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Heptadecafluorooctanesulfonic acid ($C_8F_{17}SO_3H$) catalyzed intramolecular hydroamination of olefinic sulfonamides in fluorous biphase system (FBS)

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Abstract

A practical, efficient, and environmentally benign intramolecular hydroamination of olefinic sulfonamides was carried out in fluorous biphase system (FBS) using commercially available heptadecafluorooctanesulfonic acid ($C_8F_{17}SO_3H$) as a catalyst and perfluorodecaline ($C_{10}F_{18}$, *cis*- and *trans*- mixture) as a fluorous solvent to produce the corresponding cyclic products in good yields. The Brønsted acid of $C_8F_{17}SO_3H$ is easily recovered and recycled at least five times.

Keywords: Hydroamination; Fluorous biphase system; Brønsted acid; Cyclization; Heptadecafluorooctanesulfonic acid

1. Introduction

The nitrogen-containing heterocycles (e.g., pyrrolidines, piperidines, indolines, and quinolines) are found in a lot of natural products and designed compounds with various biological activities [1]. As a consequence, much attention has been paid to the synthesis of these molecules. In general, the direct intramolecular hydroamination reaction of unsaturated amines through the addition of an N–H bond across a carbon–carbon multiple bonds, offers an efficient, atom-economical and straightforward route to nitrogen-containing molecules [2]. Various approaches catalyzed by alkali metals [3], transition metals [4], organo-f-element metal complexes [5] and the Brønsted acid [6], have been extensively studied for this seemingly simple but challenging transformation. In a previous research, we described the use of a catalytic amount of superacid of trifluoromethane-sulfonic acid (TfOH) to carry out the intramolecular hydroamination of *N*-arylsulfonyl-2-allylanilines to produce indolines or quinoline [7]. In a continuation of our research, we found that the recoverable perfluorous superacid ($C_8F_{17}SO_3H$) could efficiently catalyze the intramolecular hydroamination of olefinic sulfonamines in the fluorous biphase system (FBS), which was reported by Hováth and Rábai in 1994 [8], bearing some potential advantages, such as simplification of work-up, easy separation of product, and reuse of the catalyst. This kind of fluorous technique has been utilized for a wide variety of reactions: such as oxidation [9], reduction [10], hydroboration [11], epoxidation [12], carbon–carbon bond forming reactions [13] and so on. Herein, we wish to report the results of this protocol for intramolecular hydroamination of unactivated olefines.

2. Results and discussion

In a preliminary experiment, intramolecular hydroamination of *N*-tosyl-2-allylaniline (**1a**) was performed in the presence of a catalytic amount of perfluorinated acid ($C_8F_{17}SO_3H$) in the fluorous biphase system, which toluene and hexane were used as the solvents of organic phase, and perfluorodecalin ($C_{10}F_{18}$, *cis*- and *trans*- mixture) as the fluorous solvent. We observed that the $C_8F_{17}SO_3H$ showed good solubility in the fluorous solvent and poor solubility in the mixture of organic solvents. Upon heating up to 95 °C, the organic phase was miscible with the fluorous phase and the

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Table 1
Effect of nitrogen protecting group on the hydroamination

Entry	PG	Substrate	Time (h)	Yield of **2** (%)[a]
1	Ts	**1a**	1	95
2	Ms	**1b**	1	88
3	Ns	**1c**	1	93
4	*m*-Ns	**1d**	1	91
5	*p*-Ns	**1e**	1	92
6	PhCO	**1f**	1	Trace
7	H	**1g**	24	0

Experment were performed on a 0.5 mol scale: **1** (0.5 mmol), $C_8F_{17}SO_3H$ (5 mmol%), perfluorodecalin (1 mL), toluene (1 mL) and hexane (0.33 mL).
[a] Isolated yield.

