Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Iron-Catalyzed desulfinylative Cross-Coupling Reactions of Sulfonyl Chlorides with Grignard Reagents

Chandra M. Rao Volla and Pierre Vogel*

Corresponding Author: Prof. Pierre Vogel

Laboratory of Glycochemistry and Asymmetric Synthesis,

Institute of Molecular and Biological Chemistry,

Swiss Institute of Technology,

BCH CH-1015 Lausanne (Switzerland)

Tel: +41.21.693.93.71

Fax: +41.21.693.93.75

E-mail: Pierre.vogel@epfl.ch

Methods: Unless stated otherwise, reactions were conducted in flame-dried glassware under a vacuum. THF was distilled before to use from sodium and benzophenone. Solvents after reactions and extraction were evaporated in a rotatory evaporator under vacuum (solvents were removed cooling at – 20 °C, in the case of low boiling point or low molecular mass compounds). No effort has been taken to improve yields, especially for low boiling products that are co-distilled, in this operation, with solvent. TLC for reaction monitoring was performed on 60 F_{254} (Merck) with detection by UV light and charring with $KMnO_4$ or Pancaldi reagent. ^{1}H and ^{13}C NMR spectra were recorded by using Bruker-DPX-400, or Bruker-ARX-400 spectrometer at 400 MHz and 100.6 MHz respectively and are reported relative to Me_4Si (d 0.0) or to the solvents residual ^{1}H-signal ($CH\text{-}Cl_3$, d(H) 7.27). Data for ^{1}H NMR spectra are reported as follows: Chemical shift (d ppm), multiplicity, coupling constant (Hz) and integration. Data for ^{13}C NMR spectra reported in terms of chemical shift. IR spectra were recorded on a Perkin-Elmer-1420 spectrometer and are reported in frequency of absorption (cm^{-1}). High Resolution MALDI-TOF mass spectra were obtained from the Institute of Molecular and Biology Chemistry, Swiss Institute of Technology Mass Spectral Facility, EPFL, Lausanne.

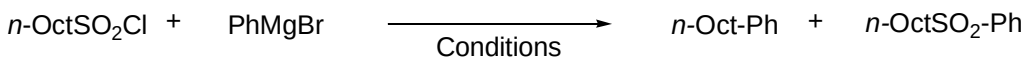
Product identification was carried out by comparison with purchased samples : Butylbenzene (Fluka), octylbenzene (Acros Chemicals), decylbenzene (Sigma-aldrich), decene (Sigma-aldrich), diphenylmethane (Fluka), cumene (Sigma-aldrich), *p*-cymene (Acros Chemicals), (*E*)-stilbene (Sigma-aldrich).

Materials: Iron acetylacetonate and iron chloride were purchased from Strem Chemicals and Acros respectively. Grignard reagents were purchased from Sigma-aldrich except for 1-naphthylmagnesium bromide (Acros Chemicals). Butane- and octanesulfonyl chlorides were purchased from Acros Chemicals. Decane-, hexadecane- and benzylsulfonyl chlorides were purchased from Alfa. 2-Propane- and camphorsulfonyl chlorides were from Fluka. Cyclopentane- and cyclohexanesulfonyl chlorides were purchased from Aldrich and 2-(1-napthyl)ethanesulfonyl chloride was purchased from TCI Chemicals. 2-Butanesulfonyl chloride was prepared following a literature procedure. [1]

[1] Y. J. Park, H. H. Shin, Y. H. Kim, *Chem. Lett.* **1992**, 1483.

Typical Experimental Procedure for Iron catalyst : In a round bottom flask dried under *vacuum* were placed under nitrogen atmosphere, the corresponding sulfonyl chloride (1 equiv.), $Fe(acac)_3$ (5 mol%) were weighed in a glove box. Then, flask connected to a *vacuum* line and filled with an argon (3 times), THF (5 mL) and NMP (2 mL) were added under an argon. The corresponding Grignard reagent (2- 3 equiv.) in 1 molar THF solution was added by a syringe pump with a rate of 2 mL per hour at 80 ^{o}C. The reaction mixture was stirred under reflux for 2 h. After cooling to room temperature, the mixture was quenched with sat. aq. soln. of NH_4Cl and diluted with ether. The aqueous layer was extracted again with ether (3 times). The combined organic phases were dried ($MgSO_4$), filtered and concentrated under reduced pressure (rotavap). The residue was purified by flash chromatography on silica gel eluting with pentane. Solvent evaporation was done on a rotavap, which was detrimental for the yields of products of low molecular weight.

