Phosphazene Base-Catalyzed Intramolecular Cascade Reactions of Aryl-Substituted Enynes

Jian-Sheng Tang,[a,b] Ye-Xiang Xie,[a] Zhi-Qiang Wang,[a] Chen-Liang Deng,[a] Jin-Heng Li*[a]

[a] Key Laboratory of Chemical Biology & Traditional Chinese Medicine Research (Ministry of Education), Hunan Normal University, Changsha 410081, P. R. of China
Fax +86(731)88872101; E-mail: jhli@hunnu.edu.cn

[b] Mathematics and Science Department, Hunan First Normal University, Changsha, 410205, P. R. of China

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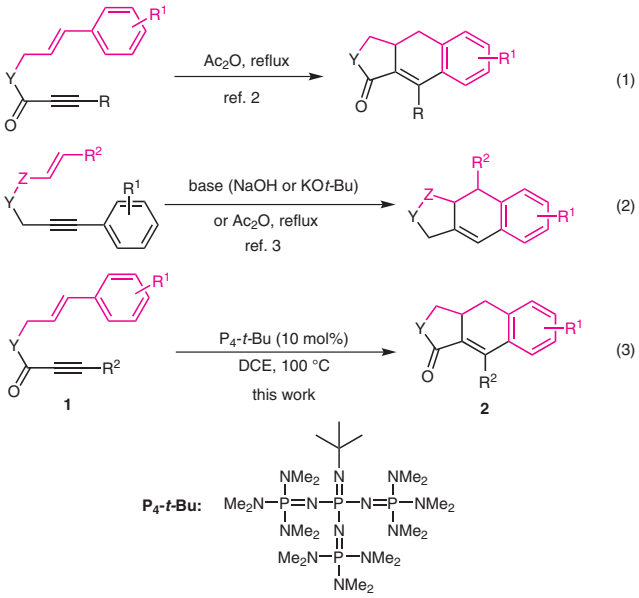
Abstract: A novel method for the synthesis of 9-aryl-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-ones has been developed by P_4-*t*-Bu-catalyzed intramolecular cascade reactions of enynes. In the presence of a catalytic amount of phosphazene P_4-*t*-Bu base, a variety of 3-arylallyl 3-arylpropiolates underwent the cascade cyclization reaction smoothly in moderate to excellent yields.

Key words: P_4-*t*-Bu base, cascade cyclization reaction, 9-aryl-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-one, 3-arylallyl 3-arylpropiolate

The cascade reaction strategy is of continuing interesting in the field of organic chemistry because it is a valuable route for the synthesis of polysubstituted polycyclic compounds.[1–3] Our interest is focused on the intramolecular Diels–Alder reactions of aryl-substituted enynes **1**, which proceeds via a cascade cyclization process (Scheme 1). Traditionally, there are two transformations for these purposes: one involves acetic anhydride mediated cyclization via the activation of the *ortho*-arene C–H bond at the terminal alkene (Scheme 1),[2] and the other is acetic anhydride[2h] or base-mediated cyclization employing the *ortho*-arene C–H bond at the terminal alkyne as a reaction partner.[3] For example, Klemm and Gopinath described intramolecular Diels–Alder cyclization of 3,4-(methylenedioxy)cinnamyl 3,4,5-trimethoxyphenylpropiolate to afford γ-apopicropodophyllin in 48% yield using acetic anhydride as the catalyst and solvent.[2a] In 1972, Laird and Ollis employed allylpropynyl ammonium cations as the substrates, shifting regioselectivity toward the *ortho*-arene C–H bond at the terminal alkyne in the presence of excess sodium methoxide.[3a] Subsequently, several papers have been reported that extend these routes in organic synthesis, but the scope has not yet been examined and it is often restricted to special substrates with unsatisfactory yields. Moreover, the high acetic anhydride or base loadings, resulting in toxic byproducts, hardly make the two transformations attractive procedures. Therefore, the development of a novel, catalytic route for the intramolecular cascade cyclization of enynes remains a challenging area. Here, we report the first intramolecular cascade cyclization protocol for the synthesis of 9-aryl-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-one using a catalytic amount of P_4-*t*-Bu (commercially available) (Scheme 1).[4,5] It is noteworthy that these products are a prevalent motif in many naturally occurring and biologically active compounds, such as the known antiviral and antitumor agents daurinol and retrochinensin.[6]



