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A general, simple catalyst for enantiospecific cross couplings of benzylic ammonium triflates and boronic acids: no phosphine ligand required

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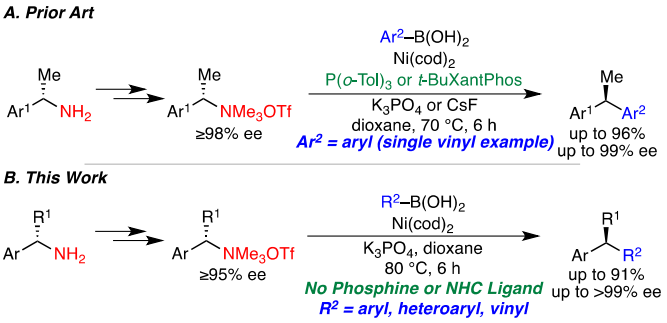
ABSTRACT

Highly improved conditions for the enantiospecific cross coupling of benzylic ammonium triflates with boronic acids are reported. This method relies on the use of $Ni(cod)_2$ without ancillary phosphine or *N*-heterocyclic carbene ligands as catalyst. These conditions enable the coupling of new classes of boronic acids and benzylic ammonium triflates. In particular, both heteroaromatic and vinyl boronic acids are well tolerated as coupling partners. In addition, these conditions enable the use of ammonium triflates with a variety of substituents at the benzylic stereocenter. Further, naphthyl-substitution is not required on the benzylic ammonium triflate; ammonium triflates with simple aromatic substituents also undergo this coupling. Good to high yields and levels of stereochemical fidelity are observed. This new catalyst system greatly expands the utility of enantiospecific cross couplings of these amine-derived substrates for the preparation of highly enantioenriched products.

1. Introduction

Diarylalkanes and triarylalkanes constitute important compounds in organic synthesis and often possess exciting biological activities.[1] An efficient strategy for the preparation of these chiral compounds is a cross coupling of a benzylic electrophile with an organometallic reagent.[2,3] However, until recently, both enantioselective and enantiospecific cross couplings of benzylic electrophiles required the use of reactive, air-sensitive organometallic coupling partners, such as Grignard or organozinc reagents.[4–7] This requirement limited the convenience and functional group tolerance of these reactions. To overcome this restriction, we developed an enantiospecific, nickel-catalyzed cross coupling of benzylic ammonium triflates with aryl boronic acids (Scheme 1A).[8] This method not only allows the use of commercially available, functional group tolerant boronic acid coupling partners, but also enables the use of amine-derived substrates. In our view, amines are ideal starting materials for enantiospecific reactions due to their wide availability in excellent enantiopurity via a variety of methods.[9] Simultaneously with the Jarvo lab,[10] we have also developed an enantiospecific, nickel-catalyzed cross coupling of alcohol-derived substrates with organoborane coupling partners; our reaction enabled the coupling of benzylic pivalates with arylboroxines.[11] Notably, this coupling relied on a simple nickel catalyst, bis(cyclooctadiene)nickel [$Ni(cod)_2$], without the need for ancillary phosphine or *N*-heterocyclic carbene (NHC) ligands.



Scheme 1. Prior art and our advances in enantiospecific cross couplings of benzylic ammonium triflates.

Although these new methods represent a significant advance by enabling the use of commercially available aryl boronic coupling partners, several limitations exist in the scope of substrates that can be used. In particular, our previous investigations of the cross couplings of benzylic ammonium triflates focused largely on the

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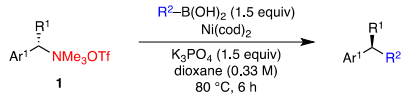
use of carbocyclic aryl boronic acids with only one example of a vinyl boronic acid.[8] Our attempts to use heteroaromatic boronic acids resulted in modest yields and ee's. In addition, substituents other than methyl were not demonstrated at the benzylic stereocenter (R^1) in the enantiospecific cross couplings of ammonium triflates. Further, enantiospecific couplings of benzylic electrophiles were limited to those that possess an aromatic substituent with an extended π system, such as 2-naphthyl or biphenyl.[12,5b,c,6,13] For example, under our previously reported conditions, the cross couplings of benzylic ammonium salts **1** with naphthyl substituents (Ar^1=2-Np) occurs with an average yield of 72%.[8] However, the cross coupling of benzylic ammonium triflates with substituted phenyl substituents occurs with an average yield of only 45%. Given the importance of heteroaromatic and substituted phenyl groups in pharmaceutical agents and other biologically active compounds,[14] we sought to develop conditions for the enantiospecific cross coupling of benzylic ammonium triflates that would overcome these limitations. We now report a general and simple catalyst system for the cross coupling of benzylic ammonium triflates with boronic acids (Scheme 1B). By using $Ni(cod)_2$ as catalyst without any ancillary phosphine or NHC ligands, we have achieved efficient cross couplings with heteroaromatic boronic acids. These conditions are also amenable to the use of vinyl boronic acids, as well as carbocyclic aryl boronic acids. In addition, these conditions are effective for ammonium triflates with a variety of substituents at the benzylic stereocenter (R^1). Finally, under these conditions, we have obtained promising results in the cross coupling of benzylic ammonium triflates substituted with non-naphthyl aromatic groups. This method greatly expands the utility of enantiospecific cross couplings of these amine-derived starting materials, which are available in exceptional enantiopurity.

2. Results and discussion

As stated above, our previous attempts to cross couple heteroaromatic boronic acids or ammonium triflates with non-naphthyl aryl substituents resulted in modest yields and/or levels of stereochemical fidelity. In an effort to overcome these limitations and identify a simpler, more convenient, and less expensive catalyst, we found that high yields and ee's were possible in the absence of an ancillary phosphine ligand. Simply using $Ni(cod)_2$ as catalyst resulted in a highly efficient catalyst system. This new 'phosphineless' catalyst system facilitates the convenience of this method, lessens the cost of the catalyst, and simplifies purification of the products by eliminating potential contamination by a phosphine ligand. As described below, these conditions are amenable to the use of new classes of boronic acids and benzylic ammonium triflate substrates.

