Synthesis of benzo[f]chromeno[3,4-b]quinoline-6-ones and chromeno[3,4-b]quinoline-6,11-diones via one-pot three component tandem Knoevenagel–Michael reaction catalyzed by $N$-tetrabutylammonium tribromide

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The synthesis of benzo[f]chromeno[3,4-b]quinoline-6-ones has been achieved via one-pot three-component reaction from substituted aromatic aldehydes, 3-aminocoumarins, and 2-naphthol in n-butanol using 10 mol% of $N$-tetrabutylammonium tribromide (TBATB) as catalyst under reflux condition. The product formation is going through tandem Knoevenagel–Michael reaction followed by concomitant cyclization. The most noteworthy features of the present protocol are environmentally benevolent reaction conditions, simplicity of procedure, high atom economy, easy accessibility of the catalyst, cost effectiveness and superior yields. In addition, TBATB has also been found to be an effective catalyst for synthesising chromeno[3,4-b]quinoline-6,11-diones from substituted aromatic aldehydes, 3-aminocoumarins and cyclic 1,3-diketones with better yields in shorter reaction time.
Synthesis of benzo[f]chromeno[3,4-b]quinoline-6-ones …

Graphical Abstract

Introduction

Multicomponent reactions (MCRs) have been considered as a handy approach for the synthesis of heterocycles [1–3] due to their powerful bond forming efficiency. These reactions have numerous advantages such as simplicity, high selectivity, variability, less time consumption and avoidance of costly purification steps [4–6]. The amalgamation of renowned elementary organic reactions such as Knoevenagel condensation [7–10] and Michael addition [11–13] into a tandem reaction has emerged as a powerful synthetic protocol for creating molecular complexity and diversity in organic synthesis. Tandem Knoevenagel-Michael reaction is being explored increasingly in MCRs for construction of new heterocyclic entities [14–16].

Quinone methides are short-lived and highly reactive intermediates which have been exploited for the synthesis of complex natural products [17–20] and pharmaceuticals [21]. These intermediates can undergo 1,4-Michael type addition reactions namely aza-Michael [22–24] and thia-Michael [25] reactions with various nucleophiles. A few years ago, Katritzky and his co-worker reported that the generation of 2-naphthoquinone-1-methide intermediated from α-(α-benzotriazolyl-alkyl)-phenols [26], and was trapped in electron-rich olefin for the construction of chroman ring system.
We perceived that 2-naphthol and aromatic aldehyde might react in presence of an appropriate acid catalyst to create 2-naphthoquinone-1-methide intermediating through Knoevenagel condensation which can react instantaneously with a carbon nucleophile like 3-aminocoumarin through Michael type reaction followed by ring closing in order to provide a new heterocyclic entity; benzo[f]chromeno[3,4-b]quinoline-6-one. A similar synthetic approach has also been revealed by other workers for the creation of 4-aza-2,3-didehydropodophyllotoxin [27] and tricyclic dihydropyridine derivatives [28].

Quinoline and its annulated derivatives are an important class of heterocycles because of their diverse applications [29–32]. Compounds containing quinoline moiety have wide utilization in medicinal chemistry [33] with a broad range of biological activities like antimalarial, antiinflammatory, antiasthmatic, antihypertensive, antibacterial, anticancer and also inhibitors of tyrosine kinase [34–37]. On the other hand, chromene nucleus is also found in many naturally occurring biologically active compounds displaying antihypertensive, anti-ischemic and anti-HIV activities [38–40]. Chromenoquinoline derivatives have been therapeutically [41, 42] used as drugs that regulate the transcriptional activity of human progesterone receptor. Some of them have been used as antagonists [43] and antiinflammatory agents such as cortisone and cortisol [44].

Few years back, chaudhuri and his collaborators first reported the environmentally benign synthesis of N-tetrabutylammonium tribromide (TBATB) and its application in bromination reactions [45]. Later on, our group also demonstrated its usefulness for the deprotection of dithioacetals [46], inter-conversion of carbonyl compounds into 1,3-oxathiolanes and vice-versa [47], synthesis of α-bromo enones [48], piperidines [49] and naturally occurring flavone derivatives [50] as well as in carbohydrate chemistry [51]. A wide variety of organic transformations have also been reported by other groups [52–57] utilizing TBATB. In continuation of our persistent efforts to develop multi-component reactions to synthesize prospective bioactive scaffolds [58, 59], we would like to report one-pot three-component reaction for synthesising benzo[f]chromeno[3,4-b]quinoline-6-one derivatives through tandem Knoevenagel-Michael reaction involving substituted aromatic aldehydes (1), 2-naphthol (2a) and 3-aminocoumarins (3) in n-butanol under reflux using 10 mol% of TBATB as catalyst as shown in Scheme 1.

