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# STUDIES OF CYCLIC DI-*tert.*-BUTYLSILYLENE DERIVATIVES OF DIOLS AND HYDROXY ACIDS BY GAS CHROMATOGRAPHY–MASS SPECTROMETRY

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## SUMMARY

Cyclic di-*tert.*-butylsilylene (DTBS) derivatives have been introduced recently as protecting groups for 1,2-, 1,3- and 1,4-diols. Analogous cyclic derivatives can also be formed from other bifunctional groupings. In this paper, based on gas chromatography–mass spectrometry, studies are reported of DTBS derivatives of twenty-one 1,2-diols, four 1,3-diols, two catechols, two α-hydroxy acids and one β-hydroxy acid. In general, the derivatives showed very satisfactory gas chromatographic properties, having retention indices (on OV-1 phase) about 150–250 units above those of analogous butaneboronates. The mass spectra showed several characteristic features. Molecular ions were almost always present, though they were in modest abundance except from aromatic substrates. DTBS derivatives of acyclic and alicyclic diols gave major ions corresponding to $[M - C_4H_9]^+$ and $[M - C_4H_9 - C_3H_6]^+$, whereas catechol derivatives yielded abundant molecular ions and distinctive fragment ions of types $[M - C_4H_8]^{+\cdot}$ and $[M - C_4H_8 - C_3H_7]^+$.

## INTRODUCTION

The selective formation of cyclic derivatives from compounds that contain suitably proximal functional groups has a variety of important applications in synthesis and analysis. Among such derivatives, cyclic borates and boronates, together with related ionic species, have proved to be particularly versatile and useful in separation processes in both condensed-phase and gas-phase systems. Cyclic silylene derivatives have not yet attained similar success, but two of the limiting factors (*i.e.* relatively difficult preparation and susceptibility to hydrolysis) have been circumvented in recent work. Simple vicinal diols tend readily to form dimeric cyclic silylene derivatives (ten-membered) and polymers, as the 1,3-dioxa-2-silacyclopentane ring requires some distortion of the relatively wide bond angles of silicon[1]. Dimethylsilylene derivatives of 1,2- and 1,3-diols[2,3] and of many other bifunctional substrates[4] have been known for more than twenty years. Such derivatives were introduced by Kelly[5,6] for the gas chromatography of thermally unstable corticosteroid diols, and were further studied for their potential value in gas chromatography–mass spectrom-

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etry (GC–MS)[7]; however, the ease of hydrolysis remained a drawback and restricted wider applications. More recently, several new protecting groups based on silicon have been developed. These include the tetraisopropyldisiloxane-1,3-diyl group[8], and the diphenylsilylene[9], diisopropylsilylene[10], and di-*tert.*-butylsilylene (DTBS) groups[11]. The preparation of dimethyl silylene and other alkyl/aryl silylene derivatives of diols, hydroxy acids, etc. has also been simplified[12]. The DTBS derivatives have special advantages as protecting groups in synthesis[11] and are relatively stable towards hydrolysis. Their preparation has been facilitated by the development of improved reagents[10]. Accordingly, the potential utility of DTBS derivatives has now been explored for a variety of bifunctional substrates. This report deals with derivatives of diols and of hydroxy acids.

## MATERIALS AND METHODS

### *Solvents and reagents*

Acetonitrile (AnalaR) was obtained from BDH (Poole, U.K.), ethyl acetate (Nanograde) from Mallinckrodt (St. Louis, MO, U.S.A.) and N-methylmorpholine from Ventron Alfa Products (Coventry, U.K.). N,O-bis(trimethylsilyltrifluoroacetamide (BSTFA) was purchased from Pierce and Warriner (Chester, U.K.) and 1-hydroxybenzotriazole from Fluka (Fluorochem, Glossop, U.K.). Di-*tert.*-butyldichlorosilane was supplied by Petrarch Systems (Bristol, PA, U.S.A.).

### *Diols and related reference compounds*

The compound numbering sequence is that depicted in Fig. 1, all chiral compounds being racemic mixtures except for compound 25, which was the (+)-enantiomer. Compounds 1 and 29 were purchased from Aldrich (Gillingham, Dorset, U.K.) and compound 2 was obtained from Fairfield Chemical Co. (Blythewood, SC, U.S.A.). Compounds 3 and 4 were prepared by lithium aluminium hydride reduction of the corresponding hydroxy acids 5 and 6, purchased from ICN (Plainview, NY, U.S.A.) and Applied Science (Pierce & Warriner, Chester, U.K.) respectively. The latter also supplied compounds 7–9. Compound 10 was obtained from the Hormel Institute (Austin, MN, U.S.A.) while Supelco (R. B. Radley & Co., Sawbridgeworth, U.K.) supplied compound 11. Compounds 12, 13, 17 and 22 were available from earlier work[13,14]. Compounds 18, 19, 23, 24 and 26–28 were synthetic samples (donated by the late Prof. J. D. Loudon, as was compound 25, originally isolated by Prof. E. Boyland from the urine of rabbits dosed with anthracene). Compounds 14 and 16 were purchased from Koch-Light (A. & J. Beveridge, Edinburgh, U.K.) and compounds 15 and 20 from Alfred Bader Chemicals (Aldrich, Gillingham, U.K.). Compound 21 (SQ 22,928) was a gift from E. R. Squibb & Sons (Princeton, NJ, U.S.A.) and compound 30 was purchased from Lancaster Synthesis (Morecambe, U.K.).

### *Gas–liquid chromatography*

Packed column gas–liquid chromatography (GLC) was performed with a Perkin-Elmer (Beaconsfield, U.K.) F-11 gas chromatograph equipped with a silanized glass column (1.8 m × 4 mm I.D.) packed with 1% OV-1 coated on Gas-Chrom Q, 100–120 mesh (Phase Separations, Queensferry, U.K.). The column was heated at

