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A TBPB Mediated C-3 Cycloalkylation and Formamidation of 4-Arylcoumarin

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Abstract. A *tert*-butyl peroxybenzoate (TBPB) mediated cycloalkylation and formamidation took place effectively in chlorobenzene or in respective formamides at 120 ^{o}C, while the former process requires the presence of acetic acid, the later goes in its absence. This radical mediated process gives moderate to good yields of the product having broad substrate scope.

Keywords: Coumarins; C–H functionalization; cycloalkylation; formamidation; metal-free; cross dehyrogenative coupling

Introduction

The direct C−H bond functionalization for the construction of carbon-carbon (C−C) bonds has emerged as one of the most powerful method which replaces the conventional cross coupling procedures thereby avoiding any prefunctionalized starting materials.[1] Such synthetic methodologies have intrinsic advantage such as higher atom economy, step economy, and environmental sustainability. In this context, cross-dehydrogenative-coupling (CDC) protocol have served as a powerful and versatile method for functionalization of different C−H bonds (sp, sp^2, sp^3).[2] In addition, CDC protocols have been successfully employed for the oxidative cross couplings between C_{sp2}−H bond of internal alkene and C_{sp3}−H bond of other coupling partners using transition metal

catalysts.[3] In view of cost economy, toxicity and heavy metal residues, transition metal catalyzed coupling reactions are not appreciated in pharmaceutical industries. Therefore, alternative route under transition metal free condition is highly sought after.

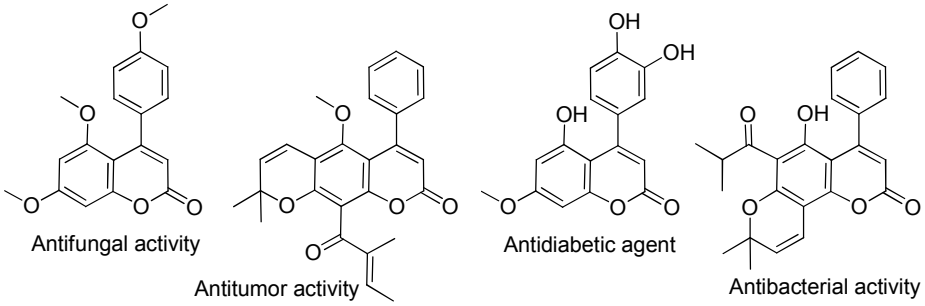
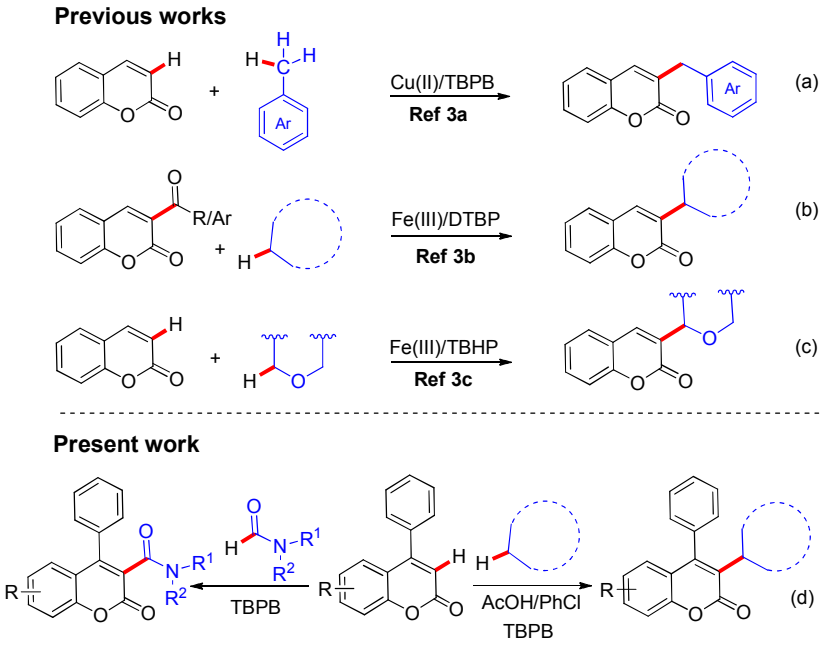


Figure 1. Representative example of bioactive 4-arylcoumarins.

4-Arylcoumarins, an important class of oxygen containing heterocycle, are prevalent in natural products.[4] They display important biological activities such as antifungal,[5] antiviral,[6] antitumor,[7] antimalarial,[8] anti-inflammatory,[9] anti-HIV,[10] antidiabetic,[11] and antibacterial properties[12] (Figure 1). Because of their impressive biological activities, further functionalization of 4-arylcoumarins may be significant in many future pharmaceutical applications.

Many coumarin functionalizations have been achieved via regioselective C-3 and C-4 arylation,[13] C-3 olefination[14] and C-3 phosphorylation[15] using transition metal catalysts. In recent years, significant efforts have been made toward the development of carbon-carbon (C-C) bond formation through C_{sp3}–H bonds functionalization of alkane.[16] The radical pathway is the effective tool for such direct C_{sp3}–H bond functionalization. In this context, Duan's group reported a Cu(II) catalyzed benzylation of coumarins (C-3 position) *via* benzylic C_{sp3}–H bond functionalization (Scheme 1a).[3a] Recently, our group also successfully demonstrated a Fe(III) catalyzed selective C-3 cycloalkylation of 3-acyl coumarin (Scheme 1b).[3b] Zhou group used coumarin as the coupling partner for C-3 functionalization with cyclic ether using a Fe(III) catalyst (Scheme 1c).[3c] However, the strategy for metal free mediated direct C-3 functionalization of 4-arylcoumarin has not yet been investigated (Scheme 1d). Herein, we report C-3 cycloalkylation and C-3 formamidation of 4-arylcoumarins under a metal free condition. The present metal-free

protocol is advantageous over the previous metal mediated methods due to their low toxicity, cost economy and high yields of the product.



Scheme 1. C-3 functionalization of coumarins.

Results and Discussion

Recently, di-*tert*-butyl peroxide (DTBP) has been used for the cycloalkylation reaction for various C–H bond functionalizations.[17] Han group demonstrated the utility of di-*tert*-butyl peroxide (DTBP) during the radical alkylation of α,α-diaryl allylic alcohols with cycloalkane.[17a] Lei group also reported a direct alkylation of ketene dithioacetals using di-*tert*-butyl peroxide (DTBP).[17c] Keeping these results in mind, we initiated the coupling reaction of 4-arylcoumarin (**1**) (0.5 mmol) with cyclohexane (**a**) (9.2 mmol) in the presence di-*tert*-butyl peroxide (DTBP) (2.0 equiv) at 120 °C for 24 h, but no coupling product was detected; only starting material (**1**) remain unconsumed. When the same reaction was carried out in the presence acetic acid (1 equiv.) in chlorobenzene (1 mL), a new product was formed after 12 h of heating. After work up and column chromatography, a white solid product was isolated in 35% yield (Table 1, entry 2). From spectroscopic analysis (^{1}H NMR and ^{13}C NMR), the structure of the product was determined to be 3-cyclohexyl-7-methoxy-4-phenyl-2*H*-chromen-2-one (**1a**). The

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structure of the compound (**1a**) was reconfirmed by X-ray crystallographic analysis as shown in Figure 2.

