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# A New Synthesis of Aryl Fluorides: The Reaction of Caesium Fluoroxysulfate with Arylboronic Acids and Derivatives†

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***Abstract:*** The *ipso* fluorination of arylboronic acids and some derivatives with caesium fluoroxysulfate has been developed. The reaction proceeds with a wide range of functionalised aromatics and is strongly solvent dependent.

## INTRODUCTION

The introduction of fluorine into aromatic systems is a highly desirable process because of the modification of the physical, biological and chemical properties of a molecule that ensue. Despite this, the number of methods available[1] to carry out this transformation is limited and the most widely used of these methods, the thermal decomposition of aryldiazonium tetrafluoroborate salts (the Balz-Schiemann reaction), is one of the oldest.[2] This reaction suffers from several drawbacks, not least of which is its intolerance to certain functional groups ortho to the diazonium group, and the production of tarry by-products from the frequently extensive side reactions of the intermediate aryl cation.

More useful would be to make use of the nucleophilicity of the arene π-system and to carry out reactions with electrophilic fluorine.[3a] Problems arise with this, however, because of the very high and indiscriminate reactivity of the most obvious source, $F_2$, and although fluorine may, under suitable conditions, act as an electrophilic fluorine equivalent it suffers from the additional problems of requiring specialised equipment and handling techniques.[4]

The problem is, therefore, to devise a regio- and chemo-specific process by which fluorine can be introduced onto the aryl ring at any appropriate stage during a synthesis without interference from other functionality or ambiguity in the site of substitution. If such a process

† Dedicated to Professor Charles W. Rees on the occasion of his 65th birthday.

can be developed then late (or last) stage fluorination becomes feasible and if the reaction time is sufficiently short, application to $^{18}F$ labelling of agents for positron emission tomography (PET) becomes possible. This is a major objective of our studies.

The problem may be tackled by reducing the reactivity of the electrophilic fluorine equivalent species, thereby increasing its specificity, and/or by controlling the site of attack by the introduction of a group which is more susceptible to displacement than hydrogen.

Over the last twenty years, a range of electrophilic fluorine reagents, based on RO-F and $R_2N$-F, species have been developed which can act as mild equivalents of $F_2$[3b] and many of these reagents are now commercially available. The alternative (or additional) tactic of directing *ipso*-substitution with a suitable functionality on the ring has resulted in the development of a range of fluorodemetallation reactions, most notably of mercury and tin.[3c]

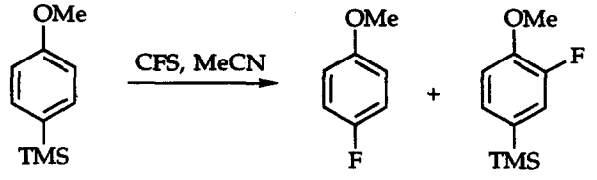
One of the most versatile of the electrophilic fluorine reagents is caesium fluoroxysulfate ($CsSO_4F$, CFS) which was first described in 1979 by Appelman.[5] This reagent has been used to introduce fluorine into a wide variety of organic substrates with varying degrees of success.[6] In a preliminary communication, we recently demonstrated that arylboronic acids and some their derivatives undergo reaction with CFS in acetonitrile to give the corresponding fluoroaromatics *via* a novel *ipso* substitution process.[7] We now report a more detailed investigation of fluorodesilylation and fluorodeboronation reactions in acetonitrile and the extension of this approach to reactions in methanol based solvent systems.

## RESULTS AND DISCUSSION

*Fluorodesilylation.*

Following a report from Chambers detailing the *ipso*-fluorination of simple aryltrimethylstannanes with CFS,[8] we were interested to see whether this process could be extended to other, less toxic, Group 14 metalloids. Our initial choice was silicon since its chemistry is similar to that of tin and electrophilic *ipso*-substitution is a well established process.[9]

**Scheme 1**




1 2 (10%) 3 (25%)

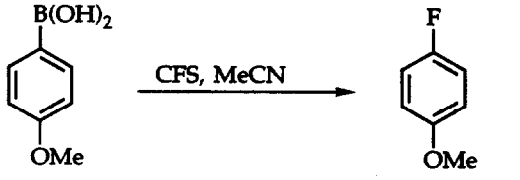
Treatment of 4-methoxyphenyltrimethylsilane (1) with CFS in acetonitrile gave a mixture of 4-fluoroanisole (2) as a minor product (10%) along with the fluorinated silane (3) in 25% yield (Scheme 1). Similar product mixtures were found in the reaction of (1) with either molecular fluorine[10] or acetyl hypofluorite.[11] The addition of boron trifluoride etherate to the reaction mixture gave the same products (2) and (3) but in higher yield (18% and 48% respectively).

The yields and product distribution in these reactions are similar to those found in the reactions with anisole itself as substrate[12] and the products are obviously determined by the directing effects of the methoxy group. Surprisingly, therefore, a trimethylsilyl group offers no relative rate enhancement over a hydrogen substituent and is not a suitable replacement for stannane. Attempts to increase the nucleophilicity of the silylated position by, for example, fluoride catalysis were not effective and the use of silicon was discontinued.

*Fluorodeboronation.*

The use of arylboronic acids in synthesis is gaining in popularity mainly because of their application in palladium-catalysed coupling reactions.[13] The halogenation of these compounds is an established process for all of the halogens except for fluorine.[14] On this basis, arylboronic acids appeared to be potential candidates for the fluorination reaction with CFS. The substrates themselves are generally readily prepared from the corresponding aryllithiums *via* transmetallation with tri*iso*propyl borate.

Scheme 2




4 2 (30%)

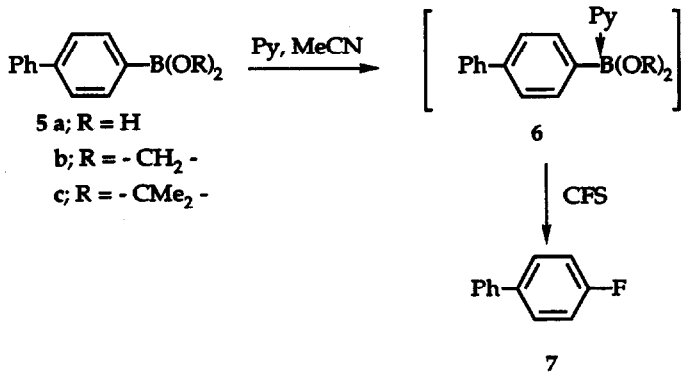
The reaction of 4-methoxyphenylboronic acid (4) with CFS in acetonitrile gave 4-fluoroanisole (2) as the major product in 30% yield (Scheme 2). Negligible quantities of *ortho*-fluorinated anisoles were detected (<1% as judged by $^{19}F$ NMR). Replacement of boron, therefore, occurs at a faster rate than that of hydrogen on this activated, electron rich, substrate. It was also possible to carry out fluorodeboronation on less activated substrates prepared from the corresponding aryl bromides such as 4-biphenylboronic acid (5a) (giving 4-fluorobiphenyl in 29% yield) and 1-naphthylboronic acid (giving 1-fluoronaphthalene in 17% yield).

Formation of cyclic boronate esters of 4-biphenylboronic acid was achieved by mixing the boronic acid (5a) and a diol in toluene and azeotropically removing the liberated water. In this way, the ethylene glycol (5b) and pinacol (5c) esters were prepared in 90% and 79% yield respectively. These substrates proved to be unreactive under the fluorination conditions. A similar lack of reactivity has been reported in the attempted halogenation of these esters with other halogens.[15]

However, the halogenolysis of boronic acids is frequently subject to general base catalysis, which is explained by the so formed 'ate' complex (as 6) enhancing the nucleophilicity of the aryl group.[16] The addition of sodium methoxide to the reaction of boronic acid (5a) with CFS resulted in complete suppression of the fluorination pathway, but a low yield of 4-fluorobiphenyl (7) could be obtained from the boronic acid (5a) if triethylamine was used. In addition,

in the presence of pyridine, it was found that boronic acid (5a) gave fluorobiphenyl (7) in a yield (15%) less than that from the free boronic acid (Scheme 3).