Table 2
Effect of different substituents of phenyl ring on the reaction

Entry	R	Substrate	Time (h)	Product (**2**)	Yield (%)[a]
1	CH_3O	**1h**	0.5	**2h**	94
2	CH_3	**1i**	1	**2i**	95
3	Br	**1j**	2	**2j**	91
4	Cl	**1k**	2	**2k**	91
5	F	**1l**	2.5	**2l**	90
6	NO_2	**1m**	5	**2m**	87

Experment were performed on a 0.5 mmol scale: **1** (0.5 mmol), $C_8F_{17}SO_3H$ (5 mol%), perfluorodecalin (1 mL), toluene (1 mL) and hexane (0.33 mL).
[a] Isolated yield.

reaction mixture became homogenous. The resulting mixture continued to reflux up to the completion of the reaction, the corresponding product *N*-tosyl-2-methylindoline (**2a**) was isolated in 95% yield in the presence of 5 mol% $C_8F_{17}SO_3H$ (Table 1, entry 1). The reduction of the catalyst loading (2 mol%) led to the lower yield (50%) in the same reaction conditions.

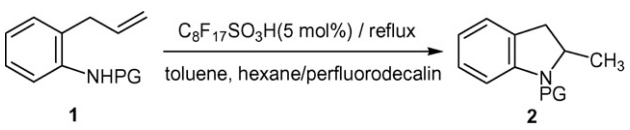
To elucidate the influence of the electronic properties of the different protecting groups of the nitrogen on the reaction, a series of *N*-protected-2-allylanilines (**1a–f**) were examined. The results are summarized in Scheme 1 and Table 1. After screening **1a–e**, it was found that all sulfonamides gave the cyclization products in good yields (Table 1, entries 1–5). *N*-Benzoyl-2-allyl-aniline (**1f**) gave only trace amount of cyclized product at refluxing in 1 h (Table 1, entry 6). While 2-allyl-aniline (**1g**) underwent this transformation, the starting material **1g** was not consumed at all even after 24 h (Table 1, entry 7). It seemed to be that the high Lewis basicity of free amine inhibited the reaction. But treated with excess acid (>1.0 equiv.), no cyclization reaction was proceeded and the superacid-promoted reaction underwent by other pathways [14]. To gain insight on the effect of the electron density of the phenyl ring of the aromatic amine, various *N*-tosyl-2-allylanilines bearing different substituents at the *para* position on the phenyl ring were readily prepared by the *N*-allylaniline Claisen rearrangements [1a,15] followed by sulfonylation with *p*-toluenesulfonyl chloride (TsCl). Under the above optimized reaction conditions, the different *para* substituted *N*-tosyl-2-allylanilines were transferred to substituted indolines in good to high yields, through a 5-*exo*-trig cyclization route favored by Baldwin's rules [16], as summarized in Scheme 2 and Table 2. The electron density of the phenyl ring had little effect on the reaction yields, but the aromatic amines with electron-withdrawing groups required longer reaction times than the electron-rich aromatic amines (Table 2, entries 1–5). It took the longest reaction time to finish the reaction of the very electron deficient alkene (**1m**) (Table 2, entry 6). It was attributed that the electron-withdrawing group decreased the electron density of the aromatic ring, and the substrate is not prone to protonation.

Then, we extended the cyclization to other tosylated amino olefins using $C_8F_{17}SO_3H$ (5 mol%) in FBS. As outlined in Table 3. Allylic tosylamide (**1n**) and homoallylic tosylamide (**1o-p**) did not undergo any reactions (Table 3, entries 1–3). We assume that the three-member or four-member ring is particularly disfavored to be formed due to their rigidity. Other acyclic substrates of tosylated γ-amino olefins (**1q** and **1r**) formed the five-member ring products through Markovnikov addition in high yields (Table 3, entries 4 and 5). In the cases of (**1s–v**) with an internal disubstituted double bond, the cyclization reaction was completely regiospecific through the benzyilic cation intermediate (Table 3, entries 6–9). Terminal monosubstituted olefins such as **1w** also was cyclized to afford a mixture of five- and six-member ring products in overall 95% yield (Table 3 entry 10).

