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A facile method for synthesis of polysubstituted naphthalene derivatives through pyrrolidine catalyzed domino reaction

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ABSTRACT

A novel synthetic method for polysubstituted naphthalene derivatives via a pyrrolidine-mediated cascade Michael/Henry reaction was developed, in which easily prepared 2-(2-oxoethyl)benzaldehydes and nitroalkenes were employed as the starting materials. The reaction consists of four consecutive reactions that include a cascade Michael/Henry reaction, a dehydration reaction, and an aromatization reaction in one pot to afford synthetically important naphthalene derivatives with moderate yields.

1. Introduction

Substituted naphthalene derivatives have emerged as very important biological entities[1] and frequently are employed as starting materials for the preparation of more complex polynuclear aromatic ring systems.[2] The development of new and efficient methodologies for the synthesis of polysubstituted naphthalene derivatives has recently attracted much attention. A variety of methods, such as transition-metal-catalyzed [2+2+2] alkyne cyclizations;[3] Lewis acid catalyzed cyclization of carbonyl compounds with alkynes;[4] and [4+2] cyclizations,[5] have been reported for their construction.[6] However, the overall process sometimes suffers relatively expensive catalysts, harsh reaction conditions, multi-step synthesis, and a mixture of isomers. To the best of our knowledge, using small organic molecules as catalysts to synthesize polysubstituted naphthalene derivatives has not been reported. In the past decade organocatalysis has been referred to as a research topic with many advantages in synthetic organic chemistry, and the field of organocatalysis has now reached adolescence[7] making many once unthinkable syntheses possible. Compared to other types of organic synthesis reaction, organocatalysts have incomparable advantages. As a further application of the organocatalyst in organic synthesis reactions, we have developed a tandem Michael/Henry reaction between 2-(2-oxoethyl)benzaldehydes and nitroalkenes to afford polysubstituted naphthalene derivatives in a single operation.

2. Results and discussion

Recently, Hayashi, etc.[8a–c] successfully used aqueous pentane-1,5-dial and nitroalkene in a highly enantioselective domino synthesis of optically active cyclohexane derivatives. Our group has developed an enantioselective synthetic method for substituted tetrahydropyridines via a proline-mediated cascade Mannich-type/intramolecular cyclization of *N*-PMP aldimines.[8d] We anticipated that 2-(2-oxoethyl)benzaldehyde, an analogue of pentane-1,5-dial, might be utilized for the formation of optically active tetrahydronaphthalenes by a cascade Michael/Henry cyclization reaction catalyzed by organic molecules. Then, the reaction between 2-(2-oxoethyl)benzaldehyde **1a** and (2-nitrovinyl)benzene **2a**, using L-proline(0.2 equiv) as a catalyst and DMAP(0.2 equiv) as an additive, was investigated in methylene chloride in the presence of water. After the completion of the reaction the dehydration and aromatization product 3-nitro-2-phenyl-1-naphthaldehyde **3a** (isolated in 44% yield) was obtained instead of the expected product (Table 1, entry 1). Based on this result, efforts were made to improve the yield of this novel synthetic reaction for synthesis of polysubstituted naphthalene derivatives (Table 1).

First, we performed a catalyst screening with various amines and found that pyrrolidine could catalyze the reaction efficiently to furnish the desired product **3a** in 58% yield, and glycine could not catalyze the reaction (Table 1, entries 2 and 3). Next we examined different solvents with pyrrolidine as the catalyst and found that methylene chloride was the optimal one for this cascade process, and both tetrahydrofuran and methanol gave lower yields of the desired product (Table 1, entries 4 and 5). To test the effect of the

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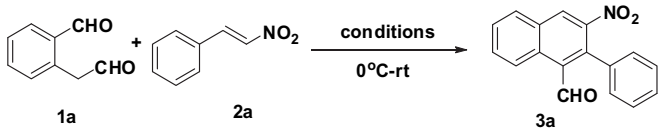
Table 1
Optimization of the reaction conditions[a]



1a 2a 3a

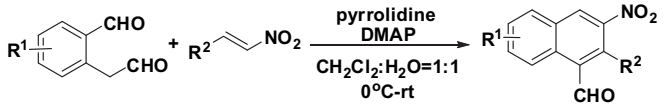
entry	Catalyst	Solvent[b]	Additive	*t*/h	Yield[c] %
1	Proline	CH_2Cl_2	DMAP	48	44
2	Pyrrolidine	CH_2Cl_2	DMAP	48	58
3	Glycine	CH_2Cl_2	DMAP	72	0
4	Pyrrolidine	THF	DMAP	72	40
5	Pyrrolidine	MeOH	DMAP	72	23
6	Pyrrolidine	CH_2Cl_2	DABCO	72	41
7	Pyrrolidine	CH_2Cl_2	K_2CO_3	72	28
8	Pyrrolidine	CH_2Cl_2	TEA	72	19
9	Pyrrolidine	CH_2Cl_2	DIPEA	72	37
10	Pyrrolidine	CH_2Cl_2	—	144	8

[a] Unless otherwise specified, all reactions were carried out with **1a** (0.4 mmol), **2a** (0.2 mmol), organocatalyst (20 mol %), and additive (20 mol %) in the indicated solvent and water (2.0 mL, $V_{solvent}/V_{water}$=1:1) at 0 °C for 4 h, and then the reaction mixture was stirred vigorously at room temperature.
[b] $V_{solvent}/V_{water}$=1:1.
[c] Isolated yield of the product **3a** after flash chromatography.

additive on the yield, we employed various bases (Table 1, entries 6–9) and found that all the additives promoted the reaction to afford the desired product **3a** in lower yields compared to DMAP. Reaction without an additive resulted in much longer reaction time and much lower yield (Table 1, entry 10). Thus, we preferred to perform this cascade reaction with DMAP as the additive.