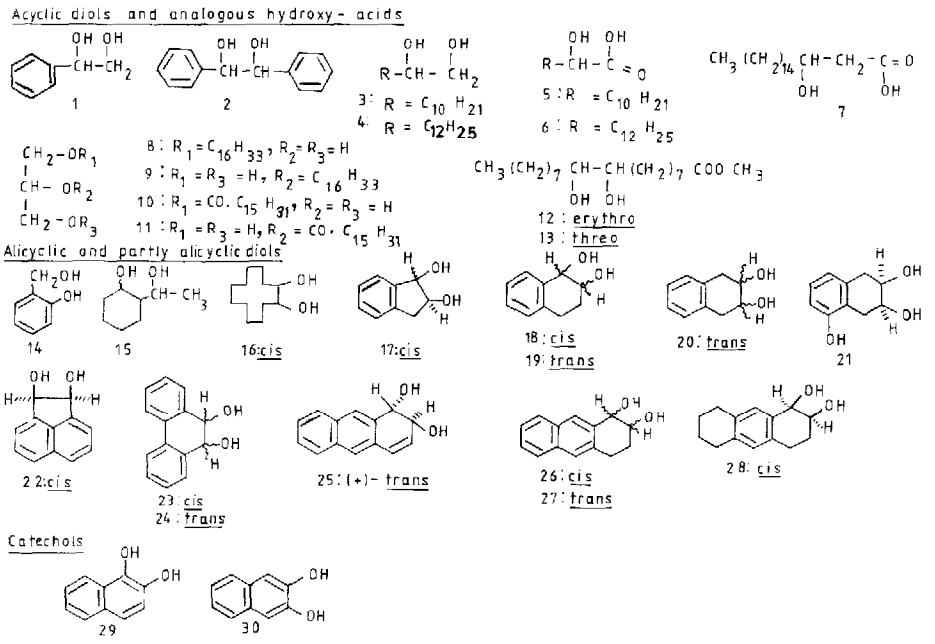


Fig. 1. Structures of parent diols and hydroxy acids. 1 = 1-phenylethane-1,2-diol; 2 = 1,2-diphenyl-1,2-ethanediol; 3 = dodecane-1,2-diol; 4 = tetradecane-1,2-diol; 5 = 2-hydroxylauric acid; 6 = 2-hydroxymyristic acid; 7 = 3-hydroxystearic acid; 8 = hexadecyl 1-glyceryl ether; 9 = hexadecyl 2-glyceryl ether; 10 = 1-monopalmitin; 11 = 2-monopalmitin; 12 = methyl *erythro*-9,10-dihydroxystearate; 13 = methyl *threo*-9,10-dihydroxystearate; 14 = 2-hydroxybenzenemethanol (saligenin); 15 = 2-(1-hydroxyethyl)cyclohexanol; 16 = cyclododecane-*cis*-1,2-diol; 17 = indane-*cis*-1,2-diol; 18 = 1,2,3,4-tetrahydronaphthalene-*cis*-1,2-diol; 19 = 1,2,3,4-tetrahydronaphthalene-*trans*-1,2-diol; 20 = 1,2,3,4-tetrahydronaphthalene-*trans*-2,3-diol; 21 = 5-hydroxy-1,2,3,4-tetrahydronaphthalene-*cis*-2,3-diol; 22 = acenaphthene-*cis*-1,2-diol; 23 = 9,10-dihydrophenanthrene-*cis*-9,10-diol; 24 = 9,10-dihydrophenanthrene-*trans*-9,10-diol; 25 = 1,2-dihydroanthracene-*trans*.-1,2-diol; 26 = 1,2,3,4-tetrahydroanthracene-*cis*-1,2-diol; 27 = 1,2,3,4-tetrahydroanthracene-*trans*-1,2-diol; 28 = 1,2,3,4,5,6,7,8-octahydroanthracene-*cis*-1,2-diol; 29 = 1,2-dihydroxynaphthalene; 30 = 2,3-dihydroxynaphthalene.

a variety of temperatures (see Tables I and II for details) and the nitrogen carrier gas flow-rate was 40 ml/min. Open-tubular GLC was carried out with a Hewlett-Packard (Winnersh, U.K.) 5880A gas chromatograph fitted with an OV-1 fused-silica capillary column, 25 m × 0.25 mm I.D. (GC², Northwich, Chester, U.K.) and a Grob-type injector operated in split mode (50:1). The column was temperature programmed either from 80°C (2 min) to 140°C (2 min) at 30°C/min, and then at 1.5°C/min to 200°C (for low molecular weight derivatives) or from 80°C (2 min) to 200°C (2 min) at 30°C/min, and then at 2°C/min to 260°C (for derivatives having $I > 2500$); the helium carrier gas flow-rate was 2 ml/min. Both instruments employed hydrogen flame-ionisation detectors.

*GC–MS*

GC–MS was performed with an LKB 9000 instrument fitted with a DB-1 fused-silica capillary column, 60 m × 0.30 mm I.D. (J. and W. Scientific, Rancho Cordova, CA, U.S.A.) and a falling needle injector[15]. Helium was used both as carrier and make-up gas (flow-rates, 7 ml/min, measured at ambient temperature,

and 25 ml/min respectively). Mass spectra were recorded under electron impact conditions (20 eV): accelerating voltage, 3.5 kV; trap current, 60 μA; source and separator temperatures, 260°C.

*Preparation of derivatives*

*DTBS derivatives.* These were prepared by two methods consisting essentially of minor modifications of the conditions published by Trost and Caldwell[11].

(A) The diol or hydroxy acid (100 μg) was dissolved in acetonitrile (30 μl). N-methylmorpholine (20 μl), 1-hydroxybenzotriazole (3 μg) (stock solution: 3 mg dissolved in 1 ml of acetonitrile) and di-*tert.*-butyldichlorosilane (3.5 μl) were added sequentially and the mixture was heated in a Reactivial at 80°C overnight (15 h).

(B) The diol or hydroxy acid (100 μg) dissolved in N-methylmorpholine (50 μl) was treated with 1-hydroxybenzotriazole (3 μg), (stock solution: 3 mg dissolved in 1 ml of N-methylmorpholine), then with di-*tert.*-butyldichlorosilane (3.5 μl) and heated at 80°C overnight. The solutions derived by methods A and B were diluted to 100 μl with ethyl acetate and used for analyses by GC and GC–MS. 1-Hydroxybenzotriazole was dried *in vacuo* at 40°C prior to preparing stock solutions. Aromatic diols 29 and 30 only required heating at 80°C for 1 h for complete derivatisation.

*Trimethylsilylation.* Compound 21 was converted to its DTBS derivative as above and the solution was filtered through cotton wool. After evaporation to dryness the product was treated with BSTFA (15 μl) and heated at 80°C for 30 min to yield the 2,3-di-*tert.*-butylsilylene 5-trimethylsilyl ether.

## RESULTS AND DISCUSSION

*Preparation of DTBS derivatives*

Among the various conditions explored by Trost and Caldwell[11] for the reactions of five diols with di-*tert.*-butyldichlorosilane, the best procedure employed acetonitrile as solvent, together with triethylamine ($\geqslant 3$ mol per mol of reagent) and 1-hydroxybenzotriazole (HBT: 0.1–0.2 molar proportions). The mixtures were heated (60–95°C) for periods from 0.5 to 5 h. In our studies, these conditions have been modified: in method A, triethylamine was replaced by N-methylmorpholine and the reaction time extended to 15 h; additionally, in method B, acetonitrile was omitted. On the 100-μg scale, both methods afforded DTBS derivatives, often in yields exceeding 95%. No evidence of dimeric derivatives was seen. Nineteen of the substrates were treated by both methods, and in ten instances method A gave better yields: the results indicated that the presence of acetonitrile was especially advantageous for the derivatisation of *trans*-diols and of catechols. The latter types of substrate reacted rapidly, as already reported[11]. Omission of HBT led to reduced yields, in agreement with the proposition that this reagent catalyses silyl transfer[11]. It is not known whether it acts at both stages of acetal formation.

