DOI: 10.1002/ejoc.201501152

DABCO-Promoted One-Pot Facile Synthesis of Angularly Fused Furoquinolinones and Furocoumarins

Monoranjan Ghosh[a] and Alakananda Hajra*[a]

Keywords: Fused-ring systems / Oxygen heterocycles / Cyclization / Michael addition / Furans / Synthetic methods

A DABCO-promoted intermolecular cyclization between enols and nitrostyrenes has been developed for the regioselective synthesis of angularly fused furan derivatives in high yields. This protocol is applicable to various enol derivatives, including 4-hydroxyquinolinones, 4-hydroxycoumarin, and 4-hydroxypyranone.

Introduction

The furans are an important class of heterocycles that are ubiquitous in the field of biologically active compounds and pharmaceuticals.[1] They have also been used as building blocks in organic synthesis.[2] Consequently, many efficient methods have been developed for the synthesis of multiply substituted furans.[3]

Angularly fused tricyclic compounds such as furoquinolinone and furocoumarin are significant among the great variety of furan derivatives. Such compounds are key structural units of numerous natural products and synthetic pharmaceuticals, and they have important biological activities, such as insecticidal, antimicrobial, antimalarial, antiarrhythmic, and sedative (Figure 1).[4]

Due to the number of applications of these derivatives in organic synthesis, as well as in pharmaceuticals, the synthesis of these compounds is highly desirable. Some attempts have been reported in the literature in recent decades.[5] However, the direct synthesis of angularly fused furoquinolinones has rarely been studied.[6]

Conjugated nitro olefins are efficient Michael acceptors that can undergo binucleophilic addition to form various heterocycles and carbocycles in a cascade fashion through a Michael addition/cyclization/denitration sequence.[7] In recent years, activated nitroalkenes (e.g., Morita–Baylis–Hillman acetates of nitroalkenes) have been used as versatile starting materials in various organic transformations for the synthesis of important heterocyclic scaffolds.[5g,8]

We are interested in the synthesis of functionalized heterocyclic compounds using undecorated nitro olefins as the Michael acceptors.[9] In a continuation of our research in the development of new methods for the synthesis of furans[9a–9c,10] from basic chemicals, in this paper, we report a simple and convenient approach to the synthesis of highly substituted angularly fused furan adducts from nitro olefins

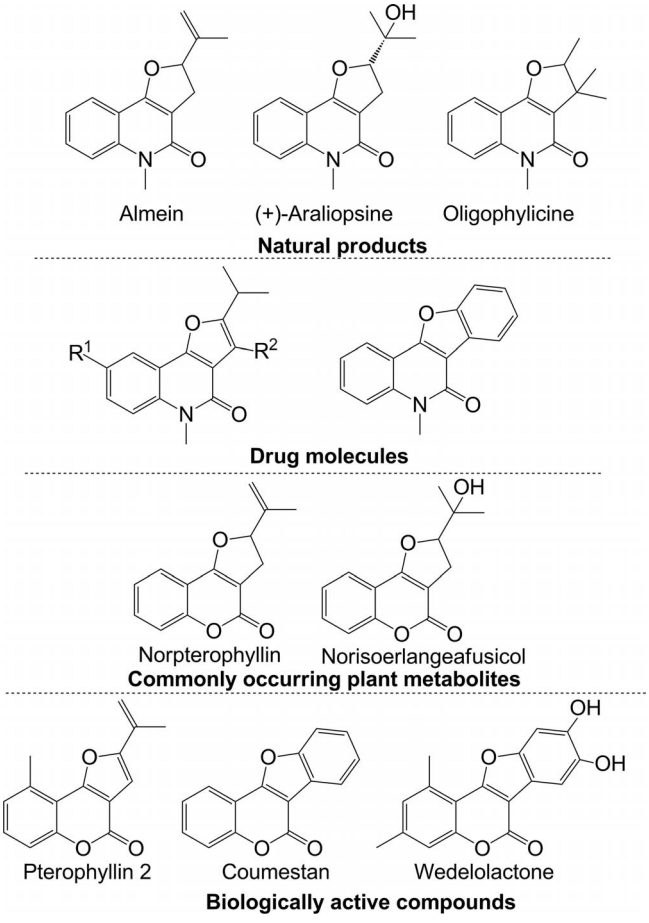
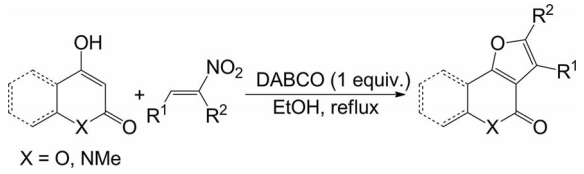


Figure 1. Some naturally occurring biologically active molecules containing the furoquinolinone and furocoumarin moieties.

[a] Department of Chemistry, Visva-Bharati (A Central University),
Santiniketan 731235, West Bengal, India
E-mail: alakananda.hajra@visva-bharati.ac.in
http://www.visvabharati.ac.in/AlakanandaHajra.html

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201501152.

and derivatives of 4-hydroxyquinolinone, 4-hydroxycoumarin, and 4-hydroxypyranone (Scheme 1).



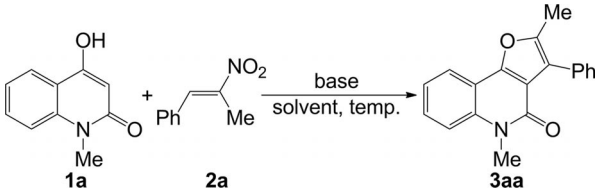
Scheme 1. Synthesis of angularly fused furan derivatives.