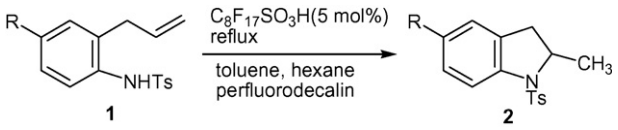
We further investigated the stereochemistry of the cyclization of the tosylated amino alkenes of **1x** and **1y** bearing stereocenters in the tether, which were prepared from styrene and β-methylstyrene [17]. Under the same reaction conditions, the racemic phenyl-substituted substrate **1y** cleanly gave the desired pyrrolidine as *trans-*/*cis-* mixture (91:9, determined by ^{1}H NMR) in 92% yield after 1 h with 5 mol% $C_8F_{17}SO_3H$. In a case of racemic substrate **1y**, the 2,3,5-trisubstituted pyrrolidine was producded as a sole isomer in 96% yield. The *trans*-isomer was obtained predominantly to indicate that the diastereoselectivity favored the thermodynamically more stable isomer (Scheme 3) and the stereochemistry is determined by 2D ^{1}H–^{1}H NOESY (see Supporting material).

Finally, recyclable peformance of $C_8F_{17}SO_3H$ was also investigated using **1a** as a substrate (Scheme 4 and Table 4). The fluorous catalytic phase was directly reused in the next reaction by combining with another mixture of reactants at least five times without loss of activity.

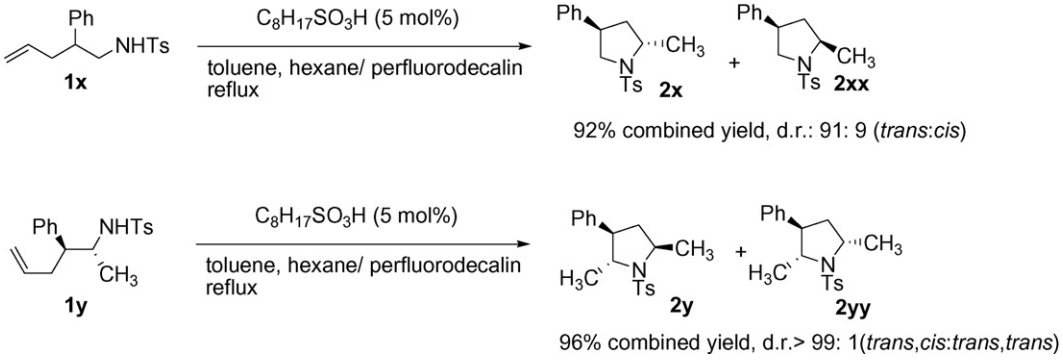
In conclusion, we report a novel catalytic alternative for the cyclization of olefinic sulfonamides to nitrogen-containing



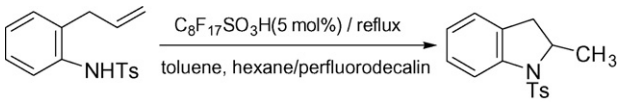
Scheme 1.



Scheme 2.



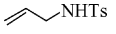
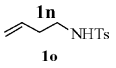
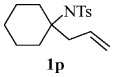
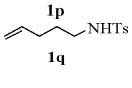
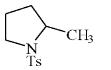
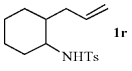
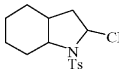
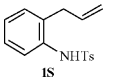
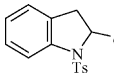
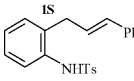
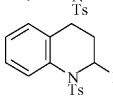
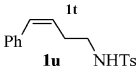
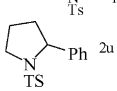
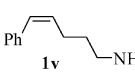
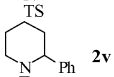
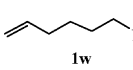
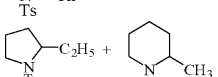
Scheme 3.