Under the optimized reaction conditions, the generality of the reaction was investigated by employing several substituted dialdehydes and nitroalkenes. The results are summarized in Table 2. The reaction is fast with electron-deficient aryl-substituted nitroethenes (Table 2, entries 2–9), while it is slow with electron-rich aryl-substituted ones (Table 2, entries 10–11). The heteroaromatic group, such as furyl, could also successfully afford the desired product in moderate yield (Table 2, entry 12). Furthermore, dialdehydes with 5-Br, 4-Br or 5-CH_3 group could act as four-carbon units in this reaction (Table 2, entries 13–18), and the corresponding cascade reaction was a little slower. And we have investigated the reaction of 3-methyl-2-(2-oxoethy l)benzaldehyde **1e** with nitroalkene in general Experimental procedure (Table 2, entry 19). However, after the completion of the reaction the dehydration product dihydronaphthalene **8s** (isolated in 53% yield) was obtained instead of the expected product 8-methyl-3-nitro-2-phenyl-1-naphthaldehyde **3s**, suggesting that the spatial effect of 3-CH_3 group prevented oxidative dehydrogenation process. A nitroalkene with an alkyl group, such as *n*-propyl did not give the corresponding naphthalene, perhaps because of the lability of the aliphatic nitroalkene in the presence of water (Table 2, entry 20).

Table 2
The synthesis of polysubstituted naphthalene derivatives[a]

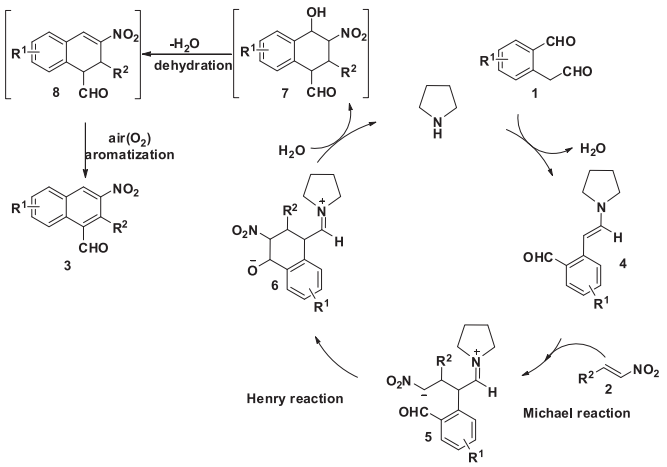


1 2 3

entry	R^1	R^2	*t*/h	Product	Yield[b] %
1	H	Ph	48	**3a**	58
2	H	2-Br–C_6H_4	48	**3b**	59
3	H	3-Br–C_6H_4	48	**3c**	62
4	H	4-Br–C_6H_4	48	**3d**	62
5	H	3-Cl–C_6H_4	48	**3e**	61
6	H	4-Cl–C_6H_4	48	**3f**	58
7	H	3-NO_2–C_6H_4	48	**3g**	46
8	H	4-NO_2–C_6H_4	48	**3h**	45
9	H	4-CN–C_6H_4	48	**3i**	62
10	H	4-CH_3–C_6H_4	72	**3j**	51
11	H	2-OCH_3–C_6H_4	72	**3k**	52
12	H	2-Furyl	72	**3l**	50
13	5-CH_3	Ph	72	**3m**	55
14	5-CH_3	3-Br–C_6H_4	72	**3n**	65
15	5-Br	Ph	72	**3o**	63
16	5-Br	3-Br–C_6H_4	72	**3p**	63
17	5-Br	4-Br–C_6H_4	72	**3q**	65
18	4-Br	Ph	72	**3r**	64
19[c]	3-CH_3	Ph	72	**3s**	53
20	H	*n*-Pr	72	—	0

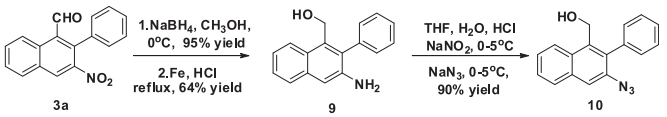
[a] Unless otherwise specified, all reactions were carried out with **1** (0.4 mmol), **2** (0.2 mmol), pyrrolidine (20 mol %), and DMAP (20 mol %) in CH_2Cl_2 and water (2.0 mL, V_{DCM}/V_{water}=1:1) at 0 °C for 4 h, and then the reaction mixture was stirred vigorously at room temperature.
[b] Isolated yield of the product **3** after flash chromatography.
[c] Isolated product was not **3s**, but dihydronaphthalene **8s**.

Based on previous experience[8a] with Michael/Henry reactions, the following stepwise cascade reaction mechanism was proposed to account for the outcome of the reaction (Scheme 1). The dialdehyde would react with pyrrolidine to form the enamine **4**, which undergoes Michael reaction with a nitroalkene to generate **5**. Zwitterion **5** would then react with the aldehyde moiety via an intramolecular Henry reaction to provide **6**, which is hydrolyzed to give the key intermediate tetrahydronaphthalene **7**. Under aqueous basic conditions, the unstable intermediate **7** undergoes dehydration to afford dihydronaphthalene **8**, which is further oxidized by air[9] to furnish the final polysubstituted naphthalene **3**.