Results and Discussion

To optimize the reaction conditions, 4-hydroxy-1-methylquinolin-2-one (**1a**) and β-methyl-β-nitrostyrene (**2a**) were initially chosen as model substrates, and the reaction was run in the presence of DABCO (1,4-diazabicyclo[2.2.2]-octane; 1 equiv.) in EtOH under reflux conditions for 6 h (Table 1, Entry 1). To our delight, the desired furan was obtained in 82% yield, and no further improvement was observed when the reaction time was increased. Encouraged by this result, we carried out the reaction using various bases in different solvents, and the results are summarized in Table 1. The common organic bases DBU (1,8-diazabicyclo[5.4.0]undec-7-ene), Et_3N, DIPEA (*N*,*N*-diisopropylethylamine), and DIPA (diisopropylamine) were screened and were found to be not as effective for the reaction in EtOH under reflux conditions (Table 1, Entries 2–5). The inorganic bases NaOH, K_2CO_3, Cs_2CO_3, and Na_2CO_3 were also tested (Table 1, Entries 6–9), but they too were found to be less effective than DABCO. Various solvents were checked, including MeOH, DMF, DMSO, acetone, MeCN, and THF (Table 1, Entries 10–14). Dry EtOH (Table 1, Entry 1) was found to be the best solvent. Water is not as effective as EtOH as the solvent for this reaction (Table 1, Entry 15). It is notable that dry EtOH gave a better yield than rectified spirit (95% EtOH; Table 1, Entry 16). Increasing the amount of base (1.5 equiv.) did not improve the yield (Table 1, Entry 17), and decreasing the amount of base (0.5 equiv.) decreased the yield significantly (Table 1, Entry 18). The reaction did not proceed at all in the absence of base (Table 1, Entry 19). Thus, the best results were obtained in the reaction of 4-hydroxy-1-methylquinolin-2-one (**1a**; 0.5 mmol) and β-methyl-β-nitrostyrene (**2a**; 0.5 mmol) in the presence of DABCO (1 equiv.) in dry EtOH under reflux for 6 h (Table 1, Entry 1).

To explore the general applicability of the method, various substituted nitro olefins were treated with 4-hydroxy-1-methylquinolin-2-one, and the results are summarized in Table 2. A nitro olefin bearing a methyl substituent on the aryl moiety produced the corresponding furan adduct in good yield (**3ab**). A dioxole-substituted nitrostyrene gave the desired furan (i.e., **3ad**) in moderate yield. Halogen-substituted nitrostyrenes (*p*-F, *p*-Cl and *p*-Br) were also compatible with the optimized reaction conditions and gave the expected products (i.e., **3ag**, **3ah**, and **3ai**) in excellent yields.

Table 1. Optimization of the reaction conditions.[a]



Entry	Base[b] (equiv.)	Solvent	Temp.	Yield [%][c]
1	DABCO (1)	EtOH	reflux (85 °C)	82
2	DBU (1)	EtOH	reflux (85 °C)	65
3	Et_3N (1)	EtOH	reflux (85 °C)	55
4	DIPEA (1)	EtOH	reflux (85 °C)	15
5	DIPA (1)	EtOH	reflux (85 °C)	17
6	NaOH (1)	EtOH	reflux (85 °C)	08
7	K_2CO_3 (1)	EtOH	reflux (85 °C)	25
8	Cs_2CO_3 (1)	EtOH	reflux (85 °C)	15
9	Na_2CO_3 (1)	EtOH	reflux (85 °C)	35
10	DABCO (1)	MeOH	reflux (70 °C)	60
11	DABCO (1)	DMF	100 °C	28
12	DABCO (1)	DMSO	100 °C	24
13	DABCO (1)	MeCN	reflux (90 °C)	55
14	DABCO (1)	THF	reflux (70 °C)	48
15	DABCO (1)	H_2O	100 °C	50
16	DABCO (1)	EtOH	reflux (85 °C)	56
17	DABCO (1.5)	EtOH	reflux (85 °C)	83
18	DABCO (0.5)	EtOH	reflux (85 °C)	48
19	–	EtOH	reflux (85 °C)	n.r.[d]

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.5 mmol), base (1 equiv.), solvent (1.5 mL), 6 h. [b] DABCO = 1,4-diazabicyclo[2.2.2]octane, DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene, DIPEA = *N*,*N*-diisopropylethylamine, DIPA = diisopropylamine. [c] Isolated yield. [d] n.r. = no reaction.