Table 1. Optimization of catalyst and solvent in iron-catalyzed cross-coupling of aliphatic sulfonyl chloride.[a]



Entry	Conditions	Cross-coupled product [b]	Sulfone [b]
1	No catalyst, 0 ^{o}C to rt, THF	-	76 %
2	$Fe(acac)_3$ (5 mol%), THF, 80 ^{o}C [c]	28 %	5 %
3	$FeCl_3$ (10 mol%), TMEDA(2 eq), THF, 80 ^{o}C [d]	-	-
4	$Fe(acac)_3$ (5 mol%), THF, 80 ^{o}C [e]	16 %	48 %
5	$Fe(acac)_3$ (5 mol %), TMEDA (10 mol %),THF, 80 ^{o}C [f]	58 %	-
6	$Fe(acac)_3$ (5 mol%), HMTA (10 mol %), THF, 80 ^{o}C [f]	65 %	-
7	$Fe(acac)_3$ (5 mol%), THF, NMP, 80 ^{o}C [f]	72 %	-

[a] **Reaction conditions:** 1.0 equiv. of octanesulfonyl chloride (1.18 mmol), iron catalyst and ligand, THF (5 mL)

and co-solvent (2 mL), 2.0-3.0 equiv. of phenylmagnesium bromide solution in Et_2O (0.8 mL of 3.0 M soln. in Et_2O, 2.36 mmol), reflux for a total of 2 hrs. [b] Determined after flash chromatography. [c] Grignard reagent was added at once. [d] Starting material was decomposed and no cross-coupled product or sulfone was observed. [e] Reaction was done in a microwave reactor, Grignard reagent was added to the reaction at -78 ^{o}C and was heated for 1.5 h at 80 ^{o}C. [f] Grignard reagent was added slowly (2 ml per hour).

Phenylbutane (Table 2, entry 1) : Following the Typical Experimental Procedure using 0.5 g (3.65 mmol) of butanesulfonyl chloride, 3 mL of phenylmagnesium bromide (3.0 M solution in Et_2O), 0.3 g (61 %) of product was obtained as colorless oil.

Phenyloctane (Table 2, entry 2) : Following the Typical Experimental Procedure using 0.25 g (1.18 mmol) of octanesulfonyl chloride, 1.2 mL of phenylmagnesium bromide (3.0 M solution in Et_2O), 0.161 g (72 %) of product was obtained as colorless oil.

Phenyldecane (Table 2, entry 3) : Following the Typical Experimental Procedure using 0.25 g (1.04 mmol) of decanesulfonyl chloride, 1 mL of phenylmagnesium bromide

(3.0 M solution in Et_2O), 0.12 g (54 %) of product was obtained as colorless oil.

Phenylhexadecane (Table 2, entry 4) : Following the Typical experimental Procedure using 0.25 g (0.77 mmol) of hexadecanesulfonyl chloride, 0.8 mL of phenylmagnesium bromide (3.0 M solution in Et_2O), 0.11 g (47 %) of product was obtained as colorless oil.

Decene (Table 2, entry 5) : Following the Typical Experimental Procedure using 0.5 g (2.36 mmol) of octanesulfonyl chloride, 7 mL of vinylmagnesium bromide (1.0 M solution in THF), 0.076 g (23 %) of product was obtained as colorless oil.

