# Synthesis of Tetrahydrobenzo[*g*]Quinoline Derivatives Using Recoverable Carbonaceous Material as Heterogeneous Catalyst

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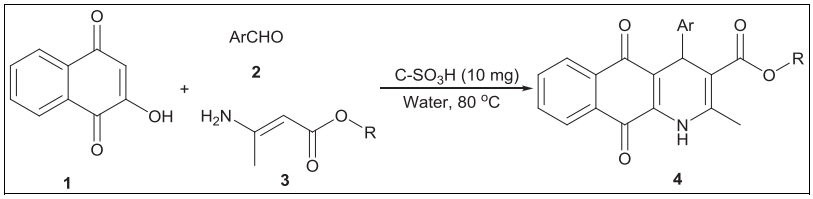


A variety of substituted benzo[*g*]quinoline-5,10-dione derivatives were synthesized via one-pot three-component reaction of 2-hydroxynaphthalene-1,4-dione, aromatic aldehydes, and (*E*)-3-aminobut-2-enoates using carbonaceous material as the heterocyclic catalyst. This procedure is simple and efficient owing to short reaction times, easy work-up, and recovery of heterogeneous catalyst. This procedure develops an efficient and promising synthetic method to construction of the benzo[*g*]quinoline-5,10-dione skeleton.

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## INTRODUCTION

Nitrogen-containing heterocycles are of great importance to both medicinal and organic chemists, and the design and synthesis of these compounds continue to represent a challenge from both an academic and industrial perspective [1]. The benzo[*g*]quinoline-5,10-dione system [2–4] represents the core skeleton of a pharmaceutically important class of heterocyclic compounds that exhibits lots of special biological activities, such as antimicrobial activity [5], anticancer activity [6], antifungal agent and sampangine [7–9], cytotoxic activity [10–13], and cytotoxic activity [14]. Owing to the important biological activities they exhibit, these compounds have distinguished themselves as heterocycles of important chemical and biological significance. Thus, developing an efficient approach to the synthesis of these azaheterocycles is of significance. Recently, many synthetic methods for tetrahydrobenzo[*g*]quinoline derivatives have been reported [15–28]. However, these methods usually suffer from one or more disadvantages, such as use of expensive substrates, poor chemoselectivity, limited tolerance of functional groups, and unreusability of the catalysts. Furthermore, the substrate scope for suitably functionalized benzo[*g*]quinoline-5,10-dione building blocks for the synthesis of structurally diverse libraries also is limited. Therefore, the development of simple and efficient synthetic routes for such azaheterocycles is a great challenge in modern organic synthesis.

Compared with liquid acid catalysts, carbonaceous material as solid acid catalyst has many advantages, such as their stability and efficiency, easy preparation and recoverability, simple synthetic procedure, and eco-friendly nature [29–33], and has attracted more and more attention and became a powerful catalyst for organic synthesis [32]. Recently, Liang synthesized a novel sulfonated carbonaceous material with polyvinyl alcohol and hydroxyethylsulfuric acid and studied its features through esterification and oxathioketalization [34]. In the past several years, our group has developed a series of synthetic methods that could provide easy access to nitrogen-containing structures of chemical and biological interest [35–37]. As a continuous work, herein we report a simple and efficient method for the synthesis of benzo [*g*]quinoline-5,10-dione derivatives through the one-pot condensation of 2-hydroxynaphthalene-1,4-dione, aromatic aldehydes, and (*E*)-3-aminobut-2-enoates using reusable sulfonated carbonaceous material as heterogeneous catalyst.

## RESULTS AND DISCUSSION

To a method from the literature [34], the sulfonated carbonaceous material (C-$SO_3H$) was prepared by mixing polyvinyl alcohol, hydroxyethylsulfuric acid, and deionized water, which was heated in an oven. Then, the mixture was filtered, washed, and dried in a vacuum oven. The acidity of the carbonaceous material (C-$SO_3H$) was 2.4 mmol/g.

We began our study by mixing 2-hydroxynaphthalene-1,4-dione (1), benzaldehyde (2a), and methyl (*E*)-3-

aminobut-2-enoate (3a) as the model reaction for condition screening (Scheme 1). First, the catalyst for the synthesis of 4a was optimized, and the results were induced in Table 1. We found that no product was given even after 24 h at 80°C in the absence of catalyst (Table 1, entry 1). HY zeolite and Amberlyst-15 as inorganic solid acid exhibit low activity and only give low yields of product 4a (Table 1, entries 2-3). The traditional liquid acid such as HOAc, TsOH, and TFA also exhibit only moderate activities and give 44–55% goal products (Table 1, entries 4–6). The solid acid catalyst obtained single polyvinyl alcohol (carbon) showed almost no activity because of little functionalities on the surface (Table 1, entry 7). However, the sulfonated carbonaceous material (C-$SO_3H$) showed very high activity in model reaction for product 4a (Table 1, entry 8). Subsequently, the model reaction was repeated many times with different amount of catalyst loading. When the catalyst loading was increased from 10 mg to 20 mg, the yield of 4a was only subtly increased from 89% to 90% (Table 1, entries 8–10). However, when the catalyst loading was decreased from 10 mg to 5 mg, the yield of 4a was decreased from 89% to 70% (Table 1, entries 8, 11). Thus, the sulfonated carbonaceous material (10 mg) was considered to be most suitable.

To further screen the reaction condition for the synthesis, the model reaction was carried out in different solvent, such as water, methanol, ethanol, dichloromethane, chloroform, acetonitrile, tetrahydrofuran, and toluene (Table 1, entries 12–18). As illustrated in Table 1, the reaction using water as solvent resulted in highest yields (Table 1, entries 12–18). Thus, water was chosen as the solvent for subsequent reactions. Then, the model substrates were mixed in water at temperatures ranging from 20°C to 100°C (Table 1, entries 8, 19–22), with an increment of 20°C. The yield of product 4a was increased from 10% to 89% as the reaction temperature was raised from 20°C to 80°C (Table 1, entries 8, 19–21). However, the yield almost leveled off when the temperature was further increased from 80°C to 100°C (Table 1, entries 8, 22). Therefore, 80°C was considered to be most suitable and chosen as the reaction conditions for all the following reactions.

