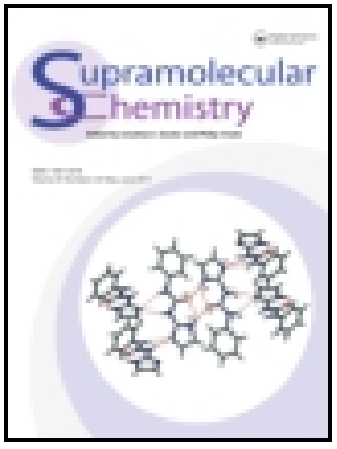

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Cucurbit[8]uril recognition of rapidly interconverting diastereomers

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The diastereoselectivity of Cucurbit[8]uril (CB[8]) binding was probed towards a series of rapidly interconverting diastereomers containing a C_{aryl}–C_{aryl} chiral axis and at least one other stereocenter. Relative binding affinities of up to 4.9 were determined when CB[8] interacted with *ortho*, *meta*, *ortho′*-substituted biphenyls bearing a chiral dialkylsulfonium substituent at their *meta*-position. Diastereoselectivities of up to 2.4-fold were obtained for *ortho′*-substituted 2-phenylpyridinium derivatives that bear a chiral myrtenyl *N*-substituent prone to CB[8] binding.

Keywords: Cucurbituril; diastereoselectivity; biaryl

Introduction

Diastereoselective recognition inside Cucurbit[*n*]urils (CB[*n*]) (*1–3*) has been exploited a few years ago, in particular by Sivaguru and Ramamurthy, towards the stereoselective [2 + 2] cycloadditions of olefin pairs encapsulated into CB[8] (*4–9*). Kim and Inoue also showed that CB[6] displays a 19-fold higher affinity towards the (*S*)-2-methylbutylammonium cation when flanked with two (*R*)-methylpiperazines at its portal than when forming an exclusion complex with two (*S*)-methylpiperazines (*10*). The same authors showed that the affinity of dipeptide L-Phe-L-Leu-NH_3^+ for CB[7] was eight times higher than its diastereomer L-Phe-D-Leu-NH_3^+ (*10*).

We have recently reported that biphenyl atropisomers, which bear various *ortho* and *ortho′*-substituents as well as a *meta*-dimethylsulfonium group, could be encapsulated into CB[7] and CB[8] (*11*). Confinement of the guests into the macrocycles triggered the ^{1}H NMR signal splitting of the two diastereotopic dimethylsulfonium groups, by propagating efficiently the dissymmetry caused by the substituents at the *ortho′*-positions. In this study, we propose first to attach two different substituents to the sulfur centre (thereby introducing a new stereocenter) and to test the recognition of CB[8] towards these new rapidly interconverting diastereomers.

Results and discussion

Biphenyls **4a**–**4d** were obtained in four steps from 2,4-difluorothiophenol. Alkylation with ethyl or isopropyl bromide afforded intermediates **1a** and **1b**, and metalation followed by electrophilic interception with iodine yielded intermediates **2a** and **2b**. Four biphenyl derivatives **3a**–**3d** were obtained after Suzuki coupling with 2-methyl- and 2-chlorophenylboronic acid, and guests **4a**–**4d** were isolated after subsequent methylation (see Scheme 1).

Although the diastereomers of guest **4a** could not be differentiated by ^{1}H NMR spectroscopy, ^{13}C NMR experiments afforded two doublets for the methylsulfonium unit in a 53:47 ratio that we attribute to two pairs of enantiomers (the multiplicity originates from a coupling with the neighbouring *ortho*-fluorine nucleus; coupling constant 2.4 ppm). Upon addition of CB[8], all aromatic hydrogens underwent an upfield shift, thereby indicating that the biphenyl units are fully encapsulated inside the cavity of the macrocycle, or that CB[8] oscillates rapidly on the NMR time scale between both aromatic units (see Figure 1). Upfield shifts are particularly significant in the case of the 2′-methyl substituent (0.76 ppm), because it is located deep inside the CB[8] cavity (see Figure 1, spectrum g, and Figure 2(i)). All signals of methyl and ethyl sulfonium groups split into two sets of singlets (methyl group), symmetrical multiplets (ethyl CH_2 group) and triplets (ethyl CH_3), each characterising one pair of enantiomers ((*P*, *R*) and (*M*, *S*) versus (*P*, *S*) and (*M*, *R*)), with differences in chemical shifts as high as 0.41 ppm in the case of the ethyl CH_3 group (noted '9' in Figure 1). Aromatic hydrogens 4 and 6′ also split into two sets of symmetrical multiplets (see Figure 1). Unfortunately, we did not manage to attribute absolute configurations to both pairs of enantiomers, even after careful evaluation of two-dimensional nuclear and rotating frame nuclear Overhauser effect spectroscopy (NOESY and ROESY) experiments. A peculiar trend is observed with H(9) hydrogens upon consecutive addition of CB[8]. While the triplet pertaining to one pair of enantiomers undergoes a monotonic upfield shift, the other triplet is first shifted

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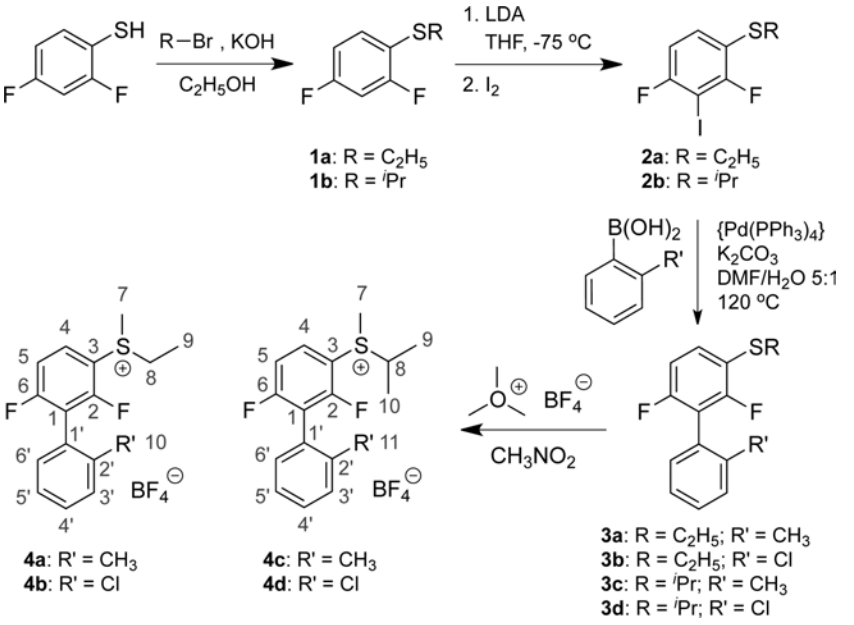


Scheme 1. Preparation of biphenyl guests **4a**–**4d**.

upfield until 0.50 equiv. CB[8] is added, and later shifts markedly downfield until saturation is reached (after the addition of approximately 1.5 equiv. CB[8], see Figure 1). This non-monotonic behavior likely indicates the concomitant formation of binary and ternary complexes **1a**·CB[8] and **1a**$_2$·CB[8] in the presence of substoichiometric amounts of the macrocycle. Once fully encapsulated into CB[8], guest **1a** coexists as a 35:65 mixture of diastereomers. This implies a 2.1-fold higher affinity of CB[8] for one of the two pairs of enantiomers.

One may reasonably question whether the ratio of diastereomers switches from 53:47 to 35:65 upon

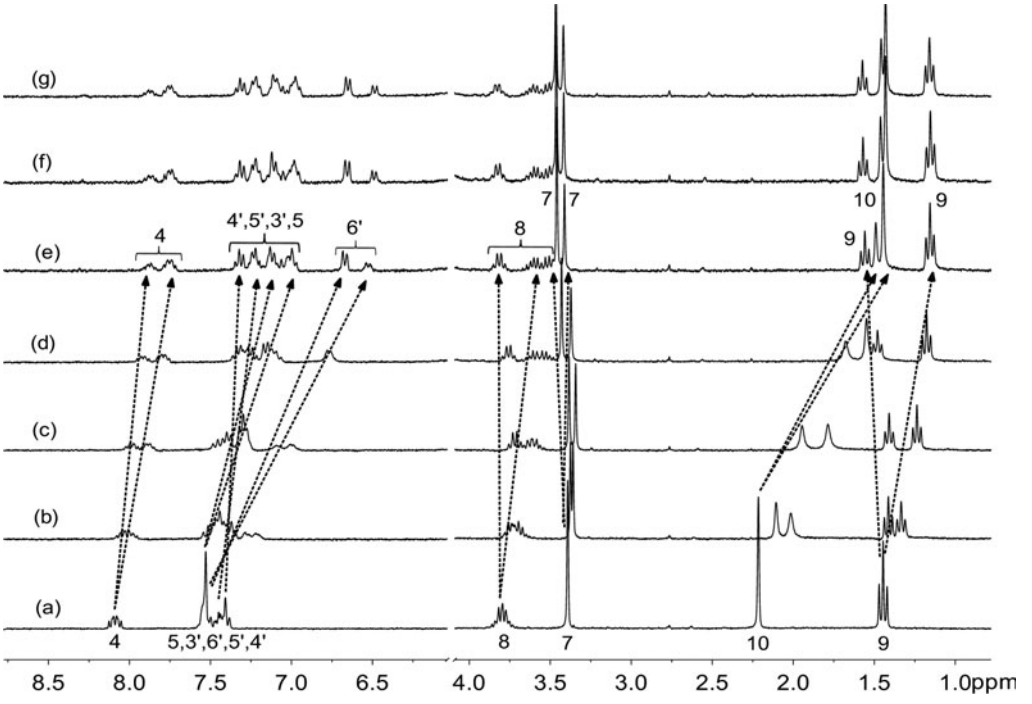


Figure 1. ^{1}H NMR spectra of biphenyl **4a** (2.0 mM) in D_2O (a) in the absence of CB[8], and (b)–(g) with increasing amounts of CB[8] (0.5, 1.0, 1.5, 2.0, 3.0 and 4.0 mM).