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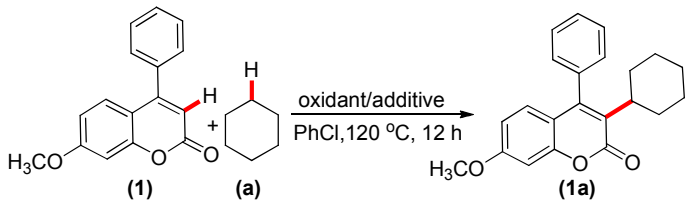
Table 1. Optimization of reaction conditions[a]



Entry	Oxidant (equiv)	Additive (equiv)	Yield (%)[b]
1	DTBP (2)	-	00
2	DTBP (2)	AcOH (1)	35
3	H_2O_2 (2)	AcOH (1)	00
4[c]	TBHP (2)	AcOH (1)	00
5	TBPB (2)	AcOH (1)	53
6	BPO (2)	AcOH (1)	30
7[d]	TBPB (2)	AcOH (1)	20
8[e]	TBPB (2)	AcOH (1)	35
9	$K_2S_2O_8$ (2)	AcOH (1)	40
10	Oxone (2)	AcOH (1)	25
11	TBPB (3)	AcOH (1)	62
12	TBPB (3)	PTSA (2)	15
13	TBPB (3)	PivOH (2)	55
14	TBPB (3)	PhCOOH (2)	25
15	TBPB (3)	HCOOH (2)	20
16	**TBPB (3)**	**AcOH (2)**	**70**
17[f]	TBPB (3)	AcOH (2)	40
18[g]	**-**	AcOH (2)	00

[a]Reaction conditions: (**1**) (0.5 mmol), (**a**) (18.4 equiv., 9.2 mmol) in chlorobenzene (1.0 mL) at 120 °C for 12 h. [b]Isolated yield.

[c]TBHP in decane.

[d] reaction in EtOH

[e] reaction in 1,2-dichloroethane.

[f]Reaction at 100 °C.

[g]Reaction in AcOH.

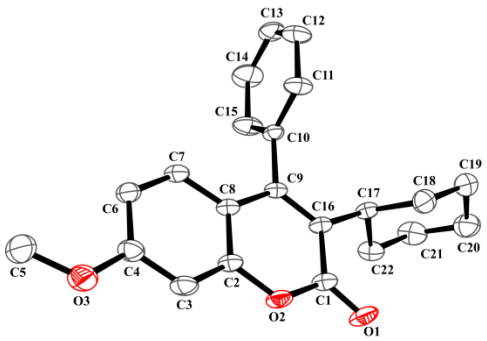
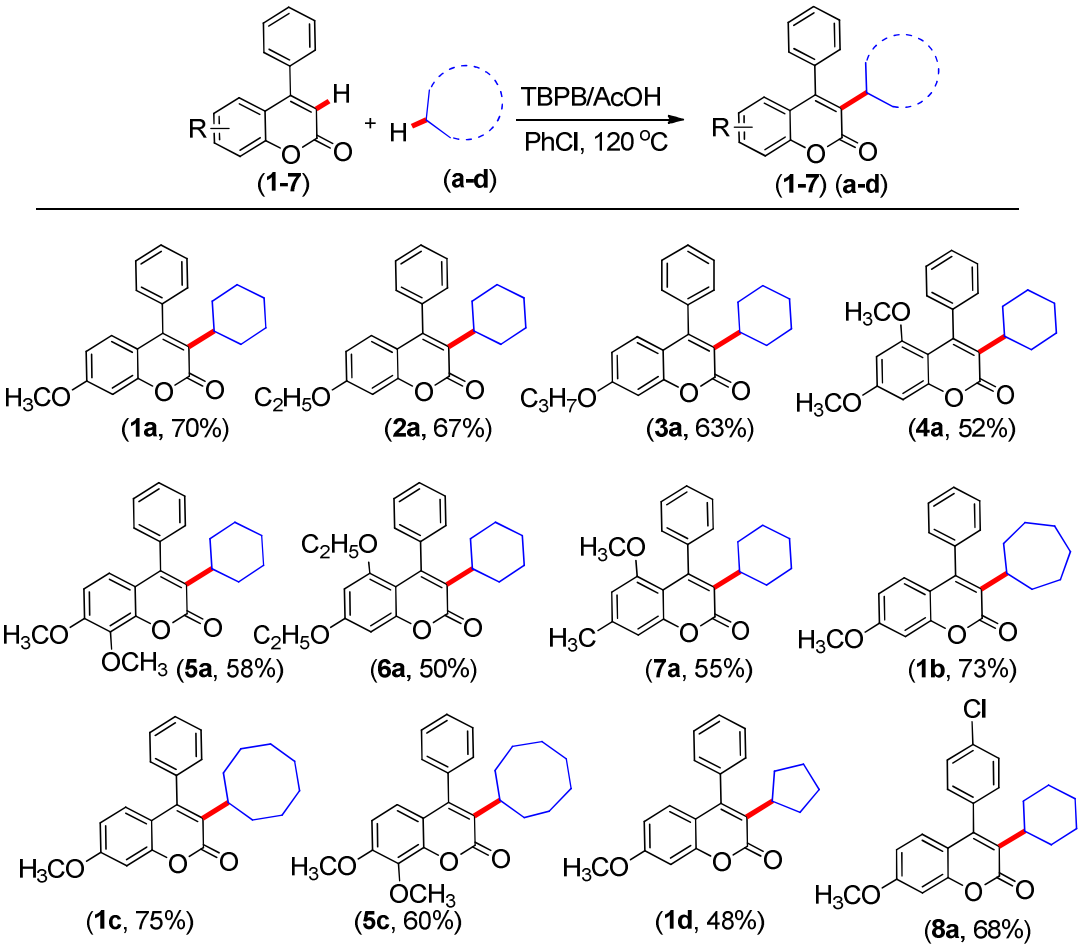


Figure 2. ORTEP diagram of (**1a)** drawn in 25% thermal probability ellipsoids. [18]

Subsequently, the effect of other oxidants such as hydrogen peroxide, *tert*-butyl hydroperoxide (TBHP), *tert*-butyl peroxybenzoate (TBPB), and benzoyl peroxide (BPO) were examined under otherwise identical reaction condition (Table 1, entries 3-6). It was found that the use of TBPB in lieu of DTBP significantly improved the yield of (**1a**) from 35% to 53% (Table 1, entry 5). While the use of hydroxyl peroxides such as hydrogen peroxide and *tert*-butyl hydroperoxide (TBHP) were not effective at all, whereas benzoyl peroxide (BPO) gave 30% yield of the product (Table 1, entry 6). The use of protic solvent such as ethanol and aprotic solvent such as 1,2-dichloroethane was not effective as compared to chlorobenzene (Table 1, entry 7-8). We examined the effect of other non-peroxide oxidants such as $K_2S_2O_8$ and oxone. However, they were found to be far inferior to TBPB (Table 1, entry 9-10). When the oxidant TBPB quantity was increased from 2 to 3 equiv., the yield of the product (**1a**) improved up to 62% (Table 1, entry 11). No further improvement in the yield of the product was observed even when the reaction was performed under O_2 atmosphere. The use of 4 equiv. of TBPB gave no further significant improvement in the yield. Screening of other additives such as *p*-toluenesulfonic acid (PTSA), pivalic acid (PivOH), benzoic acid, and HCOOH were found to be inferior to acetic acid (Table 1, entries 12-15). Further, increasing the amount of acetic acid from 1 to 2 equiv. improved the yield up to 70% (Table 1, entry 16). Performing the reaction at 100 ^{o}C, the yield of the product (**1a**) dropped to 40% (Table 1, entry 17). The reaction failed to proceed in the absence of TBPB thereby suggesting the essential requirement of peroxide oxidant. Finally, the use of 4-arylcoumarin (**1**) (0.5 mmol), cyclohexane (1 mL, 9.2 mmol), TBPB (3.0 equiv.) as the oxidant, and acetic acid (2.0 equiv.) as an additive in

chlorobenzene (1 mL) at 120 °C for 12 h was found to be the best possible optimized reaction condition.

Scheme 2. C-3 Cycloalkylation of 4-arylcoumarin using cycloalkanes.[a]



Reaction conditions:[a](**1-7**) (0.50 mmol), cycloalkane (**a-d**) (18.4 equiv., 9.2 mmol), TBPB (1.50 mmol) and AcOH (2.0 equiv) in chlorobenzene (1.0 ml) at 120 °C for 12 h. Isolated yields based on 4-phenylcoumarin.

