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Expedient synthesis of 1,2,4-triazinyl substituted benzo[c]coumarins *via* double oxidation strategy

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Abstract

Herein, we report a convenient one-pot synthesis of 1,2,4-triazinyl derivatives of benzocoumarins. The proposed approach consists of the nucleophilic addition of tetrahydrobenzo annulated dimethoxycoumarin to 1,2,4-triazines followed by double oxidation of both dihydrotriazine and tetrahydrobenzo groups with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). The nucleophilic addition of the dimethoxycoumarin to 1,2,4-triazines was carried out in the presence of three-fold excess of methanesulfonic acid in DCM at room temperature. It takes place between positions 8 and 5 of coumarin and 1,2,4-triazine, respectively. The double oxidation step was carried out with 3.6 equivalent of DDQ. Selective oxidation of dihydrotriazine moiety, without affecting the tetrahydrobenzo fragment, was achieved using 1.2 equivalent of tetrachlorobenzoquinone (TCQ). The differences in the oxidation with TCQ and DDQ appear to be related to the higher oxidative potential of DDQ in contrast to TCQ. The advantages of the method are the elimination of the use of transition metals, the availability of starting materials, and the simplicity of the procedure. The proposed approach provides a two-step one-pot protocol for the synthesis of triazinyl benzocoumarins, precursors for the preparation of push-pull pyridinyl chromophore.

Keywords

coumarin
1,2,4-triazine
nucleophilic substitution of hydrogen
quinone oxidation
push-pull chromophore

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Key findings

- One-pot synthesis of triazinyl-benzo[c]coumarin conjugate was developed.
- Oxidation of adduct with DDQ leads to double oxidation of both dihydrotriazine and tetrahydrobenzo groups.
- Oxidation of adduct with TCQ leads to chemoselective oxidation of dihydrotriazine.

Supplementary materials

1. Introduction

Azaheterocyclic coumarin derivatives provide one of most important photophysical-active compounds [1–3]. Due to good photophysical properties, such as high quantum yields and long-wavelength absorption/emission, various push-pull coumarins, containing azaheterocyclic fragment, have been studied as sensors [3–5] and fluorescent probes [6–8], components of organic light-emitting diodes (OLED) [9, 10] and solar cells [11, 12]. For example, coumarin-based terpyridine–zinc complex (Figure 1) demonstrated sensing ability for pyrophosphate (PPi) in aqueous media and was successfully applied to fluorescence imaging for PPi in Hi-5 cells and Caenorhabditis elegans [13]. Coumarin-based cyclometalated Ir(III) complex (Figure 1) was studied as an emitter in OLED, and the device based on this derivative displayed impressive electroluminescence performance [14]. Coumarin–benzothiazole–chlorambucil conjugate (Figure 1) was developed as a pH-sensitive photoresponsive drug delivery system [15].

In the literature, the synthesis of azinyl-coumarin or benzocoumarin derivatives is reported by multistep reactions sequences, involving construction of azaheterocyclic ring (Scheme 1, **a**) [16] or pyrone core (Scheme 1, **b**) [17] from corresponding precursors or transition metal (TM)-catalyzed cross-coupling reactions between prefunctionalized precursors (Scheme 1, **c**) [14].

