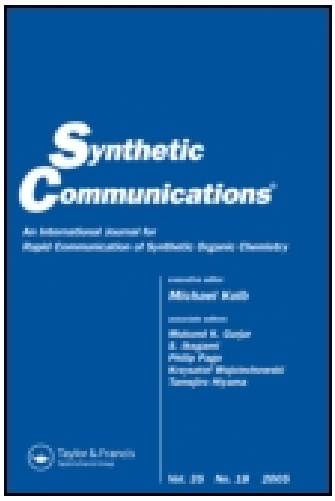


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

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

ONE POT SYNTHESIS OF N-ARYL-5-ARYL-2-FUROYL AMIDES VIA REACTION OF 5-ARYL-2-FUROIC ACID WITH ARYLAMINES

Zheng Li [a] & Xicun Wang [b]

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

[b] 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) ONE POT SYNTHESIS OF N-ARYL-5-ARYL-2-FUROYL AMIDES VIA REACTION OF 5-ARYL-2-FUROIC ACID WITH ARYLAMINES, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 32:21, 3357-3362, DOI: 10.1081/SCC-120014043

To link to this article: http://dx.doi.org/10.1081/SCC-120014043

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

SYNTHETIC COMMUNICATIONS
Vol. 32, No. 21, pp. 3357–3362, 2002

ONE POT SYNTHESIS OF *N*-ARYL-5-ARYL-2-FUROYL AMIDES VIA REACTION OF 5-ARYL-2-FUROIC ACID WITH ARYLAMINES

Zheng Li and Xicun Wang*

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

ABSTRACT

The *N*-aryl-5-aryl-2-furoyl amides (**3a–r**) are synthesized by one pot method via reaction of 5-aryl-2-furoic acids (**1**) with arylamines, using phenylsulfonyl chloride as reagent, under solid–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] anesthetic,[2] anticonvulsive[3] and plant-growth regulating[4,5] activity. However, the species of *N*-aryl-5-aryl-2-furoyl amides are very scarce because in the synthetic reactions of which, the large furan and aryl rings of 5-aryl-2-furoic acid and large aryl ring of arylamine have strong steric hindrance,

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

DOI: 10.1081/SCC-120014043
0039-7911 (Print); 1532-2432 (Online)

www.dekker.com

which makes the nucleophilic substitution between two reactants very difficult. This promotes us to develop a convenient and efficient new method to synthesize these compounds so that the properties and activities can be further investigated.

In our previous work,[5,6] a method to prepare *N*-aryl-5-aryl-2-furoyl amides had been introduced. In that method, the 5-aryl-2-furoic acids were converted into 5-aryl-2-furoyl chlorides first, and followed to react with arylamines under liquid–liquid phase transfer catalysis using polyethylene glycol-400 (PEG-400) as catalyst and sodium hydroxide as base. However, this method not only leads to more steps, but also brings other side reactions especially for carboxylic acid bearing substituents which are active to acids and bases. In this paper we report an one pot method to synthesize a new series of *N*-aryl-5-aryl-2-furoyl amides from corresponding carboxylic acids and amines under solid–liquid phase transfer catalysis using PEG-400 as catalyst and potassium carbonate as base.

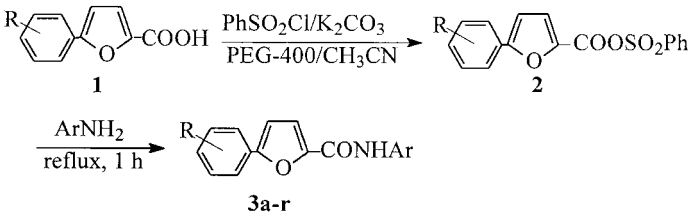
Reaction of 5-aryl-2-furoic acids (**1**) with potassium carbonate and phenylsulfonyl chloride catalyzed by PEG-400 gives a mixed anhydrides (**2**) as intermediates. Compounds **2** on treatment with arylamines in situ afford *N*-aryl-5-aryl-2-furoyl amides (**3a–r**) (Sch. 1). The yields of all compounds **3a–r** are shown in Table 1.