Using this newly optimized, simple catalyst system, high yields and levels of stereochemical fidelity were observed in the couplings of a number of heteroaromatic boronic acids. In all cases, the reactions gave inversion of the absolute stereochemistry of the benzylic stereocenter with high levels of stereochemical fidelity. Oxygen-containing heteroaromatic groups can be coupled to deliver dibenzofuran **2** and benzofuran **3** in high yields and excellent ee's (Table 1, entries 1 and 3). Although some heteroaromatic boronic acids coupled in similar yields with either phosphine-containing or phosphine-less catalysts,[15] we observed dramatic differences in yield with dibenzofuranyl boronic acid. The use of $Ni(cod)_2$/P(*o*-Tol)$_3$ as catalyst resulted in only 15–27% yield of product **3** (entry 2). Under the phosphine-less reaction conditions, pyridyl boronic acids also underwent efficient coupling to give products **4** and **5** in 70 and 88% yield, respectively (entries 4 and 5). Although product **4** was formed in 75% ee (entry 4), pyridine **5** was formed in 95% ee (entry 5).[16]

Table 1
Scope of boronic acids and ammonium triflates[a]



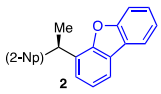
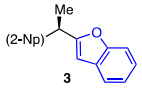
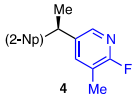
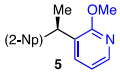
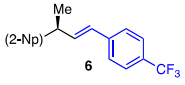
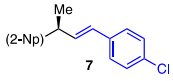
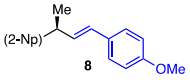
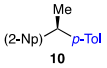
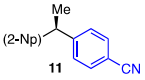
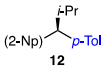
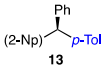
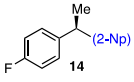
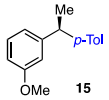
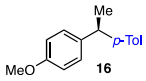
Entry	Product	mol % $Ni(cod)_2$	Yield (%)[b]	ee (%)[c]
1	 **2**	3	80	99
2[d]		3	(15–27)	97
3	 **3**	3	83	98
4	 **4**	3	70	75
5	 **5**	3	88	95[e]
6	 **6**	3	81	98
7[d]		3	(79)	>99
8	 **7**	3	76	99
9	 **8**	3	91	99
10[d]		3	(92)	96
11		0	0	n.d.[f]
12	 **9**	3	50	96
13	 **10**	10	82	>99
14	 **11**	3	(49)	>99
15[g]	 **12**	10	55	86
16[g]	 **13**	5	58	52
17	 **14**	10	75	92
18[h]		10	(29)	92
19[i]		10	(39)	88
20		0	(0.3)	n.d.[f]
21	 **15**	10	71	83

Table 1 (*continued*)

Entry	Product	mol % Ni(cod)$_2$	Yield (%)[b]	ee (%)[c]
22	 **16**	10	53	80

[a] Conditions: ammonium triflate **1** (0.20 mmol, 1.0 equiv), boronic acid (0.3 mmol, 1.5 equiv), Ni(cod)$_2$, K_3PO_4 (1.5 equiv), dioxane (0.33 M), 80 °C, 6 h. Starting materials were ≥99% ee, unless noted otherwise.

[b] Isolated yields. Yields in parentheses determined by ^{1}H NMR analysis using an internal standard.

[c] Determined by HPLC analysis using a chiral stationary phase, unless noted otherwise.

[d] P(*o*-Tol)$_3$ (7 mol %) was added to this reaction.

[e] Determined by SFC analysis using a chiral stationary phase.

[f] n.d.=not determined.

[g] Amine precursor prepared via Grignard addition to *N*-*tert*-butanesulfinyl aldimine as a single diastereomer. Starting material assumed to be >95% ee.

[h] *t*-Bu-XantPhos (12 mol %) was added to this reaction.

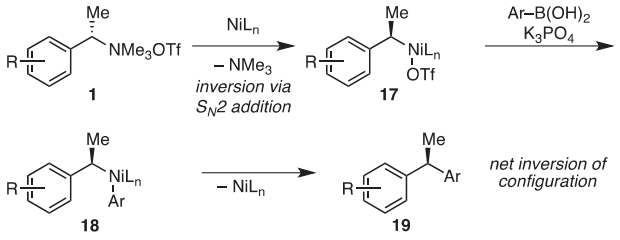
[i] P(*o*-Tol)$_3$ (22 mol %) was added to this reaction.

In addition to heteroaromatic boronic acid coupling partners, these reaction conditions are amenable to the use of vinyl boronic acids. Under our previous conditions, Ni(cod)$_2$/P(*o*-Tol)$_3$, we had found that (*E*)-2-phenylvinylboronic acid was an excellent coupling partner.[8] We were pleased to observe that these new, simpler conditions also enable the use of vinyl boronic acids. The use of both electron-rich and electron-poor phenylvinylboronic acids results in high yields and exceptional levels of stereochemical fidelity (Table 1, entries 6, 8 and 9). Notably, an aryl chloride functional group is tolerated under these reaction conditions (entry 8). With vinyl boronic acids, the use of Ni(cod)$_2$/P(*o*-Tol)$_3$ as catalyst resulted in similar yields and ee's as the phosphine-less catalyst (entries 7 and 10). Thus, in this case, the main advantage of the phosphine-less catalyst system is the ease of purification of the products by eliminating potential contamination by a phosphine ligand. Notably, these cross couplings do not occur without the Ni(cod)$_2$ catalyst (entry 11). The coupling of the more sterically demanding 1-phenylvinylboronic acid also proceeded with excellent stereochemical fidelity, albeit in reduced yield (entry 12). We also investigated the use of alkyl-substituted vinyl boronic acids; however, their use resulted in complex product mixtures, likely due to olefin isomerization.

