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Note

Analytical separation and characterisation of 1,2- and 1,3-diols as their cyclic ferroceneboronate derivatives

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Cyclic boronates are well established as effective derivatives for the selective analysis of proximally bifunctional substrates by gas–liquid chromatography (GLC) and its combination with mass spectrometry (MS). Minor drawbacks of these derivatives include their susceptibility to solvolysis, and the conformational mobility of the boronate rings: these factors can detract from the quality of gas chromatographic peaks. We considered that the use of ferroceneboronates might be advantageous. For example, electron donation to boron by the ferrocenyl group should tend to improve resistance to solvolysis. In addition, the resultant partial C–B double-bond character, together with the bulk and rigidity of the ferrocenyl ($C_{10}H_9Fe$)* moiety, would be expected to restrict the conformational range of the cyclic boronate grouping. A further aspect of interest in ferroceneboronates is their potential value for multiple-element detection in GLC combined with plasma emission spectrometry —a technique already successfully applied to the analysis of butaneboronates of catechols[1]. In this respect, ferroceneboronic acid[2] is an example of a selective "multi-element taggant"[3] for bifunctional substrates.

We have found that ferroceneboronic acid readily yields cyclic derivatives with suitably constituted 1,2-diols, 1,3-diols, and related substrates. In general, the derivatives afford sharp and symmetrical peaks in GLC, while their mass spectra (under electron impact ionisation) show abundant molecular ions, which are usually the base peaks and represent a high proportion of the total ion current. These features are exemplified in the small group of compounds (listed in Table I) that are included in this preliminary note. In general, the derivatives were prepared by adding a solution of ferroceneboronic acid (1.1 molar proportions) in dry pyridine to the substrate (100 μg) (also in dry pyridine) and heating at 70°C for 30 min. After removal of solvent in a stream of nitrogen, the residue was dissolved in ethyl acetate (100 μl) for analysis by GLC and GLC–MS. Under these conditions, there appeared to be substantially complete formation of derivatives, most of which remained stable in ethyl acetate solution for several days, as judged by GLC.

Fig. 1 shows the GLC separation of ferroceneboronates of one of the chiral forms of butane-2,3-diol and its *meso*-stereomer. The quality of the peaks is similar to that of trimethylsilyl ethers (and of cyclic di-*tert*.-butylsilylene derivatives[4]), and

* Denoted as Fc where appropriate.

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TABLE I

KOVÁTS RETENTION INDICES (*I*) AND MASS SPECTROMETRIC DATA (22 eV) FOR FERROCENEBORONATE DERIVATIVES OF 1,2- AND 1,3-DIOLS AND OF AN AMINO-ALCOHOL

Parent compound	$I_{OV\text{-}1}$	*Temperature (°C)*	$M^{+\cdot}$ *(base peak)**	$[Fc{-}B{=}O]^{+\cdot}$ *m/z 212, % abundance*
(*R,R*)-Butane-2,3-diol	1790	150	284	30
meso-Butane-2,3-diol	1840	150	284	43
Cyclohexane-*cis*-1,2-diol	2165	190	310	33
Cyclohexane-*trans*-1,2-diol	2170	190	310	82
Mephenesin**	2680	225	376	17
Chlorphenesin***	2815	225	396	20
2,2,4-Trimethylpentane-1,3-diol	2150	190	340	22
2-(2-Pyridyl)propane-1,3-diol	2610	225	347	60
(−)-2-Aminobutan-1-ol	1975	175	283	39

* Mass spectra normalised above *m/z* 40.
** 3-(2-Methylphenoxy)propane-1,2-diol.
*** 3-(4-Chlorophenoxy)propane-1,2-diol.

the separation of isomers very satisfactory. Their mass spectra are virtually identical: that of the (*R,R*)-isomer (Fig. 2) shows the characteristic isotopic pattern of the molecular ion (reflecting mainly the contributions of ^{10}B, ^{54}Fe and ^{57}Fe as relatively abundant minor isotopes). The other main ions represent the reagent moieties $[FcB(OH)_2]^{+\cdot}$ (*m/z* 230) and $[FcBO]^{+\cdot}$ (*m/z* 212). Strong metastable ions were observed in respect of the losses of C_4H_8O from the molecular ions (*m/z* 284 → *m/z* 212).