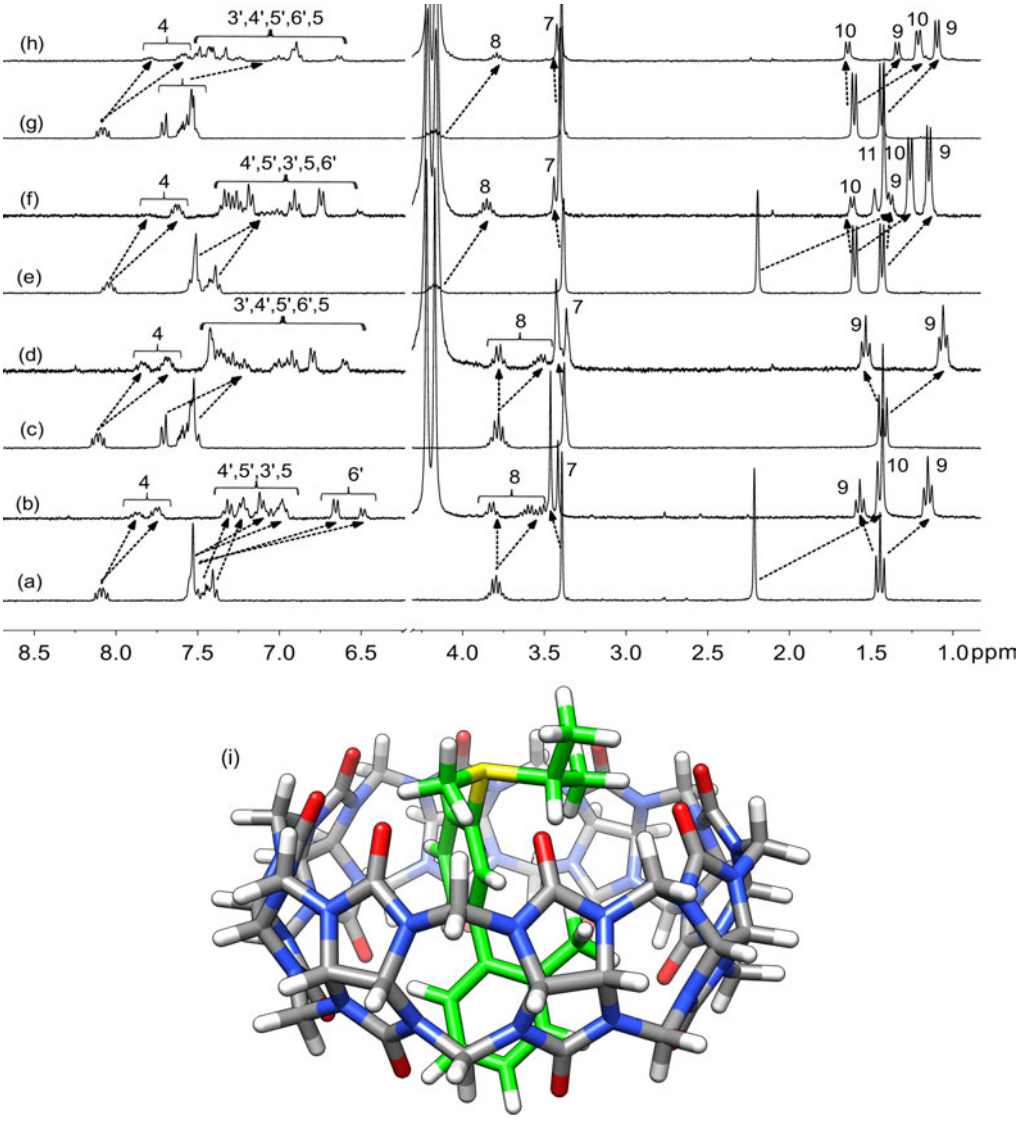


Figure 2. (Colour online) ^{1}H NMR spectra of (a) biphenyl **4a** and (b) its inclusion complex with CB[8]; (c) biphenyl **4b**, (d) assembly **4b**·CB[8], (e) biphenyl **4c**, (f) assembly **4c**·CB[8], (g) biphenyl **4d** and (h) assembly **4d**·CB[8] (see Scheme 1 for numbering). (i) TPSS-D3 (BJ)-optimised structure of complex **4d**·CB[8].

interaction with CB[8], or from 47:53 to 35:65. The ^{1}H NMR spectrum recorded in the presence of 0.25 equiv. CB [8] (Figure 1, spectrum b) shows a weaker upfield H (9) triplet at 1.33 ppm, while the weakest H(9) signal appears downfield at 1.57 ppm in the presence of 4.0 equiv. CB[8] (see spectrum g), thereby suggesting a reversal of diastereoselectivity upon encapsulation. However, we note that the concomitant formation of ternary complexes $\mathbf{1a}_2$·CB[8] in the presence of 0.25 equiv. CB[8], with their own diastereomeric ratios, may bias our reasoning.

Similar ^{1}H NMR patterns are observed upon addition of CB[8] to biphenyls **4b**–**4d** (see Figure 2). In the case of biphenyls **4c** and **4d**, the two methyl groups of the isopropyl substituents are themselves diastereotopic, appear as a pair of doublets in the absence of CB[8] and split into two pairs upon encapsulation (see Figure 2, spectra e–h). Replacing the *S*-ethyl substituent with a larger isopropyl group improves the diastereoseletive recognition of CB[8], with ratios in the absence of the macrocycles of 52:48 and 57:43 (in the case of guests **4c** and **4d**, respectively) to 18:82 and 25:75 when encapsulated by CB[8]. These ratios afford relative CB [8] binding affinities between diastereomers of 4.9 and 4.0 for biphenyls **4c** and **4d**, compared with 2.1 and 1.9 in the case of biphenyls **4a** and **4b** (see Table 1). CB[8] thus efficiently relays the steric pressure of the *S*-substituent on the remote *ortho*′-substituent (see Figure 2(i) for the optimised structure of complex **4d**·CB[8]; optimisation carried out with the dispersion-corrected TPSS-D3(BJ)

Table 1. Diastereomeric ratios of guests **4a**–**4d** in the absence and presence of CB[8].

	Diastereomeric ratio[a]		
	Free guests[b]	CB[8]-bound guests[c]	K_{rel}
4a	53:47	35:65	2.1 (±0.2)
4b	54:46	38:62	1.9 (±0.2)
4c	52:48	18:82	4.9 (±0.6)
4d	57:43	25:75	4.0 (±0.4)

Note: Relative binding affinity of CB[8] towards the diastereomers (standard deviation between parentheses).
[a] The 95% confidence interval of each term of the ratios (as obtained after repetitive integration of the relevant ^{1}H or ^{13}C NMR signals) is ±3 and ±6, respectively; signal integration is the main source of error (compared with the error calculated from a set of different experiments).
[b] Ratios obtained from relevant signals in ^{13}C NMR spectra.
[c] Ratios obtained from relevant signals in ^{1}H NMR spectra.

Table 2. Diastereomeric ratios of guests **7a**–**7d** in the absence and presence of CB[8].