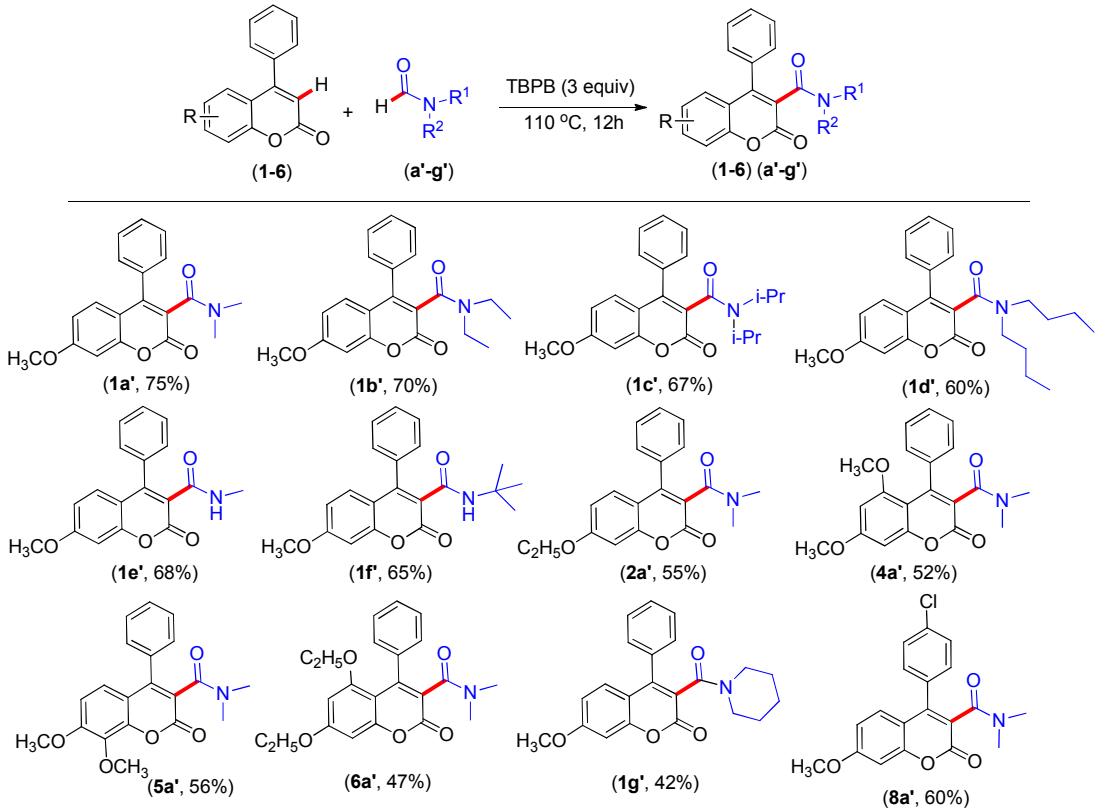
Under the optimized reaction condition, we investigated the substrate scope of various 4-arylcoumarins with different cycloalkanes as shown in Scheme 2. 4-Arylcoumarins bearing electron-donating substituents such as 7-OCH_3 (**1**), 7-OC_2H_5 (**2**) and 7-OC_3H_7 (**3**) coupled with cyclohexane (**a**) affording their desired products (**1a**), (**2a**) and (**3a**) in 70%, 67% and 63% yields, respectively. The reaction is compatible with 4-arylcoumarins having disubstituted electron-donating groups such as 5,7-di-OMe (**4**), 7,8-di-OMe (**5**), 5,7-di-OEt (**6**), and 5-OMe-7-Me (7), all afforded their corresponding C-3 cycloalkylated

products (**4a**, 52%), (**5a**, 58%) (**6a**, 50%) and (**7a**, 55%) in moderate yields. The scope of the reaction was further extended by reacting 4-arylcoumarin with other cycloalkanes such as cycloheptane (**b**), cyclooctane (**c**) and cyclopentane (**d**). As expected, all coupled efficiently, furnishing their corresponding products (**1b**, 73%), (**1c**, 75%), (**5c**, 60%), and (**1d**, 48%). This reaction is equally successful with 4-chlorophenyl substituted coumarin giving the desired product (**8a**) in 68% yield. However, substituted alkane, methylcyclohexane gave a mixture of inseparable products whereas linear alkane such as heptane, failed to give any product. This observation is consistent with our previous cycloalkylation and cycloalkylation-peroxidation of coumarins.[3b,3g]

Recent report shows that formamides can be used as amide sources via C–H bond functionalization.[19] In this context, Li group reported an oxidative coupling of terminal alkenes with formamides using $FeCl_3$ and di-*tert*-butyl peroxide (DTBP).[19a] Wang group carried out *tert*-butyl peroxybenzoate (TBPB) mediated direct C-2 amidation of azoles with formamides under metal-free condition.[19d] In this connection, in lieu of cycloalkylation we target to generate C-3 amidation of 4-aryl coumarin using formamides. After investigation of various reaction parameters, optimized reaction condition was achieved using 4-arylcoumarin (**1**) (0.5 mmol), formamides (**a'**) (1 mL, 13.0 mmol), and *tert*-butyl peroxybenzoate (TBPB) (1.5 mmol) at 120 ^{o}C for 12 h (see Supporting Information, Table S1). To further explore the scope of formamidation successful coupling of various 4-arylcoumarins with different formamides are shown in Scheme 3. 4-Arylcoumarin bearing 7-OMe (**1**) reacted smoothly with wide range of formamides such as *N,N*-dimethylformamide (**a'**), *N,N*-diethylformamide (**b'**), *N,N*-diisopropylformamide (**c'**), *N,N*-dibutylformamide (**d'**), *N*-methylformamide (**e'**), and *N*-*tert*-butylformamide (**f'**), all afforded their corresponding C-3 amidated products (**1a'**, 75%), (**1b'**, 70%), (**1c'**, 67%), (**1d',** 60%), (**1e',** 68%), and (**1f',** 65%) in good yields. Similarly, 7-OEt substituted 4-arylcoumarin (**2**) also provided amidated product (**2a'**) in 55% yield. The reaction proceed smoothly in case of di-substituted 4-arylcoumarins such as 5,7-di-OMe (**4**), 7,8-di-OMe (**5**), and 5,7-di-OEt (**6**) furnishing their corresponding products (**4a'**, 52%), (**5a'**, 56%), and (**6a'**, 47%) yields. Notably, cyclic formamide, *N*-formylpiperidine (**g'**) also

gave the desired C-3 amidated product (**1g'**) in 42% yield. 4-Chlorophenyl substituted coumarin also underwent formamidation affording the desired product (**8a'**) in 60% yield.

Scheme 3. C-3 Amidation of 4-arylcoumarin using formamides.[a](

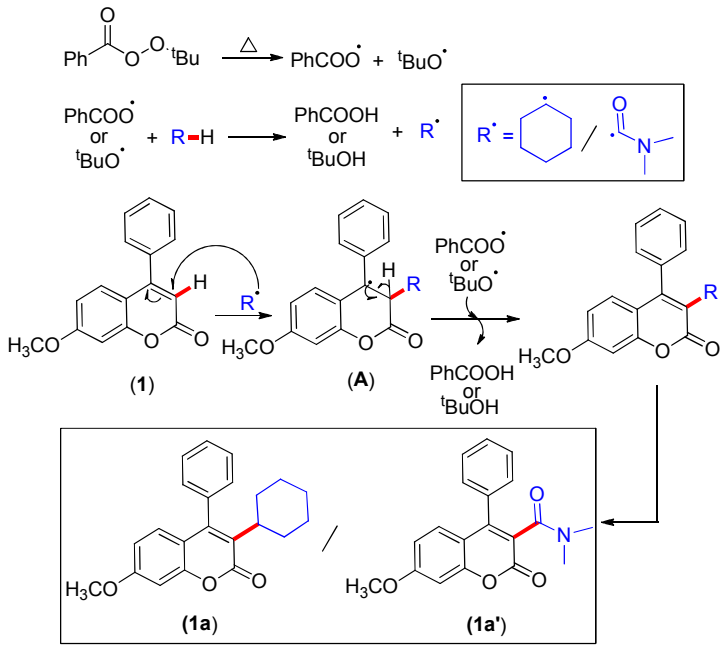


Reaction conditions: [a](**1-6**) (0.50 mmol), (**a'-g'**) (26.0 equiv., 13.0 mmol), and TBPB (1.50 mmol) at 120 °C for 12 h. Isolated yields based on 4-phenylcoumarin.

