Copper-catalysed coupling of aryl tosylates with sodium arylsulfinates

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Diaryl sulfones derivatives were easily synthesised from aryl tosylates and sodium arylsulfinates in high yields using $[Cu(CH_3CN)_4]PF_6$ as catalyst. The transformation is efficient, simple and the starting materials are readily available.

Keywords: copper-catalysed; sodium arylsulfinates; aryl tosylates; cross-coupling; diaryl sulfone synthesis

Diaryl sulfones are commonly used in organic chemistry,[1,2] and also show considerable biological activities as medicine and pesticide intermediates.[3,4] Recently they have been widely used as antibacterial, antifungal and antitumor agents.[5,6] Diaryl sulfones represent a new class of nucleoside inhibitor drug which can inhibit HIV-1 reverse transcriptase[7–9] without drug resistance and toxicity.[10,11]

Conventional synthetic methods to obtain diaryl sulfone derivatives involve Friedel–Crafts sulfonylation, which often requires strong acid and is carried out under harsh conditions.[12,13] Moreover, the site-selectivity of electrophilic substitution is restricted by the nature of the substituents. Thus, a novel method for diaryl sulfone synthesis with high regioselectivity under mild conditions is absolutely imperative.

Recent researches concerning transition metal-catalysed transformations with arylsulfinate salts have emerged.[14–25] Sodium arylsulfinates have been used as an aryl sulfonyl source with several advantages over the corresponding arylsulfonyl chlorides in that they are more stable and easily handled. The reactions can usually be carried out at low temperatures and without the need for bases or additives. Sodium arylsulfinates have provided sulfone groups by Cu(I)-catalysed cross-coupling with aryl iodides,[26,27] aryl bromides,[28–31] aryl chlorides,[32] and arylboronic acids (Fig. 1).[33–40] However, aryl triflates could only be coupled with sodium arylsulfinates under palladium catalysis.[29,30] To the best of our knowledge, no examples of copper-catalysed coupling of sodium arylsulfinates have been reported with phenyl based electrophiles. We describe here our results concerning a novel Cu(I)-catalysed cross-coupling of aryl tosylates with sodium arylsulfinates in DMSO.

Results and discussion

We optimised reaction conditions for phenyl tosylate and sodium phenylsulfinate as a template substrate in the presence of 10 mol% CuOTf in DMF. However, only a 25% yield of diphenyl sulfone was formed. In order to improve the reaction further, we tested the copper catalyst and the nature of the solvent on the yield (Table 1). The study of the reaction with several catalysts in DMF showed that copper salts are necessary to generate the desired product (entries 1–10). The cross-coupling reaction proceeds in moderate yield in the presence of CuCl as compared to CuI and CuBr (entries 2–4). Specifically, CuCN leads to higher yields as compared to other Cu(I) salts (entry 5). Tetrakis(acetonitrile)copper(I) hexafluorophosphate $[Cu(CH_3CN)_4]PF_6$ has been used as an efficient catalyst in organic synthesis.[41–47] The introduction of $[Cu(CH_3CN)_4]PF_6$ dramatically promoted the conversion to diphenyl sulfone in 84% yield (entry 6). On the contrary, Cu(II) catalysts were