**Scheme 3**

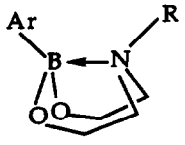



5 a; R = H
b; R = - $CH_2$ -
c; R = - $CMe_2$ -

Interestingly, the cyclic boronate esters (5b) and (5c) both gave low yields of the fluorinated product (7) (5% and 2% respectively) in the presence of one equivalent of pyridine. Both of these substrates underwent apparent initial adduct (6) formation in this reaction, indicating that this may be beneficial to the fluorodeboronation reaction with CFS. It was thought that the low yields may be due to dissociation of the adduct to give free pyridine, which was known to react with CFS in a range of solvents to give 2-substituted pyridines.[17]

The effect of added Lewis acids on the reaction of 4-biphenylboronic acid (5) in methanol (see below) was also studied. The weak Lewis acid $B(OMe)_3$ caused a slight drop in yield (to 51%), while the more powerful $BF_3.OEt_2$ caused a significant drop (to 38%).

The use of (*N-B*)-perhydro-2-aryl-1,3-dioxa-6-aza-2-boracines (8) is the classic method for the characterisation of arylboronic acids since they possess sharp melting points, unlike many of the boronic acids which may undergo initial dehydration to give the trimeric boroxines[18]. The presence of the transannular B-N bond may be recognised from the upfield shift observed in the $^{11}B$ NMR spectrum.[19] The synthesis of these substrates follows from that of the simple esters (5b) and (5c) in that the boronic acid and diethanolamine are mixed and liberated water is removed azeotropically. The products are obtained in high yield and frequently crystallise from the reaction mixture.

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In this manner, the parent (*N-B*)-perhydro-2-(4-biphenyl)-1,3-dioxa-6-aza-2-boracine (8, Ar = 4-$PhC_6H_4$, R = H) was prepared in 90% yield from diethanolamine. On treatment with CFS in

acetonitrile, this ester gave 4-fluorobiphenyl (7) in a disappointing 10% yield. It was considered that the free N-H bond present in this compound was a possible source of side reactions and to overcome this, the *N*-methylated derivatives (10, R = 4-Ph) was prepared from *N*-methyldiethanolamine (NMDE) in 96% yield (Scheme 4). Reaction of (10, R = 4-Ph) with CFS, in the presence of 10 mol% 1,3-dinitrobenzene, introduced to suppress single electron transfer reactions, gave a 41% yield of (11, R = 4-Ph). It was possible to show that, under the fluorination conditions, the ester (9, R = 4-Ph) was not degraded to the boronic acid. To test the applicability of this reaction, a range of simple substrates were prepared in high yield and subjected to the fluorination procedure (Table 1).

In the reactions where R = 4-OMe, 4-Ph (Entries 1, 2), small amounts of difluorinated products were detected (<1% by mass spectrometry), but this was not so in the other entries. No products were detected from simple substitution of hydrogen, which indicated that fluorodeboronation is a faster process. The contrast of R = 2-Ph (Entry 3), where protolysis was the only reaction, with R = 4-Ph (Entry 2), which underwent fluorination, may simply be a consequence of the severe hindrance to delivery of the fluorine by the orthogonal 2-phenyl group. It was not possible to overcome this protolysis even with added base ($NaHCO_3$).

Scheme 4

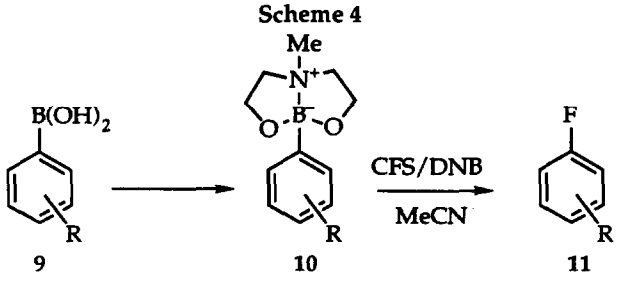



Table 1: Synthesis of fluoroaromatics from NMDE esters in acetonitrile

| *Entry* | *Substrate* 9 (R) | *Ester* 10 (% yield) | *Fluoroaromatic* 11 (% yield) |
|---|---|---|---|
| 1 | 4-MeO | 92 | 52 |
| 2 | 4-Ph | 96 | 41 |
| 3 | 2-Ph | 98 | 0 |
| 4 | 2,3-$(CH)_4$ | 94 | 35 |
| 5 | 3,4-$(CH)_4$ | 97 | 30 |
| 6 | 4-Br | 98 | 15 |
| 7 | 3-Cl-4-F | 97 | 30 |
| 8 | 2,4-$Cl_2$ | 98 | 40 |
| 9 | 3-$NO_2$ | 91 | 15* |

* Run in the presnce of $NaHCO_3$

For the case where R = 3-$NO_2$ (Entry 9), under the standard conditions, the only reaction observed was the protolysis of the C-B bond. This was suppressed if $NaHCO_3$ was added to neutralise any extraneous acid present but the yield was still modest (15%).

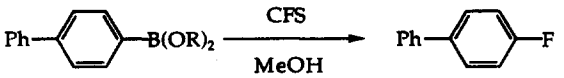
A surprising result was found in the reaction involving a bromine substituent (Entry 6). It was considered that oxidation of bromine could occur to give the arylbromine difluoride,[6a] but closer investigation of the reaction products (by GC-MS) revealed the presence of a dibromobenzene species. This implies that some *ipso* substitution of bromine by fluorine had occurred, with the bromine electrophile so generated causing bromodeboronation of the substrate.

In an attempt to improve the fluorodeboronation reaction, phase transfer catalysis with tetrabutylammonium salts or 18-crown-6 of the CFS reactions was attempted. No increase in fluorination yields resulted and generally the decomposition of CFS was accelerated. Solubilisation of the reagent was clearly not beneficial.

In acetonitrile solution, reaction times were excessive (≈ 48h), a factor which was partly attributed to the limited solubility of the substrates in this solvent. The optimum solvent, from the viewpoint of the substrate solubility, was dichloromethane but no fluorination could be achieved with 4-biphenylboronic acid or any of the ester derivatives, even on prolonged heating at reflux in this solvent.

Methanol is a useful solvent for dissolving the boronic acids (*via in situ* conversion to the dimethyl arylboronate esters). Treatment of each of the derivatives (5) of 4-biphenylboronic acid with CFS in methanol was found to give 4-fluorobiphenyl (7) in all cases although a large difference in reactivity was noted (Table 2).

Table 2: Fluorination of 4-biphenylboronic acid and derivatives in methanol.




5 7

| *Entry* | *Substrate* (5) (R) | *Fluorobiphenyl* (7). (%) |
|---|---|---|
| 1 | H | 56 |
| 2 | -$(CH_2)_2$- | 40 |
| 3 | -$(CMe_2)_2$- | 2 |
| 4 | -$(CH_2CH_2)_2NMe$ | 5 |

The arylboronic acid (Entry 1) was the most reactive substrate and the fluorination was essentially complete within 5h., which represented a great enhancement in reaction rate, together with a moderate increase in yield. The glycol esters (Entries 2, 3) did not undergo methanolysis, but the great difference in yield can be attributed to the steric differences. The NMDE ester (Entry 4) was interesting in that the yield was much lower than that of the acetonitrile based reactions. An NMR study showed that, under the reaction conditions,

methanolysis occurs to give a 9:1 mixture of the NMDE ester and the dimethyl ester.

A number of arylboronic acids were reacted under the fluorination conditions in methanol at a variety of temperatures (Table 3).

