GAS CHROMATOGRAPHY-MASS SPECTROMETRY OF CYCLIC BORONATE DERIVATIVES OF SOME ALKALOID AND TERPENOID DIOLS

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Abstract - Cyclic ferroceneboronates of the alkaloidal diols retronecine, platynecine, rosmarinecine and swainsonine, and the *bis*-methaneboronate of aphidicolin are suitable derivatives for gas chromatography-mass spectrometry.

The selective formation of cyclic derivatives is of great value in the analysis and characterisation of suitably constituted bifunctional compounds. The particular advantages of cyclic boronate esters in the study of diols by gas chromatography-mass spectrometry (GC-MS), as summarised in our original reports,[1,2] have led to widespread applications of these derivatives. The rapid detection and characterisation of diols in extracts of plant materials, for example, is aided by the ease of formation of cyclic boronates under very mild conditions. Such procedures have been used, inter alia, for pyrrolizidine alkaloids,[3-5] brassinosteroids,[6] and sesquiterpenoids.[7] Methaneboronates[8] are especially convenient for studies of compounds of relatively high molecular mass. One drawback of alkaneboronate derivatives is their susceptibility to solvolysis. We considered that ferroceneboronates might be more stable in this respect. Diols reacted smoothly with ferroceneboronic acid (1.1 molar proportions in dry pyridine, 70°C for 30 min): the resulting cyclic esters were still liable to solvolysis, but gave good gas chromatographic peaks, while the mass spectra were generally dominated by abundant molecular ion clusters.[9] The latter feature makes ferroceneboronic acid complementary to the more commonly used reagents, as outlined in the present note. The parent compounds studied are shown in Fig. 1, and GC-MS data in Table 1.

The configurations of the 1,4 - diol systems in retronecine (1) and platynecine (2) are favourable for the formation of cyclic boronate esters. In the crystalline state the left-hand rings in 1[10] and 2[11] are both exo-puckered. The ferroceneboronates of 1 and 2 were separated (ΔI = 17: Fig. 2) by gas chromatography on a CPSil5CB fused silica column (25 m x 0.32 mm I.D.). Heliotridine, the hydroxy epimer of retronecine, has been reported to yield a methaneboronate[12] in spite of its comparatively unfavourable stereochemistry:[10] however, we have not observed the formation of the analogous ferroceneboronate. In rosmarinecine (3) a seven-membered ferroceneboronate was obtained corresponding to those from 1 and 2: a six-membered ester involving the additional hydroxy group

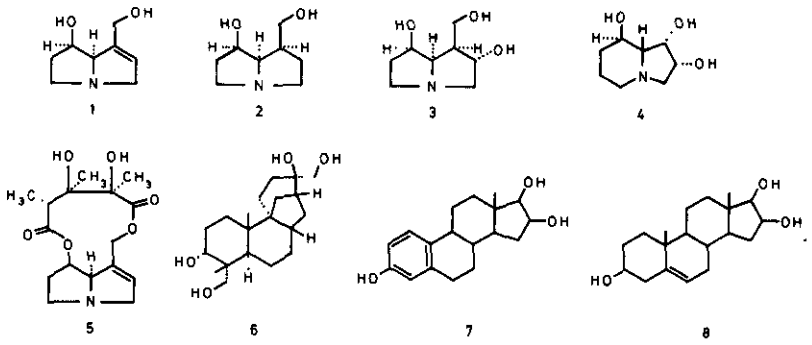

Fig. 1. Structures of diols and triols. 1 = retronecine; 2 = platynecine; 3 = rosmarinecine; 4 = swainsonine; 5 = monocrotaline; 6 = aphidicolin; 7 = estra-1,3,5(10)-triene-3,16β,17β-triol; 8 = androst-5-ene-3β,16β,17β-triol.

Table 1. Kováts retention indices (I) and salient mass spectrometric data (22 eV) for cyclic boronates of diols.

Compound	I (OV-1)	Temperature (°C)	Base peak*	$M^{+\cdot}$	% Σ
1a	2515	220	349	349	30
2a	2535	220	351	351	49
3b	2675	220	439	439	51
4b	2595	220	439	439	77
5c	2200	200	120	349(3)	-
5d	2875	255	120	411(3)	-
6e	2625	225	113	386(5)	-
7b	4100	300	554	554	89
8b	4060	300	572	572	88
8f	2655	240	129	402	8

*Mass spectra normalised above m/z 40; intensities of ions relative to the base peak are in parentheses. a = ferroceneboronate, b = ferroceneboronate TMS ether, c = methaneboronate, d = benzeneboronate, e = bis-methaneboronate, f = methaneboronate TMS ether. %Σ = the molecular ion cluster as a percentage of the total ion current.