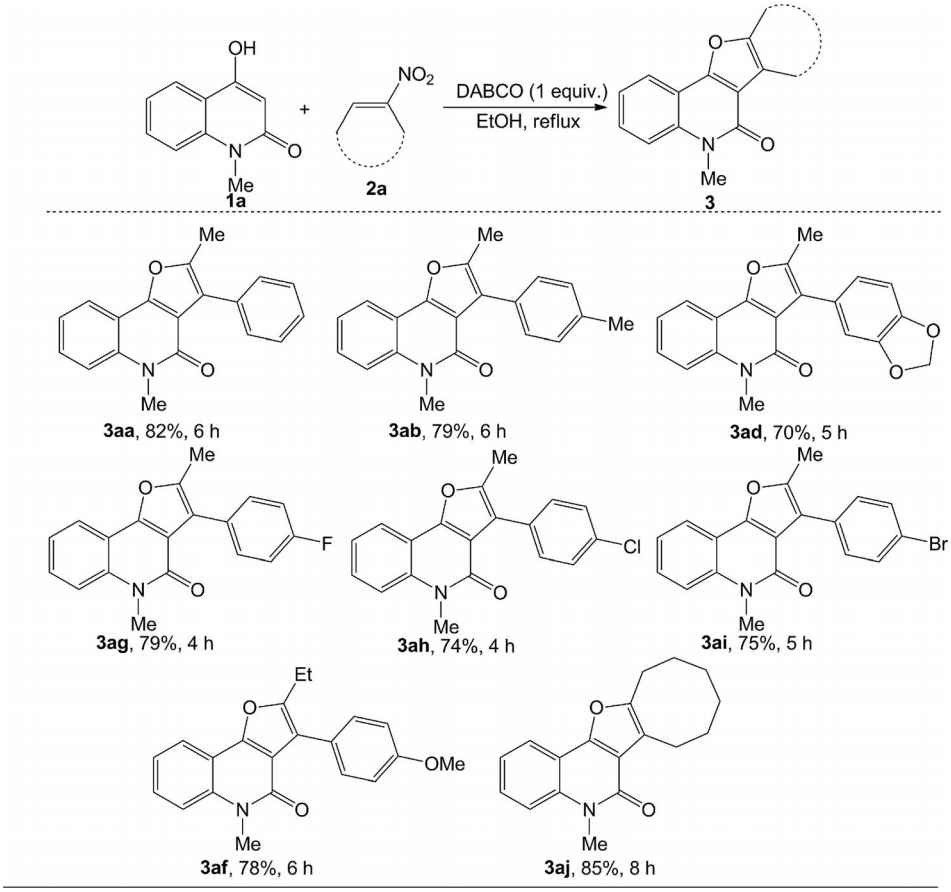
β-Ethyl-β-nitrostyrene also reacted smoothly with 4-hydroxy-1-methylquinolin-2-one to give the corresponding furan (i.e., **3af**). Moreover, the aliphatic cyclic nitroalkene 1-nitrocyclooct-1-ene gave the desired product (i.e., **3aj**). These results demonstrate the general applicability of this protocol.

Next, we went on to explore the reactivity of another hydroxy derivative (**1b**) with nitro olefins **3** under the same reaction conditions (Table 3). Nitrostyrenes bearing electron-donating groups such as Me and MeO on the phenyl ring successfully reacted with 4-hydroxycoumarin to give the corresponding furans (i.e., **4ab** and **4ac**) in good yields. A naphthyl-substituted nitrostyrene was also effective in this reaction and gave the corresponding angularly fused furan derivative (i.e., **4ae**) in good yield. β-Ethyl-β-nitrostyrene also underwent the reaction smoothly with 4-hydroxycoumarin to give the desired furan adduct (i.e., **4af**). However, β-nitrostyrene did not give the desired furan under these reaction conditions.

In addition, a structural analogue of 4-hydroxycoumarin, 4-hydroxy-6-methylpyran-2-one (**1c**), also underwent the reaction successfully to give the corresponding furans (i.e., **5aa**, **5ab**, and **5ad**) in moderate yields (Scheme 2).

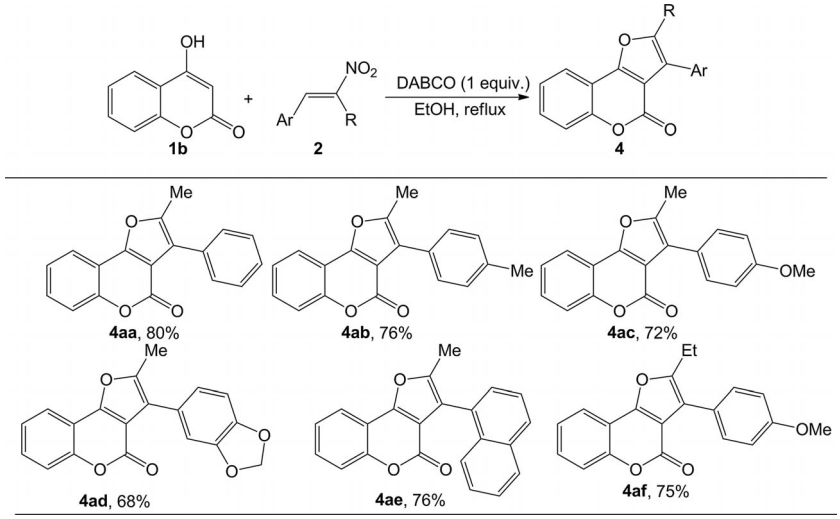
Based on literature reports[11] and our previous work,[9] a plausible mechanism is shown in Scheme 3. An initial

Table 2. Substrate scope.[a]



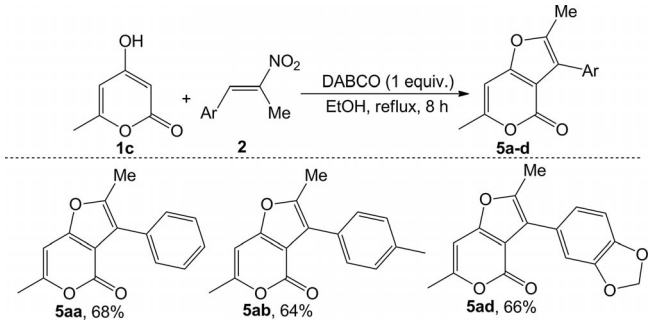
[a] Reaction conditions: enol derivative (0.5 mmol), nitro olefin (0.5 mmol), DABCO (1 equiv.), solvent (1.5 mL), reflux.

Table 3. Substrate scope.[a]

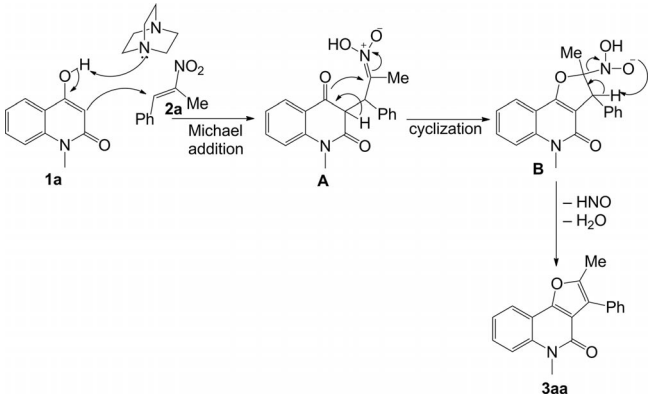


[a] Reaction conditions: enol derivative (0.5 mmol), nitro olefin (0.5 mmol), DABCO (1 equiv.), solvent (1.5 mL), reflux, 12 h.

