Journal of Chromatography, 186 (1979) 307–316

CHROM. 11,809

COMPARISON OF ELECTRON-CAPTURING BORONIC ACIDS FOR THE SELECTIVE ANALYSIS OF BIFUNCTIONAL COMPOUNDS*

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SUMMARY

The preparation and chromatographic properties of 2,6-dichlorobenzeneboronic, 2,4,6-trichlorobenzeneboronic and 3,5-di(trifluoromethyl)benzeneboronic acids are described. These reagents are compared with seven other electron-capturing boronic acids on the basis of their range of application, relative volatility, electron-capture sensitivity and derivative stability to establish some criteria for the selection of the most useful reagents. It is proposed that the four boronic acids 3,5-di(trifluoromethyl)-benzeneboronic, 2,4-dichlorobenzeneboronic, 4-bromobenzeneboronic and 4-iodobutaneboronic acid are sufficient to meet the needs of most analytical problems.

INTRODUCTION

The complete resolution of all of the components of a complex biological or environmental sample is a formidable task. However, the object of most studies is to gain some knowledge of a few specific components or a group of substances distinguished by their similar structure, physiological activity or polarity, which constitute a small part of the original sample. The use of selective reagents and selective detectors for the isolation and determination of target compounds is an attractive means of simplifying an otherwise difficult problem.

Although the number of functionalized molecules in physiological fluids is immense, only a fraction of these are bifunctional. These compounds are characterized by having at least two functional groups in close proximity. Many examples can be found among the physiologically active substances (*e.g.*, steroids, prostaglandins, catecholamines, nucleosides). Their selective analysis requires the use of chemically specific reagents capable of distinguishing the bifunctional groups from other polyfunctional arrangements. Reagents for the selective analysis of bifunctional compounds have been reviewed by Darbre[1]. For gas chromatography, the boronic acids are the most useful, being applicable to a wide range of bifunctional compounds with protonic (OH, NH_2, SH, CO_2H) or keto groups on 1,2-, 1,3- or 1,4-carbon atom systems[2,3].

The specific reaction of bifunctional compounds does not aid the determination

* Determination of Bifunctional Compounds, Part VI. For Part V see ref. 17.

of these compounds (except by changing their volatility) unless a selective means of detection is employed which enables the boronate derivative to be distinguished from the organic background. Generally, the boronates have been detected with the universal flame-ionization detector, which has not enabled full advantage to be taken of the analytical potential of the boronic esters. Hetero-element detectors for boron, the alkali flame-ionization detector (AFID)[4,5] and the flame-photometric detector[6] have been applied with limited success. Using the rubidium bead (nitrogen–phosphorus detector) (NPD) under conditions optimized for boron, only a poor selective response for boron could be obtained. With the phosphorus jet installed, an enhanced response of about four-fold was obtained for the benzeneboronate of pinacol compared to a hydrocarbon internal standard. Preliminary studies from our laboratory indicated that the introduction of an electron-capturing substituent into the organic portion of a boronic acid enabled volatile derivatives to be formed which could be selectively detected with the electron-capture detector at trace levels[7–9]. The rationale for the selection of suitable electrophores and the limitations imposed by the chemical properties of boron have been outlined previously[8,9]. Chlorobenzeneboronic acids with two chlorine substituents had excellent electron-capturing properties and were reasonably volatile on gas chromatography[8]. To complement the two reagents prepared previously, 2,6-dichlorobenzeneboronic acid and 2,4,6-trichlorobenzeneboronic acid were synthesized. As expected, the position of the chlorine substituent had a marked influence on detector sensitivity and derivative stability.