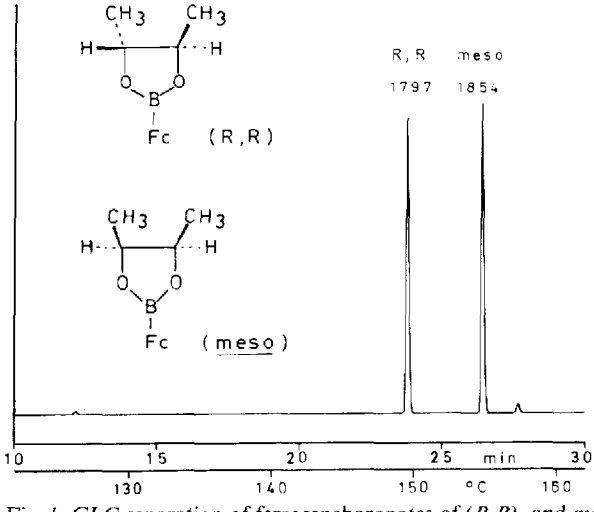

Fig. 1. GLC separation of ferroceneboronates of (*R,R*)- and *meso*-butane-2,3-diol. Column, SE-54 fused silica, 25 m × 0.32 mm I.D.; column temperature, programmed from 80°C (2 min) to 110°C (1 min) at 30°C/min, and then at 2°C/min to 200°C; helium flow-rate, 3 ml/min; flame ionization detection. Samples (*ca.* 1 μg) were introduced via a Grob-type injector operated in split mode (50:1). Fc = Ferrocenyl.

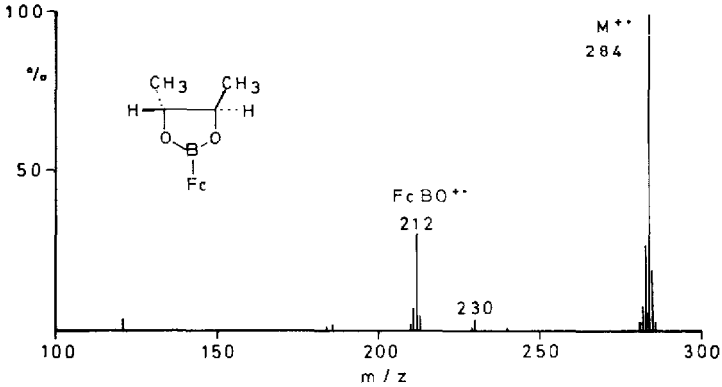

Fig. 2. Mass spectrum (22 eV) of (*R,R*)-butane-2,3-diol ferroceneboronate. The LKB 9000 gas chromatograph–mass spectrometer was operated with a DB-1 fused-silica column, 60 m × 0.32 mm I.D.; column temperature, 150°C; helium carrier gas and "make-up" gas flow-rates, 7 and 25 ml/min, respectively; accelerating voltage, 3.5 kV; source and separator temperatures, 270°C; trap current, 60 μA; filament current, 4 A. The sample (*ca.* 1 μg) was introduced via a falling-needle injector. Fc = Ferrocenyl.

The mass increment of 194 attending formation of cyclic ferroceneboronates makes these derivatives particularly suitable for the selective analysis of diols of low molecular mass. However, larger molecules can be effectively studied, as illustrated by the GLC trace in Fig. 3 for ferroceneboronates of mephenesin (a topical antifungal agent) and chlorphenesin (a muscle relaxant). The corresponding mass spectra are again dominated by molecular ions, but show a few fragment ions containing substrate moieties. In the case of mephenesin ferroceneboronate (Fig. 4), major ions derived from the reagent include *m/z* 230, 213 ($[FcBOH]^+$), 212, 186 ($FcH^{+\cdot}$) and 121 ($[C_5H_5Fe]^+$). The most prominent of the ions retaining a part of the substrate molecule occurs at *m/z* 239 ($[C_{12}H_{12}BFeO]^+$, *i.e.* $[FcBOC_2H_3]^+$).