Having established a broadened scope with respect to the boronic acid coupling partner, we turned our attention to the ammonium triflate substrate. We were pleased to observe that our new conditions provided high yields and exceptional levels of stereochemical fidelity with carbocyclic aryl boronic acids, such as *p*-tolyl boronic acid (Table 1, entry 13).[8] The coupling was also successful with electron-poor aryl boronic acids, such as *p*-cyanophenylboronic acid, albeit in reduced yields (entry 14).[17] In addition, the coupling of benzylic ammonium triflates with the bulkier *i*-propyl substituent also underwent coupling under these conditions to give diarylalkane **12** in 55% yield and 86% ee (entry 15). These conditions are also amenable to the formation of triarylmethane **13**, although in diminished ee (entry 16).

Emboldened by these results, we examined our new conditions for the coupling of simple, non-naphthyl-substituted benzylic ammonium triflates (Table 1, entries 17, 21 and 22). Although the stereochemical fidelity of these couplings is slightly diminished (80–92% ee), moderate to good yields are achieved with these highly challenging substrates.[13] In particular, electron-poor substrates efficiently undergo coupling to give *p*-fluorophenyl and *m*-methoxyphenyl products **14** and **15** in 75 and 71% yield, respectively (entries 17 and 21). With these non-naphthyl-substituted electrophiles, the phosphine-less catalyst proved crucial. The addition of *t*-Bu-XantPhos or P(*o*-Tol)$_3$ to these reactions resulted in significantly lower yields of 29% and 39%, respectively (entries 18 and 19). In addition, control experiments demonstrated that this cross coupling does not occur to any appreciable extent in the absence of Ni(cod)$_2$ (entry 20). Even electron-rich *p*-methoxyphenyl product **16** could be formed under these conditions in 53% yield. To our knowledge, these are the highest yields achieved to date for benzylic electrophiles with simple phenyl substituents (not naphthyl or biphenyl) in enantiospecific couplings with an organoborane partner.

Although detailed mechanistic experiments are required to elucidate the nature of the active catalyst under our phosphine-less conditions, we hypothesize that this reaction occurs via oxidative addition of a nickel(0) species to the benzylic ammonium triflate, likely with inversion of configuration of the benzylic stereocenter, to form either an η^1- or η^3-bound nickel complex (**17**, Scheme 2).[18] Subsequent transmetallation and reductive elimination, both with retention of configuration,[19] then result in the observed diarylalkane product with net inversion of configuration at the benzylic stereocenter.



Scheme 2. Proposed reaction mechanism.

3. Conclusion

As described above, we have identified new, general conditions for the enantiospecific cross coupling of benzylic ammonium triflates with aryl and vinyl boronic acids. These conditions rely on the use of Ni(cod)$_2$ as catalyst without ancillary phosphine or *N*-heterocyclic carbene ligands. This simple catalyst system facilitates the convenience and lowers the cost of these cross couplings. Even more importantly, these conditions enable the efficient cross coupling of heteroaromatic and vinyl boronic acids, as well as benzylic ammonium triflates with various substituents at the benzylic stereocenter. Benzylic ammonium triflates with simple, non-naphthyl aryl substituents also underwent couplings under these conditions in good yields. We are now focused on understanding the nature of the active catalyst formed under these conditions, as well as the continued development of the scope of this enantiospecific conversion of widely available amine-derived substrates into valuable, highly enantioenriched di- and tri-arylalkanes and 1,3-diaryl allylic products.

4. Experimental section

4.1. General

Reactions were performed either in a N_2-atmosphere glovebox in oven-dried 1-dram vials with Teflon-lined caps or in oven-dried round-bottomed flasks unless otherwise noted. Flasks were fitted with rubber septa, and reactions were conducted under a positive pressure of N_2. Stainless steel syringes or cannulae were used to transfer air- and moisture-sensitive liquids. Flash chromatography was performed on silica gel 60 (40–63 μm, 60 Å). Thin layer

chromatography (TLC) was performed on glass plates coated with silica gel 60 with F_{254} indicator. Commercial reagents were purchased from Sigma Aldrich, Acros, Fisher, Strem, TCI, Combi Blocks, Alfa Aesar, or Cambridge Isotopes Laboratories and used as received with the following exceptions: toluene, CH_2Cl_2, dioxane, and Et_2O were dried by passing through drying columns.[20] Toluene and dioxane were then degassed by sparging with N_2 and stored over activated 4 Å MS in a N_2-atmosphere glovebox. Anhydrous K_3PO_4 was purchased from Acros and stored in an N_2-atmosphere glovebox. MeOTf was purchased from TCI, America, and used as received. $CDCl_3$ was stored over oven-dried potassium carbonate. Proton nuclear magnetic resonance (^{1}H NMR), carbon nuclear magnetic resonance (^{13}C NMR), and fluorine nuclear magnetic resonance (^{19}F NMR) spectra were recorded on 400 MHz spectrometers. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$=δ 7.28; $(CD_3)_2CO$=δ 2.07). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent ($CDCl_3$=δ 77.07; $(CD_3)_2CO$=δ 28.94). Data are represented as follows: chemical shift, multiplicity (br=broad, s=singlet, d=doublet, t=triplet, q=quartet, p=pentet, m=multiplet, dd=doublet of doublets, h=heptet), coupling constants in Hertz (Hz), integration. Infrared (IR) spectra were obtained using FTIR spectrophotometers with material loaded onto a NaCl plate. The mass spectral data were obtained at the University of Delaware mass spectrometry facility. Optical rotations were measured using a 2.5 mL cell with a 0.1 dm path length. Melting points were taken on an uni-melt Thomas Hoover capillary melting point apparatus.