**Table 1**

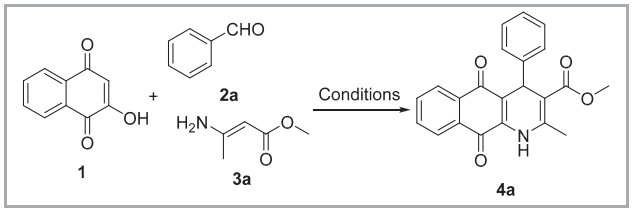
Reaction conditions for the synthesis of benzo[*g*]quinoline-5,10-dione 4a.[a]

| Entry | Catalyst (mg) | Solvent | T (°C) | Yield (%)[b] |
|---|---|---|---|---|
| 1 | — | $H_2O$ | 80 | 0 |
| 2 | HY zeolite (10) | $H_2O$ | 80 | 31 |
| 3 | Amberlyst-15 (10) | $H_2O$ | 80 | 21 |
| 4 | HOAc (10)[c] | $H_2O$ | 80 | 44 |
| 5 | TsOH (10)[c] | $H_2O$ | 80 | 55 |
| 6 | TFA (10)[c] | $H_2O$ | 80 | 51 |
| 7 | Carbon (10)[d] | $H_2O$ | 80 | 10 |
| 8 | C-$SO_3H$ (10) | $H_2O$ | 80 | 89 |
| 9 | C-$SO_3H$ (15) | $H_2O$ | 80 | 89 |
| 10 | C-$SO_3H$ (20) | $H_2O$ | 80 | 90 |
| 11 | C-$SO_3H$ (5) | $H_2O$ | 80 | 70 |
| 12 | C-$SO_3H$ (10) | MeOH | 80 | 55 |
| 13 | C-$SO_3H$ (10) | EtOH | 80 | 76 |
| 14 | C-$SO_3H$ (10) | $CH_2Cl_2$ | 80 | 23 |
| 15 | C-$SO_3H$ (10) | $CHCl_3$ | 80 | 41 |
| 16 | C-$SO_3H$ (10) | $CH_3CN$ | 80 | 52 |
| 17 | C-$SO_3H$ (10) | THF | 80 | 31 |
| 18 | C-$SO_3H$ (10) | Toluene | 80 | 40 |
| 19 | C-$SO_3H$ (10) | $H_2O$ | 20 | 10 |
| 20 | C-$SO_3H$ (10) | $H_2O$ | 40 | 30 |
| 21 | C-$SO_3H$ (10) | $H_2O$ | 60 | 72 |
| 22 | C-$SO_3H$ (10) | $H_2O$ | 100 | 88 |

[a]Reaction conditions: 1 (1.0 mmol), 2a (1.0 mmol), 3a (1.0 mmol), C-$SO_3H$ (10 mg), and solvent (3.0 mL) in the sealed tube in 6 h.
[b]Isolated yields.
[c]10 mol%.
[d]The carbonaceous material obtained from the single polyvinyl alcohol.

Using the most suitable condition, the reaction scope was evaluated by using different substrates 2 and 3 (Scheme 2). To our delight, aromatic aldehydes bearing either electron-withdrawing or electron-donating functional groups, such as fluoro, chloro, nitro, trifluoromethyl, methyl, methoxyl, or isopropyl, were all found to be suitable for the reaction with 2-hydroxynaphthalene-1,4-dione (1), and methyl (*E*)-3-aminobut-2-enoate (3a) to obtain benzo[*g*]quinoline-5,10-diones (4) in good to excellent yields (Table 2). Meanwhile, we also noted that the aromatic aldehydes with electron-deficient functional groups, such as chloro, fluoro, bromo, nitro, or trifluoromethyl showed higher reactivities than those with electron-rich functional groups, such as methyl, methoxyl, or isopropyl and gave higher yields. We attributed the higher reactivities of electron-deficient functional groups aromatic aldehydes to their electron absorption effect. Particularly noteworthy was the fact that the bulky aromatic aldehyde, such as 1-naphthaldehyde and less reactive heterocyclic aldehyde,

**Scheme 1.** Synthesis of benzo[*g*]quinoline-5,10-dione 4a.




**Scheme 2.** Synthesis of benzo[*g*]quinoline-5,10-diones 4a–4t.

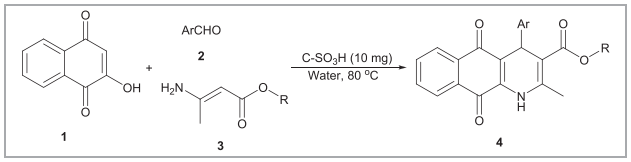


**Table 2**

Synthesis of benzo[*g*]quinoline-5,10-dione derivatives catalyzed by sulfonated carbonaceous material.[a]