DABCO-promoted Michael addition of 4-hydroxyquinolone (**1a**) to nitro olefin **2a** occurs to form intermediate **A**. Intramolecular cyclization of intermediate **A** leads to the formation of cyclic intermediate **B**, which subsequently gives the final product (i.e., **3a**) through elimination of water and HNO.



Scheme 2. Synthesis of furo[3,2-*c*]pyran-4-one derivatives.



Scheme 3. Probable mechanism.

Conclusions

We have developed a simple and versatile straightforward protocol for the synthesis of highly substituted angularly fused furans in high yields. The method is applicable to various enol systems, including 4-hydroxyquinolinones as well as 4-hydroxycoumarin and its structural analogue 4-hydroxypyranone. The reaction involves Michael addition, cyclization, and denitration to give the desired furans. The reaction has great advantages in terms of its operational simplicity, cost-effectiveness, and environmental impact.

Experimental Section

General Information: ^{1}H NMR spectra were determined with a 400 MHz spectrometer in $CDCl_3$ solution. Chemical shifts are expressed in ppm (δ), and referenced to tetramethylsilane (TMS), which was used as an internal standard. Signals are reported as s (singlet), d (doublet), t (triplet), or m (multiplet), and coupling constants J are given in Hz. ^{13}C NMR spectra were recorded at 100 MHz in $CDCl_3$. IR spectra were recorded with a Shimadzu 8400S FTIR spectrometer. TLC was carried out on aluminium sheets coated with silica gel 60 F_{254} (Merck). Silica gel (60–120 mesh) was used for column chromatography. Petroleum ether refers to the fraction boiling in the range 60–80 °C, unless otherwise stated. All solvents were dried and distilled before use. Commercially available substrates were freshly distilled before use. Solvents, reagents, and chemicals were purchased from Aldrich and Merck. All reactions involving moisture-sensitive reactants were carried out using oven-dried glassware.

Typical Experimental Procedure for the Synthesis of 2,5-Dimethyl-3-phenylfuro[3,2-*c*]quinolin-4-(5*H*)-one (3aa): Table 2. A mixture of 4-hydroxy-1-methylquinolin-2-one (**1a**) (87 mg, 0.5 mmol), β-methyl-β-nitrostyrene (**2a**) (81 mg, 0.5 mmol) and DABCO (56 mg, 1 equiv.) were placed in a round-bottom flask fitted with a condenser. Dry EtOH (1.5 mL) was added, and the mixture was stirred under reflux condition (85 °C) for 6 h. After TLC indicated that the reaction was complete, the reaction mixture was cooled to room temperature. Then the reaction mixture was concentrated to dryness under reduced pressure, and the residue was extracted with ethyl acetate. The organic phase was dried with anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel (60–120 mesh) using petroleum ether/ethyl acetate (9:1) as eluent to give the desired product (**3aa**; 118 mg, 82%) as a white solid.

2,5-Dimethyl-3-phenylfuro[3,2-*c*]quinolin-4-(5*H*)-one (3aa): White solid (118 mg, 82%). M.p. 124–126 °C. IR (KBr): $\tilde{\nu}$ = 3058, 1652, 1105 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, J = 8.0 Hz, 1 H), 7.57–7.53 (m, 2 H), 7.51–7.46 (m, 3 H), 7.43–7.37 (m, 2 H), 7.33–7.28 (m, 1 H), 3.74 (s, 3 H), 2.53 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.2, 153.9, 150.9, 137.8, 131.3, 130.4, 129.1, 127.9, 127.3, 122.1, 120.9, 120.6, 114.9, 114.1, 112.9, 29.2, 12.6 ppm. $C_{19}H_{15}NO_2$ (289.33): calcd. C 78.87, H 5.23, N 4.84; found C 78.69, H 5.39, N 4.72.

2,5-Dimethyl-3-(*p*-tolyl)furo[3,2-*c*]quinolin-4-(5*H*)-one (3ab): White solid (119 mg, 79%). M.p. 120–122 °C. IR (KBr): $\tilde{\nu}$ = 3067, 1655, 1106 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02 (d, J = 9.2 Hz, 1 H), 7.53 (t, J = 8.8 Hz, 1 H), 7.44–7.41 (m, 3 H), 7.30 (t, J = 8.0 Hz, 1 H), 7.26–7.25 (m, 2 H), 3.74 (s, 3 H), 2.50 (s, 3 H), 2.40 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.4, 153.9, 150.8, 137.9, 137.1, 130.3, 129.1, 129.0, 128.7, 128.3, 126.5, 122.2, 121.0, 114.9, 113.1, 29.2, 21.4, 12.6 ppm. $C_{20}H_{17}NO_2$ (303.36): calcd. C 79.19, H 5.65, N 4.62; found C 79.01, H 5.48, N 4.79.

3-(Benzo[*d*][1,3]dioxol-5-yl)-2,5-dimethylfuro[3,2-*c*]quinolin-4-(5*H*)-one (3ad): Gummy mass (116 mg, 70%). IR (KBr): $\tilde{\nu}$ = 3060, 1650, 1103 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02 (d, J = 9.2 Hz, 1 H), 7.54–7.51 (m, 1 H), 7.43 (d, J = 8.4 Hz, 1 H), 7.31 (t, J = 8.0 Hz, 1 H), 7.02 (s, 1 H), 6.96 (d, J = 8.4 Hz, 1 H), 6.89 (d, J = 8.0 Hz, 1 H), 5.99 (s, 2 H), 3.74 (s, 3 H), 2.49 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.1, 151.0, 147.4, 147.1, 143.9, 138.1, 129.2, 125.0, 123.9, 122.7, 122.2, 121.1, 119.6, 115.0, 113.2, 111.1, 108.0, 101.1, 29.3, 12.6 ppm. $C_{20}H_{15}NO_4$ (333.34): calcd. C 72.06, H 4.54, N 4.20; found C 71.89, H 4.64, N 4.05.