In order to understand the mechanistic pathway of this reaction, a control experiment was carried out. When the radical scavenger 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) (0.5 mmol) was added into the reaction mixture, only a trace of C-3 cycloalkylated product (**1a**) (5%) was formed along with the formation of TEMPO-cyclohexyl adduct (50%) thereby suggesting the radical nature for this reaction (see Supporting Information, Scheme S2).

On the basis of experimental results and previous reports, a possible mechanistic pathway is outlined in Scheme 4. Initially, a thermal homolytic cleavage of *tert*-butyl peroxybenzoate (TBPB) produces peroxybenzoate radical and *tert*-butoxy radical, which

abstract a proton from cyclohexane (**a**) or *N,N*-dimethylformamide (**a'**) to form a radical species (**R**·) with the release of *tert*-butyl alcohol and/or benzoic acid. Then, the addition of radical species (**R**·) to 4-phenylcoumarin (**1**) gave the stable benzyl radical species (**A**), from which a proton is abstracted by another *tert*-butoxy radical or peroxybenzoate radical to furnish the desired C-3 functionalized product (**1a**) or (**1a'**).



Scheme 4. Proposed mechanism for C-3 functionalization of 4-arylcoumarins.

CONCLUSION

In conclusion, we have reported C-3 cycloalkylation, and amidation of 4-arylcoumarin. A wide range of 4-arylcoumarins, cycloalkanes, and formamides are suitable under this reaction condition, provided corresponding C-3 functionalized products. This protocol is an operationally simple and convenient route for C-3 fuctionalization of 4-arylcoumarins and a new strategy to increase the efficiency of C-H bond functionalization, particularly in internal alkene.

Experimental Section

General Information: All reagents were commercial grade and used without further purification. Reactions were monitored by TLC on silica gel 60 GF254 (0.25 mm). 1H NMR spectra (400 and 600 MHz) and 13C NMR spectra (100 MHz) were recorded at room temperature on a Bruker NMR instrument. High-resolution mass spectral analysis (HRMS) data were recorded using ESI mode (Q-TOF type Mass Analyzer). IR spectra were recorded in KBr. All the reagents and solvents were procured from Sigma Aldrich, and Merck. 4-Arylcoumarins were prepared according to the literature procedure (C. A. Silva et.al./Med Chem Res 2016, 26, 131–139).

General procedure for the synthesis of 3-cyclohexyl-7-methoxy-4-phenyl-2*H*-chromen-2-one (1a): In an oven-dried 10 mL round-bottom flask, 4-arylcoumarin (**1**) (126 mg, 0.5 mmol), cyclohexane (1 mL, 9.2 mmol), TBPB (285 µL, 1.50 mmol), AcOH (57 µL, 1.0 mmol) and were added, followed by the addition of chlorobenzene (1 mL). The reaction mixture was then heated at 120 °C. After completion of the reaction (12 h), the solvents were evaporated under reduced pressure. The reaction mixture was then admixed with water (3 mL) and then extracted with ethyl acetate (2 x 10 mL), dried over anhydrous sodium sulphate, Na_2SO_4, and again evaporated under reduced pressure. The crude products were purified on a silica gel column chromatography using a 10% EtOAc/hexane to afford the corresponding product, 3-cyclohexyl-7-methoxy-4-phenyl-2*H*-chromen-2-one (**1a**) (118 mg, 70%).

General procedure for the synthesis of 7-methoxy-*N,N*-dimethyl-2-oxo-4-phenyl-2*H*-chromene-3-carboxamide (1a'): In an oven-dried 10 mL round-bottom flask, 4-arylcoumarin (**1**) (126 mg, 0.5 mmol), and *N,N*-dimethylformamide (**a'**) (1 mL, 13.0 mmol) and *tert*-butyl peroxybenzoate (TBPB) (285 µL, 1.50 mmol) were added. The reaction mixture was then heated at 120 °C. After completion of the reaction (12 h), the reaction mixture was then admixed with water (5 mL) and then extracted with ethyl acetate (3 x 10 mL), dried over anhydrous sodium sulphate, Na_2SO_4, and again evaporated under reduced pressure. The crude products were purified on a silica gel column chromatography using a 30% EtOAc/hexane to afford the corresponding product, 7-

methoxy-*N,N*-dimethyl-2-oxo-4-phenyl-2*H*-chromene-3-carboxamide (**1a'**) (122 mg, 75%,).

3-Cyclohexyl-7-methoxy-4-phenyl-2*H*-chromen-2-one (1a): White solid, (118 mg, 70%). m.p. 178-179 °C. R_f = 0.7 (20% EtOAc/hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.95-1.05 (m, 2H), 1.17-1.12 (m, 1H), 1.45-1.56 (m, 3H), 2.07-2.16 (m, 2H), 2.27-2.34 (m, 1H), 1.66-1.70 (m, 2H), 3.83 (s, 3H), 6.63 (dd, J_1 = 2.0 Hz, J_2 = 2.4 Hz, 1H), 6.74 (d, J = 8.8 Hz, 1H), 6.82 (d, J = 2.4 Hz, 1H), 7.17 (d, J = 6.0 Hz, 2H), 7.47-7.52 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 25.4, 26.4, 29.3, 40.8, 55.6, 99.9, 111.7, 114.5, 127.5, 127.8, 128.2, 128.3, 128.6, 135.6, 150.6, 154.0, 160.6, 161.5 ppm. IR (KBr): ῡ = 2927, 2843, 1718, 1614, 1549, 1509, 1452, 1357, 1368, 1248, 1162, 1139, 1068, 1027, 985, 854, 823, 782, 718, 700 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{22}O_3$ $[M + H]^+$ 335.1642; found 335.1647.

3-Cyclohexyl-7-ethoxy-4-phenyl-2*H*-chromen-2-one (2a): White solid, (116 mg, 67%). m.p. 106-107 °C. R_f = 0.7 (20% EtOAc/hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.96-1.03 (m, 2H), 1.19-1.25 (m, 1H), 1.41-1.48 (m, 5H), 1.53 (d, J = 13.2 Hz, 1H), 1.67 (d, J = 13.2 Hz, 2H), 2.08-2.15 (m, 2H), 2.29 (t, J = 12.0 Hz), 4.03 (q, J = 7.2 Hz, 2H), 6.63 (dd, J_1 = J_2 = 2.4 Hz, 1H), 6.73 (d, J = 9.0 Hz, 1H), 6.81 (d, J = 2.4 Hz, 1H), 7.17 (d, J = 7.2 Hz, 2H), 7.47-7.53 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.2, 22.3, 26.6, 29.4, 40.9, 64.3, 100.1, 111.8, 114.7, 127.4, 127.9, 128.4, 128.5, 128.7, 135.7, 150.7, 154.2, 160.4, 161.6 ppm. IR (KBr): ῡ = 2924, 2850, 1709, 1683, 1583, 1508, 1452, 1426, 1326, 1293, 1166, 1072, 1038, 933, 852, 808, 779, 707 cm^{-1}. HRMS (ESI): calcd. for $C_{23}H_{24}O_3$ $[M + H]^+$ 349.1798; found 349.1801.