| Entry | Ar | R | Product | Time (h) | Yield (%)[b] | Mp (°C) | |
|---|---|---|---|---|---|---|---|
| | | | | | | Found | Reported [15] |
| 1 | $C_6H_5$ | Me | 4a | 6 | 89 | 250–252 | 248 |
| 2 | 4-$FC_6H_4$ | Me | 4b | 6 | 87 | 246–248 | — |
| 3 | 4-$ClCC_6H_4$ | Me | 4c | 6 | 89 | 221–222 | 225 |
| 4 | 4-$NO_2C_6H_4$ | Me | 4d | 6 | 86 | 228–230 | — |
| 5 | 4-$CF_3C_6H_4$ | Me | 4e | 6 | 83 | 235–236 | — |
| 6 | 2-$ClC_6H_4$ | Me | 4f | 6 | 80 | 238–240 | 239 |
| 7 | 2-$NO_2C_6H_4$ | Me | 4 g | 6 | 82 | 199–200 | — |
| 8 | 2,4-$Cl_2C_6H_3$ | Me | 4 h | 6 | 85 | 201–202 | 199 |
| 9 | 2,6-$Cl_2C_6H_3$ | Me | 4i | 6 | 81 | 298–300 | — |
| 10 | 4-$MeC_6H_4$ | Me | 4j | 6 | 82 | 210–212 | 207 |
| 11 | 4-$OMeC_6H_4$ | Me | 4 k | 6 | 84 | 229–230 | — |
| 12 | 4-$^i$Pr$C_6H_4$ | Me | 4 l | 8 | 76 | 202–204 | — |
| 13 | 1-Naphthyl | Me | 4 m | 8 | 80 | 185–186 | 189 |
| 14 | 2-Thienyl | Me | 4n | 8 | 68 | 208–210 | — |
| 15 | $C_6H_5$ | Et | 4o | 6 | 83 | 236–238 | 232 |
| 16 | 4-$ClC_6H_4$ | Et | 4p | 6 | 88 | 206–208 | 209 |
| 17 | 2,4-$Cl_2C_6H_3$ | Et | 4q | 6 | 83 | 184–186 | 182 |
| 18 | 4-$NO_2C_6H_4$ | Et | 4r | 6 | 84 | 200–202 | 198 |
| 19 | 4-$MeC_6H_4$ | Et | 4 s | 6 | 81 | 225–226 | 222 |
| 20 | 2-Thienyl | Et | 4 t | 8 | 71 | 203–204 | 207 |

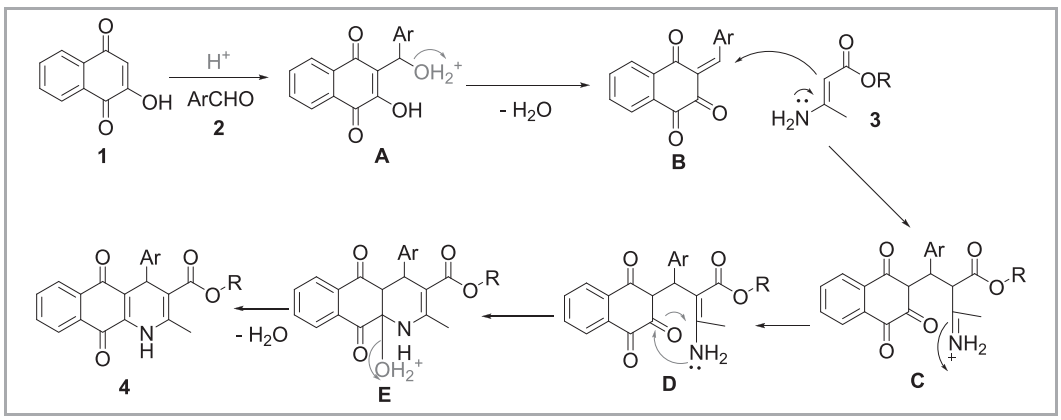
[a]Reaction conditions: 1 (1.0 mmol), 2 (1.0 mmol), 3 (1.0 mmol), C-$SO_3H$ (10 mg), and water (3.0 mL) at 80°C.
[b]Isolated yields.

such as thiophene-2-carbaldehyde, also exhibited good reactivities and gave corresponding products with 80% and 68% yields, respectively.

To further study the scope of this methodology, a variety of aromatic aldehydes were submitted to react with 2-hydroxynaphthalene-1,4-dione (1), and ethyl (*E*)-3-aminobut-2-enoate (3b). In all these cases, the reaction proceeded smoothly to give the corresponding goal products with 71% to 88% yields. Additionally, to further demonstrate the efficiency of the methodology, aliphatic aldehyde such as 3-methylbutanal was also employed with 2-hydroxynaphthalene-1,4-dione (1), and methyl (*E*)-3-aminobut-2-enoate (3a). Unfortunately, the corresponding goal product was not obtained under similar reaction conditions, probably because of the low reactivity of aliphatic aldehyde.

The domino reaction of 2-hydroxynaphthalene-1,4-dione, aromatic aldehydes, and (*E*)-3-aminobut-2-enoate probably follows the regular mechanism of acid-catalyzed condensations. We speculated that the mechanism of the domino reaction involves the reaction of sulfonated carbonaceous material with the 2-hydroxynaphthalene-1,4-dione by acting as an acid and playing a complex role to give radical condensation intermediate between 2-hydroxynaphthalene-1,4-dione and benzaldehyde (Scheme 3).

**Scheme 3.** Mechanism of the synthesis of 4.



The reaction proceeds via intermediate A, formed by the activation of 1 with solid acid. Subsequently, the intermediate B, which could be isolated from the reaction mixture [38], was formed via dehydration reaction under the effect of catalyst. Then, the intermediate C was generated from the reaction of enamine 3 with intermediate B. Ultimately, the goal product 4 was given followed by regioselective intramolecular condensation of cyclization and dehydration. The differences of electrophilicity of carbonyl and steric hindrance of intermediate B explained that the formation of benzo[*g*] quinoline-5,10-diones was highly regioselective. In addition, the stabilizing electron-withdrawing group of benzo[*g*]quinoline-5,10-dione [15,39,40] prevents the aromatization of it even under severe reaction condition, such as microwave or high reaction temperature, or high active oxidants such as peroxide [41].

Subsequently, the recoverability of the sulfonated carbonaceous material catalyst was examined using the model reaction of 2-hydroxynaphthalene-1,4-dione (1), benzaldehyde (2a), and methyl (*E*)-3-aminobut-2-enoate (3a) under optimized conditions. Upon completion, the crude solid was resolved with hot ethanol, and the catalyst was filtered and dried in vacuum oven at 100°C for 4–6 h, it was used. To our delight, the recycled catalyst could be reused four times without any further treatment and only subtle loss in the catalytic activity was observed. We attribute the slight loss in the catalytic activity after the several runs to the minor losses in the recyclability process.