PEG-400 used in these reactions plays a very important role in the first step. It can easily form complex (PEG-400-K^+)$FuCOO^-$ (here Fu is 5-aryl-2-furyl). This complex makes the $FuCOO^-$ possible to readily react with phenylsulfonyl chloride to give compounds **2**. In contrast, if no PEG-400 is used, there are no any compounds **2** formed at all.

The compound **2** includes a very easily leaving group, $PhSO_3$, and can readily react with arylamines to give **3a–r** by eliminating $PhSO_3H$ although the arylamines are weak nucleophilic substitution reagents.

The described method above can be extended to the preparation of various aromatic and aliphatic carboxamides.

The characterization of compounds **3a–r** is based on their IR (KBr), ^1H NMR MS and elemental analyses. The IR spectra exhibit characteristic



Scheme 1.

Table 1. The Isolated Yields of **3a–r**

Compd.	Ar	*R*	Yield	Compd.	Ar	*R*	Yield
3a	C_6H_5	2-O_2N	90	**3j**	C_6H_5	3-O_2N	91
3b	2-$CH_3C_6H_4$	2-O_2N	92	**3k**	2-$CH_3C_6H_4$	3-O_2N	89
3c	2-$CH_3OC_6H_4$	2-O_2N	90	**3l**	2-$CH_3OC_6H_4$	3-O_2N	96
3d	1-Naphthyl	2-O_2N	86	**3m**	1-Naphthyl	3-O_2N	90
3e	2-ClC_6H_4	2-O_2N	87	**3n**	2-ClC_6H_4	3-O_2N	92
3f	4-BrC_6H_4	2-O_2N	89	**3o**	4-BrC_6H_4	3-O_2N	93
3g	2-$O_2NC_6H_4$	2-O_2N	86	**3p**	2-$O_2NC_6H_4$	3-O_2N	93
3h	3-$O_2NC_6H_4$	2-O_2N	89	**3q**	3-$O_2NC_6H_4$	3-O_2N	96
3i	4-$O_2NC_6H_4$	2-O_2N	88	**3r**	4-$O_2NC_6H_4$	3-O_2N	90

strong absorption at 1654–1685 cm^{-1} attributable to the carbonyl of **3a–r**. NH absorptions are observed at 3310–3330 cm^{-1}. The ^1H NMR spectral data of **3a–r** in d_6-dimethylsulfoxide show peaks at 10.14–10.52 for proton of NH. All elemental analyses and MS of **3a–r** are good agreement with the structure prepared.

EXPERIMENTAL

IR spectra were recorded using KBr pellets on an Alpha Centauri FT-IR spectrophotometer and ^1H NMR spectra on a FT-80A instrument using DMSO-d_6 as solvent and Me_4Si as internal standard. Elemental analyses were performed on a Vario EI 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-Aryl-2-furoic acid (**1**) was prepared according to literature procedure.[7] Arylamines, phenylsulfonyl chloride and PEG-400 were commercially available and used as received.

General Procedure for the Preparation of Compounds 3a–r

The mixture of 5 mmol of 5-aryl-2-furoic acid (**1**), 5 mmol (0.88 g) of $PhSO_2Cl$ and 20 mmol (2.76 g) of anhydrous K_2CO_3, 0.15 mmol (0.06 g) of PEG-400 in 15 mL of CH_3CN was refluxed for 0.5 h. Then 5 mmol of arylamine was added, and the resulting mixture was refluxed for another 1 h. The solvent was removed by evaporation. To the residue, 10 mL of water was added so that the inorganic salts were dissolved, then the slurry was

filtered, the solid was washed with 2×5 mL water and recrystallized from DMF-H_2O (3 : 1), and the product was given. The yield of the product was calculated according to the compound **1**. The physical and spectral data of compounds **3a–r** are reported below.

