



## Catalyst-free Friedel–Crafts alkylation of naphthols with nitrostyrenes in the presence of water

Azim Ziyaei Halimehjani<sup>a</sup>, Fezzeh Aryanasab<sup>b</sup>, Mohammad R. Saidi<sup>b,\*</sup>

<sup>a</sup> Faculty of Chemistry, Tarbiat Moallem University, 49 Mofateh St., Tehran, Iran

<sup>b</sup> Department of Chemistry, Sharif University of Technology, PO Box 11365-9516 Tehran 11365, Iran

### ARTICLE INFO

#### Article history:

Received 22 October 2008

Revised 21 December 2008

Accepted 13 January 2009

Available online 19 January 2009

### ABSTRACT

Accelerated Michael-type Friedel–Crafts alkylation of naphthols with nitrostyrenes in the presence of water is reported. The procedure is simple, catalyst-free, and affords good yields of the products.

© 2009 Elsevier Ltd. All rights reserved.

The environment calls on the entire research community to define long-term strategic goals for clean chemistry and to reduce pollutants, especially organic solvents, whose recovery is mandated by evermore strict laws. To reduce the use of ecologically hazardous chemicals, it is advantageous to carry out organic reactions in aqueous media. Indeed, water is recognized as an attractive medium for many organic reactions. Reactions in aqueous media are more environmentally safe, simple to handle, cheaper to operate, and are especially important in industry.<sup>1,2</sup>

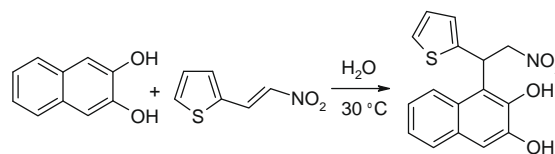
The Friedel–Crafts alkylation is a very important process for C–C bond formation in organic chemistry.<sup>3</sup> Various aromatic compounds, including benzenes with electron-donating substituents, furans, pyrroles, and indoles, have been applied successfully in a number of Friedel–Crafts reactions with diverse electrophiles. Enantioselective variants of this reaction have also been studied in the presence of chiral metal complexes.<sup>4,5</sup> Nevertheless, most reports in this area are focused on relatively more reactive indole or pyrrole derivatives.<sup>6</sup> There are only a few reports on the Friedel–Crafts reaction of benzene derivatives bearing highly electron-donating groups.<sup>4e</sup> Hence, there is a need to develop novel Friedel–Crafts reactions, especially for electron-rich arenes. Naphthols have been demonstrated to be good donors in Friedel–Crafts alkylations with a range of electrophiles, and various biologically active compounds and useful chiral ligands for asymmetric catalysis can be prepared easily by this method.<sup>7,8</sup> Although Friedel–Crafts alkylations of naphthol derivatives with activated species such as iminium ions,<sup>9</sup>  $\alpha,\beta$ -unsaturated olefins<sup>8a</sup>, and aza-dicarboxylate<sup>7b</sup> are well studied, there is only one report on the reaction of 2-naphthol and nitroolefins in the literature.<sup>10</sup>

In continuation of our studies using water as catalyst or solvent for organic transformations, and encouraged by our results using water for Michael addition of amines and thiols to activated olefins,<sup>11</sup> and ring-opening of epoxides by amines in water,<sup>12</sup> we envi-

sioned that the Friedel–Crafts reaction between a nitrostyrene and a 2,3-dihydroxy-naphthalene would be possible through activation of the nitro group in the nitrostyrene and hydroxy groups in 2,3-dihydroxynaphthalene through hydrogen bonding in aqueous medium, **Scheme 1**.

A range of organic solvents were screened for the Friedel–Crafts reaction of 2,3-dihydroxynaphthalene and 2-(2-nitrovinyl)thiophene.<sup>13</sup> As shown in **Table 1**, we found that the best yield was obtained in the presence of water. After optimization of the solvent, we studied the reaction at different temperatures, and found out that the best yield was obtained at 30 °C.

Having established the optimal reaction conditions, we next expanded our study to other naphthols such as 2-naphthol **2** and 2,7-dihydroxynaphthalene **3**. As shown in **Table 2**, 2,3-dihydroxynaphthalene and 2,7-dihydroxynaphthalene showed very good reactivity towards 2-(2-nitrovinyl)-thiophene in the presence of water, and good to excellent yields of products were obtained. However, 2-naphthol gave only a moderate yield. Also, electron-donating and electron-withdrawing groups on the phenyl ring of the nitrostyrene decreased the yield of the reaction. Reaction of 1-naphthol with nitrostyrene gave low yields of the Friedel–Crafts products (ca. less than 10%). We did not observe O-alkylation products in these reactions, and only C-alkylation products were obtained in all cases. Work-up was very simple, involving filtration of the solid material or decanting the water. Purification was accomplished by washing with hot petroleum ether or by using



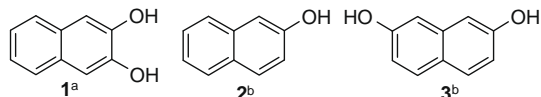
**Scheme 1.** Reaction of 2,3-dihydroxynaphthalene with 2-(2-nitrovinyl)thiophene in the presence of water.