Dimethyl benzyl amines were prepared either from the benzyl amines using Escheweiler–Clarke conditions[21] or via reductive amination of benzaldehyde or acetophenone derivatives.[22] It has been reported that epimerization does not occur under the Escheweiler–Clarke conditions.[23] The amine precursors for salts **1b** and **1c** were prepared via Grignard addition to *N*-*tert*-butanesulfinyl aldimines, isolated as single diastereomers as determined by ^{1}H NMR analysis, and therefore assumed to be >95% ee.[24] Precursors for racemic ammonium triflates were synthesized via reductive amination of the corresponding acetophenone derivatives. Ammonium triflates **1a**, **1d**, and **1e** were prepared as previously described.[8]

4.2. General procedure for enantiospecific cross coupling

In a N_2-atmosphere glovebox, $Ni(cod)_2$ (either 1.6 mg, 0.006 mmol, 3 mol % or 5.5 mg, 0.020 mmol, 10 mol %) and K_3PO_4 (64.0 mg, 0.30 mmol, 1.5 equiv) were weighed into a 1-dram vial. Benzyl ammonium triflate **1** (0.20 mmol, 1.0 equiv) and boronic acid (0.30 mmol, 1.5 equiv) were added, followed by dioxane (0.6 mL, 0.33 M). The vial was capped with a Teflon-lined cap and removed from the glovebox. The mixture was stirred for 6 h at 80 °C. After cooling to room temperature, the reaction mixture was then diluted with Et_2O (1.5 mL) and filtered through a short plug of silica gel, which was rinsed with Et_2O (10 mL). The filtrate was concentrated and purified by silica gel chromatography to give the cross-coupled product.

*4.2.1. (R)-4-(1-(Naphthalen-2-yl)ethyl)dibenzo[b,d]furan (**2**).* General procedure was followed using 3 mol % $Ni(cod)_2$ and benzylic ammonium triflate **1a** prepared in 99.6% ee. The crude material was purified by silica gel chromatography (100% hexanes) to give compound **2** (51 mg, 80%) as a white solid (mp 98–101 °C). The enantiomeric excess was determined to be 99% ee by chiral HPLC analysis (CHIRALPAK IB, 1.0 mL/min, 0.2% *i*-PrOH/hexane, λ=254 nm); t_R (major)=7.996 min, t_R (minor)=10.60 min. $[\alpha]_D^{24}$ +124.5 (*c* 1.11, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J*=7.7 Hz, 2H), 7.85–7.71 (m, 5H), 7.58 (d, *J*=8.2 Hz, 1H), 7.49–7.38 (m, 4H), 7.33 (t, *J*=7.5 Hz, 1H), 7.28 (d, *J*=4.5 Hz, 1H), 5.01 (q, *J*=7.2 Hz, 1H), 1.90 (d, *J*=7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.1, 154.3, 142.7, 133.6, 132.3, 130.5, 128.0, 127.9, 127.7, 127.1, 127.0, 126.0, 125.7, 125.6, 125.5, 124.6, 124.2, 123.0, 122.7, 120.8, 118.7, 111.9, 39.0, 20.9; FTIR (NaCl/thin film) 3054, 2968, 1451, 1421, 1184, 751 cm^{-1}; HRMS (EI$^+$) $[M]^+$ calculated for $C_{24}H_{18}O$: 322.1358, found: 322.1342.

*4.2.2. (R)-2-(1-(Naphthalen-2-yl)ethyl)benzofuran (**3**).* General procedure was followed using 3 mol % $Ni(cod)_2$ and benzylic ammonium triflate **1a** prepared in 99.6% ee. The crude material was purified by silica gel chromatography (100% hexanes) to give compound **3** (45.0 mg, 83%) as a white solid (mp 97–100 °C). The enantiomeric excess was determined to be 98% ee by chiral HPLC analysis (CHIRALPAK IC, 1.0 mL/min, 0.2% *i*-PrOH/hexane, λ=254 nm); t_R (minor)=6.26 min, t_R (major)=6.84 min. $[\alpha]_D^{24}$ −38.3 (*c* 1.46, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94–7.91 (m, 3H), 7.86 (s, 1H), 7.67–7.46 (m, 5H), 7.38–7.25 (m, 2H), 6.61 (s, 1H), 4.55 (q, *J*=7.2 Hz, 1H), 1.91 (d, *J*=7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 155.0, 140.8, 133.7, 132.6, 128.8, 128.4, 127.9, 127.8, 126.2, 126.1, 126.0, 125.8, 123.6, 122.6, 120.6, 111.1, 102.4, 39.9, 20.4; FTIR (NaCl/thin film) 3053, 2973, 1455, 1255 cm^{-1}; HRMS (EI$^+$) $[M]^+$ calculated for $C_{20}H_{16}O$: 272.1201, found: 272.1186.