Before attempting a final evaluation and comparison of all available electron-capturing boronic acids, it was considered that there was still a need for a reagent which provided more volatile derivatives than those prepared previously. The introduction of a benzene ring with pendant substituents can add substantially to the retention time of a compound and becomes of considerable importance for compounds of intermediate and high molecular weight. A solution to this enigma is the use of fluoroaromatic substituents as fluorocarbon compounds have exceptional volatility in spite of their high molecular weights. Chambers[10] has given an explanation of this phenomenon in terms of intramolecular forces. Pentafluorobenzeneboronic acid was found to be unsuitable as under the conditions necessary for derivative formation the boron aryl bond was labile. Zlatkis and Lovelock[11] reported that compounds containing two or more weakly electron-capturing centers connected by some intramolecular pathway can behave synergistically with the production of a detector response many-fold greater than that recorded for either center in isolation. Compounds of this type were said to contain conjugated electrophores. 3,5-Di(trifluoromethyl)benzeneboronic acid was synthesized as a volatile reagent with a conjugated electrophore consisting of the benzeneboronate group as one part and the two trifluoromethyl substituents as the other. Although benzene is virtually non-electron-capturing, the benzeneboronate group captures electrons to a moderate extent[8]. The trifluoromethyl group is a poor electrophore[12–14].

EXPERIMENTAL

Reagents

Benzeneboronic acid, 4-bromobenzeneboronic acid (Aldrich, Milwaukee, Wisc., U.S.A.) and 3-nitrobenzeneboronic acid (K & K Labs., ICN Pharmaceuticals,

Plainview, N.Y., U.S.A.) were obtained commercially. 2,4-Dichlorobenzeneboronic acid[8], 4-iodobutaneboronic acid[9] and 3,5-di(trifluoromethyl)benzeneboronic acid are available from Lancaster Synthesis (Lancaster, Great Britain) or the Alfa Products Division of Ventron Corp. (Danvers, Mass., U.S.A.) and were prepared for the first time in this laboratory. 3,5-Dichlorobenzeneboronic acid[7] and naphthaleneboronic acid[8] were available from previous studies. 2,6-Dichloroaniline (Aldrich) and 2,4,6-trichloroaniline (Eastman Kodak, Rochester, N.Y., U.S.A.) were diazotized and converted into the iodochlorobenzene compound with potassium iodide, essentially by the method of Hodgson and Mahadevan[15]. 3,5-Di(trifluoromethyl)bromobenzene was obtained from the Fairfield Chemical Co. (Blythewood, S.C., U.S.A.).

The general experimental technique for the synthesis of boronic acids by the low-temperature reaction of a Grignard reagent with trimethylborate (Aldrich) was used with minor modifications[7,8] for the preparation of 2,6-dichlorobenzeneboronic, 2,4,6-trichlorobenzeneboronic and 3,5-di(trifluoromethyl)benzeneboronic acids. The Grignard reagents were prepared in diethyl ether using a crystal of iodine to initiate the reaction. Refluxing for 7–16 h was required for the chlorobenzene compounds and for 2 h for 3,5-di(trifluoromethyl)bromobenzene. The boronic acids were not stable to the aqueous acid–base work-up employed previously. The Grignard–boronate complexes were decomposed with a saturated solution of ammonium chloride and the ether layer collected and dried over magnesium sulphate. The oily residues obtained by evaporation of the ether solution were triturated with methanol (2,6-dichloro- and 2,4,6-trichlorobenzeneboronic acids) or *n*-hexane [3,5-di(trifluoromethyl)benzeneboronic acid] in a dry-ice–acetone bath and the crystals collected and dried on the filter. The boronic acids were recrystallized from methanol or *n*-hexane and characterized as their pinacol derivatives[16]. The physical constants and experimental yields are given in Table I.

TABLE I

PHYSICAL CONSTANTS FOR THE BORONIC ACIDS

Boronic acid	*Melting point (°C)*	*Yield (%)*	*Melting point of pinacol derivative (°C)*
2,6-Dichlorobenzeneboronic acid (methanol)	149–151	30	103.5–105.5 (*n*-hexane)
2,4,6-Trichlorobenzeneboronic acid (*n*-hexane)	54–55	14	94–95 (methanol)
3,5-Di(trifluoromethyl)benzeneboronic acid (*n*-hexane)	212–215	25	67–67.5 (ethanol–water)

Preparation of derivatives

Equal volumes of 0.1 *M* tetrahydrofuran solution of the bifunctional compound and boronic acid were added to a 1.0-ml Reacti-vial (Pierce, Rockford, Ill., U.S.A.) and mixed briefly on a vortex mixer. All reactions were complete within 15 min at room temperature. Alternative reaction techniques for the formation of boronic ester derivatives have been discussed elsewhere[17].