Two diols with tertiary hydroxyl groups (*i.e.* 2-methylpentane-2,4-diol and 9-methyl-9,10-dihydrophenanthrene-*cis*-9,10-diol) did not form DTBS derivatives under the conditions used. A steric effect was also apparent in the reaction of methyl *erythro*-9,10-dihydroxystearate, as described below. The formation of DTBS derivatives from tertiary and other hindered diols has been achieved by means of the more active silyl transfer reagent, di-*tert.*-butylsilyl ditriflate[10].

TABLE I

KOVÁTS RETENTION INDICES ($I$) AND MASS SPECTROMETRIC DATA (20 eV) FOR DI-*tert.*-BUTYLSILYLENE DERIVATIVES OF ACYCLIC DIOLS AND ANALOGOUS HYDROXY ACIDS

| *Compound* | $I^{1\%}_{OV\text{-}1}$ | *Temperature (°C)* | *M* | *Base peak** | *Other principal ions (m/z) (intensities relative to base peak in parentheses)* |
|---|---|---|---|---|---|
| 1 | 1715 | 155 | 278(9) | 179 | 221(74) 204(2) 165(3) 161(32) 143(2) 104(4) 101(9) 77(4) |
| 2 | 2330 | 200 | 354(17) | 297 | 339(1) 279(1) 255(34) 237(10) 219(4) 191(3) 180(3) 179(3) 177(4) 165(2) 149(3) 132(2) 127(5) 101(2) 91(3) |
| 3 | 2030 | 190 | 342(2) | 285 | 243(79) 225(2) 201(2) 165(4) 159(2) 157(2) 145(10) 131(3) 123(5) 117(3) 115(2) 109(14) 103(10) 101(2) 97(4) 95(18) 91(4) 83(8) 81(9) 77(10) |
| 4 | 2225 | 200 | 370(2) | 313 | 271(71) 253(2) 201(3) 193(4) 159(2) 151(2) 145(12) 137(5) 131(3) 123(7) 117(3) 115(2) 111(6) 109(13) 103(10) 101(2) 97(7) 95(19) 91(5) 83(7) 81(11) |
| 5 | 2175 | 190 | 356(9) | 255 | 312(8) 301(54) 300(30) 299(44) 281(12) 271(8) 243(16) 239(7) 229(8) 216(17) 213(4) 199(10) 195(5) 173(8) 160(4) 157(5) 151(9) 143(4) 131(4) 127(8) 117(5) 115(5) 109(4) 103(30) 101(5) 95(9) |
| 6 | 2385 | 200 | 384(11) | 283 | 340(7) 329(49) 328(30) 327(39) 309(9) 299(9) 271(13) 267(4) 257(5) 229(6) 227(7) 225(5) 216(21) 199(4) 179(7) 173(7) 160(4) 157(6) 143(5) 131(5) 129(4) 127(8) 123(5) 117(6) 115(4) 109(7) 103(35) 101(5) |
| 7 | 2800 | 235 | 440(1) | 383 | 425(1) 365(6) 341(21) 339(5) 323(2) 299(2) 263(2) 229(6) 221(2) 173(5) 131(2) 129(2) 117(2) 109(2) 103(3) 101(2) 97(2) 95(2) |
| 8 | 2815 | 235 | 456(−) | 175 | 399(34) 201(5) 157(3) 145(1) 141(1) 133(2) 127(1) 119(22) 117(3) 113(2) 103(2) 99(4) 85(12) |
| 9 | 2855 | 235 | 456(−) | 117 | 399(64) 215(1) 189(7) 177(15) 175(18) 159(56) 149(2) 133(5) 125(4) 121(3) 119(18) 111(11) 103(2) 97(18) 91(3) 85(10) 83(17) |
| 10 | 2905 | 235 | 470(2) | 413 | 455(1) 383(4) 357(15) 287(4) 274(5) 239(20) 217(3) 215(4) 214(5) 201(10) 175(53) 161(5) 157(9) 123(3) 119(8) 117(6) 115(5) 111(3) 109(6) 103(6) 99(5) 97(6) 95(10) 85(17) 83(17) 81(5) |
| 11 | 2925 | 235 | 470(1) | 413 | 455(1) 383(1) 357(84) 339(4) 287(3) 239(60) 217(3) 215(10) 214(3) 201(1) 175(32) 161(14) 159(10) 157(10) 137(5) 123(7) 119(12) 117(23) 115(12) 111(3) 109(12) 103(3) 99(10) 97(11) 95(20) 85(31) 83(17) 81(10) |
| 12 | 2750 | 235 | 470(−) | 413 | 439(3) 421(5) 395(38) 381(74) 363(4) 357(5) 313(5) 271(14) 255(3) 245(6) 141(3) 133(7) 123(3) 109(5) 107(4) 97(4) 95(6) 91(14) 83(6) 81(6) |
| 13 | 2690 | 235 | 470(−) | 413 | 439(1) 421(7) 395(52) 381(80) 363(5) 357(2) 313(3) 271(19) 263(4) 255(4) 245(8) 151(3) 133(10) 123(5) 109(7) 107(6) 97(6) 95(8) 91(15) 83(9) 81(7) |

* Mass spectra normalised above *m/z* 75.

The DTBS derivatives of saturated diols proved to be stable in solution for at least a week, whereas the derivatives of hydroxy acids and of catechols underwent decomposition within 24 h. The detector response in GLC of the DTBS derivatives of saligenin, 1,2,3,4-tetrahydroanthracene-*cis*-1,2-diol, and naphthalene-2,3-diol was linear with respect to the amount of sample injected over the range 1 μg to 50 ng, indicating that no appreciable adsorption occurred in the column.

*DTBS derivatives of acyclic diols and hydroxy acids*

Gas chromatographic retention data and salient features of the mass spectra of DTBS derivatives of the thirteen compounds studied are summarised in Table I. The influence, on the retention index, of the mass increment ($\Delta m$) of 140 conferred by derivatisation, is moderated by the low polarity of the DTBS group, so that (on the OV-1 phase) the retention indices are merely some 150–250 units above those of corresponding 1-butaneboronates for which $\Delta m$ is only +66.