*4.2.3. (R)-2-Fluoro-3-methyl-5-(1-(naphthalen-2-yl)ethyl)pyridine (**4**).* General procedure was followed using 3 mol % $Ni(cod)_2$ and benzylic ammonium triflate **1a** prepared in 99.6% ee. The crude material was purified by silica gel chromatography (5% EtOAc/1% Et_3N/hexanes) to give compound **4** (37 mg, 70%) as a pale yellow oil. The enantiomeric excess was determined to be 75% ee by chiral HPLC analysis (CHIRALPAK IB, 1.0 mL/min, 5.0% *i*-PrOH/hexane, λ=254 nm); t_R (minor)=5.99 min, t_R (major)=7.18 min. $[\alpha]_D^{24}$ −89.6 (*c* 0.73, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30–8.11 (m, 1H), 7.86–7.70 (m, 3H), 7.61–7.51 (m, 1H), 7.52–7.37 (m, 2H), 7.33–7.22 (m, 1H), 6.79–6.67 (m, 1H), 4.39 (q, *J*=7.1 Hz, 1H), 2.21 (s, 3H), 1.74 (d, *J*=7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7 (d, J_{C-F}=238.4 Hz), 151.8 (d, J_{C-F}=8.1 Hz), 145.7 (d, J_{C-F}=15.15 Hz), 142.3, 136.9 (d, J_{C-F}=5.1 Hz), 133.6, 132.2, 128.5, 127.7 (d, J_{C-F}=4.0 Hz), 126.3, 125.8, 125.6, 110.7, 110.4, 39.6, 22.0, 19.8 (d, J_{C-F}=3.0 Hz); ^{13}C NMR (101 MHz, $(CD_3)_2CO$) δ 162.6 (d, J_{C-F}=232.3 Hz), 151.9 (d, J_{C-F}=8.1 Hz), 145.6 (d, J_{C-F}=16.2 Hz), 142.6, 137.4 (d, J_{C-F}=4.0 Hz), 133.7, 132.3, 128.2, 127.7, 127.5, 126.4, 126.1, 125.6, 125.5, 109.9 (d, J_{C-F}=19.2 Hz), 39.0, 21.2, 18.6 (d, J_{C-F}=3.0 Hz); FTIR (NaCl/thin film) 3053, 2968, 1608, 1485, 1373, 962 cm^{-1}; HRMS (EI$^+$) $[M]^+$ calculated for $C_{18}H_{16}FN$: 265.1267, found:265.1252. Please note: Although two ^{13}C NMR peaks are coincident when $CDCl_3$ is used as solvent, all 18 ^{13}C NMR peaks are seen when $(CD_3)_2CO$ is used as solvent.

*4.2.4. (R)-2-Methoxy-3-(1-(naphthalen-2-yl)ethyl)pyridine (**5**).* General procedure was followed using 3 mol % $Ni(cod)_2$ and benzylic ammonium triflate **1a** prepared in 99.6% ee. The crude material was purified by silica gel chromatography (5% EtOAc/1% EtN_3/hexanes) to give compound **5** (47 mg, 88%) as an oil. The enantiomeric excess was determined to be 95% ee by chiral SFC analysis (OJ-H, 3.0 mL/min, 40% *i*-PrOH(0.1% DEA)/CO_2, λ=254 and 220 nm); t_R (major)=2.46 min, t_R (minor)=3.07 min. $[\alpha]_D^{24}$ +58.4 (*c* 1.73, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09–8.02 (m, 1H), 7.85–7.74 (m, 3H), 7.73–7.67 (m, 1H), 7.52–7.31 (m, 4H), 6.88–6.78 (m, 1H), 4.61 (q, *J*=7.1, 6.0 Hz, 1H), 3.95 (s, 3H), 1.68 (d, *J*=7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.6, 144.4, 142.7, 136.1, 133.6, 132.2, 129.1, 127.9, 127.8, 127.7, 127.1, 126.0, 125.6, 125.5, 116.9, 53.5, 37.9, 20.5; FTIR (NaCl/thin film) 3055, 2969, 2948, 1589, 1507, 1463, 1409,

1321, 1253, 1020 cm^{-1}; HRMS (EI^+) $[M]^+$ calculated for $C_{18}H_{17}NO$: 263.1310, found: 263.1297.

*4.2.5. (S,E)-2-(4-(4-(Trifluoromethyl)phenyl)but-3-en-2-yl)naphthalene (**6**).* General procedure was followed using 3 mol % $Ni(cod)_2$ and benzylic ammonium triflate **1a** prepared in 99.6% ee. The crude material was purified by silica gel chromatography (100% hexanes) to give compound **6** (53.0 mg, 81%) as a white solid (mp 70–73 °C). The enantiomeric excess was determined to be 98% ee by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 100% hexane, λ=254 nm); t_R (major)=24.21 min, t_R (minor)=30.68 min. $[\alpha]_D^{24}$ −30.5 (*c* 1.18, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 7.90–7.76 (m, 3H), 7.76–7.64 (m, 1H), 7.54 (d, *J*=8.2 Hz, 2H), 7.51–7.37 (m, 5H), 6.63–6.43 (m, 2H), 3.99–3.69 (m, 1H), 1.58 (d, *J*=7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.5, 141.13, 141.11, 138.0, 133.8, 132.4, 129.0 (q, J_{C-F}=32.3 Hz), 128.3, 127.78, 127.76, 126.4, 126.3, 126.2, 125.64, 125.57 (q, J_{C-F}=4.0 Hz), 125.5, 124.4 (q, J_{C-F}=272.7 Hz), 42.8, 21.1; FTIR (NaCl/thin film) 3053, 2967, 1615, 1325, 1164, 1121, 1067 cm^{-1}; HRMS (EI^+) $[M]^+$ calculated for $C_{21}H_{17}F_3$: 326.1282, found: 326.1284.

*4.2.6. (S,E)-2-(4-(4-Chlorophenyl)but-3-en-2-yl)naphthalene (**7**).* General procedure was followed using 3 mol % $Ni(cod)_2$ and benzylic ammonium triflate **1a** prepared in 99.6% ee. The crude material was purified by silica gel chromatography (100% hexanes) to give **7** (44.0 mg, 76%) as a white solid (mp 68–71 °C). The enantiomeric excess was determined to be 99% ee by chiral HPLC analysis (CHIRALPAK IB, 1.0 mL/min, 100% hexane, λ=254 nm); t_R (major)=22.47 min, t_R (minor)=28.85 min. $[\alpha]_D^{24}$ −40.8 (*c* 1.42, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 7.98–7.82 (m, 3H), 7.77 (s, 1H), 7.63–7.43 (m, 3H), 7.43–7.25 (m, 4H), 6.59–6.38 (m, 2H), 3.98–3.80 (m, 1H), 1.63 (d, *J*=7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.4, 141.0, 141.0, 137.9, 133.7, 132.3, 128.2, 127.69, 127.66, 126.3, 126.2, 126.1, 125.6, 125.4, 42.7, 21.0; ^{13}C NMR (101 MHz, $(CD_3)_2CO$) δ 143.8, 137.2, 136.8, 134.5, 133.1, 132.7, 129.2, 128.7, 128.4, 128.3, 128.2, 128.1, 126.9, 126.6, 126.1, 125.8, 43.4, 21.4; FTIR (NaCl/thin film) 3052, 2965, 1490, 1091, 966 cm^{-1}; HRMS (EI^+) $[M]^+$ calculated for $C_{20}H_{17}Cl$: 292.1019, found: 292.0993. Please note: Although two ^{13}C NMR peaks are coincident when $CDCl_3$ is used as solvent, all 18 ^{13}C NMR peaks are seen when $(CD_3)_2CO$ is used as solvent.