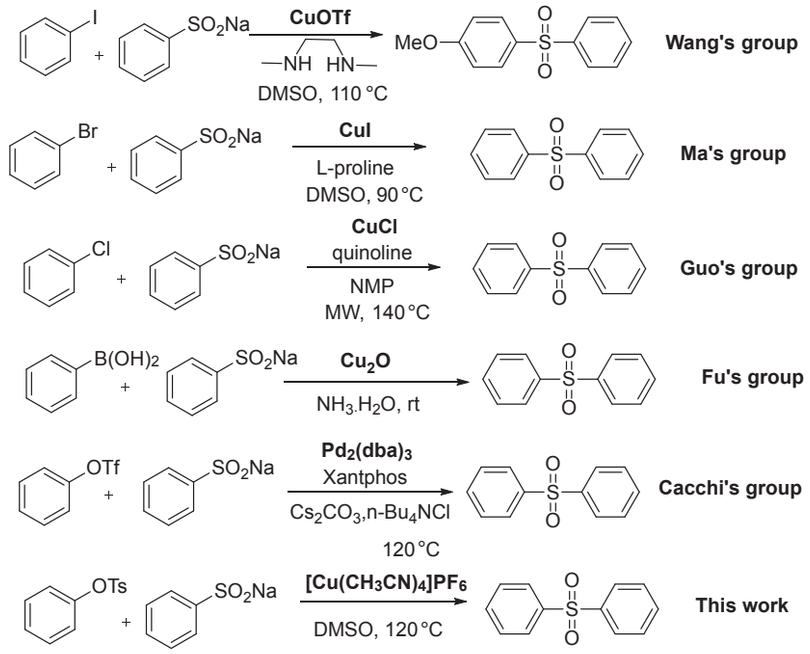

Fig. 1 Diaryl sulfone synthesis with sodium arylsulfinates.

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Table 1 Catalyst and solvent selection on the reaction[a]

Entry	Catalyst	Yield/%[b]	Entry	Solvent	Yield/%[c]
1	CuOTf	25	11	Toluene	20
2	CuCl	38	12	Xylene	32
3	CuBr	39	13	*t*-BuOH	39
4	CuI	35	14	Toluene	33
5	CuCN	59	15	Dioxane	40
6	$[Cu(CH_3CN)_4]PF_6$	84	16	DME	39
7	$Cu(OAc)_2$	–	17	CH_3CN	75
8	$CuCl_2$	–	18	NMP	87
9	$Cu(OTf)_2$	–	19	DMA	86
10	–	–	20	DMSO	95

[a]Reaction conditions: PhOTs (1.0 mmol), $PhSO_2Na$ (1.0 mmol), catalyst (0.1 mmol), solvent (2 mL), 120 °C, 3 h.
Isolated yield using [b]DMF as solvent; [c]$Cu(CH_3CN)_4]PF_6$ as catalyst.

totally ineffective (entries 7–9). None of the desired products have been detected without a copper catalyst (entry 10). The solvent for the coupling reactions was investigated carefully in order to uncover optimum reaction conditions (entries 11–20). Reactions conducted in various organic solvents occurred in low yield with $[Cu(CH_3CN)_4]PF_6$ under 120 °C, possibly due to the poor solubility of sodium phenylsulfinate in the solvent (entries 11–16). Specifically, aprotic polar solvents lead to a much higher yield compared to other solvents (entries 17–19). The brief survey indicated that reaction efficiencies are highest when $[Cu(CH_3CN)_4]PF_6$ is the catalyst and DMSO is used as solvent (Table 1, entry 20).

To establish a relative reactivity profile, reactions of sodium arylsulfinates with aryl tosylates, promoted by 10 mol% of $[Cu(CH_3CN)_4]PF_6$ in hot DMSO, were probed (Table 2). Both electron-rich and electron-deficient aryl tosylates reacted with sodium phenylsulfinate to give the respective sulfonylation products in high yields (entries 1–5). Aryl tosylates bearing a fluoride group are particularly attractive, since they display high selectivity in cross-coupling reactions (entry 6). On the other hand, the sterically hindered aryl tosylates reacts only slowly with sodium phenylsulfinate to give somewhat lower yields of the corresponding coupling products (entries 7 and 8).

Next, we explored the coupling procedure utilising other sodium arylsulfinates with phenyl tosylates. Electron-rich arylsulfinate salts displayed slightly higher reactivity than electron-deficient arylsulfinate salts in the cross-coupling reactions (entries 9–13). As shown in entry 14, our procedure afforded 1-fluoro-4-(phenylsulfonyl)benzene in 86% yields. The components in entries 15 and 16 underwent the cross-coupling reaction in slightly lower yields, owing to the steric effect of the *ortho*-aryl substituent.

Conclusions

In conclusion, we report a new method to synthesise unsymmetrical diaryl sulfone derivatives through copper-catalysed cross-coupling of sodium arylsulfinates and aryl tosylates. Further investigation of the mechanism is undergoing in our laboratory.