## CONCLUSIONS

In conclusion, we have developed sulfonated carbonaceous material as heterogeneous catalyst catalyzed domino reaction leading to synthesis of benzo[*g*]quinoline-5,10-dione derivatives in good to excellent yields. The reactions were conducted in water using readily available and inexpensive substrates. This procedure shows several advantages, such as concise reaction condition, water as eco-friendly media, short reaction periods, the structural diversity of products, and using sulfonated carbonaceous material as recoverable catalyst.

## EXPERIMENTAL

**General.** Analytical thin layer chromatography (TLC) was performed using Merck silica gel GF254 plates. Flash column chromatography was performed on silica gel (300–400 mesh). Melting points were measured on an X-4 melting point apparatus. $^1$H-NMR spectra were recorded on a 400-MHz instrument (Bruker Avance 400 Spectrometer). Chemical shifts ($\delta$) are given in ppm relative to TMS as the internal reference, with coupling constants ($J$) in Hz. $^{13}$C-NMR spectra were recorded at 100 MHz. Chemical shift were reported in ppm with the internal chloroform signal at 77.0 ppm as a standard. Elemental analysis was carried out on EuroEA elemental analyzer.

**Synthesis and characterization of the sulfuric acid groups functionalized carbon [34].** According to literature method, the polyvinyl alcohol (5.0 g), hydroxyethylsulfuric acid (3.5 g), and deionized water (50 mL) were added in Teflon-lined stainless steel autoclaves, and heated at 180°C for 4 h. Then, the resulting mixture were filtered, washed with water and methanol, and dried in a vacuum oven at 100°C for 4 h. The black goal product was obtained with about 50% yield (according to polyvinyl alcohol).

Neutralization titration indicated that the acidity of the solid acid was 2.4 mmol/g. According to XPS analysis, almost all the S existed in the forms of sulfonic acid groups, and many oxygen-containing groups besides the carbonyl acid groups exist. The BET surface of the solid acid was 146 $m^2$/g. The 1040 and 1195 $cm^{-1}$ absorbability of IR spectra indicated the existence of the sulfuric acid groups. FT-IR spectra showed that the solid acid contains resident functionalities such as hydroxyl (3500 $cm^{-1}$), carboxylate (1704 $cm^{-1}$), C=C groups (1604 $cm^{-1}$), and C—O groups (1204 $cm^{-1}$).

**General procedure for the synthesis of benzo[g]quinoline-5,10-dione derivatives 4a–4t.** 2-Hydroxynaphthalene-1,4-dione (1, 1.0 mmol), aromatic aldehyde (2, 1.0 mmol), (*E*)-3-aminobut-2-enoate (3, 1.0 mmol), C-$SO_3$H (10 mg), and water (3.0 mL) were mixed and heated at 80°C for 6–8 h. When the reaction was finished indicated by TLC monitoring, the precipitate was filtered and dried along with the catalyst. Then, the catalyst was recovered by filtration, and the goal product was further purified by recrystalization from EtOH (95%) to give the pure goal product 4a–t.

***Methyl 2-methyl-5,10-dioxo-4-phenyl-1,4,5,10-tetrahydrobenzo[g] quinoline-3-carboxylate (4a) [15].*** Red brown solid. M.p. 250–252°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.04 (d, 2H, $J$ = 7.2 Hz, ArH), 7.64–7.71 (m, 2H, ArH), 7.35–7.37 (m, 2H, ArH), 7.22–7.24 (m, 2H, ArH), 7.12–7.16 (m, 2H, ArH + NH), 5.37 (s, 1H, CH), 3.66 (s, 3H, OMe), 2.54 (s, 3H, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 182.5, 180.1, 167.3, 145.1, 144.0, 136.8, 134.7, 133.0, 132.8, 130.3, 128.2, 128.1, 126.8, 126.5, 126.1, 119.4, 104.6, 51.2, 37.6, 19.5.

***Methyl 4-(4-fluorophenyl)-2-methyl-5,10-dioxo-1,4,5,10-tetrahydrobenzo[g]quinoline-3-carboxylate (4b).*** Red brown solid. M.p. 246–248°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.04–8.06 (m, 2H, ArH), 7.71–7.75 (m, 1H, ArH), 7.64–7.68 (m, 1H, ArH), 7.31–7.35 (m, 2H, ArH), 7.10 (s, 1H, NH), 5.37

(s, 1H, CH), 3.67 (s, 3H, OMe), 2.54 (s, 3H, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 180.1, 179.9, 156.9, 155.4, 133.4, 132.8, 129.8, 126.6, 126.1, 124.9, 115.3, 115.1, 112.0, 51.3, 36.8, 19.6. *Anal*. Calcd for $C_{22}H_{16}FNO_4$ (377.37): C 70.02, H 4.27, N 3.71; Found: C 69.87, H 4.57, N 3.66.

***Methyl 4-(4-chlorophenyl)-2-methyl-5,10-dioxo-1,4,5,10-tetrahydrobenzo[g]quinoline-3-carboxylate (4c).*** [15]. Red brown solid. M.p. 221–222°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.03–8.06 (m, 2H, ArH), 7.63–7.74 (m, 2H, ArH), 7.19–7.30 (m, 2H, ArH), 7.12 (s, 1H, NH), 5.36 (s, 1H, CH), 3.66 (s, 3H, OMe), 2.53 (s, 3H, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 182.4, 179.9, 167.2, 144.3, 136.8, 134.8, 132.8, 132.7, 132.6, 130.1, 129.5, 128.5, 126.5, 126.1, 118.9, 104.3, 51.2, 37.1, 19.6.