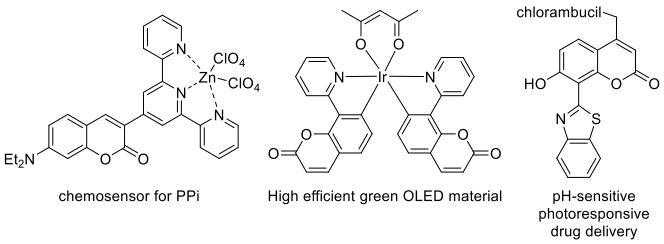
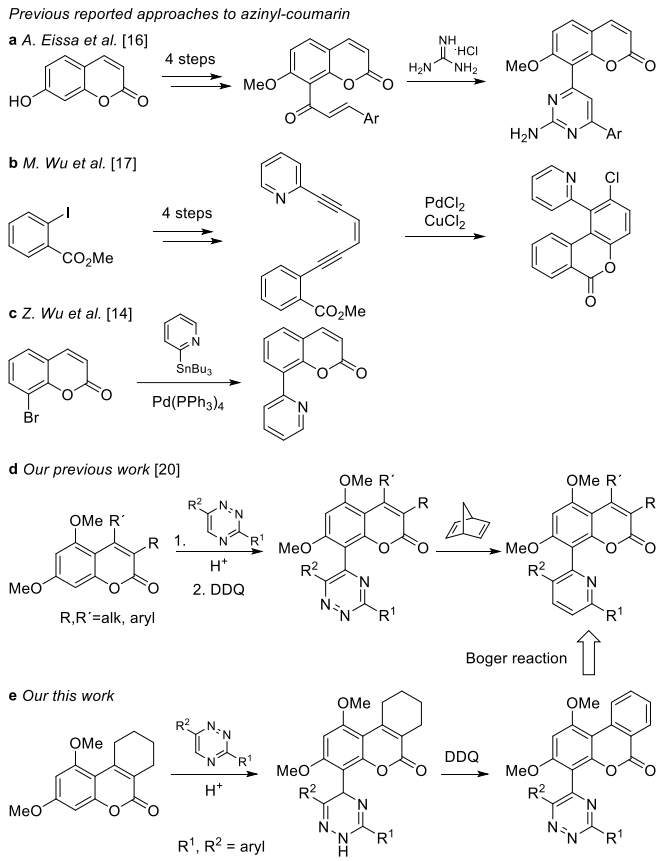


Figure 1 Some important azaheterocyclic coumarin derivatives.



Scheme 1 Approaches to azinyl-coumarin.

Nucleophilic substitution of hydrogen (S_NH) [18] in nitrogen-containing heterocycles represents a powerful tool for the construction of a novel C–C bond, conforming to the requirements of "green" chemistry and PASE (pot, atom, step economy) approaches. The advantages of this approach are the avoidance of TM catalysts and the so-called "chlorine technologies", mild reaction conditions, which, in turn, leads to a decrease in the number of steps and an increase in the overall yield of the desired product. S_NH reactions often proceed as the addition of a nucleophile to an electrophilic azine with the formation of a σ^H-adduct, which can subsequently be oxidized in the presence of an external oxidizing agent (air oxygen [19], 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) [20–23], $K_3[Fe(CN)_6]$ [24–26], MnO_2 [22, 27]) to a product of nucleophilic substitution of hydrogen.

Earlier, we proposed a convenient synthetic approach to push-pull 8-pyridinylcoumarin chromophores (Scheme 1, **d**) by using a sequence of reactions of nucleophilic substitution of hydrogen and Boger pyridine synthesis in the series of 3,6-diaryl-substituted 1,2,4-triazines and 5,7-dimethoxycoumarins [20, 28]. Thus, at the first step, coumarin was added to the triazine core with the formation of a 1,4-dihydrotriazine derivative, which then easily underwent aromatization under the action of the external oxidant such as DDQ with the formation of S_NH product in high yield, which then transformed to pyridine derivative with 2,5-norbornadiene. In order to study the scope and limitations of this S_NH approach, we adopted synthetic protocol of the oxidative cross-coupling of 1,3-dimethoxy-7,8,9,10-tetrahydro-6*H*-benzo[c]coumarin **1** with 3,6-substituted triazines **2**. In the present work, we report the double aromatization of both the dihydrotriazine and tetrahydrobenzene moieties (Scheme 1, **e**). This double aromatization strategy allowed us to extend the opportunities of S_NH reactions in triazines providing stringboard access to 1,2,4-triazinyl substituted benzo[c]coumarins.

2. Experimental

^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra were recorded on a Bruker DRX-400 Avance spectrometer with DMSO-d_6 or $CDCl_3$ as a solvent at ambient temperature. Chemical shifts are reported in ppm and coupling constants are given in Hz. Data for ^{1}H NMR are recorded as follows: chemical shift (ppm), multiplicity (*s*, singlet; *d*, doublet; *t*, triplet; *m*, multiplet; *br s*, broad signal), coupling constant (Hz), integration. High resolution mass spectra were recorded on an Agilent UHPLC/MS Accurate-Mass Q-TOF 1290/6545. Thin layer chromatography (TLC) was performed on silica gel coated glass slide (Merck, Silica gel G for TLC). Aluminium oxide 90 (70–230 mesh, Merck) was used for column chromatography. All solvents were dried and distilled before use. Commercially available substrates were freshly distilled before the reaction. Solvents, reagents and chemicals were purchased from Aldrich, Fluka, Merck, SRL, Spectrochem and Process Chemicals. All reactions involving moisture sensitive reactants were carried out using oven dried glassware.