2-Methyldec-1-ene (Table 2, entry 6) : Following the Typical Experimental Procedure using 0.25 g (1.18 mmol) of octanesulfonyl chloride, 7 mL of isopropenylmagnesium bromide (0.5 M solution in THF), 0.09 g (46 %) of product was obtained as colorless oil. Its spectral data were identical to those reported for this compound. [2]

2-Methylundec-2-ene (Table 2, entry 7) : Following the Typical Experimental Procedure using 0.25 g (1.18 mmol) of octanesulfonyl chloride, 7 mL of 2-methyl-1-propenylmagnesium bromide (0.5 M solution in THF), 0.07 g (35 %) of product was obtained as colorless oil. Its

[2] Farhat, S.; Zouev, I.; Marek, I. *Tetrahedron* **2004**, 1329.

spectral data were identical to those reported for this compound. [3]

1-Methyl-4-octylbenzene (Table 2, entry 8) : Following the Typical Experimental Procedure using 0.25 g (1.18 mmol) of octanesulfonyl chloride, 3.6 mL of *p*-tolylmagnesium bromide (1.0 M solution in THF), 0.163 g (68 %) of product was obtained as colorless oil. Its spectral data were identical to those reported for this compound. [4]

1-Methoxy-4-octylbenzene (Table 2, entry 9) : Following the Typical Experimental Procedure using 0.25 g (1.18 mmol) of octanesulfonyl chloride, 7 mL of 4-methoxyphenylmagnesium bromide (0.5 M solution in THF), 0.212 g (82 %) of product was obtained as colorless oil. Its spectral data were identical to those reported for this compound. [5]

Diphenylmethane (Table 2, entry 11) : Following the Typical Experimental Procedure using 0.2 g (1.1 mmol) of benzylsulfonyl chloride, 1 mL of phenylmagnesium bromide

---

[3] Ishihara, K.; Kubota, M.; Kurihara, H.; Yamamota, H. *J. Org. Chem.* **1996**, *61*, 4560.

[4] Bedford, R. B.; Betham, M.; Bruce, D. W.; Danopoulos A. A.; Frost, R. M.; Hird, M. *J. Org. Chem.* **2006**,*71*, 1104.

[5] Brenstrum, T.; Gerristma, D. A.; Adjabeng, G. M.; Frampton, C. S.; Britten, J.; Robertson, A. J.; McNulty, J.; Capretta, A. *J. Org. Chem.* **2004**, *69*, 7635.

(3.0 M solution in Et_2O), 0.102 g (55 %) of product was obtained as colorless oil.

1-Benzyl-4-methylbenzene (Table 2, entry 12) : Following the Typical Experimental Procedure using 0.2 g (1.1 mmol) of benzylsulfonyl chloride, 3 mL of p-tolylmagnesium bromide (1.0 M solution in THF), 0.110 g (58 %) of product was obtained as colorless oil. Its spectral data were identical to those reported for this compound. [6]

Phenyldecane (Table 2, entry 13) : Following the Typical Experimental Procedure using 0.25 g (1.18 mmol) of octanesulfonyl chloride, 3 mL of phenethylmagnesium chloride (1.0 M solution in THF), 0.015 g (6 %) of product was obtained as colorless oil.

1-(1-Naphthyl)-2-phenylethane (Table 2, entry 15) : Following the Typical Experimental Procedure using 0.5 g (2.0 mmol) of 2-(1-naphthyl)ethanesulfonyl chloride, 2 mL of phenylmagnesium bromide (3.0 M solution in Et_2O), 0.362 g (78 %) of product was obtained as colorless oil. Its spectral data were identical to those reported for this compound. [7]

Cumene (Table 2, entry 17) : Following the Typical Experimental Procedure using 0.5 g (3.50 mmol) of isopropanesulfonyl chloride, 3 mL of phenylmagnesium

[6] Molander, G. A.; Elia, M. D.; *J. Org. Chem.* **2006**, *71*, 9198.

[7] Molander, G. A.; Yun, C-S.; *Tetrahedron* **2002**, *58*, 1465.

bromide (3.0 M solution in Et_2O), 0.101 g (24 %) of product was obtained as colorless oil.

Cymene (Table 2, entry 18) : Following the Typical Experimental Procedure using 0.5 g (3.50 mmol) of isopropanesulfonyl chloride, 9 mL of *p*-tolylmagnesium bromide (1.0 M solution in THF), 0.136 g (29 %) of product was obtained as colorless oil.