\* Corresponding author. Tel.: +98 21 66005718; fax: +98 21 66012983.  
E-mail address: [Saidi@sharif.edu](mailto:Saidi@sharif.edu) (M.R. Saidi).

**Table 1**

Friedel–Crafts alkylation of 2,3-dihydroxy-naphthalene with 2-(2-nitrovinyl)thiophene in different solvents

Entry	Solvent	Yield <sup>a</sup> (%)
1	H <sub>2</sub> O	92
2	C <sub>2</sub> H <sub>5</sub> OH	30
3	CH <sub>3</sub> OH	38
4	CH <sub>3</sub> CN	60
5	CHCl <sub>3</sub>	52
6	THF	14
7	DMSO	50

<sup>a</sup> Yields based on 2-(2-nitrovinyl)thiophene.**Table 2**Catalyst-free Friedel–Crafts alkylation of naphthol **1**, **2** or **3** with 2-(2-nitrovinyl)thiophene, nitrostyrenes and 2-(2-nitrovinyl)furan in the presence of water at 30 °C

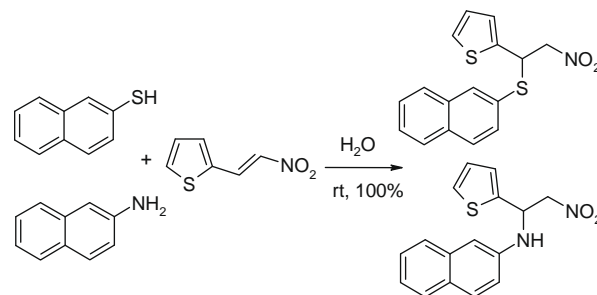
Entry	Naphthol	Yield <sup>c</sup> (%)
1	<b>1</b>	92
2	<b>2</b>	57
3	<b>3</b>	75
4	<b>1</b>	87
5	<b>2</b>	55
6	<b>3</b>	60
7	<b>1</b>	50
8	<b>2</b>	45
9	<b>1</b>	93
10	<b>2</b>	55
11	<b>3</b>	80
12	<b>1</b>	75
13	<b>2</b>	40
14	<b>3</b>	33
15	<b>2</b>	40

<sup>a</sup> Reaction conditions: naphthol **1** (1 mmol), nitrostyrene (1.1 mmol).<sup>b</sup> Reaction conditions: naphthol **2** or **3** (1.1 mmol), nitrostyrene (1 mmol).<sup>c</sup> Isolated yields.

column chromatography (silica gel, ethyl acetate: petroleum ether). Reaction of 2-naphthalenethiol and 2-amino-naphthalene with 2-(2-nitrovinyl)thiophene gave the corresponding thia and aza-Michael addition products in 100% yields, **Scheme 2**.

Theoretical calculations to determine the optimized parameters (dipole moment, solvation energy, and partial charge on the  $\alpha$ -position) of 2,3-dihydroxynaphthalene were performed with the HF/6-311G\*\* basis set using Gaussian software. As shown in **Table 3**, the dipole moment and the partial charge on the  $\alpha$ -position of 2,3-dihydroxynaphthalene in water are greater than in organic solvents, which may ascribe the higher nucleophilic ability of the  $\alpha$ -carbon in 2,3-dihydroxy-naphthalene toward electrophiles.

In conclusion, we have reported a very mild, simple, and catalyst-free method for the Friedel–Crafts alkylation of naphthols in

**Scheme 2.** Reaction of 2-naphthalenethiol and 2-amino-naphthalene with 2-(2-nitrovinyl)thiophene in the presence of water.**Table 3**

Calculated parameters for 2,3-dihydroxynaphthalene in different solvents using the HF/6-311G\*\* basis set