2.1. 4-(3,6-Diphenyl-2,5-dihydro-1,2,4-triazin-5-yl)-1,3-dimethoxy-7,8,9,10-tetrahydro-6H-benzo[c]chromen-6-one 3a

To a solution of coumarin **1** (260 mg, 1 mmol) and triazine **2a** (233 mg, 1 mmol) in dichloromethane (DCM,6 ml) was added $MeSO_3H$ (288 mg, 3 mmol). The resulting solution was left for 3 h; the progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was washed with a saturated Na_2CO_3 solution. The organic layer was separated, dried with anhydrous sodium sulfate, and the solvent was removed under reduced pressure. The residue was recrystallized from benzene to give pure adduct **3a**.

White precipitate. Yield 449 mg (91%). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 11.14–10.93 (*br s*, 1H), 7.86–7.77 (*m*, 2H), 7.67–7.58 (*m*, 2H), 7.47–7.35 (*m*, 3H), 7.30–7.20 (*m*, 3H), 6.57 (*s*, 1H), 6.41 (*s*, 1H), 3.92 (*s*, 3H),

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3.85 (*s*, 3H), 2.97–2.85 (*m*, 2H), 2.42–2.29 (*m*, 2H), 1.67–1.54 (*m*, 4H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.8, 159.2, 158.1, 151.7, 149.3, 149.2, 139.3, 136.0, 133.4, 130.1, 128.6, 128.2, 128.1, 126.2, 124.9, 118.0, 111.2, 103.9, 92.7, 56.3, 56.1, 45.8, 29.4, 24.2, 21.7, 20.6. **HRMS** (ESI): $C_{30}H_{28}N_3O_4^+$ [(M+H)$^+$]: calcd.: 494.2074; found: 494.2069.

2.2. 4-(3,6-Diphenyl-1,2,4-triazin-5-yl)-1,3-dimethoxy-7,8,9,10-tetrahydro-6H-benzo[c]chromen-6-one 4a

Dihydrotriazine **3a** (493 mg, 1 mmol) was dissolved in 1,2-dichloroethane (DCE, 10 ml), tetrachloro-1,4-benzoquinone (TCQ) (340 mg, 1.2 mmol) was added, and the mixture was refluxed for 6 h. The solvent was removed under reduced pressure, and the residue was recrystallized from butanol-1 to give pure **4a**.

Pale yellow precipitate. Yield 417 mg, 85%. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.60–8.54 (*m*, 2H), 7.58–7.49 (*m*, 5H), 7.35–7.27 (*m*, 3H), 6.21 (*s*, 1H), 3.90 (*s*, 3H), 3.51 (*s*, 3H), 3.11–3.10 (*m*, 2H), 2.57–2.46 (*m*, 2H), 1.80–1.69 (*m*, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.3, 160.8, 160.3, 158.4, 152.4, 152.3, 149.3, 135.9, 135.3, 131.4, 129.3, 128.8, 128.6, 128.5, 128.2, 120.2, 107.2, 105.5, 91.2, 66.0, 55.8, 30.1, 24.8, 22.5, 21.4. **HRMS** (ESI): $C_{30}H_{26}N_3O_4^+$ [(M+H)$^+$]: calcd.: 492.1918; found: 492.1923.

2.3. General method for synthesis of compounds 5

To a solution of coumarin **1** (260 mg, 1 mmol) and corresponding triazine **2a–i** (1 mmol) in DCM (6 ml) was added $MeSO_3H$ (288 mg, 3 mmol). The resulting solution was left for 3 h. After completion of the reaction, the reaction mixture was washed with a saturated Na_2CO_3 solution. The organic layer was separated, dried with anhydrous sodium sulfate, and the solvent was removed under reduced pressure to give adduct **3**, which then was dissolved in DCE (10 ml). Then, DDQ (3.6 mmol, 817 mg) was added, and the mixture was refluxed for 6 h. The resulting mixture was purified using flash chromatography (Al_2O_3/ethyl acetate). The solvent was removed under reduced pressure, and the residue was recrystallized from butanol-1 to give pure **5**.