Gas chromatograms and mass spectral line diagrams for representative derivatives are depicted in Figs. 2–7. Fig. 2 shows a gas chromatographic separation of DTBS derivatives of dodecane-1,2-diol (compound 3), tetradecane-1,2-diol (compound 4) and the corresponding α-hydroxy acids (compounds 5 and 6). The carbonyl group in the latter derivatives is associated with a retention index increment of *ca.* 150. The chromatograms in Fig. 2, and others below, illustrate the generally very satisfactory peak quality obtained for the DTBS derivatives of both the neutral and the acidic types of substrate. Mass spectra of the derivatives of compounds 4 and 6 are shown in Fig. 3. In the former, the preponderant ions corresponding to [M − 57] and [M − 57 − 42] are major fragments observed from DTBS derivatives of all diols of the type $R^1R^2CH(OH)CH(OH)R^3R^4$ where the R groups lack any strong fragmentation-directing substituents. The sequential losses of a *tert.*-butyl radical and a

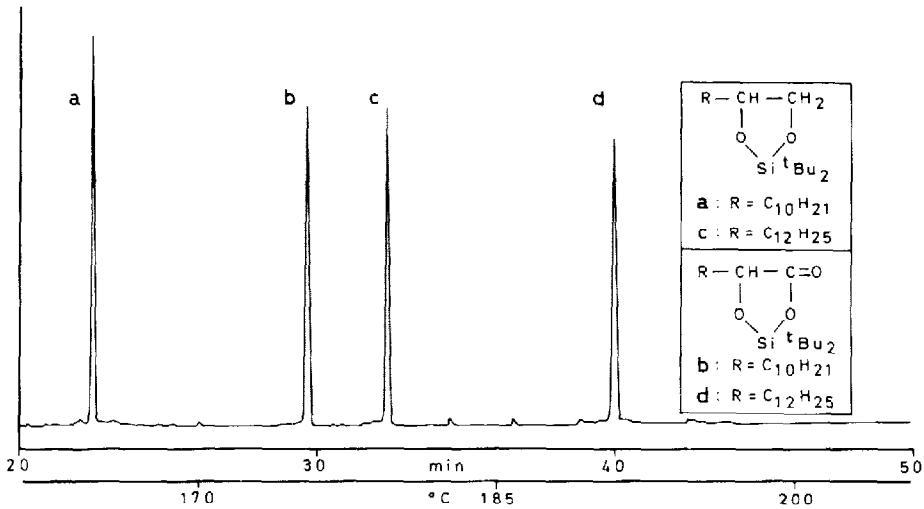


Fig. 2. Gas chromatographic separation of the DTBS derivatives of dodecane-1,2-diol (peak a, $I$ = 2014), 2-hydroxylauric acid (peak b, $I$ = 2160), tetradecane-1,2-diol (peak c, $I$ = 2214), and 2-hydroxymyristic acid (peak d, $I$ = 2372). Column, OV-1 fused-silica capillary (25 m × 0.25 mm I.D.); column temperature, programmed from 80°C (2 min) to 140°C (2 min) at 30°C/min, and then at 1.5°C/min to 200°C; helium flow-rate, 2 ml/min. $^t$Bu = *tert.*-butyl.

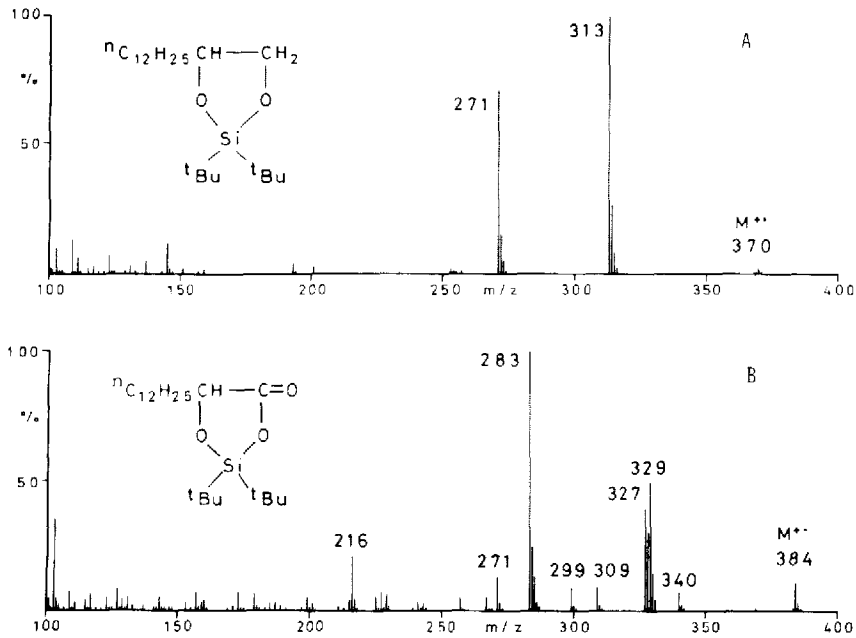


Fig. 3. Mass spectra (20 eV) of the DTBS derivatives of tetradecane-1,2-diol (A) and 2-hydroxymyristic acid (B) measured on an LKB 9000 gas chromatograph–mass spectrometer. Column, DB-1 fused-silica capillary (60 m × 0.30 mm I.D.); column temperatures as in Table I; helium carrier gas and make-up gas flow-rates, 7 ml/min and 25 ml/min, respectively; accelerating voltage, 3.5 kV; source temperature, 260°C; trap current, 60 μA. $^t$Bu = *tert.*-butyl.

neutral propene equivalent are indicated by strong metastable ions in most of the mass spectra recorded in the present work. In the case of the hydroxy acid DTBS derivative (Fig. 3, lower spectrum) the [M − 57] ion is again prominent, but [M − 57 − 42] is not; instead, ions resulting from losses of carbon dioxide, notably [M − 44] and the base peak at [M − 57 − 44], are characteristic. In addition, loss of dodecene via McLafferty rearrangement is possible only for the hydroxy acid DTBS derivative, affording a prominent ion at *m/z* 216.

The one β-hydroxy-acid DTBS derivative cited (Table I, compound 7) yielded [M − 57] as the base peak. The only other abundant ions were of nominal mass [M − 57 − 42] resulting both from losses of ketene and of $C_3H_6$, as shown by accurate mass measurements (*m/z* 341.2890 and 341.2519, respectively).