Scheme 1. Proposed mechanism for the cascade reaction.

As illustrated in Scheme 2, the polysubstituted naphthalene derivates **3** could be smoothly converted to some versatile building blocks for organic syntheses. The compound **3a** was converted into (3-amino-2-phenylnaphthalen-1-yl)methanol **9** by reduction with $NaBH_4$ and subsequent deoxidation under the catalysis of Fe/HCl. Furthermore, we converted **9** into (3-azido-2-phenylnaphthalen-1-yl)methanol **10**, which was used to react with NaN_3 in the presence of $NaNO_2$ and HCl.[11] These successful reactions provide evidence that the current domino reaction is a useful methodology in the synthesis of polysubstituted naphthalene derivatives.



3a 9 10

Scheme 2. Synthesis of compounds **9** and **10**.

3. Conclusion

In summary, we have developed a novel synthetic method for polysubstituted naphthalene derivatives via a pyrrolidine-mediated cascade cyclization reaction, in which easily prepared 2-(2-oxoethyl) benzaldehydes and nitroalkenes are employed as the starting materials. The reaction consists of four consecutive reactions that include a cascade Michael/Henry reaction, a dehydration reaction, and an aromatization reaction in one pot to afford synthetically important naphthalene derivatives in moderate yields. Based on the important results, the synthetic applications of this cascade reaction are currently under active investigations.

4. Experimental section

4.1. General

All reactions were performed under an air atmosphere unless otherwise stated. All glass apparatuses were dried and cooled before use. Reagents used were obtained from commercial suppliers or redistilled. In all cases of chromatography, distilled solvents were used as eluents. Flash chromatography was performed on silica gel (200–300 mesh). Thin-layer chromatography (TLC) was carried out using GF_{254} (200–300 mesh) fluorescent treated silica, which was visualised under UV light (250 nm) or by staining with phosphomolybdic acid solutions as a chromogenic reagent.

All ^1H and ^{13}C NMR spectra were recorded using a Bruker 400 MHz and 100 MHz spectrometers. Chemical shifts (δ) are given in parts per million, and coupling constants (J) are given in hertz (Hz). Melting points were determined on an uncorrected XT-4 melting point apparatus. MS was measured on a VG-7070E spectrometer (EI at 70 eV). IR spectra were recorded using Nicolet NEXUS 670 FTIR instrument. Starting materials **1** were prepared according to the published methods,[10] the Experimental procedure and characterization data are available in the Supplementary data.

4.2. General experimental procedure for synthesis of polysubstituted naphthalene derivatives

2-(2-Oxoethyl)benzaldehyde **1** (0.4 mmol) was added to a mixture of nitroalkene **2** (0.2 mmol), pyrrolidine (0.04 mmol), and DMAP (0.04 mmol) in CH_2Cl_2 and water (2.0 mL, V_{DCM}/V_{water}=1:1) at 0 °C. The reaction mixture was stirred at 0 °C for 4 h, and then it was stirred vigorously at room temperature until the intermediate was consumed as monitored by TLC. The mixture was extracted with CH_2Cl_2. The combined organic fractions were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (PE/EtOAc) to afford the corresponding naphthalene **3**.

*4.2.1. 3-Nitro-2-phenylnaphthalene-1-carbaldehyde (**3a**).* Light yellow solid, mp 158–159 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.98 (s, 1H), 9.13 (d, J=8.8 Hz, 1H), 8.55 (s, 1H), 8.04 (d, J=8.0 Hz, 1H), 7.86–7.82 (m, 1H), 7.75–7.71 (m, 1H), 7.50–7.48 (m, 3H), 7.38–7.36 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 193.1, 147.7, 138.8, 132.6, 132.0, 131.8, 131.7, 131.2, 129.9, 129.4, 129.2, 128.7, 128.6, 128.5, 126.0; IR (KBr): 3365, 2879, 1685, 1527, 1057, 756 cm^{-1}; MS (EI, 70 eV), m/z (%): 277 (M^+, 22), 260 (89), 230 (100), 202 (83), 189 (17), 176(10), 88 (21).

*4.2.2. 2-(2-Bromophenyl)-3-nitronaphthalene-1-carbaldehyde (**3b**).* Light yellow solid, mp 112–113 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.98 (s, 1H), 9.17 (d, J=8.4 Hz, 1H), 8.78 (s, 1H), 8.09 (d, J=8.4 Hz, 1H), 7.89–7.86 (m, 1H), 7.80–7.72 (m, 2H), 7.45 (t, J=7.2 Hz, 1H), 7.39–7.32 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 192.6, 146.2, 138.0, 134.4, 132.8, 132.4, 132.2, 131.6, 131.5, 131.3, 130.6, 130.0, 129.8, 128.9, 127.5, 126.2, 123.8; IR (KBr): 3373, 3068, 2957, 2869, 1694, 1531, 1344, 1218, 762 cm^{-1}; MS (EI, 70 eV), m/z (%): 276 (100), 230 (51), 200 (32), 189 (15), 100(9).