Conditions for gas chromatography

For gas chromatography with flame-ionization detection a Sigma 2 (Perkin-

Elmer) chromatograph and a 90 × 0.2 cm I.D. nickel column packed with 1% OV-17 on Gas-Chrom Q (100–120 mesh) was used. The carrier gas was nitrogen at a flow-rate of 60 ml·min^{-1} and the injector and detector temperatures were 200 and 300°C, respectively.

For electron-capture studies two different detectors were used. Detector A was of the coaxial displaced cylinder type with a nickel-63 (8 mCi) source, operated in the pulse-modulated constant-current mode and fitted to a Varian 3700 gas chromatograph. With this detector configuration, the temperature of the source is lower than that monitored by the instrument which takes measurements at the detector block. Detector B was custom-designed[18] and of the coaxial cylinder type with a nickel-63 (30 mCi) source and operated in the pulse mode with a pulse width of 4 μsec and a pulse period of 2000 μsec. Detector B was mounted on a Victoreen 4000 gas chromatograph.

Hydrolysis of pinacol boronates

A stock solution of pinacol boronate (0.08 *M*) and internal standard (C_{16}, C_{20} or C_{22}) in *n*-hexane was diluted 1:2 with *n*-hexane and extracted with an equal volume of either 1 or 3 *N* sodium hydroxide solution saturated with sodium chloride. The solutions were mixed vigorously for 8 min on a vortex mixer and the phases allowed to separate (0.5 min) prior to injection of an aliquot from the organic phase.

RESULTS AND DISCUSSION

Chlorobenzeneboronic acids

The position of the chlorine atoms on the benzene ring had little effect on the range of application of the reagents to a test set of bifunctional compounds selected to represent a broad range of functional group type and environment. 2,4,6-Trichlorobenzeneboronate derivatives of aliphatic amino bifunctional compounds were generally less stable than the dichlorobenzeneboronate derivatives. The results are summarized in Table II and compounds not forming derivatives of any type are listed in the footnotes. As expected, the position of the chlorine atom has little effect on the volatility of the derivatives for the relatively non-selective OV-17 stationary phase. The introduction of two chlorine atoms into the benzene ring increases the retention time about 4- to 7-fold compared with the benzeneboronate derivatives and the addition of a third chlorine atom in 2,4,6-trichlorobenzeneboronates adds a further increment of about 1.5-fold to this.

To establish the sensitivity of the electron-capture detector towards the chlorobenzeneboronates, the minimal detectable quantity (MDQ) of pinacol was determined under optimal conditions. Of importance in studies of detector optimization is the correct selection of detector temperature[18]. The temperature dependence of the detector response arises from the mechanism of electron capture and is conveniently evaluated graphically by a plot of ln $AT^{3/2}$ against $1/T$ (A = peak area for a fixed mass of derivative and T is the detector temperature in °K)[19]. For the chlorobenzeneboronates (Fig. 1), all derivatives capture electrons in a dissociative manner with the largest detector response being obtained at high detector temperatures. The relative position of the chlorine atoms on the benzene ring has a significant effect on detector sensitivity. For the pinacol boronates the MDQ values are 2,4-dichlorobenzeneboronate