3-Cyclohexyl-7-propoxy-4-phenyl-2*H*-chromen-2-one (3a): White solid, (114 mg, 63%). m.p. 120-121 °C. R_f = 0.7 (20% EtOAc/hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.98-1.044 (m, 5H), 1.21-1.24 (m, 1H), 1.45 (d, J = 12.6 Hz, 2H), 1.52 (d, J = 13.2 Hz, 1H), 1.64-1.68 (m, 2H), 1.78-1.84 (m, 2H), 2.07-2.14 (m, 2H), 2.27-2.31 (m, 1H), 3.92 (t, J = 6.6 Hz, 2H), 6.63 (dd, J_1 = 2.4 Hz, J_2 = 3.0 Hz, 1H), 6.72 (d, J = 9. Hz, 1H), 6.80 (d, J = 2.4 Hz, 1H), 7.17 (d, J = 6.6 Hz, 2H), 7.41-7.51 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 10.4, 22.7, 25.6, 26.6, 29.5, 41.0, 69.6, 100.1, 111.9, 114.7, 127.7, 128.0,

128.4, 128.5, 128.8, 135.8, 150.8, 154.2, 160.8, 161.7 ppm. IR (KBr): ῡ = 2930, 2851, 1700, 1687, 1603, 1584, 1550, 1506, 1496, 1453, 1425, 1372, 1326, 1292, 1178, 1128, 1073, 1027, 1000, 934, 848, 835, 809, 753, 707 cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{26}O_3$ $[M + H]^+$ 363.1955; found 363.2000.

3-Cyclohexyl-5,7-dimethoxy-4-phenyl-2*H*-chromen-2-one (4a): White solid, (95 mg, 52%). m.p. 150-151 °C. R_f = 0.6 (20% EtOAc/hexane). ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.88-0.96 (m, 2H), 1.19-1.26 (m, 1H), 1.40 (d, *J* = 11.4 Hz, 2H), 1.51 (d, *J* = 12.6 Hz, 1H), 1.57-1.69 (m, 2H), 2.11-2.20 (m, 3H), 3.26 (s, 3H), 3.85 (s, 3H), 6.13 (d, *J* = 2.4 Hz, 1H), 6.48 (d, *J* = 2.4 Hz, 1H), 7.08 (d, *J* = 7.2 Hz, 2H), 7.35-7.41 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 25.5, 26.5, 29.3, 39.5, 55.6, 57.8, 92.8, 95.2, 103.5, 127.5, 127.9, 128.3, 128.4, 128.6, 135.6, 150.6, 154.1, 160.6, 161.5 ppm. IR (KBr): ῡ = 2930, 2841, 1712, 1615, 1580, 1562, 1505, 1471, 1360, 1350, 1293, 1167, 1105, 1071, 982, 880, 804, 790, 771, 723, 708 cm^{-1}. HRMS (ESI): calcd. for $C_{23}H_{24}O_4$ $[M + H]^+$ 365.1747; found 365.1746.

3-Cyclohexyl-7,8-dimethoxy-4-phenyl-2*H*-chromen-2-one (5a): White solid, (106 mg, 58%). m.p. 175-178 °C. R_f = 0.6 (20% EtOAc/hexane). ^1H NMR ($CDCl_3$, 600 MHz): δ = 0.96-1.02 (m, 2H), 1.22-1.27 (m, 1H), 1.46 (d, *J* = 12.0 Hz, 2H), 1.53 (d, *J* = 12.6 Hz, 1H), 1.67 (d, *J* = 13.2 Hz, 2H), 2.08-2.15 (m, 2H), 2.27-2.32 (m, 1H), 3.89 (s, 3H), 4.02 (s, 3H), 6.53 (d, *J* = 9.0 Hz, 1H), 6.66 (d, *J* = 9.0 Hz, 1H), 7.17 (d, *J* = 12.0 Hz, 2H), 7.46-7.52 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 25.4, 26.4, 29.2, 40.9, 56.1, 61.4, 107.6, 115.8, 122.4, 127.8, 128.4, 129.2, 130.1, 133.7, 135.5, 146.5, 150.6, 154.1, 160.0 ppm. IR (KBr): ῡ = 2929, 2846, 1718, 1601, 1591, 1559, 1505, 1464, 1366, 1350, 1293, 1168, 1106, 1074, 986, 886, 805, 784, 769, 714, 697 cm^{-1}. HRMS (ESI): calcd. for $C_{23}H_{24}O_4$ $[M + H]^+$ 365.1747; found 365.1748.

3-Cyclohexyl-5,7-diethoxy-4-phenyl-2*H*-chromen-2-one (6a): White solid, (98 mg, 50%). m.p. 180-181 °C. R_f = 0.6 (20% EtOAc/hexane). ^1H NMR ($CDCl_3$, 600 MHz): δ = 0.85-0.93 (m, 2H), 1.22-1.31 (m, 2H), 1.37-1.40 (m, 2H), 1.43 (t, *J* = 8.4 Hz, 6H), 1.64 (d, *J* = 13.8 Hz, 2H), 1.86-1.93 (m, 1H), 2.13-2.16 (m, 2H), 3.53-3.57 (m, 2H), 4.05-4.08 (m, 2H), 6.12 (d, *J* = 2.4 Hz), 6.45 (d, *J* = 2.4 Hz, 1H), 7.09 (dd, $J_1 = J_2$ = 1.8 Hz), 7.35-7.39

(m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.3, 14.4, 26.1, 26.5, 29.0, 39.8, 63.3, 63.8, 92.9, 96.1, 104.2, 126.4, 128.4, 130.1, 133.7, 139.9, 150.1, 155.3, 157.2, 160.4, 161.4 ppm. IR (KBr): ῡ = 2934, 2830, 1715, 1602, 1575, 1552, 1501, 1482, 1363, 1352, 1287, 1160, 1102, 1083, 985, 886, 802, 775, 771, 723, 705 cm^{-1}. HRMS (ESI): calcd. for $C_{25}H_{28}O_4$ $[M + H]^+$ 393.2060; found 393.2065.

3-Cyclohexyl-5-methoxy-7-methyl-4-phenyl-2*H*-chromen-2-one (7a): White solid, (96 mg, 55%). m.p. 111-112 °C. R_f = 0.7 (20% EtOAc/hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.89-0.97 (m, 2H), 1.23-1.31 (m, 3H), 1.41-1.48 (m, 1H), 1.66 (d, J = 12.0 Hz, 2H), 1.85-1.93 (m, 1H), 2.11-2.15 (m, 2H), 2.38 (s, 3H), 3.27 (s, 3H), 6.38 (s, 1H), 6.79 (s, 1H), 7.09 (d, J = 7.2 Hz, 2H), 7.36-7.42 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 21.5, 27.8, 27.9, 31.8, 35.2, 55.5, 100.0, 111.7, 114.3, 122.9, 127.8, 128.3, 130.0, 133.6, 135.5, 149.0, 153.9, 160.7, 161.4 ppm. IR (KBr): ῡ = 2922, 2850, 1687, 1618, 1602, 1583, 1495, 1453, 1424, 1326, 1292, 1185, 1127, 1100, 1072, 1026, 996, 934, 808, 708 cm^{-1}. (HRMS (ESI): calcd. for $C_{23}H_{24}O_3$ $[M + H]^+$ 349.1798; found 349.1803.

3-Cycloheptyl-7-methoxy-4-phenyl-2*H*-chromen-2-one (1b): White solid, (127 mg, 73%). m.p. 203-204 °C. R_f = 0.7 (20% EtOAc/hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 1.20-1.23 (m, 2H), 1.35-1.45 (m, 4H), 1.52-1.55 (m, 2H), 1.66-1.69 (m, 2H), 2.09 (s, 2H), 2.44 (s, 1H), 3.83 (s, 3H), 6.64 (dd, $J_1 = J_2$ = 2.4 Hz, 1H), 6.76 (d, J = 8.4 Hz, 1H), 6.82 (d, J = 2.4 Hz, 1H), 7.18 (d, J = 6.6 Hz, 2H), 7.46-7.51 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 27.9, 28.0, 31.9, 41.5, 55.5, 100.1, 111.8, 114.4, 127.9, 128.4, 128.6, 130.1, 133.7, 135.6, 149.1, 154.0, 160.8, 161.5 ppm. IR (KBr): ῡ = 2915, 2840, 1720, 1618, 1570, 1506, 1450, 1360, 1352, 1255, 1175, 1190, 1062, 1025, 973, 835, 816, 778, 710, 703 cm^{-1}. HRMS (ESI): calcd. for $C_{23}H_{24}O_3$ $[M + H]^+$ 349.1798; found 349.1803.