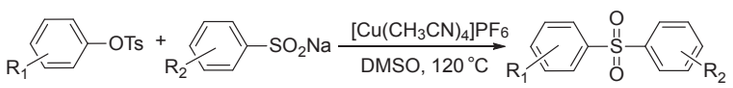
Experimental

All solvents were purified and dried according to standard methods prior to use. Proton NMR spectra were recorded in $CDCl_3$ on a Bruker Avance III 400 MHz spectrometer. Proton chemical shifts are reported in parts per million (ppm) relative to tetramethylsilane (TMS) with the residual solvent peak as the internal reference. Multiplicities are reported as: singlet (s), doublet (d), triplet (t) and multiplet (m). HRMS (EI) data were collected on High resolution mass spectrometer (MAT 900 XL, Thermo Finnigan, USA). The tosylates and sulfinates were prepared according to literature procedures.[48,49] Other materials were purchased from common commercial sources and used without additional purification.

Synthesis of aryl tosylates; general procedure[48]

p-Toluenesulfonyl chloride (1.9 g, 10 mmol) and the corresponding phenol (10 mmol) were dissolved in dichloromethane (15 mL). DABCO (1.35 g, 12 mmol) in dichloromethane (5 mL) was added, resulting in rapid warming and precipitate formation. After

Table 2 Cu-catalysed coupling of aryl tosylates with arylsulfinic salts



Entry	R^1	R^2	Yield/%[b]
1	4-OCH_3	H	92
2	4-CH_3	H	94
3	4-$COOCH_3$	H	87
4	4-NO_2	H	83
5	4-CF_3	H	80
6	4-F	H	90
7	2-CH_3	H	81
8	2-F	H	76
9	H	4-OCH_3	91
10	H	4-CH_3	95
11	H	4-$COCH_3$	90
12	H	4-CF_3	87
13	H	4-NO_2	85
14	H	4-F	86
15	H	2-OCH_3	81
16	H	2-F	82

[a]Reaction conditions: ArOTs (1.0 mmol), $ArSO_2Na$ (1.0 mmol), $[Cu(CH_3CN)_4]PF_6$ (0.1 mmol), DMSO (2 mL), 120 °C, 3 h.
[b]Isolated yield.

completion, 1 M NaOH (3 mL) was added and the reaction mixture was diluted into ethyl acetate (100 mL). The organic layer was extracted with 5% $NaHCO_3$ (3 × 50 mL), 0.1 M HCl (3 × 50 mL), water (25 mL), and brine (25 mL). The solvent was dried with sodium sulfate and removed *in vacuo*.

Synthesis of sodium arylsulfinates; general procedure[49]

Sodium arylsulfinates were prepared by heating 2.5 g of sodium sulfite (2.5 g), the appropriate $ArSO_2Cl$ (10 mmol) and sodium hydrogen carbonate (1.68 g) in water (9.6 mL) at 70–80 °C for 4 h. After cooling to room temperature, water was removed under vacuum and the residue was extracted with ethanol.

Synthesis of diphenyl sulfone derivatives; general procedure

A mixture of the sodium arylsulfinate (1 mmol), aryl tosylate (1 mmol), $[Cu(CH_3CN)_4]PF_6$ (0.1 mmol) and DMSO (2 mL) was stirred at 120 °C under air for 6 h. Afterwards, water (2 mL) was added to the reaction solution which was then filtered and the solution extracted by Et_2O (3 × 2 mL). The organic phases were combined and evaporated under reduced pressure. The residue was purified on a SiO_2 column to afford the desired product (eluent; ethyl acetate/hexane 1 : 15).

All products are known compounds and were characterised by their ^{1}H NMR spectra and by HRMS.

Diphenyl sulfone: White solid, m.p. 125–127 °C (lit.[37] 125–126 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 7.2 Hz, 4H), 7.54 (t, *J* = 7.6 Hz, 2H), 7.50 (t, *J* = 7.2 Hz, 4H); HRMS calcd for $C_{12}H_{10}O_2S$: [M^+] 218.0402; found: 218.0403.