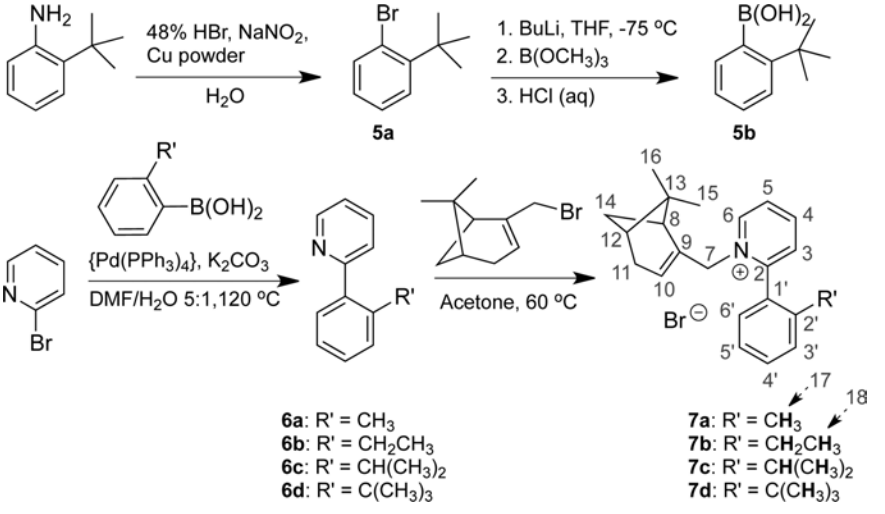
	Diastereomeric ratio		
	Free guests	CB[8]-bound guests	K_{rel}
7a[a]	50:50	35:65	1.9 (±0.1)
7b[a]	50:50	30:70	2.3 (±0.2)
7c[a]	43:57	24:76	2.4 (±0.2)
7d[b]	43:57	35:65	1.4 (±0.1)

Note: Relative binding affinity of CB[8] towards the diastereomers (standard deviation between parentheses).
[a] The 95% confidence interval of each term of the ratios (as obtained after repetitive integration of the relevant ^{1}H NMR signals) is ±3.
[b] Ratios obtained by fitting myrtenyl H(16) NMR signals with a sum of two Gaussian functions; standard deviation ±1.

functional (*12*,*13*) and def2-SVP basis sets, together with the COSMO (*14*,*15*) solvation model).

We then tested whether CB[8] could influence diastereomeric distributions when it encapsulates a chiral substituent, and not the biaryl unit itself. We replaced the biphenyl scaffold with a 2-phenylpyridium unit bearing *ortho*′-substituents (methyl, ethyl, isopropyl or *tert*-butyl) and a chiral *N*-substituent prone to CB[8] binding. The (−)-myrtenyl substituent is ideal in that regard, because it is rigid, fits very well into the cavity of CB[8] and can be easily grafted to the 2-phenylpyridine scaffold. Biaryls **6a**–**6d** were obtained after coupling *ortho*-substituted phenylboronic acids to 2-bromopyridine (2-*tert*-butylphenylboronic acid **5b** was prepared from the corresponding aniline via Gattermann reaction to afford bromobenzene **5a**, followed by bromine/lithium permutation, reaction with trimethyl borate and hydrolysis). *N*-allylation with (−)-myrtenyl bromide (obtained by radical allylic bromination of (−)-β-pinene) (*16*) afforded the desired pyridinium guests **7a**–**7d** (see Scheme 2).

The ratios of dynamic diastereomers in the absence of CB[8] (see Table 2) could be readily determined by integrating the ^{1}H NMR signals of their 6-methyl hydrogens (appearing as two pairs of singlets at 1.18 and 0.61 ppm, see H(15) and H(16) in Figure 3, spectra a, c, e and g). Upon addition of CB[8], all myrtenyl signals as well as the hydrogen at position 6 of the pyridinium unit underwent upfield shifts (up to 0.73 ppm), thereby confirming encapsulation of the myrtenyl substituent. All other hydrogens underwent slight downfield shifts as anticipated when hydrogen nuclei are located close to the carbonyl portal of the macrocycle. Myrtenyl 6-methyl hydrogens were used again to determine diastereomeric ratios in the case of CB[8]-bound guests **7a** and **7b**. Relative CB[8] binding affinities for both diastereomers were 1.9 in the case of guest **7a** (ratios shifting from 50:50 to 35:65, see Figure 3, spectra a and b) and 2.3 for guest **7b** (ratios shifting from 50:50 to 30:70, spectra c and d). In the case of guest **7c**, H(15) and H(17) signals were used to determine the diastereomeric ratios (24:76,



Scheme 2. Preparation of CB[8] guests **7a**–**7d**.

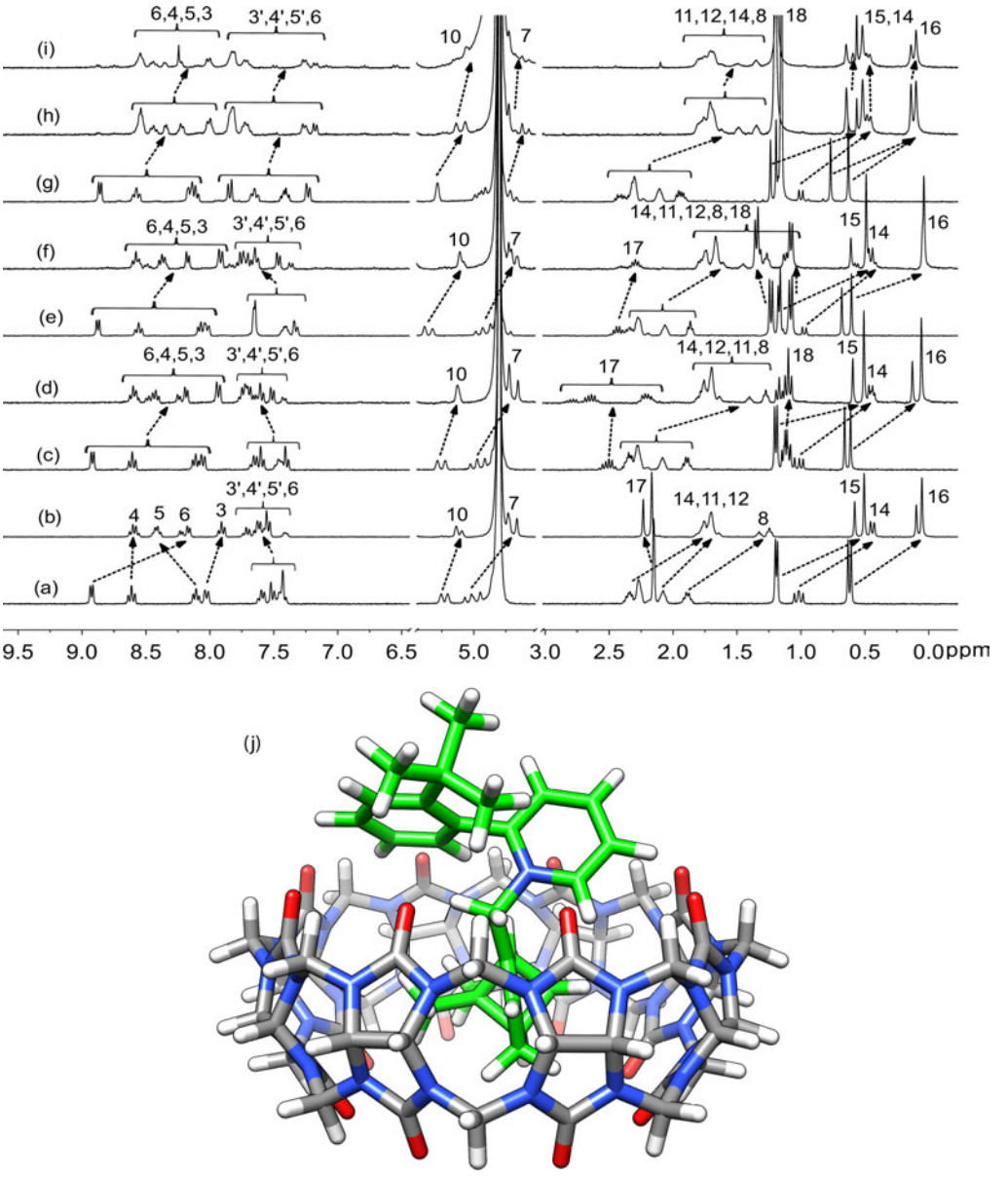


Figure 3. (Colour online) ^{1}H NMR spectra of (a) pyridinium **7a** and (b) its inclusion complex with CB[8]; (c) pyridinium **7b**, (d) assembly **7b**·CB[8], (e) pyridinium **7c**, (f) assembly **7c**·CB[8], (g) pyridinium **7d**, (h) assembly **7d**·CB[8] and (i) assembly **7d**·CB[8] after heating to 95°C for 10 days (see Scheme 1 for numbering). (j) TPSS-D3(BJ)-optimised structure of complex **7d**·CB[8].

compared with 43:57 in the absence of the macrocycle, see spectra e and f), leading to a 2.4-fold selectivity for CB[8] towards one of the two diastereomers. We noticed that upon addition of CB[8] to guest **7d**, the ratio of diastereomers remained steady at 43:57 (see spectra g and h). This led us to suspect that the bulky *tert*-butyl substituent may prevent rotation along the C_{aryl}–C_{aryl} axis at 25°C. Indeed, equilibrium could only be reached upon heating the sample to 95°C for 10 days; a 35:65 ratio was then determined using H(16) signals (see Figure 3, spectrum i; due to the poor resolution of the two singlets, the ratios were obtained by fitting the signal with a sum of two Gaussian functions). We also confirmed that 43:57 represented the ratio of diastereomers at equilibrium in the absence of CB[8], and not merely a kinetic distribution arising from a weakly diastereoselective allylation of 2-phenylpyridine **6d** with (−)-myrtenyl bromide. The mixture of diastereomers was heated to 95°C for up to 2 weeks without observing a variation in distribution. CB[8] thus displays a mere 1.4-fold preference for one of the two diastereomers (see Table 2).