*4.2.3. 2-(3-Bromophenyl)-3-nitronaphthalene-1-carbaldehyde (**3c**).* Light yellow solid, mp 153–154 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 10.00 (s, 1H), 9.12 (d, J=8.4 Hz, 1H), 8.61 (s, 1H), 8.06 (d, J=8.4 Hz, 1H), 7.88–7.84 (m, 1H), 7.75 (t, J=7.6 Hz, 1H), 7.64 (dd, J=1.2, 8.0 Hz, 1H), 7.54 (s, 1H), 7.37 (t, J=8.0 Hz, 1H), 7.31 (d, J=7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 192.6, 147.1, 137.1, 134.8, 132.5, 132.3, 132.2, 132.0, 131.8, 131.2, 130.0, 129.6, 129.2, 128.9, 128.5, 126.1, 122.8; IR (KBr): 3399, 2922, 2853, 1687, 1528, 1341, 757 cm^{-1}; MS (EI, 70 eV), m/z (%): 355 (M^+, 21), 338 (62), 308 (59), 259 (40), 229 (27), 200 (100), 189 (38), 100 (67).

*4.2.4. 2-(4-Bromophenyl)-3-nitro-1-naphthaldehyde (**3d**).* Light yellow solid, mp 114–115 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.99 (s, 1H), 9.10 (d, J=8.4 Hz, 1H), 8.58 (s, 1H), 8.05 (d, J=8.4 Hz, 1H), 7.87–7.83 (m, 1H), 7.74 (t, J=7.6 Hz, 1H), 7.63 (d, J=8.4 Hz, 2H), 7.24 (d, J=8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 192.6, 147.2, 137.4, 132.2, 131.9, 131.8, 131.8, 131.7, 131.4, 131.2, 129.6, 129.0, 128.9, 126.0, 123.7; IR (KBr): 3364, 3072, 2922, 1690, 1530, 1340, 1068, 761 cm^{-1}; MS (EI, 70 eV), m/z (%): 355 (M^+, 31), 338 (52), 308 (52), 259 (45), 229 (32), 200(100), 189 (38), 100 (73).

*4.2.5. 2-(3-Chlorophenyl)-3-nitro-1-naphthaldehyde (**3e**).* Light yellow solid, mp 166–167 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 10.00 (s, 1H), 9.12 (d, J=8.4 Hz, 1H), 8.61 (s, 1H), 8.06 (d, J=8.4 Hz, 1H), 7.88–7.84 (m, 1H), 7.75 (t, J=7.6 Hz, 1H), 7.49 (d, J=8.0 Hz, 1H), 7.43 (t, J=7.6 Hz, 1H), 7.38 (s, 1H), 7.26 (d, J=6.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 192.6, 147.1, 137.2, 134.8, 134.6, 132.3, 132.0, 131.8, 131.2, 129.8, 129.7, 129.6, 129.4, 129.2, 128.9, 128.1, 126.1; IR (KBr): 3399, 2924, 1692, 1530, 1344, 1060, 763 cm^{-1}; MS (EI, 70 eV), m/z (%): 311 (M^+, 23), 294 (75), 264 (100), 236 (24), 200 (68), 189 (21), 100 (47).

*4.2.6. 2-(4-Chlorophenyl)-3-nitronaphthalene-1-carbaldehyde (**3f**).* Light yellow solid, mp 129–130 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.99 (s, 1H), 9.10 (d, J=8.8 Hz, 1H), 8.58 (s, 1H), 8.05 (d, J=8.0 Hz, 1H), 7.87–7.83 (m, 1H), 7.76–7.72 (m, 1H), 7.49–7.46 (m, 2H), 7.32–7.29 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 192.7, 147.4, 137.4, 135.6, 132.2, 131.9, 131.8, 131.2, 131.1, 129.5, 129.0, 128.9, 128.8, 126.0; IR (KBr): 3743, 3361, 2920, 1686, 1529, 1335, 1058, 854, 762 cm^{-1}; MS (EI, 70 eV), m/z (%): 311 (M^+, 37), 294 (70), 264 (100), 236 (17), 200 (68), 189 (18), 100 (39).

*4.2.7. 3-Nitro-2-(3-nitrophenyl)naphthalene-1-carbaldehyde (**3g**).* Light yellow solid, mp 199–200 °C; ^1H NMR (DMSO-d_6, 400 MHz) δ 9.97 (s, 1H), 9.15 (s, 1H), 8.95 (d, J=8.8 Hz, 1H), 8.39–8.36 (m, 3H), 7.99–7.93 (m, 2H), 7.89–7.80 (m, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 193.0, 147.5, 146.5, 136.4, 135.1, 135.0, 132.4, 131.9, 131.7, 130.7, 130.3, 129.9, 129.7, 129.0, 125.2, 124.4, 123.7; IR (KBr): 3416, 2920, 1957, 1678, 1526, 1340, 1212, 716 cm^{-1}; MS (EI, 70 eV), m/z (%): 322 (M^+, 27), 305 (99), 275 (66), 229 (49), 200 (100), 189 (41), 176 (18), 100 (29).

*4.2.8. 3-Nitro-2-(4-nitrophenyl)naphthalene-1-carbaldehyde (**3h**).* Light yellow solid, mp 182–183 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 10.00 (s, 1H), 9.10 (d, J=8.8 Hz, 1H), 8.74 (s, 1H), 8.38 (d, J=8.4 Hz, 2H), 8.12 (d, J=7.6 Hz, 1H), 7.93–7.89 (m, 1H), 7.80 (t, J=7.6 Hz, 1H), 7.58 (d, J=8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 191.8, 148.2, 146.3, 140.1, 136.1, 132.7, 132.2, 131.8, 131.3, 130.8129.8, 129.7, 129.3, 126.1, 123.7; IR (KBr): 3403, 1933, 1526, 1343, 1111, 711 cm^{-1}; MS (EI, 70 eV), m/z (%): 322 (M^+, 14), 305 (66), 275 (21), 229 (35), 200 (100), 189 (46), 176 (18), 100 (35).