Table 3: Fluorination of phenylboronic acids in methanol


9 11

| *Entry* | *Substrate* 9 (R =) | *Temperature* (°C) | *Fluoroaromatic* 11 (% yield) |
|---|---|---|---|
| 1 | 4-MeO | 0 | 35 (+ 45% 2-fluoro) |
| 2 | 3-MeO | rt | 0 (+ 40% 2-fluoro, 4-fluoro) |
| 3 | 3-MeO | 0 | 10 (+ 40% 2-fluoro, 4-fluoro) |
| 4 | 3-MeO | –30 | 10 (+ 20% 2-fluoro, 4-fluoro) |
| 5 | 4-Ph | rt | 56 |
| 6 | 4-Ph | 0 | 45 |
| 7 | 4-Ph | –40 | 21 |
| 8 | 2-Ph | 0 | 28 |
| 9 | 3,4-$(CH)_4$ | rt | 0 |
| 10 | 3,4-$(CH)_4$ | 0 | 0 |
| 11 | 4-Br | 0 | 20 |
| 12 | 2,4-$Cl_2$ | –10 | 28 |
| 13 | 3-$NO_2$ | 0 | 14 |

The reactivities observed in these reactions are clearly different to those found using acetonitrile as solvent. Several substrates give different results to those found with either the NMDE esters or boronic acids.

For R = 4-OMe (Entry 1), the change of solvent resulted in a complete loss of regiocontrol since the major product resulted from fluorination *ortho* to the methoxy group with *ipso*-fluorination as a slightly lower yielding pathway. The use of R = 3-OMe (Entries 2, 3, 4) was to test the degree of regiocontrol and selectivity which could be exerted on an activated substrate. It was required that fluorine be introduced into a position which was not activated by the methoxy substituent. The results show that this was carried out to some extent but, even at -30°C, a greater amount of fluorination, directed by the methoxy group, was observed. This inability of the fluorodemetallation reaction to overcome directional effects from activating

substituents appears to be widespread, since literature reactions invariably have the metal at a centre inherently activated to substitution.[8,21]

The variable temperature reactions with R = 4-Ph (Entries 5, 6, 7) illustrate that, even at -40°C, a poorly activated system will undergo reaction to give moderate yields of fluoroarenes. At greater than ambient temperature, the products obtained included a wide range of fluorinated aromatics besides the desired product. It is notable that with R = 2-Ph (Entry 8) fluorination occurred whereas only protolysis was seen in reactions in acetonitrile. Also notable is the failure of 2-naphthaleneboronic acid (Entry 9) to give any fluoronaphthalenes at either 0°C or room temperature although an intense colour change (to a deep yellow colour) was observed.

Previous reactions with CFS in methanol have concentrated on adding the elements of MeO-F to alkenes[6a-d] with Markovnikov addition of electrophilic fluorine. This correlates with our reactions exhibiting electrophilic fluorination. CFS reacts vigorously with methanol to give an oxidising solution, $^{19}F$ NMR spectroscopy of which indicates the presence of a new species ($\delta_F$ -185 ppm).This is different from CFS in acetonitrile ($\delta_F$ 132 ppm)[5] or MeOF ($\delta_F$ 120.3 ppm).[22] The identity of the $\delta_F$ -185 species and the nature of the fluorination process are under investigation.

The short reaction time necessary, as indicated above, for radiochemical application, was achieved with a totally homogeneous reaction. A saturated, aqueous solution of CFS (4 equiv.) on reaction with a methanol solution of 4-biphenylboronic acid (5) at room temperature gave 4-fluorobiphenyl in 26% yield after only 15 minutes. Application for this purpose has been reported elsewhere.[29]

We thank the SERC for a studentship (to L.J.D) and for access to the Swansea Mass Spectroscopy Service, and ICI Agrochemicals for financial support.

## EXPERIMENTAL

Melting points were determined on a Kofler hot stage apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 1700 FT spectrometer. $^1H$ NMR spectra were recorded on a Bruker WM250 (250 MHz), JEOL GSX270 (270 MHz) and a Bruker AM500 (500 MHz) spectrometer using residual undeuterated solvent as reference. Apparent J values are measured in Hertz and multiplicities are assigned; s, singlet; d, doublet; t, triplet; m, multiplet. $^{19}F$ NMR were recorded on a JEOL FX90Q (84 MHz) with $CFCl_3$ as reference. Quantitative $^{19}F$ NMR spectra were calibrated against a measured quantity of 2-bromobenzotrifluoride. Tetrahydrofuran and diethyl ether were distilled immediately before use from sodium benzophenone ketyl, dichloromethane and acetonitrile were distilled from calcium hydride, methanol was distilled from magnesium methoxide. Petrol refers to that fraction boiling in the range 40-60°C. Other materials were purified according to literature procedures.[23] Caesium fluoroxysulfate was prepared according to the method of Zupan.[24] 4-Methoxyphenyltrimethylsilane was prepared by the method of Gilman.[25]

*Fluorination of 4-methoxyphenyltrimethylsilane* (1). — A suspension of caesium fluoroxysulfate (250 mg, 1.01 mmol) in acetonitrile (5 ml) was stirred for 5 min. under a nitrogen atmosphere at room temperature and then a solution of 4-

methoxyphenyltrimethylsilane (270 mg, 1.51 mmol) in acetonitrile (2 ml) was added in one portion followed by boron trifluoride etherate (3 drops). The reaction mixture was allowed to stir overnight after which GC and NMR analysis showed starting material (20%), 4-fluoroanisole (20%, $\delta_F$ -125) and 3-fluoro-4-methoxyphenyltrimethylsilane (48%, $\delta_F$ -137)

In the absence of boron trifluoride etherate, the corresponding yields were 60%, 10% and 25%.

*3-Methoxyphenyl boronic acid* (9, R = 3-OMe). — A solution of 3-bromoanisole (3.74 g, 20 mmol, 2.53 ml) in dry ether (20 ml) was stirred at 0°C and butyllithium (15 ml of 1.47M solution in hexanes, 1.1 eq) was added *via* syringe over a period of 10 min. The reaction mixture was stirred at 0°C for 1.25h. and then transferred *via* cannula to a cold (-78°C) solution of tri*iso*propyl borate (6 ml, 25 mmol, 1.25 eq) in THF (30 ml) over 20 minutes. After stirring for 1h. at -78°C, the reaction mixture was allowed to warm to room temperature over a period of 3h. The cloudy suspension was poured onto dilute 2M aqueous HCl (30 ml) and the layers were separated. The aqueous phase was extracted with ether (2 x 30 ml) and the combined organic phases were washed with saturated brine solution (2 x 40 ml), dried ($MgSO_4$), and evaporated to leave a white solid which was washed with petrol (2 x 30 ml) to yield the title compound (9, R = 3-OMe) (2.158 g, 71%); m.p. 165-166°C (Found, *m/z* 152.0645; $C_7H_9BO_3$ requires *m/z* 152.0645); $\nu_{max}$ (Nujol)/cm$^{-1}$ 1458, 1357, 1234; $\delta_H$ ($CDCl_3$, 270 MHz) 7.83 (1H, dd, *J* 7.33, 0.98 Hz, 6-H), 7.75 (1H, d, *J* 2.69 Hz, 2-H), 7.44 (1H, t, *J* 7.69 Hz, 5-H), 7.15 (1H, ddd, *J* 8.30, 2.69, 0.98 Hz, 4-H), 3.92 (s, 3H, $OCH_3$); *m/z* (EI) 402 ($M^+$ of trimer, 100%), 152 ($M^+$), 134, 108, 91, 78, 65.