3-(4-Fluorophenyl)-2,5-dimethylfuro[3,2-*c*]quinolin-4-(5*H*)-one (3ag): White solid (121 mg, 79%). M.p. 152–154 °C. IR (KBr): $\tilde{\nu}$ = 3063, 1648, 1103 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, J = 7.6 Hz, 1 H), 7.55–7.48 (m, 3 H), 7.41 (d, J = 8.8 Hz, 1 H), 7.32–7.28 (m, 1 H), 7.16–7.11 (m, 2 H), 3.72 (s, 3 H), 2.49 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.3 (d, $J_{C,F}$ = 245 Hz), 159.3, 154.0, 150.9, 137.9, 132.0 (d, $J_{C,F}$ = 9 Hz), 129.3, 127.2 (d, $J_{C,F}$ = 3 Hz), 122.2, 121.0, 119.7, 115.0, 114.9 (d, $J_{C,F}$ = 12 Hz), 114.0, 112.9, 29.2, 12.5 ppm. $C_{19}H_{14}FNO_2$ (307.32): calcd. C 74.26, H 4.59, N 4.56; found C 74.02, H 4.71, N 4.68.

3-(4-Chlorophenyl)-2,5-dimethylfuro[3,2-*c*]quinolin-4-(5*H*)-one (3ah): Yellow solid (119 mg, 74%). M.p. 158–160 °C. IR (KBr): $\tilde{\nu}$ = 3048, 1654, 1102 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, J = 9.2 Hz, 1 H), 7.52–7.48 (m, 3 H), 7.43 (d, J = 8.4 Hz, 2 H), 7.39 (d, J = 8.4 Hz, 1 H), 7.29 (t, J = 7.6 Hz, 1 H), 3.71 (s, 3 H), 2.50 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.4, 159.1, 153.9, 150.9, 137.7, 133.2, 131.6, 129.2, 128.1, 122.1, 120.9, 119.5, 114.8, 112.7, 109.4, 29.1, 12.5 ppm. $C_{19}H_{14}ClNO_2$ (323.78): calcd. C 70.48, H 4.36, N 4.33; found C 70.29, H 4.15, N 4.59.

3-(4-Bromophenyl)-2,5-dimethylfuro[3,2-*c*]quinolin-4-(5*H*)-one (3ai): White solid (138 mg, 75%). M.p. 153–155 °C. IR (KBr): $\tilde{\nu}$ = 3042, 1659, 1103, 524 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, J = 8.0 Hz, 1 H), 7.55–7.48 (m, 3 H), 7.44–7.40 (m, 3 H), 7.32–7.29 (m, 1 H), 3.72 (s, 3 H), 2.50 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.2, 154.0, 151.0, 137.8, 133.3, 131.7, 129.7, 129.3, 128.1, 122.2, 120.9, 119.6, 114.9, 113.8, 112.8, 29.2, 12.6 ppm. $C_{19}H_{14}BrNO_2$ (368.23): calcd. C 61.97, H 3.83, N 3.80; found C 62.09, H 3.69, N 3.70.

2-Ethyl-3-(4-methoxyphenyl)-5-methylfuro[3,2-*c*]quinolin-4(5*H*)-one (3af): Colourless liquid (129 mg, 78%). IR (KBr): $\tilde{\nu}$ = 3060, 1653, 1109 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.93 (d, J = 8.0 Hz, 1 H), 7.44–7.40 (m, 1 H), 7.37–7.31 (m, 3 H), 7.22–7.18 (m, 1 H), 6.90 (d, J = 8.4 Hz, 2 H), 3.77 (s, 3 H), 3.63 (s, 3 H), 2.75 (q, J = 7.6 Hz, 2 H), 1.26 (t, J = 7.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.5, 159.0, 155.6, 153.8, 137.9, 131.5, 129.0, 123.6, 122.1, 121.0, 119.5, 114.9, 114.2, 113.5, 113.1, 55.3, 29.2, 20.0, 13.3 ppm. $C_{21}H_{19}NO_3$ (333.39): calcd. C 75.66, H 5.74, N 4.20; found C 75.52, H 5.92, N 4.05.

5-Methyl-7,8,9,10,11,12-hexahydrocycloocta[4,5]furo[3,2-*c*]quinolin-6(5*H*)-one (3aj): Pale yellow oil (119 mg, 85%). IR (KBr): $\tilde{\nu}$ = 3068, 1655, 1101 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, J = 8.8 Hz, 1 H), 7.36–7.31 (m, 1 H), 7.24 (d, J = 8.4 Hz, 1 H), 7.13 (t, J = 7.6 Hz, 1 H), 3.61 (s, 3 H), 2.95 (t, J = 6.4 Hz, 2 H), 2.81 (t, J = 6.4 Hz, 2 H), 1.72–1.68 (m, 4 H), 1.44–1.36 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.2, 154.3, 153.0, 137.5, 128.4, 121.9, 120.6, 118.2, 115.0, 114.7, 113.3, 28.9, 28.5, 27.9, 26.0, 25.9, 25.5, 21.4 ppm. $C_{18}H_{19}NO_2$ (281.35): calcd. C 76.84, H 6.81, N 4.98; found C 76.72, H 6.72, N 4.80.