Examples of substrate diols containing additional oxygen groups are the glycerol 1- and 2-ethers (compounds 8 and 9). The satisfactory gas chromatographic separation of the isomeric hexadecyl glyceryl ethers ($\Delta I = 36$) is illustrated in Fig. 4. (The apparent "tail" on the peak of the 2-isomer was consistently observed. It is not known whether this resulted from some adsorption of this derivative, possibly with reversible ring-opening, or from an otherwise undetected impurity). The mass spectra of these derivatives (Fig. 5) showed no molecular ions, although the expected ions of type [M − 57] were prominent. The DTBS derivative of the 1-isomer (upper diagram) yielded a base peak at *m/z* 175 resulting from a further loss of hexadecene (*i.e.*

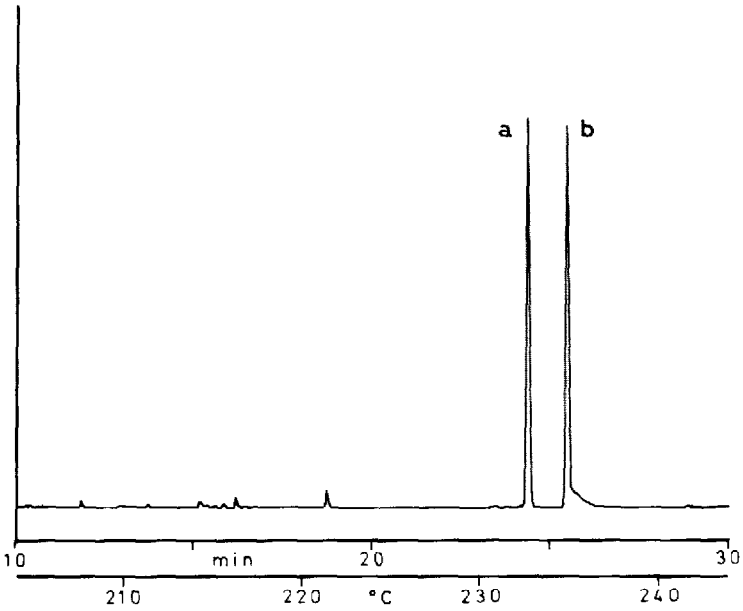


Fig. 4. Gas chromatographic separation of the DTBS derivatives of hexadecyl 1-glyceryl ether (peak a, $I$ = 2814) and hexadecyl 2-glyceryl ether (peak b, $I$ = 2850). Column, OV-1 fused-silica capillary (25 m × 0.25 mm I.D.); column temperature, programmed from 80°C (2 min) to 200°C (2 min) at 30°C/min, and then at 2°C/min to 260°C; helium flow-rate, 2 ml/min.

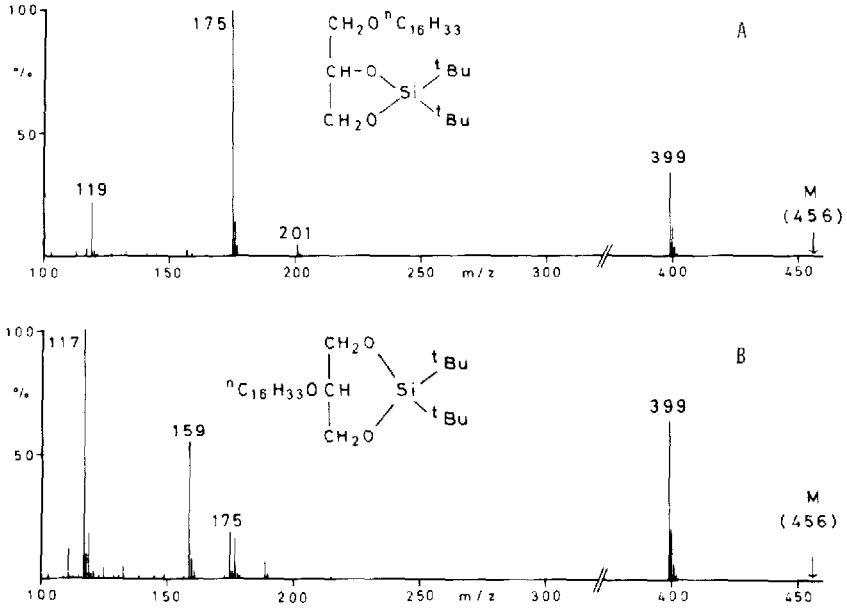


Fig. 5. Mass spectra (20 eV) of the DTBS derivatives of hexadecyl 1-glyceryl ether (A) and hexadecyl 2-glyceryl ether (B). GC–MS conditions as in Fig. 3. $^{t}$Bu = *tert.*-butyl.

[M − 57 − 224]). A minor ion at *m/z* 201 corresponded to the cyclic oxonium ion formed by α-cleavage with loss of the $CH_2OC_{16}H_{33}$ radical. The 2-isomer was very well distinguished by its mass spectrum (Fig. 5, lower diagram): the base peak of *m/z* 117 has the composition $C_4H_9O_2Si^+$ and probably arises from the ion of *m/z* 159. Formation of the latter is presumed to occur by successive losses of *tert.*-butyl radical and of a hexadecanal equivalent from the molecular ion.

An example of markedly different rates of derivative formation from isomeric diols is shown in Fig. 6. Under the usual reaction conditions, the *erythro* isomer of methyl 9,10-dihydroxystearate (compound 12) was only partly converted into its DTBS derivative while the *threo* isomer (compound 13) underwent complete reaction. On the OV-1 phase, the separation between the isomers ($\Delta I$ = 56) was much better than that observed for the analogous methaneboronate derivatives ($\Delta I$ = 32) even though the latter required column temperatures about 40°C lower. This gas chromatographic discrimination is of importance because the two isomers gave virtually identical mass spectra. The mass spectrum of the *threo* isomer derivative is illustrated in Fig. 7. The three major ions are [M − 57], [M − 57 − 18] and [M − 57 − 32] (*i.e.* [M − $C(CH_3)_3^{\cdot}$ − $CH_3OH$]. Strong metastable ions corresponding to the formation of the latter two were seen at *m/z* 377.7 and 351.5 respectively. A further metastable ion at *m/z* 345.7 attested to the process [(M − 57 − 32) − 18]. Alpha cleavages resulting in loss of the alkyl and ester side-chains, respectively, yielded cyclic oxonium ions at *m/z* 357 and 313 indicating the original site of the diol group in the chain; and a further prominent ion at *m/z* 271 appeared to represent a loss of $C_3H_6$ from the latter.

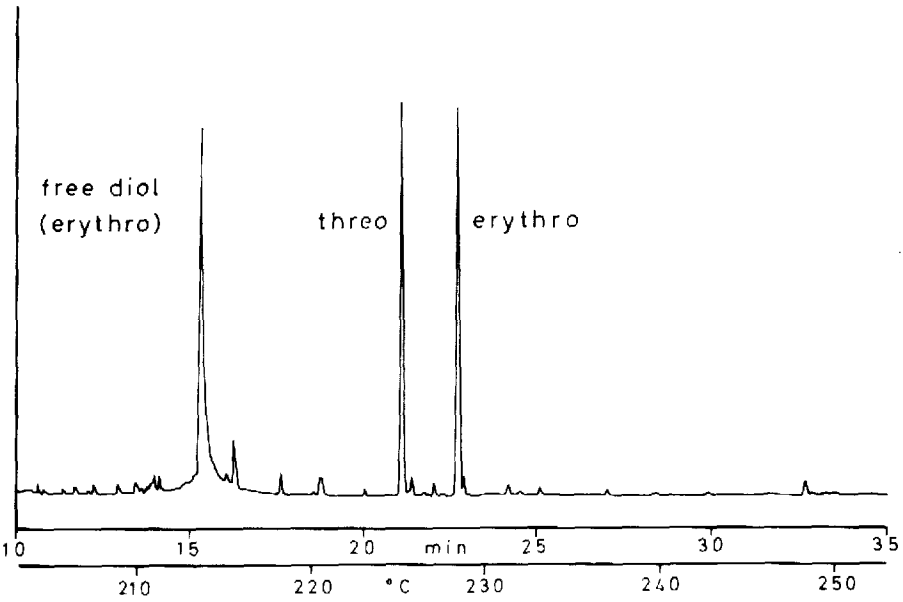


Fig. 6. Gas chromatographic separation of the DTBS derivatives of *threo* ($I$ = 2700) and *erythro* ($I$ = 2756) methyl 9,10-dihydroxystearate. GLC conditions as in Fig. 4.