***Methyl 4-(4-nitrophenyl)-2-methyl-5,10-dioxo-1,4,5,10-tetrahydrobenzo[g]quinoline-3-carboxylate (4d).*** Red brown solid. M.p. 228–230°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.12 (d, 2H, $J$ = 8.8 Hz, ArH), 8.03–8.09 (m, 2H, ArH), 7.74 (t, 1H, $J$ = 7.6 Hz, ArH), 7.68 (t, 1H, $J$ = 7.6 Hz, ArH), 7.55 (d, 2H, $J$ = 8.8 Hz, ArH), 7.17 (s, 1H, NH), 5.50 (s, 1H, CH), 3.67 (s, 3H, OMe), 2.57 (s, 3H, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 182.5, 179.6, 167.1, 152.4, 137.1, 135.1, 133.1, 133.0, 129.2, 126.6, 126.2, 123.8, 117.9, 113.8, 51.5, 37.9, 19.8. *Anal*. Calcd for $C_{22}H_{16}N_2O_6$ (404.38): C 65.35, H 3.99, N 6.93; Found: C 65.08, H 4.28, N 6.68.

***Methyl 2-methyl-5,10-dioxo-4-(4-(trifluoromethyl)phenyl)-1,4,5,10-tetrahydrobenzo[g] quinoline-3-carboxylate (4e).*** Red brown solid. M.p. 235–236°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.06 (t, 2H, $J$ = 7.6 Hz, ArH), 7.71–7.75 (m, 1H, ArH), 7.63–7.69 (m, 1H, ArH), 7.48–7.52 (m, 4H, ArH), 7.14 (s, 1H, NH), 5.46 (s, 1H, CH), 3.67 (s, 3H, OMe), 2.56 (s, 3H, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 182.3, 179.7, 167.3, 152.4, 138.8, 137.1, 135.2, 133.0, 129.1, 126.6, 126.3, 123.9, 117.8, 104.3, 52.1, 37.9, 19.8. *Anal*. Calcd for $C_{23}H_{16}F_3NO_4$ (427.38): C 64.64, H 3.77, N 3.28; Found: C 64.55, H 4.01, N 3.00.

***Methyl 4-(2-chlorophenyl)-2-methyl-5,10-dioxo-1,4,5,10-tetrahydrobenzo[g]quinoline-3-carboxylate (4f) [15].*** Red brown solid M.p. 238–240°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.01–8.06 (m, 2H, ArH), 7.63–7.72 (m, 2H, ArH), 7.37–7.41 (m, 2H, ArH), 7.26–7.32 (m, 1H, ArH), 7.07–7.16 (m, 3H, ArH + NH), 5.75 (s, 1H, CH), 3.66 (s, 3H, OMe), 2.49 (s, 3H, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 182.2, 179.9, 167.3, 143.8, 143.6, 137.3, 134.7, 133.2, 132.8, 132.6, 131.5, 130.1, 129.7, 128.0, 126.8, 126.5, 126.0, 118.8, 104.6, 51.0, 36.2, 19.4.

***Methyl 4-(2-nitrophenyl)-2-methyl-5,10-dioxo-1,4,5,10-tetrahydrobenzo[g]quinoline-3-carboxylate (4g).*** Red brown solid. M.p. 199–200°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.06 (t, 2H, $J$ = 8.4 Hz, ArH), 7.81 (m, 1H, $J$ = 8.0 Hz, ArH), 7.66–7.72 (m, 2H, ArH), 7.46–7.48 (m, 2H, ArH), 7.12 (s, 1H, NH), 6.22 (s, 1H, CH), 3.62 (s, 3H, OMe), 2.52 (s, 3H, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 182.0, 179.8, 167.0, 144.5, 140.2, 137.4, 135.1, 133.0, 132.9, 132.6, 131.2, 129.9, 127.7, 126.8, 126.1, 124.5, 104.4, 51.4, 33.2, 19.7. *Anal*. Calcd for $C_{22}H_{16}N_2O_6$ (404.38): C 65.35, H 3.99, N 6.93; Found: C 64.98, H 4.06, N 7.11.

***Methyl 4-(2,4-dichlorophenyl)-2-methyl-5,10-dioxo-1,4,5,10-tetrahydrobenzo[g]quinoline-3-carboxylate (4h) [15].*** Red brown solid. M.p. 201–202°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.01–8.07 (m, 2H, ArH), 7.62–7.74 (m, 2H, ArH), 7.31–7.36 (m, 2H, ArH), 7.11–7.14 (m, 2H, ArH + NH), 5.71 (s, 1H, CH), 3.65 (s, 3H, OMe), 2.49 (s, 3H, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 182.1, 179.9, 167.1, 143.8, 142.1, 137.3, 134.8, 134.0, 133.0, 132.8, 132.5, 129.5, 128.2, 127.2, 126.5, 126.1, 118.2, 104.4, 51.2, 36.2, 19.4.

***Methyl 4-(2,6-dichlorophenyl)-2-methyl-5,10-dioxo-1,4,5,10-tetrahydrobenzo[g]quinoline-3-carboxylate (4i).*** Red brown solid. M.p. 298–300°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.04–8.06 (m, 1H, ArH), 7.99–8.01 (m, 1H, ArH), 7.76–7.77 (m, 1H, ArH), 7.62–7.71 (m, 2H, ArH), 7.23–7.25 (m, 1H, ArH), 7.22 (s, 1H, NH), 7.04 (t, 1H, $J$ = 8.0 Hz, ArH), 6.26 (s, 1H, CH), 3.59 (s, 3H, OMe), 2.42 (s, 3H, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 182.3, 179.7, 167.3, 145.0, 138.7, 138.2, 135.0, 132.7, 129.8, 128.3, 127.9, 126.5, 126.0, 116.0, 101.5, 50.8, 36.5, 19.5. *Anal*. Calcd for $C_{22}H_{15}Cl_2NO_4$ (428.27): C 61.70, H 3.53, N 3.27; Found: C 61.52, H 3.67, N 2.96.