Scheme 4.

heterocycles in good to high yields, using a catalytic amount of commercially available $C_8F_{17}SO_3H$ as a catalyst. And this fluorous biphase system (FBS) approach offers an easy work-up procedure and good to high yield for the cyclization product under mild reaction conditions.

Table 3
$C_8F_{17}SO_3H$ catalyzed the cyclization reaction of tosylated amino olefins

Entry	Substrate	Product	Yield (%)[a]
1		–[b]	
2		–[b]	
3		–[b]	
4			97
5			94
6			79
7			83
8			91
9			88
10			95

Experment were performed on a 0.5 mmol scale: **1** (0.5 mmol), $C_8F_{17}SO_3H$ (5 mol%), perfluorodecalin (1 mL), toluene (1 mL) and hexane (0.33 mL), reflux, 1 h.

[a] Isolated yield.

[b] No desired product was observed.

3. Experimental

General: ^1H and ^{13}C NMR spectra were recorded on a Bruker DPX 300 MHz spectrometer (300 and 75 MHz, respectively) with TMS as an internal standard. Coupling constants are reported in Hertz (Hz). All ^{13}C NMR spectra were proton decoupled. Mass spectral analyzed was measured on a HP-5989. HRMS (EI) was measured on a Finnigan MA+. IR was measured on Perkin 983. Elemental analysis was determined on an Italian Carlo-Erba 110. The melting points were measure on a Melting point SGW X-4. All the products were purified by column chromatography on silica gel with ethyl acetate–hexane in an appropriate ratio as the eluent. Spectroscopic data and combustion or HRMS analyses are reported for all new compounds.

3.1. General procedure of $C_8F_{17}SO_3H$-catalyzed hydroamination of olefinic sulfonamides in FBS

$C_8F_{17}SO_3H$ (0.025 mmol) was added into a mixture of substrate (0.5 mmol), dry toluene (1 mL), hexane (0.33 mL) and perfluorodecalin (*cis*- and *trans*- mixture, 1 mL). The reaction mixture was stirred and heated to reflux. At the end of the reaction, the reaction mixture was cooled to room temperature and settled down for 2 min. The mixture was separated into two liquid phases. The upper organic layer afforded the corresponding product by silica gel column chromatography (hexane:AcOEt = 10:1), while the lower fluorous phase containing the catalyst was used in subsequent reaction.

Table 4
Recycling performance of $C_8F_{17}SO_3H$ in FBS

Run	Catalyst loading (mol%)	Time (h)	Yield (%)[a]
1	5	1	95
2	5	1	95
3	5	1	93
4	5	1	94
5	5	1.5	92

Experment were performed on a 2.5 mmol scale: **1** (2.5 mmol), $C_8F_{17}SO_3H$ (5 mol%), perfluorodecalin (5 mL), toluene (5 mL) and hexane (1.67 mL).

[a] Isolated yield.

3.2. 2-Methyl-1-(toluene-4-sulfonyl)-2,3-dihydro-1H-indole (**2a**) [18]

White solid; 95% yield; mp 63–64 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.66–7.64 (m, 1H), 7.56–7.53 (m, 2H), 7.26–6.98 (m, 5H), 4.35 (ddq, J = 3, 6.6, 9.6 Hz, 1H), 2.89 (dd, J = 9.6, 15.9 Hz, 1H), 2.43 (dd, J = 3.0, 15.9 Hz, 1H), 2.34 (s, 3H), 1.42 (d, J = 6.6 Hz, 3H).

IR (KBr): υ 3067, 2966, 2925, 2855, 1599, 1479, 1461, 1352, 1167, 1103, 1091, 814, 756 cm^{-1}.

3.3. Methylanesulfonyl-2-methyl-2,3-dihydro-1H-indole (**2b**) [19]

White solid; mp 58–59 °C; 88% yield; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42–7.02 (m, 4H), 4.44 (ddq, J = 3.6, 6.6, 9.6 Hz, 1H), 3.45 (dd, J = 9.6, 16.2 Hz, 1H), 2.70 (dd, J = 3.6, 16.2 Hz, 1H), 2.41 (s, 3H), 1.45 (d, J = 6.6 Hz, 3H).