2-Methyl-3-phenyl-4*H*-furo[3,2-*c*]chromen-4-one (4aa): White solid (110 mg, 80%). M.p. 145–147 °C. IR (KBr): $\tilde{\nu}$ = 3064, 1731, 1075 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, J = 9.2 Hz, 1 H), 7.44–7.41 (m, 3 H), 7.40–7.35 (m, 3 H), 7.31–7.29 (m, 1 H), 7.27–7.23 (m, 1 H), 2.44 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.8, 156.4, 152.4, 151.8, 130.4, 130.1, 130.0, 128.3, 127.9, 124.4, 120.7, 120.6, 117.2, 112.9, 109.7, 12.7 ppm. $C_{18}H_{12}O_3$ (276.29): calcd. C 78.25, H 4.38; found C 78.42, H 4.21.

2-Methyl-3-(*p*-tolyl)-4*H*-furo[3,2-*c*]chromen-4-one (4ab): White solid (110 mg, 76%). M.p. 139–141 °C. IR (KBr): $\tilde{\nu}$ = 3067, 1730, 1068 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, J = 9.2 Hz, 1 H), 7.43–7.39 (m, 1 H), 7.36–7.31 (m, 3 H), 7.27–7.23 (m, 1 H), 7.20–7.18 (m, 2 H), 2.44 (s, 3 H), 2.33 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.9, 156.3, 152.4, 151.5, 137.7, 130.3, 129.8, 129.6, 129.1, 127.1, 124.4, 120.7, 117.2, 112.9, 109.8, 21.4, 12.7 ppm. $C_{19}H_{14}O_3$ (290.32): calcd. C 78.61, H 4.86; found C 78.79, H 4.71.

3-(4-Methoxyphenyl)-2-methyl-4*H*-furo[3,2-*c*]chromen-4-one (4ac): Gummy mass (110 mg, 72%). IR (KBr): $\tilde{\nu}$ = 3058, 1738, 1078 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, J = 9.2 Hz, 1 H), 7.52–7.49 (m, 1 H), 7.47–7.44 (m, 3 H), 7.38–7.34 (m, 1 H), 7.02 (d, J = 8.8 Hz, 2 H), 3.88 (s, 3 H), 2.54 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3, 158.0, 156.3, 152.4, 151.4, 131.2, 130.3, 124.4, 122.3, 120.7, 120.2, 117.2, 113.9, 113.0, 109.9, 55.4, 12.7 ppm. $C_{19}H_{14}O_4$ (306.32): calcd. C 74.50, H 4.61; found C 74.38, H 4.79.

3-(Benzo[*d*][1,3]dioxol-5-yl)-2-methyl-4*H*-furo[3,2-*c*]chromen-4-one (4ad): Yellow solid (108 mg, 68%). M.p. 159–161 °C. IR (KBr): $\tilde{\nu}$ = 3068, 1739, 1079 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, J = 9.2 Hz, 1 H), 7.42–7.40 (m, 1 H), 7.36–7.34 (m, 1 H), 7.31–7.24 (m, 2 H), 6.88–6.81 (m, 2 H), 5.91 (s, 2 H), 2.43 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.9, 156.3, 152.4, 151.6, 147.6, 147.4, 132.7, 130.4, 124.9, 124.4, 124.1, 123.6, 120.7, 117.2, 116.8, 110.6, 108.3, 101.3, 12.7 ppm. $C_{19}H_{12}O_5$ (320.30): calcd. C 71.25, H 3.78; found C 71.10, H 3.98.

2-Methyl-3-(naphthalen-1-yl)-4*H*-furo[3,2-*c*]chromen-4-one (4ae): Gummy mass (123 mg, 76%). IR (KBr): $\tilde{\nu}$ = 3042, 1736, 1069 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.96 (t, J = 8.8 Hz, 3 H), 7.71 (d, J = 8.4 Hz, 1 H), 7.60–7.56 (m, 1 H), 7.54–7.50 (m, 3 H), 7.48–7.45 (m, 2 H), 7.41–7.38 (m, 1 H), 2.37 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.5, 156.4, 153.0, 152.6, 133.8, 132.4, 130.4, 128.9, 128.6, 127.8, 126.4, 126.0, 125.6, 125.4, 124.4, 120.7, 118.4, 117.3, 113.1, 111.5, 12.6 ppm. $C_{22}H_{14}O_3$ (326.35): calcd. C 80.97, H 4.32; found C 80.82, H 4.15.

2-Ethyl-3-(4-methoxyphenyl)-4*H*-furo[3,2-*c*]chromen-4-one (4af): Yellow liquid (120 mg, 75%). IR (KBr): $\tilde{\nu}$ = 3059, 1689, 1075 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, J = 8.4 Hz, 1 H), 7.49–7.42 (m, 4 H), 7.36–7.32 (m, 1 H), 7.01 (d, J = 8.8 Hz, 2 H), 3.87 (s, 3 H), 2.86 (q, J = 7.6 Hz, 2 H), 1.37 (t, J = 7.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3, 158.0, 156.3, 156.2, 152.3, 131.1, 130.2, 124.3, 122.3, 120.6, 119.5, 117.1, 113.8, 112.9, 109.7, 55.3, 20.0, 13.1 ppm. $C_{20}H_{16}O_4$ (320.34): calcd. C 74.99, H 5.03; found C 75.12, H 4.89.

2,6-Dimethyl-3-phenyl-4*H*-furo[3,2-*c*]pyran-4-one (5aa): Gummy mass (81 mg, 68%). IR (KBr): $\tilde{\nu}$ = 3068, 1721, 1070 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.39 (m, 2 H), 7.38–7.34 (m, 2 H), 7.29–7.26 (m, 1 H), 6.31 (s, 1 H), 2.36 (s, 3 H), 2.27 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.9, 159.5, 159.4, 150.1, 130.4, 129.9, 128.9, 128.3, 127.7, 119.2, 95.6, 20.3, 12.6 ppm. $C_{15}H_{12}O_3$ (240.26): calcd. C 74.99, H 5.03; found C 75.12, H 4.89.