2.3.1. 4-(3,6-Diphenyl-1,2,4-triazin-5-yl)-1,3-dimethoxy-6H-benzo[c]chromen-6-one 5a

Yellow powder. Yield 429 mg, 88%; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.89 (*d*, *J* = 8.4 Hz, 1H), 8.64–8.57 (*m*, 2H), 8.34 (*d*, *J* = 7.9 Hz, 1H), 7.76 (*t*, *J* = 7.6 Hz, 1H), 7.61–7.56 (*m*, 2H), 7.55–7.46 (*m*, 4H), 7.34–7.27 (*m*, 3H), 4.08 (*s*, 3H), 3.60 (*s*, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.3, 160.7, 160.4, 158.4, 158.3, 152.4, 151.2, 135.9, 135.3, 135.0, 134.6, 131.4, 130.4, 129.3, 128.9, 128.6, 128.5, 128.2, 127.6, 126.7, 119.9, 108.0, 102.5, 91.8, 56.2, 56.0. **HRMS** (ESI): $C_{30}H_{22}N_3O_4^+$ [(M+H)$^+$]: calcd.: 488.1605; found: 488.1609.

2.3.2. 4-(3,6-bis(4-Methoxyphenyl)-1,2,4-triazin-5-yl)-1,3-dimethoxy-6*H*-benzo[c]chromen-6-one 5b

Yellow powder. Yield 421 mg, 77%. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.88 (*d*, *J* = 8.5 Hz, 1H), 8.58–8.51 (*m*, 2H), 8.33 (*dd*, *J* = 7.5, 1.6 Hz, 1H), 7.75 (*ddd*, *J* = 8.5, 7.5, 1.6 Hz, 1H), 7.56–7.43 (*m*, 3H), 7.06–6.98 (*m*, 2H), 6.85–6.75 (*m*, 2H), 6.41 (*s*, 1H), 4.08 (s, 3H), 3.87 (*s*, 3H), 3.75 (*s*, 3H), 3.63 (*s*, 3H). **^{13}C NMR** (101 MHz, CDCl3) δ 162.4, 161.6, 160.6, 160.5 (2C), 158.3, 157.3, 152.0, 151.1, 135.0, 134.6, 130.4, 130.2, 129.8, 128.4, 128.0, 127.5, 126.7, 119.9, 114.2, 113.7, 108.3, 102.4, 91.9, 56.2, 56.1, 55.5, 55.3. **HRMS** (ESI): $C_{32}H_{26}N_3O_6^+$ [(M+H)$^+$]: calcd.: 548.1816; found: 548.1820.

2.3.3. 1,3-Dimethoxy-4-(6-(4-methoxyphenyl)-3-(p-tolyl)-1,2,4-triazin-5-yl)-6*H*-benzo[c]chromen-6-one 5c

Yellow powder. Yield 405 mg, 74%. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.87 (*d*, *J* = 8.4 Hz, 1H), 8.48 (*d*, *J* = 7.9 Hz, 2H), 8.32 (*d*, *J* = 7.9 Hz, 1H), 7.74 (*t*, *J* = 7.9 Hz, 1H), 7.53 (*d*, *J* = 8.4 Hz, 2H), 7.47 (t, *J* = 7.9 Hz, 1H), 7.31 (d, *J* = 7.9 Hz, 2H), 6.78 (d, *J* = 8.4 Hz, 2H), 6.41 (s, 1H), 4.07 (s, 3H), 3.74 (s, 3H), 3.62 (s, 3H), 2.42 (s, 3H). **^{13}C NMR** (101 MHz, CDCl3) δ 161.9, 160.6, 160.5, 160.4, 158.3, 157.7, 152.1, 151.1, 141.6, 134.9, 134.6, 132.6, 130.3, 129.8, 129.6, 128.4, 128.3, 127.5, 126.7, 119.8, 113.7, 108.2, 102.4, 91.9, 56.2, 56.0, 55.3, 21.7. **HRMS** (ESI): $C_{32}H_{26}N_3O_5^+$ [(M+H)$^+$]: calcd.: 532.1867; found: 532.1871.