Solvent	$\mu$ (Debye) <sup>a</sup>	$\delta^b$	$\Delta G^{#c}$
H <sub>2</sub> O	3.7116	-0.116498	-11.63
Gas phase	2.6349	-0.085354	—
C <sub>2</sub> H <sub>5</sub> OH	3.6459	-0.115057	-11.26
CH <sub>3</sub> OH	3.6702	-0.115678	-14.29
CHCl <sub>3</sub>	3.1458	-0.092739	-3.75
Toluene	2.9555	-0.089616	-2.95
CH <sub>3</sub> CN	3.3577	-0.095791	-2.13
DMSO	3.3669	-0.095831	-5.95
Acetone	3.3282	-0.095397	-6.27
THF	3.2263	-0.093837	-4.57
CH <sub>3</sub> NO <sub>2</sub>	3.3595	-0.095824	-5.07

<sup>a</sup> Dipole moment for 2,3-dihydroxynaphthalene in different solvents.<sup>b</sup> Partial charge on C-1 of 2,3-dihydroxynaphthalene.<sup>c</sup> Solvation energy.

aqueous medium. The yields are good to excellent, and the work-up is very simple especially on large scale.

## Acknowledgments

We are grateful to the research council of Sharif University of Technology for financial support. We also thank the Faculty of Chemistry of Tarbiat Moallem University for supporting this work.

## References and notes

- Meijer, A.; Otto, S.; Engberts, J. B. F. *N. J. Org. Chem.* **1998**, *63*, 8989.
- Li, C. *J. Chem. Rev.* **1993**, *93*, 2023.
- For a general review on Friedel–Crafts reactions, see: Olah, G. A.; Krishnamurti, R.; Prakash, G. K. S. *Friedel–Crafts Alkylations*. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 3, p 293.
- For selected examples, see: (a) Jensen, K. B.; Thorhaug, J.; Hazell, R. G.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 160; (b) Zhou, J.; Tang, Y. *J. Am. Chem. Soc.* **2002**, *124*, 9030; (c) Palomo, C.; Oiarbide, M.; Kardak, B. G.; Garcia, J. M.; Linden, A. *J. Am. Chem. Soc.* **2005**, *127*, 4154; (d) Evans, D. A.; Fandrick, K. R.; Song, H.-J. *J. Am. Chem. Soc.* **2005**, *127*, 8942; (e) Zhao, J.-L.; Liu, L.; Sui, Y.; Liu, Y.-L.; Wang, D.; Chen, Y.-J. *Org. Lett.* **2006**, *8*, 6127, and references therein.
- For selected examples, see: (a) Paras, N. A.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2001**, *123*, 4370; (b) Terada, M.; Sorimachi, K. *J. Am. Chem. Soc.* **2007**, *129*, 292; (c) Kang, Q.; Zhao, Z.-A.; You, S.-L. *J. Am. Chem. Soc.* **2007**, *129*, 1484; (d) Chen, W.; Du, W.; Yue, L.; Li, R.; Wu, Y.; Ding, L.-S.; Chen, Y.-C. *Org. Biomol. Chem.* **2007**, *5*, 816, and references therein.
- For recent reviews on catalytic asymmetric Friedel–Crafts reactions, see: (a) Bandini, M.; Melloni, A.; Tommasi, S.; Umani-Ronchi, A. *Synlett* **2005**, 1199; (b) Bandini, M.; Melloni, A.; Umani-Ronchi, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 550; (c) Jørgensen, K. A. *Synthesis* **2003**, 1117.
- For limited examples of naphthols in asymmetric Friedel–Crafts reactions, see: (a) Erker, G.; van der Zeijden, A. A. H. *Angew. Chem., Int. Ed.* **1990**, *29*, 512; (b) Brandes, S.; Bella, M.; Kjærsgaard, A.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 1147.
- For limited examples of naphthols in Michael-type Friedel–Crafts reaction in a racemic form, see: (a) Kidwai, M.; Saxena, S.; Khan, M. K. R.; Thukral, S. S. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 4295; (b) Aoki, S.; Amamoto, C.; Oyamada, J.;