*4-Methoxyphenyl boronic acid* (4). — A solution of 4-bromoanisole (3.740 g, 20 mmol) in dry ether (20 ml) was cooled to 0°C under a nitrogen atmosphere and a solution of butyllithium (17 ml of 1.45 M solution, 1.25 eq) was added via syringe over a period of 5 minutes. After stirring for 1h. at 0°C, the pale yellow solution was transferred via cannula to a cold (-78°C) solution of tri*iso*propyl borate (9.2 ml, 40 mmol, 2 eq) in dry ether (10 ml) over a period of 0.5h. and stirring continued at this temperature for a further 1h. The reaction mixture was then allowed to reach room temperature over a period of 2h. during which time, a flocculent, white precipitate was formed. It was then transferred to a separating funnel and partitioned between 2M HCl (50 ml) and ether (100 ml). The aqueous layer was washed with ether (1 x 30 ml) and the combined organic phases were washed with water (1 x 50 ml), saturated aqueous brine (2 x 40 ml) then dried ($MgSO_4$). The crude solution was concentrated to approximately 30 ml under reduced pressure and petrol (30 ml) was added to deposit the title compound (4) as white crystals (1.811 g, 60%); m.p. 209-210°C (Found C, 55.4; H, 5.9%; $C_7H_9BO_3$ requires C, 55.3; H, 6.0%); $\nu_{max}$ (Nujol)/cm$^{-1}$ 1585, 1460, 1410, 1355, 1230; $\delta_H$ (90 MHz, $CDCl_3$) 7.75 (2H, d, *J* 7.8 Hz, 2-H, 6-H), 6.97 (2H, d, *J* 7.7 Hz, 3-H, 5-H), 6.51 (2H, s, B-OH), 3.87 (3H, s, $OCH_3$); *m/z* (EI) 402 ($M^+$ of trimer, 100%), 152 ($M^+$), 108, 65.

*2-Biphenylboronic acid* (9, R = 2-Ph). — A solution of 2-bromobiphenyl (4.662 g, 20 mmol, 3.45 ml) in ether (50 ml) was cooled to 0°C and butyllithium (9.5 ml of 2.4M solution, 1.2 eq) was added *via* syringe over 15 minutes. After the addition, the reaction mixture was allowed to warm to room temperature and stirred for a further 40 minutes. The cloudy solution was transferred *via* cannula to a cold (-78°C) solution of tri*iso*propyl borate (7 ml, xs) in ether (30 ml) over a period of 30 minutes. After stirring for a further 2h. at -78°C, the reaction mixture was allowed to reach room temperature over 1h. and the thick suspension was partitioned between 10% aqueous HCl (30 ml) and ether (50 ml). The combined organic phases were washed

with saturated brine solution (2 x 50 ml), dried ($MgSO_4$), and concentrated to approximately 30 ml. Hexane (50 ml) was added and concentration continued to give a precipitate which was collected by filtration and washed with hexane to give the title compound (9, R = 2-Ph) as a white solid (1.202 g, 30%); m.p. >300°C (Found C, 72.6; H, 5.55%; $C_{12}H_{11}BO_2$ requires C, 72.7; H, 5.6%); $\nu_{max}$ (Nujol)/$cm^{-1}$ 3326 (BO-H), 1595, 1374, 1341, 1012; $\delta_H$ (90 MHz, $CDCl_3$) 7.81-7.13 (9H, m, Ar-H), 5.42 2H, s, B-OH); *m/z* (EI) 198 ($M^+$), 180, 153.

*4-Biphenylboronic acid* (5, R = H). — A stirred solution of 4-bromobiphenyl (2.332 g, 10 mmol) in dry ether (25 ml) was cooled to 0°C under a nitrogen atmosphere and a solution of butyllithium (8.35 ml of 1.2M, 1.03 eq) was added *via* syringe over a period of 5 minutes. The reaction mixture was stirred at 0°C for 1.5h. after which time, the yellow solution was transferred *via* cannula to a cold (-78°C) solution of tri*iso*propyl borate (2.45 ml, 1.1 eq) in dry ether (50 ml) over a period of 20 minutes. After a further 40 minutes at -78°C, the reaction mixture was allowed to warm to room temperature over a 3h. during which time a thick, white precipitate formed. The mixture was stirred at room temperature for 0.5h. and then poured into a separating funnel where it was partitioned between 2M aqueous HCl (40 ml) and ether (50 ml). The ether layer was washed with brine (2 x 30 ml), dried ($MgSO_4$) and evaporated to a white solid. This was recrystallised from toluene to yield the title compound (5, R = H) as white crystals (1.260 g, 64%); m.p. 246°C (Found C, 72.7; H, 5.5%; $C_{12}H_{11}BO_2$ requires C, 72.8; H, 5.6%); $\nu_{max}$ (Nujol)/$cm^{-1}$ 3407, 1398, 1335, 993; $\delta_H$ (270 MHz, $d_6$-acetone) 8.08-7.36 (9H, m, Ar-H), 3.31 (2H, s, B-OH); *m/z* (EI) 198 ($M^+$), 180, 153.

*2-(4-Biphenyl)-1,3-dioxa-2-borolane* (5, R = -$CH_2$-). — A solution of 4-biphenylboronic acid (5, R = H) (597.6 mg, 3.01 mmol) and ethylene glycol (187.3 mg, 3.01 mmol) in toluene (20 ml) was concentrated under reduced pressure on a rotary evaporator to a volume of approximately 3 ml. Trituration of the resulting solution with petrol (2 ml) yielded a white solid which was collected by filtration, washed with cold petrol (1 x 5 ml) and dried *in vacuo* to give the title compound (5, R = -$CH_2$-) (614.3 mg, 90%); m.p. 99-101°C (Found C, 75.3; H, 5.8%; $C_{14}H_{13}BO_2$ requires C, 75.1; H, 5.85%); $\nu_{max}$ (Nujol)/$cm^{-1}$ 1606, 1400, 1338, 1225, 1212; $\delta_H$ ($CDCl_3$, 90 MHz) 8.1-7.3 (9H, m, Ar-H), 4.24 (4H, s, $OCH_2$); *m/z* (EI) 224 ($M^+$, 100%), 167, 152.

*2-(4-Biphenyl)-4,4,5,5-tetramethyl-1,3-dioxa-2-borolane* (5, R = -$CMe_2$-). — A mixture of 4-biphenylboronic acid (5, R = H) (1.409 g, 7.12 mmol) and pinacol (844.8 mg, 7.12 mmol) in toluene (35 ml) was heated in a distillation apparatus until approximately 5 ml of solvent remained. On cooling, the remainder of the solvent was removed under reduced pressure to yield an oil. This was purified by rapid (<5 minutes) flash chromatography ($SiO_2$; petrol-ether 9:1) to yield the title compound (5, R = -$CMe_2$-) as a white solid (1.569 g, 79%); m.p. 103-104°C (Found C, 77.3; H, 7.8%; $C_{18}H_{21}BO_2$ requires C, 77.2; H, 7.55%); $\nu_{max}$ (Nujol)/$cm^{-1}$ 1610, 1398, 1324, 1142, 1094; $\delta_H$ ($CDCl_3$, 90 MHz) 8.05-7.30 (9H, m, Ar-H), 1.01 (6H, s, $CH_3$), 0.92 (6H, s, $CH_3$); *m/z* (EI) 280 ($M^+$), 265, 194, 180 (100%), 152.

*1-Naphthylboronic acid* [9, R = 2,3-$(CH)_4$]. — A solution of 1-bromonaphthalene (1.242 g, 6 mmol) in dry ether (20 ml) was added *via* cannula to a solution of *tert*-butyllithium (10 ml of 1.2M, 2 eq.) in ether (30 ml) at -78°C over a period of 30 minutes. After a further 30 minutes the resulting precipitate was dissolved by addition of THF (2 ml) and then transferred *via* cannula to a cold (-78°C) solution of tri*iso*propyl borate (2.33 ml, 10 mmol) in ether (10 ml) over a period of 45 minutes then stirred for a further 1h. at this temperature before allowing the solution to warm slowly to room temperature over 3h. The resulting suspension was

partitioned between 2M aqueous HCl (40 ml) and ether (50 ml) and the ether phase was washed with saturated, aqueous brine (2 x 30 ml), dried ($MgSO_4$) and evaporated to yield a light brown solid. This was recrystallised from hot benzene then precipitated from an ethanol solution by trituration with water to yield a microcrystalline solid which was air-dried on the sinter then dried *in vacuo* to yield 1-naphthylboronic acid [9, R = 2,3-$(CH)_4$] (666 mg, 77%); m.p. 210-211°C (lit.,[26] 210-211°C); $\delta_H$ (90 MHz, $CDCl_3$) 7.94-7.38 (7H, m, Ar-H), 5.44 (2H, s, B-OH)

