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Mass Spectra of Tetrahydrofuran Derivatives

Hajime Nagano,* Makiko Ijiri, Xiao Hong Xu, and Michio Shiota
Department of Chemistry, Faculty of Science, Ochanomizu University,
Otsuka, Bunkyo-ku, Tokyo 112
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Synopsis. Mass spectra of 2-(4,5-dialkyloxacyclopent-2-yl)-2-propanols exhibited a characteristic cleavage of tetrahydrofuran ring yielding an ion at *m/z* 102 ($C_5H_{10}O_2$) and/or an ion ($M^+-C_5H_{10}O_2-H$).

In the course of structure determination of magydardienediol, a diterpene isolated from *Magydaris panacifolia* (Vahl) Lange (Umbelliferae), we found a new characteristic mass spectral cleavage of tetrahydrofurans (**1**) derived from the diterpene.[1] The cleavage yielded ions at *m/z* 250 ($M^+-C_5H_{10}O_2$) and at *m/z* 167 ($M^+-C_5H_{10}O_2-CH_2CH_2CH=C(CH_3)_2$) as intense peaks. The other possible structure 2-(5-alkyl-5-methyloxacycopent-2-yl)-2-propanol expected for **1** was disproved as the mass spectra of tetrahydrofurans of the general type are well known to show an ion at *m/z* 143.[2] This difference in fragmentations shows that mass spectroscopy is efficient for the discrimination of these tetrahydrofurans.

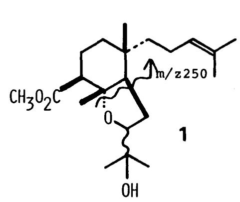
We report here the mass spectral fragmentations of tetrahydrofurans (**2**—**5**) which verify the cleavage of tetrahydrofuran ring mentioned above.

Tetrahydrofurans **2**—**5** were prepared from 5α-cholestan-3-one, 5-undecanone, cyclooctanone, and androsterone, respectively ((i) LiN(*i*-Pr)$_2$, $(CH_3)_2C=CHCH_2Br$, (ii) $NaBH_4$, (iii) *m*-chloroperbenzoic acid, H^+).

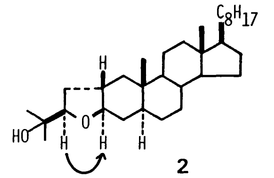
Mass spectrum of **2**, mp 132—134 °C, obtained at an electron beam energy of 70 eV showed a prominent peak at *m/z* 102 (relative intensity 52%) due to ion **a** ($C_5H_{10}O_2^+$). The formation of ion **a**, which was scarcely observed in the spectrum of **1**, firmly established the fragmentation process of tetrahydrofuran ring as shown in Scheme. At a lower electron beam energy (25 eV) the cleavage occurred predominantly to give the base peak at *m/z* 102 and loss of water from the molecular ion to a lesser extent. The predominancy of tetrahydrofuran ring cleavage over other fragmentations was also shown in the spectrum of **1** obtained at 18 eV (*m/z* 250 (54%) and 167 (100)).

Mass spectra of diastereomeric mixtures, **3a**, **3b**, **4a**, and **4b**, also showed an intense peak at *m/z* 102 (70 eV: **3a**(58%), **3b**(57), **4a**(53), and **4b**(53); 25 eV: **3a**(81%), **3b**(88), **4a**(87), and **4b**(100)).

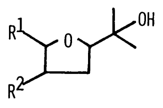
In the spectra of **5** (diastereomeric mixture) fragment ions at *m/z* 273 (70 eV (77%) and 25 eV (67); $M^+-C_5H_{10}O_2-H$) and 255 (70 eV (70%), 25 eV (100); $M^+-H_2O-C_5H_{10}O_2-H$) were observed as predominant peaks, whereas the intensities of ion **a** were moderate (70 eV (21%) and 25 eV (20)). The tendency for charge to reside on the methoxycarbonyl group in **1** and the hydroxyl group at C-3 in **5** may decrease the intensities of ion **a**. In the spectra of **4a** and **4b** a fragment ion ($M^+-C_5H_{10}O_2-H$) was also observed as an intense peak at *m/z* 109 (70 eV: **4a**(72%) and **4b**(75); 18 eV: **4a**(54%) and **4b**(46)).



1

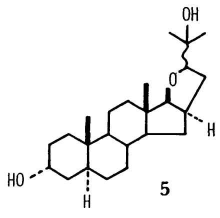


2

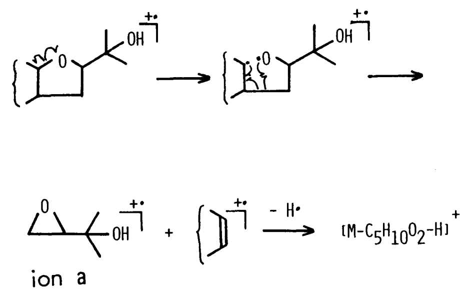


3a **3b** $R^1=C_5H_{11}$, $R^2=C_4H_9$

4a **4b** R^1, $R^2=-(CH_2)_6-$



5



Scheme

Experimental

Mass spectra were measured on a JEOL DX-300 spectrometer using direct inlet system. NMR Spectra were recorded on a JEOL GX270 spectrometer in $CDCl_3$.