IR (KBr): υ 3015, 2970, 2929, 2852, 1602, 1479, 1460, 1346, 1159, 961, 767 cm^{-1}.

3.4. 2-Methyl-1-(2-nitro-benzenesulfonyl)-2,3-dihydro-1H-indole (**2c**) [20]

White solid; 93% yield; mp 107–108 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85–7.03 (m, 8H), 4.71 (m, 1H), 3.29 (m, 1H), 2.58 (m, 1H), 1.40 (d, J = 6.3Hz, 3H).

IR (KBr): υ 3096, 2922, 2851, 1592, 1545, 1478, 1371, 1172, 1126, 756, 597.

3.5. 2-Methyl-1-(3-nitro-benzenesulfonyl)-2,3-dihydro-1H-indole (**2d**) [20]

White solid; 91% yield; mp 104–105 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56–7.06 (m, 8H), 4.42 (ddq, J = 2.7, 6.3, 9.3 Hz, 1H), 2.94 (dd, J = 9.3, 16.2 Hz, 1H), 2.52 (dd, J = 2.7, 16.2 Hz, 1H), 1.47 (d, J = 6.3Hz, 3H).

IR (KBr): υ 3082, 2926, 1605, 1533, 1479, 1352, 1176, 1127, 762 cm^{-1}.

3.6. 2-Methyl-1-(4-nitro-benzenesulfonyl)-2,3-dihydro-1H-indole (**2e**) [20]

White solid; 92% yield; mp 137–138 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23 (d, J = 8.7 Hz, 2H), 7.87 (d, J = 8.7 Hz, 2H), 7.69–7.66 (m, 1H), 7.27–7.07 (m, 3H), 4.37 (ddq, J = 2.4, 6, 9.3 Hz, 1H), 2.91 (dd, J = 9.3, 16.2 Hz, 1H), 2.50 (dd, J = 2.4, 16.2 Hz, 1H), 1.46 (d, J = 6Hz, 3H).

IR (KBr): υ 3104, 2958, 2924, 2853, 1604, 1531, 1349, 1309, 1171, 1087, 740 cm^{-1}.

3.7. (2-Methyl-2, 3-dihydro-indol-1-yl)-phenyl-methanone (**2f**) [21]

White solid; trace yield; mp 92–93 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (m, 5H), 7.22 (m, 2H), 7.02 (m, 2H), 4.75 (m, 1H), 3.42 (m, 1H), 2.65 (m, 1H), 1.25 (d, J = 4.8 Hz, 3H).

IR (KBr): υ 3059, 2956, 2920, 2850, 1640, 1598, 1481, 1390, 1288, 756, 701 cm^{-1}.

3.8. 5-Methoxyl-1-(toluene-4-sulfonyl)-2,3-dihydro-1H-indole (**2h**) [20]

White solid; 94% yield; mp 76–77 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58–7.48 (m, 3H), 7.15 (m, 2H), 6.77–6.60 (m, 2H), 4.36–4.27 (m, 1H), 3.76 (s, 3H), 2.78–2.70 (m, 1H), 2.40–2.30 (m, 4H), 1.38 (d, J = 6.6 Hz, 3H).

IR (KBr): υ 3030, 2926, 2836, 1736, 1597, 1489, 1351, 1164, 1090, 1033, 813, 750, 669 cm^{-1}.

3.9. 5-Methyl-1-(toluene-4-sulfonyl)-2,3-dihydro-1H-indole (**2i**) [20]

White solid; mp 64–65 °C; 96% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55–7.52 (m, 3H), 7.16–6.85 (m, 4H), 4.31 (ddq, J = 2.7, 6.6, 9.6 Hz, 1H), 2.81 (dd, J = 9.6, 15.9 Hz, 1H), 2.39 (dd, J = 2.7, 15.9 Hz, 4H), 2.34 (m, 3H), 2.27 (s, 3H), 1.40 (d, J = 6.6Hz, 3H).