*4.2.7. (S,E)-2-(4-(4-Methoxyphenyl)but-3-en-2-yl)naphthalene (**8**).* General procedure was followed using 3 mol % $Ni(cod)_2$ and benzylic ammonium triflate **1a** prepared in 99.6% ee. The crude material was purified by silica gel chromatography (100% hexanes) to give compound **8** (53.0 mg, 91%) as a white solid (mp 78–80 °C). The enantiomeric excess was determined to be 99% ee by chiral HPLC analysis (CHIRALPAK IA, 0.6 mL/min, 1% EtOAc/hexane, λ=254 nm); t_R (major)=27.88 min, t_R (minor)=30.19 min. $[\alpha]_D^{24}$ −35.7 (*c* 1.43, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 7.86–7.77 (m, 3H), 7.72–7.68 (m, 1H), 7.50–7.38 (m, 3H), 7.34–7.28 (m, 2H), 6.90–6.80 (m, 2H), 6.48–6.26 (m, 2H), 3.81–3.78 (m, 4H), 1.55 (d, *J*=7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 143.4, 133.7, 133.1, 132.3, 130.4, 128.3, 128.1, 127.8, 127.7, 127.4, 126.5, 126.0, 125.4, 125.3, 114.0, 55.4, 42.7, 21.4; FTIR (NaCl/thin film) 2962, 1607, 1511, 1250, 1175, 1034 cm^{-1}; HRMS (EI^+) $[M]^+$ calculated for $C_{21}H_{20}O$: 288.1514, found: 288.1517.

*4.2.8. (R)-2-(3-Phenylbut-3-en-2-yl)naphthalene (**9**).* General procedure was followed using 3 mol % $Ni(cod)_2$ and benzylic ammonium triflate **1a** prepared in 99.6% ee. The crude material was purified by silica gel chromatography (100% hexane) to give compound **9** (26 mg, 50%) as a white solid (mp 64–65 °C). The enantiomeric excess was determined to be 96% ee by chiral HPLC analysis (CHIRALCEL OD-H, 0.8 mL/min, 1% *i*-PrOH/hexane, λ=254 nm); t_R (minor)=6.33 min, t_R (major)=6.73 min. $[\alpha]_D^{24}$ −64.0 (*c* 0.64, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 7.88–7.76 (m, 3H), 7.76–7.70 (m, 1H), 7.53–7.42 (m, 3H), 7.42–7.33 (m, 2H), 7.33–7.16 (m, 3H), 5.53 (s, 1H), 5.27 (t, *J*=1.3 Hz, 1H), 4.24 (q, *J*=7.0 Hz, 1H), 1.60 (d, *J*=7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.5, 142.7, 142.2, 133.7, 132.3, 128.2, 128.2, 127.8, 127.7, 127.3, 126.8, 126.6, 125.9, 125.4, 113.5, 44.4, 21.8; ^{13}C NMR (101 MHz, $(CD_3)_2CO$) δ 152.6, 142.8, 142.1, 133.7, 132.2, 128.0, 127.9, 127.53, 127.46, 127.2, 126.6, 126.4, 125.82, 125.79, 125.3, 112.5, 43.7, 21.2; FTIR (NaCl/thin film) 3053, 2967, 2930, 2361, 2337, 1624, 1599, 1506 cm^{-1}; HRMS (EI^+) $[M]^+$ calculated for $C_{20}H_{18}$: 258.1409, found: 258.1422. Please note: Although two ^{13}C NMR peaks are coincident when $CDCl_3$ is used as solvent, all 18 ^{13}C NMR peaks are seen when $(CD_3)_2CO$ is used as solvent.

*4.2.9. (S)-2-(1-p-Tolylethyl)naphthalene (**10**).* General procedure was followed using 10 mol % $Ni(cod)_2$ and benzylic ammonium triflate **1a** prepared in 99.6% ee. The crude material was purified by silica gel chromatography (100% hexanes) to give compound **10** (40 mg, 82%) as a white solid. The enantiomeric excess was determined to be >99% ee by chiral HPLC analysis (CHIRALPAK IB, 0.4 mL/min, 100% hexane, λ=254 nm); t_R (major)=21.65: ^1H NMR (400 MHz, $CDCl_3$) δ 7.86–7.66 (m, 4H), 7.52–7.36 (m, 2H), 7.31 (dd, *J*=8.4, 1.8 Hz, 1H), 7.21–7.06 (m, 4H), 4.29 (q, *J*=7.2 Hz, 1H), 2.32 (s, 3H), 1.72 (d, *J*=7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0, 143.3, 135.6, 133.5, 132.1, 129.1, 128.0, 127.8, 127.7, 127.6, 126.9, 126.0, 125.4, 125.3, 44.5, 21.9, 21.1. The spectral data for this compound matches that reported in the literature.[8] Comparison of the HPLC spectrum of this product to that previously obtained in our laboratory confirmed that the absolute configuration of this product is *S*.[8]