Scheme 1 Intramolecular cascade reactions

Our initial investigation began with the cyclization of cinnamyl 3-phenylpropiolate (**1a**) to optimize the reaction conditions (Table 1). Generally, base-mediated intramolecular Diels–Alder reactions of aryl-substituted enyne **1a** are used with the *ortho*-arene C–H bond at the terminal alkyne as a reaction partner.[3] However, we found that only product **2a** was obtained by activating the *ortho*-arene C–H bond at the terminal alkene using various bases (entries 1–13). The results demonstrated that the amount of potassium carbonate affected the reaction (entries 1–4). While treatment of substrate **1a** with two equivalents of potassium carbonate afforded the target product **2a** in 20% yield (entry 1), 5 equivalents of potassium carbonate enhanced the yield to 80% (entry 3), and an identical result was obtained in the presence of six equivalents of potassium carbonate (entry 4). Prompted by these results, a variety of other bases, such as Cs_2CO_3, K_3PO_4, NaOH, NaOEt,

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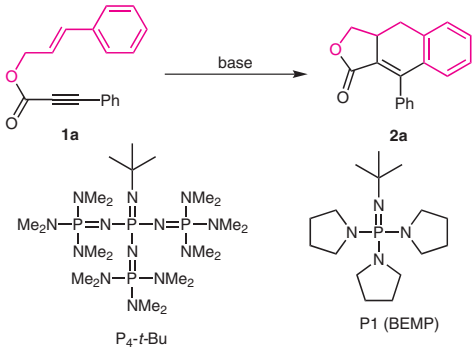
Table 1 Screening Optimal Conditions[a]



Entry	Base (equiv)	Solvent	Temp (°C)	Isolated yield (%)
1	K_2CO_3 (2)	DCE	100	20
2	K_2CO_3 (4)	DCE	100	52
3	K_2CO_3 (5)	DCE	100	80
4	K_2CO_3 (6)	DCE	100	75
5	Cs_2CO_3 (5)	DCE	100	44
6	K_3PO_4 (5)	DCE	100	61
7	NaOH (5)	DCE	100	trace
8	NaOEt (5)	DCE	100	70
9	DABCO (5)	DCE	100	20
10	DBU (5)	DCE	100	35
11[b]	P_4-*t*-Bu (0.05)	DCE	100	52
12[b]	P_4-*t*-Bu (0.1)	DCE	100	82
13[b]	P_4-*t*-Bu (0.2)	DCE	100	46
14[b]	P1 (0.1)	DCE	100	80
15[b]	Ph_3P (0.1)	DCE	100	trace
16	K_2CO_3 (5)	toluene	100	45
17	K_2CO_3 (5)	THF	100	53
18	K_2CO_3 (5)	DMF	100	trace
19	K_2CO_3 (5)	DCE	80	34
20	K_2CO_3 (5)	DCE	120	65

[a] Conditions: **1a** (0.2 mmol), base, solvent (2 mL), 24 h.
[b] For 60 h.

DABCO, DBU, and P_4-*t*-Bu, were examined (entries 5–13). We found that all but one were inferior to potassium carbonate (entries 5–10). To our delight, 10 mol% of P_4-*t*-Bu, an organic superbase, gave the best results after prolonged the reaction time (entry 12). Identical results were observed using P1 (BEMP) base (entry 14). Triphenylphosphine was also evaluated as the catalyst, however, no reaction occurred (entry 15). Subsequently, a number of other solvents, including toluene, tetrahydrofuran, and *N*,*N*-dimethylformamide, were tested, and they were less effective than 1,2-dichloroethane (entries 16–18). Finally, the effect of the reaction temperature was evaluated, and it turned out that both 80 °C and 120 °C decreased the yield (entries 19 and 20). The structure of **2a** was unambiguously confirmed by X-ray single-crystal diffraction analysis (Figure 1).[7]