Kováts indices (I) were determined on a glass column (2 m x 4 mm I.D.) packed with 1% OV-1 on Gas Chrom Q (100-120 mesh).

would be highly strained. Rosmarinecine acetonide also has the seven-membered structure (H.A. Kelly and D.J. Robins, unpublished results). Acyclic boronate esters, which may be formed from isolated hydroxy groups such as that in 3, are easily displaced by mild acylation[12] or silylation.[1,2] Ferroceneboronates of 3 and of the indolizidine alkaloid swainsonine (4) were each treated (in the initial reaction mixture) with N,O-bis(trimethylsilyl)trifluoroacetamide at 70°C for 5 min to yield derivatives suitable for gas chromatography. In the latter case the ester was formed from the cis-1,2-diol, in which the hydroxyl groups are virtually coplanar. The mass spectra of the derivatives from compounds 1-4 are notable for the great abundance of the molecular ion clusters (Table 1). Apart from these, the fragment ions comprise two main groups as exemplified in Fig. 3: (i) ions containing the ferrocenyl (Fc) group, principally $FcB(OH)_2^{+\bullet}$ (m/z 230), $FcBO^{+\bullet}$ (m/z 212) and $FcH^{+\bullet}$ (m/z 186) and (ii) nitrogenous fragments such as (for retronecine ferroceneboronate) $C_8H_{10}NO^+$([M - FcBOH]), $C_8H_{10}N^+$, $C_8H_9N^{+\bullet}$, $C_7H_8N^+$ and $C_6H_7N^{+\bullet}$ - all of which were verified by accurate mass measurements at m/z 136, 120, 119, 106 and 93 respectively. A major ion at m/z 122 in the mass spectrum of platynecine ferroceneboronate was similarly verified as $C_8H_{12}N^+$.

Monocrotaline (5), which contains a vicinal diol in the cyclic diester moiety, was examined as its methaneboronate (already found satisfactory by others)[4] and its benzeneboronate. (The ferroceneboronate would have had an unduly high retention time.) Although molecular ions were quite clear

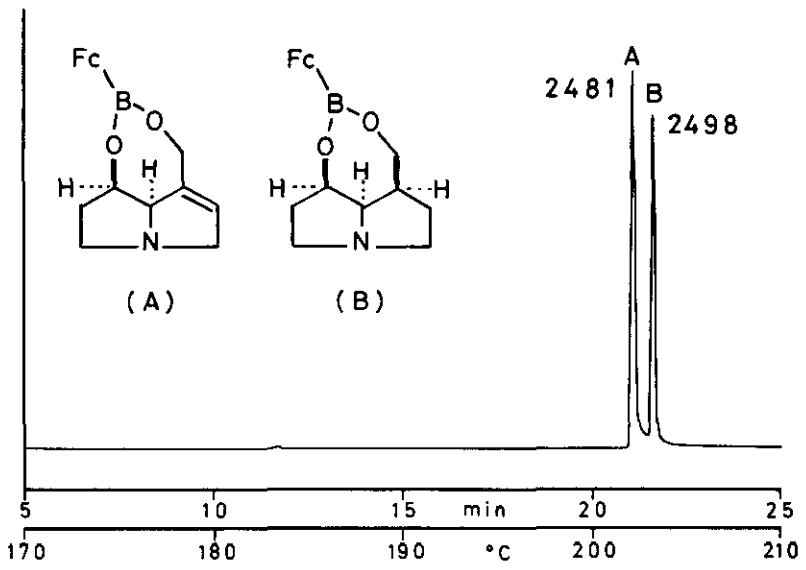

Fig. 2. Capillary gas chromatographic separation of the ferroceneboronates of (A) retronecine and (B) platynecine.

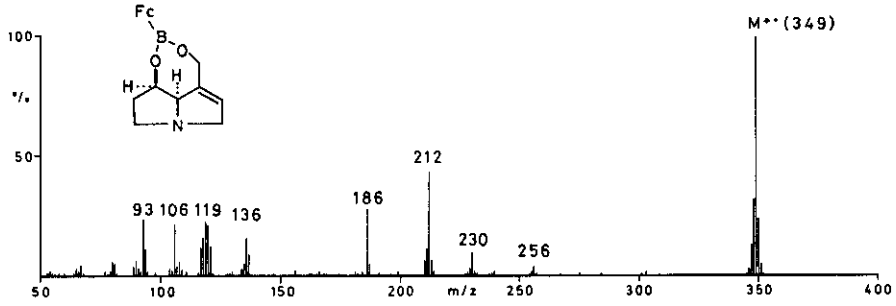

Fig. 3. Mass spectrum (22 eV) of retronecine ferroceneboronate

in the mass spectra, their relative abundance was low, as there was major fragmentation, the most abundant ions being at m/z 120 ($C_8H_{10}N^+$). Ions at m/z 112 and 174 respectively were ascribed to fragments of type $R.BO_2.C_4H_6^{+\bullet}$ - the only major ions that contained part of the macrocyclic ring. Cyclic boronates of certain non-nitrogenous compounds have also been briefly examined. Small molecules such as threitol and erythritol readily form bis-ferroceneboronates that are very convenient derivatives for GC-MS (C.J.W. Brooks and W.J. Cole, unpublished results). Aphidicolin (6) has too high a molecular mass for similar treatment, but - like the brassinosteroids[6] of comparable molecular masses - afforded a bis-methaneboronate quite suitable for gas chromatography. The mass spectrum (Fig. 4) showed as major features a complementary pair of ions (m/z 273 and 113), each containing one boronate moiety: these are ascribed to cleavage through ring A with one hydrogen transfer.