*4.2.10. (S)-2-(2-Methyl-1-p-tolylpropyl)naphthalene (**12**).* General procedure was followed using 10 mol % $Ni(cod)_2$ and benzylic ammonium triflate **1b** prepared in >95% ee. The crude material was purified by silica gel chromatography (100% hexanes) to give compound **12** (30 mg, 55%) as a white solid (mp 77–78 °C). The enantiomeric excess was determined to be 86% ee by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 100% hexane, λ=254 nm); t_R (major)=8.24 min, t_R (minor)=8.93 min. $[\alpha]_D^{24}$ −33.5 (*c* 0.864, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 7.85–7.61 (m, 4H), 7.49–7.31 (m, 3H), 7.31–7.16 (m, 2H), 7.05 (d, *J*=7.8 Hz, 2H), 3.53 (d, *J*=10.8 Hz, 1H), 2.67–2.47 (m, 1H), 2.25 (s, 3H), 0.91 (d, *J*=6.4 Hz, 3H), 0.87 (d, *J*=6.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.7, 141.7, 135.5, 133.6, 132.1, 129.1, 128.0, 127.9, 127.6, 127.5, 126.5, 126.2, 125.8, 125.1, 60.5, 31.6, 22.0, 21.9, 21.0; FTIR (NaCl/thin film) 3053, 3019, 2955, 2922, 2868, 1508, 1457, 1385, 813, 760, 741 cm^{-1}; HRMS (EI^+) $[M]^+$ calculated for $C_{21}H_{22}$: 274.1722, found: 274.1724.

*4.2.11. (S)-2-(Phenyl(p-tolyl)methyl)naphthalene (**13**).* General procedure was followed using 10 mol % $Ni(cod)_2$ and benzylic ammonium triflate **1c** prepared in >95% ee. The crude material was purified by silica gel chromatography (100% hexanes) to give compound **13** (36 mg, 58%) as an oil. The enantiomeric excess was determined to be 52% ee by chiral HPLC analysis (CHIRALCEL OD-H, 0.3 mL/min, 0.2% *i*-PrOH/pentane, λ=254 nm); t_R (major)= 38.59 min, t_R (minor)=40.72 min. $[\alpha]_D^{24}$ +37.6 (*c* 1.88, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 7.95–7.71 (m, 3H), 7.54 (s, 1H), 7.49 (dt, *J*=6.1, 3.5 Hz, 2H), 7.40–7.33 (m, 3H), 7.33–7.26 (m, 1H), 7.26–7.20 (m, 2H), 7.20–7.09 (m, 4H), 5.74 (s, 1H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.9, 141.7, 140.7, 135.9, 133.4, 132.1, 129.5, 129.4, 129.1, 128.3, 128.1, 127.9, 127.8, 127.7, 127.5, 126.3, 125.9, 125.6, 56.5, 21.1. The spectral data for this compound matches that reported in the literature.[5c]

*4.2.12. (R)-2-(1-(4-Fluorophenyl)ethyl)naphthalene (**14**).* General procedure was followed using 10 mol % $Ni(cod)_2$ and benzylic

ammonium triflate **1d** prepared in 99% ee. The crude material was purified by silica gel chromatography (100% petroleum ether) to give compound **14** (38 mg, 75%) as an oil. The enantiomeric excess was determined to be 92% ee by chiral HPLC analysis (CHIRALCEL OD-H, 0.8 mL/min, 100% hexane, λ=254 nm); t_R (minor)=24.62 min, t_R (major)=31.78 min: ^{1}H NMR (400 MHz, CDCl3) δ 7.81–7.76 (m, 2H), 7.74 (d, J=8.5 Hz, 1H), 7.68–7.64 (m, 1H), 7.49–7.37 (m, 2H), 7.29–7.23 (m, 1H), 7.23–7.16 (m, 2H), 7.01–6.91 (m, 2H), 4.29 (q, J=7.2 Hz, 1H), 1.70 (d, J=7.2 Hz, 3H); ^{13}C NMR (101 MHz, CDCl3) δ 161.3 (d, J_{C-F}=245.4 Hz), 143.6, 141.9 (d, J_{C-F}=4.0 Hz), 133.5, 132.1, 129.1 (d, J_{C-F}=7.1 Hz), 128.1, 127.7, 127.6, 126.7, 126.1, 125.5, 125.3, 115.1 (d, J_{C-F}=21.2 Hz), 44.1, 21.9. The spectral data for this compound matches that reported in the literature.[8] Comparison of the HPLC spectrum of this product to that previously obtained in our laboratory confirmed that the absolute configuration of this product is *R*.[8]

*4.2.13. (S)-1-Methoxy-3-(1-p-tolylethyl)benzene (**15**).* General procedure was followed using 10 mol % Ni(cod)$_2$ and benzylic ammonium triflate **1e** prepared in >99% ee. The crude material was purified by silica gel chromatography (0–1% Et$_2$O/hexanes) to give compound **15** (32 mg, 71%) as an oil. The enantiomeric excess was determined to be 83% ee by chiral HPLC analysis (CHIRALPAK IA, 10.8 mL/min, 1% *i*-PrOH/hexane, λ=254 nm); t_R (minor)=5.55 min, t_R (major)=5.81 min: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.32–7.21 (m, 1H), 7.20–7.08 (m, 4H), 6.92–6.82 (m, 2H), 6.77 (ddt, J=8.1, 2.4, 1.4 Hz, 1H), 4.14 (q, J=7.1 Hz, 1H), 3.82 (s, 3H), 2.36 (s, 3H), 1.66 (d, J=7.2 Hz, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 159.7, 148.4, 143.3, 135.6, 129.4, 129.2, 127.5, 120.2, 113.8, 110.9, 55.2, 44.5, 22.0, 21.1. The spectral data for this compound matches that reported in the literature.[8] Comparison of the HPLC spectrum of this product to that previously obtained in our laboratory confirmed that the absolute configuration of this product is *S*.[8]