1-*sec*-Butyl-4-methylbenzene (Table 2, entry 19) : Following the Typical Experimental Procedure using 0.5 g (3.65 mmol) of butane-2-sulfonyl chloride, 9 mL of *p*-tolylmagnesium bromide (1.0 M solution in THF), 0.345 g (64 %) of product was obtained as colorless oil. Its spectral data were identical to those reported for this compound. [8]

1-*sec*-Butylbenzene (Table 2, entry 20) : Following the Typical Experimental Procedure using 0.5 g (3.65 mmol) of butane-2-sulfonyl chloride, 3 mL of phenylmagnesium bromide (3.0 M solution in Et_2O), 0.278 g (57 %) of product was obtained as colorless oil. Its spectral data were identical to those reported for this compound. [9]

Phenylcyclopentane (Table 2, entry 21) : Following the Typical Experimental Procedure using 0.25 g (1.50 mmol) of cyclopentanesulfonyl chloride, 1.5 mL of phenylmagnesium bromide (3.0 M solution in Et_2O), 0.138 g (63 %) of product

[8] Lee, P. H.; Lee, S. W.; Seomoon, D. *Org. Lett.* **2003**, *5*, 4963.

[9] Barton, D. H.; Bohe, L.; Lusinchi, X. *Tetrahedron*, **1990**, *46*, 5273.

was obtained as colorless oil. Its spectral data were identical to those reported for this compound. [10]

1-Cyclopentyl-4-methoxybenzene (Table 2, entry 22) : Following the Typical Experimental Procedure using 0.25 g (1.50 mmol) of cyclopentanesulfonyl chloride, 9.0 mL of 4-methoxyphenylmagnesium bromide (0.5 M solution in THF), 0.187 g (71 %) of product was obtained as colorless oil. Its spectral data were identical to those reported for this compound. [11]

Phenylcyclohexane (Table 2, entry 23) : Following the Typical Experimental Procedure using 0.25 g (1.37 mmol) of cyclohexanesulfonyl chloride, 1.3 mL of phenylmagnesium bromide (3.0 M solution in Et_2O), 0.148 g (68 %) of product was obtained as colorless oil.

(Prop-1-en-2-yl)cyclohexane (Table 2, entry 24) : Following the Typical Experimental Procedure using 0.25 g (1.37 mmol) of cyclohexanesulfonyl chloride, 8 mL of isopropenylmagnesium bromide (0.5 M solution in THF), 0.082 g (48 %) of product was obtained as colorless oil. Its spectral data were identical to those reported for this compound. [12]

---

[10] Marvell, E. N.; Lin, C. *J. Am. Chem. Soc.* **1978**, *100*, 877.

[11] Gonzalez-Bobes, F.; Fu, G. C. *J. Am. Chem. Soc.* **2006**, *128*, 5360.

[12] Olah, G. A.; Reddy, V. P.; Prakash, G. K. S. *Synthesis* **1991**, 29.

(*E*)-1-(Oct-1-enyl)benzene (Table 2, Entry 25) : Following the Typical Experimental Procedure using 0.25 g (1.24 mmol) of β-styrenesulfonyl chloride, 1.3 mL of hexylmagnesium bromide (2.0 M solution in Et_2O), 0.158 g (68 %) of product was obtained as colorless oil.[13]

(*E*)-1-(Dec-1-enyl)benzene (Table 2, Entry 26) : Following the Typical Experimental Procedure using 0.25 g (1.24 mmol) of β-styrenesulfonyl chloride, 1.3 mL of octylmagnesium bromide (2.0 M solution in Et_2O), 0.163 g (61 %) of product was obtained as colorless oil.[14]

(*E*)-Stilbene (Table 2, Entry 27) : Following the Typical Experimental Procedure using 0.25 g (1.24 mmol) of β-styrenesulfonyl chloride, 0.85 mL of phenylmagnesium bromide (3.0 M solution in Et_2O), 0.123 g (55 %) of product was obtained as white solid.

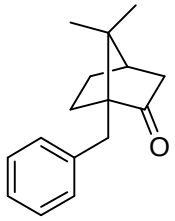
---

[13] Wang, Z.; Zhang, G.; Guzei, I.; Verkade, J. G. *J. Org. Chem.* **2001**, *66*, 3521.

[14] Farhat, S.; Zouev, I.; Marek, I. *Tetrahedron*, **2004**, *60*, 1329.