Synthesis of chromeno[3,4-b]quinoline-6,11-diones via Michael reaction of 3-aminocoumarin on in situ created benzylidene cyclohexane-1,3-diones has been reported by our group [60]. Knowing the unique behaviour and properties of TBATB and influenced by its efficacy as a catalyst in tandem Knoevenagel–Michael reaction, we conceived that TBATB might also act as a useful catalyst for the one-pot synthesis of chromeno[3,4-b]quinoline-6,11-diones. So we report the TBATB catalyzed
one-pot synthesis of chromeno[3,4-b]quinoline-6,11-diones from substituted aromatic aldehydes (1), cyclic 1,3-diketones (2b) and 3-aminocoumarins (3) as shown in Scheme 2.

**Experimental**

*Materials and methods*

Melting points were recorded on a Büchi melting point apparatus and are uncorrected. IR spectra were recorded on Perkin-Elmer 281 IR spectrophotometer. $^1$H and $^{13}$C NMR spectra were recorded on Varian 400 spectrometer using TMS as internal reference; chemical shifts ($\delta$ scale) are reported in parts per million (ppm). Elemental analyses were carried out using Perkin-Elmer 2400 Series II CHNS/O analyzer at the Department of Chemistry, Indian Institute of Technology Guwahati. The X-ray crystal structures were determined with a Siemens P-4 diffractometer. Complete crystallographic data of 4d and 5o have been deposited with the Cambridge Crystallographic Data Centre. Besides, CCDC nos. are 897315 and 910378 respectively. Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK, (Fax: +44 1223 336033, e-mail: deposit@ccdc.cam.ac.uk or www.ccdc.cam.ac.uk).

*General procedure for the synthesis of benzo[f]chromeno[3,4-b]quinoline-6-ones (4)*

In a 25 mL round bottomed flask was taken aromatic aldehyde (1 mmol), 2-naphthol (1 mmol) and 3-aminocoumarin (1 mmol) in 3 mL of n-butanol. Then, the catalyst $N$-tetrabutylammonium tribromide (TBATB) (0.048 g, 0.1 mmol) was added into the reaction mixture which was then kept for refluxing in a pre-heated oil bath. The progress of the reaction was monitored time to time by performing thin layer chromatography. After that the completion of the reaction has been confirmed, the reaction mixture was cooled to room temperature and the solvent n-butanol was then removed in a rotary evaporator. The crude residue was extracted with dichloromethane (2×10 mL) and it was washed with water and dried over anhydrous sodium sulfate. The organic layer was concentrated in a rotary evaporator and the crude residue was purified through silica gel (60-120 mesh) column chromatography. The product was eluted with ethyl acetate/n-hexane (05:95) mixture.

*General procedure for synthesising chromeno[3,4-b]quinoline-6,11-diones (5)*

To a solution of a mixture of cyclic 1,3-diketone (1 mmol), aromatic aldehydes (1 mmol) and 3-aminocoumarins (1 mmol) in ethanol (3 mL) was added $N$-tetrabutylammonium tribromide (TBATB) (0.048 g, 0.1 mmol) and the resulting reaction mixture was refluxed for 2 h in a pre-heated
Scheme 1. One-pot synthesis of benzo[f]chromeno[3,4-b]quinoline-6-one derivatives

Oil bath. After completion of reaction, the reaction mixture was brought to room temperature and the solid product was precipitated out. The precipitate was filtered off through a Büchner funnel, was washed with 1 mL of ethanol and finally dried in a vacuum pump to get the pure product. The filtrate was concentrated further and kept for recrystallization in DCM-EtOH (1:1) mixture.

The selected spectral data for the benzo[f]chromeno[3,4-b]quinoline-6-one derivatives (4a-l)

14-(4-chlorophenyl)-7,14-dihydro-6H-benzo[f]chromeno[3,4-b]quinolin-6-one (4a)

Yellow solid, yield 78%, mp 254–255 °C, IR (KBr) (νmax / cm⁻¹): 3362, 2924, 1702, 1524 and 741. ¹H NMR (400 MHz, CDCl₃): δ 6.22 (1H, s), 7.14 (1H, d, J = 7.2 Hz), 7.19 (4H, d, J = 8.8 Hz), 7.33-7.38 (4H, m), 7.42 (1H, d, J = 7.2 Hz), 7.52 (1H, t, J = 8 Hz), 7.74 (1H, d, J = 9.2 Hz), 7.77 (1H, d, J = 8.0 Hz), 7.93 (1H, d, J = 8.0 Hz), 8.10 (1H, d, J = 8.4 Hz). ¹³C NMR (100 MHz, CDCl₃): δ 39.0, 112.5, 117.2, 117.3, 119.7, 120.1, 122.0, 122.4, 123.6, 124.1, 125.1, 127.5, 128.1, 129.1 (3C), 129.2, 129.5 (2C), 131.1, 131.6, 133.1, 134.6, 142.8, 150.1, 158.3. Anal. Calcd for C₂₆H₁₆ClNO₂: C, 76.19; H, 3.93; N, 3.42; Found: C, 76.32; H, 3.99; N, 3.53.
14-(p-tolyl)-7,14-dihydro-6H-benzo[f]chromeno[3,4-b]quinolin-6-one (4e)