3-Cyclooctyl-7-methoxy-4-phenyl-2*H*-chromen-2-one (1c): White solid, (136 mg, 75%). m.p. 120-121 °C; R_f = 0.7 (20% EtOAc/hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.98-1.03 (m, 1H), 1.21-1.28 (m, 4H), 1.39-1.50 (m, 5H), 1.61-1.65 (m, 2H), 2.08-2.13 (m, 2H), 2.58 (s, 1H), 3.84 (s, 3H), 6.66 (dd, $J_1 = J_2$ = 2.4 Hz, 1H), 6.80 (d, J = 8.4 Hz, 1H), 6.83 (d, J = 2.4 Hz, 1H), 7.20 (d, J = 7.2 Hz, 2H), 7.46-7.53 (m, 3H) ppm. ^{13}C NMR

($CDCl_3$, 100 MHz): δ = 19.0, 19.2, 19.7, 24.5, 31.1, 48.6, 93.1, 104.8, 107.4, 120.9, 121.4, 121.6, 123.1, 126.7, 128.6, 142.2, 147.0, 154.4, 165.2 ppm. IR (KBr): ῡ = 2907, 2844, 1722, 1616, 1594, 1507, 1445, 1375, 1325, 1280, 1252, 1195, 1151, 1121, 1058, 1030, 996, 835, 816, 774, 704 cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{26}O_3$ $[M + H]^+$ 363.1955; found 363.1956.

3-Cyclooctyl-7,8-dimethoxy-4-phenyl-2*H*-chromen-2-one (5c): White solid, (118 mg, 60%). m.p. 213-214 °C; R_f = 0.6 (20% EtOAc/hexane). ^1H NMR ($CDCl_3$, 600 MHz): δ = 0.97-1.03 (m, 1H), 1.22-1.27 (m, 4H), 1.36-1.51 (m, 5H), 1.59-1.66 (m, 2H), 2.06-2.13 (m, 2H), 2.54-2.60 (m, 1H), 3.88 (s, 3H), 4.01 (s, 3H), 6.57 (d, *J* = 13.2 Hz, 1H), 6.67 (d, *J* = 13.2 Hz, 1H), 7.19 (d, *J* = 9.6 Hz, 2H), 7.46-7.53 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 26.0, 26.2, 26.7, 31.5, 38.2, 56.2, 61.4, 107.6, 115.7, 122.4, 127.9, 128.3, 128.6, 130.1, 130.7, 135.6, 146.6, 149.0, 154.0, 160.0 ppm. IR (KBr): ῡ = 2909, 2860, 1722, 1650, 1613, 1561, 1509, 1428, 1349, 1288, 1218, 1174, 986, 918, 872, 827, 812, 787, 723, 705 cm^{-1}. HRMS (ESI): calcd. for $C_{25}H_{28}O_4$ $[M + H]^+$ 393.2060; found 393.2062.

3-Cyclopentyl-7-methoxy-4-phenyl-2*H*-chromen-2-one (1d): White solid, (77 mg, 48%). m.p. 175-176 °C; R_f = 0.7 (20% EtOAc/hexane). ^1H NMR ($CDCl_3$, 600 MHz): δ = 1.41-1.47 (m, 2H), 1.52-1.58 (m, 2H), 1.80-1.85 (m, 2H), 1.99-2.08 (m, 2H), 2.65-2.73 (m, 1H), 3.84 (s, 3H), 6.64 (dd, J_1 = 3.6 Hz, J_2 = 2.4 Hz, 1H), 6.76 (d, *J* = 8.8 Hz, 1H), 6.83 (d, *J* = 2.4 Hz, 1H), 7.20 (d, *J* = 6.4 Hz, 2H), 7.46-7.52 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 26.7, 30.4, 40.5, 55.6, 100.0, 111.7, 114.5, 124.2, 126.1, 128.1, 128.2, 128.6, 135.7, 150.9, 154.0, 160.2, 161.4 ppm. IR (KBr): ῡ = 2947, 2867, 1705, 1616, 1553, 1509, 1433, 1362, 1329, 1294, 1256, 1161, 1137, 1071, 1027, 846, 825, 784, 775, 701 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{20}O_3$ $[M + H]^+$ 321.1485; found 321.1490.

4-(4-Chlorophenyl)-3-cyclohexyl-7-methoxy-2H-chromen-2-one (**8a**): White solid, (125 mg, 68%). m.p. 170-171 °C. R_f = 0.7 (20% EtOAc/hexane). ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.97-1.06 (m, 2H), 1.17-1.27 (m, 1H), 1.43 (d, *J* = 12.4 Hz, 2H), 1.53 (d, *J* = 13.6 Hz, 1H), 1.66-1.70 (d, *J* = 12.8 Hz, 2H), 2.07-2.15 (m, 2H), 2.24-2.30 (m, 1H), 3.82 (s, 3H), 6.64-6.66 (m, 1H), 6.70 (d, *J* = 9.2 Hz, 1H), 6.81 (s, 1H), 7.11 (d, *J* = 8.4 Hz, 1H),

7.44-7.50 (m, 2H), 8.10 (d, *J* = 7.2 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 25.4, 26.4, 29.3, 40.9, 55.6, 100.1, 111.8, 114.1, 128.0, 128.3, 129.0, 129.3, 130.0, 134.0, 149.3, 154.0, 160.3, 161.7 ppm. IR (KBr): ῡ = 2930, 2840, 1720, 1615, 1550, 1509, 1451, 1355, 1368, 1250, 1162, 1140, 1068, 1030, 985, 850, 823, 780, 720, 701 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{21}ClO_3$ $[M + H]^+$ 369.1179; found 369.1185.

7-Methoxy-*N,N*-dimethyl-2-oxo-4-phenyl-2*H*-chromene-3-carboxamide (1a'): Red gummy (122 mg, 75%). R_f = 0.3 (20% EtOAc/hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 2.78 (s, 3H), 2.79 (s, 3H), 3.85 (s, 3H), 6.74 (dd, $J_1 = J_2$ = 2.4 Hz, 1H), 6.84 (d, *J* = 2.4 Hz, 1H), 7.13 (d, *J* = 9.0 Hz, 1H), 7.22 (d, *J* = 4.8 Hz, 1H), 7.44-7.50 (m, 4H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 34.1, 37.5, 55.6, 100.6, 112.5, 119.6, 127.2, 127.9, 128.6, 128.8, 129.4, 132.7, 151.2, 155.0, 158.5, 162.9, 164.5 ppm. IR (KBr): ῡ = 2918, 2849, 1712, 1647, 1608, 1555, 1494, 1442, 1333, 1397, 1361, 1333, 1297, 1260, 1239, 1194, 1162, 1134, 1041, 849, 825, 790, 751, 700 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{17}NO_4$ $[M + H]^+$ 324.1230; found 324.1234.

***N,N*-Dimethyl-7-methoxy-2-oxo-4-phenyl-2*H*-chromene-3-carboxamide (1b'):** Red gummy (123 mg, 70%). R_f = 0.3 (20% EtOAc/hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.75 (t, *J* = 7.2 Hz, 3H), 1.01 (t, *J* = 7.2 Hz, 3H), 2.92-2.97 (m, 2H), 3.29-3.33 (m, 2H), 3.89 (s, 3H), 6.77 (dd, $J_1 = J_2$ = 7.2 Hz, 1H), 6.89 (d, *J* = 3.0 Hz, 1H), 7.16 (d, *J* = 8.4 Hz, 1H), 7.25 (d, *J* = 6.6 Hz, 1H), 7.46-7.51 (m, 3H), 7.60 (d, *J* = 7.8 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 11.4, 13.3, 38.2, 42.6, 55.5, 100.6, 112.5, 119.4, 127.3, 128.0, 128.5, 128.8, 129.7, 133.1, 151.0, 155.0, 158.8, 162.9, 164.1 ppm. IR (KBr): ῡ = 2933, 2860, 1718, 1684, 1617, 1553, 1493, 1374, 1313, 1293, 1255, 1239, 1161, 1114, 1070, 1026, 1000, 822, 786, 759, 707 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{21}NO_4$ $[M + H]^+$ 352.1543; found 352.1540.