IR (KBr): υ 2957, 2924, 2853, 1597, 1486, 1349, 1164, 1090, 983, 813, 666, 614, 584, 542 cm^{-1}.

3.10. 5-Bromo-1-(toluene-4-sulfonyl)-2,3-dihydro-1H-indole (**2j**) [20]

White solid; 90% yield; mp 84–85 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53–7.51 (m, 3H), 7.33–7.30 (m, 1H), 7.20–7.17 (m, 3H), 4.33 (ddq, J = 2.4, 6.3, 9.3 Hz, 1H), 2.82 (dd, J = 9.3, 15.9 Hz, 1H), 2.42 (dd, J = 2.4, 15.9 Hz, 4H), 2.36 (s, 3H), 1.42 (d, J = 6.3 Hz, 3H).

IR (KBr): υ 2957, 2924, 2853, 1736, 1597, 1470, 1353, 1168, 1097, 814, 725, 666, 581, 540 cm^{-1}.

3.11. 5-Chloro-1-(toluene-4-sulfonyl)-2,3-dihydro-1H-indole (**2k**) [20]

White solid, 91% yield; mp 81–82 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58–7.53 (m, 3H), 7.19–7.01 (m, 4H), 4.34 (m, 1H), 2.85 (m, 1H), 2.43–2.35 (m, 4H), 1.41 (d, J = 6.6 Hz, 3H).

IR (KBr): υ 2963, 2927, 2852, 1598, 1472, 1353, 1165, 1090, 814, 666, 582 cm^{-1}.

3.12. 5-Fluoro-1-(toluene-4-sulfonyl)-2,3-dihydro-1H-indole (**2l**) [20]

White solid; 91% yield; mp 116–117 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62–7.50 (m, 3H), 7.19–7.16 (m, 2H), 6.93–6.74 (m, 2H), 4.36 (m, 1H), 2.80 (m, 1H), 2.41–2.34 (m, 4H), 1.40 (d, J = 6.6 Hz, 3H).

IR (KBr): υ 2970, 2926, 2859, 1594, 1481, 1348, 1164, 1084, 668, 589 cm^{-1}.

3.13. 5-Nitro-1-(toluene-4-sulfonyl)-2,3-dihydro-1H-indole (**2m**) [20]

White solid; 87% yield; mp 122–123 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (m, 1H), 7.94 (m, 1H), 7.72–7.63 (m, 3H), 7.26–7.23 (m, 2H), 4.49 (ddt, J = 3.3, 6.6, 9.6 Hz, 1H), 3.12 (dd, J = 9.6, 16.2 Hz, 1H), 2.63 (dd, J = 3.3, 16.2 Hz, 1H), 2.38 (s, 3H), 1.50 (d, J = 6.6Hz, 3H).

IR (KBr): υ 3089, 2970, 2927, 2852, 1712, 1598, 1518, 1338, 1166, 1074, 749, 666 cm^{-1}.

3.14. 2-Methyl-1-(toluene-4-sulfonyl)-pyrrolidine (**2q**) [14]

White solid; 97% yield; mp 94–95 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (d, J = 8.1 Hz, 2H), 7.29 (d, J = 8.1 Hz, 2H), 3.72–3.66 (m, 1H), 3.46–3.39 (m, 1H), 3.17–3.09 (m, 1H), 2.41 (s, 3H), 1.86–1.44 (m, 4H), 1.30 (d, J = 6.3 Hz, 3H).

IR (KBr): υ 2966, 2927, 1597, 1460, 1341, 1158, 1092, 661, 549 cm^{-1}.

3.15. 2-Methyl-1-(toluene-4-sulfonyl)-octahydro-indole (**2r**)

White solid; 94% yield; mp 58–59 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75–7.71 (m, 2H), 7.32–7.25 (m, 2H), 3.83 (m, 1H), 3.63-3.50 (m, 1H), 2.42 (s, 3H), 2.27–1.05 (m, 14H).