Yellow solid, yield 86%, mp 276–277 °C, IR (KBr) (ν_max / cm⁻¹): 3337, 1701, 1527 and 736. ¹H NMR (400 MHz, CDCl₃): δ 2.15 (3H, s), 6.18 (1H, s), 6.98 (1H, d, J = 8.8 Hz), 7.17 (2H, d, J = 8.8 Hz), 7.29-7.35 (5H, m), 7.38 (2H, d, J = 8.0 Hz), 7.50 (1H, td, J = 1.6, 8.4 Hz), 7.71 (1H, d, J = 8.8 Hz), 7.75 (1H, d, J = 7.6 Hz), 7.97-8.01 (1H, m), 8.16 (1H, d, J = 8.4 Hz). ¹³C NMR (100 MHz, CDCl₃): δ 21.1, 39.2, 113.1, 117.1, 117.2, 120.0, 120.8, 122.3, 122.6, 123.4, 123.9, 125.0, 127.3, 127.8, 128.1, 129.1, 129.2, 129.6, 131.0, 131.7, 134.5, 137.0, 141.6, 150.1, 158.4. Anal. Calcd for C₂₇H₁₉NO₂: C, 83.27; H, 4.92; N, 3.60; Found: C, 83.44; H, 4.99; N, 3.72.

14-(naphthalen-2-yl)-7,14-dihydro-6H-benzo[f]chromeno[3,4-b]quinolin-6-one (4g)

Yellow solid, yield 86%, mp 310–312 °C, IR (KBr) (ν_max / cm⁻¹): 3341, 1685, 1527 and 743. ¹H NMR (400 MHz, CDCl₃): δ 6.39 (1H, s), 7.21 (2H, m), 7.29-7.41 (6H, m), 7.50 (1H, t, J = 8.0 Hz), 7.63-7.66 (3H, m), 7.72-7.76 (3H, m), 8.13 (1H, s), 8.06-8.08 (1H, m), 8.28 (1H, d, J = 8.4 Hz). ¹³C NMR (100 MHz, CDCl₃): δ 40.0, 112.8, 117.2, 117.2, 120.0, 120.5, 122.3, 122.7, 123.6, 124.0, 125.0, 126.1, 126.5, 126.7 (2C), 127.4, 127.7, 127.9, 128.1, 129.0, 129.2, 129.5, 131.1, 131.8, 132.6, 133.4, 134.7, 141.8, 150.1, 158.5. Anal. Calcd for C₃₉H₂₇NO₂: C, 84.69; H, 4.50; N, 3.29; Found: C, 84.85; H, 4.58; N, 3.40.

2-methoxy-14-(p-tolyl)-7,14-dihydro-6H-benzo[f]chromeno[3,4-b]quinolin-6-one (4j)

Yellow solid, yield 83%, mp 281–283 °C. IR (KBr) (ν_max / cm⁻¹): 3335, 2923 1702, 1529 and 736. ¹H NMR (400 MHz, CDCl₃): δ 2.16 (3H, s), 3.91 (3H, s), 6.11 (1H, s), 6.90 (1H, d, J = 8.4 Hz), 7.01 (2H, d, J = 7.2 Hz), 7.17 (1H, d, J = 8.8 Hz), 7.25 (1H, d, J = 8.8 Hz), 7.40-7.34 (5H, m), 7.50 (1H, t, J = 7.6 Hz), 7.71 (1H, d, J = 8.8 Hz), 7.75 (1H, d, J = 8.0 Hz), 8.16 (1H, d, J = 8.4 Hz). ¹³C NMR (100 MHz, CDCl₃): δ 20.0, 38.0, 54.9, 105.2, 111.7, 113.1, 116.3, 117.1, 118.5, 119.6, 121.4, 122.5, 122.9, 125.1, 127.1 (2C), 127.6 (2C), 128.3(2C), 129.7, 130.5, 134.2, 135.5, 141.3, 143.1, 155.4, 156.9. Anal. Calcd for C₃₈H₂₉NO₂: C, 80.17; H, 5.05; N, 3.34; Found: C, 80.32; H, 5.12; N, 3.42.

2-bromo-14-(p-tolyl)-7,14-dihydro-6H-benzo[f]chromeno[3,4-b]quinolin-6-one (4k)

Yellow solid, yield 82%, mp 268–269 °C. IR (KBr) (ν_max / cm⁻¹): 3331, 1701, 1618 and 1529. ¹H NMR (400 MHz, CDCl₃): δ 2.17 (3H, s), 6.06 (1H, s), 7.01 (2H, d, J = 8.0 Hz), 7.16 (1H, d, J = 8.8 Hz), 7.18 (1H, d, J = 3.2 Hz), 7.31-7.40 (5H, m), 7.50 (1H, t, J = 8.0 Hz), 7.71 (1H, d, J = 8.8 Hz), 7.73 (1H, d, J = 8.4 Hz), 8.05 (1H, d, J = 2.0 Hz), 8.15 (1H, d, J = 8.4 Hz). ¹³C NMR (100 MHz, CDCl₃): δ 21.1, 39.2, 113.2, 117.1, 118.0, 118.7, 121.9, 122.4, 124.0, 124.1, 125.3, 127.5, 128.1(2C), 129.1, 129.4,
129.8(2C), 130.4, 131.2, 131.6, 134.1, 137.2, 141.2, 142.2, 149.0, 157.9. Anal. Calcd for C_{27}H_{18}BrNO_{2}: C, 69.40; H, 3.94; N, 2.91 Found: C, 69.24; H, 3.87; N, 2.99.