2.3.4. 1,3-Dimethoxy-4-(3-phenyl-6-(p-tolyl)-1,2,4-triazin-5-yl)-6*H*-benzo[c]chromen-6-one 5d

Yellow powder. Yield 296 mg, 59%. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.88 (*d*, *J* = 8.5 Hz, 1H), 8.64–8.55 (*m*, 2H), 8.34 (*dd*, *J* = 7.9, 1.6 Hz, 1H), 7.76 (*ddd*, *J* = 8.5, 7.9, 1.6 Hz, 1H), 7.56–7.44 (*m*, 6H), 7.11–7.04 (*m*, 2H), 6.41 (*s*, 1H), 4.08 (*s*, 3H), 3.61 (*s*, 3H), 2.28 (*s*, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.0, 160.7, 160.4, 158.3, 152.3, 151.2, 134.9, 135.4, 135.0, 134.6, 132.9, 131.3, 130.4, 129.0, 128.8, 128.6, 128.4, 128.4, 127.5, 126.7, 119.9, 108.2, 102.4, 91.9, 56.2, 56.0, 21.5. **HRMS** (ESI): $C_{32}H_{26}N_3O_5$: calcd.: 532.1867; found: 532.1871.

2.3.5. 1,3-Dimethoxy-4-(6-(naphthalen-2-yl)-3-phenyl-1,2,4-triazin-5-yl)-6*H*-benzo[c]chromen-6-one 5e

Yellow powder. Yield 381 mg, 71%. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.86 (*d*, *J* = 8.5 Hz, 1H), 8.69–8.60 (*m*, 2H), 8.33 (*dd*, *J* = 7.9, 1.6 Hz, 1H), 8.15 (*s*, 1H), 7.80–7.71 (*m*, 4H), 7.67 (*dd*, *J* = 8.5, 1.6 Hz, 1H), 7.60–7.50 (*m*, 3H), 7.51–7.38 (*m*, 3H), 6.34 (s, 1H), 4.03 (*s*, 3H), 3.54 (*s*, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.2, 160.7, 160.5, 158.4, 158.3, 152.6, 151.3, 135.3, 135.0, 134.6, 133.6, 133.3, 133.0, 131.4, 130.4, 128.9, 128.8, 128.6, 128.5, 127.9, 127.7, 127.6, 126.9, 126.7, 126.3, 125.6, 119.8, 108.0, 102.5, 91.8, 56.2, 56.0. **HRMS** (ESI): $C_{34}H_{24}N_3O_4^+$ [(M+H)$^+$]: calcd.: 538.1761; found: 538.1757.

2.3.6. 4-(6-(4-Bromophenyl)-3-phenyl-1,2,4-triazin-5-yl)-1,3-dimethoxy-6*H*-benzo[c]chromen-6-one 5f

Yellow powder. Yield 441 mg, 78%. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.89 (*d*, *J* = 8.5 Hz, 1H), 8.63–8.56 (*m*, 2H), 8.34 (*dd*, *J* = 7.5, 1.6 Hz, 1H), 7.77 (*ddd*, *J* = 8.5, 7.5, 1.6 Hz, 1H), 7.61–7.44 (*m*, 6H), 7.44–7.37 (*m*, 2H), 6.41 (*s*, 1H), 4.10 (*s*, 3H), 3.64 (*s*, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.5, 160.9, 160.3, 158.2, 157.5, 152.3, 151.1, 135.1, 135.1, 134.9, 134.5, 131.6, 131.5, 130.4, 130.0, 128.9, 128.7, 127.7, 126.7,

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124.0, 119.8, 107.5, 102.5, 91.8, 56.3, 56.0. **HRMS** (ESI): $C_{30}H_{21}BrN_3O_4^+$ [(M+H)$^+$]: calcd.: 566.0710; found: 566.0715.

2.3.7. 4-(6-(4-Bromophenyl)-3-(4-methoxyphenyl)-1,2,4-triazin-5-yl)-1,3-dimethoxy-6*H*-benzo[c]chromen-6-one 5g

Yellow powder. Yield 446 mg, 75%. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.89 (*d*, *J* = 8.5 Hz, 1H), 8.59–8.51 (*m*, 2H), 8.34 (*dd*, *J* = 7.5, 1.6 Hz, 1H), 7.77 (*ddd*, *J* = 8.5, 7.5, 1.6 Hz, 1H), 7.54–7.38 (*m*, 4H), 7.07–6.98 (*m*, 2H), 6.41 (*s*, 1H), 4.10 (*s*, 3H), 3.88 (*s*, 3H), 3.63 (*s*, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.6, 162.2, 160.8, 160.4, 158.2, 156.8, 152.1, 151.2, 135.1, 134.5, 131.5, 130.4, 130.4, 130.0, 127.7, 127.7, 126.7, 123.8, 119.8, 114.3 (2C), 107.7, 102.5, 91.8, 56.3, 56.0, 55.5. **HRMS** (ESI): $C_{31}H_{23}BrN_3O_5^+$ [(M+H)$^+$]: calcd.: 596.0816; found: 596.0822.