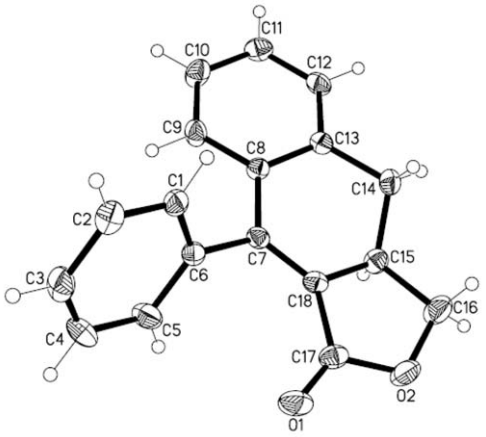


Figure 1 ORTEP diagram of the single-crystal X-ray structure of compound **2a**

With the optimized reaction conditions in hand, the enyne scope was investigated (Table 2).[8] Initially, a series of 3-arylallyl 3-phenylpropiolates **1b–d**, bearing electron-rich or electron-deficient arylallyl groups, were treated with P_4-*t*-Bu smoothly in good yields (entries 1–3). Gratifyingly, a moderate yield of **2e** was still isolated from heteroarylallyl substrate **1e** (entry 4). The results showed that several functional groups, such as methyl, methoxy, iodo, bromo, fluoro, acetyl, and nitro groups, on the aryl ring of the 3-arylpropiolate moiety were tolerated (entries 5–15). The cyclization reaction of substrates **1f–h** with a *p*-, *m*-, or *o*-methyl group, for instance, successfully proceeded with P_4-*t*-Bu in moderate yields (entries 5–7). It is pleasing to observe that the optimized conditions were compatible with halo-substituted substrates **1k–m** (entries 10–12). Electron-deficient substrates **1n–p** also underwent the cyclization reaction with P_4-*t*-Bu in excellent yields (entries 13–15). It was noted that cinnamyl 3-(thiophen-2-yl)propiolate (**1q**) was suitable for the reaction, affording the corresponding product **2q** in 90% yield (entry 16). In the presence of P_4-*t*-Bu, two *N*-cinnamyl-3-phenylpropiolamides **1r** and **1s** were also consistent with the reaction conditions, and they were transformed into the desired products **2r** and **2s** in 70% and 81% yields, respectively (entries 17 and 18). However, (*E*)-[3-(cinnamyloxy)prop-1-ynyl]benzene was not a suitable substrate under the optimized conditions.

Table 2 P_4-*t*-Bu-Catalyzed Intramolecular Cyclization Reactions of Enynes **1**[a]

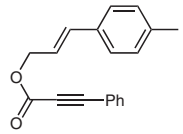
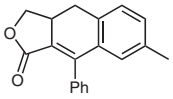
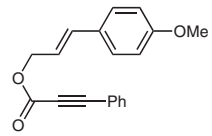
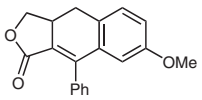
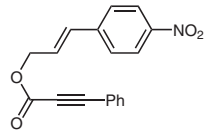
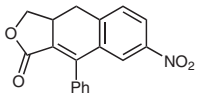
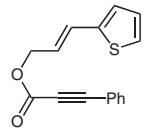
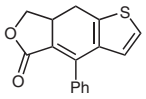
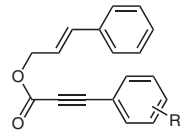
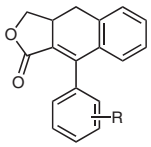
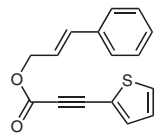
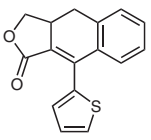
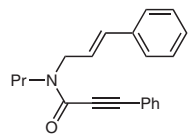
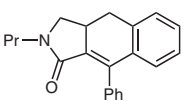
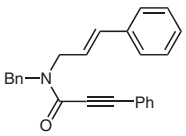
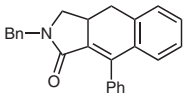
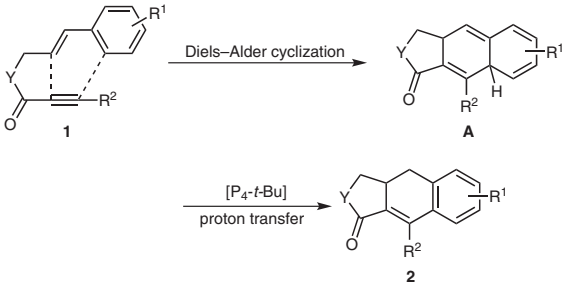
Entry	Enyne **1**	Product **2**	Yield[b] (%)
1	 **1b**	 **2b**	92
2	 **1c**	 **2c**	72
3	 **1d**	 **2d**	80
4	 **1e**	 **2e**	63
			
