preferentially gave M − 105 (X = S). This process was more favored in the 5-hydroxymethyl pyrimidine derivatives **13** and **14** due to stabilization afforded by the



13 14

adjacent aromatic ring, but their high-resolution spectra showed minor contributions at the same nominal mass from ions equivalent to M − CH_4 − Me_3Si.

Disruption of the aromatic ring with expulsion of MeSiOCN (ion e) was observed as a minor process in several pyrimidines, including **1** (*m/e* 141, 0.6% rel intensity), **3** (*m/e* 140, Figure 1c), and the trimethylsilyl ethers of 5-hydroxyuracil (*m/e* 229, 1.3%), 6-azauracil (*m/e* 142, 6.3%), and 6-azathymine (*m/e* 156, 2.0%). Analogous ions of the correct nominal mass, containing NH instead of O, were observed in the spectra of **4**, **9**, and **11** but failed tests of either exact mass measurement or required shifts of nine mass units in d_9-tri-

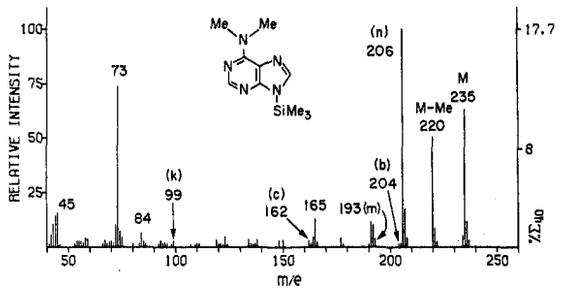


Figure 4.—Mass spectrum of N^6,N^6-dimethyl-9-(trimethylsilyl)adenine (**8**).

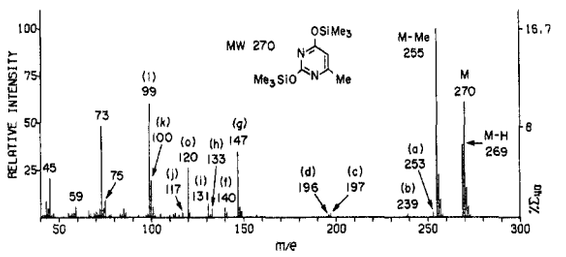
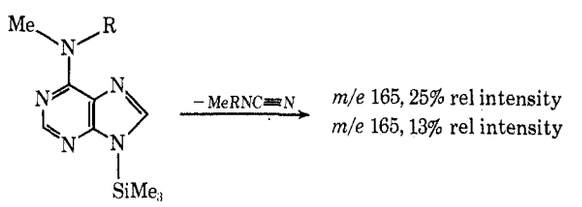


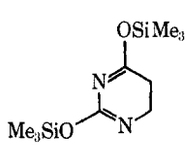
Figure 5.—Mass spectrum of O^2,O^4-bis(trimethylsilyl)-6-methyluracil (**10**).

methylsilyl derivatives. However, a similar process involving expulsion of a C–N fragment of the aromatic nucleus occurs in the spectra of N^6-methylated adenine derivatives **15** and **8** (Figure 4), in which N-1 and C-6 and its substituents are lost.



15, R = H
8, R = Me

If the elimination of Me_3SiXCN (X = O, S, NR) proceeds from M − Me rather than the molecular ion, an additional peak in the spectrum (ion f) appears 15 mass units lower than ion e. This ion is produced in the fragmentation of numerous compounds, including **1**, **10** (Figure 5), and O^2,O^4-bis(trimethylsilyl)-5,6-dihydrouracil (**16**) (Figure 6), as well as **8** and **15**. The



16

6-methylpurine derivative **11** shows the same behavior, CH_3CN being lost (*m/e* 150, 4.4% rel intensity). When its d_9-labeled counterpart was examined it was found that ion f (*m/e* 156) also contained contributions at *m/e* 155 and 154. These latter ions reflect hydrogen exchange between the trimethylsilyl function and the base as previously discussed, in support of the identity of M − Me as the precursor of ion f. Comparison of ion f from the thiated models (Figure 3) shows retention of the heteroatom at C-4 (*m/e* 126, 142). From this it can be inferred that expulsion of Me_3-