***Methyl 2-methyl-5,10-dioxo-4-(p-tolyl)-1,4,5,10-tetrahydrobenzo[g] quinoline-3-carboxylate (4j) [15].*** Red brown solid. M.p. 210–212°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.04 (d, 2H, $J$ = 8.0 Hz, ArH), 7.68–7.73 (m, 1H, ArH), 7.62–7.66 (m, 1H, ArH), 7.25 (d, 2H, $J$ = 8.0 Hz, ArH), 7.10 (s, 1H, NH), 7.05 (d, 2H, $J$ = 8.0 Hz, ArH), 5.35 (s, 1H, CH), 3.67 (s, 3H, OMe), 2.54 (s, 3H, $CH_3$), 2.26 (s, 3H, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 182.4, 180.1, 167.4, 143.9, 142.5, 136.8, 136.4, 134.7, 132.9, 132.6, 130.6, 129.1, 128.1, 126.6, 125.9, 119.4, 104.6, 51.2, 36.9, 21.0.

***Methyl 4-(4-methoxyphenyl)-2-methyl-5,10-dioxo-1,4,5,10-tetrahydrobenzo[g]quinoline-3-carboxylate (4k).*** Red brown solid. M.p. 229–230°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.05 (d, 2H, $J$ = 7.6 Hz, ArH), 7.73 (t, 1H, $J$ = 6.8 Hz, ArH), 7.65 (t, 1H, $J$ = 7.6 Hz, ArH), 7.30 (d, 2H, $J$ = 8.4 Hz, ArH), 7.08 (s, 1H, NH), 6.78 (d, 2H, $J$ = 8.4 Hz, ArH), 5.33 (s, 1H, CH), 3.74 (s, 3H, OMe), 3.67 (s, 3H, OMe), 2.53 (s, 3H, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 183.9, 182.6, 168.4, 158.4, 143.8, 137.8, 136.6, 134.8, 132.7, 130.2, 129.2, 126.5, 126.0, 113.8, 55.2, 51.3, 36.5, 19.6. *Anal*. Calcd for $C_{23}H_{19}NO_5$ (389.41): C 70.94, H 4.92, N 3.60; Found: C 70.83, H 4.60, N 3.89.

***Methyl 4-(4-isopropylphenyl)-2-methyl-5,10-dioxo-1,4,5,10-tetrahydrobenzo[g]quinoline-3-carboxylate (4l).*** Red brown solid. M.p. 202–204°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.06 (d, 2H, $J$ = 7.6 Hz, ArH), 7.65–7.72 (m, 2H, ArH), 7.26–7.28 (m, 3H, ArH + NH), 7.10 (d, 2H, $J$ = 8.0 Hz, ArH), 5.39 (s, 1H, CH), 3.69 (s, 3H, OMe),

2.80–2.83 (m, 1H, CH), 2.55 (s, 3H, $CH_3$), 1.19 (d, 6H, $J$ = 6.8 Hz, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 182.5, 180.1, 167.3, 144.0, 142.3, 136.8, 136.6, 134.7, 132.8, 132.6, 130.2, 129.3, 128.0, 126.5, 125.9, 119.0, 104.2, 51.0, 37.0, 32.9, 23.5, 19.5. *Anal*. Calcd for $C_{25}H_{23}NO_4$ (401.46): C 74.80, H 5.77, N 3.49; Found: C 75.12, H 6.01, N 3.31.

***Methyl 2-methyl-4-(naphthalen-1-yl)-5,10-dioxo-1,4,5,10-tetrahydrobenzo[g]quinoline-3-carboxylate (4m) [15].*** Red brown solid. M.p. 185–186°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.88 (d, 1H, $J$ = 8.4 Hz, ArH), 8.04–8.08 (m, 1H, ArH), 7.90–7.93 (m, 1H, ArH), 7.78 (d, 1H, $J$ = 8.0 Hz, ArH), 7.58–7.72 (m, 4H, ArH), 7.45–7.50 (m, 2H, ArH), 7.30–7.35 (m, 1H, ArH), 7.15 (s, 1H, NH), 6.12 (s, 1H, CH), 3.54 (s, 3H, OMe), 2.55 (s, 3H, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 182.4, 180.2, 167.4, 144.7, 142.9, 136.8, 134.7, 133.4, 133.0, 132.7, 130.9, 130.3, 128.2, 127.8, 127.5, 126.6, 126.5, 126.1, 125.8, 125.6, 125.1, 120.6, 106.6, 50.9, 32.7, 19.5.

***Methyl 2-methyl-5,10-dioxo-4-(thiophen-2-yl)-1,4,5,10-tetrahydrobenzo[g]quinoline-3-carboxylate (4n).*** Red brown solid. M.p. 208–210°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.12 (d, 1H, $J$ = 6.8 Hz, ArH), 8.07 (d, 1H, $J$ = 7.2 Hz, ArH), 7.73–7.77 (m, 1H, ArH), 7.68 (t, 1H, $J$ = 7.2 Hz, ArH), 7.41–7.43 (m, 1H, ArH), 7.21 (s, 1H, NH), 7.10–7.12 (m, 1H, ArH), 6.88-6.90 (m, 1H, ArH), 5.72 (s, 1H, CH), 3.68 (s, 3H, OMe), 2.58 (s, 3H, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 182.9, 180.3, 167.1, 157.4, 142.9, 137.9, 136.5, 132.5, 130.3, 129.1, 126.0, 104.8, 55.6, 36.4, 19.6. *Anal*. Calcd for $C_{20}H_{15}NO_4S$ (365.40): C 65.74, H 4.14, N 3.83; Found: C 65.58, H 4.41, N 4.11.