**12-(3-fluorophenyl)-9,10-dihydro-9,9-dimethyl-7H-chromeno[3,4-b]quinoline-6,11(8H,12H)-dione (5f)**

Yellow solid, yield 0.67 g (85%), mp 243–245 °C, IR (KBr) (ν_{max} / cm⁻¹): 3414, 1712, 1618 and 1596. ¹H NMR (400 MHz, CDCl₃): δ 0.96 (3H, s), 1.11 (3H, s), 2.23 (1H, d, J = 16.8 Hz), 2.30 (1H, d, J = 16.8 Hz), 2.42 (1H, d, J = 16.8 Hz), 2.50 (1H, d, J = 16.8 Hz), 5.60 (1H, s), 6.80-6.85 (1H, m), 7.07-7.09 (2H, m), 7.16-7.26 (3H, m), 7.33 (1H, d, J = 7.2 Hz), 7.39 (1H, t, J = 8.4 Hz), 7.60 (1H, d, J = 7.6 Hz). ¹³C NMR (100 MHz, CDCl₃): δ 27.2, 29.4, 32.8, 36.4, 41.3, 50.8, 108.4, 114.2, 115.3, 116.9, 119.0, 122.1, 124.0, 125.3, 126.0, 129.4, 130.1, 146.5, 149.4, 150.6, 157.4, 162.0, 164.4, 195.3. Anal. Calcd for C_{24}H_{20}FNO_3: C, 74.02; H, 5.18; N, 3.60 Found: C, 74.09; H, 5.12; N, 3.56.

**12-(4-Cyanophenyl)-9,10-dihydro-9,9-dimethyl-7H-chromeno[3,4-b]quinoline-6,11(8H,12H)-dione (5g)**

Yellow solid, yield 87%, mp 261–263 °C, IR (KBr) (ν_{max} / cm⁻¹): 3414, 1729, 1638 and 1617. ¹H NMR (400 MHz, CDCl₃): δ 0.93 (3H, s), 1.12 (3H, s), 2.22 (1H, d, J = 16.0 Hz), 2.30 (1H, d, J = 16.4 Hz), 2.43 (1H, d, J = 16.8 Hz), 2.50 (1H, d, J = 16.8 Hz), 5.66 (1H, s), 7.15 (1H, s), 7.23 (1H, t, J = 8 Hz), 7.34 (1H, d, J = 8.4 Hz), 7.41 (1H, t, J = 8.4 Hz), 7.50-7.57 (5H, m). ¹³C NMR (100 MHz, CDCl₃): δ 27.2, 29.3, 32.8, 37.0, 41.3, 50.7, 107.8, 110.9, 117.0, 118.7, 118.8, 122.3, 123.7, 125.1, 125.4, 129.1, 129.7, 132.6, 148.9, 149.7, 150.6, 157.3, 195.2. Anal. Calcd for C_{25}H_{20}N_{2}O_3: C, 75.74; H, 5.08; N, 7.07 Found: C, 75.69; H, 5.13; N, 7.01.

**2-Methoxy-12-phenyl-9,10-dihydro-9,9-dimethyl-6H-chromeno[3,4-b]quinoline-6,11(8H,12H)-dione (5i)**

Yellow solid, yield 84%, mp 247–249 °C, IR (KBr) (ν_{max} / cm⁻¹): 3414, 1698, 1632 and 1599. ¹H NMR (400 MHz, CDCl₃): δ 0.95 (3H, s), 1.11 (3H, s), 2.22 (1H, d, J = 16.4 Hz), 2.29 (1H, d, J = 16.4 Hz), 2.41 (1H, d, J = 16.4 Hz), 2.48 (1H, d, J = 16.8 Hz), 3.76 (3H, s), 5.53 (1H, s), 6.92 (1H, d, d, J = 2.8 Hz, 8.8 Hz), 7.06-7.13 (2H, m), 7.15 (1H, s), 7.22-7.27 (3H, m), 7.40-7.42 (2H, m). ¹³C NMR (100 MHz, CDCl₃): δ 27.2, 29.4, 32.9, 37.0, 41.4, 50.9, 55.8, 106.6, 108.9, 117.0, 117.8, 119.7, 122.1, 126.6, 127.2, 128.3, 128.8, 144.3, 145.0, 149.0, 156.7, 157.7, 195.3. Anal. Calcd for C_{25}H_{23}NO_4: C, 74.79; H, 5.77; N, 3.49 Found: C, 74.73; H, 5.83; N, 3.42.