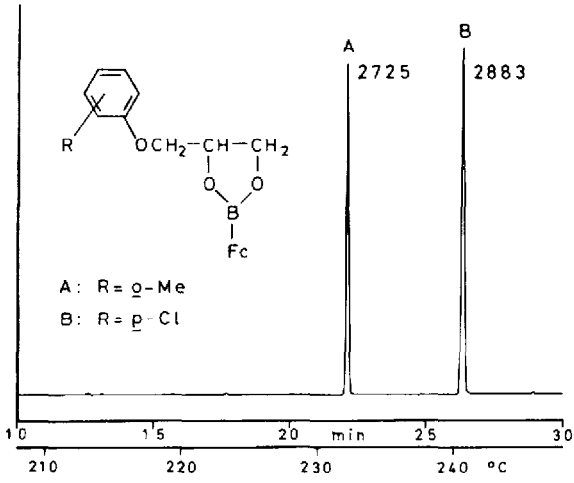

Fig. 3. GLC separation of the ferroceneboronates of mephenesin (A) and chlorphenesin (B). Column as in Fig. 1; column temperature, programmed from 80°C (2 min) to 200°C (2 min) at 30°C/min, and then at 2°C/min to 260°C; other conditions as in Fig. 1. Fc = Ferrocenyl.

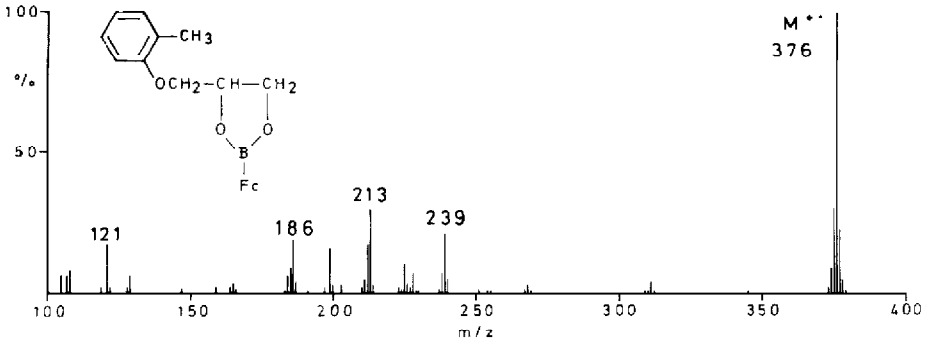

Fig. 4. Mass spectrum (22 eV) of the ferroceneboronate of mephenesin. Conditions as in Fig. 2, except for column temperature (225°C). Fc = Ferrocenyl.

Satisfactory ferroceneboronates have been obtained from a wide range of other substrates. Salient data for cyclohexane-*cis*- and -*trans*-1,2-diols (for which the derivatives were just separable by GLC), for two 1,3-diols, and for 2-aminobutan-1-ol, are given in Table I. Our results indicate that ferroceneboronic acid resembles other boronic acids in its ready reaction with most of the bifunctional substrate types for which the latter reagents are well established. The cyclic ferroceneboronates of diols also possess some special features: for example, (i) the GLC peaks are, in most instances, strikingly sharp and symmetrical; (ii) the electron impact mass spectra show strongly preponderant molecular ions (with characteristic isotopic patterns) and relatively few other substrate-derived ions; (iii) the high abundances of molecular ions, and of reagent-derived ions (*e.g.* *m/z* 230, 212, 186 and 121) provide potentially sensitive means of detecting, respectively, the individual boronates or the boronates as a group, by selected ion monitoring. Further aspects of the applications of ferroceneboronic acid to the analysis and characterisation of bifunctional substrates are described in a fuller paper[5].

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