IR (KBr): υ 2927, 2861, 1599, 1449, 1337, 1161, 1095, 664 cm^{-1}; ESI calculated for $C_{16}H_{23}NO_2S$ [M + Na^{+1}] 316.1344; found 316.1342. Anal. Calcd. for $C_{16}H_{23}NO_2S$: C, 65.49; H, 7.90; N, 4.77; Found: C, 65.56; H, 8.00; N, 4.62.

3.16. 2-Phenyl-1-(toluene-4-sulfonyl)-2,3-dihydro-1H-indole (**2s**) [20]

White solid; 79% yield; mp 101–102 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72–7.52 (m, 3H), 7.29–7.03 (m, 10H), 5.42 (dd, J = 2.7, 10.2 Hz, 1H), 3.26 (dd, J = 10.2, 16.2 Hz, 1H), 2.86 (dd, J = 2.7, 16.2 Hz, 1H), 2.34 (s, 3H).

IR (KBr): υ 3064, 3031, 2920, 2852, 1598, 1494, 1478, 1460, 1355, 1168, 1091, 1028, 814, 756, 576 cm^{-1}.

3.17. 2-Phenyl-1-(toluene-4-sulfonyl)-1,2,3,4-tetrahydro-quinoline (**2t**) [20]

White solid; 83% yield; mp 109–110 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89–7.86 (m, 1H), 7.44–6.94 (m, 12H), 5.35 (t, J = 7.2 Hz, 1H), 2.38 (s, 3H), 2.35–2.29 (m, 1H), 2.23–2.12 (m, 1H), 1.89–1.72 (m, 2H).

IR (KBr): υ 3062, 3029, 2948, 2844, 1599, 1486, 1454, 1347, 1164, 1090, 972, 813, 759, 660, 584, 570, 549 cm^{-1}.

3.18. 2-Phenyl-1-(toluene-4-sulfonyl)-pyrrolidine (**2u**) [22]

White solid; 91% yield; mp 102–103 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68–7.66 (m, 2H), 7.31–7.22 (m, 7H), 4.81–4.77 (m, 1H), 3.65–3.58 (m, 1H), 3.47–3.39 (m, 1H), 2.42 (s, 3H), 2.00–1.56 (m, 4H).

IR (KBr): υ 2975, 2873, 1598, 1494, 1346, 1159, 1094, 667, 588 cm^{-1}.

3.19. 2-Phenyl-1-(toluene-4-sulfonyl)-piperidine (**2v**) [22]

White solid; 88% yield; mp 136–137 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79–7.75 (m, 2H), 7.35–7.10 (m, 7H), 5.27 (m, 1H), 3.85 (m, 1H), 3.01 (m, 1H), 2.44 (s, 3H), 1.69–1.30 (m, 6H).

IR (KBr): υ 2940, 1449, 1337, 1155, 1103, 946, 722, 665 cm^{-1}.

3.20. 2-Ethyl-1-(toluene-4-sulfonyl)-pyrrolidine (**2w**) [23] and 2-methyl-1-(toluene-4-sulfonyl)-piperidine (**2ww**) [23]

They were obtained as a mixture. Since they were difficult to isolate from each other, the measurement of ^{1}H NMR was carried out for the mixtures. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73–7.26 (m, 8H), 4.25–4.23 (m, 1H), 3.73–3.69 (m, 1H), 3.56–3.52 (m, 1H), 3.42–3.34 (m, 1H), 3.23–3.17 (m, 1H), 3.02–2.94 (m, 1H), 2.42 (s, 3 H), 2.41 (s, 3H), 1.90–1.49 (m, 12H), 1.06 (d, J = 7.2 Hz, 3H), 0.91 (t, J = 7.8 Hz, 3H).