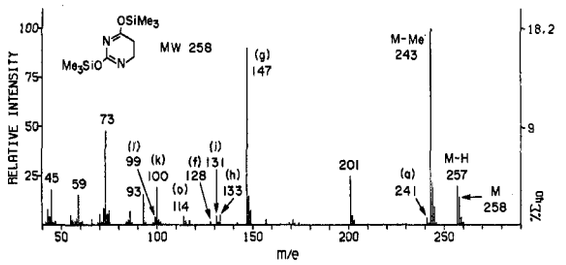
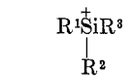


Figure 6.—Mass spectrum of O^2,O^4-bis(trimethylsilyl)-5,6-dihydrouracil (**16**).

SiXCN in forming the precursor (ion e) from pyrimidines occurs predominantly from C-2, with loss of either N-1 or N-3.

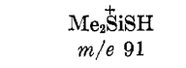
In the spectra of all compounds examined a substantial portion of the total ion current was carried by silicon-containing ions which include little or none of the base skeleton. The simplest of these are the rearranged species *m/e* 45 and 59,[13] and the ubiquitous trimethylsiliconium ion *m/e* 73. Deuterium labeling in the trimethylsilyl moiety shows that both rearranged hydrogens in *m/e* 45 originate to greater than 80% from trimethylsilyl groups, while, for *m/e* 59, 20% (**16**) to 60% (**1**) of the single rearranged hydrogen sta-



m/e 45, $R^1 = R^2 = H$; $R^3 = Me$
m/e 59, $R^1 = H$; $R^2 = R^3 = Me$
m/e 73, $R^1 = R^2 = R^3 = Me$
m/e 82, $R^1 = R^2 = R^3 = CD_3$

tistically comes from the same or another trimethylsilyl function. In the case of *m/e* 73, which one would assume to arise by simple cleavage, over 90% of the original hydrogens were generally retained. Exceptions were the derivatives of 6-methylpurine and 7-methyladenine, which showed the incorporation of about 16 and 22%, respectively, of hydrogen from the base skeleton in *m/e* 73. These data are in qualitative agreement with the $(M - CD_2H)/(M - CD_3)$ ratios shown in Table II, which indicate the relatively greater tendency for hydrogen scrambling in those compounds. The ubiquitous fragment $MeSi^+$ (*m/e* 43)[13] is also formed as a common fragment in the low-mass region of all spectra.

The oxygen-containing fragment *m/e* 75 is a common product of trimethylsilyl ether fragmentation[14] which normally serves no diagnostic purpose. However, all five thiouracils examined (see Figure 3) showed contributions at *m/e* 91 from the sulfur analog of *m/e* 75, while the analogous nitrogen ion (*m/e* 74) was



essentially absent in the high-resolution spectra of *N*-silyl model compounds. By contrast, the sulfur analog *m/e* 163[10] of the well known *m/e* 147[8,15] (ion g)

(13) J. H. Beynon, R. A. Saunders, and A. E. Williams, "The Mass Spectra of Organic Molecules," Elsevier, New York, N. Y., 1968, p 424.

(14) H. Budzikiewicz, D. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967, p 471.

(15) J. Diekman, J. B. Thomson, and C. Djerassi, *J. Org. Chem.*, **33**, 2271 (1968), and references cited therein.

was generally not found in the spectra of the thiated bases (*e.g.*, Figure 3), while the corresponding amino

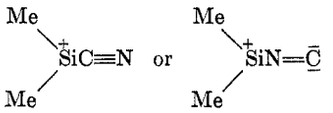
$Me_3SiX\overset{+}{S}iMe_2$
g
X = O, *m/e* 147
X = S, *m/e* 163
X = NH, *m/e* 146

species *m/e* 146 was observed in the spectra of all three cytosine derivatives, **3**, **14**, and O^2,N^4-bis(trimethylsilyl)-5-methylcytosine. Several additional interesting but diagnostically unimportant ions which are structurally though not necessarily mechanistically related to ion g were present in most spectra. These may be represented as ion h in the case of ethers. Companion

$Me_2HSiO\overset{+}{S}iMe_2$
h, *m/e* 133

ions 16 mass units lower than g and h were also usually present (ions i and j). Measurement of exact mass showed that their compositions differ by CH_4, but no metastable ion evidence was found to indicate the formation of i or j by expulsion of methane from ions g or h.

