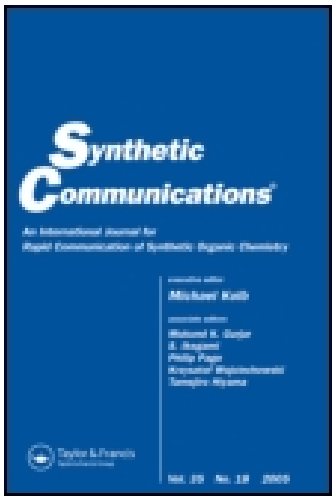


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

SYNTHESIS OF ARYL 5-(2-CHLOROPHENYL)-2-FUROATES UNDER PHASE TRANSFER CATALYSIS

Zheng Li [a] & Xicun Wang [a]

[a] College of Chemistry and Chemical Engineering , Northwest Normal University , Lanzhou, Gansu, 730070, P.R. China

Published online: 16 Aug 2006.

To cite this article: Zheng Li & Xicun Wang (2002) SYNTHESIS OF ARYL 5-(2-CHLOROPHENYL)-2-FUROATES UNDER PHASE TRANSFER CATALYSIS, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 32:20, 3081-3086, DOI: 10.1081/SCC-120013716

To link to this article: http://dx.doi.org/10.1081/SCC-120013716

MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016

SYNTHETIC COMMUNICATIONS
Vol. 32, No. 20, pp. 3081–3086, 2002

SYNTHESIS OF ARYL 5-(2-CHLOROPHENYL)-2-FUROATES UNDER PHASE TRANSFER CATALYSIS

Zheng Li* and Xicun Wang

College of Chemistry and Chemical Engineering,
Northwest Normal University, Lanzhou,
Gansu, 730070, P.R. China

ABSTRACT

The steric hindered esters, aryl 5-(2-chlorophenyl)-2-furoates **(3a–o)**, are synthesized via the reaction of 5-(2-chlorophenyl)-2-furoic acid (**1**) with thionyl chloride and phenols under liquid–liquid phase transfer catalysis in excellent yield.

5-Aryl-2-furoic acid derivatives have attracted much attention due to their diverse biological activities, such as antibacterial,[1,2] anesthetic[3] anticonvulsive[4] and plant-growth regulating[5,6] activity. However, the species of aryl 5-aryl-2-furoates are very scarce[2] because of the steric hindrance. This promotes us to investigate a convenient and efficient method to synthesize these compounds so that the properties and activities can be further investigated.

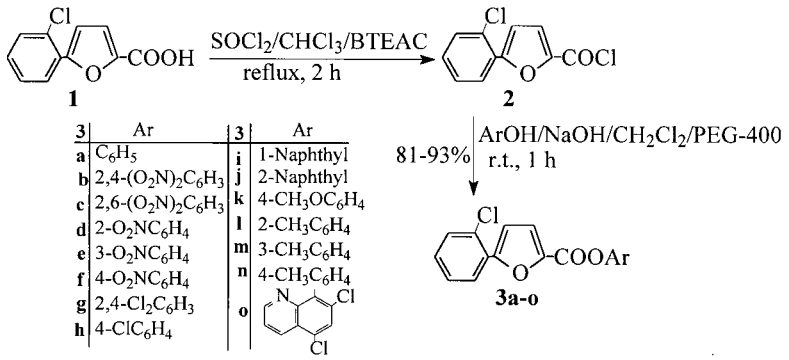
*Corresponding author. E-mail: lizheng@nwnu.edu.cn

DOI: 10.1081/SCC-120013716 0039-7911 (Print); 1532-2432 (Online)

Reaction of 5-(2-chlorophenyl)-2-furoic acid (**1**) with thionyl chloride catalyzed by benzyl triethyl ammonium chloride (BTEAC) gives 5-(2-chlorophenyl)-2-furoyl chloride (**2**) in 95% yield. Compound **2** on further treatment with phenols catalyzed by polyethylene glycol-400 (PEG-400) affords aryl 5-(2-chlorophenyl)-2-furoates **(3a–o)** in excellent yield (Sch. 1).

It is worthy to mention that this is a very simple, facile and one pot synthetic method for the steric hindered furoates under mild condition.

In order to confirm the optimal synthetic condition, different phase transfer catalysts, including 18-crown-6, $(C_4H_9)_4NI$, $(C_4H_9)_4NBr$, BTEAC, $(C_{16}H_{33})N(CH_3)_3Br$, PEG-400, PEG-600 and PEG-1000, are tested for the selected compound **3a**. The results are shown in Table 1.