Conclusions

We showed that CB[8] binding can be moderately diastereoselective, with relative binding affinities of up to 4.9. To the best of our knowledge, this study is the first attempt at determining the binding affinities of any macrocycle towards rapidly interconverting diastereomers.

Experimental section

Generalities

Reagents were ordered from Sigma-Aldrich (St. Louis, MO), Alfa Aesar (Ward Hill, MA) and AK scientific (Union City, CA). CB[6], CB[7] and CB[8] were prepared using known procedures, from glycoluril and excess amounts of formaldehyde (*17–20*). (−)-Myrtenyl bromide was prepared as described in literature from (−)-β-pinene (*16*). All ^{1}H NMR experiments were performed using a 300-MHz Bruker NMR instrument. ^{1}H-decoupled ^{13}C NMR spectra were obtained at 75.5 MHz using the same Bruker 300 spectrometer. Unless specified otherwise, NMR experiments were performed at 25°C, the solvent was CD_3CN and the internal reference was tetramethylsilane-d^{12} ($\delta = 0.00$ ppm). When D_2O was the solvent, chemical shifts δ refer to the residual signal of HDO ($\delta = 4.80$ ppm). High-resolution mass spectra were obtained at the COSMIC facility of the Old Dominion University (Norfolk, VA) using a Bruker Daltonics 12 Tesla APEX-Qe FTICR mass spectrometer with an Apollo II ion source. Density functional calculations were performed at the Ohio Supercomputer Center (Columbus, OH), using the TURBOMOLE suite of programs (version 6.3.1).[1]

*(2,4-Difluorophenyl)(ethyl)sulfane (**1a**)*

Potassium hydroxide (0.42 g, 7.5 mmol) was added to a solution of 2,4-difluorothiophenol (1.0 g, 6.8 mmol) in ethanol under inert atmosphere. After stirring for 30 min, ethyl bromide (1.1 g, 10 mmol) was added and the reaction mixture kept at 25°C for 12 h. Aqueous sodium hydroxide (2.0 M, 4.0 mL) was then added, and ethanol was removed under vacuum. The reaction mixture was diluted with water (40 mL), extracted with dichloromethane (3 × 30 mL), and the combined extracts were washed with water (50 mL), brine (50 mL), dried with sodium sulfate and evaporated. The product was purified by chromatography (silica gel; eluent: hexane/chloroform, 9:1) to afford a colourless liquid (0.80 g, 67%). ^{1}H NMR: δ 7.48 (q, $J = 8.4$ Hz, Ar—*H*, 1H), 7.01 (m, Ar—*H*, 2H), 2.93 (q, $J = 7.4$ Hz, S—C*H*$_2$, 2H), 1.24 (t, $J = 7.3$ Hz, CH$_2$—C*H*$_3$) ppm. ^{13}C NMR: 161.7 (dd, $J = 245.3$, 11.3 Hz, Ar*C*F), 162.6 (dd, $J = 244.5$, 12.0 Hz, Ar*C*F), 134.7 (dd, $J = 9.8$, 3.0 Hz, Ar*C*), 119.7 (dd, $J = 18.0$, 3.8 Hz, Ar*C*S), 112.9 (dd, $J = 21.5$, 3.8 Hz, Ar*C*), 105.1 (t, $J = 26.9$ Hz, Ar*C*), 28.5 (d, $J = 2.3$ Hz, ArS*C*H$_2$), 14.8 (ArSCH$_2$*C*H$_3$) ppm.

*(2,4-Difluorophenyl)(isopropyl)sulfane (**1b**)*

Prepared similarly from 2,4-difluorothiophenol (3.0 g, 20 mmol) and 2-bromopropane (7.6 g, 62 mmol); colourless liquid (2.6 g, 67%). ^{1}H NMR: δ 7.55 (q, $J = 8.4$ Hz, Ar—*H*), 7.02 (q, $J = 8.6$ Hz, Ar—*H*), 3.39 (o, $J = 6.7$ Hz, SC*H*), 1.25 (d, $J = 6.7$ Hz, (CH(C*H*$_3$)$_2$) ppm. ^{13}C NMR: 165.3 (t, $J = 11.8$ Hz, Ar*C*F), 162.1 (t, $J = 11.3$ Hz, Ar*C*F), 137.8 (dd, $J = 6.9$, 2.3 Hz, Ar*C*), 118.6 (d, $J = 3.8$ Hz, Ar*C*), 112.8 (dd, $J = 17.6$, 3.8 Hz, Ar*C*), 105.2 (t, $J = 26.1$ Hz, Ar*C*), 39.2 (S*C*H), 23.4 (C(*C*H$_3$)$_2$) ppm.

*(2,4-Difluoro-3-iodophenyl)(ethyl)sulfane (**2a**)*

A solution of butyllithium (1.8 mL, 3.6 mmol) in hexane was added to a solution of diisopropylamine (0.39 g, 3.9 mmol) in dry THF (30 mL) and the reaction mixture was kept at −75°C for 20 min. A solution of sulfide **1a** (0.50 g, 2.9 mmol) in THF (5.0 mL) was added dropwise, and the reaction mixture was kept at −75°C for 2 h before adding iodine (0.87 g, 3.4 mmol). The resulting reaction mixture was allowed to warm to 25°C before adding an aqueous solution of $Na_2S_2O_3$ (23 mg, 0.14 mmol). The solution was diluted with water (20 mL) and extracted with diethyl ether (3 × 25 mL). The combined organic layers were washed with water (50 mL) and brine (40 mL), dried with sodium sulfate and evaporated. The title compound was isolated as a light yellow oil (0.74 g, 86%). ^{1}H NMR: δ 7.47 (q, $J = 8.5$ Hz, Ar—*H*, 1H), 7.02 (t, $J = 7.7$ Hz, Ar—*H*, 1H), 2.94 (q, $J = 7.2$ Hz, SC*H*$_2$, 2H), 1.26 (t, $J = 7.4$ Hz, CH$_2$C*H*$_3$, 3H) ppm. ^{13}C NMR: 162.5 (dd, $J = 243.0$, 5.3 Hz, Ar*C*F), 161.6 (dd, $J = 240.8$, 6.0 Hz, Ar*C*F), 134.1 (dd, $J = 8.6$, 3.0 Hz, Ar*C*), 120.4 (dd, $J = 21.0$, 3.8 Hz, Ar*C*S), 112.6 (dd, $J = 24.8$, 3.8 Hz, Ar*C*), 72.3 (t, $J = 30.8$ Hz, Ar*C*I), 28.4 (d, $J = 2.3$ Hz, S*C*H$_2$), 14.7 (CH$_2$*C*H$_3$) ppm.

*(2,4-Difluoro-3-iodophenyl)(isopropyl)sulfane (**2b**)*

Prepared similarly to sulfide **2a**, with (2,4-difluorophenyl)(isopropyl)sulfane **1b** (2.2 g, 12 mmol) instead of (2,4-difluorophenyl)(ethyl)sulfane **1a**. The product was purified by chromatography (silica gel; eluent: hexane/chloroform, 18:2) to afford a light yellow liquid (3.0 g, 83%). ^{1}H NMR: δ 7.48 (q, $J = 8.4$ Hz, Ar—*H*, 1H), 6.96 (t, $J = 7.5$ Hz, Ar—*H*, 1H), 3.37 (octet, $J = 6.9$ Hz, C*H*(CH$_3$)$_2$, 1H), 1.21 (d, $J = 6.6$ Hz, CH(C*H*$_3$)$_2$) ppm. ^{13}C NMR: 163.3 (dd, $J = 244$, 5.4 Hz, Ar*C*), 162.8 (dd, $J = 241$, 6.2 Hz, Ar*C*), 137.3 (dd, $J = 9.0$, 2.3 Hz, Ar*C*), 119.2 (dd, $J = 21.5$, 3.9 Hz, Ar*C*), 112.6 (dd, $J = 24.2$, 4.0 Hz, Ar*C*), 72.4 (t, $J = 30.0$ Hz, Ar*C*), 39.2 (S*C*H), 23.3 (C(*C*H$_3$)$_2$) ppm.