*4.2.14. (S)-1-Methoxy-4-(1-p-tolylethyl)benzene (**16**).* General procedure was followed using 10 mol % Ni(cod)$_2$ and benzylic ammonium triflate **1f** prepared in 99.5% ee. The crude material was purified by silica gel chromatography (0–1% Et$_2$O/hexane) to give compound **16** (24 mg, 53%) as an oil. The enantiomeric excess was determined to be 81% ee by chiral HPLC analysis (CHIRALCEL OJ-H, 0.8 mL/min, 100% hexane, λ=254 nm); t_R (major)=45.54 min, t_R (minor)=55.21 min. $[\alpha]_D^{24}$ −23.0 (*c* 1.02, CHCl$_3$): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.21–7.07 (m, 6H), 6.90–6.79 (m, 2H), 4.09 (q, J=7.2 Hz, 1H), 3.79 (s, 3H), 2.33 (s, 3H), 1.62 (d, J=7.2 Hz, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 157.9, 143.9, 138.9, 135.5, 129.2, 128.6, 127.5, 113.8, 55.4, 43.6, 22.3, 21.1. The spectral data for this compound matches that reported in the literature.[25]

4.3. Procedure for benzyl ammonium triflates

*4.3.1. (S)-N,N,N,2-Tetramethyl-1-(naphthalen-2-yl)propan-1-aminiumtrifluoromethane sulfonate (**1b**).* The dimethylbenzylamine (179 mg, 0.79 mmol, 1.0 equiv) was dissolved in Et$_2$O (0.17 mL, 4.0 M). MeOTf (0.17 mL, 1.0 mmol, 1.3 equiv) was added dropwise at 0 °C. The formation of two layers was observed. After complete addition the reaction mixture was stirred for an additional 15 min at 0 °C. The top layer was decanted off. The bottom layer was then washed with Et$_2$O (5 mL×3) and then hexanes (5 mL×3). Residual solvent was removed from the resulting oil in vacuo to give **1b** (298 mg, 97%) as an oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.97 (s, 1H), 7.96–7.86 (m, 2H), 7.86–7.80 (m, 1H), 7.58–7.44 (m, 3H), 4.61 (d, J=5.2 Hz, 1H), 3.20 (s, 9H), 2.89–2.70 (m, 1H), 1.15–0.99 (m, 6H); ^{19}F NMR (565 MHz, CDCl$_3$) δ −78.4; FTIR (NaCl/thin film) 2975, 1490, 1278, 1166, 1030, 828, 638 cm^{-1}; LRMS (ESI) [M−OTf]$^+$ calculated for [C$_{17}$H$_{24}$ N]$^+$: 242.2, found: 242. The ^{13}C NMR spectrum of **1b** was complex due to the presence of rotamers. Please see the spectrum in the Supplementary data.

*4.3.2. (S)-N,N,N-Trimethyl-1-(naphthalen-2-yl)-1-phenylmethanaminiumtrifluoromethane sulfonate (**1c**).* The dimethylbenzylamine (245 mg, 0.94 mmol, 1.0 equiv) was dissolved in Et$_2$O (0.24 mL, 4.0 M). MeOTf (0.13 mL, 1.2 mmol, 1.3 equiv) was added dropwise at 0 °C. The formation of two layers was observed. After complete addition the reaction mixture was stirred for an additional 15 min at 0 °C. The top layer was decanted off. The bottom layer was washed with washed with Et$_2$O (5 mL×3) and then hexanes (5 mL×3). Residual solvent was removed from the resulting oil in vacuo to give salt **1c** (225 mg, 57%) as a white fluffy solid (mp 61–63 °C): ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.32 (s, 1H), 7.98–7.76 (m, 6H), 7.58–7.39 (m, 5H), 6.12 (s, 1H), 3.25 (s, 9H); FTIR (NaCl/thin film) 3042, 1489, 1262, 1225, 1158, 1030, 735 cm^{-1}; ^{19}F NMR (565 MHz, CDCl$_3$) δ −78.3; LRMS (ESI) [M−OTf]$^+$ calculated for [C$_{20}$H$_{22}$N]$^+$: 276.2, found: 276. The ^{13}C NMR spectrum of **1b** was complex due to the presence of rotamers. Please see the spectrum in the Supplementary data.

*4.3.3. (S)-1-(4-Methoxyphenyl)-N,N,N-trimethylethanaminium trifluoromethanesulfonate (**1f**).* The dimethylbenzylamine (426 mg, 2.4 mmol, 1.0 equiv) was dissolved in Et$_2$O (0.6 mL, 4.0 M). MeOTf (0.30 mL, 3.1 mmol, 1.3 equiv) was added dropwise at 0 °C. White precipitate formed immediately. After complete addition the reaction mixture was stirred for an additional 15 min at 0 °C. The precipitate was isolated by filtration and washed with Et$_2$O (2×5 mL). The resulting solid was dried under vacuum to give salt **1f** (783 mg, 73%) as a white solid (mp 94–95 °C): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.52–7.36 (m, 2H), 7.06–6.81 (m, 2H), 4.79 (q, J=13.7, 6.8 Hz, 1H), 3.81 (s, 3H), 3.09 (s, 9H), 1.77 (d, J=6.7 Hz, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 161.3, 131.8, 124.0, 120.7 (q, J_{C-F}=321.2 Hz), 114.6, 73.8, 55.5, 50.8, 15.0; ^{19}F NMR (565 MHz, CDCl$_3$) δ −78.5; FTIR (NaCl/thin film) 2967, 1611, 1518, 1258, 1157, 1029, 838 cm^{-1}; LRMS (ESI) [M−OTf]$^+$ calculated for [C$_{12}$H$_{30}$NO]$^+$: 194.2, found: 194.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2014.03.039.

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