***N,N*-Diisopropyl-7-methoxy-2-oxo-4-phenyl-2*H*-chromene-3-carboxamide (1c'):** White solid, (127 mg, 67%). m.p. 212-213 °C. R_f = 0.3 (20% EtOAc/hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.62 (d, *J* = 6.6 Hz, 3H), 1.03 (d, *J* = 6.6 Hz, 3H), 1.12 (d, *J* = 7.2 Hz, 3H), 1.48 (d, *J* = 7.2 Hz, 3H), 3.18-3.23 (m, 2H), 3.74-3.78 (m, 2H), 3.87 (s, 3H), 6.75

(dd, $J_1 = J_2 = 2.4$ Hz, 1H), 6.78 (d, $J = 2.4$ Hz, 1H), 7.17 (d, $J = 9.0$ Hz, 1H), 7.24 (d, $J = 2.4$ Hz, 1H), 7.43-7.48 (m, 3H), 7.68 (d, $J = 6.0$ Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 19.5, 20.1, 20.2, 20.8, 45.7, 51.1, 55.7, 100.7, 112.4, 121.5, 127.5, 128.2, 128.6, 129.3, 130.0, 132.7, 149.1, 155.0, 158.9, 162.7, 163.3 ppm. IR (KBr): ῡ = 2930, 2844, 1712, 1621, 1559, 1429, 1457, 1443, 1365, 1328, 1297, 1265, 1233, 1210, 1166, 1139, 1039, 874, 825, 808, 761, 730, 703 cm^{-1}. HRMS (ESI): calcd. for $C_{23}H_{25}NO_4$ $[M + H]^+$ 380.1856; found 380.1854.

***N,N*-Dibutyl-7-methoxy-2-oxo-4-phenyl-2*H*-chromene-3-carboxamide (1d'):** Red gummy (123 mg, 60%). R_f = 0.3 (20% EtOAc/hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.73 (t, $J = 7.8$ Hz, 3H), 0.77 (t, $J = 6.0$ Hz, 3H), 1.25-1.30 (m, 4H), 1.45-1.50 (m, 4H), 3.16 (t, $J = 7.2$ Hz, 4H), 3.84 (s, 3H), 6.74 (d, $J = 9.0$ Hz, 1H), 6.86 (s, 1H), 7.10 (d, $J = 9.0$ Hz, 1H), 7.21 (d, ($J = 5.4$ Hz, 3H), 7.38-7.44 (m, 4H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 28.4, 29.0, 29.8, 30.3, 41.7, 43.5, 47.1, 48.2, 55.6, 100.6, 112.4, 119.8, 127.6, 127.9, 128.4, 129.2, 129.6, 132.6, 150.4, 154.9, 158.7, 162.9, 164.1 ppm. IR (KBr): ῡ = 2926, 2872, 1718, 1674, 1636, 1611, 1553, 1491, 1466, 1372, 1295, 1280, 1254, 1211, 1160, 1115, 1042, 959, 838, 786, 759, 713, 700 cm^{-1}. HRMS (ESI): calcd. for $C_{25}H_{29}NO_4$ $[M + H]^+$ 408.2169; found 408.2171.

7-Methoxy-*N*-methyl-2-oxo-4-phenyl-2*H*-chromene-3-carboxamide (1e'): Red gummy (105 mg, 68%). R_f = 0.2 (20% EtOAc/hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 2.77 (d, $J = 4.8$ Hz, 3H), 3.88 (s, 3H), 8.76 (dd, $J_1 = J_2 = 2.4$ Hz, 1H), 6.83 (s, 1H), 7.06 (d, $J = 9.0$ Hz, 1H), 7.29 (d, $J = 6.0$ Hz, 1H), 7.37 (s, 1H), 7.46-7.49 (m, 3H), 8.10 (d, $J = 7.8$ Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 26.2, 55.5, 100.1, 112.8, 117.4, 127.5, 128.1, 128.7, 129.4, 129.7, 133.0, 154.7, 155.8, 160.3, 163.3, 164.0 ppm IR (KBr): ῡ = 3303, 2942, 2842, 1746, 1693, 1555, 1490, 1444, 1413, 1371, 1282, 1259, 1217, 1159, 1119, 1059, 1026, 1001, 968, 982, 826, 788, 754, 705 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{15}NO_4$ $[M + H]^+$ 310.1074; found 310.1073.

***N*-(*tert-butyl*)-7-Methoxy-2-oxo-4-phenyl-2*H*-chromene-3-carboxamide (1f'):** White solid, (113 mg, 65%). m.p. 192-193 °C. R_f = 0.2 (20% EtOAc/hexane). ^{1}H NMR ($CDCl_3$,

600 MHz): δ = 1.19 (s, 9H), 3.89 (s, 3H), 5.99 (s, 1H), 6.76 (dd, J_1 = 2.4 Hz, J_2 = 1.8 Hz, 1H), 6.84 (s, 1H), 7.12 (d, J = 9.0 Hz, 1H), 7.36-7.38 (m, 2H), 7.50-7.52 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 28.1, 51.6, 55.7, 100.4, 112.6, 112.8, 120.3, 128.0, 128.4, 129.0, 129.8, 133.7, 153.3, 154.9, 159.6, 162.5, 163.0 ppm. IR (KBr): ῡ = 3302, 2940, 2850, 1726, 1639, 1549, 1508, 1477, 1444, 1376, 1283, 1262, 1227, 1155, 1118, 1038, 1023, 974, 941, 853, 813, 794, 749, 703 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{21}NO_4$ $[M + H]^+$ 349.1798; found 349.1800.

7-Ethoxy-*N,N*-diethyl-2-oxo-4-phenyl-2*H*-chromene-3-carboxamide (2a'): Red gummy (93 mg, 55%). R_f = 0.3 (20% EtOAc/hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 1.34 (d, J = 6.6 Hz, 3H), 2.72 (s, 3H), 2.74 (s, 3H), 3.98-4.01 (m, 2H), 6.66 (d, J = 8.4 Hz, 1H), 6.76 (s, 1H), 7.06 (d, J = 9.0 Hz, 1H), 7.17 (s, 1H), 7.39-7.47 (m, 3H), 7.95 (d, J = 7.8 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.2, 34.1, 37.5, 64.0, 100.9, 112.8, 119.2, 127.1, 128.0, 128.7, 129.3, 129.6, 132.6, 151.4, 154.9, 158.6, 162.3, 164.7 ppm. IR (KBr): ῡ = 2939, 2850, 1718, 1645, 1597, 1554, 1500, 1445, 1399, 1371, 1295, 1280, 1252, 1234, 1170, 1133, 1039, 840, 823, 786, 759, 703 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{19}NO_4$ $[M + H]^+$ 338.1387; found 338.1386.