5	R = 4-Me **1f**	R = 4-Me **2f**	61
6	R = 3-Me **1g**	R = 3-Me **2g**	60
7	R = 2-Me **1h**	R = 2-Me **2h**	55
8	R = 4-OMe **1i**	R = 4-OMe **2i**	86
9	R = 2-OMe **1j**	R = 2-OMe **2j**	92
10	R = 4-I **1k**	R = 4-I **2k**	48
11	R = 2-Br **1l**	R = 2-Br **2l**	91
12	R = 4-F **1m**	R = 4-F **2m**	54
13	R = 4-Ac **1n**	R = 4-Ac **2n**	91
14	R = 3-Ac **1o**	R = 3-Ac **2o**	98
15	R = 3-NO_2 **1p**	R = 3-NO_2 **2p**	92
16	 **1q**	 **2q**	90
17	 **1r**	 **2r**	70

Table 2 P_4-*t*-Bu-Catalyzed Intramolecular Cyclization Reactions of Enynes **1**[a] (continued)

Entry	Enyne **1**	Product **2**	Yield[b] (%)
18	 **1s**	 **2s**	81

[a] Reaction conditions: **1** (0.2 mmol), P_4-*t*-Bu (10 mol%), DCE (2 mL), 100 °C, 60 h.
[b] Isolated yield.

Compared with the results for the base-mediated intramolecular Diels–Alder reactions of aryl-substituted enynes **1**,[3] different chemoselectivity was observed in the present reaction: the chemoselectivity was shifted towards the *ortho*-arene C–H bond at the terminal alkene, which is identical to the acetic anhydride mediated cyclization process. Thus, we deduced that the present reaction proceeds via a Diels–Alder mechanism,[2] and the role of P_4-*t*-Bu base is as an acid scavenger that promotes the reaction by a proton-transfer process (Scheme 2).



Scheme 2 A possible mechanism

In summary, we have disclosed phosphazene P_4-*t*-Bu base as an efficient catalyst for the intramolecular cascade cyclization of enynes. This work is the first to demonstrate that the intramolecular Diels–Alder cyclization reaction of enynes can be carried out successfully using a catalytic amount of phosphazene P_4-*t*-Bu base. Importantly, this new route allows the base-catalyzed mediated intramolecular cascade cyclization of enynes by activating the *ortho*-arene C–H bond at the terminal alkene, not the *ortho*-arene C–H bond at the terminal alkyne.[3]

NMR spectroscopy was performed on a Bruker-500 spectrometer operating at 500 MHz (^{1}H NMR) and 125 MHz (^{13}C NMR), TMS internal standard and $CDCl_3$ solvent. MS analysis was performed by GC-MS analysis (Shimadzu GCMS-QP2010 plus). Melting points are uncorrected.

Phosphazene Base Catalyzed Intramolecular Cascade Reactions of Aryl-Substituted Enynes; Typical Procedure

3-Arylallyl 3-arylpropiolate **1** (0.2 mmol), P_4-*t*-Bu (10 mol%), and DCE (2 mL) were added to a Schlenk tube and the soln was stirred at 100 °C for the indicated time until complete consumption of start-

ing material (TLC and GC-MS monitoring). When the reaction was finished, the mixture was washed with brine and extracted with Et_2O. The combined extracts were dried (anhyd Na_2SO_4) and evaporated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane–EtOAc) to afford the desired product.

9-Phenyl-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-one (2a)[6e]
White solid; mp 182.1–183.3 °C.

IR (KBr): 1748 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.46–7.38 (m, 3 H), 7.34–7.29 (m, 4 H), 7.18 (t, *J* = 7.5 Hz, 1 H), 6.95 (d, *J* = 8.0 Hz, 1 H), 4.73 (t, *J* = 9.0 Hz, 1 H), 4.04 (t, *J* = 8.5 Hz, 1 H), 3.50–3.42 (m, 1 H), 3.07, 3.05 (dd, *J* = 6.5, 6.5 Hz, 1 H), 2.90, 2.87 (dd, *J* = 15.0, 15.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.2, 147.3, 135.9, 135.4, 134.2, 129.8, 129.1, 128.5, 128.0, 127.8, 127.2, 126.4, 122.1, 71.2, 35.5, 33.0.

LRMS (EI, 70 eV): *m*/*z* (%) = 262 (M^+, 100), 231 (46), 217 (72), 203 (70), 101 (41).