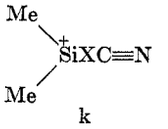
An ion of composition C_3H_6NSi (*m/e* 84) was observed in every mass spectrum except that of the trimethylsilyl derivative of barbituric acid. In some instances, such as compound **2**, contributions from other ions of different compositions were apparent. Mass 84 was found to be most abundant in spectra of purine derivatives, with a maximum value of 26% in **12**. Deuterium labeling revealed the presence of two trimethylsilyl methyl groups, which leads to the possible isomeric structures shown below. The greater



m/e 84

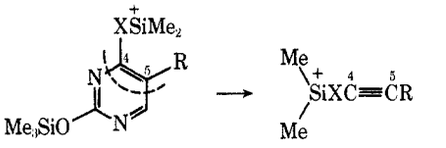
prominence of this ion in the spectra of purines (Table I) suggests the inclusion of N-9; however, the spectrum of 8-^{14}C-**4** indicates that C-8 is not involved. Although its formation from many of the pyrimidines requires extensive rearrangement, the structures shown are well stabilized, and there is ample precedent for rearrangement of partial or intact trimethylsilyl groups.[16]

A structurally similar ion containing a heteroatom was observed in the spectra of nearly all bases. Deuterium labeling and measurement of exact mass leads to the structure as ion k. Its presence in the spectra of five 2-thiouracil derivatives at both *m/e* 100 and *m/e* 116 (*e.g.*, Figure 3a) indicates no positional preference for the origin of the heteroatom. Carbon-14 labeling showed the absence of C-8 in ion k from **4** (Figure 1d), even though structural rearrangement would not be required.



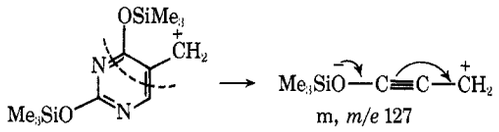
k
X = O, *m/e* 100
X = S, *m/e* 116
X = NH, *m/e* 99

Ions Characteristic of Either Pyrimidines or Purines. —The most structurally diagnostic ion in the spectra of pyrimidine derivatives arises from opening of the aromatic nucleus after formation of M − Me. Measurement of exact mass and deuterium labeling leads to the formulation shown as ion l. Spectra of the isomeric thiouracils shown in Figure 3 indicate that the heteroatom attached to C-4 is exclusively involved, thus also requiring the presence of C-5 and its substituents.



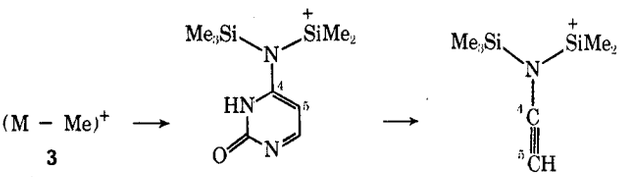
	m/e		
R	O	S	NH
H	99	115	98
Me	113	129	112

As shown by comparison of Figures 1a, 1b, and 6, ion l can be used as a prominent indicator of the position of C-methylation in pyrimidines, in addition to the determination of the position of thiation. A similar cleavage across the aromatic ring in fragment ions of several 5-substituted pyrimidines (*e.g.*, **2**, **13**, **14**) also produces a minor but characteristic fragment, such as *m/e* 127 in Figure 1b.



m/e 269 (**2**)

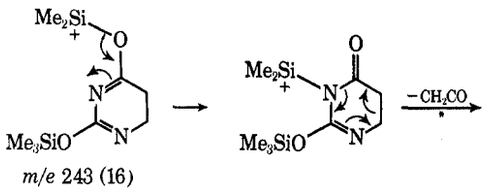
In the spectrum of the cytosine derivative **3**, rupture of the aromatic ring in M − 15 is preceded by migration of a trimethylsilyl function to N^4. The resulting prominent peak (*m/e* 170, Figure 1c) shifts to *m/e* 184 in the spectrum of the 5-methyl derivative (5% rel intensity), confirming the inclusion of C-4 and CH5, and providing a means of distinguishing methylation at C-5 *vs.* C-6.