The ion seen at m/z 213 corresponds to the loss of methaneboronic acid from m/z 273, but no metastable ion for this process was observed.

Finally, cyclic ferroceneboronates of 16-epiestriol (7) and androst-5-ene-3β,16β,17β-triol (8) were examined after trimethylsilylation of the 3-hydroxy groups. The resulting derivatives had retention index values above 4000, but with recent improvements in gas chromatography, such high values have become practicable. The mass spectra (Fig. 5) show the great stability of the molecular ions, which carry almost 90% of the total ion current above m/z 40. This effect is very striking for the androstenetriol derivative, in which the ions of m/z 129 and (M-129), which are normally abundant in the mass spectra of 5-ene-3-trimethylsilyloxysteroids,[13] are negligible. In the corresponding methaneboronate 3-trimethylsilyl ether of 8 (see Table 1) ions of m/z 129 and (M-129) are respectively of 100% and 26% relative abundance.

It may be concluded that for diols of moderate molecular mass the cyclic ferroceneboronates, obtainable from 1,2-, 1,3- and 1,4-diols of appropriate geometry, are usefully characteristic derivatives, which are easily formed even from sterically hindered diols. The remarkably stable

molecular ions formed under electron impact, and their isotopic patterns, are features useful for the detection and characterisation of diols in mixtures by selected ion monitoring, according to established practice for alkaneboronates.[6]

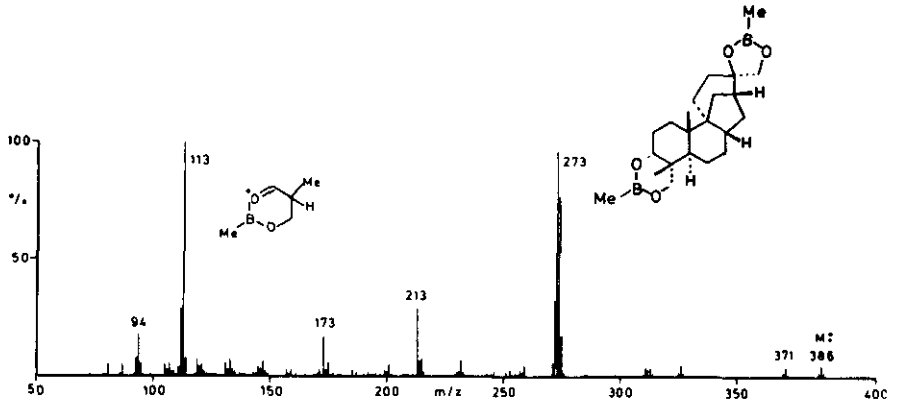

Fig. 4. Mass spectrum (22 eV) of aphidicolin bis-methaneboronate.

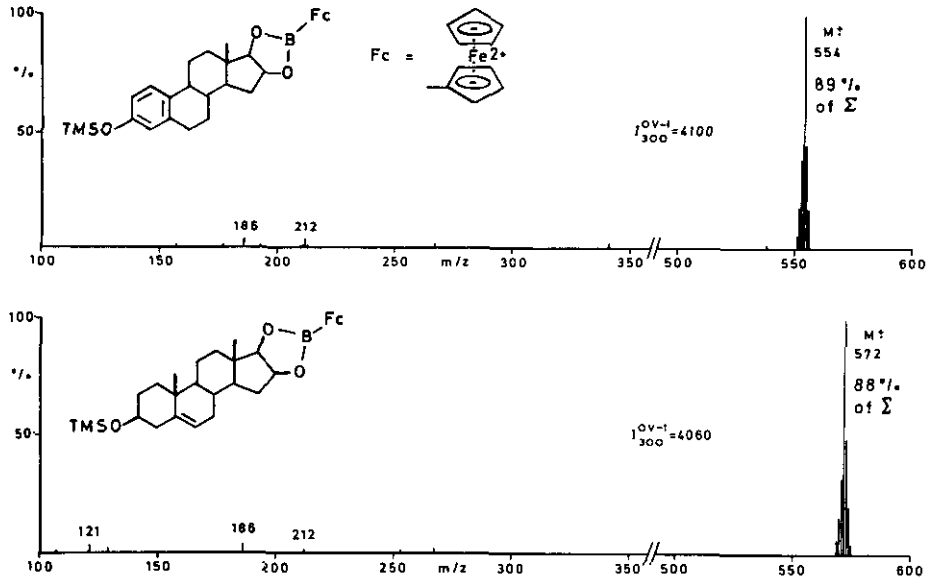

Fig. 5. Mass spectra (22 eV) of the ferroceneboronate 3-trimethylsilyl ethers of estra-1,3,5(10)-triene-3,16β,17β-triol (top) and androst-5-ene-3β,16β,17β-triol (bottom).

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