***Ethyl 2-methyl-5,10-dioxo-4-phenyl-1,4,5,10-tetrahydrobenzo[g]quinoline-3-carboxylate (4o) [15].*** Red brown solid. M.p. 236–238°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.03 (d, 2H, $J$ = 7.6 Hz, ArH), 7.60–7.70 (m, 2H, ArH), 7.36–7.39 (m, 2H, ArH), 7.22–7.25 (m, 2H, ArH), 7.12–7.16 (m, 2H, ArH + NH), 5.37 (s, 1H, CH), 4.10 (m, 2H, $CH_2$), 3.66 (s, 3H, OMe), 2.52 (s, 3H, $CH_3$), 1.20 (t, 3H, $J$ = 7.2 Hz, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 182.4, 179.9, 166.8, 145.4, 143.6, 136.8, 134.7, 132.8, 132.6, 130.2, 128.3, 128.1, 126.7, 126.5, 125.1, 119.3, 104.6, 60.0, 37.6, 19.4, 14.1.

***Ethyl 4-(4-chlorophenyl)-2-methyl-5,10-dioxo-1,4,5,10-tetrahydrobenzo[g]quinoline-3-carboxylate (4p) [15].*** Red brown solid M.p. 206–208°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.01–8.05 (m, 2H, ArH), 7.60–7.72 (m, 2H, ArH), 7.31 (d, 2H, $J$ = 8.0 Hz, ArH), 7.21 (d, 2H, $J$ = 8.4 Hz, ArH), 7.13 (s, 1H, NH), 5.35 (s, 1H, CH), 4.08–4.15 (m, 2H, $CH_2$), 2.53 (s, 3H, $CH_3$), 1.22 (t, 3H, $J$ = 7.2 Hz, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 182.4, 179.9, 166.7, 144.1, 143.8, 136.8, 134.7, 132.8, 132.5, 130.3, 129.7, 128.3, 128.1, 126.5, 126.1, 118.7, 104.5, 60.2, 37.2, 19.5, 14.2.

***Ethyl 4-(2,4-dichlorophenyl)-2-methyl-5,10-dioxo-1,4,5,10-tetrahydrobenzo[g]quinoline-3-carboxylate (4q) [15].*** Red brown solid. M.p. 184–186°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.01–8.06 (m, 2H, ArH), 7.61–7.73 (m, 2H, ArH), 7.31–7.36 (m, 2H, ArH), 7.11–7.16 (m, 2H, ArH + NH), 5.70 (s, 1H, CH), 4.08–4.16 (m, 2H, $CH_2$), 2.42 (s, 3H, $CH_3$), 1.23 (t, 3H, $J$ = 7.2 Hz, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 182.2, 179.8, 166.7, 144.1, 143.8, 142.0, 137.4, 135.0, 133.8, 133.0, 132.8, 132.6, 130.3, 129.4, 127.1, 126.5, 126.1, 117.8, 104.4, 60.2, 36.1, 19.5, 14.2.

***Ethyl 2-methyl-4-(4-nitrophenyl)-5,10-dioxo-1,4,5,10-tetrahydrobenzo[g]quinoline-3-carboxylate (4r) [15].*** Red brown solid. M.p. 200–202°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.11 (d, 2H, $J$ = 8.8 Hz, ArH), 8.01–8.07 (m, 2H, ArH), 7.65–7.75 (m, 2H, ArH), 7.56 (d, 2H, $J$ = 8.8 Hz, ArH), 7.18 (s, 1H, NH), 5.50 (s, 1H, CH), 4.09-4.17 (m, 2H, $CH_2$), 2.56 (s, 3H, $CH_3$), 1.21 (t, 3H, $J$ = 7.2 Hz, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 182.2, 179.6, 166.4, 152.6, 144.6, 137.2, 135.0, 133.1, 132.6, 130.1, 129.4, 126.6, 126.3, 123.6, 117.9, 104.0, 60.2, 38.4, 19.5, 14.2.

***Ethyl 2-methyl-5,10-dioxo-4-(p-tolyl)-1,4,5,10-tetrahydrobenzo[g]quinoline-3-carboxy-late (4s) [15].*** Red brown solid. M.p. 225–226°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.01–8.06 (m, 2H, ArH), 7.61–7.71 (m, 2H, ArH), 7.24–7.27 (m, 2H, ArH), 7.03–7.07 (m, 2H, ArH), 5.33 (s, 1H, CH), 4.09–4.15 (m, 2H, $CH_2$), 2.52 (s, 3H, $CH_3$), 2.25 (s, 3H, $CH_3$), 1.22 (t, 3H, $J$ = 7.2 Hz, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 182.4, 178.0, 166.8, 143.3, 142.7, 136.8, 136.3, 134.7, 132.8, 132.5, 130.2, 129.0, 128.2, 126.5, 125.9, 119.4, 104.9, 60.0, 37.1, 20.9, 19.5, 14.1.

***Ethyl 2-methyl-5,10-dioxo-4-(thiophen-2-yl)-1,4,5,10-tetrahydrobenzo[g]quinoline-3-carboxylate (4t) [15].*** Red brown solid. M.p. 203–204°C. $^1$H-NMR (400 MHz, $CDCl_3$, $\delta$ ppm): 8.05–8.12 (m, 2H, ArH), 7.64–7.77 (m, 2H, ArH), 7.20 (s, 1H, ArH), 7.09–7.11 (m, 1H, ArH), 6.85–6.89 (m, 2H, ArH), 5.71 (s, 1H, CH), 4.14–4.20 (m, 2H, $CH_2$), 2.53 (s, 3H, $CH_3$), 1.25 (t, 3H, $J$ = 7.2 Hz, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$, $\delta$ ppm): 182.3, 179.9, 166.7, 148.9, 144.1, 136.8, 134.7, 132.8, 130.2, 126.8, 126.7, 126.1, 124.6, 124.3, 118.1, 104.5, 60.2, 32.1, 19.4, 14.2.

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## REFERENCES AND NOTES

[1] Wender, P. A.; Verma, V. A.; Paxton, T. J.; Pillow, T. H. Acc Chem Res 2008, 41, 40.