*2-Naphthylboronic acid* [9, R = 3,4-$(CH)_4$]. — A solution of 2-bromonaphthalene (2.063 g, 9.94 mmol) in dry ether (50 ml) was stirred at -78°C and a solution of *tert*-butyllithium (12.5 ml of 1.6M solution, 2 eq) was added via syringe over 5 minutes. The reaction mixture turned orange immediately and was stirred at this temperature for a further 50 minutes then transferred via cannula to a cold (-78°C) solution of tri*iso*propyl borate (4.6 ml, 2 eq) in dry ether (50 ml) over a period of 1h. The cloudy solution was allowed to reach room temperature over a period of 4h. The resulting suspension was transferred to a separating funnel and partitioned between 2M HCl (50 ml) and ether (100 ml). The aqueous layer was washed with ether (1 x 30 ml) and the combined organic phases were washed with water (1 x 50 ml), saturated, aqueous brine (2 x 40 ml) and dried ($MgSO_4$). The solution was concentrated to approximately 50 ml under reduced pressure and petrol (20 ml) was added. Further concentration yielded the product [9, R = 3,4-$(CH)_4$] as white crystals (1.031 g, 60%); m.p. 225°C (dec.) (Found C, 69.5; H, 5.1%; $C_{10}H_9BO_2$ requires C, 69.7; H, 5.3%); $\nu_{max}$ (Nujol)/$cm^{-1}$ 3256, 1319, 1033; $\delta_H$ (90 MHz, $CDCl_3$) 8.40 (1H, s, 1-H), 7.91-7.80 (4H, m, 5-H, 6-H, 7-H, 8-H), 7.57-7.46 (2H, m, 3-H, 4-H), 4.44 (2H, s B-OH); *m/z* (EI) 172 ($M^+$, 100%), 154, 149, 128.

*General method for the preparation of (N-B)-perhydro-2-aryl-6-methyl-1,3-dioxa-6-aza-2-boracines* (10). — The arylboronic acid and *N*-methyldiethanolamine were suspended in toluene in a distillation apparatus and heated to distill off the toluene. Solvent was collected until the volume of toluene remaining was approximately 5-10 ml. The hot solution was rapidly filtered and then allowed to cool to room temperature. If the product precipitated from the solution, it was collected by filtration, washed with cold ether and and dried *in vacuo*. If no solid was deposited, the solution was further concentrated and, if necessary, triturated with cold petrol to give the product. So prepared were:—

(N-B)-*Perhydro-2-(4-methoxyphenyl)-6-methyl-1,3-dioxa-6-aza-2-boracine* (10, R = 4-OMe) in 92% yield; m.p. 96-97°C (Found, *m/z* 235.1380; $C_{12}H_{18}BNO_3$ requires 235.1380); $\nu_{max}$ (Nujol)/$cm^{-1}$ 1277, 1231, 1205, 1115; $\delta_H$ ($CDCl_3$, 250 MHz) 7.53 (2H, d, *J* 8.08 Hz, 2-H, 6-H), 6.85 (2H, d, *J* 8.05 Hz, 3-H, 5-H), 4.26-4.01 (4H, m, $OCH_2$), 3.78 (3H, s, $OCH_3$), 3.23-2.87 (4H, m, $NCH_2$), 2.29 (3H, s, $NCH_3$); *m/z* (EI) 235 ($M^+$), 149 , 128 (100%).

(N-B)-*Perhydro-2-(2-biphenyl)-6-methyl-1,3-dioxa-6-aza-2-boracine* (10, R = 2-Ph) in 98% yield; m.p. 154-155°C (Found C, 72.3; H, 7.0; N, 4.9%; $C_{17}H_{20}BNO_2$ requires C, 72.6; H, 7.2; N, 5.0%); $\nu_{max}$ (Nujol)/$cm^{-1}$ 3049, 3016, 1444, 1275, 1232; $\delta_H$ (270 MHz, $CDCl_3$) 7.91 (1H, m, Ar-H), 7.48-7.10 (8H, m, Ar-H), 3.97 (4H, m, $OCH_2$), 2.91-2.32 (4H, m, $NCH_2$), 2.20 (3H, s, $NCH_3$); *m/z* (EI) 281 ($M^+$), 280, 195, 180, 128 (100%); *m/z* (CI, $NH_3$) 282 ($MH^+$, 100%).

(N-B)-*Perhydro-2-(4-biphenyl)-1,3-dioxa-6-aza-2-boracine* (8, Ar = 4-$PhC_6H_4$, R = H) in 80% yield; m.p. 243-244°C (Found, *m/z* 268.1509; $C_{16}H_{19}BNO_2$ requires *m/z* 268.1509); $\nu_{max}$ (Nujol)/$cm^{-1}$ 3093, 1272, 1232, 1097; $\delta_H$ (90 MHz, $d_6$-DMSO) 7.69-7.15 (9H, m, Ar-H), 6.89 (1H, br.s, N*H*), 4.01-3.73 (4H, m, $OCH_2$), 3.48-3.08 (4H, m, $NCH_2$); *m/z* (EI) 267 ($M^+$), 236, 180, 170, 154, 114, 74, 56 (100%).

(N-B)-*Perhydro-2-(4-biphenyl)-6-methyl-1,3-dioxa-6-aza-2-boracine* (10, R = 4-Ph) in 96% yield; m.p. 150-151°C (Found C, 72.4; H, 7.2; N, 4.9%; $C_{17}H_{20}BNO_2$ requires C, 72.6; H, 7.2; N, 5.0%); $\upsilon_{max}$ (Nujol) 2923, 1096, 1075 $cm^{-1}$; $\delta_H$ ($CDCl_3$, 270 MHz) 7.80-7.31 (9H, m, Ar-H), 4.30-4.15 (4H, m, $OCH_2$), 3.31-2.97 (4H, m, $NCH_2$), 2.41 (3H, s, $NCH_3$); *m/z* (EI) 281 ($M^+$), 195, 180, 128 (100%).

(N-B)-*Perhydro-2-(1-naphthyl)-6-methyl-1,3-dioxa-6-aza-2-boracine* [10, R = 2,3-$(CH)_4$] in 94% yield; m.p. 138-140°C (Found C, 70.4; H, 7.0; N, 5.6%; $C_{15}H_{18}BNO_2$ requires C, 70.55; H, 7.1; N, 5.5%); $\nu_{max}$ (Nujol)/$cm^{-1}$ 1265, 1240, 1172; $\delta_H$ ($CDCl_3$, 90 MHz) 7.94-7.11 (7H, m, Ar-H), 4.41-4.12 (4H, m, $OCH_2$), 3.41-3.12 (4H, m, $NCH_2$), 3.03 (3H, s, $NCH_3$); *m/z* (EI) 255 ($M^+$), 169, 154, 128 (100%).

(N-B)-*Perhydro-2-(2-naphthyl)-6-methyl-1,3-dioxa-6-aza-2-boracine* [10, R = 3,4-$(CH)_4$] in 97% yield; m.p. 140-142°C (Found C, 70.8; H, 7.2; N, 5.3%; $C_{15}H_{18}BNO_2$ requires C, 70.6; H, 7.1; N, 5.5%.); $\upsilon_{max}$ (Nujol)/$cm^{-1}$ 3040, 1270, 1240; $\delta_H$ ($CDCl_3$, 250 MHz) 8.13 (1H, s, 1-H), 7.90-7.70 (4H, m, Ar-H), 7.45-7.38 (2H, m, Ar-H), 4.31-4.17 (4H, m, $OCH_2$), 3.26-3.15 (4H, m, $NCH_2$), 2.29 (3H, s, $NCH_3$);*m/z* (EI) 255 ($M^+$), 169, 154, 128 (100%).