2,6-Dimethyl-3-(*p*-tolyl)-4*H*-furo[3,2-*c*]pyran-4-one (5ab): Yellow gummy mass (81 mg, 64%). IR (KBr): $\tilde{\nu}$ = 3058, 1720, 1085 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.29 (d, J = 8.0 Hz, 2 H), 7.17 (d, J = 8.0 Hz, 2 H), 6.30 (s, 1 H), 2.35 (s, 3 H), 2.31 (s, 3 H), 2.26 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.8, 159.6, 159.2, 149.8, 137.4, 129.7, 129.0, 127.3, 119.1, 107.6, 95.6, 21.4, 20.2, 12.5 ppm. $C_{16}H_{14}O_3$ (254.28): calcd. C 75.57, H 5.55; found C 75.69, H 5.41.

3-(Benzo[*d*][1,3]dioxol-5-yl)-2,6-dimethyl-4*H*-furo[3,2-*c*]pyran-4-one (5ad): Yellow oil (93 mg, 66%). IR (KBr): $\tilde{\nu}$ = 3042, 1701, 1103 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.18 (s, 1 H), 6.88–6.84 (m, 1 H), 6.82–6.77 (m, 1 H), 6.29 (s, 1 H), 5.91 (s, 2 H), 2.32 (s, 3 H), 2.25 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.7, 159.5, 159.3, 149.8, 147.2, 124.0, 123.5, 118.9, 110.4, 108.2, 105.7, 101.5, 101.2, 95.6, 20.2, 12.5 ppm. $C_{16}H_{12}O_5$ (284.27): calcd. C 67.60, H 4.25; found C 67.42, H 4.39.

Acknowledgments

A. H. acknowledges financial support from the Council of Scientific and Industrial Research (CSIR), New Delhi [grant no. 02(0168)/13/EMR-II]. M. G. thanks the University Grants Commission [UGC (SRF)], India for a senior research fellowship.

[1] a) B. H. Lipshutz, *Chem. Rev.* **1986**, *86*, 795; b) G. Feuer in *Progress in Medicinal Chemistry* (Eds.: G. P. Ellis, G. B. West), North-Holland Publishing Co., New York, **1974**; c) O. Thastrup, B. Fjalland, J. Lemmich, *Acta Pharmacol. Toxicol.* **1983**, *52*, 246; d) R. D. H. Murray, *Prog. Chem. Org. Nat. Prod.* **1991**, *58*, 83; e) R. D. H. Murray, *Nat. Prod. Rep.* **1995**, *12*, 477; f) D. Guilet, J.-J. Helesbeux, D. Seraphin, T. Sevenet, P. Richomme, J. Bruneton, *J. Nat. Prod.* **2001**, *64*, 563; g) S. Y. Kang, K. Y. Lee, S. H. Sung, M. J. Park, Y. C. Kim, *J. Nat.*

Prod. **2001**, *64*, 683; h) T. L. Gilchrist, *J. Chem. Soc. Perkin Trans. 1* **2001**, 2491.

[2] a) A. R. Katritzky, *Comprehensive Heterocyclic Chemistry III*, 1st ed., Elsevier, Amsterdam, New York, **2008**; b) X. L. Hou, H. Y. Cheung, T. Y. Hon, P. L. Kwan, T. H. Lo, S. Y. Tong, H. N. C. Wong, *Tetrahedron* **1998**, *54*, 1955; c) S. F. Kirsch, *Org. Biomol. Chem.* **2006**, *4*, 2076.

[3] a) S. J. Hayes, D. W. Knight, M. D. Menzies, M. O'Halloran, W.-F. Tan, *Tetrahedron Lett.* **2007**, *48*, 7709; b) H. Tsuji, K. Yamagata, Y. Ueda, E. Nakamura, *Synlett* **2011**, 1015; c) C. He, S. Guo, J. Ke, J. Hao, H. Xu, H. Chen, A. Lei, *J. Am. Chem. Soc.* **2012**, *134*, 5766; d) H. Cao, H. Zhan, J. Cen, J. Lin, Y. Lin, Q. Zhu, M. Fu, H. Jiang, *Org. Lett.* **2013**, *15*, 1080; e) U. Sharma, T. Naveen, A. Maji, S. Manna, D. Maiti, *Angew. Chem. Int. Ed.* **2013**, *52*, 12669; *Angew. Chem.* **2013**, *125*, 12901; f) M. R. Kuram, M. Bhanuchandra, A. K. Sahoo, *Angew. Chem. Int. Ed.* **2013**, *52*, 4607; *Angew. Chem.* **2013**, *125*, 4705; g) H. Tsuji, G. Cantagrel, Y. Ueda, T. Chen, L.-J. Wan, E. Nakamura, *Chem. Asian J.* **2013**, *8*, 2377; h) F. Boberg, J. Knoop, *Justus Liebigs Ann. Chem.* **1967**, *708*, 148; i) S. Niwas, S. Kumar, A. P. Bhaduri, *Indian J. Chem.* **1983**, *22B*, 914; j) A. Gomez-Sanchez, R. Femandez-Fernandez, C. Pascual, J. Bellanato, *J. Chem. Res. Synop.* **1986**, 318; k) B. Konig in *Science of Synthesis* (Eds.: B. M. Trost, G. Maas), Thieme, Stuttgart, **2002**, vol. 9, p. 183.