Typical Experimental Procedure for the coupling of camphorsulfonyl chloride with aromatic Grignard reagents : In a round bottom flask dried under *vacuum* were placed under nitrogen atmosphere, (-)-10-camphor sulfonyl chloride (1.00 mmol), $Fe(acac)_3$ (0.05 mmol) were weighed in a glove box. Then, flask connected to a *vacuum* line and filled with argon (3 times), THF (5 mL) and NMP (2 mL) were added under argon. The corresponding Grignard reagent (3.00 mmol) was added by a syringe pump with a rate of 2 mL per hour at 80 ^{o}C. The reaction mixture was stirred under reflux for 2 h. After cooling to room temperature, the mixture was quenched with sat. aq. soln. of NH_4Cl and diluted with ether. The aqueous layer was extracted again with ether (3 times). The combined organic phases were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel. Solvent evaporation was done on a rotavap.

1-Benzyl-7,7-dimethylbicyclo[2.2.1]heptan-2-one (Table 2, Entry 28) : Following the Typical Experimental procedure using 0.25 g (1.00 mmol) of (-)-10-camphorsulfonyl chloride, 1 mL of phenylmagnesium bromide (3.0 M solution in Et_2O), 0.078 g of product was obtained.



Colorless oil, R_f = 0.65 (pentane).

[a] $^{25}_{589}$ = -42 (c = 0.1, $CHCl_3$)

IR (film) : 3026, 2958, 1741, 1495, 1453, 1417, 1047, 748, 702 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ= 7.29- 7.35 (m, 3H, Ph), 7.21-7.26 (m, 2H, Ph), 2.98 (d, ^2J = 13.9 Hz, 1H, $\underline{CH_2}$-Ph), 2.61 (d, ^2J = 13.9 Hz, 1H, $\underline{CH_2}$-Ph), 2.37 (ddd, ^2J = 18.2 Hz, ^3J = 4.5 Hz, ^4J = 2.8 Hz, 1H, H- C(3)), 2.03 (t, ^3J = 4.5 Hz, 1H, H- C(4)), 1.88 (m, 1H, H- C(5)), 1.85 (d, ^2J = 18.2 Hz, 1H, H- C(3)), 1.77 (td, ^2J = ^3J = 12.7 Hz, ^3J = 3.1 Hz, 1H, H- C(6)), 1.18 – 1.35 (m, 2H, H- C(4), H- C(5)), 0.93 (s, 3H, Me- C(7)), 0.85 (s, 3H, Me- C(7)).

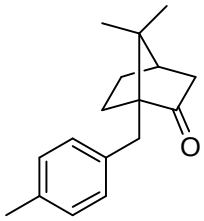
^{13}C NMR (100.6 MHz, $CDCl_3$): 218.9, 139.1, 130.6, 127.8, 125.8, 68.7, 43.6, 43.2, 34.6, 31.6, 27.4, 26.8, 20.3, 19.8.

CI-MS (NH_3): m/z = 229 (39, $[M+1]^+$), 228 (14, $[M]^+$), 184 (15, $[M-44]^+$), 171 (14, $[M-57]^+$), 229 (39, $[M+1]^+$), 91 (100, $[M-137]^+$), 77 (13, $[M-151]^+$).

MALDI-HRMS : Calcd. for $C_{16}H_{21}O^+$ 229.1592, found 229.1587.

7,7-Dimethyl-1-(4-methylbenzyl)bicyclo[2.2.1]heptan-2-one (Table 2, Entry 29) : Following the Typical Experimental procedure using 0.25 g (1.00 mmol) of (-)-10-camphorsulfonyl chloride, 3 mL of *p*-tolylmagnesium bromide

(1.0 M solution in THF), 0.077 (32 %) g of product was obtained.



Colorless oil, R_f = 0.68 (pentane).