4-Methoxyphenyl phenyl sulfone: Yellow solid, m.p. 91–92 °C (lit.[28] 88–90 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85–7.95 (m, 4H), 7.47–7.54 (m, 3H), 6.93–6.99 (m, 2H), 3.85 (s, 3H); HRMS calcd for $C_{13}H_{12}O_3S$: [M^+] 248.0507; found: 248.0506.

4-Methylphenyl phenyl sulfone: White solid, m.p.125–126 °C (lit.[37] 126–127 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, *J* = 8.0 Hz, 2H), 7.81 (d, *J* = 7.6 Hz, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 2.37 (s, 3H); HRMS calcd for $C_{13}H_{12}O_2S$: 232.0558; found: 232.0559.

Methyl 4-(phenylsulfonyl)benzoate: Colourless oil[37]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 7.6 Hz, 2H), 8.01 (d, *J* = 7.6 Hz, 2H), 7.94 (d, *J* = 7.6 Hz, 2H), 7.61 (d, *J* = 6.8 Hz, 1H), 7.52 (m, 2 H), 3.94 (s, 3H); HRMS calcd for $C_{14}H_{12}O_4S$: [M^+] 276.0456; found: 276.0458.

4-Nitrophenyl phenyl sulfone: Yellow solid, m.p. 145–147 °C (lit.[38] 143–145 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27–8.37 (m, 2H), 8.07–8.16 (m, 2H), 7.92–8.01 (m, 2H), 7.58–7.66 (m, 1H), 7.51–7.60 (m, 2H); HRMS calcd for $C_{12}H_9NO_4S$: [M^+] 263.0252; found: 263.0251.

4-Trifluoromethylphenyl phenyl sulfone: Colourless solid, m.p. 89–91 °C (lit.[38] 90–91 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 8.0 Hz, 2H), 7.90–8.02 (m, 2H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.50–7.64 (m, 3H); HRMS calcd for $C_{13}H_9F_3O_2S$: [M^+] 286.0275; found: 286.0278.

4-Fluorophenyl phenyl sulfone: White solid, m.p. 103–105 °C (lit.[37] 105–107 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93–8.01 (m, 4H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 7.2 Hz, 2H), 7.14–7.22 (m, 2H); HRMS calcd for $C_{12}H_9FO_2S$: 236.0307: [M^+] found: 236.0309.

2-Methylphenyl phenyl sulfone: White solid, m.p. 125–127 °C (lit.[38] 125–127 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65–7.75 (m, 5H), 7.19–7.35 (m, 4 H), 3.33 (s, 3 H); HRMS calcd for $C_{13}H_{12}O_2S$: [M^+] 232.0558; found: 232.0556.

2-Fluorophenyl phenyl sulfone: White solid; (m.p. 93–95 °C (lit.[38] 92–94 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.52 (m, 5 H), 7.09–7.22 (m, 4 H); HRMS calcd for $C_{12}H_9FO_2S$: [M^+] 236.0307; found: 236.0310.

4-Acetylphenyl phenyl sulfone: Yellow solid, m.p. 131–133 °C (lit.[28] 132–134 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94–8.03 (m, 6H), 7.50–7.62 (m, 3H), 2.61 (s, 3H); HRMS calcd for $C_{14}H_{12}O_3S$: [M^+] 260.0507; found: 260.0504.

2-Methoxyphenyl phenyl sulfone: White solid, m.p. 76–77 °C (lit.[38] 75 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.55 (m, 5 H), 7.13–7.23 (m, 4 H), 3.81 (s, 3H); HRMS calcd for $C_{13}H_{12}O_3S$: [M^+] 248.0507; found: 248.0506.