(N-B)-*Perhydro-2-(3-chloro-4-fluorophenyl)-6-methyl-1,3-dioxa-6-aza-2-boracine* (10, R = 3-Cl-4-F) in 97% yield (Found C, 50.8; H, 6.2; N, 5.35%; $C_{11}H_{16}BClFNO_2$ requires C, 50.95; H, 6.2; N, 5.4%); $\nu_{max}$ (Nujol)/$cm^{-1}$ 1266, 1235; $\delta_H$ (250 MHz, $CDCl_3$) 7.63 (1H, dd, *J* 19.55, 3.91 Hz, 2-H), 7.46 (1H, ddd, *J* 20.33, 12.82, 3.36 Hz, 6-H), 7.05 (1H, dd, *J* 25.02, 20.33 Hz, 5-H), 4.25-4.07 (4H, m, $OCH_2$), 3.26-3.17 (2H, m, $NCH_2$), 3.06-2.95 (2H, m, $NCH_2$), 2.33 (3H, s, $NCH_3$); $\delta_F$ (84.27 MHz, $CDCl_3$) -118.6; *m/z* (EI) 259, 257 ($M^+$), 171, 156, 128 (100%).

(N-B)-*Perhydro-2-(4-bromophenyl)-6-methyl-1,3-dioxa-6-aza-2-boracine* (10, R = 4-Br) in 98% yield; m.p. 142-143°C (Found C 46.55, H 5.1, N 4.8%; $C_{11}H_{15}BBrNO_2$ requires C, 46.5, H, 5.3, N, 4.9%); $\upsilon_{max}$ (Nujol)/$cm^{-1}$ 1577, 1212, 1198, 1098; $\delta_H$ (270 MHz, $CDCl_3$) 7.51-7.39 (4H, m, Ar-H), 4.24-4.06 (4H, m, $OCH_2$), 3.22-2.94 (4H, m, $NCH_2$), 2.31 (3H, s, $NCH_3$); *m/z* (EI) 285, 283 ($M^+$) 240, 199, 197, 184, 182, 128 (100%).

(N-B)-*Perhydro-2-(3-nitrophenyl)-6-methyl-1,3-dioxa-6-aza-2-boracine* (10, R = 3-$NO_2$) in 91% yield; m.p. 119-123°C (Found C, 52.9; H, 5.8; N, 11.1%; $C_{11}H_{15}BN_2O_4$ requires C, 52.8; H, 6.05; N, 11.2%); $\upsilon_{max}$ (Nujol)/$cm^{-1}$ 1519, 1352, 1199; $\delta_H$ (270 MHz, $CDCl_3$) 8.39(1H, dd, *J* 1.8, 1.6 Hz, 2-H), 8.05 (1H, ddd, *J* 7.1, 1.7, 1.6 Hz, 4-H), 7.91 (1H, d, *J* 7.1 Hz, 6-H), 7.40 (1H, t, *J* 6.9 Hz, 5-H), 4.21-4.06 (4H, m, $OCH_2$), 3.27-3.17(2H, m, $NCH_2$), 3.09-2.94 (2H, m, $NCH_2$), 2.29 (3H, s, $NCH_3$); *m/z* (CI, $NH_3$) 251 ($MH^+$, 100%), 221, 145, 128, 102.

(N-B)-*Perhydro-2-(2,4-dichlorophenyl)-6-methyl-1,3-dioxa-6-aza-2-boracine* (10, R = 2,4-$Cl_2$) in 98% yield; m.p. 99-101°C (Found, *m/z* 274.0573; $C_{11}H_{14}BCl_2NO_2$ requires *m/z* 274.0573); $\upsilon_{max}$ (Nujol)/$cm^{-1}$ 1576, 1364, 1255, 1174; $\delta_H$ (250 MHz, $CDCl_3$) 7.72 (1H, d, *J* 8.1 Hz, 6-H), 7.31 (1H, d, *J* 1.5 Hz, 3-H), 6.77 (1H, dd, *J* 8.1, 1.5 Hz, 5-H), 4.14 (4H, m, $OCH_2$), 3.21 (4H, m, $NCH_2$), 2.56 (3H, s, $NCH_3$); *m/z* (EI) 273 ($M^+$), 195, 128 (100%).

*General procedure for the fluorination of boronic acids with CFS in acetonitrile*: — A suspension of caesium fluoroxysulfate (1 – 1.5 equiv.) and the boronic acid (1 equiv.) in dry MeCN (to give ≈ 5% w/v) was stirred at room temperature under a nitrogen atmosphere. After 2.5 – 20h., the reaction mixture was diluted x 10 with DCM and the insoluble products were removed by filtration. The filtrate was washed with water, dried ($MgSO_4$) and evaporated. The product(s) were isolated by chromatography of the residue on $SiO_2$ with petrol as eluant. Thus

reacted were:—

*4-Methoxyphenyl boronic acid* (9, R = 4-MeO): (70 mg, 0.53 mmol); reaction time 2.5h. Analysis of the reaction mixture by GC and $^{19}F$ NMR showed the presence of 4-fluoroanisole (30%) $\delta_F$ (84 MHz, $CDCl_3$) -124.

*4-Biphenylboronic acid* (9, R = 4-Ph): (79 mg, 0.40 mmol); reaction time 20h.; product, 4-fluorobiphenyl (11, R = 4-Ph), white solid (20.1 mg, 29%); m.p. 73-74°C (lit.,[27] 74-76°C); $\delta_F$ (84 MHz, $CDCl_3$) -116.

*1-Naphthylboronic acid* [9, R = 2,3-$(CH)_4$]: (75.3 mg, 0.44 mmol);reaction time 20h.; product, 1-fluoronaphthalene (11 mg, 17%); $\delta_F$ (84 MHz, $CDCl_3$) -123, identical with an authentic sample

*General procedure for the fluorination of* (N-B)-*perhydro-2-(aryl)-6-methyl-1,3-dioxa-6-aza-2-boracines (9) in acetonitrile.* — A suspension of caesium fluoroxysulfate in dry acetonitrile was stirred at room temperature for 10 minutes and the boracine ester and 1,3-dinitrobenzene (10 mol%) were added. Stirring was continued under a nitrogen atmosphere and product formation was followed by GC. Further portions of caesium fluoroxysulfate (0.5 eq.) were added after 6, 20, 28 and 38h. and after 48h. the reaction mixture was analysed by either method A or B.

*Method A* (non-volatile products): The reaction mixture was diluted with DCM (20 ml) and filtered to remove inorganic products. The filtrate was washed with water (1 x 5 ml), dried ($MgSO_4$) and evaporated. Pure product was obtained by flash chromatography and compared with an authentic sample.

*Method B* (volatile products): The product was not isolated pure and so the reaction mixture was diluted with DCM (10 ml) and filtered. The resulting solution was analysed by GC against authentic samples and, subsequently, GC-MS. The solution was then evaporated in order to obtain the $^{19}F$ NMR spectrum.

So fluorinated were:—

(N-B)-*Perhydro-2-(4-biphenyl)-6-methyl-1,3-dioxa-6-aza-2-boracine* (10, R = 4-Ph). Work up as for method A gave 4-fluorobiphenyl (28.8 mg, 41%); m.p. 75-76°C (lit.,[27] 74-76°C); $\delta_F$ (84 MHz, $CDCl_3$) -116.

(N-B)-*Perhydro-2-(1-naphthyl)-6-methyl-1,3-dioxa-6-aza-2-boracine* [10, R = 2,3-$(CH)_4$]. Work up and assay as for method B showed 1-fluoronapthalene (35%); $\delta_F$ (84 MHz, $CDCl_3$) -123.

(N-B)-*Perhydro-2-(2-naphthyl)-6-methyl-1,3-dioxa-6-aza-2-boracine* [10, R = 3,4-$(CH)_4$]. Work up and assay as for method B showed 2-fluoronapthalene (30%); $\delta_F$ (84 MHz, $CDCl_3$) -115.