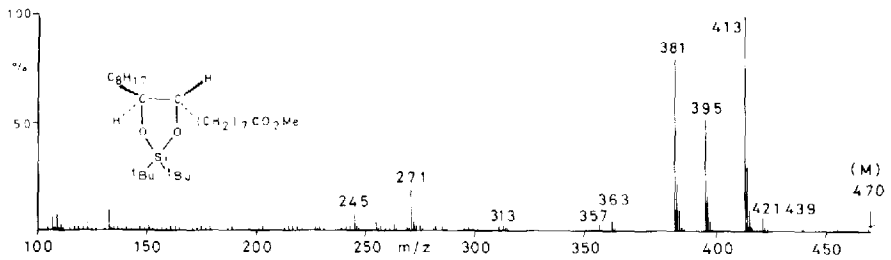


Fig. 7. Mass spectrum (20 eV) of the DTBS derivative of methyl *threo*-9,10-dihydroxystearate. GC–MS conditions as in Fig. 3. $^tBu$ = *tert.*-butyl.

The occurrence of rearrangement ions formed by losses of $H_2O$, most typically as [M − 57 − 18] and [M − 57 − 42 − 18], was a striking feature of the mass spectra of many of the DTBS derivatives studied. In several instances, such ions were prominent (cf. Table I, compounds 1 and 2).

The only derivatives not so far mentioned are those of the isomeric monopalmitins (compounds 10 and 11). These were adequately separated by GLC ($\Delta I$ = 20) but the mass spectra were more closely similar to each other than those of the analogous glyceryl monoethers shown in Fig. 5. Major ions corresponded to [M − $C(CH_3)_3$] (base peaks); [M − $C(CH_3)_3$ − $C_4H_8$] ($C_{15}H_{31}CO^+$: *m/z* 239); and [M − $C(CH_3)_3$ − $C_{14}H_{29}CH{=}C{=}O$] (*m/z* 175). However, the ion at *m/z* 201 was much more abundant from the 1-monoglyceride [from which it could arise by simple α-cleavage (cf. Fig. 5)] than from the 2-isomer.

*DTBS derivatives of alicyclic and aromatic diols*

Principal data recorded by GLC and GC–MS for derivatives of fifteen alicyclic diols and two catechols are set out in Table II. The quality of the gas chromatographic peaks was as good (at least for *cis*-diol derivatives) as that seen in the acyclic group discussed above. In this series, retention indices of some free diols have been recorded in earlier work[16], and the increments ($\Delta I$) for DTBS derivatisation were (for the OV-1 phase) between 280 and 410 units, for the diols 17, 18, 20, 22, 23 and 26. Major features of the mass spectra of alicyclic diol DTBS derivatives were, as for the acyclic group, ions of types [M − 57] and [M − 57 − 42] which together accounted for base peaks in thirteen of the examples. Molecular ions were distinctly more abundant for compounds containing aromatic rings. Thus, saligenin DTBS derivative (compound 14) showed 18% relative intensity for $M^{+\cdot}$, whereas its alicyclic analogue (compound 15) yielded no observable molecular ion.

A gas chromatogram derived from a mixture of three representative *cis*-1,2-diols (compounds 16, 18 and 22) is shown in Fig. 8. Slight tailing of the peak of the cyclododecanediol DTBS derivative was consistently observed. Whether this was due to partial adsorption or to a minor impurity has not been determined. The peaks from the 5- and 6-membered cycloalkanediol derivatives were as sharp and symmetrical as those of corresponding di-trimethylsilyl ethers. In view of the preponderant fragmentation modes already mentioned, only the mass spectrum of the cyclododecanediol DTBS derivative is shown (Fig. 9). The ion of *m/z* 77 is presumed to be $C_6H_5^+$ derived from the cycloalkane ring. [Studies of the formation of DTBS

KOVÁTS RETENTION INDICES ($I$) AND MASS SPECTROMETRIC DATA (20 eV) FOR DI-*tert.*-BUTYLSILYLENE DERIVATIVES OF ALICYCLIC AND AROMATIC DIOLS