*4.2.9. 4-(1-Formyl-3-nitronaphthalen-2-yl) benzonitrile (**3i**).* Light yellow solid, mp 158–159 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.98 (s,

1H), 9.09 (d, *J*=8.8 Hz, 1H), 8.70 (s, 1H), 8.10 (d, *J*=8.0 Hz, 1H), 7.92–7.88 (m, 1H), 7.79 (t, *J*=8.8 Hz, 3H), 7.51 (d, *J*=8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 191.9, 146.5, 138.1, 136.5, 132.7, 132.2, 132.1, 131.7, 131.3, 130.5, 129.8, 129.7, 129.2, 126.1, 118.0, 113.2; IR (KBr): 3404, 3075, 2223, 1681, 1525, 1335, 1054, 859, 747 cm^{-1}; MS (EI, 70 eV), *m*/*z* (%): 302 (M^+, 18), 285 (69), 255 (100), 227 (70), 200 (19), 125 (11), 100 (32), 87 (20).

*4.2.10. 3-Nitro-2-p-tolylnaphthalene-1-carbaldehyde (**3j**).* Light yellow solid, mp 120–121 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.98 (s, 1H), 9.13 (dd, *J*=0.8, 8.8 Hz, 1H), 8.52 (s, 1H), 8.03 (d, *J*=8.0 Hz, 1H), 7.85–7.81 (m, 1H), 7.74–7.70 (m, 1H), 7.29 (d, *J*=8.0 Hz, 2H), 7.25 (d, *J*=8.0 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 193.3, 148.0, 139.3, 138.9, 131.9, 131.8, 131.7, 131.2, 129.8, 129.5, 129.4, 129.3, 129.2, 128.5, 126.0, 21.3; IR (KBr): 3363, 2921, 1690, 1530, 1347, 1059, 755 cm^{-1}; MS (EI, 70 eV), *m*/*z* (%): 291 (M^+, 53), 274 (100), 244 (90), 215 (84), 202 (46), 189 (31), 107 (18), 95 (22).

*4.2.11. 2-(2-Methoxyphenyl)-3-nitro-1-naphthaldehyde (**3k**).* Light yellow solid, mp 135–136 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.97 (s, 1H), 9.13 (d, *J*=8.8 Hz, 1H), 8.63 (s, 1H), 8.05 (d, *J*=8.4 Hz, 1H), 7.84–7.80 (m, 1H), 7.73–7.69 (m, 1H), 7.51–7.47 (m, 1H), 7.21 (dd, *J*=1.6, 7.6 Hz, 1H), 7.10 (t, *J*=7.6 Hz, 1H), 7.01 (d, *J*=8.4 Hz, 1H), 3.74 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 193.5, 156.5, 147.5, 136.0, 132.2, 131.8, 131.7, 131.7, 131.6, 131.0, 129.5, 128.9, 128.4, 125.9, 121.7, 120.9, 110.8, 55.5; IR (KBr): 3401, 2932, 1690, 1529, 1345, 1020, 758 cm^{-1}; MS (EI, 70 eV), *m*/*z* (%): 307 (M^+, 99), 290 (60), 273 (62), 245 (48), 231 (68), 217 (50), 202 (34), 189 (100), 163 (25), 95 (50).

*4.2.12. 2-(Furan-2-yl)-3-nitronaphthalene-1-carbaldehyde (**3l**).* Light yellow solid, mp 105–106 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.08 (s, 1H), 9.00 (d, *J*=8.8 Hz, 1H), 8.55 (s, 1H), 8.03 (d, *J*=8.4 Hz, 1H), 7.85–7.81 (m, 1H), 7.75–7.65 (m, 1H), 7.64 (s, 1H), 6.69–6.62 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 192.2, 146.4, 145.1, 143.5, 132.8, 132.0, 131.9, 130.8, 129.6, 129.1, 129.0, 126.5, 126.0, 116.6, 111.9; IR (KBr): 3343, 2867, 1680, 1531, 1349, 1215, 1013, 756 cm^{-1}; MS (EI, 70 eV), *m*/*z* (%): 267 (M^+, 7), 238 (6), 222 (35), 194 (25), 166 (100), 152 (94), 139 (78), 126 (72).

*4.2.13. 6-Methyl-3-nitro-2-phenylnaphthalene-1-carbaldehyde (**3m**).* Light yellow solid, mp 153–154 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.96 (s, 1H), 9.02 (d, *J*=8.8 Hz, 1H), 8.45 (s, 1H), 7.79 (s, 1H) 7.66 (d, *J*=8.8 Hz, 1H), 7.49–7.48 (m, 3H), 7.37–7.35 (m, 2H), 2.59 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 193.3, 147.8, 138.9, 138.0, 134.3, 132.7, 132.1, 131.4, 129.9, 129.4, 129.0, 128.5, 128.3, 128.1, 125.7, 21.5; IR (KBr): 3401, 1956, 1677, 1523, 1328, 1214, 1055, 820, 704 cm^{-1}; MS (EI, 70 eV), *m*/*z* (%): 291 (M^+, 41), 274 (100), 244 (97), 215 (76), 202 (43), 189 (27), 139 (11), 95 (26).