7-Methyl-9-phenyl-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-one (2b)
White solid; mp 165.8–167.0 °C.

IR (KBr): 1748 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.45–7.44 (m, 3 H), 7.29–7.26 (m, 2 H), 7.17 (d, *J* = 7.5 Hz, 1 H), 7.11 (d, *J* = 8.0 Hz, 1 H), 6.75 (s, 1 H), 4.71 (t, *J* = 9.0 Hz, 1 H), 4.03 (t, *J* = 8.5 Hz, 1 H), 3.46–3.38 (m, 1 H), 3.03, 3.01 (dd, *J* = 6.5, 6.5 Hz, 1 H), 2.84, 2.81 (dd, *J* = 15.5, 15.5 Hz, 1 H), 2.22 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.3, 147.5, 136.9, 135.8, 134.3, 132.4, 130.5, 129.7, 128.5, 128.0, 127.9, 127.8, 122.1, 71.1, 35.8, 32.7, 21.1.

LRMS (EI, 70 eV): *m*/*z* (%) = 276 (M^+, 53), 215 (27), 202 (29), 71 (77), 57 (100), 43 (98).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{16}O_2$: 276.1150; found: 276.1148.

7-Methoxy-9-phenyl-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-one (2c)[8]
White solid; mp 142.0–143.8 °C.

IR (KBr): 1745 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.43–7.42 (m, 3 H), 7.31–7.29 (m, 2 H), 7.19 (d, *J* = 7.5 Hz, 1 H), 6.85–6.83 (m, 1 H), 6.50 (d, *J* = 2.5 Hz, 1 H), 4.71 (t, *J* = 9.0 Hz, 1 H), 4.03 (t, *J* = 7.5 Hz, 1 H), 3.65 (s, 3 H), 3.46–3.38 (m, 1 H), 3.02, 2.99 (dd, *J* = 7.0, 6.5 Hz, 1 H), 2.81, 2.77 (dd, *J* = 15.0, 15.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.2, 158.7, 147.2, 137.0, 134.1, 129.7, 128.7, 128.5, 127.8, 127.4, 122.6, 115.3, 114.6, 71.1, 55.3, 35.9, 32.1.

LRMS (EI, 70 eV): *m*/*z* (%) = 292 (M^+, 100), 247 (47), 231 (14), 215 (28), 203 (20).

7-Nitro-9-phenyl-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-one (2d)
Yellow solid; mp 188.0–189.9 °C.

IR (KBr): 1748 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.16–8.14 (m, 1 H), 7.80 (d, *J* = 2.5 Hz, 1 H), 7.49–7.46 (m, 4 H), 7.30–7.26 (m, 2 H), 4.76 (t, *J* = 7.5 Hz, 1 H), 4.08 (t, *J* = 9.0 Hz, 1 H), 3.55–3.47 (m, 1 H), 3.23, 3.20 (dd, *J* = 6.5, 6.5 Hz, 1 H), 2.97, 2.94 (dd, *J* = 15.5, 15.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.3, 147.5, 145.3, 142.3, 137.4, 132.6, 130.0, 129.3, 128.9, 128.3, 124.4, 124.3, 123.4, 70.9, 35.2, 32.8.

LRMS (EI, 70 eV): *m*/*z* (%) = 307 (M^+, 100), 290 (33), 260 (17), 215 (36), 101 (35).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{13}NO_4$: 307.0845; found: 307.0848.

4-Phenyl-7a,8-dihydrothieno[2,3-*f*][2]benzofuran-5(7*H*)-one (2e)[6e]
Yellow solid; mp 136.5–138.0 °C.

IR (KBr): 1748 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.51–7.49 (m, 1 H), 7.48–7.38 (m, 4 H), 7.07 (t, *J* = 6.0 Hz, 1 H), 6.72 (d, *J* = 5.0 Hz, 1 H), 4.71 (t, *J* = 7.5 Hz, 1 H), 4.05 (t, *J* = 9.0 Hz, 1 H), 3.69–3.60 (m, 1 H), 3.24, 3.20 (dd, *J* = 8.0, 7.5 Hz, 1 H), 2.85, 2.81 (dd, *J* = 16.5, 16.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.0, 144.2, 139.2, 138.1, 134.3, 129.4, 128.8, 127.8, 126.8, 122.9, 117.5, 70.5, 37.4, 27.8.