TABLE II

RELATIVE VOLATILITIES OF CHLOROBENZENEBORONATES

*Compound**	*2,4-DCBB*	*3,5-DCBB*	*2,6-DCBB*	*2,4,6-Tri-CBB*	*Column temperature (°C)*
Ethylene glycol	0.40	0.32	0.32	0.51	140**
Pinacol	0.47	0.40	0.56	0.96	140
1,3-Propanediol	0.75	0.71	0.55	0.95	140
1,4-Butanediol	1.26	1.15	0.93	1.58	140
1,3-Cyclopentanediol	1.59	1.45	1.55	2.35	140
cis-1,2-Cyclohexanediol	2.54	2.13	2.41	3.93	140
Lactic acid	0.71	0.54	0.47	—	140
1,3-Propanediamine	0.90	1.30	—	—	140
3-Amino-1-propanol	0.79	1.30	0.78	—	140
2-Amino-1-butanol	0.70	1.00	0.86	—	140
Catechol	2.36	1.89	1.87	3.02	140
Phenyl-1,2-ethanediol	0.41	0.35	0.38	0.54	210***
o-Phenylenediamine	0.71	0.85	0.58	0.90	210
o-Aminophenol	0.32	0.43	0.33	0.52	210
D,L-Mandelic acid	0.63	0.53	0.53	0.68	210
Salicylic acid	0.64	0.64	0.50	0.67	210
Anthranilic acid	1.61	—	1.93	2.95	210

* Compounds not forming boronate derivatives: 2,3-butanedione, 2,4-pentanedione, 2,5-hexanedione, 3-hydroxy-2-butanone, propane-1,3-dithiol; 2-anilinoethanol, 2-amino-2-hydroxymethyl-1,3-propanediol, ethylenediamine, methylguanidine; isophthalic acid, *trans*-1,2-cyclobutanedicarboxylic acid, oxalic acid, 2,3-pyridinecarboxylic acid, pyruvic acid, gallic acid, isoleucine, succinic acid, citric acid, malonic acid; pentane-1,5-diol, sorbitol; *m*-phenylenediamine, resorcinol, 3-aminophenol.

Compounds forming 4-iodobutaneboronates but not 2,4-DCBB: 3-hydroxypropionic acid, 1,2-;5,6-dianhydrogalactitol.

Compound forming 2,4-DCBB but not 4-iodobutaneboronates: 1,3-propanediamine.

** Internal standard C_{20}, $R_t = 5.7$ min.

*** Internal standard C_{28}, $R_t = 5.6$ min.

($4 \cdot 10^{-12}$ g) ≈ 2,4,6-trichlorobenzeneboronate ($4 \cdot 10^{-12}$ g) < 3,5-dichlorobenzeneboronate ($11 \cdot 10^{-12}$ g) < 2,6-dichlorobenzeneboronate ($18 \cdot 10^{-12}$ g).

Further discussion of the properties of the chlorobenzeneboronic acids is deferred to the section *Comparison of electron-capturing boronic acids.*

3,5-Di(trifluoromethyl)benzeneboronic acid

A representative series of bifunctional compounds was used to assess the range of application and derivative volatility. Derivatives were formed with all compounds (Table III) except for those containing carboxylic acid groups, which were generally unstable. Both the benzeneboronate and the 3,5-di(trifluoromethyl)benzeneboronate derivatives had good peak shapes on the OV-17 column. Of particular interest is the remarkable volatility of the 3,5-di(trifluoromethyl)benzeneboronate derivatives. These were approximately 2.5–3.5 times more volatile than the benzeneboronates and are the most volatile of the electron-capturing boronic acids prepared to date. The 3,5-di(trifluoromethyl)benzeneboronate of pinacol captures electrons in a non-dissociative manner (Fig. 1). Conjugated electrophores invariably show this type of temperature