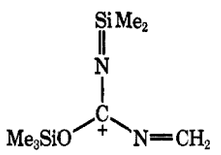
m/e 170

The presence of a saturated 5,6 moiety in the pyrimidine nucleus was observed to lead to several significant changes in fragmentation behavior. As shown in Figure 6, formation of ion l (*m/e* 99) is suppressed, but the prominent ion *m/e* 201 occurs, which has no counterpart in the mass spectrum of **1**. Metastable ion evidence for the transition *m/e* 243 → 201 supported by measurement of exact mass points to a mechanism involving expulsion of ketene from C-4,5.

(16) For leading references, see E. White, V, and J. A. McCloskey, *J. Org. Chem.*, **35**, 4241 (1970).

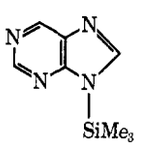


m/e 243 (16)

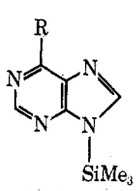


m/e 201

The most common fragmentation reactions of free (underivatized) purines involve sequential expulsion of HCN.[1c,17,18] In the present case the presence of the trimethylsilyl moiety changes the course of fragmentation such that direct elimination of HCN from M is a minor process, occuring in few cases (*e.g.*, **9**, **11**, **12**, **17**, and **18**). Loss of HCN from the even-electron M − Me ion was found to be somewhat more common (ion m, Table I) and was most abundant in the purine derivatives **11**, **17**, and **18**. The spectrum of 8-^{14}C-**4**



17



18, R = Cl
19, R = SMe

showed that about half of the carbon lost as HCN to form ion m originated from C-8, in contrast to the expulsion of HCN from the molecular ion of adenine, which does not involve C-8.[1d]

As demonstrated by the above discussion, disruption of the aromatic purine nucleus appears to be most extensive in compounds which have the least opportunity for charge delocalization outside of the ring system. Another example of this effect is represented by a relatively common fragment ion of mass 123, $C_5H_7N_2Si$. Deuterium labeling shows the presence of two silyl methyl groups, and 8-^{14}C-**4** indicates retention of C-8, so that the ion apparently represents the imidazole portion of the base. Its abundance is greatest in the spectra of **11** and **17** (Table I), and is zero in spectra of polyfunctional molecules such as trimethylsilyl derivatives of guanine (**5**) and uric acid.

Opening of the ring is also demonstrated by the models **18** and **19**, in which external heteroatoms (Cl, S) are spatially removed from the trimethylsilyl function at N-9. In both cases a series of ions is produced by direct interaction of the two groups presumably after ring opening, although the possibility of silyl migration from N-9 to N-7 across the intact ring cannot be excluded. The isotopic pair *m/e* 93, 95 (Me_2SiCl^+)

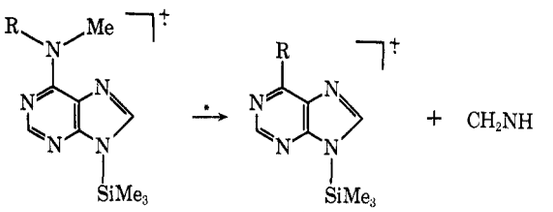
		% rel intensity	
		^{35}Cl	MeS
18, 19 ⟶	Me_2SiR^+	48	3.1
	$MeHSiR^+$	4.3	1.2
	SiR^+	8.4	<1

(17) S. J. Shaw, D. M. Desiderio, K. Tsuboyama, and J. A. McCloskey, *J. Amer. Chem. Soc.*, **92**, 2510 (1970).