2.3.8. 4-(6-(4-Bromophenyl)-3-(p-tolyl)-1,2,4-triazin-5-yl)-1,3-dimethoxy-6*H*-benzo[c]chromen-6-one 5h

Yellow powder. Yield 428 mg, 74%. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.89 (*d*, *J* = 8.5 Hz, 1H), 8.49 (*d*, *J* = 8.0 Hz, 2H), 8.34 (*dd*, *J* = 7.9, 1.6 Hz, 1H), 7.77 (*ddd*, *J* = 8.5, 7.9, 1.6 Hz, 1H), 7.54–7.38 (*m*, 5H), 7.33 (*d*, *J* = 8.0 Hz, 2H), 6.41 (*s*, 1H), 4.10 (*s*, 3H), 3.64 (*s*, 3H), 2.44 (*s*, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.5, 160.8, 160.3, 158.2, 157.3, 152.2, 151.1, 142.0, 135.1, 135.0, 134.5, 132.4, 131.5, 130.4, 130.0, 129.7, 128.6, 127.7, 126.7, 123.9, 119.8, 107.6, 102.5, 91.8, 56.2, 56.0, 21.7. **HRMS** (ESI): $C_{31}H_{23}BrN_3O_4^+$ [(M+H)$^+$]: calcd.: 580.0866; found: 580.0870.

2.3.9. 1,3-Dimethoxy-4-(3-phenyl-1,2,4-triazin-5-yl)-6*H*-benzo[c]chromen-6-one 5i

Yellow powder. Yield 275 mg, 67%. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.53 (*s*, 1H), 8.96–8.90 (*m*, 1H), 8.50–8.43 (*m*, 2H), 8.26–8.19 (*m*, 1H), 7.93–7.88 (*m*, 1H), 7.68–7.56 (*m*, 4H), 6.92 (*s*, 1H), 4.19 (*s*, 3H), 3.96 (*s*, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 162.8, 160.9, 159.5, 158.9, 153.7, 150.5, 150.3, 135.4, 134.8, 133.9, 131.8, 129.6, 129.1, 127.9, 127.8, 126.4, 119.0, 104.9, 101.1, 93.2, 56.8, 56.7. **HRMS** (ESI): $C_{24}H_{18}BrN_3O_4^+$ [(M+H)$^+$]: calcd.: 412.1292; found: 412.1297.

3. Results and Discussion

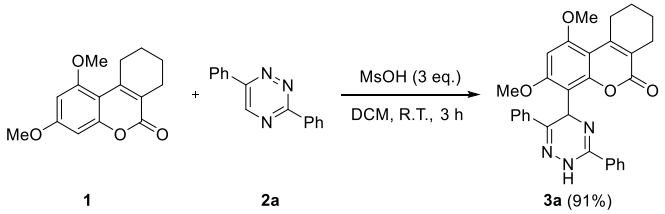
We started our research with the reaction of dimethoxycoumarin **1** with 3,6-diphenyl-1,2,4-triazine **2a**, which was carried out in the presence of three-fold excess of methanesulfonic acid (MsOH) in DCM at room temperature, yielding dihydrotriazine **3a** in high yield (Scheme 2), in accordance with the previously described procedure [20].

Aromatization of the adduct **3a** with 1.5 equivalent of DDQ (Table 1, entry 1) [20] provided a complex mixture of products. We hypothesized that, in contrast to our previous work [20, 28], DDQ not only oxidizes 1,4-dihydrotriazine core to give expected product of the nucleophilic substitution of hydrogen **4a**, but also aromatizes tetrahydrobenzene moiety yielding **5a** and **6a**, which is confirmed by the literature data [29, 30].