[2] Tadic, D.; Cassels, B. K.; Leboeuf, M.; Cave, A. Phytochemistry 1987, 26, 537.

[3] Bou-Abdullah, E.; Jossang, A.; Tadic, D.; Leboeuf, M.; Cave, A. J Nat Prod 1989, 52, 273.

[4] Rios, J. L.; Cortes, D.; Valverde, S. Planta Med 1989, 55, 321.

[5] Koyama, J.; Morita, I.; Kobayashi, N.; Osakai, T.; Usuki, Y.; Taniguchi, M. Bioorg Med Chem Lett 2001, 15, 1079.
[6] Lee, H.; Hong, S.-S.; Choi, J.-Y.; Cho, J.; Kim, Y.-H. Arch Pharm Res 1998, 21, 73.
[7] Bracher, F. Liebigs Ann Chem 1989, 87.
[8] Peterson, J. R.; Zjawiony, J. K.; Liu, S.; Hufford, C. D.; Clark, A. M.; Rogers, R. D. J Med Chem 1992, 35, 4069.
[9] Zjawiony, J. K.; Srivastava, A. R.; Hufford, C. D.; Clark, A. M. Heterocycles 1994, 39, 779.
[10] Boger, D. L.; Hong, J.; Hikota, M.; Ishida, M. J Am Chem Soc 1999, 121, 2471.
[11] Kogl, F.; Sparenburg, J. Recl Trav Chim Pays-Bas 1940, 59, 1180.
[12] Kogl, F.; Quackenbush, F. W. Recl Trav Chim Pays-Bas 1944, 63, 251.
[13] Kogl, F.; van Wessem, G. C.; Elsbach, O. I. Recl Trav Chim Pays-Bas 1945, 64, 23.
[14] Soonthornchareonnon, N.; Suwanborirux, K.; Bavovada, R.; Patarapanich, C.; Cassady, J. M. J Nat Prod 1999, 62, 1390.
[15] Bala, B. D.; Balamurugan, K.; Perumal, S. Tetrahedron Lett 2011, 52, 4562.
[16] Jiang, C. H.; Xu, M.; Wang, S.; Wang, H.; Yao, Z. J Org Chem 2010, 75, 4323.
[17] Koyama, J.; Morita, I.; Yamori, T. Molecules 2010, 15, 6559.
[18] Rebstock, A. S.; Mongin, F.; Trécourt, F.; Quéguiner, G. Org Biomol Chem 2004, 2, 291.
[19] Jacobs, J.; Kesteleyn, B.; De Kimp, N. Tetrahedron 2008, 64, 4985.
[20] Jacobs, J.; Deblander, J.; Kesteleyn, B.; Tehrani, K. A.; De Kimp, N. Tetrahedron 2008, 64, 5345.
[21] Echavarren, A. M. J Org Chem 1990, 55, 4255.
[22] Nebois, P.; Barret, R.; Fillion, H. Tetrahedron Lett 1990, 31, 2569.
[23] Nicolaides, D. N.; Awad, R. W.; Papageorgiou, G. K.; Stephanidou-Stephanatou, J. J Org Chem 1994, 59, 1083.
[24] Krapcho, A. P.; Gallagher, C. E.; Mammach, A.; Ellis, M.; Menta, E.; Oliva, A. J Heterocyclic Chem 1997, 34, 27.
[25] Meghani, P.; Mills, O. S.; Joule, J. A. Heterocycles 1990, 30, 1121.
[26] Berghot, M. A. Chem Pap 2002, 56, 202.
[27] Cuerva, J. M.; Cárdenas, D. J.; Echavarren, A. M. Chem Commun 1999, 17, 1721.
[28] Heravi, M. M.; Hashhemi, E.; Beheshtiha, Y. S.; Kamjou, K.; Toolabi, M.; Hosseintash, N. J Mol Catal A Chem 2014, 392, 173.
[29] Nakajima, K.; Okamura, M.; Kondo, J. N.; Domen, K.; Tatsumi, T.; Hayashi, S. Chem Mater 2009, 21, 186.
[30] Budarin, V.; Luque, R.; Macquarrie, D. J.; Clark, J. H. Chem Eur J 2007, 13, 6914.
[31] Toda, M.; Takagaki, A.; Okamura, M.; Kondo, J. N.; Domen, K.; Hayashi, S. Nature 2005, 438, 178.
[32] Hara, M.; Yoshida, T.; Takagaki, A.; Takata, T. J.; Kondo, N.; Domen, K. Angew Chem Int Ed 2004, 43, 2955.
[33] Comerford, J. W.; Clark, J. H.; Macquarrie, D. J.; Breeden, S. W. Chem Commun 2009, 2562.
[34] Liang, X. Z.; Xiao, H. Q.; Shen, Y. M.; Qi, C. Z. Mater Lett 2010, 64, 953.
[35] Li, C. M.; Liang, X. Z.; Zhang, F. R.; Qi, C. Z. Catal Commun 2015, 62, 6.
[36] Zhang, F. R.; Li, C. M.; Wang, C.; Qi, C. Z. Org Biomol Chem 2015, 13, 5022.
[37] Chen, Z.; Shi, Y. X.; Shen, Q. Q.; Xu, H. X.; Zhang, F. R. Tetrahedron Lett 2015, 56, 4749.
[38] Patil, S. R.; Choudhary, A. S.; Sekar, N. Fibers and Polymers 2015, 16, 1068.
[39] Tu, S. J.; Li, C. M.; Shi, F.; Zhou, D. X.; Shao, Q. Q.; Cao, L. J.; Jiang, B. Synthesis 2008, 369.
[40] Shi, F.; Ding, J.; Zhang, S.; Hao, W. J.; Cheng, C.; Tu, S. J. Bioorg Med Chem Lett 2011, 21, 1554.
[41] Jacobs, J.; Abbaspour Tehrani, K.; De Kimpe, N. Tetrahedron 2011, 67, 9459.