[a] $^{25}_{589}$ = -22 (c = 0.15, $CHCl_3$)

IR (film) : 2957, 2875, 1741, 1514, 1452, 1417, 1047, 813, 767, 648 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ= 7.19 (d, ^3J =7.6 Hz, 2H, Arom.), 7.05 (d, ^3J =7.6 Hz, 2H, Arom.), 2.94 (d, ^2J = 14.2 Hz, 1H, $\underline{CH_2}$-Ph), 2.57 (d, ^2J = 14.2 Hz, 1H, $\underline{CH_2}$-Ph), 2.36 (ddd, ^2J = 17.6 Hz, ^3J = 4.5 Hz, ^4J = 2.7 Hz, 1H, H- C(3)), 2.30 (s, 3H, Me- Ph), 2.01 (t, ^3J = 4.5 Hz, 1H, H- C(4)), 1.92 (m, 1H, H- C(5)), 1.84 (dd, ^2J = 17.6 Hz, ^3J = 4.3 Hz, 1H, H- C(3)), 1.76 (td, ^2J = ^3J = 12.7 Hz, ^3J = 3.4 Hz, 1H, H- C(6)), 1.17 – 1.45 (m, 2H, H- C(4), H- C(5)), 0.92 (s, 3H, Me- C(7)), 0.88 (s, 3H, Me- C(7)).

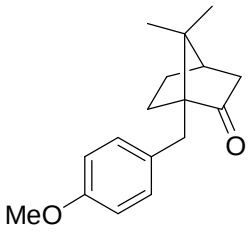
^{13}C NMR (100.6 MHz, $CDCl_3$): 218.9, 135.9, 135.3, 130.5, 128.5, 68.6, 43.6, 43.3, 34.5, 31.1, 27.4, 26.8, 21.0, 20.3, 19.8.

CI-MS (NH_3): m/z = 260 (23, $[M+18]^+$), 243 (100, $[M+1]^+$), 242 (17, $[M]^+$), 198 (6, $[M-44]^+$), 185 (5, $[M-57]^+$), 105 (12, $[M-137]^+$), 91 (5, $[M-151]^+$).

MALDI-HRMS : Calcd. for $C_{17}H_{23}O^+$ 243.1749, found 243.1737.

1-(4-Methoxybenzyl)-7,7-dimethylbicyclo[2.2.1]heptan-2-one (Table 2, Entry 30) : Following the Typical Experimental procedure using 0.25 g (1.00 mmol) of (-)-10-

camphorsulfonyl chloride, 6 mL of 4-methoxyphenylmagnesium bromide (0.5 M solution in THF), 0.108 g (42 %) of product was obtained.



Colorless oil, R_f = 0.54 (pentane/Et_2O = 9 : 1).

[a] $^{25}_{589}$ = -19.5 (c = 0.22, $CHCl_3$)

IR (film) : 2956, 2854, 1738, 1607, 1511, 1245, 1178, 1040, 910, 823, 732, 632 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ= 7.22 (d, ^3J =8.8 Hz, 2H, Arom.), 6.78 (d, ^3J =8.8 Hz, 2H, Arom.), 3.78 (s, 3H, OMe), 2.90 (d, ^2J = 14.3 Hz, 1H, $\underline{CH_2}$-Ph), 2.56 (d, ^2J = 14.3 Hz, 1H, $\underline{CH_2}$-Ph), 2.36 (ddd, ^2J = 18.2 Hz, ^3J = 4.5 Hz, ^4J = 3.0 Hz, 1H, H- C(3)), 2.01 (t, ^3J = 4.5 Hz, 1H, H- C(4)), 1.90 (m, 1H, H- C(5)), 1.83 (d, ^2J = 18.2 Hz, 1H, H- C(3)), 1.75 (td, ^2J = ^3J = 12.5 Hz, ^3J = 3.0 Hz, 1H, H- C(6)), 1.16 – 1.34 (m, 2H, H- C(4), H- C(5)), 0.92 (s, 3H, Me- C(7)), 0.83 (s, 3H, Me- C(7)).

^{13}C NMR (100.6 MHz, $CDCl_3$): 220.6, 157.8, 131.6, 127.7, 113.2, 69.6, 55.2, 43.6, 43.3, 39.5, 30.7, 27.5, 26.8, 20.3, 19.8.

CI-MS (NH_3): m/z = 276 (14, $[M+18]^+$), 259 (100, $[M+1]^+$), 258 (67, $[M]^+$), 188 (10, $[M-70]^+$), 120 (13, $[M-138]^+$), 91 (5, $[M-167]^+$).

MALDI-HRMS : Calcd. for $C_{17}H_{23}O_2^+$ 259.1698, found 259.1687.