*4.2.14. 2-(3-Bromophenyl)-6-methyl-3-nitronaphthalene-1-carbaldehyde (**3n**).* Light yellow solid, mp 162–163 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.99 (s, 1H), 9.02 (d, *J*=8.8 Hz, 1H), 8.53 (s, 1H), 7.82 (s, 1H), 7.70–7.62 (m, 2H), 7.53 (t, *J*=1.6 Hz, 1H), 7.38–7.30 (m, 2H), 2.60 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 192.7, 147.1, 139.3, 136.3, 135.0, 134.7, 132.6, 132.3, 132.2, 131.5, 129.9, 129.5, 128.6, 128.6, 128.5, 125.8, 122.8, 21.5; IR (KBr): 3355, 3063, 1685, 1526, 1343, 1217, 829, 690 cm^{-1}; MS (EI, 70 eV), *m*/*z* (%): 369 (M^+, 21), 352 (48), 322 (37), 273 (42), 243 (30), 215 (100), 189 (29), 139 (15), 107 (35), 95 (43).

*4.2.15. 6-Bromo-3-nitro-2-phenylnaphthalene-1-carbaldehyde (**3o**).* Light yellow solid, mp 172–173 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.94 (s, 1H), 9.03 (d, *J*=9.2 Hz, 1H), 8.42 (s, 1H), 8.19 (d, *J*=2.0 Hz, 1H), 7.88 (dd, *J*=2.0 Hz, 9.2 Hz, 1H), 7.52–7.48 (m, 3H), 7.37–7.35 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 192.7, 148.6, 139.0, 135.2, 132.9, 132.1, 131.7, 131.1, 129.8, 129.6, 129.4, 128.7, 127.7, 127.3, 123.2; IR (KBr): 3405, 3073, 2924, 1949, 1683, 1529, 1050, 698 cm^{-1}; MS (EI, 70 eV), *m*/*z* (%): 355 (M^+, 20), 338 (62), 310 (62), 229 (14), 200 (100), 189 (28), 150 (16), 100 (73).

*4.2.16. 6-Bromo-2-(3-bromophenyl)-3-nitronaphthalene-1-carbaldehyde (**3p**).* Light yellow solid, mp 114–115 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.97 (s, 1H), 9.03 (d, *J*=9.6 Hz, 1H), 8.49 (s, 1H), 8.22 (d, *J*=2.0 Hz, 1H), 7.91 (dd, *J*=2.0, 9.6 Hz, 1H), 7.66 (d, *J*=8.0 Hz, 1H), 7.53 (d, *J*=2.0 Hz, 1H), 7.38 (t, *J*=7.6 Hz, 1H), 7.31 (d, *J*=7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 192.1, 148.0, 137.3, 135.5, 134.3, 133.1, 132.6, 132.5, 131.8, 131.3, 130.1, 129.6, 128.5, 127.8, 123.6, 122.9; IR (KBr): 3366, 3114, 2920, 1694, 1531, 1344, 909, 725 cm^{-1}; MS (EI, 70 eV), *m*/*z* (%): 433 (M^+, 8), 418 (40), 388 (34), 339 (21), 309 (16), 281(9), 200 (100), 150 (12), 100 (80).

*4.2.17. 6-Bromo-2-(4-bromophenyl)-3-nitronaphthalene-1-carbaldehyde (**3q**).* Light yellow solid, mp 132–133 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.96 (s, 1H), 9.01 (d, *J*=9.6 Hz, 1H), 8.47 (s, 1H), 8.21 (d, *J*=1.6 Hz, 1H), 7.91 (dd, *J*=1.6, 9.6 Hz, 1H), 7.65 (d, *J*=8.4 Hz, 2H), 7.24 (d, *J*=8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 192.2, 148.1, 137.6, 135.4, 133.1, 132.0, 131.9, 131.3, 131.2, 131.1, 129.6, 127.8, 127.6, 124.1, 123.5; IR (KBr): 3367, 3110, 2923, 1693, 1531, 1484, 1344, 1073, 824 cm^{-1}; MS (EI, 70 eV), *m*/*z* (%): 433 (M^+, 11), 418 (31), 388 (30), 339 (21), 309 (18), 281(7), 200 (100), 189 (17), 150 (12), 100 (70).

*4.2.18. 7-Bromo-3-nitro-2-phenylnaphthalene-1-carbaldehyde (**3r**).* Light yellow solid, mp 152–153 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.93 (s, 1H), 9.41 (s, 1H), 8.52 (s, 1H), 7.90 (d, *J*=8.4 Hz, 1H), 7.82 (dd, *J*=1.6, 8.4 Hz, 1H), 7.52–7.50 (m, 3H), 7.37–7.35 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 192.5, 148.0, 140.1, 132.4, 132.1, 132.0, 130.6, 130.3, 129.9, 129.5, 128.7, 128.6, 128.5, 127.6; IR (KBr): 3092, 2921, 2853, 1962, 1863, 1767, 1680, 1586, 1535, 1482, 1337, 1200, 1055, 892, 806, 707, 661, 492 cm^{-1}; MS (EI, 70 eV), *m*/*z* (%): 355 (M^+, 10), 338 (66), 310 (58), 229 (40), 200 (100), 189(73), 149 (53), 100 (75), 57 (86), 40 (93).