**2-Methoxy-12-(thiophen-2-yl)-9,10-dihydro-9,9-dimethyl-6H-chromeno[3,4-b]quinoline-6,11(8H,12H)-dione (5k)**
Yellow solid, yield 87%, mp 232–235 °C, IR (KBr) (ν_{max} / cm^{-1}): 3413, 1698, 1637, 1573. ¹H NMR (400 MHz, CDCl₃): δ 1.04 (3H, s), 1.13 (3H, s), 2.31-2.32 (2H, m), 2.47 (1H, d, J = 16.8 Hz), 2.49 (1H, d, J = 16.4 Hz), 3.81 (3H, s), 6.82 (1H, d.d, J = 3.2 Hz, 4.8 Hz), 6.89-6.90 (1H, m), 6.96 (1H, d, J = 2.4 Hz, 8.8 Hz), 7.01 (1H, d, d, J = 1.2 Hz, 5.2 Hz), 7.14 (1H, d, J = 2.8 Hz), 7.25 (2H, m). ¹³C NMR (100 MHz, CDCl₃): δ 27.3, 29.5, 31.3, 32.8, 41.1, 50.7, 55.9, 106.2, 108.1, 117.1, 117.8, 119.5, 121.8, 124.6, 125.1, 125.4, 126.7, 145.0, 147.0, 156.7, 157.5, 195.3. Anal. Calcd for C_{23}H_{21}NO_{4}S: C, 67.79; H, 5.19; N, 3.44. Found: C, 67.75; H, 5.25; N, 3.39.

2-Methoxy-12-(naphthalene-2-yl)-9,10-dihydro-9,9-dimethyl-6H-chromeno[3,4-b]quinoline-6,11(8H,12H)-dione (5I)

Yellow solid, yield 88%, mp 253–255 °C, IR (KBr) (ν_{max} / cm^{-1}): 3413, 1699, 1636, 1600. ¹H NMR (400 MHz, CDCl₃): δ 0.92 (3H, s), 1.10 (3H, s), 2.19 (1H, d, J = 16.4 Hz), 2.30 (1H, d, J = 16.4 Hz), 2.42 (1H, d, J = 16.8 Hz), 2.49 (1H, d, J = 16.4 Hz), 3.73 (3H, s), 5.70 (1H, s), 6.88 (1H, d, d, J = 2.8 Hz, 8.8 Hz), 7.11-7.12 (2H, m), 7.21 (1H, d, J = 9.2 Hz), 7.37-7.43 (2H, m), 7.59 (1H, d, d, J = 1.6 Hz, 8.4 Hz), 7.74 (3H, m), 7.81 (1H, s). ¹³C NMR (100 MHz, CDCl₃): δ 27.1, 29.4, 32.7, 37.2, 41.2, 50.8, 55.7, 106.6, 108.6, 116.8, 117.7, 119.7, 122.5, 125.9, 126.2, 126.3, 126.7, 127.0, 127.6, 128.0, 128.5, 132.5, 133.5, 141.8, 144.9, 149.3, 156.5, 157.6, 195.4. Anal. Calcd for C_{29}H_{25}NO_{4}: C, 77.14; H, 5.58; N, 3.10. Found: C, 77.08; H, 5.62; N, 3.14.

Results and discussion

For synthesising benzo[f]chromeno[3,4-b]quinoline-6-ones 4, a mixture of 4-chlorobenzaldehyde (1 mmol), 2-naphthol (1 mmol), and 3-aminocoumarin (1 mmol) in 3 mL of ethanol was stirred under reflux condition in presence of 5, 10 and 20 mol% of TBATB, respectively. The reaction was very sluggish and even incomplete after 24 hours. However, we observed a yellow fluorescent spot on TLC along with unreacted starting materials.

The new spot was characterized by IR, ¹H NMR, ¹³C NMR spectra and elemental analysis and was found to be benzo[f]chromeno[3,4-b]quinoline-6-one derivative 4a. In IR spectrum, it showed characteristic absorptions peaks at 3362 (NH) and 1702 (C=O). Similarly, the compound showed a diagnostic signal at δ 6.22 in the ¹H NMR spectrum assignable to the proton at the point of attachment of dihydropyridine ring to the aryl moiety.

Then we tried the same set of reaction in different solvents like n-butanol, dichloroethane, methanol and acetonitrile (Table 1, entries 2–7). It was observed that when the reaction was performed in n-butanol in presence of 10 mol% TBATB, the yield of the product 4a increased significantly (Table 1, entry 3). With 10 mol% of other catalysts such as anhydrous Fe₂(SO₄)₃·xH₂O,
ZnCl\(_2\), Iodine, Triflic acid and InCl\(_3\) one could not improve the reaction either in terms of time or yield (Table 1, entries 8–12). Also, in absence of catalyst, no product formation was observed (Table 1, entry 13). So, we came to this conclusion that 10 mol% of TBATB in 3 mL of \(n\)-butanol is the best reaction condition in terms of both yield and reaction time.