(18) J. S. Shannon and D. S. Letham, *New Zealand J. Sci.*, **9**, 833 (1966).

is undoubtedly a general ion in the spectra of molecules containing both chlorine and a trimethylsilyl function, and is therefore not restricted to purines, since its presence in the spectra of long-chain halo ethers and halo esters has been established.[16]

Methylation of amino groups, as in compounds **8** and **15**, is readily characterized by ions (ion n) resulting from expulsion of methylene imine, which has been visualized as proceeding by migration of methyl or hydrogen to either N-1[12] or C-6.[17] As shown in Figure 4 (**8**) and Table I (**15**) the production of ion n rep-



8, R = CH_3 — *m/e* 206
15, R = H — *m/e* 192
20, R = $SiMe_3$

resents a major and therefore highly diagnostic process. The corresponding reactions have been documented for free bases[12,18] and nucleosides.[17,19] There is presently no reason to believe the reaction would not occur in the case of pyrimidines, such as N^4-methylcytosine or its trimethylsilyl derivative, but relevant data have not been reported. Ion n in the spectrum of **15** is accompanied by a peak of nearly equal intensity one mass unit higher, confirmed by measurement of exact mass to represent the loss of CH_2N from the molecular ion. If the derivatization reaction is carried out at higher temperatures, the disilyl compound **20** is produced in significant amount, but the characteristic ion n is essentially absent.

The presence of certain functional groups, such as propyl or methylthio, was observed to lead to a number of characteristic fragmentation paths, in addition to those discussed above. Although the details of these reactions are not included in the present communication, they can in general be ascertained by consideration of deuterium labeling and metastable ion data,[20] and by examination of the literature pertinent to each specific functional group.[21]

Multiply Charged Ions.—The presence of abundant doubly charged ions in a mass spectrum often provides a useful means of characterization, if the structural features[22] that are responsible can be identified. In the present study the most abundant doubly charged ions are associated primarily with loss of two methyl radicals from different silyl functions, a process which has been observed in other systems.[10,23] The resulting ions (o) occur at *m/e* (M − 30)/2 and can be recognized by their occurence at half-mass values (odd molecular mass), or by their half-mass first isotope

(19) S. H. Eggers, S. I. Biedron, and A. O. Hawtrey, *Tetrahedron Lett.*, 3271 (1966).

(20) E. White, V, and J. A. McCloskey, unpublished results.

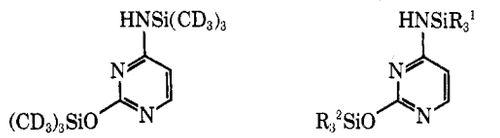
(21) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967.

(22) For example, (a) P. Vouros and K. Biemann, *Org. Mass Spectrom.*, **2**, 375 (1969); (b) G. G. Smith and C. Djerassi, *ibid.*, **5**, 505 (1971).

(23) (a) J. L. Smith, J. L. Beck, and W. J. A. VandenHeuvel, *ibid.*, **5**, 473 (1971), and references cited therein to these authors' previous work; (b) V. Y. Orlov, N. S. Nametkin, L. E. Gusel'nikov, and T. H. Islamov, *ibid.*, **4**, 195 (1970).

peaks (even molecular mass). In Figure 1c–e the intensity values for ion o (not shown) follow: **3**, *m/e* 112.5, 27%; **4**, *m/e* 124.5, 4%; **5**, *m/e* 168.5, 1%. The relatively high abundance of ion o, particularly in the spectra of pyrimidine derivatives, provides a potentially useful means of identifying bases and confirming the value of M in multicomponent mixtures such as nucleic acid hydrolysates.

In order to determine to what extent silyl methyls are lost from different functions, a mixture of trimethylsilyl derivatives of cytosine (**3**, **3a**, or the isomers **3b**) was prepared using a mixture of labeled and unlabeled reagents.[8] The three possible values of ion o from **3a** [(M − 30)/2, (M − 33)/2, (M − 36)/2] were separated in mass from those of **3b**, and showed that at least 95% of the methyl groups lost are from different silyl moieties. In the spectra of d_9-trimethylsilyl derivatives of methylated bases, a variety of combinations