LRMS (EI, 70 eV): *m*/*z* (%) = 268 (M^+, 38), 223 (33), 165 (11), 43 (100).

9-(4-Tolyl)-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-one (2f)
White solid; mp 151.1–152.8 °C.

IR (KBr): 1748 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.30–7.26 (m, 2 H), 7.26–7.20 (m, 2 H), 7.20–7.17 (m, 3 H), 6.99 (d, *J* = 7.5 Hz, 1 H), 4.72 (t, *J* = 9.0 Hz, 1 H), 4.04 (t, *J* = 7.5 Hz, 1 H), 3.48–3.40 (m, 1 H), 3.06, 3.01 (dd, *J* = 6.5, 6.5 Hz, 1 H), 2.88, 2.86 (dd, *J* = 15.5, 15.5 Hz, 1 H), 2.42 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.3, 147.6, 138.4, 136.1, 135.5, 131.2, 129.7, 129.2, 128.7, 128.0, 127.2, 121.8, 71.1, 35.6, 33.1, 21.4.

LRMS (EI, 70 eV): *m*/*z* (%) = 276 (M^+, 100), 231 (98), 217 (58), 202 (60), 101 (26).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{16}O_2$: 276.1150; found: 276.1149.

9-(3-Tolyl)-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-one (2g)
White solid; mp 152.2–153.0 °C.

IR (KBr): 1748 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.24 (m, 3 H), 7.22–7.19 (m, 1 H), 7.18–7.09 (m, 3 H), 6.97 (d, *J* = 8.0 Hz, 1 H), 4.72 (t, *J* = 7.5 Hz, 1 H), 4.03 (t, *J* = 8.0 Hz, 1 H), 3.48–3.40 (m, 1 H), 3.06, 3.03, (dd, *J* = 6.5, 6.5 Hz, 1 H), 2.88, 2.85 (dd, *J* = 15.5, 15.5 Hz, 1 H), 2.38 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.2, 147.5, 137.4, 136.0, 135.4, 134.2, 129.8, 129.3, 129.2, 128.0, 127.8, 127.2, 122.0, 71.7, 35.6, 33.1, 21.4.

LRMS (EI, 70 eV): *m*/*z* (%) = 276 (M^+, 100), 231 (93), 215 (49), 202 (62), 101 (23).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{16}O_2$: 276.1150; found: 276.1145.

9-(2-Tolyl)-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-one (2h)
White solid; mp 126.9–128.2 °C.

IR (KBr): 1748 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.32–7.26 (m, 4 H), 7.22–7.14 (m, 2 H), 6.91 (d, *J* = 7.5 Hz, 1 H), 6.80 (d, *J* = 8.0 Hz, 1 H), 4.74 (t, *J* = 6.5 Hz, 1 H), 4.07 (t, *J* = 9.0 Hz, 1 H), 3.51–3.46 (m, 1 H), 3.09,

3.08 (dd, *J* = 3.0, 3.5 Hz, 1 H), 2.92, 2.88 (dd, *J* = 16.0, 15.0 Hz, 1 H), 2.24 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.1, 168.0, 146.2, 137.0, 135.4, 135.2, 135.1, 134.7, 134.0, 131.2, 130.2, 130.1, 130.0, 129.9, 129.7, 128.6, 128.5, 128.2, 128.2, 128.0, 127.9, 127.7, 127.5, 126.5, 125.8, 125.4, 123.0, 122.7, 71.4, 35.3, 32.8, 19.5.

LRMS (EI, 70 eV): *m*/*z* (%) = 276 (M^+, 74), 231 (100), 215 (84), 202 (63), 101 (21).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{16}O_2$: 276.1150; found: 276.1148.

9-(4-Methoxyphenyl)-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-one (2i)
White solid; mp 130.0–131.5 °C.

IR (KBr): 1748 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32–7.26 (m, 4 H), 7.20–7.17 (m, 1 H), 7.01 (d, *J* = 7.5 Hz, 1 H), 6.96 (d, *J* = 7.5 Hz, 2 H), 4.72 (t, *J* = 8.5 Hz, 1 H), 4.04 (t, *J* = 8.5 Hz, 1 H), 3.86 (s, 3 H), 3.45–3.40 (m, 1 H), 3.05, 3.02 (dd, *J* = 6.5, 6.5 Hz, 1 H), 2.88, 2.85 (dd, *J* = 15.5, 15.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.4, 159.9, 147.4, 136.2, 135.6, 131.5, 129.8, 129.3, 128.0, 127.2, 126.2, 121.4, 113.2, 71.1, 55.2, 35.7, 33.1.