After optimization of the reaction conditions, reaction of various other substituted aromatic aldehydes were examined with 2-napthol and 3-aminocoumarin under identical reaction conditions which resulted in products 4b–g (Table 2, entries 2–7) in good yields. However, 4-nitrobenzaldehyde did not provide the desired product even after prolonging the reaction for 24 hours. The substrate scope of some substituted 3-aminocoumarins, for example 6-bromo-3-aminocoumarin and 6-methoxy-3-aminocoumarin, were also examined with substituted aromatic aldehyde and 2-naphthol under identical reaction condition and it was found that they also afforded the desired benzo[f]chromeno[3,4-b]quinoline-6-one derivatives 4h–l (Table 2, entries 8–12) in good yields.

**Table 1.** Optimization of reaction conditions for synthesising benzo[f]chromeno[3,4-b]quinoline-6-one (4a)

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<th>Entry</th>
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<th>Solvent</th>
<th>Mol% of Catalyst</th>
<th>Time (h)</th>
<th>Yield%(^{b})</th>
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<td>21</td>
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<td>(n)-BuOH</td>
<td>10</td>
<td>8</td>
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<td>10</td>
<td>Iodine</td>
<td>(n)-BuOH</td>
<td>10</td>
<td>8</td>
<td>33</td>
</tr>
<tr>
<td>11</td>
<td>Triflic acid</td>
<td>(n)-BuOH</td>
<td>10</td>
<td>8</td>
<td>37</td>
</tr>
<tr>
<td>12</td>
<td>InCl(_3)</td>
<td>(n)-BuOH</td>
<td>10</td>
<td>8</td>
<td>00</td>
</tr>
<tr>
<td>13</td>
<td>No Catalyst</td>
<td>(n)-BuOH</td>
<td>10</td>
<td>12.0</td>
<td>00</td>
</tr>
</tbody>
</table>

\(^{a}\)All the reactions were performed with 4-chlorobenzaldehyde (1 mmol), 2-naphthol (1 mmol) and 3-aminocoumarin (1 mmol)

\(^{b}\)Isolated yields
Table 2. Scope of various benzo[f]chromeno[3,4-b]quinoline-6-one derivatives\textsuperscript{a}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>X</th>
<th>Product</th>
<th>Time</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4-Cl-C\textsubscript{6}H\textsubscript{5}</td>
<td>H</td>
<td>4a</td>
<td>8</td>
<td>78</td>
</tr>
<tr>
<td>2</td>
<td>C\textsubscript{6}H\textsubscript{5}</td>
<td>H</td>
<td>4b</td>
<td>8</td>
<td>72</td>
</tr>
<tr>
<td>3</td>
<td>4-Br-C\textsubscript{6}H\textsubscript{5}</td>
<td>H</td>
<td>4c</td>
<td>8</td>
<td>73</td>
</tr>
<tr>
<td>4</td>
<td>4-F-C\textsubscript{6}H\textsubscript{5}</td>
<td>H</td>
<td>4d</td>
<td>6</td>
<td>78</td>
</tr>
<tr>
<td>5</td>
<td>4-Me-C\textsubscript{6}H\textsubscript{5}</td>
<td>H</td>
<td>4e</td>
<td>6</td>
<td>86</td>
</tr>
<tr>
<td>6</td>
<td>4-MeO-C\textsubscript{6}H\textsubscript{5}</td>
<td>H</td>
<td>4f</td>
<td>6</td>
<td>71</td>
</tr>
<tr>
<td>7</td>
<td>2-C\textsubscript{10}H\textsubscript{7}</td>
<td>H</td>
<td>4g</td>
<td>8</td>
<td>86</td>
</tr>
<tr>
<td>8</td>
<td>4-Cl-C\textsubscript{6}H\textsubscript{5}</td>
<td>MeO</td>
<td>4h</td>
<td>8</td>
<td>79</td>
</tr>
<tr>
<td>9</td>
<td>4-F-C\textsubscript{6}H\textsubscript{5}</td>
<td>MeO</td>
<td>4i</td>
<td>8</td>
<td>76</td>
</tr>
<tr>
<td>10</td>
<td>4-Me-C\textsubscript{6}H\textsubscript{5}</td>
<td>MeO</td>
<td>4j</td>
<td>8</td>
<td>83</td>
</tr>
<tr>
<td>11</td>
<td>4-Me-C\textsubscript{6}H\textsubscript{5}</td>
<td>Br</td>
<td>4k</td>
<td>6</td>
<td>82</td>
</tr>
<tr>
<td>12</td>
<td>4-F-C\textsubscript{6}H\textsubscript{5}</td>
<td>Br</td>
<td>4l</td>
<td>6</td>
<td>81</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Reaction Condition: aromatic aldehyde, 2-naphthol and 3-aminocoumarin were reacted in 1:1:1 ratio in presence of 10 mol\% of TBATB in \textit{n}-butanol under reflux

\textsuperscript{b}Isolated Yields

Next, we turned our attention to investigate the scope and applicability of catalyst TBATB for the reaction of dimedone, aromatic aldehydes and 3-aminocoumarin for the synthesis of Chromeno[3,4-b]quinoline-6,11-diones.