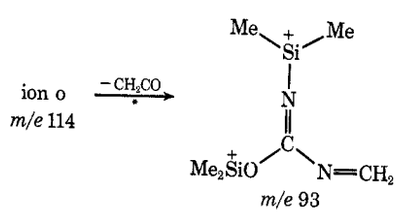
3a

3b, $R^1 = CH_3$; $R^2 = CD_3$
or
$R^1 = CD_3$; $R^2 = CH_3$

was observed. Derivatives of 6-methylpurine (**11**) and 7-methyladenine (**12**) showed a maximum of 11% of ion o to involve the native methyl function [(M − 33)/2], while the *N*,*N*-dimethyl derivative **8** produced 59% (M − 33)/2, 15% (M − 30)/2, and 26% (M − 36)/2 in accordance with the mixed nature of ion a (M − CH_3) previously discussed. Surprisingly, the 3-methyladine derivative **9**, which produced the most abundant ion o of any purine derivative examined (11% rel intensity), showed essentially quantitative (>99%) loss of two methyls from a single silyl group. This behavior indicates that the formation of ion o is mechanistically diverse and in some cases requires rearrangement or opening of the ring.

Other less prominent doubly charged ions are also formed, apparently by fragmentation of ion o. In the pyrimidines the principal species corresponds to elimination of methane to produce *m/e* (M − 2Me − CH_4)/2 (**1**, *m/e* 105, 2%; **2**, *m/e* 112, 1%; **3**, *m/e* 104.5, 3%). By contrast, most purines characteristically undergo further expulsion of HCN to provide *m/e* (M − 2Me − HCN)/2, which corresponds to *m/e* 111 in Figure 1d, and is absent (incorrect exact mass) in the spectrum of **5**.

Also worthy of note is the prominent doubly charged ion of *m/e* 93 in the mass spectrum of the dihydrouracil derivative **16** (Figure 6). High-resolution data indicate the composition $C_6H_{14}N_2OSi_2$, while labeling in the trimethylsilyl moiety shows the presence of four methyl groups (shift of six mass units, or 12/2). A metastable peak at *m/e* 75.9 confirms the formation



of *m/e* 93 from the doubly charged ion o (*m/e* 114). Its mechanism of formation therefore involves elimination of the elements of ketene from C-4,5, in parallel to production of singly charged *m/e* 201 as discussed previously.

The triply charged species $(M - 3Me)^{3+}$ was observed in approximately one-third of the spectra which were studied, with a maximum intensity of 0.6% in the spectrum of the tris(trimethylsilyl) derivative of 6-hydroxyuracil.

Experimental Section

Low-resolution mass spectra were recorded using an LKB 9000 instrument, with sample introduction through the gas chromatographic inlet system (3, 6, and 9 ft, 1% SE-30 and 1% OV-17). Ion source and carrier gas separator temperatures were 250–270°, ionizing energy was 70 eV. Particular care was taken to record the spectra on the apex of the eluting peak in order to avoid bias due to changing sample concentration during the scan.

High-resolution mass spectra of **1–5**, **8**, **10**, **11**, **13–16**, **18**, **19**, and the trimethylsilyl derivatives of 5-methylcytosine, 6-methyl-