Scheme 1.

Table 1. The Influence of Phase Transfer Catalysts on the Yield of **3a**

Catalyst	Solvent	Yield
18-Crown-6	CH_2Cl_2	70
$(C_4H_9)_4NI$	CH_2Cl_2	68
$(C_4H_9)_4NBr$	CH_2Cl_2	74
BTEAC	CH_2Cl_2	69
$(C_{16}H_{33})N(CH_3)_3Br$	CH_2Cl_2	70
PEG-1000	CH_2Cl_2	75
PEG-600	CH_2Cl_2	80
PEG-400	CH_2Cl_2	86
PEG-400	CH_3CN	85
PEG-400	C_6H_6	75
–	CH_2Cl_2	0

From Table 1, we can see that all of the catalysts used in the reactions are able to catalyze the reaction to give the title compounds in good to excellent yield. Among of them, PEG-400 is the best under the studied condition. However, if no catalyst used, the product cannot be obtained at all in the same condition. In addition, the solvents can also influence the yield of the reaction.

The characterization of compounds **3a–o** is based on their IR (KBr), ^{1}H NMR MS and elemental analyses. The IR spectra exhibit a characteristic strong absorption at 1732–1748 cm^{-1} attributable to the carbonyl of **3a–o**. All elemental analyses and MS of **3a–o** are good agreement with the structure prepared.

EXPERIMENTAL

IR spectra were recorded using KBr pellets on an Alpha Centauri FT-IR spectrophotometer and ^{1}H NMR spectra on a FT-80A instrument using $CDCl_3$ as solvent and Me_4Si as internal standard. Elemental analyses were performed on a Vario El Elemental Analysis instrument. Mass spectra were recorded on a QP-1000A GC-MS using the impact mode (70 eV). Melting points were observed in an open capillary tube and uncorrected. 5-(2-Chlorophenyl)-2-furoic acid (**1**) was prepared according to literature procedure.[5] Phenols, thionyl chloride, 18-crown-6, $(C_4H_9)_4NI$, $(C_4H_9)_4NBr$, $(C_{16}H_{33})N(CH_3)_3Br$, PEG-400, PEG-600 and PEG-1000 were commercially available and used as received.

General Procedure for the Preparation of Compounds 3a–o

The mixture of 0.49 g (2.2 mmol) of 5-(2-chlorophenyl)-2-furoic acid (**1**), 5 mL of $SOCl_2$ and 0.05 g (0.22 mmol) of BTEAC in 10 mL of $CHCl_3$ was refluxed for 2 h. Then the excess of $SOCl_2$ and $CHCl_3$ was removed by evaporation. The residue was extracted with petroleum ether. After removal of the solvent, a solution of 0.08 g (2.00 mmol) of NaOH in 8 mL of H_2O, 2.00 mmol of phenol, 0.024 g (0.06 mmol) of PEG-400 and 15 mL CH_2Cl_2 were added. The resulting mixture was stirred for 1 h at room temperature. Then the organic layer was separated and the water layer was extracted with CH_2Cl_2 (2×5 mL). The resulting organic solution was dried with anhydrous Na_2SO_4. After the solvent was removed by evaporation, the residue was recrystallized from C_2H_5OH

to give **3a–o**. The physical and spectral data of compounds **3a–o** are reported below.

Phenyl 5-(2-chlorophenyl)-2-furoate (3a): White solid. Yield: 86%. M.p.: 82–83°C. ^{1}H NMR ($CDCl_3$) δ 7.15–8.13 (m, 11H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 1732 (C=O), 1301, 1222, 1109 (C-O-C). MS: m/z, 298 (M^+). Anal. Calcd. for $C_{17}H_{11}O_3Cl$: C, 68.35; H, 3.71. Found: C, 68.12; H, 3.68.

2,4-Dinitrophenyl 5-(2-chlorophenyl)-2-furoate (3b): White solid. Yield: 85%. M.p.: 152–153°C. ^{1}H NMR ($CDCl_3$) δ 7.21–8.87 (m, 9H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 1746 (C=O), 1307, 1239, 1104 (C-O-C). MS: m/z, 388 (M^+). Anal. Calcd. for $C_{17}H_9N_2O_7Cl$: C, 52.53; H, 2.33; N, 7.21. Found: C, 52.29; H, 2.24; N, 7.16.