5,7-Dimethoxy-*N,N*-dimethyl-2-oxo-4-phenyl-2*H*-chromene-3-carboxamide (4a'): Red gummy (92mg, 52%). R_f = 0.2 (20% EtOAc/hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 2.67 (s, 3H), 2.72 (s, 3H), 3.26 (s, 3H), 3.79 (s, 3H), 6.13 (d, J = 2.4 Hz, 1H), 6.44 (d, J = 2.4 Hz, 1H), 7.02 (d, J = 6.6 Hz, 1H), 7.31-7.38 (m, 3H), 7.99 (d, J = 8.4 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 34.1, 37.7, 55.4, 55.7, 93.3, 95.9, 103.1, 119.8, 126.7, 128.1, 129.8, 132.9, 136.6, 151.0, 156.3, 158.6, 163.6, 164.7 ppm. IR (KBr): ῡ = 2926, 2852, 1718, 1641, 1611, 1584, 1550, 1500, 1475, 1429, 1393, 1353, 1339, 1265, 1244, 1226, 1162, 1150, 1114, 1053, 1022, 983, 939, 885, 835, 758, 744, 697 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{19}NO_5$ $[M + H]^+$ 354.1336; found 354.1331.

7,8-Dimethoxy-*N,N*-dimethyl-2-oxo-4-phenyl-2*H*-chromene-3-carboxamide (5a'): Red gummy (99mg, 56%). R_f = 0.2 (20% EtOAc/hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 2.82 (s, 3H), 2.83 (s, 3H), 3.93 (s, 3H), 4.00 (s, 3H), 6.80 (d, J = 9.0 Hz, 1H), 6.95 (d, J

= 9.0 Hz, 1H), 7.24 (d, *J* = 6.0 Hz, 1H), 7.40-7.48 (m, 3H), 8.07 (d, *J* = 7.2 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 34.2, 37.6, 56.2, 61.4, 108.2, 113.6, 122.9, 127.2, 128.2, 128.9, 129.8, 133.1, 136.0, 147.4, 151.4, 155.7, 158.1, 164.7 ppm. IR (KBr): ῡ = 2928, 2849, 1704, 1652, 1601, 1561, 1505, 1452, 1394, 1355, 1298, 1258, 1105, 1019, 987, 894, 866, 813, 787, 752, 701 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{19}NO_5$ [M + H]$^+$ 354.1336; found 354.1334.

5,7-Diethoxy-*N,N*-dimethyl-2-oxo-4-phenyl-2*H*-chromene-3-carboxamide (6a'): Red gummy (90 mg, 47%). R_f = 0.2 (20% EtOAc/hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.63 (t, *J* = 6.6 Hz, 3H), 1.44 (t, *J* = 7.2 Hz, 3H), 2.76 (s, 3H), 2.83 (s, 3H), 3.59-3.64 (m, 2H), 4.07-4.10 (m, 2H), 6.18 (d, *J* = 2.4 Hz, 1H), 6.49 (d, *J* = 1.8 Hz, 1H), 7.11 (d, *J* = 7.2 Hz, 1H), 7.28-7.40 (m, 3H), 8.11 (d, *J* = 7.2 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.0, 14.2, 34.0, 37.7, 63.5, 63.9, 93.4, 96.4, 102.8, 119.3, 125.7, 128.1, 129.7, 133.0, 136.8, 151.4, 156.2, 157.9, 162.9, 164.9 ppm. IR (KBr): ῡ = 2937, 2860, 1717, 1676, 1616, 1584, 1550, 1449, 1395, 1376, 1349, 1246, 1226, 1159, 1139, 1116, 1051, 1010, 941, 870, 839, 823, 760, 751, 706 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{23}NO_4$ [M + H]$^+$ 382.1649; found 382.1654.

7-Methoxy-4-phenyl-3-(piperidine-1-carbonyl)-2*H*-chromen-2one (1g'): Red gummy (76 mg, 42%). R_f = 0.3 (20% EtOAc/hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.92-0.95 (m, 1H), 1.12-1.17 (m, 1H), 1.45-1.49 (m, 3H), 1.54-1.56 (m, 1H), 3.13-3.17 (m, 1H), 3.24-3.28 (m, 1H), 3.32-3.39 (m, 1H), 3.56-3.60 (m, 1H), 3.89 (s, 1H), 6.77 (dd, $J_1 = J_2$ = 2.4 Hz, 1H), 6.88 (d, *J* = 2.4 Hz, 1H), 7.19 (d, *J* = 9.0 Hz, 1H), 7.45-7.50 (m, 3H), 8.10 (d, *J* = 7.2 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 24.2, 24.7, 46.6, 55.5, 100.5, 112.3, 119.5, 127.6, 127.8, 128.4, 128.9, 129.50, 132.3, 150.4, 154.9, 158.5, 160.7, 162.7 ppm. IR (KBr): ῡ = 2930, 2868, 1712, 1670, 1636, 1609, 1556, 1498, 1459, 1361, 1290, 1275, 1246, 1210, 1175, 1110, 1030, 960, 835, 782, 750, 712, 7003 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{21}NO_4$ [M + H]$^+$ 364.1543; found 364.1541.

4-(4-Chlorophenyl)-7-methoxy-*N,N*-dimethyl-2-oxo-2H-chromene-3-carboxamide (8a'): Red gummy (107.5 mg, 60%). R_f = 0.3 (20% EtOAc/hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 2.78 (S, 3H), 2.80 (S, 3H), 3.86 (S, 3H), 6.75-6.77 (m, 1H), 6.85 (d, *J* = 2.4

Hz, 1H), 7.14 (d, J = 9.0 Hz, 1H), 7.45-7.57 (m, 4H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 34.2, 37.6, 55.7, 100.6, 112.5, 119.6, 127.3, 128.0, 128.6, 128.8, 129.4, 132.7, 151.3, 155.0, 158.6, 163.0, 164.6 ppm. IR (KBr): ῡ = 2920, 2850, 1715, 1650, 1608, 1552, 1494, 1440, 1335, 1397, 1367, 1333, 1298, 1261, 1239, 1195, 1162, 1137, 1045, 849, 827, 793, 750, 701 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{16}ClNO_4$ $[M + H]^+$ 358.0768; found 358.0772.

1-(Cyclohexyloxy)-2,2,6,6-tetramethylpiperidine (1C): Red gummy (60 mg; 50%). R_f = 0.8 (20% EtOAc/hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 1.10-1.25 (m, 18H), 1.42-1.53 (m, 6H), 1.73 (s, 2H), 2.04 (s, 2H), 3.57-3.61 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 17.2, 25.0, 25.9, 32.8, 34.3, 40.2, 59.5, 81.6 ppm. IR (KBr): ῡ = 2933, 2854, 1456, 1374, 1359, 1255, 1240, 1208, 1180, 1132, 1060, 1045, 1021, 995, 967, 914, 890, 783, 710 cm^{-1}. HRMS (ESI): calcd. for $C_{15}H_{29}NO$ $[M + H]^+$ 240.2328; found 240.2330.

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[18] CCDC 1570811 of the compound (**1a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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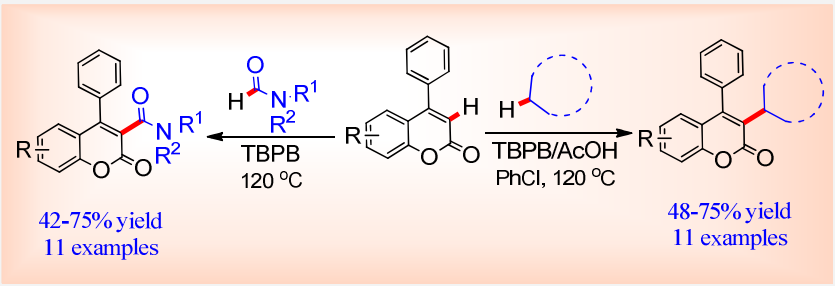
Graphical Abstract



A *tert*-butyl peroxybenzoate (TBPB) mediated cycloalkylation and formamidation take place effectively in chlorobenzene or in respective formamides at 120 °C, while the former process requires the presence of acetic acid, the later goes in its absence. This radical mediated process gives moderate yield of the products with good substrate scope.

sp^2–sp^3 and sp^2–sp^2 C–H bond functionalization
S. J. Singh, and B. K Patel*
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A TBPB Mediated C-3 Cycloalkylation and Formamidation of 4-Arylcoumarin

keywords: Coumarins; C–H functionalization; cycloalkylation; formamidation; metal-free; cross dehyrogenative coupling