| *Compound* | $I^{1\%}_{OV\text{-}1}$ | *Temperature (°C)* | *M* | *Base peak** | *Other principal ions (m/z) (intensities relative to base peak in parentheses)* |
|---|---|---|---|---|---|
| 14 | 1560 | 130 | 264(18) | 165 | 207(28) 177(2) 175(1) 152(6) 151(2) 150(2) |
| 15 | 1625 | 130 | 284(–) | 185 | 227(58) 183(2) 141(2) 109(2) 107(2) 105(2) 101(1) 77(7) |
| 16 | 2140 | 190 | 340(2) | 283 | 338(2) 325(1) 281(6) 241(94) 227(2) 163(2) 121(3) 119(2) 109(2) 107(2) 101(2) 95(5) 83(3) 81(6) 77(24) |
| 17 | 1760 | 155 | 290(5) | 191 | 233(52) 177(2) 157(2) 131(1) 115(32) 101(2) 77(4) |
| 18 | 1890 | 170 | 304(10) | 247 | 302(1) 300(2) 229(2) 205(91) 203(10) 187(5) 169(3) 146(2) 129(13) 117(2) 104(2) 101(3) 77(60) |
| 19 | 1920 | 170 | 304(19) | 247 | 302(1) 300(2) 289(1) 229(1) 220(3) 205(68) 203(10) 187(7) 169(5) 146(1) 129(15) 117(3) 104(2) 101(5) 77(76) |
| 20 | 1960 | 170 | 304(7) | 205 | 247(68) 190(2) 187(2) 131(5) 129(14) 101(1) 89(3) 77(12) |
| 21 | 2200 | 190 | 320(3) | 221 | 263(18) 245(1) 203(3) 195(2) 191(2) 185(3) 145(5) 131(2) 120(1) 115(1) 103(2) 101(2) 77(4) |
| 21a** | 2195 | 190 | 392(10) | 149 | 377(1) 335(18) 317(14) 305(3) 293(8) 275(38) 263(7) 261(4) 259(8) 219(4) 217(1) 201(1) 191(44) 177(2) 173(5) 169(5) 145(14) 133(2) 117(1) 101(1) |
| 22 | 2070 | 170 | 326(22) | 227 | 269(48) 214(2) 212(2) 199(14) 193(8) 181(3) 168(4) 152(8) 140(2) 101(3) |
| 23 | 2360 | 215 | 352(18) | 295 | 350(5) 277(12) 253(54) 235(30) 219(34) 178(20) 101(3) 77(26) |
| 24 | 2370 | 215 | 352(40) | 295 | 350(2) 337(2) 285(3) 277(4) 253(21) 251(3) 235(23) 219(10) 194(8) 178(8) 165(6) 119(3) 114(3) 95(3) 77(15) |
| 25 | 2500 | 220 | 352(100) | 352 | 337(2) 295(39) 277(6) 253(40) 239(15) 235(16) 225(2) 219(32) 204(1) 195(2) 194(2) 178(12) 165(2) 101(3) 77(5) |
| 26 | 2455 | 220 | 354(45) | 255 | 352(3) 350(7) 297(95) 279(3) 253(3) 237(7) 221(11) 219(17) 205(2) 196(2) 179(19) 178(9) 167(2) 165(2) 154(2) 141(7) 101(4) 77(30) |
| 27 | 2505 | 220 | 354(90) | 255 | 352(3) 350(1) 339(2) 297(65) 279(4) 253(3) 250(2) 237(8) 221(12) 219(17) 196(2) 179(19) 178(4) 167(3) 165(2) 154(2) 141(7) 101(4) 77(33) |
| 28 | 2380 | 220 | 358(11) | 77 | 356(2) 354(4) 301(34) 297(3) 259(11) 257(2) 255(2) 225(4) 223(5) 200(5) 183(18) 181(11) 158(5) 145(3) 141(4) 119(10) 104(2) 101(7) 91(2) |
| 29 | 1915 | 170 | 300(100) | 300*** | 244(34) 201(21) 187(3) 186(6) 57(20) |
| 30 | 1990 | 170 | 300(100) | 300*** | 244(64) 201(54) 188(4) 187(4) 186(7) 57(24) |

* Mass spectra normalised above $m/z$ 75.
** 5-OTMS ether.
*** Mass spectra normalised above $m/z$ 59.

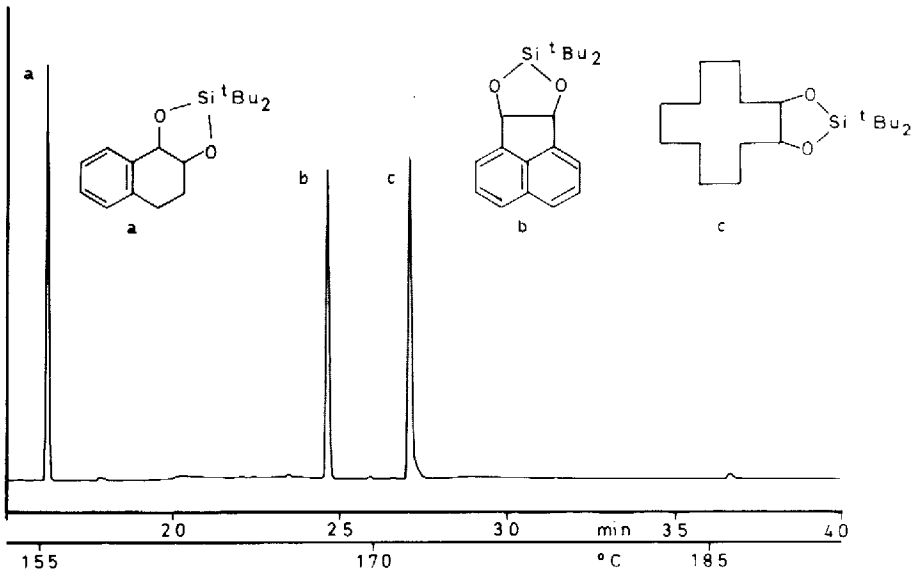


Fig. 8. Gas chromatographic separation of the DTBS derivatives of 1,2,3,4-tetrahydronaphthalene-*cis*-1,2-diol (peak a, $I$ = 1888), acenaphthene-*cis*-1,2-diol (peak b, $I$ = 2056) and cyclododecane-*cis*-1,2-diol (peak c, $I$ = 2106). GLC conditions as in Fig. 2. $^t$Bu = *tert.*-butyl.

derivatives by reaction of "metabolic" dihydrodiols and related tetrahydrodiols with di-*tert.*-butyldichlorosilane will be reported more fully in a separate paper. One derivative worthy of note here is that of the metabolic dihydroanthracenediol (compound 25), which was exceptional in yielding the molecular ion as base peak.]

Compound 21, 5-hydroxytetrahydronaphthalene-*cis*-1,2-diol, was the only substrate containing an extra reactive group and was studied as the DTBS and DTBS trimethylsilyl ether derivatives. The base peak in the mass spectrum of the latter was shown to have the composition $C_4H_{13}O_2Si_2$ ($m/z$ observed and calculated 149.0454; [$^2H_9$]trimethylsilyl analogue, 158.1019) and constitutes a rearrangement ion such as $(CH_3)_3\overset{+}{S}iO=Si(OH)CH_3$. Another major ion was that of $m/z$ 191 ($C_7H_{19}O_2Si_2$),

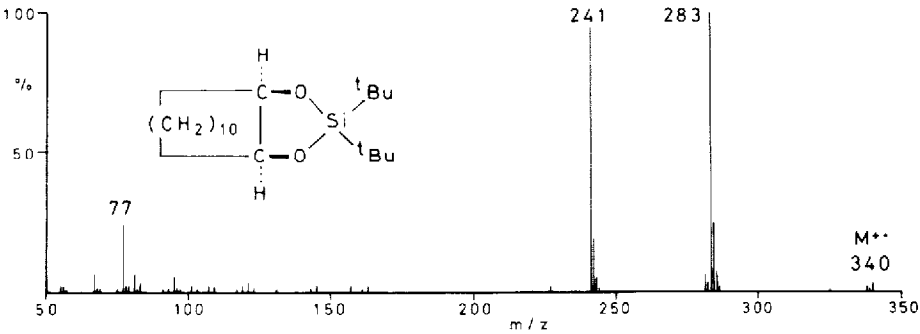


Fig. 9. Mass spectrum (20 eV) of the DTBS derivative of cyclododecane-*cis*-1,2-diol. GC–MS conditions as in Fig. 3, column temperature as in Table II. $^t$Bu = *tert.*-butyl.

possibly corresponding to $(CH_3)_3SiO-CH=\overset{+}{O}\ Si(CH_3)_3$ which is well known[17] in the mass spectra of diol di-trimethylsilyl ethers. The origin of the prominent ion of *m/z* 275 ($C_{14}H_{19}O_2Si_2^+$: observed *m/z* 275.0937) is at present obscure.