***N*-Phenyl-5-(2-nitrophenyl)-2-furoyl amide (3a):** White solid. M.p.: 123–124°C. ^{1}H NMR (DMSO-d_6) δ 10.30 (s, 1H, NH), 7.15–8.30 (m, 11H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 3320 (NH), 1656 (C=O). MS: m/z, 308 (M^+). Anal. calcd. for $C_{17}H_{12}N_2O_4$: C, 66.23; H, 3.92; N, 9.09. Found: C, 66.03; H, 3.86; N, 8.90.

***N*-(2-Methylphenyl)-5-(2-nitrophenyl)-2-furoyl amide (3b):** White solid. M.p.: 136–137°C. ^{1}H NMR (DMSO-d_6) δ 10.14 (s, 1H, NH), 7.28–8.31 (m, 10H, Ar-H and Fu-H), 2.26 (s, 3H, CH_3). IR (KBr, ν, cm^{-1}): 3315 (NH), 1654 (C=O). MS: m/z, 322 (M^+). Anal. calcd. for $C_{18}H_{14}N_2O_4$: C, 67.07; H, 4.38; N, 8.69. Found: C, 67.20; H, 4.43; N, 8.76.

***N*-(2-Methoxylphenyl)-5-(2-nitrophenyl)-2-furoyl amide (3c):** White solid. M.p.: 119–120°C. ^{1}H NMR (DMSO-d_6) δ 10.22 (s, 1H, NH), 7.20–8.24 (m, 10H, Ar-H and Fu-H), 3.74 (s, 3H, CH_3). IR (KBr, ν, cm^{-1}): 3320 (NH), 1664 (C=O). MS: m/z, 338 (M^+). Anal. calcd. for $C_{18}H_{14}N_2O_5$: C, 63.90; H, 4.17; N, 8.28. Found: C, 64.01; H, 4.25; N, 8.39.

***N*-Naphthyl-5-(2-nitrophenyl)-2-furoyl amide (3d):** White solid. M.p.: 127–128°C. ^{1}H NMR (DMSO-d_6) δ 10.51 (s, 1H, NH), 7.27–8.30 (m, 13H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 3278 (NH), 1657 (C=O). MS: m/z, 358 (M^+). Anal. calcd. for $C_{21}H_{14}N_2O_4$: C, 70.39; H, 3.94; N, 7.82. Found: C, 70.50; H, 4.01; N, 7.89.

***N*-(2-Chlorophenyl)-5-(2-nitrophenyl)-2-furoyl amide (3e):** White solid. M.p.: 151–152°C. ^{1}H NMR (DMSO-d_6) δ 10.24 (s, 1H, NH), 7.20–8.18 (m, 10H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 3328 (NH), 1666 (C=O). MS: m/z, 342 (M^+). Anal. calcd. for $C_{17}H_{11}N_2O_4Cl$: C, 59.57; H, 3.23; N, 8.17. Found: C, 59.70; H, 3.30; N, 8.30.

***N*-(4-Bromophenyl)-5-(2-nitrophenyl)-2-furoyl amide (3f):** White solid. M.p.: 159–160°C. ^{1}H NMR (DMSO-d_6) δ 10.16 (s, 1H, NH), 7.23–8.26 (m, 10H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 3326 (NH), 1684 (C=O). MS: m/z, 387 (M^+). Anal. calcd. for $C_{17}H_{11}N_2O_4Br$: C, 52.74; H, 2.86; N, 7.24. Found: C, 52.64; H, 2.90; N, 7.34.

***N*-(2-Nitrophenyl)-5-(2-nitrophenyl)-2-furoyl amide (3g):** White solid. M.p.: 131–132°C. ^{1}H NMR (DMSO-d_6) δ 10.41 (s, 1H, NH), 7.12–8.29 (m, 10H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 3310 (NH), 1658 (C=O). MS: m/z, 353 (M^+). Anal. calcd. for $C_{17}H_{11}N_3O_6$: C, 57.80; H, 3.14; N, 11.89. Found: C, 57.68; H, 3.02; N, 11.79.