Under similar reaction conditions, we carried out the reaction of dimedone (1 mmol), benzaldehyde (1 mmol) and 3-aminocoumarin (1 mmol) for 12 h in presence of 10 mol\% of TBATB in 3 mL of \textit{n}-butanol under reflux condition. Finally, the desired product chromeno[3,4-b]quinoline-6,11-diones 5a was obtained in 46\% yield. Thus, we tried to improve the yield of product and decrease the reaction time by carrying out further optimisation.

To find out the optimized reaction condition for synthesising chromeno[3,4-b]quinoline-6,11-diones, one-pot three-component reaction was carried out using dimedone (1 mmol), benzaldehyde (1 mmol) and 3-aminocoumarin (1 mmol) in ethanol under reflux condition in presence of 5 mol\% of TBATB and the desired product 5a was isolated in 54\% yield. The same reaction was then executed successively using 10 mol\% and 20 mol\% of TBATB (Table 3, entries 2 and 3), which gave rise to the desired product 5a in 85\% and 86\% yield, respectively. Since the yield of product did not enhance considerably by increasing the quantity of catalyst from 10\% to 20\%, we inferred that 10 mol\% of the catalyst is the sufficient amount to obtain best result.
For determining the appropriate solvent system, parallel reactions were also performed in methanol and acetonitrile (Table 3, entry 4 and 5) and it was found that the maximum yield was obtained in ethanol. As a result, ethanol was chosen as the solvent. To inspect the effectiveness of the catalyst, similar reactions were carried out in presence of some other catalysts such as FeCl$_3$/6H$_2$O, HCl, aq 48% HBr and HClO$_4$-SiO$_2$ (Table 3, entries 7–10). It was observed that the reaction does not proceed on using HCl as catalyst while, on using 20 mol% of aq 48% HBr, only a trace amount of product was obtained. From these observations, we concluded that the utmost yields under shortest reaction times were obtained on using 10 mol% of TBATB as catalyst. The results are summarized in Table 3. Compared to the previous method [25] the current protocol improves the yield of the Chromeno[3,4-b]quinoline-6,11-diones product and decrease the reaction time for product formation appreciably.

Table 3. Optimization of reaction conditions for synthesising Chromeno[3,4-b]quinoline-6,11-dione derivative 5a

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Catalyst (mol%)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TBATB</td>
<td>EtOH</td>
<td>5</td>
<td>4</td>
<td>54</td>
</tr>
<tr>
<td>2</td>
<td>TBATB</td>
<td>EtOH</td>
<td>10</td>
<td>2</td>
<td>85</td>
</tr>
<tr>
<td>3</td>
<td>TBATB</td>
<td>EtOH</td>
<td>20</td>
<td>2</td>
<td>86</td>
</tr>
<tr>
<td>4</td>
<td>TBATB</td>
<td>MeOH</td>
<td>10</td>
<td>4</td>
<td>66</td>
</tr>
<tr>
<td>5</td>
<td>TBATB</td>
<td>MeCN</td>
<td>10</td>
<td>4</td>
<td>62</td>
</tr>
<tr>
<td>6</td>
<td>p-TSA$^c$</td>
<td>EtCN</td>
<td>20</td>
<td>7</td>
<td>77</td>
</tr>
<tr>
<td>7</td>
<td>FeCl$_3$</td>
<td>EtOH</td>
<td>10</td>
<td>4</td>
<td>48</td>
</tr>
<tr>
<td>8</td>
<td>HCl</td>
<td>EtOH</td>
<td>20</td>
<td>4</td>
<td>Trace</td>
</tr>
<tr>
<td>9</td>
<td>HBr</td>
<td>EtOH</td>
<td>20</td>
<td>4</td>
<td>33</td>
</tr>
<tr>
<td>10</td>
<td>HClO$_4$-SiO$_2$</td>
<td>EtOH</td>
<td>10</td>
<td>4</td>
<td>44</td>
</tr>
</tbody>
</table>

$^a$All the reactions were carried out with benzaldehyde, dimedone and 3-aminocoumarin in 1:1:1 ratio in presence of catalyst in 3 mL of indicated solvent

$^b$Isolated yields

$^c$Reference [60]