*4.2.19. 8-Methyl-3-nitro-2-phenyl-1,2-dihydronaphthalene-1-carbaldehyde (**8s**).* Light yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.55 (s, 1H), 8.01 (s, 1H), 7.38–7.34 (m, 3H), 7.21 (t, *J*=3.2 Hz, 3H), 7.11–7.09 (m, 2H), 5.08 (s, 1H), 4.16 (s, 1H), 2.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.5, 148.2, 138.3, 137.8, 134.6, 131.6, 130.2, 129.2, 129.0, 128.9, 127.9, 127.8, 126.9, 57.1, 38.1, 19.4; IR (KBr): 3425, 3065, 2826, 2725, 2255, 1952, 1878, 1721, 1648, 1516, 1466, 1324, 1257, 1062, 1027, 930, 910, 789, 733, 700, 590 cm^{-1}; MS (EI, 70 eV), *m*/*z* (%): 293 (M^+, 31), 276 (100), 246 (83), 217 (79), 204 (43), 191 (29), 97 (20).

4.3. General experimental procedure for synthesis of (3-amino-2-phenylnaphthalen-1-yl)methanol 9

$NaBH_4$ (31 mg, 0.81 mmol) was added in portions to a solution of **3a** (150 mg, 0.54 mmol) in MeOH (5 mL) at 0 °C. The mixture was stirred for 30 min, diluted with water (10 mL), and extracted with EtOAc. The organic layer was dried over $NaSO_4$ and the solvent was removed under reduced pressure. The crude alcohol was resuspended in ethanol (12 mL) and treated with H_2O (3 mL), iron dust (287 mg, 5.1 mmol), and a catalytic amount of concentrated hydrochloric acid. The mixture was stirred at reflux for 30 min, and filtered to remove iron dust. The filtrate was concentrated to one-fifth of its original volume, and extracted with EtOAc. The combined organic fractions were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (PE/EtOAc) to afford **9** as a brown liquid. Yield, 82 mg (64%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.11 (d, *J*=8.4 Hz, 1H), 7.64 (d, *J*=8.4 Hz, 1H), 7.51 (t, *J*=7.2 Hz, 2H), 7.46–7.39 (m, 2H), 7.34–7.30 (m, 3H), 7.07 (s, 1H), 4.77 (s, 2H), 3.61 (s, 2H), 1.60 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.3, 137.0, 134.8, 134.5, 131.2, 129.9, 129.1, 128.0, 126.3, 126.2,

124.4, 123.2, 109.2, 59.8; IR (KBr): 3551, 3469, 3372, 3055, 2923, 1952, 1726, 1624, 1501, 1447, 1384, 1272, 1064, 983, 869, 750, 704, 663 cm^{-1}; MS (EI, 70 eV), *m*/*z* (%): 249 (M^+, 35), 220 (26), 202 (8), 149 (5), 115 (12), 97 (7), 57 (13), 45 (100).

4.4. General experimental procedure for synthesis of (3-azido-2-phenylnaphthalen-1-yl)methanol 10

A solution of $NaNO_2$ (11 mg, 0.16 mmol) in water was added dropwise to a solution of **9** (40 mg, 0.16 mmol) in THF (3 mL) and 10% HCl (3 mL) at 0–5 °C with vigorous stirring. The mixture was kept below 5 °C for 30 min, and then a solution of NaN_3 (15.6 mg, 0.24 mmol) in water (3 mL) was added dropwise while the temperature was kept below 5 °C. After being stirred for 1 h, the reaction mixture was allowed to reach at room temperature, then it was extracted with EtOAc. The extract was dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (PE/EtOAc) to afford **10** as a brown liquid. Yield, 39 mg (90%). ^1H NMR ($CDCl_3$, 400 MHz) δ 8.24 (t, *J*=3.2 Hz, 1H), 7.85–7.81 (m, 1H), 7.60 (s, 1H), 7.56–7.53 (m, 2H), 7.48–7.44 (m, 3H), 7.29–7.25 (m, 2H), 4.82 (s, 2H), 1.61 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.8, 136.6, 135.8, 133.9, 133.7, 130.0, 129.8, 128.2, 127.9, 127.3, 126.9, 126.4, 124.8, 116.0, 59.5; IR (KBr): 3568, 3355, 3057, 2897, 2246, 2111, 1590, 1433, 1339, 1291, 1243, 1027, 1008, 909, 843, 746, 704, 652, 540 cm^{-1}; MS (EI, 70 eV), *m*/*z* (%): 275 (M^+, 2), 229 (37), 217 (31), 189 (8), 149 (4), 114 (8), 84 (17), 61 (13), 43 (100).

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Supplementary data

Experimental procedures, NMR spectra data for new compounds analyses are available in the Supplementary data. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.08.069. These data include MOL files and InChIKeys of the most important compounds described in this article.