[4] a) L. Piccagli, M. Borgatti, E. Nicolis, N. Bianchi, I. Mancini, I. Lampronti, D. Vevaldi, F. Dall'Acqua, G. Cabrini, R. Gambari, *Bioorg. Med. Chem.* **2010**, *18*, 8341; b) A. G. Al-Sehemi, S. R. El-Gogary, *Chin. J. Chem.* **2012**, *30*, 316; c) M. Borgatti, A. Chilin, L. Piccagli, I. Lampronti, N. Bianchi, I. Mancini, G. Marzaro, F. dall'Acqua, A. Guiotto, R. Gambari, *Eur. J. Med. Chem.* **2011**, *46*, 4870; d) M. F. Grundon, *Nat. Prod. Rep.* **1990**, *7*, 131; e) C. Moulis, K. R. Wirasutisna, J. Gleye, P. Loiseau, E. Stanislas, C. Moretti, *Phytochemistry* **1983**, *22*, 2095; f) B. Wolters, U. Eilert, *Planta Med.* **1981**, *43*, 166; g) L. K. Basco, S. Mitaku, A. L. Skaltsounis, N. Ravelomanantsoa, F. Tillequin, M. Koch, L. Bras, *Antimicrob. Agents Chemother.* **1994**, *38*, 1169; h) T.-S. Wu, C.-Y. Li, Y.-L. Leu, C.-Q. Hu, *Phytochemistry* **1999**, *50*, 509; i) I. Butenschon, K. Moller, W. Hansel, *J. Med. Chem.* **2001**, *44*, 1249.

[5] a) F. Risitano, G. Grassi, F. Foti, C. Bilardo, *Tetrahedron Lett.* **2001**, *42*, 3503; b) V. Nair, R. S. Menon, A. U. Vinod, S. Viji, *Tetrahedron Lett.* **2002**, *43*, 2293; c) G. Raffa, M. Rusch, G. Balme, N. Monteiro, *Org. Lett.* **2009**, *11*, 5254; d) C.-J. Lee, Y.-J. Jang, Z.-Z. Wu, W. Lin, *Org. Lett.* **2012**, *14*, 1906; e) Z. Zareai, M. Khoobi, A. Ramazani, A. Foroumadi, A. Souldozi, K. Slepokura, T. Lis, A. Shafiee, *Tetrahedron* **2012**, *68*, 6721; f) Z. Zhou, H. Liu, Y. Li, J. Liu, Y. Li, J. Liu, J. Yao, C. Wang, *ACS Comb. Sci.* **2013**, *15*, 363; g) S. Singh, A. Srivastava, S. M. Mobin, S. Samanta, *RSC Adv.* **2015**, *5*, 5010.

[6] a) Y. R. Lee, B. S. Kim, D. H. Kim, *Tetrahedron* **2000**, *56*, 8845; b) D. K. Barange, V. Kavala, C.-W. Kuo, P.-M. Lei, C.-F. Yao, *Tetrahedron* **2011**, *67*, 2870; c) S. Indumathi, S. Perumal, N. Anbananthan, *Green Chem.* **2012**, *14*, 3361.

[7] a) G. Rosini, R. Ballini, *Synthesis* **1988**, 833; b) N. Ono, *The Nitro Group in Organic Synthesis* Wiley-VCH, New York, **2001**; c) R. Ballini, G. Bosica, D. Fiorini, A. Palmieri, M. Petrini, *Chem. Rev.* **2005**, *105*, 933; d) L. Li, M.-N. Zhao, Z.-H. Ren, J. Li, Z.-H. Guan, *Synthesis* **2012**, *44*, 532; e) A. Z. Halimehjani, I. N. N. Namboothiri, S. E. Hooshmand, *RSC Adv.* **2014**, *4*, 48022; f) A. Z. Halimehjani, I. N. N. Namboothiri, S. E. Hooshmand, *RSC Adv.* **2014**, *4*, 31261.

[8] a) D. K. Nair, S. M. Mobin, I. N. N. Namboothiri, *Tetrahedron Lett.* **2012**, *53*, 3349; b) W.-Y. Huang, Y.-C. Chen, K. Chen, *Chem. Asian J.* **2012**, *7*, 688; c) S. Anwar, W.-Y. Huang, C.-H. Chen, Y.-S. Cheng, K. Chen, *Chem. Eur. J.* **2013**, *19*, 4344; d) T. Kumar, S. M. Mobin, I. N. N. Namboothiri, *Tetrahedron* **2013**, *69*, 4964.

[9] a) D. Kundu, M. Samim, A. Majee, A. Hajra, *Chem. Asian J.* **2011**, *6*, 406; b) M. Ghosh, S. Mishra, A. Hajra, *J. Org. Chem.* **2015**, *80*, 5364; c) M. Ghosh, S. Santra, P. Mondal, D. Kundu, A. Hajra, *Chem. Asian J.* **2015**, DOI: 10.1002/asia.201500710; d) S. Santra, A. K. Bagdi, A. Majee, A. Hajra, *Adv. Synth. Catal.* **2013**, *355*, 1065; e) S. Mitra, A. K. Bagdi, A. Majee, A. Hajra, *Tetrahedron Lett.* **2013**, *54*, 4982; f) S. Santra, S. Mitra, A. K. Bagdi, A. Majee, A. Hajra, *Tetrahedron Lett.* **2014**, *55*, 5151.

[10] M. Ghosh, S. Mishra, K. Monir, A. Hajra, *Org. Biomol. Chem.* **2015**, *13*, 309.

[11] a) H. Shiraishi, T. Nishitani, S. Sakaguchi, Y. Ishii, *J. Org. Chem.* **1998**, *63*, 6234; b) S. Maiti, S. Biswas, U. Jana, *J. Org. Chem.* **2010**, *75*, 1674; c) C. M. Simpkins, D. A. Hunt, *Tetrahedron Lett.* **2013**, *54*, 5544.

Received: September 4, 2015
Published Online: November 6, 2015