*(2,6-Difluoro-2′-methylbiphenyl-3-yl)(ethyl)sulfane (**3a**)*

A solution of potassium carbonate (0.37 g, 2.7 mmol) in water (5.0 mL) was added to a solution of sulfide **2a**

(0.40 g, 1.3 mmol), *o*-tolylboronic acid (0.27 g, 2.0 mmol) and palladium(0)tetrakis(triphenylphosphine) (0.14 g, 0.13 mmol) in *N*,*N*-dimethylformamide (25 mL) under inert atmosphere. The resulting mixture was heated at 120°C for 12 h. After cooling to 25°C, the reaction mixture was filtered through a pad of celite. The filtrate was then poured into ice-cold water (40 mL), acidified with 1.0 M HCl and extracted with dichloromethane (3 × 30 mL). The organic fractions were washed with water (60 mL) and brine (60 mL), dried with sodium sulfate and concentrated *in vacuo*. The product was purified by column chromatography (silica gel; eluent: hexane/ethyl acetate, 98:2) to afford a colourless oil (0.26 g, 74%). ^{1}H NMR: δ 7.53 (q, $J = 8.5$ Hz, Ar—*H*, 1H), 7.4–7.3 (m, Ar—*H*, 3H), 7.27 (t, $J = 7.5$ Hz, Ar—*H*, 1H), 7.11 (t, $J = 8.8$ Hz, Ar—*H*, 1H), 2.98 (q, $J = 7.4$ Hz, S—CH_2, 2H), 2.16 (s, Ar—CH_3, 3H), 1.29 (t, $J = 7.4$ Hz, CH_2CH_3, 3H) ppm. ^{13}C NMR: 160.1 (dd, $J = 243.0$, 6.8 Hz, Ar*C*F), 159.4 (dd, $J = 242.3$, 7.5 Hz, Ar*C*F), 138.3 (*C*CH_3), 133.0 (dd, $J = 9.8$, 3.0 Hz, Ar*C*), 131.5, 131.2, 130.2, 129.9, 126.8 (Ar*C*), 120.0 (dd, $J = 19.5$, 3.8 Hz, Ar*C*S), 119.2 (t, $J = 22.5$ Hz, Ar*C*), 112.8 (dd, $J = 23.3$, 3.8 Hz, Ar*C*), 28.4 (d, $J = 2.3$ Hz, S*C*H_3), 19.9 (C*C*H_3), 144.9 (CH_2*C*H_3) ppm.

*(2′-Chloro-2,6-difluorobiphenyl-3-yl)(ethyl)sulfane (**3b**)*

Prepared similarly to biphenyl **3a**, with 2-chlorophenylboronic acid (0.91 g, 5.80 mmol) instead of *o*-tolylboronic acid. The product was purified by chromatography (silica gel; eluent: hexane/ethyl acetate, 99:1) to afford a colourless oil (0.30 g, 27%). ^{1}H NMR: δ 7.61–7.43 (m, Ar—*H*, 5H), 7.11 (t, $J = 9.0$ Hz, Ar—*H*, 1H), 2.95 (q, $J = 7.3$ Hz, S—CH_2, 2H), 1.27 (t, $J = 7.4$ Hz, CH_2—CH_3, 3H) ppm. ^{13}C NMR: 160.0 (dd, $J = 245.2$, 6.8 Hz, Ar*C*F), 159.3 (dd, $J = 243.8$, 7.5 Hz, Ar*C*F), 134.8 (Ar*C*), 133.8 (dd, $J = 9.8$, 3.0 Hz, Ar*C*), 133.24 (Ar*C*), 131.7 (Ar*C*), 130.6 (Ar*C*), 129.4 (Ar*C*), 128.2 (Ar*C*), 120.1 (dd, $J = 19.5$, 4.5 Hz, Ar*C*), 117.3 (t, $J = 21.8$ Hz, Ar*C*), 112.8 (dd, $J = 22.5$, 3.8 Hz, Ar*C*), 28.4 (d, $J = 2.3$ Hz, S*C*H_2), 14.8 (CH_2*C*H_3) ppm.

*(2,6-Difluoro-2′-methylbiphenyl-3-yl)(isopropyl)sulfane (**3c**)*

Prepared similarly to biphenyl **3a**, with isopropyl sulfide **2b** (0.70 g, 2.2 mmol) instead of ethyl sulfide **2a**. The product was purified by chromatography (silica gel; eluent: hexane/chloroform, 49:1) to afford a colourless oil (0.44 g, 71%). ^{1}H NMR: δ 7.59–7.40 (m, Ar—*H*, 1H), 7.35–7.25 (m, Ar—*H*, 4H), 7.11 (t, $J = 8.9$ Hz, Ar—*H*, 1H), 3.44 (o, $J = 6.7$ Hz, S*CH*, 1H), 2.16 (s, Ar—CH_3, 3H), 1.28 (d, $J = 6.7$ Hz, CH–(CH_3)$_2$, 6H) ppm. ^{13}C NMR: 160.7 (dd, $J = 244.5$, 6.8 Hz, Ar*C*F), C161.0 (dd, $J = 243.0$, 8.3 Hz, Ar*C*F), 138.22 (Ar*C*), 136.1 (dd, $J = 9.8$, 3.0 Hz, Ar*C*), 131.4, 131.2, 129.9, 129.8, 126.8 (Ar*C*), 119.2 (t, $J = 21.8$ Hz, Ar*C*), 118.7 (dd, $J = 20.3$, 3.8 Hz, Ar*C*), 112.7 (dd, $J = 23.3$, 4.5 Hz, Ar*C*), 39.1 (S*C*H), 23.5 (C(*C*H_3)$_2$), 19.9 (Ar*C*H_3) ppm.

*(2′-Chloro-2,6-difluorobiphenyl-3-yl)(isopropyl)sulfane (**3d**)*

Prepared similarly to biphenyl **3b**, with isopropyl sulfide **2b** (0.90 g, 2.9 mmol) instead of ethyl sulfide **2a**. The product was purified by chromatography (silica gel; eluent: hexane/chloroform, 99:1) to afford a colourless oil (0.30 g, 35%). ^{1}H NMR: δ 7.60 (q, $J = 6.0$ Hz, Ar—*H*, 2H), 7.52–7.41 (m, Ar—*H*, 3H), 7.11 (t, $J = 8.7$ Hz, Ar—*H*, 1H), 3.43 (o, $J = 6.7$Hz, S—C*H*, 1H), 1.27 (d, $J = 6.7$ Hz, CH(CH_3)$_2$, 6H) ppm. ^{13}C NMR: 160.7 (dd, $J = 246.8$, 6.8 Hz, Ar*C*F), 160.5 (dd, $J = 243.8$, 7.5 Hz, Ar*C*F), 136.5 (dd, $J = 9.8$, 2.3 Hz, Ar*C*), 134.8, 133.2, 131.7, 130.6, 129.4, 128.2 (Ar*C*), 119.0 (dd, $J = 19.5$, 3.8 Hz, Ar*C*), 117.3 (t, $J = 21.8$ Hz, Ar*C*), 112.8 (dd, $J = 22.5$, 3.8 Hz, Ar*C*), 39.2 (S*C*H), 23.4 (CH(*C*H_3)$_2$) ppm.

*(2,6-Fluoro-2′-methylbiphenyl-3-yl)(ethyl)(methyl) sulfonium tetrafluoroborate (**4a**)*

Trimethyloxonium tetrafluoroborate (70 mg, 0.45 mmol) was added to a solution of biphenyl **3a** (0.10 g, 0.38 mmol) in nitromethane (4.0 mL) under a nitrogen atmosphere. The reaction mixture was heated to 60°C for 12 h. After cooling to 25°C, methanol (10 mL) was added, and the solvent was evaporated under vacuum. Addition of diethyl ether resulted in the formation of the title compound as a light yellow solid (0.12 g, 87%); mp 130–131°C. ^{1}H NMR: δ 8.0 (q, $J = 8.7$ Hz, Ar—*H*, 1H), 7.52–7.30 (m, Ar—*H*, 5H), 3.70 (m, S—CH_2, 2H), 3.28 (S, S—CH_3, 3H), 2.20 (s, Ar—CH_3, 3H), 1.40 (t, $J = 7.3$ Hz, CH_2—CH_3, 3H) ppm. ^{13}C NMR: 165.4 (dd, $J = 255.0$, 8.3 Hz, Ar*C*F), 161.1 (dd, $J = 252.0$, 8.3 Hz, Ar*C*F), 138.5 (Ar*C*CH_3), 133.6 (dd, $J = 13.5$, 6.0 Hz, Ar*C*), 131.6, 131.5, 130.9 (Ar*C*), 127.5 (d, $J = 2.3$ Hz, Ar*C*), 127.2 (d, $J = 1.5$ Hz, Ar*C*), 121.5 (t, $J = 23.2$ Hz, Ar*C*), 115.8 (dt, $J = 24.8$, 3.0 Hz, Ar*C*), 107.5 (dt, $J = 16.0$, 3.0 Hz, Ar*C*S), 47.6 (d, $J = 3.0$ Hz, S*C*H_2), 26.03 (d, $J = 3.0$ Hz, S*C*H_3), 25.8 (d, $J = 1.5$ Hz, S*C*H_3), 19.8 (Ar*C*H_3), 9.8 (d, $J = 6.8$ Hz, CH_2*C*H_3) ppm. HRMS (ESI) *m*/*z* calcd for $C_{16}H_{17}F_2S$ ($[M]^+$) 279.101354, found 279.100712.