- Kitamura, T. *Tetrahedron* **2005**, *61*, 9291; (c) Nakazawa, T.; Furukawa, H.; Torii, K.; Itabashi, K. *Nippon Kagaku Kaishi* **1989**, 244.
9. Saidi, M. R.; Azizi, N. *Tetrahedron: Asymmetry* **2003**, *14*, 389.
10. Liu, T.-Y.; Cui, H.-L.; Chai, O.; Long, J.; Li, B.-J.; Wu, Y.; Ding, L.-S.; Chen, Y.-C. *Chem. Commun.* **2007**, 2228.
11. (a) Ziyaei, A.; Saidi, M. R. *Tetrahedron Lett.* **2008**, *49*, 1244; (b) Azizi, N.; Arynasab, F.; Saidi, M. R. *Org. Biomol. Chem.* **2006**, *4*, 4275; (c) Azizi, N.; Torkian, L.; Saidi, M. R. *J. Mol. Catal. A: Chem.* **2007**, *275*, 109; (d) Ziyaei-Halimjani, A.; Saidi, M. R. *Can. J. Chem.* **2006**, *84*, 1515; (e) Azizi, N.; Aryanadab, F.; Torkian, L.; Ziyaei-Halimehjani, A.; Saidi, M. R. *J. Org. Chem.* **2006**, *71*, 3634.
12. Azizi, N.; Saidi, M. R. *Org. Lett.* **2006**, *7*, 3649.
13. *General procedure for the reaction of naphthol derivatives with nitrostyrene*: In a round-bottomed flask equipped with a magnetic stirrer, naphthol, nitrostyrene (as noted in Table 2), and water (3 mL) were added. The mixture was stirred at room temperature, and the progress of the reaction was monitored by TLC (silica gel, ethyl acetate: petroleum ether 1:3). After completion of the reaction (8 h), the products were extracted with ethyl acetate (2 × 10 mL). Evaporation of the solvent gave a crude product. Purification was accomplished by washing with hot petroleum ether (Table 2, entries 1, 4, 9, and 12) or using column chromatography (silica gel, ethyl acetate: petroleum ether 1:3).
- Selected spectroscopic data*: Table 2, entry 1: IR (KBr):  $\nu = 3422, 1638, 1549, 1377, 1259, 1184, 1008 \text{ cm}^{-1}$ ;  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3/\text{DMSO}$ ),  $\delta$ , 5.20–5.30 (m, 2H), 5.71 (t,  $J = 7.4 \text{ Hz}$ , 1H), 6.66 (dd,  $J = 4.9, 3.6 \text{ Hz}$ , 1H), 6.81 (d,  $J = 3.3 \text{ Hz}$ , 1H), 6.90 (d,  $J = 5.1 \text{ Hz}$ , 1H), 6.97 (s, 1H), 7.04–7.11 (m, 2H), 7.37 (d,  $J = 8.0 \text{ Hz}$ , 1H), 7.60 (br, 1H, –OH), 7.73 (d,  $J = 8.4 \text{ Hz}$ , 1H), 9.85 (br s, 1H, –OH) ppm;  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3/\text{DMSO}$ ),  $\delta$ , 37.2, 78.9, 109.9, 116.8, 121.8, 123.2, 123.9, 124.3, 125.0, 126.6, 126.9, 127.2, 129.4, 142.5, 145.5, 145.7 ppm. Decomposed at 130 °C. Anal. Calcd for  $\text{C}_{16}\text{H}_{13}\text{NO}_4\text{S}$ : C, 60.95; H, 4.12; N, 4.44. Found: C, 60.40; H, 3.90; N, 4.54.
- Table 2, entry 3:  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3/\text{DMSO}$ ),  $\delta$ , 4.85 (dd,  $J = 13.0 \text{ Hz}$ , 6.7, 1H) 4.96 (dd,  $J = 12.9, 7.7 \text{ Hz}$ , 1H), 5.29 (t,  $J = 7.3 \text{ Hz}$ , 1H), 6.35 (m, 2H), 6.44 (d,  $J = 8.8 \text{ Hz}$ , 1H), 6.51 (d,  $J = 3.2 \text{ Hz}$ , 1H), 6.61 (d,  $J = 5.1 \text{ Hz}$ , 1H), 6.82 (s, 1H), 6.99 (d,  $J = 8.7 \text{ Hz}$ , 1H), 7.03 (d,  $J = 8.7 \text{ Hz}$ , 1H), 8.99 (br s, 1H, OH), 9.36 (br s, 1H, OH) ppm;  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3/\text{DMSO}$ ),  $\delta$ , 29.5, 79.2, 104.3, 114.7, 115.2, 115.4, 123.4, 124.3, 125.0, 125.5, 129.4, 130.3, 134.5, 143.5, 153.8, 156.5 ppm. Table 2, entry 4: IR (KBr):  $\nu = 3440, 1632, 1547, 1516, 