2,6-Dinitrophenyl 5-(2-chlorophenyl)-2-furoate (3c): White solid. Yield: 82%. M.p.: 122–123°C. ^{1}H NMR ($CDCl_3$) δ 7.19–8.55 (m, 9H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 1748 (C=O), 1306, 1245, 1108 (C-O-C). MS: m/z, 388 (M^+). Anal. Calcd. for $C_{17}H_9N_2O_7Cl$: C, 52.53; H, 2.33; N, 7.21. Found: C, 52.41; H, 2.28; N, 7.13.

2-Nitrophenyl 5-(2-chlorophenyl)-2-furoate (3d): White solid. Yield: 90%. M.p.: 132–133°C. ^{1}H NMR ($CDCl_3$) δ 7.12–8.20 (m, 10H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 1745 (C=O), 1307, 1227, 1105 (C-O-C). MS: m/z, 343 (M^+). Anal. Calcd. for $C_{17}H_{10}NO_5Cl$: C, 59.40; H, 2.93; N, 4.08. Found: C, 59.26; H, 2.86; N, 3.89.

3-Nitrophenyl 5-(2-chlorophenyl)-2-furoate (3e): White solid. Yield: 81%. M.p.: 142–143°C. ^{1}H NMR ($CDCl_3$) δ 7.14–8.22 (m, 10H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 1743 (C=O), 1303, 1221, 1101 (C-O-C). MS: m/z, 343 (M^+). Anal. Calcd. for $C_{17}H_{10}NO_5Cl$: C, 59.40; H, 2.93; N, 4.08. Found: C, 59.29; H, 2.90; N, 3.99.

4-Nitrophenyl 5-(2-chlorophenyl)-2-furoate (3f): White solid. Yield: 84%. M.p.: 146–147°C. ^{1}H NMR ($CDCl_3$) δ 7.12–8.19 (m, 10H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 1748 (C=O), 1305, 1224, 1104 (C-O-C). MS: m/z, 343 (M^+). Anal. Calcd. for $C_{17}H_{10}NO_5Cl$: C, 59.40; H, 2.93; N, 4.08. Found: C, 59.56; H, 2.89; N, 3.98.

2,4-Dichlorophenyl 5-(2-chlorophenyl)-2-furoate (3g): White solid. Yield: 87%. M.p.: 121–122°C. ^{1}H NMR ($CDCl_3$) δ 7.13–8.08 (m, 9H, Ar–H and Fu-H). IR (KBr, ν, cm^{-1}): 1744 (C=O), 1304, 1223, 1120 (C-O-C). MS: m/z, 367 (M^+). Anal. Calcd. for $C_{17}H_9O_3Cl_3$: C, 55.54; H, 2.47. Found: C, 55.34; H, 2.41.

4-Chlorophenyl 5-(2-chlorophenyl)-2-furoate (3h): White solid. Yield: 84%. M.p.: 110–111°C. ^{1}H NMR ($CDCl_3$) δ 7.18–8.15 (m, 10H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 1740 (C=O), 1303, 1221, 1097 (C-O-C). MS: m/z, 333 (M^+). Anal. Calcd. for $C_{17}H_{10}O_3Cl_2$: C, 61.29; H, 3.03. Found: C, 61.03; H, 2.96.

1-Naphthyl 5-(2-chlorophenyl)-2-furoate (3i): White solid. Yield: 83%. M.p.: 78–79°C. ^{1}H NMR ($CDCl_3$) δ 7.19–8.12 (m, 13H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 1735 (C=O), 1304, 1215, 1110 (C-O-C). MS: m/z, 348 (M^+). Anal. Calcd. for $C_{21}H_{13}O_3Cl$: C, 72.32; H, 3.76. Found: C, 72.08; H, 3.68.

2-Naphthyl 5-(2-chlorophenyl)-2-furoate (3j): White solid. Yield: 87%. M.p.: 126–127°C. ^{1}H NMR ($CDCl_3$) δ 7.21–8.14 (m, 13H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 1733 (C=O), 1305, 1206, 1105 (C-O-C). MS: m/z, 348 (M^+). Anal. Calcd. for $C_{21}H_{13}O_3Cl$: C, 72.32; H, 3.76. Found: C, 72.12; H, 3.70.