LRMS (EI, 70 eV): *m*/*z* (%) = 292 (M^+, 100), 261 (10), 247 (62), 203 (32), 189 (39).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{16}O_3$: 292.1099; found: 292.1105.

9-(2-Methoxyphenyl)-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-one (2j)
Colorless oil.

IR (KBr): 1748 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42–7.39 (m, 1 H), 7.29–7.26 (m, 2 H), 7.14–7.09 (m, 1 H), 7.00–6.91 (m, 4 H), 4.70 (t, *J* = 8.5 Hz, 1 H), 4.05 (t, *J* = 9.0 Hz, 1 H), 3.55–3.38 (m, 1 H), 3.07–3.02 (m, 1 H), 3.00–2.86 (m, 1 H), 2.04 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.1, 168.3, 167.9, 157.8, 156.4, 144.5, 142.9, 135.5, 135.4, 135.3, 134.8, 131.9, 130.0, 129.8, 129.6, 129.6, 129.4, 128.6, 128.0, 127.5, 127.3, 127.0, 124.0, 123.4, 123.0, 122.8, 120.4, 120.1, 111.1, 111.0, 71.2, 71.2, 55.7, 55.5, 35.4, 35.3, 32.9, 32.8.

LRMS (EI, 70 eV): *m*/*z* (%) = 292 (M^+, 100), 261 (41), 247 (31), 231 (43), 215 (23), 202 (36), 101 (22).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{16}O_3$: 292.1099; found: 292.1100.

9-(4-Iodophenyl)-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-one (2k)
Yellow solid; mp 223.7–225.1 °C.

IR (KBr): 1748 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 8.5 Hz, 2 H), 7.33–7.28 (m, 2 H), 7.18 (t, *J* = 8.5 Hz, 1 H), 7.06–7.03 (m, 2 H), 6.93 (d, *J* = 8.0 Hz, 1 H), 4.73 (t, *J* = 8.5 Hz, 1 H), 4.04 (t, *J* = 8.0 Hz, 1 H), 3.48–3.40 (m, 1 H), 3.07, 3.04 (dd, *J* = 7.0, 7.0 Hz, 1 H), 2.88, 2.85 (dd, *J* = 16.0, 15.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.1, 146.1, 137.0, 135.4, 133.7, 131.7, 130.1, 128.9, 128.2, 127.4, 122.5, 94.8, 71.2, 35.6, 32.9.

LRMS (EI, 70 eV): *m*/*z* (%) = 388 (M^+, 100), 231 (34), 217 (39), 202 (73), 101 (30).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{13}IO_2$: 387.9960; found: 387.9956.

9-(2-Bromophenyl)-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-one (2l)
Pale–yellow solid; mp 137.5–139.0 °C.

IR (KBr): 1748 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.48–7.40 (m, 8 H), 4.31–4.27 (m, 1 H), 4.22–4.17 (m, 1 H), 4.05–4.02 (m, 1 H), 3.94, 3.92 (dd, *J* = 3.5, 5.0 Hz, 1 H), 3.80, 3.79 (dd, *J* = 8.5, 8.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.9, 145.5, 135.4, 135.1, 134.4, 132.9, 132.5, 131.6, 129.9, 128.2, 127.4, 126.9, 124.2, 123.8, 122.1, 71.4, 35.3, 32.7.

LRMS (EI, 70 eV): *m*/*z* (%) = 342 (M^+ + 2, 1), 340 (M^+, 1), 261 (100), 233 (10), 215 (15), 202 (68).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{13}BrO_2$: 340.0099; found: 340.0093.

9-(4-Fluorophenyl)-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-one (2m)
Yellow solid; mp 175.1–176.9 °C.

IR (KBr): 1748 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.28 (m, 4 H), 7.26–7.24 (m, 1 H), 7.21–7.10 (m, 2 H), 6.94 (d, *J* = 7.5 Hz, 1 H), 4.74 (t, *J* = 9.0 Hz, 1 H), 4.05 (t, *J* = 8.5 Hz, 1 H), 3.49–3.41 (m, 1 H), 3.07, 3.04 (dd, *J* = 6.5, 7.0 Hz, 1 H), 2.89, 2.86 (dd, *J* = 15.5, 15.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.2, 162.9 (d, *J* = 246.5 Hz, 1 C), 146.3, 135.7, 135.4, 129.9, 128.9, 128.1, 127.3, 122.4, 115.0, 114.9, 71.2, 35.6, 32.9.