1458, 1366, 1259, 1180, 1012 \text{ cm}^{-1}$ ;  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3/\text{DMSO}$ ),  $\delta$ , 5.28–5.34 (m, 2H), 5.58 (t,  $J = 7.5 \text{ Hz}$ , 1H), 7.01–7.16 (m, 6H), 7.25–7.31 (m, 3H), 7.42 (d,  $J = 7.8 \text{ Hz}$ , 1H), 7.79 (d,  $J = 8.5 \text{ Hz}$ , 1H), 9.81 (br s, 1H, –OH) ppm;  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3/\text{DMSO}$ ),  $\delta$ , 41.9, 78.5, 110.0, 117.7, 122.5, 123.6, 124.2, 127.2, 127.3, 128.0, 128.2, 128.9, 129.9, 140.7, 145.8, 146.2 ppm. Decomposed at 150 °C. Anal. Calcd for  $\text{C}_{18}\text{H}_{15}\text{NO}_4$ : C, 69.90; H, 4.85; N, 4.53. Found: C, 69.45; H, 4.66; N, 4.58.
- Table 2, entry 6:  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3/\text{DMSO}$ ),  $\delta$ , 5.08–5.23 (m, 3H), 6.55–6.65 (m, 2H), 6.9 (m, 3H), 7.10–7.23 (m, 5H), 8.99 (br s, 1H), 9.17 (br s, 1H) ppm;  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3/\text{DMSO}$ ),  $\delta$ , 40.3, 79.2, 104.9, 115.3, 115.6, 115.8, 123.7, 126.8, 128.0, 128.5, 129.3, 130.4, 135.1, 140.7, 155.7, 156.5 ppm.
- Table 2, entry 9: IR (KBr):  $\nu = 3515, 3412, 1635, 1551, 1379, 1280, 1182, 1015 \text{ cm}^{-1}$ ;  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3/\text{DMSO}$ ),  $\delta$ , 4.96 (dd,  $J = 13.2, 6.9 \text{ Hz}$ , 1H), 5.21 (dd,  $J = 13.2, 7.6 \text{ Hz}$ , 1H), 5.62 (t,  $J = 7.1 \text{ Hz}$ , 1H), 5.79 (d,  $J = 2.7 \text{ Hz}$ , 1H), 6.0 (t,  $J = 7.2 \text{ Hz}$ , 1H), 6.92 (s, 1H), 6.96–7.03 (m, 2H), 7.05 (s, 1H), 7.31 (d,  $J = 7.9 \text{ Hz}$ , 1H), 7.58 (d,  $J = 8.3 \text{ Hz}$ , 1H), 7.7 (br s, 1H, OH), 9.81 (br s, 1H, OH) ppm;  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3/\text{DMSO}$ ),  $\delta$ , 35.9, 77.0, 106.9, 110.3, 111.1, 115.2, 122.5, 123.5, 124.1, 127.3, 127.9, 129.8, 141.8, 146.2, 146.3, 153.5 ppm. Decomposed at 172 °C. Anal. Calcd For  $\text{C}_{16}\text{H}_{13}\text{NO}_5$ : C, 64.21; H, 4.35; N, 4.68. Found: C, 63.98; H, 3.90; N, 4.54.
- Table 2, entry 11:  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3/\text{DMSO}$ ),  $\delta$ , 5.0 (dd,  $J = 13.3, 6.9 \text{ Hz}$ , 1H), 5.40 (dd,  $J = 13.2, 8.1 \text{ Hz}$ , 1H), 5.75 (t,  $J = 7.3 \text{ Hz}$ , 1H), 5.93 (d,  $J = 3.1 \text{ Hz}$ , 1H), 6.14 (t,  $J = 2.42 \text{ Hz}$ , 1H), 6.80–6.85 (m, 3H), 6.9 (s, 1H), 6.95 (s, 1H), 7.41 (d,  $J = 8.7 \text{ Hz}$ , 1H), 7.46 (d,  $J = 8.7 \text{ Hz}$ , 1H), 9.3 (br s, 1H, OH) ppm;  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3/\text{DMSO}$ ),  $\delta$ , 35.6, 76.9, 104.6, 106.5, 110.7, 112.6, 115.4, 115.5, 123.6, 129.5, 130.5, 134.9, 141.2, 153.5, 154.3, 156.3 ppm.
- Table 2, entry 14:  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3/\text{DMSO}$ ),  $\delta$ , 5.14 (dd,  $J = 12.9, 7.0 \text{ Hz}$ , 1H), 5.16–5.36 (m, 2H), 6.50–6.80 (m, 2H), 7.03 (d,  $J = 7.7, 2.3 \text{ Hz}$ , 2H), 7.24 (m, 3H), 7.34 (d,  $J = 8.7 \text{ Hz}$ , 1H), 7.40 (d,  $J = 8.7 \text{ Hz}$ , 1H), 9.0 (br s, 1H, OH), 9.2 (br s, 1H, OH) ppm;  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3/\text{DMSO}$ ),  $\delta$ , 40.5, 79.1, 104.9, 115.2, 115.5, 115.8, 123.9, 128.7, 129.4, 129.6, 130.6, 132.5, 135.0, 139.5, 154.0, 156.7 ppm.