4-Methoxylphenyl 5-(2-chlorophenyl)-2-furoate (3k): White solid. Yield: 93%. M.p.: 122–123°C. ^{1}H NMR ($CDCl_3$) δ 7.08–8.07 (m, 10H, Ar-H and Fu-H), 3.75 (s, 3H, CH_3). IR (KBr, ν, cm^{-1}): 1742 (C=O), 1305, 1214, 1109 (C-O-C). MS: m/z, 328 (M^+). Anal. Calcd. for $C_{18}H_{13}O_4Cl$: C, 65.76; H, 3.99. Found: C, 65.59; H, 4.08.

2-Methylphenyl 5-(2-chlorophenyl)-2-furoate (3l): White solid. Yield: 92%. M.p.: 80–81°C. ^{1}H NMR ($CDCl_3$) δ 7.20–8.12 (m, 10H, Ar-H and Fu-H), 2.27 (s, 3H, CH_3). IR (KBr, ν, cm^{-1}): 1742 (C=O), 1306, 1223, 1116 (C-O-C). MS: m/z, 312 (M^+). Anal. Calcd. for $C_{18}H_{13}O_3Cl$: C, 69.13; H, 4.19. Found: C, 68.92; H, 4.11.

3-Methylphenyl 5-(2-chlorophenyl)-2-furoate (3m): White solid. Yield: 84%. M.p.: 104–105°C. ^{1}H NMR ($CDCl_3$) δ 7.23–8.14 (m, 10H, Ar-H and Fu-H), 2.31 (s, 3H, CH_3). IR (KBr, ν, cm^{-1}): 1739 (C=O), 1305, 1227, 1121 (C-O-C). MS: m/z, 312 (M^+). Anal. Calcd. for $C_{18}H_{13}O_3Cl$: C, 69.13; H, 4.19. Found: C, 68.85; H, 4.14.

2-Methylphenyl 5-(2-chlorophenyl)-2-furoate (3n): White solid. Yield: 82%. M.p.: 102–103°C. ^{1}H NMR ($CDCl_3$) δ 7.19–8.13 (m, 10H, Ar-H and Fu-H), 2.29 (s, 3H, CH_3). IR (KBr, ν, cm^{-1}): 1741 (C=O), 1304, 1217, 1112 (C-O-C). MS: m/z, 312 (M^+). Anal. Calcd. for $C_{18}H_{13}O_3Cl$: C, 69.13; H, 4.19. Found: C, 69.28; H, 4.23.

5,7-Dichloro-8-quinolyl 5-(2-chlorophenyl)-2-furoate (3o): White solid. Yield: 85%. M.p.: 154–155°C. ^{1}H NMR ($CDCl_3$) δ 7.14–8.17 (m, 10H, Ar–H, Py-H and Fu-H). IR (KBr, ν, cm^{-1}): 1743 (C=O), 1297, 1226, 1118 (C-O-C). MS: m/z, 418 (M^+). Anal. Calcd. for $C_{20}H_{10}NO_3Cl_3$: C, 57.38; H, 2.41; N, 3.35. Found: C, 57.13; H, 2.49; N, 3.21.

ACKNOWLEDGMENT

The authors thank the Scientific and Technological Innovation Engineering of Northwest Normal University and Natural Science Foundation of Gansu Province for the financial support of this work.

REFERENCES

1. Oleinlik, A.F.; Vozyakova, T.I.; Filitis, L.N.; Okinshevich, O.V.; Perschin, G.N.; Shestakovskii, V.M. Khim. Farm. Zh. **1984**, *18*, 697; Chem. Abstr. *101*, 230269.
2. Dai, Y.J.; Li, Y.J.; Chen, J.C. Youji Huaxue (Chinese) **1988**, *8*, 443; Chem. Abstr. *110*, 94889.
3. Koretskaya, N.I.; Trubisksyna, T.K.; Mashkovskii, M.D.; Olenik, A.F. Khim. Farm. Zh. **1977**, *11*, 33; Chem. Abstr. *87*, 39715.
4. Burch, H.A.; Write, R.E.; Wright, G.C.; Goldenberg, M.M. J. Pharm. Sci. **1980**, *69*, 107.
5. Wei, T.B.; Chen, J.C.; Wang, X.C.; Yang, S.Y. Chem. J. Univ. (Chinese) **1992**, *13*, 1217; Chem. Abstr. *118*, 191447.
6. Wang, X.C.; Chen, J.C.; Wang, X.C. Chem. J. Univ. (Chinese) **1998**, *19*, 1274; Chem. Abstr. *129*, 275795.

Received in Japan April 16, 2001