TABLE III
PREPARATION AND GAS CHROMATOGRAPHY OF TRIMETHYLSILYL DERIVATIVES

Compd	Methods of preparation	Column temp, °C	Column
Uracil-($SiMe_3$)$_2$ (**1**)	A, B	80	A
Thymine-($SiMe_3$)$_2$ (**2**)	A, B	89	B
Cytosine-($SiMe_3$)$_2$ (**3**)	B	140	D
Adenine-($SiMe_3$)$_2$ (**4**)	B	180[a]	D
Guanine-($SiMe_3$)$_3$ (**5**)	B[b]	208[a]	D
2-Thiouracil-($SiMe_3$)$_2$ (**6**)	A, B	110	A
4-Thiouracil-($SiMe_3$)$_2$ (**7**)	A, B	97	F
N^6,N^6-Dimethyladenine-($SiMe_3$) (**8**)	A, B	133	C
3-Methyladenine-($SiMe_3$) (**9**)	C	177	D
6-Methyluracil-($SiMe_3$)$_2$ (**10**)	B	123	D
6-Methylpurine-($SiMe_3$) (**11**)	B	160	D
7-Methyladenine-($SiMe_3$)$_2$ (**12**)	C	174	D
5-Hydroxymethyluracil-($SiMe_3$)$_3$ (**13**)	B	155[a]	D
5-Hydroxymethylcytosine-($SiMe_3$)$_3$ (**14**)	B	136	A
N^6-Methyladenine-($SiMe_3$) (**15**)	B	150	A
5,6-Dihydrouracil-($SiMe_3$)$_2$[d] (**16**)	C	120	A
Purine-($SiMe_3$) (**17**)	A, B	119	D
6-Chloropurine-($SiMe_3$) (**18**)	A, B	139	D
6-Methylthiopurine-($SiMe_3$) (**19**)	B	200	D
5-Methylcytosine-($SiMe_3$)$_2$	B	150	D
Hypoxanthine-($SiMe_3$)$_2$	B	150	A
1-Methyladenine-($SiMe_3$)$_2$	C	160	A
2-Methyladenine-($SiMe_3$)$_2$	A	148	A
7-Methylguanine-($SiMe_3$)$_2$	C	185	D
7-Methylxanthine-($SiMe_3$)$_2$	B[c]	145	A
5-Hydroxyuracil-($SiMe_3$)$_3$	B	123	A
6-Hydroxyuracil-($SiMe_3$)$_3$	B	128	E
Xanthine-($SiMe_3$)$_3$	B	170	A
Orotic acid-($SiMe_3$)$_3$	A, B	119	C
Uric acid-($SiMe_3$)$_4$	B[c]	163	A
5-Methyl-2-thiouracil-($SiMe_3$)$_2$	A, B	107	F
6-Methyl-2-thiouracil-($SiMe_3$)$_2$	A, B	112	A
6-Propyl-2-thiouracil-($SiMe_3$)$_2$	A, B	123	A

[a] Starting temperature; temperature programmed at 2 or 3°/min. [b] Heated for 3 hr. [c] Heated for 12 hr. [d] Methods of preparation which require heating resulted in partial conversion to **1**.

2-thiouracil, 6-propyl-2-thiouracil, hypoxanthine, 2-methyladenine, xanthine, and orotic acid were photographically recorded on a CEC 21-110B instrument using a gas chromatographic inlet system[24] (6 ft, 1% OV-17). Ion source and carrier gas separator temperatures were 250°; ionizing energy was 70 eV. Exact masses were measured of all ions having relative abundances greater than ~0.5%.

All pyrimidine and purine bases were purchased commercially with the exception of 4-thiouracil (7), which was obtained from the Cancer Chemotherapy National Service Center of the National Institutes of Health. 8-^{14}C-4 containing 67 mol % ^{14}C (equivalent to 40 mCi/mmol) was purchased from International Chemical and Nuclear Corp. Compounds were checked for purity by gas chromatography and mass spectrometry of their trimethylsilyl derivatives.

Formation of Trimethylsilyl Derivatives.—Derivatives were prepared from 0.5–1.5 mg of base at concentrations of 4–10 $\mu g/\mu l$, by one of the three following methods. (A) The base was heated at 100° for 1–2 hr with bis(trimethylsilyl)trifluoroacetamide (BSTFA) (Peninsular ChemResearch, Inc.) and 1% added trimethylchlorosilane in a screw-capped vial. (B) The same procedure as A was followed using bis(trimethylsilyl)acetamide (BSA) (Pierce Chemical Co., distilled before use) in place of BSTFA. (C) The base was allowed to stand at room temperature for 1 hr with occasional shaking in a mixture of BSA and acetonitrile (1:3) with trimethylchlorosilane (1%). d_9-Trimethylsilyl derivatives were prepared by method C, using bis(d_9-trimethylsilyl)acetamide and d_9-trimethylsilylchlorosilane (Merck Sharp and Dohme of Canada, Ltd.).

The method of preparation and column temperature for the LKB gas chromatograph are shown for each compound in Table III. The columns used at a flow rate of 30–40 cc He/min were (A) 9 ft, 1% SE-30; (B) 3 ft, 1% SE-30; (C) 3 ft, 1% OV-17; (D) 6 ft, 1% OV-17; (E) 9 ft, 1% OV-17; (F) 6 ft, 1% SE-30.