3.21. 2-Methyl-4-phenyl-1-(toluenesulfonyl)-pyrrolidine (**2x + 2xx**)

White solid; 92% yield; mp 83–84 °C; mixture of *trans*-, *cis*-isomers: 91:9 (^{1}H NMR). The relative stereochemistry was determined by NOESY-experiment. ^{1}H NMR (300 MHz, $CDCl_3$) (mixture of *syn* and *anti* isomers): δ 7.78 (d, J = 8.2 Hz, 0.91 H) (*anti*), 7.75 (d, J = 8.2 Hz, 0.09H) (*syn*), 7.35 (d, J = 8.2 Hz, 0.91 H) (*anti*), 7.30 (m, 0.09 H) (*syn*), 7.25 (d, J = 7.2 Hz, 0.91H) (*anti.*), 7.20 (m, 0.09 H) (*syn*), 7.10 (d, J = 7.2 Hz, 0.91H) (*anti*), 7.05 (d, J = 7.2 Hz, 0.09H), 3.95 (m, 0.09 H) (*syn*), 3.80 (m, 0.91 H) (*anti*), 3.70 (m, 0.91H) (*anti*), 3.55 (m, 0.09 H) (*syn*), 3.39 (t, J = 11.2 Hz, 0.91 H) (*anti*), 3.00 (t, J = 11.2 Hz, 0.09 H) (*syn*), 2.68 (m, 1H), 2.43 (s, 3 H), 2.32 (m, 1H), 1.85 (m, 0.09 H) (*syn*), 1.74 (m, 0.91 H) (*anti*), 1.48 (d, J = 6.2 Hz, 2.73 H) (*anti*), 1.42 (d, J = 6.2 Hz, 0.27 H) (*syn*).

^{13}C NMR (75 MHz, $CDCl_3$) (mixture of *syn* and *anti* isomers): δ 18.0 (*syn*), 21.4 (*anti*), 22.5 (*anti*), 23.4 (*syn*), 39.7 (*syn*), 41.5 (*syn*), 42.1 (*anti*), 42.8 (*anti*), 55.0 (*anti*), 55.9 (*syn*), 56.9 (*anti*), 60.0 (*syn*), 126.8 (*anti*), 127.3 (*anti*), 128.5 (*anti*), 129.6 (*anti*), 132.0 (*syn*), 135.3 (*syn*), 139.6 (*syn*), 143.3 (*syn*).

IR (KBr): υ 2967, 1598, 1495, 1341, 1160, 1090 cm^{-1}.

ESI-LRMS: m/z 316.2 (M + 1)$^+$.

Anal. Calcd. for $C_{18}H_{21}NO_2S$: C, 68.54; H, 6.71; N, 4.44. Found: C, 68.78; H, 6.50; N, 4.28.

3.22. (Trans,cis)-2,5-dimethyl-3-phenyl-1-(toluenesulfonyl)-pyrrodiline (**2y**)

White solid; 96% yield; mp 120–121 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, J = 8.1 Hz, 2H), 7.31–7.20 (m, 5H), 7.15 (d, J = 8.1 Hz, 2H) 4.12–4.01 (m, 1H), 3.95–3.86

(m, 1H), 2.83–2.75 (m, 1H), 2.54–2.47 (m, 1H), 2.43 (s, 3H), 1.74–1.64 (m, 1H), 1.39 (d, J = 6.6 Hz, 3H), 1.29 (d, J = 6 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 142.7, 141.6, 140.2, 129.5, 128.6, 127.5, 127.0, 126.9, 63.2, 56.6, 52.0, 41.8, 21.7, 21.5, 19.2.

IR (KBr): υ 2970, 2929, 1600, 1495, 1335, 1165, 1091; MS (EI) (m/z) 329, 314, 238, 174, 155, 91 $cm^{-1.}$

MALDI-HMRS m/z calcd. for $C_{19}H_{24}NO_2S$ $[M + H^+]$: 330.1529; found: 330.1522.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/jfluchem.2006.09.012.

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