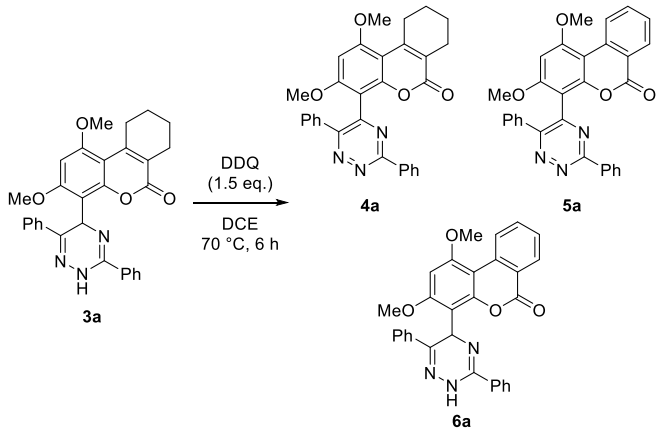
However, it was found that increasing amount of oxidant up to 3.6 equivalents (1.2 equiv. per σ-bond) in 1,2-dichloroethane (DCE) at 70 °C allows producing 4-triazinyl-benzo[c]coumarin derivative **5a** in 90% yield (Scheme 4). Further increasing of DDQ amount up to 5 equivalents did not improve the yield (Table 1, entry 3).

In addition, we also demonstrated that using even four-fold excess of TCQ (Table 1, entry 4) instead of DDQ as the oxidizing agent in the same oxidation process led to aromatization of dihydrotriazine moiety with excellent chemoselectivity to give S_N^H product (Scheme 5).

After quick reoptimization of the reaction conditions, we found that the use of 1.2 eq. TCQ in DCE at 70 °C (Table 1, entry 5) could allow the formation of **4a** in best yield. One can assume that the differences in the oxidation with TCQ and DDQ are related to the higher oxidative potential of DDQ in contrast to TCQ (0.51 vs. 0.01 volts [31]).



Scheme 2 Synthesis of adduct **3a**.



Scheme 3 Formation of the complex mixture of products during the oxidation of adduct **3a** with 1.5 equivalents of DDQ.

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

Entry	Oxidant (equivalents)	Product	Yield [b]
1	DDQ (1.5 eq.)	– [c]	
2	DDQ (3.6 eq.)	**5a**	90
3	DDQ (5.0 eq.)	**5a**	88
4	TCQ (4.0 eq.)	**4a**	84
5	TCQ (1.2 eq.)	**4a**	85
6	air (bubbling)	– [d]	
7	oxygen (bubbling)	– [d]	
8	MnO_2 (10 eq.)	**4a**	51

[a] Conditions: **3a** (1 mmol), DCE (10 ml), 70°C;
[b] Isolated yield;
[c] Hard-to-separate mixture;
[d] Starting material was isolated.

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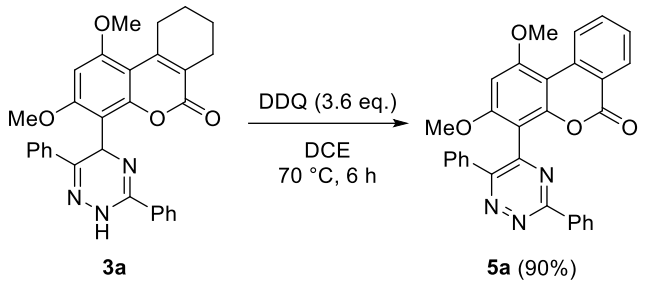
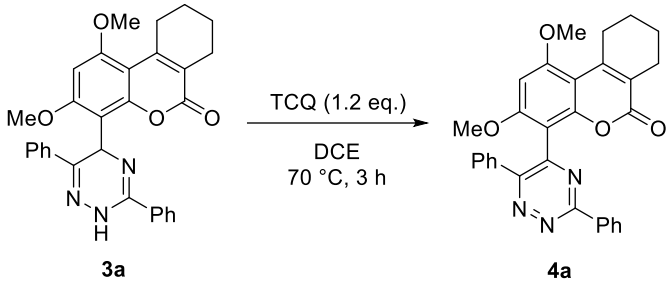


Scheme 4 Oxidation of adduct **3a** with 3.6 equivalents of DDQ.



Scheme 5 Oxidation of adduct **3a** with TCQ.