(N-B)-*Perhydro-2-(4-methoxyphenyl)-6-methyl-1,3-dioxa-6-aza-2-boracine* (10, R = 4-OMe). Work up and assay as for method B showed 4-fluoroanisole (52%); $\delta_F$ (84 MHz, $CDCl_3$) -124; *m/z* (EI) 126 ($M^+$), 111, 95, 83 (100%), 75, 63, 57.

(N-B)-*Perhydro-2-(3-nitrophenyl)-6-methyl-1,3-dioxa-6-aza-2-boracine* (10, R = 3-$NO_2$) Addition of $NaHCO_3$ to the general procedure followed by work up as for method B showed 1-fluoro-3-nitrobenzene (15%); $\delta_F$ (84 MHz, $CDCl_3$) -110; *m/z* (EI) 141 ($M^+$), 111, 95 (100%), 83, 75.

(N-B)-*Perhydro-2-(4-bromophenyl)-6-methyl-1,3-dioxa-6-aza-2-boracine* (10, R = 4-Br) Work up and assay as for method B showed 1-bromo-4-fluorobenzene (15%); $\delta_F$ (84 MHz, $CDCl_3$) -115; *m/z* (EI) 176 ($M^+$), 174, 95(100%), 75.

(N-B)-*Perhydro-2-(2,4-dichlorophenyl)-6-methyl-1,3-dioxa-6-aza-2-boracine* (10, R = 2,4-$Cl_2$) Work up and assay as for method B showed 1,3-dichloro-4-fluorobenzene (40%); $\delta_F$ (84

MHz, $CDCl_3$) -119; *m/z* (EI) 166, 164 ($M^+$), 148, 146 (100%), 113, 111, 75.

*(N-B)-Perhydro-2-(3-chloro-4-fluorophenyl)-6-methyl-1,3-dioxa-6-aza-2-boracine* (10, R = 3-Cl-4-F) Work up and assay as for method B showed 1-chloro-2,5-difluorobenzene (30%); $\delta_F$ (84 MHz, $CDCl_3$) -116 (5-F), -122 (2-F); *m/z* (EI) 150, 148 ($M^+$), 129 (100%).

*General procedure for the fluorination of arylboronic acids in methanol.* —A solution of the boronic acid in dry methanol was stirred at 0°C and caesium fluoroxysulfate was added in one portion. The reaction mixture was monitored by TLC for disappearance of the dimethyl ester and further portions of CFS (0.5 equiv.) were added at 2-4h. intervals. If the reaction was not complete within 10h., it was worked up after 24h. Workup was carried out by either method A or B as described above according to the volatility of the product. So reacted were:—

*3-Methoxyphenylboronic acid.* After 24h. at -30°C, workup by method B showed 3-fluoroanisole (10% vs. internal standard); $\delta_F$ (84 MHz, $CDCl_3$) -112. The presence of 2-fluoro- and 4-fluoroanisoles (combined yield 20% vs. internal standard) was also observed.

A similar amount of 3-fluoroanisole was also formed if reaction was carried out at 0°C although the amount of byproducts increased to 40%.

*4-Methoxyphenylboronic acid.*After 2h., workup by method B showed 4-fluoroanisole (35% vs. internal standard) $\delta_F$ ($CDCl_3$, 84 MHz) -124 was detected together with 2-fluoroanisole isomer (45%, $\delta_F$ -137).

*2-Biphenylboronic acid.* After 10h., workup by method A showed 2-fluorobiphenyl (40 mg, 28%); m.p. 73-74°C (lit.,[27] 74°C); $\delta_F$ ($CDCl_3$, 84 MHz) -118.

*4-Bromophenylboronic acid.* After 24h., workup by method B showed 1-bromo-4-fluorobenzene (20% vs. internal standard) $\delta_F$ ($CDCl_3$, 84 MHz) -115.

*2,4-Dichlorophenylboronic acid.* After 24h. at -10°C, workup by method B showed 1,3-dichloro-4-fluorobenzene (28% vs. internal standard) $\delta_F$ ($CDCl_3$, 84 MHz) -119.

*3-Nitrophenylboronic acid.* After 24h., workup by method B showed 1-fluoro-3-nitrobenzene (14% vs. internal standard) $\delta_F$ ($CDCl_3$, 84 MHz) -110.

*Effect of added Lewis bases and acids on fluorination of 4-biphenyl boronic acid and derivatives:* —

*Pyridine.* a) A suspension of 4-biphenyl boronic acid (5, R = H) (94.3 mg, 0.55 mmol) in MeCN (3 ml) was stirred at room temperature and neat pyridine (43 mg, 44 µl, 1 eq) was added. There was no observable effect and on addition of caesium fluoroxysulfate (134 mg, 0.54 mmol) the reaction mixture became yellow in colour and an exothermic reaction was noted. After a further 3h. a further portion of caesium fluoroxysulfate (140 mg, 0.58 mmol) was added. After a total of 6h. the reaction mixture was diluted with DCM (10 ml) and filtered giving a yellow solution. This was evaporated and the residue subjected to flash chromatography to give 4-fluorobiphenyl as a white solid (14 mg, 15%); m.p. 73-74°C Identical to the above.

b) A suspension of 2-(4-biphenyl)-1,3-dioxa-2-borolane (5, R = $-CH_2-$) (113.1 mg, 0.50 mmol) in MeCN (2 ml) was stirred at room temperature and neat pyridine (45 mg, 0.48 mmol) was added. The suspension dissolved giving a homogeneous solution. Caesium fluoroxysulfate (160 mg, 0.665 mmol) was added to the solution in one portion and the solution became a yellow suspension. After 30h., a further portion of caesium fluoroxysulfate (163 mg, 0.66 mmol) was added and stirring continued for a further 30h. after which DCM (10 ml) was added and the reaction mixture was filtered, washed with water (1 x 5 ml), dried and evaporated. $^{19}F$ NMR analysis of the crude product indicated the presence of 4-fluorobiphenyl (5% vs. an internal

standard).

c) A suspension of 2-(4-biphenyl)-1,3-dioxa-4,4,5,5-tetramethyl-2-borolane (5, R = -$CMe_2$-) (161 mg, 0.575 mmol) in acetonitrile (2 ml) was stirred at room temperature and pyridine (52 mg, 0.55 mmol) was added. Over a period of 5 minutes, the suspension dissolved giving a homogeneous solution and solid caesium fluoroxysulfate (206 mg, 0.83 mmol) was added in one portion. After 48h., TLC indicated a trace of product and a further portion of caesium fluoroxysulfate was added. After 66h., the reaction mixture was diluted with DCM (15 ml), filtered to remove insoluble material and the resulting solution evaporated. $^{19}F$ NMR analysis of the resulting solid showed the presence of 4-fluorobiphenyl (2% vs. internal standard).

*Trimethyl borate.* A solution of 4-biphenylboronic acid (5, R = H) (48.5 mg, 196 μmol) in methanol (2 ml) was stirred at 0°C and neat trimethyl borate (~50 μl) was added *via* syringe followed by solid caesium fluoroxysulfate (125.1 mg, 500 μmol). After 5 minutes the cooling bath was removed and the reaction mixture was stirred at room temperature. After 2h., a further portion of caesium fluoroxysulfate (119 mg, 480 μmol) was added and the reaction mixture was diluted with DCM (15 ml) after 5h. and filtered. The resulting solution was washed with water (5 ml), dried ($MgSO_4$) and evaporated under reduced pressure to yield an orange oil. This was purified by flash chromatography ($SiO_2$; petrol) to give 4-fluorobiphenyl (17.2 mg, 51%).

*Boron trifluoride.* A solution of 4-biphenylboronic acid (5, R = H) (55 mg, 0.277 mmol) in dry methanol (1 ml) was stirred at 0°C and boron trifluoride-etherate (2 drops) was added *via* syringe. After 1 minute, solid caesium fluoroxysulfate (155 mg, 0.625) was added in two portions and, after 10 minutes, the cooling bath was removed. The reaction mixture was diluted with DCM (20 ml) after 4h. and filtered then evaporated. The resulting oil was purified by flash chromatography ($SiO_2$; petrol) to yield 4-fluorobiphenyl (17.3 mg, 38%).