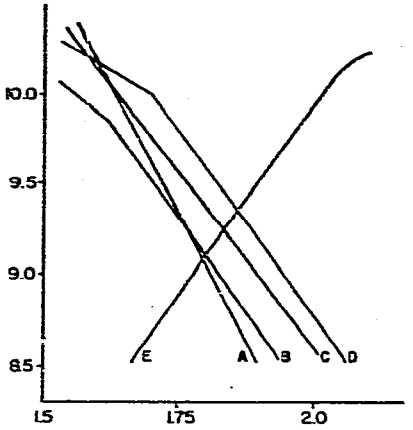

Fig. 1. Plot of ln $AT^{3/2}$ (vertical axis) against $1/T$ (A = peak area for a fixed mass of derivative and T °K = detector temperature) for the pinacol derivatives of (A) 3,5-dichlorobenzeneboronic acid, (B) 2,6-dichlorobenzeneboronic acid, (C) 2,4-dichlorobenzeneboronic acid, (D) 2,4,6-trichlorobenzeneboronic acid and (E) 3,5-di(trifluoromethyl)benzeneboronic acid.

dependence[20]. Maximal detector response was obtained at low detector temperatures with a minimal detectable amount of 3.0 pg obtained at 180°C.

Further discussion of the properties of the 3,5-di(trifluoromethyl)benzeneboronic acid is deferred to the next section.

Comparison of electron-capturing boronic acids

In previous reports, eight boronic acids with electron-capturing properties were

TABLE III

RETENTION TIME DATA FOR THE BORONATE DERIVATIVES OF SOME REPRESENTATIVE BIFUNCTIONAL COMPOUNDS

Compound	*Derivative*		*Column temperature (°C)*
	BB	*3,5-DTFMBB*	
Ethylene glycol	1.00	0.33	80*
Pinacol	1.73	0.41	80
1,3-Propanediol	2.60	0.97	80
Lactic acid	2.39	—	80
1,4-Butanediol	1.25	0.47	100**
cis-1,2-Cyclohexanediol	2.84	0.79	100
1,3-Propanediamine	1.21	0.52	100
3-Amino-1-propanol	1.16	0.47	100
2-Amino-1-butanol	1.08	0.42	100
Catechol	2.45	0.74	100
Phenyl-1,2-ethanediol	0.67	0.19	160***
o-Phenylenediamine	1.43	0.57	160
o-Aminophenol	0.64	0.25	160

* Internal standard C_{14}, R_t = 3.0 min.
** Internal standard C_{16}, R_t = 3.8 min.
*** Internal standard C_{22}, R_t = 4.2 min.

described[7–9] and in this paper a further three new boronic acids have been introduced. With such a large number of reagents available, some rational means of selection is necessary. A comparison of all of these electron-capturing boronic acids can be made in terms of range of application, relative volatility, electron-capture detector response and hydrolytic stability to provide some criteria for reagent selection.

Range of application. All reagents can be used to derivatize a wide range of bifunctional compounds. Some bifunctional compounds did not produce derivatives with any boronic acid; these include bifunctional ketone compounds, thiol-containing compounds, dicarboxylic acids and 1,3-substituted aromatic compounds. The boronate derivatives of aromatic carboxylic acids showed both solution and thermal degradation and are unsuitable for trace analysis. 3,5-Di(trifluoromethyl)benzeneboronic acid did not produce derivatives with compounds containing carboxylic acid groups. The 4-iodobutaneboronates of diamines and the 2,4,6-trichlorobenzeneboronates of diamines and hydroxyamines often exhibit poor thermal stability. Many of the boronate derivatives are quantitatively decomposed on stainless-steel columns and the use of nickel[21] or glass is essential for successful trace analysis.

Relative volatility. The bifunctional compounds used to assess the range of application of the boronic acids were chromatographed on the OV-17 column. The benzeneboronate derivatives were used as internal standards and assigned a value of 1.0. Thus the relative volatility was calculated by division of the retention time of the boronate derivative by that of the benzeneboronate of the same compound under identical chromatographic conditions. These values are assigned in descending order (*i.e.*, the order of decreasing volatility or increasing retention time) in Table IV together with suggested abbreviations for the boronate derivatives. The first seven entries (3,5-DTFMBB, BB, 4-IBuB, 4-BrBB, 2,6-DCBB, 2,4-DCBB and 3,5-DCBB) show adequate volatility for general use in gas chromatography while the other derivatives (2,4,6-TriCBB, 3-NBB and NAPB) have unfavorable properties. The first three (3,5-DTFMBB, BB and 4-IBuB) are significantly more volatile than the other derivatives and would be the reagents of choice if volatility was the only criterion for selection.