*(2′-Chloro-2,6-difluorobiphenyl-3-yl)(ethyl)(methyl) sulfonium tetrafluoroborate (**4b**)*

Obtained similarly to sulfonium **4a**, using biphenyl **3b** (0.10 g, 0.35 mmol) instead of biphenyl **3a**. White solid (0.70 g, 54%); mp 139–140°C. ^{1}H NMR: δ 8.06 (q, $J = 7.7$ Hz, Ar—*H*, 1H), 7.68–7.52 (m, Ar—*H*, 5H), 3.68 (m, S—CH_2, 2H), 3.28 (s, S(CH_3), 3H), 1.39 (t, $J = 7.2$ Hz, CH_2—CH_3, 3H) ppm. ^{13}C NMR: 165.3 (ddd, $J = 256.5$,

6.8, 3.8 Hz, Ar*C*F), 161.1 (ddd, $J = 254.3$, 6.0, 2.3 Hz, Ar*C*F), 134.7 (Ar*C*), 134.5 (t, $J = 11.3$ Hz, ArC), 133.2 (d, $J = 3.0$ Hz, Ar*C*), 132.8 (Ar*C*), 130.9 (Ar*C*), 128.7 (Ar*C*), 127.1 (d, $J = 2.3$ Hz, Ar*C*), 119.4 (t, $J = 21.8$ Hz, Ar*C*), 115.7 (ddd, $J = 24.8$, 8.3, 3.8 Hz, Ar*C*), 107.6 (t, $J = 15.8$ Hz, Ar*C*), 41.6 (d, $J = 6.0$ Hz, S*C*H_3), 25.9 & 25.7 (d, $J = 2.3$ Hz, S*C*H_2), 9.8 (d, $J = 7.5$ Hz, $CH_2C\,H_3$) ppm. HRMS (ESI) *m/z* calcd for $C_{15}H_{14}ClF_2S$ ($[M]^+$) 299.046732, found 299.046874.

*(2,6-Difluoro-2′-methylbiphenyl-3-yl)(isopropyl)(methyl) sulfonium tetrafluoroborate (**4c**)*

Obtained similarly to sulfonium **4a**, using biphenyl **3c** (0.10 g, 0.36 mmol) instead of biphenyl **3a**. White solid (0.11 g, 81%); m.p. 128–129°C. ^{1}H NMR: δ 7.94 (m, Ar—*H*, 1H), 7.53–7.43 (m, Ar—*H*, 3H), 7.40–7.28 (m, Ar—*H*, 2H), 4.06 (m, S—C*H*, 1H), 3.26 (s, S-(C*H*$_3$), 3H), 2.19 (s, Ar—C*H*$_3$, 3H), 1.56 & 1.39 (d, $J = 6.7$ Hz, CH-(C*H*$_3$)$_2$, 6H) ppm. ^{13}C NMR: 165.4 (dd, $J = 255.0$, 7.5 Hz, Ar*C*F), 161.1 (dd, $J = 251.9$, 7.5 Hz, Ar*C*F), 138.5 (Ar*C*), 133.7 (dd, $J = 11.3$, 6.0 Hz, ArC), 131.6 (d, $J = 3.8$ Hz, Ar*C*), 131.4 (d, $J = 2.3$ Hz, Ar*C*), 130.9 (d, $J = 2.3$ Hz, Ar*C*), 127.5 (d, $J = 3.8$ Hz, Ar*C*), 127.2 (d, $J = 2.3$ Hz, Ar*C*), 121.5 (t, $J = 22.2$ Hz, Ar*C*), 115.8 (ddd, $J = 28.5$, 3.8 Hz, Ar*C*), 106.7 (dt, $J = 15.8$, 3.8 Hz, Ar*C*), 53.4 (d, $J = 4.5$ Hz, S*C*H), 23.3 & 23.2 (d, $J = 2.3$ Hz, S(*C*H_3)), 19.8 (Ar*C*H_3), 18.5 (d, $J = 3.8$ Hz, CH(*C*H_3)), 18.2 (d, $J = 5.3$ Hz, CH(*C*H_3)) ppm. HRMS (ESI) *m/z* calcd for $C_{19}H_{19}F_2S$ ($[M]^+$) 293.117004, found 293.117180.

*(2′-Chloro-2,6-difluorobiphenyl-3-yl)(isopropyl)(methyl) sulfonium tetrafluoroborate (**4d**)*

Obtained similarly to sulfonium **4a**, using biphenyl **3d** (60 mg, 0.20 mmol) instead of biphenyl **3a**. White solid (45 mg, 56%); m.p. 127–128°C. ^{1}H NMR (CD_3CN): δ 8.03–7.96 (m, Ar—*H*, 1H), 7.67 (d, $J = 8.1$ Hz, Ar—*H*, 1H), 7.61–7.48 (m, Ar—*H*, 4H), 4.12–4.00 (m, C*H*(CH$_3$)$_2$, 1H), 3.27 (s, S(C*H*$_3$), 3H), 1.56 (d, $J = 6.6$ Hz, CH(C*H*$_3$)$_2$, 3H), 1.38 (d, J = 6.6 Hz, CH(C*H*$_3$)$_2$, 3H) ppm. ^{13}C NMR: 165.3 (dt, $J = 256.8$, 7.3 Hz, Ar*C*), 161.0 (dd, $J = 245.3$, 3.8 Hz, Ar*C*), 134.9–134.4 (m, Ar*C* × 2), 133.1 (d, $J = 7.1$ Hz, Ar*C*), 132.7 (d, $J = 1.8$ Hz, Ar*C*), 130.9 (Ar*C*), 128.6 (d, $J = 3.1$ Hz, Ar*C*), 127.1 (d, $J = 3.6$ Hz, Ar*C*), 119.8–119.1 (m, Ar*C*), 115.8 (dd, $J = 24.2$, 3.6 Hz, Ar*C*), 106.8 (t, $J = 11.8$ Hz, Ar*C*), 53.5 (d, $J = 18.8$ Hz, S*C*H$_3$), 23.2 (t, $J = 2.25$ Hz, S*C*H), 18.5 (d, $J = 5.0$ Hz, CH(*C*H$_3$)$_2$), 18.2 (CH(*C*H$_3$)$_2$) ppm. HRMS (ESI) *m/z* calcd for $C_{16}H_{16}ClF_2S$ ($[M]^+$) 313.062382, found 313.062629.

*1-Bromo-2-*tert*-butylbenzene (**5a**) (21)*

To a solution of 2-*tert*-butylphenylamine (7.5 g, 50 mmol) in 48% HBr (13 mL) at 0°C was added a solution of sodium nitrite (7.6 g, 0.11 mol) in water (10 mL). The solution was kept at 0°C for 2 h until the addition of 0.20 g of copper powder. The resulting solution was stirred at 0°C until bubbling stopped, and finally heated to 50°C for 30 min. The reaction mixture was diluted with water (40 mL), extracted with diethyl ether (3 × 50 mL) and combined organic layers were washed with an aqueous solution of potassium hydroxide (10%). The product was purified by chromatography (silica gel; eluent:hexane) to afford a light brown liquid (3.1 g, 30%). ^{1}H NMR: δ 7.65 (d, $J = 7.8$ Hz, Ar—*H*, 1H), 7.54 (d, $J = 8.0$ Hz, Ar—*H*, 1H), 7.34 (t, $J = 7.1$ Hz, Ar—*H*, 1H), 7.11 (t, $J = 8.7$ Hz, Ar—*H*, 1H), 1.53 (s, (C*H*$_3$)$_2$, 9H) ppm.

*2-*tert*-Butylphenylboronic acid (**5b**) (21)*

A solution of butyllithium (2.5 M) in hexane (1.0 g, 16 mmol) was added to a solution of 1-bromo-2-*tert*-butylbenzene (3.0 g, 14 mmol) in dry THF (0.10 L), and the solution was kept at −75°C for 2 h. The reaction mixture was then added to a solution of trimethyl borate (4.4 mL, 42 mmol) in THF (25 mL) and the solution kept at −75°C for 1 h followed by 2 h at 25°C. The reaction mixture was acidified with dilute HCl, diluted with water (0.10 L) and extracted with diethyl ether (3 × 50 mL). The title compound crystallised as white needles in hexane (1.8 g, 71 %); m.p. 128–129°C. ^{1}H NMR: δ 7.75 (d, $J = 7.9$ Hz, Ar—*H*, 1H), 7.30–7.26 (m, Ar—*H*, 2H), 7.15 (t, $J = 7.2$ Hz, Ar—*H*, 1H), 5.99 (s, B(O*H*)$_2$, 2H), 1.40 (s, C(C*H*$_3$)$_2$, 9H) ppm.