***N*-(3-Nitrophenyl)-5-(2-nitrophenyl)-2-furoyl amide (3h):** White solid. M.p.: 173–174°C. ^{1}H NMR (DMSO-d_6) δ 10.29 (s, 1H, NH), 7.13–8.30 (m, 10H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 3318 (NH), 1660 (C=O).

MS: *m*/*z*, 353 (M^+). Anal. calcd. for $C_{17}H_{11}N_3O_6$: C, 57.80; H, 3.14; N, 11.89. Found: C, 57.89; H, 3.17; N, 11.98.

***N*-(4-Nitrophenyl)-5-(2-nitrophenyl)-2-furoyl Amide (3i):** White solid. M.p.: 183–184°C. ^{1}H NMR (DMSO-d_6) δ 10.50 (s, 1H, NH), 7.10–8.32 (m, 10H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 3316 (NH), 1654 (C=O). MS: *m*/*z*, 353 (M^+). Anal. calcd. for $C_{17}H_{11}N_3O_6$: C, 57.80; H, 3.14; N, 11.89. Found: C, 57.92; H, 3.20; N, 12.01.

***N*-Phenyl-5-(3-nitrophenyl)-2-furoyl amide (3j):** White solid. M.p.: 136–137°C. ^{1}H NMR (DMSO-d_6) δ 10.32 (s, 1H, NH), 7.13–8.31 (m, 11H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 3324 (NH), 1658 (C=O). MS: *m*/*z*, 308 (M^+). Anal. calcd. for $C_{17}H_{12}N_2O_4$: C, 66.23; H, 3.92; N, 9.09. Found: C, 66.31; H, 4.05; N, 9.18.

***N*-(2-Methylphenyl)-5-(3-nitrophenyl)-2-furoyl amide (3k):** White solid. M.p.: 143–144°C. ^{1}H NMR (DMSO-d_6) δ 10.15 (s, 1H, NH), 6.90–8.07 (m, 10H, Ar-H and Fu-H), 2.27 (s, 3H, CH_3). IR (KBr, ν, cm^{-1}): 3320 (NH), 1657 (C=O). MS: *m*/*z*, 322 (M^+). Anal. calcd. for $C_{18}H_{14}N_2O_4$: C, 67.07; H, 4.38; N, 8.69. Found: C, 67.18; H, 4.41; N, 8.79.

***N*-(2-Methoxylphenyl)-5-(3-nitrophenyl)-2-furoyl amide (3l):** White solid. M.p.: 159–160°C. ^{1}H NMR (DMSO-d_6) δ 10.21 (s, 1H, NH), 7.22–8.21 (m, 10H, Ar-H and Fu-H), 3.76 (s, 3H, CH_3). IR (KBr, ν, cm^{-1}): 3322 (NH), 1659 (C=O). MS: *m*/*z*, 338 (M^+). Anal. calcd. for $C_{18}H_{14}N_2O_5$: C, 63.90; H, 4.17; N, 8.28. Found: C, 63.72; H, 4.13; N, 8.16.

***N*-Naphthyl-5-(3-nitrophenyl)-2-furoyl amide (3m):** White solid. M.p.: 144–145°C. ^{1}H NMR (DMSO-d_6) δ 10.48 (s, 1H, NH), 7.24–8.26 (m, 13H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 3281 (NH), 1659 (C=O). MS: *m*/*z*, 358 (M^+). Anal. calcd. for $C_{21}H_{14}N_2O_4$: C, 70.39; H, 3.94; N, 7.82. Found: C, 70.48; H, 4.01; N, 7.92.

***N*-(2-Chlorophenyl)-5-(3-nitrophenyl)-2-furoyl amide (3n):** White solid. M.p.: 156–157°C. ^{1}H NMR (DMSO-d_6) δ 10.25 (s, 1H, NH), 7.19–8.22 (m, 10H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 3330 (NH), 1664 (C=O). MS: *m*/*z*, 342 (M^+). Anal. calcd. for $C_{17}H_{11}N_2O_4Cl$: C, 59.57; H, 3.23; N, 8.17. Found: C, 59.49; H, 3.19; N, 8.09.