Table 4. Substrate scope of chromeno[3,4-b]quinoline-6,11-dione derivatives

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>X</th>
<th>Product</th>
<th>Yield$^b$ (%)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C$_6$H$_5$</td>
<td>H</td>
<td>5a</td>
<td>85</td>
<td>77</td>
</tr>
<tr>
<td>2</td>
<td>4-Me-C$_6$H$_4$</td>
<td>H</td>
<td>5b</td>
<td>91</td>
<td>82</td>
</tr>
<tr>
<td>3</td>
<td>4-F-C$_6$H$_4$</td>
<td>H</td>
<td>5c</td>
<td>87</td>
<td>73</td>
</tr>
<tr>
<td>No</td>
<td>Substituent</td>
<td>Reaction conditions</td>
<td>Yield</td>
<td>Combined yield</td>
<td></td>
</tr>
<tr>
<td>----</td>
<td>-------------------</td>
<td>---------------------</td>
<td>-------</td>
<td>----------------</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>4-Cl-C(_6)H(_4)</td>
<td></td>
<td>5d</td>
<td>88</td>
<td>78</td>
</tr>
<tr>
<td>5</td>
<td>4-Br-C(_6)H(_4)</td>
<td></td>
<td>5e</td>
<td>90</td>
<td>82</td>
</tr>
<tr>
<td>6</td>
<td>3-F-C(_6)H(_4)</td>
<td></td>
<td>5f</td>
<td>85</td>
<td>--</td>
</tr>
<tr>
<td>7</td>
<td>4-CN-C(_6)H(_4)</td>
<td></td>
<td>5g</td>
<td>87</td>
<td>--</td>
</tr>
<tr>
<td>8</td>
<td>2-Thiophene</td>
<td></td>
<td>5h</td>
<td>85</td>
<td>--</td>
</tr>
<tr>
<td>9</td>
<td>C(_6)H(_5)</td>
<td>OMe</td>
<td>5i</td>
<td>84</td>
<td>--</td>
</tr>
<tr>
<td>10</td>
<td>4-Cl-C(_6)H(_4)</td>
<td>OMe</td>
<td>5j</td>
<td>89</td>
<td>--</td>
</tr>
<tr>
<td>11</td>
<td>2-Thiophene</td>
<td>OMe</td>
<td>5k</td>
<td>87</td>
<td>--</td>
</tr>
<tr>
<td>12</td>
<td>2-Napthyl</td>
<td>OMe</td>
<td>5l</td>
<td>88</td>
<td>--</td>
</tr>
<tr>
<td>13</td>
<td>4-Cl-C(_6)H(_4)</td>
<td>NO(_2)</td>
<td>5m</td>
<td>89</td>
<td>--</td>
</tr>
<tr>
<td>14</td>
<td>4-F-C(_6)H(_4)</td>
<td>NO(_2)</td>
<td>5n</td>
<td>86</td>
<td>--</td>
</tr>
<tr>
<td>15</td>
<td>4-Br-C(_6)H(_4)</td>
<td>Br</td>
<td>5o</td>
<td>85</td>
<td>76</td>
</tr>
<tr>
<td>16</td>
<td>4-Me-C(_6)H(_4)</td>
<td>Br</td>
<td>5p</td>
<td>91</td>
<td>81</td>
</tr>
</tbody>
</table>

*a* Reaction conditions: aromatic aldehydes, dimedone and 3-aminocoumarin were reacted in 1:1:1 ratio in presence of TBATB (0.048 g, 0.1 mmol) in 3 mL ethanol

*b* Combined yield after recrystallization

To explore the synthetic scope and the generality of the present protocol, reactions under optimized conditions were performed using dimedone, a broad variety of substituted aromatic aldehydes and 3-aminocoumarins. The percentage yield of the products (5b–p) along with their reaction time are shown in Table 4. It is worth mentioning that pure products can be obtained from these reactions just by filtering the solid products followed by recrystallizing the crude products thus obtained from a mixture of dichloromethane and ethanol and consequently avoiding aqueous work-up and dreary column-chromatographic separation process.

The formation of the products 4 and 5 may be explained as follows: It was previously reported that benzyltrimethyl ammonium bromide on reaction with ethanol can produce dry HBr in the reaction medium [61]. We believe that TBATB reacts with n-butanol/ethanol to generate dry HBr in the reaction medium which actually catalyzes the product formation. First, the aromatic aldehyde reacts with 2-naphthol/dimedone in presence of dry HBr to provide Knoevenagel product A which is either o-quinonemethide or benzylidenecyclohexane-1,3-dione intermediate. The intermediate A which acts a suitable Michael acceptor and reacts with 3-aminocoumarin to give intermediate B by Michael reaction undergoes intra-molecular ring closure reaction followed by elimination of one molecule of H\(_2\)O to give product 4 or 5 as shown in Scheme 3.
The structures of the representative compounds 4d (CCDC 897315) and 5o (CCDC 910378) were confirmed unambiguously by single crystal X-ray diffraction analysis as shown in Figure 1.

Figure 1. X-ray crystal structures of 4d (CCDC 897315) and 5o (CCDC 910378)
Scheme 3. Possible mechanistic pathway for the formation of products

Conclusion

To conclude, we have demonstrated the synthesis of a new type of heterocyclic compound benzo[f]chromeno[3,4-b]quinoline-6-ones via one-pot three-component tandem Knoevenagel–Michael reaction catalyzed by $N$-tetrabutylammonium tribromide. It is also notable that in the course of reaction three new sigma bonds (two $C\text{–}C$ and one $C\text{–}N$) and one stereocenter are formed. Environmentally benevolent reaction conditions, simplicity of procedure, high atom economy, easy accessibility of the catalyst, cost effectiveness and superior yields are some of the most important features of the present protocol. We have also provided an efficient route for synthesising a series of chromeno[3,4-b]quinoline-6,11-diones with better yields under shorter reaction time using $N$-tetrabutylammonium tribromide as catalyst.

Acknowledgments

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Disclosure statement

No potential conflict of interest was reported by the authors.

Supporting Information

Additional supporting information related to this article can be found, in the online version, at http://www.ajgreenchem.com/article_55290.html.

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