*2-*o*-Tolylpyridine (**6a**)*

Prepared similarly to biphenyl **3a**, with 2-bromopyridine (0.50 g, 3.2 mmol) and tolylboronic acid (0.64 g, 4.7 mmol). The product was purified by chromatography (silica gel; hexane/dichloromethane, 7:3) to afford a light brown oil (0.52 g, 96%). ^{1}H NMR: δ 8.68 (d, $J = 4.7$ Hz, Ar—*H*, 1H), 7.82 (t, $J = 7.7$ Hz, Ar—*H*, 1H), 7.47–7.40 (m, Ar—*H*, 2H), 7.33–7.30 (m, Ar—*H*, 4H), 2.37 (s, Ar—C*H*$_3$, 3H) ppm. ^{13}C NMR: 160.8, 150.1, 141.7, 137.3, 136.9, 131.7, 130.6, 129.2, 126.9, 125.0, 122.9 (Ar*C*), 20.7 (Ar*C*H$_3$) ppm.

*2-(2-Ethylphenyl)pyridine (**6b**)*

Prepared similarly to tolylpyridine **6a**, with 2-ethylbenzeneboronic acid (0.71 g, 4.7 mmol) instead of tolylboronic acid. The product was purified by chromatography (silica gel; eluent: hexane–ethyl acetate, 8:2) to afford a colourless oil (0.46 g, 79%). ^{1}H NMR: δ 8.67 (d, $J = 5.6$ Hz, Ar—*H*, 1H), 7.81 (t, $J = 7.7$ Hz, Ar—*H*, 1H), 7.45–7.29 (m, Ar—*H*, 6H), 2.74 (q, $J = 7.5$ Hz, Ar—C*H*$_2$, 2H), 1.09 (t, $J = 7.5$ Hz, C*H*$_3$, 3H) ppm. ^{13}C NMR: 161.1, 150.0, 143.2, 141.4, 137.4, 130.8, 130.2, 129.4, 126.8, 125.0, 122.9 (Ar*C*), 26.9 (Ar*C*H$_2$), 16.2 (*C*H$_3$) ppm.

*2-(2-Isopropylphenyl)pyridine (**6c**)*

Prepared similarly to tolylpyridine **6a**, with 2-isopropylphenylboronic acid (0.58 g, 3.5 mmol) instead of tolylboronic acid. The product was purified by chromatography (silica gel; eluent: hexane–ethyl acetate, 9:1) to afford light brown oil (0.39 g, 78%). ^{1}H NMR: δ 8.68 (d, $J = 4.8$ Hz, Ar—*H*, 1H), 7.82 (t, $J = 7.7$ Hz, Ar—*H*, 1H), 7.51–7.34 (m, Ar—*H*, 3H), 7.33–7.28 (m, Ar—*H*, 3H) ppm. ^{13}C NMR: 161.3, 150.0, 147.6, 141.2, 137.3, 130.7, 129.6, 126.7, 126.5, 125.3, 122.9 (Ar*C*), 30.1 (Ar*C*H), 24.4 (*C*H$_3$) ppm.

*2-(2-*tert*-Butylphenyl)pyridine (**6d**)*

Prepared similarly to tolylpyridine **6a**, with 2-*tert*-butylphenylboronic acid (**5b**; 0.70 g, 4.0 mmol) instead of tolylboronic acid. The product was purified by chromatography (silica gel; eluent: hexane–ethyl acetate, 17:3) to afford colourless oil (0.15 g, 22%). ^{1}H NMR: δ 8.59 (d, $J = 4.6$ Hz, Ar—*H*, 1H), 7.79 (t, $J = 7.8$ Hz, Ar—*H*, 1H), 7.62 (d, $J = 8.0$ Hz, Ar—*H*, 1H), 7.42–7.32 (m, Ar—*H*, 3H), 7.25 (t, $J = 7.4$ Hz, Ar—*H*, 1H), 7.06 (d, $J = 7.5$ Hz, Ar—*H*, 1H), 1.19 (s, C(C*H*$_3$)$_3$, 9H) ppm. ^{13}C NMR: 164.5, 149.0, 148.8, 142.3, 136.9, 132.5, 128.9, 127.9, 126.2, 126.0, 122.9 (Ar—*C*), 37.2 (*C*(CH$_3$)$_2$), 32.7 (C(*C*H$_3$)$_2$) ppm.

N-*Myrtenyl-(2-*o*-tolyl)pyridinium bromide (**7a**)*

A mixture of *o*-tolylpyridine (**6a**; 50 mg, 0.30 mmol) and (−)-myrtenyl bromide (64 mg, 0.3 mmol) in acetone (15 mL) was refluxed for 12 h. Addition of diethyl ether (10 mL) resulted in the formation of the title compound as a white solid (31 mg, 27%); m.p. 167–168°C. ^{1}H NMR (D_2O): δ 8.93 (d, $J = 6.3$ Hz, Ar—*H*, 1H), 8.62 (t, $J = 7.2$ Hz, Ar—*H*, 1H), 8.11 (t, $J = 6.3$ Hz, Ar—*H*, 1H), 8.03 (d, $J = 7.8$ Hz, Ar—*H*, 1H), 7.60 (t, $J = 6.3$ Hz, Ar—*H*, 1H), 7.52–7.41 (m, Ar—*H*, 3H), 5.23 (d, $J = 14.7$ Hz, C = C*H*, 1H), 4.98 (m, N–C*H*$_2$, 2H), 2.34 (m, CH$_2$, 1H), 2.27 (br, CH$_2$, 2H), 2.16 (s, Ar—C*H*$_3$, 3H), 2.08 (br, C*H*, 1H), 1.88 (m, C*H*$_2$, 1H), 1.19 (d, $J = 4.8$ Hz, CH$_3$, 3H), 1.01 (t, $J = 11.4$ Hz, C*H*$_2$, 1H), 0.62 (d, $J = 7.5$ Hz, C*H*$_3$, 3H) ppm. ^{13}C NMR (D_2O): 156.2 (d, $J = 6.0$ Hz, Ar*C*), 146.5 (d, $J = 4.5$ Hz, Ar*C*), 145.9 (s, Ar*C*), 141.6 (s, Ar*C*), 137.0 (d, $J = 21$ Hz, Ar*C*), 132.0 (Ar*C*), 131.5 (d, $J = 12.8$ Hz, Ar*C*), 131.4 (s, Ar*C*), 131.3 (d, $J = 8.3$ Hz, Ar*C*), 129.9 (s, Ar*C*), 129.5 (Ar*C*), 127.6 (Ar*C*), 126.5 (d, $J = 7.5$ Hz, Ar*C*), 124.8 (d, $J = 7.5$ Hz, Ar*C*), 62.4 (d, $J = 3.2$ Hz, NC*H*$_2$), 44.0 (d, $J = 10.5$ Hz, myrtenyl-C), 40.5 (d, $J = 2.6$ Hz, myrtenyl-C), 38.1 (d, $J = 8.3$ Hz, myrtenyl-C), 31.5 (myrtenyl-C), 31.3 (d, $J = 6.3$ Hz, myrtenyl-C), 25.7 (myrtenyl-C), 20.6 (d, $J = 19.5$ Hz, myrtenyl-C), 19.3 (d, $J = 11.3$ Hz, myrtenyl-C) ppm. HRMS (ESI) *m/z* calcd for $C_{22}H_{26}N$ ([M]$^+$) 304.205976, found 304.206121.