2α-(3-Methyl-2-butenyl)-5α-cholestan-3-one. To a solution of the enolate of 5α-cholestan-3-one (569 mg) prepared using LiN(*i*-Pr)$_2$ (1.5 mmole) in dry THF (5 ml) and HMPA (0.2 ml) was added a solution of 4-bromo-2-methyl-2-butene (249 mg) in THF (1 ml) at −78 °C and the solution was stirred for 3 h. After work-up as usual the product was submitted to preparative TLC to give 2α-(3-methyl-2-butenyl)-5α-cholestan-3-one (31 mg), mp 115.5—116.5 °C; IR (KBr) 1708 cm^{-1}; ^{1}H NMR δ=1.59 (3H, s, Me), 1.69 (3H, s, Me), and 5.06 (1H, t, *J*=6.7 Hz); ^{13}C NMR δ=45.85 (C-1), 48.07 (C-2), 45.03 (C-4), and 46.85 (C-5); Found: *m/z* 454.4141. Calcd for $C_{32}H_{54}O$: M, 454.4173.

2α-(3-Methyl-2-butenyl)-5α-cholestan-3β-ol. The above ketone (30 mg) was reduced with $NaBH_4$ (17 mg) in ethanol to give 3β-ol (21 mg), mp 97—98 °C; IR (KBr) 3350 cm^{-1}; ^{1}H NMR δ=3.29 (1H, ddd, J=10.5, 10.5, and 5 Hz, 3α-H); Found: m/z 456.4416. Calcd for $C_{32}H_{56}O$: M, 456.4331.

Tetrahydrofuran 2. A solution of the 3β-ol (21 mg) and m-chloroperbenzoic acid (18 mg) in CH_2Cl_2 was allowed to stand at room temperature and then treated with dilute HCl to give **2** (7.6 mg); IR (KBr) 3520 and 3440 cm^{-1}; ^{1}H NMR δ=1.15 (3H, s, Me), 1.22 (3H, s, Me), 3.09 (1H, ddd, J=10.5, 10.5, and 4 Hz, 3α-H), and 3.83 (1H, dd, J=9 and 3.5 Hz, CH-O); HRMS: m/z 454.4170 (Calcd for $C_{32}H_{54}O$, M$-H_2O$, m/z 454.4173) and 102.0777 (Calcd for $C_5H_{10}O_2$, 102.0681).

Tetrahydrofurans 3a and 3b. A diastereomeric mixture of tetrahydrofurans derived similarly from 5-undecanone was separated into two fractions, **3a** (a mixture of two less polar diastereomers) and **3b** (a mixture of two polar diastereomers) using silica gel column chromatography. **3a**: an oil, IR (neat) 3450 cm^{-1}; ^{1}H NMR δ=0.89 (6H, m, Me), 1.105 (1.5H, s, Me), 1.109 (1.5H, s, Me), 1.21 (3H, s, Me), 3.46 (1H, m), and 3.73 (1H, m); MS (70 eV): m/z 241 (5%, M$^+-$Me), 238 (6, M$^+-H_2O$), and 153 (23, M$^+-C_5H_{10}O_2$-H); HRMS: m/z 197.1940 (Calcd for $C_{13}H_{25}O$, M$-C_3H_7O$, 197.1905), 153.1654 (Calcd for $C_{11}H_{21}$, 153.1644), and 102.0692 (Calcd for $C_5H_{10}O_2$, 102.0681). **3b**: an oil, IR (neat) 3450 cm^{-1}; ^{1}H NMR δ=0.89 (6H, m, Me), 1.10 (3H, s, Me), 1.20 (1.8H, s, Me), 1.23 (1.2H, s, Me), 3.69 (0.4H, dd, J=9.7 and 5.6 Hz), 3.78 (0.6H, t, J=7.5 Hz), and 3.91 (1H, m); MS: m/z 241 (4%), 238 (4) and 153 (19); HRMS: m/z 197.1928 and 102.0696.

Tetrahydrofurans 4a and 4b. A diastereomeric mixture of tetrahydrofurans derived from cyclooctanone was separated into two fractions, **4a** (a mixture of two less polar diastereomers) and **4b** (a mixture of two polar diastereomers). **4a**: an oil, IR (neat) 3450 cm^{-1}; ^{1}H NMR δ=1.10 (1.8H, s, Me), 1.11 (1.2H, s, Me), 1.21 (3H, s, Me), 3.5—3.85 (1.4H, m), 4.13 (0.6H, m); MS: m/z 212 (M$^+$, 0.3%); HRMS: m/z 194.1733 (Calcd for $C_{13}H_{22}O$, M$-H_2O$, 194.1671), 109.1011 (Calcd for C_8H_{13}, 109.1016), and 102.0693 (Calcd for $C_5H_{10}O_2$, 102.0681). **4b**: an oil, IR (neat) 3450 cm^{-1}; ^{1}H NMR δ=1.10 (3H, s, Me), 1.20 (3H, s, Me), 3.71 (1H, t, J=7.5 Hz), and 4.04 (1H, m); MS: m/z 212 (M$^+$, 1%); HRMS: m/z 197.1556, 109.1020, and 102.0707.

Tetrahydrofurans 5. The spectral data of **5** (a mixture of diastereomers), colorless plates, mp 199.5—200.5 °C, are as follows. IR (KBr) 3350 cm^{-1}; ^{1}H NMR δ=0.73 (1.8H, s, 18-H or 19-H), 0.78 (4.2H, s, 18-H and 19-H), 1.08 (1.8H, s, Me), 1.14 (1.2H, s, Me), 1.18 (1.8H, s, Me), 1.25 (1.2H, s, Me), 2.18 (1H, br s, OH), 2.29 (1H, br s, OH), 2.65 (1H, m,), 3.81 (0.4H, dd, J=11.3 and 4.4 Hz,), and 3.9—4.1 (2.6H, m); HRMS: m/z 376.2983 (Calcd for $C_{24}H_{40}O_3$, M, 376.2977), 273.2176 (Calcd for $C_{19}H_{29}O$, 273.2217), 255.1401 (Calcd for $C_{17}H_{19}O_2$, 255.1384), and 102.0735 (Calcd for $C_5H_{10}O_2$, 102.0681).

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