The two naphthalenediols (compounds 29 and 30) yielded, in rapid reactions, DTBS derivatives that showed excellent gas chromatographic properties (Fig. 10). Their mass spectra (Fig. 11) showed fragmentations that were distinctive for the catechol DTBS systems, *viz.*, predominant ions of types [M − 56] of *m/z* 244, and [M − 56 − 43] of *m/z* 201, together with strong metastable ions; the only other significant fragments were the *tert.*-butyl cation and an ion of *m/z* 186 formed by further loss of a methyl radical from the ion of *m/z* 201, as indicated by a metastable ion at 172.0.

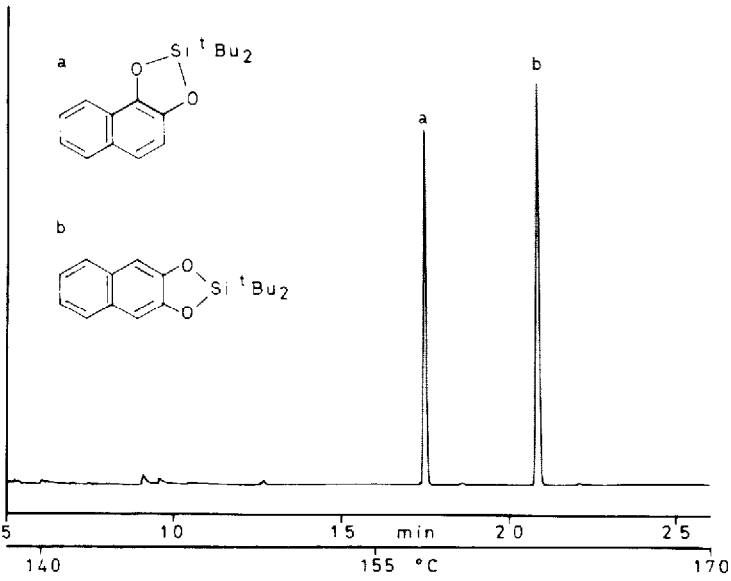


Fig. 10. Gas chromatographic separation of the DTBS derivatives of 1,2-dihydroxynaphthalene (peak a, $I$ = 1916) and 2,3-dihydroxynaphthalene (peak b, $I$ = 1984). GLC conditions as in Fig. 2. $^t$Bu = *tert.*-butyl.

There are comparatively few data in the literature on the mass spectra of heterocyclic compounds containing 1,3-dioxa-2-sila groupings. A brief report has appeared on 2,2,4,4,5,5-hexamethyl-1,3-dioxa-2-silacyclopentane and on four analogous 2-aryl-2-methyl compounds[18]. The mass spectrum of 2,2-dimethyl-1,3-dithia-2-silacyclopentane has been studied: the major fragment, as expected, was [M − 15][19]. Mass spectra of 2,2-dimethyl-4-oxo-5,6-benzo-1,3-dioxa-2-silacyclohexene[4] and related compounds have been studied[20]. We are unaware of any other previous reports on either the gas chromatography or mass spectrometry of derivatives more closely related to the DTBS acetals*.

* After this manuscript was submitted, a report appeared on the gas chromatographic and mass spectrometric properties of diethylsiliconide (diethylsilylene) derivatives of steroidal diols: H. Miyazaki, M. Ishibashi, M. Itoh and K. Yamashita, *Biomed. Mass Spectrom.*, 11 (1984) 377.

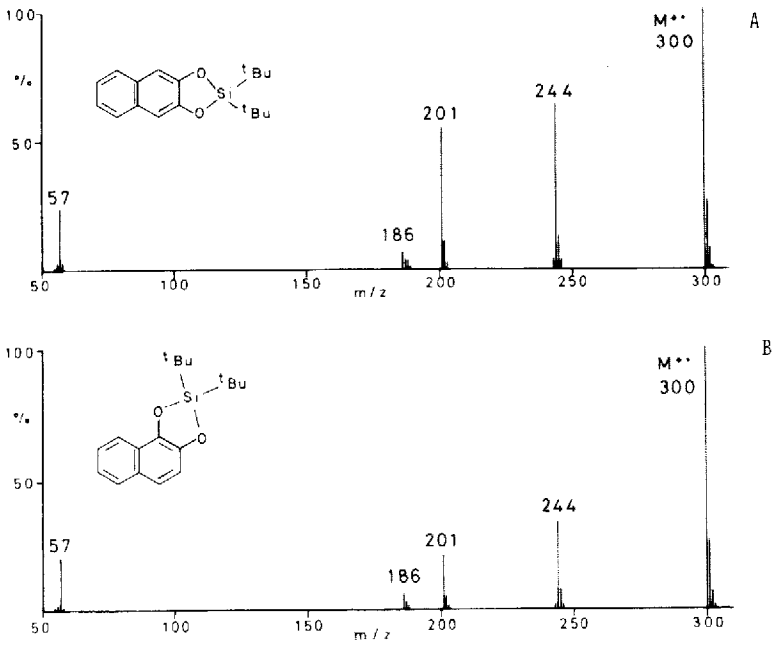


Fig. 11. Mass spectra (20 eV) of the DTBS derivatives of 2,3-dihydroxynaphthalene (A) and 1,2-dihydroxynaphthalene (B). GC–MS conditions as in Fig. 3, column temperatures as in Table II. $^tBu$ = *tert.*-butyl.

## CONCLUSIONS

The results described above indicate that DTBS derivatives are readily obtainable from unhindered 1,2- and 1,3-diols and from α- and β-hydroxy acids. The DTBS derivatives show good gas chromatographic properties, and are effective in separating both diastereomeric and structurally isomeric diols. The mass spectra are generally characterised by two major sequential cleavages of the Si–$C(CH_3)_3$ bonds, the second cleavage involving rearrangement with retention of $CH_3$. Thus, alkanediol DTBS derivatives yield [M − 57] and [M − 57 − 42] ions. By a variant of this sequence, catechol DTBS derivatives yield [M − 56] and [M − 56 − 43] ions. Rearrangement ions formed by losses of $H_2O$ are strikingly prominent in several examples. Many of these major fragmentations are accompanied by the observation of strong metastable ions. Ions resulting from cleavages alpha to the heterocyclic ring constitute minor but informative fragments in some instances.

We conclude that the DTBS derivatives are usefully selective for diols and hydroxy acids, as studied here, and potentially for a wide range of related substrates (cf. refs. 4, 12, 19 and 20). In more recent work[21], we have obtained DTBS derivatives from further bifunctional compounds including *o*-hydroxybenzoic acids (cf. refs. 4, 12 and 20 for dimethylsilylene analogues) and have found these satisfactory for GC–MS. The DTBS derivatives of saturated diols are likely to be particularly useful by virtue of their resistance to hydrolysis.

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