N-*Myrtenyl-[2-(2-ethylphenyl)]pyridinium bromide (**7b**)*

Obtained similarly to pyridinium **7a**, using phenylpyridine **6b** (0.10 g, 0.55 mmol) instead of phenylpyridine **6a**. White solid (89 mg, 41%); m.p. 141–142°C. ^{1}H NMR (D_2O): δ 8.92 (d, $J = 6.0$ Hz, Ar—*H*, 1H), 8.61 (t, $J = 8.1$ Hz, Ar—*H*, 1H), 8.12 (d, $J = 6.9$ Hz, Ar—*H*, 1H), 8.07 (t, $J = 7.2$ Hz, Ar—*H*, 1H), 7.66 (t, $J = 7.2$ Hz, Ar—*H*, 1H), 7.58 (d, $J = 7.0$ Hz, Ar—*H*, 1H), 7.49–7.39 (m, Ar—*H*, 2H), 5.26 (d, $J = 17.7$ Hz, C = C*H*, 1H), 5.03–4.86 (m, N–C*H*$_2$, 2H), 2.57–2.45 (m, C*H*, 1H), 2.40–2.31 (m, Ar—C*H*$_2$, 2H), 2.31–2.20 (m, C*H*, 2H), 2.08 (br, C*H*, 1H), 1.89 (q, $J = 6.3$ Hz, C*H*, 1H), 1.19 (d, $J = 6.0$ Hz, C*H*$_3$, 3H), 1.15–0.98 (m, C*H*$_3$,CH, 4H), 0.64 (d, $J = 13.8$ Hz, C*H*$_3$, 3H) ppm. ^{13}C NMR (D_2O): 155.3 (d, $J = 6.8$ Hz, Ar*C*), 146.0 (d, $J = 3.2$ Hz, Ar*C*), 145.6 (d, $J = 3.2$ Hz, Ar*C*), 142.3 (d, $J = 19.5$ Hz, Ar*C*), 140.9 (d, $J = 3.8$ Hz, Ar*C*), 131.7 (Ar*C*), 130.9 (d, $J = 6.0$ Hz, Ar*C*), 130.3 (Ar*C*), 129.4 (m, Ar*C*), 129.1, 127.3 (Ar*C*), 126.5 (d, $J = 8.6$ Hz, Ar*C*), 124.3 (d, $J = 4.5$ Hz, Ar*C*), 61.9 (d, $J = 3.4$ Hz, NC*H*$_2$), 43.5 (d, $J = 9.8$ Hz, myrtenyl-C), 40.0 (myrtenyl-C), 37.7 (d, $J = 7.5$ Hz, myrtenyl-C),31.0, 30.9 (myrtenyl-C), 25.8 (d, $J = 10.5$ Hz, myrtenyl-C), 25.4 (d, $J = 2.3$ Hz, myrtenyl-C), 20.4 (d, $J = 17.3$ Hz, myrtenyl-C), 14.4 (d, $J = 4.5$ Hz, myrtenyl-C) ppm. HRMS (ESI) *m/z* calcd for $C_{23}H_{28}N$ ([M]$^+$) 318.221626, found 318.221780.

N-*Myrtenyl-[2-(2-isopropylphenyl)]pyridinium bromide (**7c**)*

A mixture of phenylpyridine **6c** (0.10 g, 0.51 mmol) and (−)-myrtenyl bromide (0.11 g, 0.51 mmol) in acetonitrile was heated to 50°C for 12 h. The product was crystallised from acetonitrile/diethyl ether (2:1) to afford a white solid that immediately turned to a thick oil when exposed to air (50 mg, 24%). ^{1}H NMR (D_2O): δ 8.87 (d, $J = 6.0$ Hz, Ar—*H*, 1H), 8.56 (t, $J = 7.5$ Hz, Ar—*H*, 1H), 8.09–8.00 (m, Ar—*H*, 2H), 7.68–7.64 (m, Ar—*H*, 2H), 7.44–7.38 (m, Ar—*H*, 2H), 7.34–7.32 (m, Ar—*H*, 1H), 5.34 (d, $J = 19.2$ Hz, C = C*H*, 1H), 4.98–4.71 (m, NC*H*$_2$, 2H), 2.48–2.38 (m, Ar—C*H*, 1H), 2.38–2.19 (m, C*H*$_2$, C*H*, 3H), 2.06 (br, C*H*, 1H), 1.87 (t, $J = 5.4$ Hz, C*H*, 1H), 1.23 (d, $J = 6.9$ Hz, C*H*$_3$, 3H), 1.17 (d, $J = 4.8$ Hz, C*H*$_3$, 3H), 1.08 (d, $J = 6.6$ Hz, C*H*$_3$, 3H), 0.97 (m, C*H*$_2$, 1H), 0.65 (d, $J = 22.8$ Hz, C*H*$_3$, 3H) ppm. ^{13}C NMR (D_2O): 156.2 (d, $J = 5.6$ Hz, Ar*C*), 147.8, 147.5 (Ar*C*), 146.2 (d, $J = 2.6$ Hz, Ar*C*), 145.6 (d, $J = 5.0$ Hz, Ar*C*), 141.4, 141.1, 132.5 (Ar*C*), 131.4 (d, $J = 7.2$ Hz, Ar*C*), 130.11–129.3 (Ar*C* × 2), 127.5–126.8 (Ar*C*), 126.1–125.7 (m, Ar*C*), 62.8 (NC*H*$_2$), 43.9, 40.8 (myrtenyl-C), 38.1 (d, $J = 4.5$ Hz, myrtenyl-C), 31.6–31.2 (myrtenyl-C × 2), 25.6 (myrtenyl-C), 24.6 (d, $J = 7.2$ Hz, myrtenyl-C), 23.7 (myrtenyl-C), 22.6 (d, $J = 8.9$ Hz, myrtenyl-C), 20.7 (d, $J = 11.4$ Hz, myrtenyl-C) ppm. HRMS (ESI) *m/z* calcd for $C_{24}H_{30}N$ ([M]$^+$) 332.237276, found 332.237442.

N-*Myrtenyl-[2-(2*-tert-*butylphenyl)]pyridinium bromide (**7d**)*

Prepared similarly to pyridinium **7c** with phenylpyridine **6d** (0.10 g, 0.47 mmol). White solid (51 mg, 25%); m.p. 58–59°C. ^{1}H NMR (D_2O): δ 8.86 (d, $J = 6.0$ Hz, Ar—*H*, 1H), 8.57 (t, $J = 6.9$ Hz, Ar—*H*, 1H), 8.17–8.09 (m, Ar—*H*, 2H), 7.85 (d, $J = 8.1$ Hz, Ar—*H*, 1H), 7.65 (t, $J = 7.5$ Hz, Ar—*H*, 1H), 7.45–7.38 (m, Ar—*H*, 1H), 7.22 (d, $J = 7.8$ Hz, Ar—*H*, 1H), 5.29 (s, C = C*H*, 1H), 5.00–4.67 (m, NCH_2, 2H), 2.45–2.24 (m, CH_2, C*H*, 3H), 2.10 (br, C*H*, 1H), 1.97–1.90 (m, C*H*, 1H), 1.24 & 1.19 (s, CH_3, 3H), 1.16 (s, C(CH_3)$_3$, 9H), 1.06 (m, C*H*, 1H), 0.77 & 0.63 (s, CH_3, 3H) ppm. ^{13}C NMR (D_2O): 158.6 (Ar*C*), 148.8 (d, $J = 21.8$ Hz, Ar*C*), 145.8 (d, $J = 4.8$ Hz, Ar*C*), 145.2 (d, $J = 9.4$ Hz, Ar*C*), 141.3 (d, $J = 10.1$ Hz, Ar*C*), 141.4 (d, $J = 10.1$ Hz, Ar*C*), 132.1–131.9 (m, Ar*C* × 2), 131.1 (d, $J = 33$ Hz, Ar*C*), 129.6 (d, $J = 3.7$ Hz, Ar*C*), 129.1 (Ar*C*), 127.7 (d, $J = 10.1$ Hz, Ar*C*), 126.7 (d, $J = 14.5$ Hz, Ar*C*), 125.2 (d, $J = 20.2$, Ar*C*), 62.8 (d, $J = 16.4$ Hz, N*C*H$_2$), 44.1, 40.5 (myrtenyl-C), 38.5 (d, $J = 17.0$ Hz, myrtenyl-C), 36.8, 32.3 (myrtenyl-C), 31.9 (d, $J = 4.4$ Hz, myrtenyl-C), 31.5 (d, $J = 8.3$ Hz, myrtenyl-C), 25.8 (myrtenyl-C), 20.9 (d, $J = 32.0$ Hz, myrtenyl-C) ppm. HRMS (ESI) *m/z* calcd for $C_{25}H_{32}N$ ([M]$^+$) 346.252926, found 346.253111.

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Note

1. A development of the University of Karlsruhe and Forschungszentrum Karlsruhe GmbH, 1989–2007; TURBOMOLE GmbH since 2007; available from www.turbomole.com and distributed by COSMO*logic* GmbH & Co. KG, D–51381 Leverkusen (http://www.cosmologic.de).

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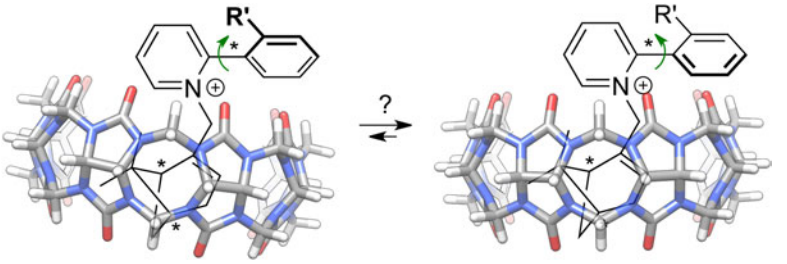

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