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References

1 S. Patai, Z. Rappoport and C.J.M. Stirlin eds, *The Chemistry of sulfones and sulfoxides,* John Wiley, New York, 1981.
2 N.S. Simpkins, *Sulfones in organic synthesis,* Pergamon Press, Oxford, 1993.
3 R.A. Hartz, A.G. Arvanitis, C. Arnold, J.P. Rescinito, K.L. Hung, G. Zhang, H. Wong, D.R. Langley, P.J. Gilligan and G.L. Trainor, *Bioorg. Med. Chem. Lett*., 2006, **16**, 934.
4 T. Otzen, E.G. Wempe, B. Kunz, R. Bartels, G. Lehwark-Yvetot, W. Hänsel, K.J. Schaper and J.K. Seydel, *J. Med. Chem*., 2004, **47**, 240.
5 T.R. Jones, S.E. Webber, M.D. Varney, M.R. Reddy, K.K. Lewis, V. Kathardekar, H. Mazdiyasni, J. Deal, D. Nguyen, K.M. Welsh, S. Webber, A. Johnson, D.A. Matthews, W.W. Smith, C.A. Janson, R.J. Bacquet, E.F. Howland, C.L.J. Booth, R.W. Ward, S.M. Herrmann, J. White, C.A. Bartlett and C.A. Morse, *J. Med. Chem.,* 1997, **40**, 677.
6 C.J. Dinsmore, T.M. Williams, T.J. O'Neill, D. Liu, E. Rands, J.C. Culberson, R.B. Lobell, K.S. Koblan, N.E. Kohl, J.B. Gibbs, A.I. Oliff, S.L. Graham and G.D. Hartman, *Biorg. Med. Chem. Lett.,* 1999, **9**, 3301.
7 N. Neamati, A. Mazumder, H. Zhao, S. Sunder, T.R. Burke Jr, R.J. Schultz and Y. Pommier, *Antimicrob. Agents Chemother*., 1997, **41**, 385.
8 M. Artico, R. Silvestri, S. Massa, A.G. Loi, S. Corrias, G. Piras and P. La Colla, *J. Med. Chem*., 1996, **39**, 522.
9 J.B. McMahon, R.J. Gulakowsky, O.S. Weislow, R.J. Schultz, V.L. Narayanan, D.J. Clanton, R. Pedemonte, F.W. Wassmundt, R.W. Buckheit Jr, W.D. Decker, E.L. White, J.P. Bader, M.R. Boyd, *Antimicrob. Agents Chemother*., 1993, **37**, 754.
10 T.M. Williams, T.M. Ciccarone, S.C. MacTough, C.S. Rooney, S.K. Balani, J.H. Condra, E.A. Emini, M.E. Goldman, W.J. Greenlee, L.R. Kauffman, J.A. O'Bnen, V.V. Sardana, W.A. Schleif, A.D. Theoharides and P.S. Anderson, *J. Med. Chem*., 1993, **36**, 1291.
11 M. Artico, R. Silvestri, E. Pagnozzi, B. Bruno, E. Novellino, G. Greco, S. Massa, A. Ettorre, A.G. Loi, F. Scintu and P. La Colla, *J. Med. Chem*., 2000, **43**, 1886.
12 P. Laidlaw, D. Bethell, S.M. Brown, G. Watson, D.J. Willock and G.J. Hutchings, *J. Mol. Catal. A: Chem*., 2002, **178**, 205.
13 X. Zhou, J. Luo, J. Liu, S. Peng and G.-J. Deng, *Org. Lett*., 2011, **13**, 1432.
14 F. Zhao, Q. Tan, F. Xiao, S. Zhang and G.-J. Deng, *Org. Lett*., **2013**, *15*, 1520.
15 G.-W. Wang and T. Miao, *Chem. Eur. J*., **2011**, *17*, 5787.
16 R. Chen, S. Liu, X. Liu, L. Yang and G.-J. Deng, *Org. Biomol. Chem*., 2011, **9**, 7675.
17 M. Wu, J. Luo, F. Xiao, S. Zhang, G.-J. Deng and H.-A. Luo, *Adv. Synth. Catal*., 2012, **354**, 335.
18 M. Wang, D. Li, W. Zhou and L. Wang, *Tetrahedron*, 2012, **68**, 1926.
19 M. Behrends, J. Sävmarker, P.J.R. Sjöberg and M. Larhed, *ACS Catal*., 2011, **1**, 1455.
20 J. Liu, X. Zhou, H. Rao, F. Xiao, C.-J. Li and G.-J. Deng, *Chem. Eur. J*., 2011, **17**, 7996.
21 W. Chen, X. Zhou, F. Xiao, J. Luo and G.-J. Deng, *Tetrahedron Lett*., 2012, **53**, 4347.
22 H. Wang, Y. Li, R. Zhang, K. Jin, D. Zhao and C. Duan, *J. Org. Chem*., 2012, **77**, 4849.
23 C. Zhou, Q. Liu, Y. Li, R. Zhang, X. Fu and C. Duan, *J. Org. Chem*., 2012, **77**, 10468.
24 K. Cheng, S. Hu, B. Zhao, X.-M. Zhang and C. Qi, *J. Org. Chem*., 2013, **78**, 5022.
25 S. Hu, P. Xia, K. Cheng and C. Qi, *Appl. Organometal. Chem*., 2013, **27**, 188.
26 S. Cacchi, G. Fabrizi, A. Goggiamani and L.M. Parisi, *Org. Lett*., 2002, **4**, 4719.
27 J.M. Baskin and Z. Wang, *Org. Lett*., 2002, **4**, 4423.
28 W. Zhu and D. Ma, *J. Org. Chem*., 2005, **70**, 2696.
29 S. Cacchi, G. Fabrizi, A. Goggiamani and L.M. Parisi, *Synlett,* 2003, 361.