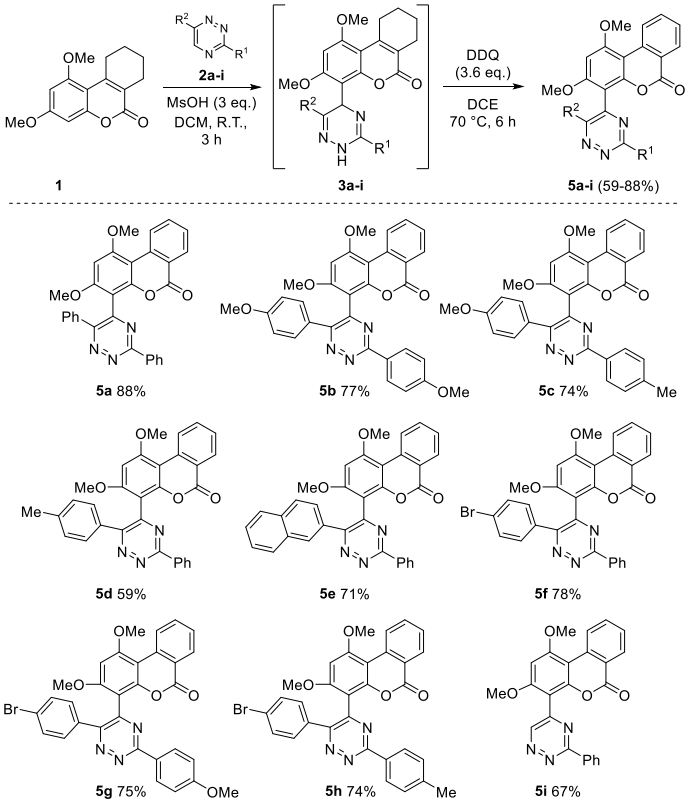
Air or oxygen bubbling through the reaction mixture did not produce desired products (Table 1, entries 6 and 7, respectively), and only the starting material was isolated from the reaction mixture.

Manganese oxide (IV) is another oxidizing agent that can oxidize dihydrotriazines to aromatic triazines [27]. When dihydrotriazine **3a** was refluxed with 10 equivalents of MnO_2 in dichloroethane, product **4a** was formed in 51% yield (Table 1, entry 8).

Formation of compound **5a** was proven by ^1H and ^{13}C NMR spectroscopy data. In particular, multipletes of protons of the methylene groups were not observed in the 3.5–1.5 ppm region. In addition, signals of sp^3-hybridized carbons of the tetrahydrobenzene ring were also absent in the high field of ^{13}C NMR spectrum.

After optimizing the reaction conditions, we examined the applicability and scope of this reaction sequence with respect to 3,6-diaryl-substituted 1,2,4-triazines **2a–h**. The results are summarized in Scheme 6. 1,2,4-Triazines **2** bearing *p*-tolyl, 4-methoxyphenyl (PMP), 4-bromophenyl and even bulky naphthalenyl group at the C6 position were tolerated, and corresponding products **5a–h** were isolated in 59–88% yields after recrystallization. The reduced yield for compound **5d** may be due to oxidation of the p-tolyl group with DDQ [32]. On the other hand, all attempts to involve 3-pyridin-2-yl substituted 1,2,4-triazines in this reaction sequence were unsuccessful. In addition, using 3-phenyl-1,2,4-triaizine **2i** also provided desired product **5i** in good yield.

It is well known that 1,2,4-triazines are readily accessible and cheap building block for construction of pyridine derivatives, which are used as functional materials [33]. At the same time, the annulation of an additional benzene cycle to the coumarin framework often improves the photophysical characteristics: it leads to a bathochromic shift of the absorption and emission maxima and can also increase the fluorescence quantum yield [34, 35].



Scheme 6 Synthesis of benzo[*c*]coumarin **5**.

Thus, the obtained products may be considered as precursors for pyridyl-coumarin conjugate chromophores. Further transformations and detailed photophysical studies are in progress and will be published later.

4. Limitations

We proposed the method of synthesis of 1,2,4-triazinyl substituted benzo[*c*]coumarins *via* double aromatization strategy. Various 3,6-biaryl-1,2,4-triazines were involved in this transformation. However, in the case of 3-pyridinyl substituted 1,2,4-triaines, desired benzo[*c*]coumarin derivatives were not observed. In the course of our further research, we will attempt to overcome those limitations and develop a method of the oxidative cross-coupling 3-pyridin-2-yl 1,2,4-triazines with coumarins.

5. Conclusion

We proposed a new protocol of the synthesis of triazinyl-benzo[*c*]coumarin derivatives by means of simultaneous oxidation dihydrotriazine and tetrahydrobenzene frameworks under the action of DDQ as an oxidant. In contrast to DDQ, oxidation in the presence of TCQ exclusively provided the S_NH products. The obtained products could serve as precursors for push-pull pyridyl-coumarin conjugate chromophores for potential applications in material science.

• Supplementary materials

This manuscript contains supplementary materials, which are available on the corresponding online page.

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• Conflict of interest

The authors declare no conflict of interest.

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