References and notes

1. Some representative examples from this century include: (a) Dalton King, H.; Denhart, D. J.; Deskus, J. A.; Ditta, J. L.; Epperson, J. R.; Higgins, M. A.; Kung, J. E.; Marcin, L. R.; Sloan, C. P.; Mattson, G. K.; Molski, T. F.; Krause, R. G.; Bertekap, R. L.; Lodge, N. J.; Mattson, R. J.; Macor, J. E. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5647; (b) Wang, Z.; Elokdah, H.; McFarlane, G.; Pan, S.; Antane, M. *Tetrahedron Lett.* **2006**, *47*, 3365; (c) Saeki, K.; Matsuda, T.; Kato, T.; Yamada, K.; Mizutani, T.; Matsui, S.; Fukuhara, K.; Miyata, N. *Biol. Pharm. Bull.* **2003**, *26*, 448; (d) Hartmann, R. W.; Palusczak, A.; Lacan, F.; Ricci, G.; Ruzziconi, R. *J. Enzyme Inhib. Med. Chem.* **2004**, *19*, 145; (e) Silva, O.; Gomes, E. T. *J. Nat. Prod.* **2003**, *66*, 447; (f) Dai, J.; Liu, Y.; Zhou, Y.-D.; Nagle, D. G. *J. Nat. Prod.* **2007**, *70*, 1824; (g) Brasholz, M.; Sörgel, S.; Azap, C.; Reissig, H.-U. *Eur. J. Org. Chem.* **2007**, 3801; (h) Krohn, K.; Kounam, S. F.; Cludius-Brandt, S.; Draeger, S.; Schulz, B. *Eur. J. Org. Chem.* **2008**, 3615; (i) Lowell, A. N.; Fennie, M. W.; Kozlowski, M. C. *J. Org. Chem.* **2008**, *73*, 1911.
2. De Koning, C. B.; Rousseau, A. L.; van Otterlo, W. A. L. *Tetrahedron* **2003**, *59*, 7.
3. For reviews, see: (a) Saito, S.; Yamamoto, Y. *Chem. Rev.* **2000**, *100*, 2901; (b) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081; (c) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49; (d) Trost, B. M. *Angew. Chem.* **1995**, *107*, 285; *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 259; (e) Grotjahn, D. B. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; Vol. 12, pp 741–770; (f) Schore, N. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 1129–1162.
4. (a) Viswanathan, G. S.; Wang, M.; Li, C.-J. *Angew. Chem.* **2002**, *114*, 2242; *Angew. Chem., Int. Ed.* **2002**, *41*, 2138; (b) Kabalka, G. W.; Ju, Y.; Wu, Z. *J. Org. Chem.* **2003**, *68*, 7915; (c) Asao, A.; Takahashi, K.; Lee, S.; Kasahara, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2002**, *124*, 12650; (d) Asao, A.; Nogami, T.; Lee, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2003**, *125*, 10921.
5. (a) Rengarajan, B.; Vanajakshi, G. *Org. Lett.* **2009**, *11*, 3116; (b) See Ref. 3a and references therein.
6. For the other latest syntheses, see: (a) Dudnik, A. S.; Schwier, T.; Gevorgyan, V. *Tetrahedron* **2009**, *65*, 1859; (b) Dudnik, A. S.; Schwier, T.; Gevorgyan, V. *Org. Lett.* **2008**, *10*, 1465; (c) Duan, S.; Sinha-Mahapatra, D. K.; Herndon, J. W. *Org. Lett.* **2008**, *10*, 1541; (d) Wang, Y.; Xu, J.; Burton, D. J. *J. Org. Chem.* **2006**, *71*, 7780; (e) Zhang, X.; Sarkar, S.; Larock, R. C. *J. Org. Chem.* **2006**, *71*, 236; (f) Barluenga, J.; Vázquez-Villa, H.; Ballesteros, A.; González, J. M. *Org. Lett.* **2003**, *5*, 4121.
7. For reviews on organocatalytic reactions, see: (a) Dondoni, A.; Massi, A. *Angew. Chem.* **2008**, *120*, 4716; *Angew. Chem., Int. Ed.* **2008**, *47*, 4638; (b) Enders, D.; Grondal, M.; Hüttl, R. M. *Angew. Chem.* **2007**, *119*, 1590; *Angew. Chem., Int. Ed.* **2007**, *46*, 1570; (c) Dalko, P. I.; Moisan, L. *Angew. Chem.* **2004**, *116*, 5248; *Angew. Chem., Int. Ed.* **2004**, *43*, 5138 and references therein.
8. (a) Hayashi, Y.; Okano, T.; Aratake, S.; Hazelard, D. *Angew. Chem.* **2007**, *119*, 5010; *Angew. Chem., Int. Ed.* **2007**, *46*, 4922; (b) Hong, B.-C.; Nimje, R. Y.; Sadani, A. A.; Liao, J.-H. *Org. Lett.* **2008**, *10*, 2345; (c) Hazelard, D.; Ishikawa, H.; Hashizume, D.; Koshino, H.; Hayashi, Y. *Org. Lett.* **2008**, *10*, 1445; (d) Han, R.-G.; Wang, Y.; Li, Y.-Y.; Xu, P.-F. *Adv. Synth. Catal.* **2008**, *350*, 1474.
9. (a) Wang, X.-S.; Li, Q.; Zhang, M.-M.; Yao, C.-S.; Tu, S.-J. *J. Heterocycl. Chem.* **2008**, *45*, 1027; (b) Wu, Y.-C.; Liu, L.; Li, H.-J.; Wang, D.; Chen, Y.-J. *J. Org. Chem.* **2006**, *71*, 6592; (c) Eisch, J.-J.; Dluzniewski, T. *J. Org. Chem.* **1989**, *54*, 1269.
10. (a) Frank, M. H.; Subbarao, P. *Synthesis* **1980**, 621; (b) Garratt, P. J.; Vollhardt, K. P. C. *Synthesis* **1971**, 423.
11. Masayuki, T.; Shoko, S.; Shozo, K. *Chem. Pharm. Bull.* **1982**, 3125.