30 S. Cacchi, G. Fabrizi, A. Goggiamani, L.M. Parisi and R. Bernini, *J. Org. Chem*., 2004, **69**, 5608.
31 Y. Peng. *J. Chem. Res*., 2014, **38**, 447.
32 Y. Yuan and S. Guo. *Synlett*, 2011, **18**, 2750.
33 A. Kar, I.A. Sayyed, W.F. Lo, H.M. Kaiser, M. Beller and M.K. Tse. *Org. Lett*., 2007, **9**, 3405.
34 V. Garzya, I.T. Forbes, S. Lauru and P. Maragni, *Tetrahedron Lett*., 2004, **45**, 1499.
35 K. Bahrami, M.M. Khodei and F. Shahbazi. *Tetrahedron Lett*., 2008, **49**, 3931.
36 F. Huang and R.A. Batey, *Tetrahedron*, 2007, **63**, 7667.
37 H. Yang, Y. Li, M. Jiang, J. Wang and H. Fu, *Chem. Eur. J*., 2011, **17**, 5652.
38 B.P. Bandgar, S.V. Bettigeri and J. Phopase, *Org. Lett*., 2004, **6**, 2105.
39 K.M. Lakshmi, B. Neelima, B. Sreedhar and R. Chakravarti, *Synlett*, 2008, 1455.
40 W. Zhang, K. Li and B. Zhao, *J. Chem. Res.,* 2014, **38**, 269.
41 M. Presset, D. Oehlrich, F. Rombouts and G.A. Molander. *J. Org. Chem.,* 2013, **78**, 12837.
42 W. Kong, M. Casimiro, E. Merino and C. Nevado, *J. Am. Chem. Soc*., 2013, **135**, 14480.
43 P. Maity, H.D. Srinivas and M.P. Watson, *J. Am. Chem. Soc*., 2011, **133**, 17142.
44 M. Nakanishi, C. Minard, P. Retailleau, K. Cariou and R.H. Dodd, *Org. Lett*., 2011, **13**, 5792.
45 D.A. Powell and H. Fan, *J. Org. Chem*., 2010, **75**, 2726.
46 C. Peng, J. Cheng and J. Wang, *Adv. Syn. Catal*., 2008, **350**, 2359.
47 R. Bhuyan and K.M. Nicholas, *Org. Lett*., 2007, **9**, 3957.
48 S.C. Miller, *J. Org. Chem*., 2010, **75**, 4632.
49 L. Liu, Y. Chi and K. Jen, *J. Org. Chem*., 1980, **45**, 406.