The successful gas chromatography of 9-(trimethylsilyl)purine (17) was found to depend strongly on the age and condition of the column. The chromatogram of N^6,9-bis(trimethylsilyl)-1-methyladenine showed a broad, low peak followed closely by a normal peak. Mass spectra of the two peaks showed the same fragment ions but differing relative abundances. Data given in Table I relate to the sharp chromatographic peak, but include some contamination from the second component.

Mass spectra of all compounds were free of peaks above that of the molecular ion, and at improbable mass values below that of the molecular ion. The number of trimethylsilyl groups exchanged during the derivatization reaction was determined from the mass spectra. In some instances, derivatives of purine bases can have structures isomeric with those shown in the text. In most cases silylation is assumed to occur at enolizable carbonyl groups, on amino groups external to the ring, and at N-9, based on infrared[3c,4] and nmr data,[4] and by known reactions of these derivatives in synthetic procedures.[3b,d] In particular, other structures cannot be completely excluded for derivatives of 3-methyladenine (9), 7-methyladenine (12), purine (17), 6-chloropurine (18), and 1-methyladenine (discussed above).

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Registry No.—**1**, 10457-14-4; **2**, 7288-28-0; **3**, 18037-10-0; **4**, 17995-04-9; **5**, 18602-85-2; **6**, 32865-74-0; **7**, 32865-75-1; **8**, 32865-76-2; **9**, 32865-77-3; **10**, 32865-78-4; **11**, 32865-79-5; **12**, 32865-80-8; **13**, 31517-04-1; **14**, 32865-82-0; **15**, 32865-83-11; **16**, 32865-84-2; **17**, 32865-85-3; **18**, 32865-86-4; **19**, 32865-87-5; 5-methylcytosine-$(SiMe_3)_2$, 32865-88-6; hypoxanthine-$(SiMe_3)_2$, 17962-89-9; 1-methyladenine-$(SiMe_3)_2$, 32958-85-3; 2-methyladenine-$(SiMe_3)_2$, 32865-90-0; 7-methylguanine-$(SiMe_3)_2$, 32958-86-4; 7-methylxanthine-$(SiMe_3)_2$, 32865-91-1; 5-hydroxyuracil-$(SiMe_3)_3$, 32865-92-2; 6-hydroxyuracil-$(SiMe_3)_3$, 31111-39-4; xanthine-$(SiMe_3)_3$, 18551-03-6; orotic acid-$(SiMe_3)_3$, 32865-94-4; uric acid-$(SiMe_3)_4$, 18547-59-6; 5-methyl-2-thiouracil-$(SiMe_3)_2$, 32865-96-6; 6-methyl-2-thiouracil-$(SiMe_3)_2$, 32865-97-7; 6-propyl-2-thiouracil-$(SiMe_3)_2$, 32958-88-6.

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Photochemical Oxidations. V. Concerted *vs.* Radical Stepwise Addition of Oxygen to the Carbon–Hydrogen Bond of Hydrocarbons

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The stereochemistry of the initial stage of the photooxidation of hydrocarbons was studied. During this stage, the reaction products originate directly from the excitation of a contact charge transfer complex between oxygen and the hydrocarbons. The liquid-phase oxidation of (+)-3-methylhexane produces a racemic tertiary alcohol, and the *cis*- and *trans*-decalins give mixtures of cis and trans tertiary decalols. Thus, a radical, stepwise mechanism for the formation of the intermediate alkyl hydroperoxides is postulated rather than a concerted oxygen insertion into the carbon–hydrogen bond.

The primary process occurring during the photooxidation of saturated hydrocarbons has now been shown to be the excitation of a contact charge transfer complex between oxygen and hydrocarbons.[1–4] Product accumulation studies on the photooxidation of hydrocarbons have demonstrated that alkylhydroperoxides are the primary products and the secondary products are alcohols and ketones.[1] Relative reactivity studies of primary, secondary, and tertiary C–H bonds of several hydrocarbons proved that the C–H bond rather than the C–C bond was the donor site in the contact charge transfer complex.[5]

Equations 1–3 summarize the initial steps in the

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