***N*-(4-Bromophenyl)-5-(3-nitrophenyl)-2-furoyl amide (3o):** White solid. 93%. M.p.: 203–204°C. ^{1}H NMR (DMSO-d_6) δ 10.18 (s, 1H, NH), 7.22–8.25 (m, 10H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 3328 (NH), 1685 (C=O). MS: *m*/*z*, 387 (M^+). Anal. calcd. for $C_{17}H_{11}N_2O_4Br$: C, 52.74; H, 2.86; N, 7.24. Found: C, 52.80; H, 2.90; N, 7.31.

***N*-(2-Nitrophenyl)-5-(3-nitrophenyl)-2-furoyl amide (3p):** White solid. M.p.: 173–174°C. ^{1}H NMR (DMSO-d_6) δ 10.43 (s, 1H, NH), 7.18–8.31 (m, 10H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 3312 (NH), 1660 (C=O). MS: *m*/*z*, 353 (M^+). Anal. calcd. for $C_{17}H_{11}N_3O_6$: C, 57.80; H, 3.14; N, 11.89. Found: C, 57.73; H, 3.06; N, 11.98.

***N*-(3-Nitrophenyl)-5-(3-nitrophenyl)-2-furoyl amide (3q):** White solid. M.p.: 191–192°C. ^{1}H NMR (DMSO-d_6) δ 10.30 (s, 1H, NH), 7.10–8.32 (m, 10H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 3320 (NH), 1658 (C=O). MS: m/z, 353 (M^+). Anal. calcd. for $C_{17}H_{11}N_3O_6$: C, 57.80; H, 3.14; N, 11.89. Found: C, 57.90; H, 3.20; N, 11.74.

***N*-(4-Nitrophenyl)-5-(3-nitrophenyl)-2-furoyl amide (3r):** White solid. M.p.: 208–209°C. ^{1}H NMR (DMSO-d_6) δ 10.52 (s, 1H, NH), 7.15–8.30 (m, 10H, Ar-H and Fu-H). IR (KBr, ν, cm^{-1}): 3318 (NH), 1656 (C=O). MS: m/z, 353 (M^+). Anal. calcd. for $C_{17}H_{11}N_3O_6$: C, 57.80; H, 3.14; N, 11.89. Found: C, 57.94; H, 3.19; N, 12.00.

ACKNOWLEDGMENTS

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

REFERENCES

1. Dai,. Y.J.; Li, Y.J.; Chen, J.C. Youji Huaxue (Chinese) **1988**, *8*, 443; Chem. Abstr. *110*, 94889.
2. Koretskaya, N.I.; Trubisksyna, T.K.; Mashkovskii, M.D.; Olenik, A.F. Khim. Farm. Zh. **1977**, *11*, 33; Chem. Abstr. *87*, 39715.
3. Burch, H.A.; Write, R.E.; Wright, G.C.; Goldenberg, M.M. J. Pharm. Sci. **1980**, *69*, 107.
4. Wei, T.B.; Chen, J.C.; Wang, X.C.; Yang, S.Y. Chem. J. Univ. (Chinese) **1992**, *13*, 1217; Chem. Abstr. *118*, 191447.
5. Wang, X.C.; Chen, J.C.; Wang, X.C. Chem. J. Univ. (Chinese) **1998**, *19*, 1274; Chem. Abstr. *129*, 275795.
6. Wang, X.C.; Li, Z.; Gao, L.M.; Wei, T.B.; Chen, J.C. Synth. Commun. **2000**.
7. Kvatosikova, A.; Kovac, J.; Sykova, V. Collect. Czech. Chem. Communs. **1974**, *39*, 1892.

Received in Japan April 25, 2001