Electron-capture detector sensitivity. The minimal detectable quantities (MDQ) of the pinacol boronates are arranged in descending order of sensitivity in Table V. With the exception of the last two entries (BB, NAPB), all of the reagents show

TABLE IV

RELATIVE VOLATILITIES OF THE BORONATE DERIVATIVES

Boronic ester	*Abbreviation*	*Relative volatility*
3,5-Di(trifluoromethyl)benzeneboronates	3,5-DTFMBB	0.3 ± 0.05
Benzeneboronates	BB	1.0
4-Iodobutaneboronates	4-IBuB	1.8 ± 0.5
4-Bromobenzeneboronates	4-BrBB	3.9 ± 0.8
2,6-Dichlorobenzeneboronates	2,6-DCBB	4.3 ± 2.0
2,4-Dichlorobenzeneboronates	2,4-DCBB	4.7 ± 1.7
3,5-Dichlorobenzeneboronates	3,5-DCBB	5.0 ± 1.1
2,4,6-Trichlorobenzeneboronates	2,4,6-TriCBB	6.9 ± 1.8
3-Nitrobenzeneboronates	3-NBB	11.7 ± 3.4
Naphthaleneboronates	NAPB	18.5 ± 4.6

TABLE V

RELATIVE ELECTRON-CAPTURE DETECTOR SENSITIVITY OF THE PINACOL BORONATES

Pinacol boronate	*Optimal detector temperature (°C)*	*Detector type*	*MDQ* $\times 10^{-12}$ *(g)*
2,4-Dichlorobenzeneboronate	325	B	2.0
	380	A	4.0
4-Bromobenzeneboronate	350	B	3.0
3,5-Di(trifluoromethyl)benzeneboronate	180	A	3.0
2,4,6-Trichlorobenzeneboronate	380	A	4.0
3-Nitrobenzeneboronate	300	B	4.0
3,5-Dichlorobenzeneboronate	380	A	11.0
	325	B	9.0
4-Iodobutaneboronate	325	B	16.0
2,6-Dichlorobenzeneboronate	380	A	18.0
Benzeneboronate	200	B*	150.0
Naphthaleneboronate	350	B	2550.0

* This detector temperature is not optimal.

adequate sensitivity for trace analysis when used in conjunction with the electron-capture detector.

If high sensitivity is required then operation at the optimal detector temperature is essential. From a practical point of view, the use of high detector temperatures is preferred as this enables detector contamination to be minimized. Of the entries in Table V, only the benzeneboronate and 3,5-di(trifluoromethyl)benzeneboronate derivatives have their highest response at low detector temperatures. For the 3,5-DTFMBB derivative, the detector response varies by a factor of 17 over a detector temperature

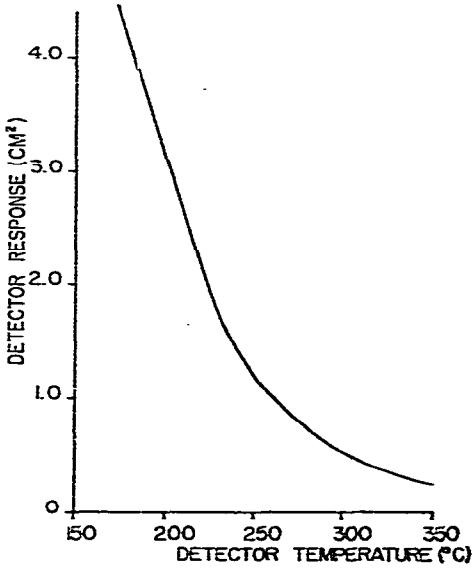

Fig. 2. Influence of detector temperature on detector response for a constant mass of the 3,5-di-(trifluoromethyl)benzeneboronate of pinacol.

range of 170°C. The variation of detector response with temperature is not linear (Fig. 2) and a small change in detector temperature close to the optimal value has a greater influence on detector response than the same temperature change close to the maximal operating temperature of the detector. For example, the detection limit for the 3,5-DTFMBB of pinacol is approximately $12 \cdot 10^{-12}$ g at 250°C and $50 \cdot 10^{-12}$ g at 350°C using detector A for the determinations. Although the analysis of complex biological mixtures after conversion into their 3,5-DTFMBB derivatives may not be practical at the optimal detector temperature (in all instances), these derivatives have sufficient sensitivity to be used at more suitable detector temperatures and still allow trace level determinations to be performed.