A similar result was obtained if boron trifluoride-methanol complex was used. A lower yield (~25%) was found if the reaction was run at -10°C with either source.

## REFERENCES


1. *Carbon-Fluorine Compounds - Chemistry, Biochemistry and Biological Activities;* Ciba Foundation Symposium, 13-15 September 1971, Associated Scientific Publishers, Amsterdam, 1972; M. Hudlicky, *Chemistry of Organic Fluorine Compounds,* Ellis Horwood, Chichester, 1976; W. A. Sheppard and C. M. Sharts, *Organic Fluorine Chemistry,* Benjamin, New York, 1969; R. D. Chambers, *Fluorine in Organic Chemistry,* Wiley, New York, 1973; J. T. Welch and S. Eswarakrishnan, *Fluorine in Bioorganic Chemistry,* Wiley, New York, 1991.
2. G. Balz and G. Schiemann; Chem. Ber.,1927, 60, 1189.
3 a) For discussions of electrophilic fluorination mechanisms, see: O. Lerman, Y. Tor, D. Hebel and S. Rozen *J. Org. Chem.*, 1984, 49, 806; D.D. DesMarteau, Z.-Q. Xu and M. Witz, *J. Org. Chem., 1992,* 57, 629. b) See *inter alia,* Trifluoromethyl hypofluorite: C. Chavis and M. Mousseron-Canet; *Bull. Soc. Chim. Fr.*, 1971, 632; Acetyl hypofluorite: S. Rozen, O. Lerman and M. Lerman; *J. Chem. Soc., Chem. Commun.*, 1981, 443; N-Fluorosulfonamides: W. E. Barnette; *J. Am. Chem. Soc.*, 1984, 106, 452; N-Fluorosultams: E. Differding and R. W. Lang; *Helv. Chim. Acta*, 1989, 72, 1248; N-Fluorosulfonimides: S. Singh, D. D. DesMarteau, S. S. Zuberi, M. Witz and H-N. Huang; *J. Am. Chem. Soc.*, 1987, 109, 7194; N-Fluoropyridinium triflates: T. Umemoto, K. Kawada and K. Tomita; *Tetrahedron Lett.*, 1986, 27, 4465; N-

Fluoroquinuclidinium fluoride: R. E. Banks, R. A. Du Boisson and E. Tsiliopoulos; *J. Fluorine Chem.*,1986, 32, 461; Perchloryl fluoride: R. E. Erhenkaufer and R. T. McGregor; *Int. J. Appl. Radiat. Isot.*, 1983, 25, 613; Xenon difluoride: M. J. Shaw, J. A. Weil, H. H. Hyman and R. Filler; *J. Am. Chem. Soc.*, 1970, 92, 5096; c) See *inter alia* G.W.M.Visser, B.W.v.Halteren, J.D.M.Herscheid, G.A.Brinkman, A. Hoekstra; *J. Chem. Soc., Chem. Commun.*, 1984, 655; G.W.M.Visser, C.N.M.Bakker, B.W.v.Halteren, J.D.M.Herscheid, G.A. Brinkman, A.Hoekstra; *J. Org. Chem.*, 1986, 51, 1886

4. S. Misaki; *J. Fluorine Chem.*, 1981, 17, 159: S. Misaki; *J. Fluorine Chem.*, 1982, 21, 191.
5. E. H. Appelman, L. J. Basile and R. C. Thompson; *J. Am. Chem. Soc.*, 1979, 101, 3384.
6. See *inter alia*, (a) S. Stavber and M. Zupan; *J. Chem. Soc., Chem. Commun.*, 1983, 563; (b) S. Stavber and M. Zupan; *J. Org. Chem.*, 1987, 52, 919; (c) S. Stavber and M. Zupan; *Tetrahedron*, 1986, 42, 5035; (d) S. Stavber and M. Zupan; *Tetrahedron*, 1990, 46, 3093; (e) L. E. Andrews, R. Bonnett, A. N. Kozyrev and E. H. Appelman; *J. Chem. Soc., Perkin Trans. I*, 1988, 1735; (f) T. B. Patrick and R. Mortezania; *J. Org. Chem.*, 1988, 53, 515; (g) S. Stavber and M. Zupan; *Tetrahedron*, 1989, 45, 2737; (h) T. J. Michalski, E. H. Appelman, M. K. Bowman, J. E. Hunt, J. R. Norris, T. M. Cotton and L. Raser; *Tetrahedron Lett.*, 1990, 47, 6847.
7. J. M. Clough, L. J. Diorazio and D. A. Widdowson; *Synlett*, 1990, 761.
8. M. R. Bryce, R. D. Chambers, S. T. Mullins and A. Parkin; *J. Chem. Soc., Chem. Commun.*, 1986, 1623: M. R. Bryce, R. D. Chambers, S. T. Mullins and A. Parkin; *Bull. Soc. Chim. Fr.*, 1986, 930.
9. T. H. Chan and I. Fleming; *Synthesis*, 1979, 761.
10. M. P. Speranza, C. Y. Shiue, A. P. Wolf, D. S. Wilbur and G. Angelini; *J. Fluorine Chem.*, 1985, 30, 97.
11. H. H. Coenen and S. M. Coerlain; *J. Fluorine Chem.*,1987, 36, 63.
12. D. P. Ip, C. D. Arthur, R. E. Winans and E. H. Appelman; *J. Am. Chem. Soc.*, 1981, 103, 1964.
13. N. Miyaura, T. Yanagi and A. Suzuki; *Synth. Commun.*, 1981, 11, 513.
14. H. R. Snyder, J. A. Kuck and J. R. Johnson; *J. Am. Chem. Soc.*, 1938, 60, 105.
15. K. Torsell; *Acta Chem. Scand.*, 1954, 8, 1779.
16. H. G. Kuivila and E. K. Easterbrook; *J. Am. Chem. Soc.*, 1951, 73, 4629.
17. S. Stavber and M. Zupan; *Tetrahedron Lett.*, 1990, 31, 775.
18. R. L. Letsinger and I. Skoog; *J. Am. Chem. Soc.*, 1955, 77, 2491.
19. R. Contreras, C. Garcia, T. Mancilla and B. Wrackmeyer; *J. Organomet. Chem.*, 1983, 246, 213.
20. P. K. Gowick and T. M. Klapotke; *J. Chem. Soc., Chem. Commun.*, 1990, 1433
21. See *inter alia*, G. W. M. Visser, B. W. v. Halteren, J. D. M. Herscheid, G. A. Brinkman and A. Hoekstra; *J. Chem. Soc., Chem. Commun.*, 1984, 655; S. G. Mislankar, D. L. Gildersleeve, D. M. Wieland, C. C. Massin, G. K. Mulholland and S. A. Toorongian; *J. Med. Chem.*, 1988, 31, 362.
22. M. Kol, S. Rozen and E. H. Appelman; *J. Am. Chem. Soc.*, 1991, 113, 2648.
23. D. D. Perrin, W. L. F. Armarego and D. R. Perrin, *Purification of Laboratory Chemicals*, 2nd Edition, Pergammon Press, Oxford, 1980.
24. S. Stavber and M. Zupan; *J. Org. Chem.*, 1985, 50, 3609.
25. H. Gilman and J. F. Nobis; *J. Am. Chem. Soc.*, 1950, 72, 2629.
26. Lancaster Synthesis Ltd., Eastgate, White Lund, Morecambe, Lancs., LA3 3DY, England, UK.
27. Aldrich Chemicals Ltd., The Old Brickyard, New Road, Gillingham, Dorset, SP8 4JL, England, UK
28. S. Misaki; *J. Fluorine Chem.*,1982, 21, 191.
29. L.J. Diorazio, D.A. Widdowson and J.M. Clough; *J. Chem. Soc., Perkin Trans. I*, 1992, 421.