Relative hydrolytic stability. As a model system of hydrolytic stability, an *n*-hexane solution of the pinacol boronate was extracted for 8 min with sodium hydroxide solution. Full details of the procedure are given under Experimental. A time of 8 min for the extraction was chosen as this provided a convenient scale on which the degree of hydrolysis of all of the boronate derivatives could be included. The experimental results are summarized in Table VI, in order of decreasing hydrolytic stability. The first three entries (BB, 4-IBuB and 4-BrBB) are the most stable to base hydrolysis while 2,4,6-TriCBB and 2,4-DCBB are labile. However, the 2,4-DCBB derivatives are suitable for trace analysis when careful control is maintained over the experimental conditions.

TABLE VI

RELATIVE HYDROLYTIC STABILITIES OF PINACOL BORONATES

Pinacol boronate	*Hydrolysis (%)*	
	1 N NaOH	*3 N NaOH*
Benzeneboronate	5	30
4-Iodobutaneboronate	5	22
4-Bromobenzeneboronate	15	31
2,6-Dichlorobenzeneboronate	24	—
3,5-Di(trifluoromethyl)benzeneboronate	25	35
3,5-Dichlorobenzeneboronate	26	65
2,4,6-Trichlorobenzeneboronate	72	92
2,4-Dichlorobenzeneboronate	76	94

Our experience with the use of these reagents also enables us to make several qualitative observations on their general stability under conditions which might be encountered in practical analytical use. The pinacol derivatives are stable to thin-layer chromatography on silica gel but most other derivatives are readily hydrolyzed[22]. The products encountered on the thin-layer plate are the boronic acid and the bifunctional compound, indicating that hydrolysis (or dissociation) of the boronic ester is the process taking place and this is influenced by the nature of the functional group (for example, hydroxyl groups form the most stable derivatives while carboxylic acids are among the least stable) and the steric environment at the point of contact of the functional group (pinacol boronates are more stable than ethylene glycol boronates). Other workers have shown that ring size (6- > 5- > 7-membered) is also an important parameter in determining hydrolytic stability[23].

Polyfunctional compounds generally require complete derivatization for successful analysis by gas chromatography. This will require the use of multiple derivatization techniques to protect functional groups not reacting with the boronic acids. Carboxylic acids can be esterified and carbonyl groups converted into their oximes without interfering with the subsequent boronate formation if excess of reagent is first removed. The cleavage of boronate derivatives with trimethylsilylimidazole (TMSIM) and trifluoroacetylimidazole is a general and facile reaction. Heating the boronate derivative with excess of imidazole will produce extensive cleavage in many instances. N,O-Bis-(trimetyisilyl)trifluoroacetamide (BSTFA) and BSTFA–trimethylchlorosilane mixtures can often be used successfully under conditions which produce extensive cleavage with TMSIM.

CONCLUSIONS

The excellent volatility, stability and sensitivity to the electron-capture detector of the 3,5-di(trifluoromethyl)benzeneboronates makes them very useful derivatives for trace analysis. It has been our experience that the above boronic acid and 2,4-dichlorobenzeneboronic, 4-bromobenzeneboronic and 4-iodobutaneboronic acids provide a sufficient selection of reagents to meet the needs of a laboratory determining bifunctional compounds with electron-capture detection.

ACKNOWLEDGEMENT

This paper is based upon work supported by the National Science Foundation under Grant No. CHE78-12386.

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