LRMS (EI, 70 eV): *m*/*z* (%) = 280 (M^+, 100), 249 (31), 221 (74).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{13}FO_2$: 280.0900; found: 280.0899.

9-(4-Acetylphenyl)-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-one (2n)
White solid; mp 170.9–172.1 °C.

IR (KBr): 1741, 1678 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.20 (d, *J* = 8.5 Hz, 2 H), 7.41–7.39 (m, 2 H), 7.34–7.29 (m, 2 H), 7.19–7.16 (m, 1 H), 6.87 (d, *J* = 7.5 Hz, 1 H), 4.75 (t, *J* = 7.5 Hz, 1 H), 4.06 (t, *J* = 9.0 Hz, 1 H), 3.51–3.43 (m, 1 H), 3.09, 3.07 (dd, *J* = 6.5, 6.5 Hz, 1 H), 2.89, 2.88 (dd, *J* = 16.0, 15.0 Hz, 1 H), 2.65 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 197.8, 168.1, 146.1, 136.8, 135.4, 134.7, 130.1, 128.8, 128.4, 128.2, 128.1, 127.6, 127.4, 123.0, 71.3, 35.6, 32.9, 26.6.

LRMS (EI, 70 eV): *m*/*z* (%) = 304 (M^+, 100), 289 (72), 261 (12), 231 (48), 217 (35), 202 (62), 101 (30).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{20}H_{16}O_3$: 304.1099; found: 304.1097.

9-(3-Acetylphenyl)-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-one (2o)
White solid; mp 170.0–171.6 °C.

IR (KBr): 1740, 1675 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.04–8.02 (m, 1 H), 7.90–7.83 (m, 1 H), 7.59–7.53 (m, 2 H), 7.37–7.29 (m, 2 H), 7.19–7.16 (m, 1 H), 6.69 (d, *J* = 9.0 Hz, 1 H), 4.74 (t, *J* = 8.5 Hz, 1 H), 4.06 (t, *J* = 6.5 Hz, 1 H), 3.52–3.44 (m, 1 H), 3.09, 3.06 (dd, *J* = 6.5, 6.5 Hz, 1 H), 2.91, 2.88 (dd, *J* = 15.5, 16.0 Hz, 1 H), 2.61 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 197.7, 168.0, 146.0, 139.4, 136.9, 135.3, 135.2, 130.4, 130., 128.8, 128.2, 128.0, 127.9, 127.6, 127.4, 123.0, 71.3, 35.5, 32.8, 26.6.

LRMS (EI, 70 eV): *m*/*z* (%) = 304 (M^+, 100), 289 (65), 261 (13), 217 (37), 202 (56), 101 (43).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{20}H_{16}O_3$: 304.1099; found: 304.1098.

9-(3-Nitrophenyl)-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-one (2p)
Yellow solid; mp 203.0–204.3 °C.

IR (KBr): 1772, 1732, 1719 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.32–8.28 (m, 1 H), 8.18–8.10 (m, 1 H), 7.74–7.61 (m, 2 H), 7.36–7.31 (m, 2 H), 7.22–7.19 (m, 1 H), 6.86 (d, *J* = 8.0 Hz, 1 H), 4.77 (t, *J* = 8.5 Hz, 1 H), 4.09 (t, *J* = 9.0 Hz, 1 H), 3.52–3.48 (m, 1 H), 3.12, 3.00 (dd, *J* = 6.5, 6.5 Hz, 1 H), 2.93, 2.90 (dd, *J* = 16.0, 15.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.9, 148.0, 144.4, 135.9, 135.3, 134.8, 130.4, 129.1, 128.9, 128.5, 128.4, 127.6, 127.5, 123.9, 123.5, 71.4, 35.5, 32.7.

LRMS (EI, 70 eV): *m*/*z* (%) = 307 (M^+, 88), 263 (25), 215 (29), 202 (100), 101 (21).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{13}NO_4$: 307.0845; found: 307.0848.

9-(Thiophen-2-yl)-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-one (2q)
Yellow solid; mp 128.0–130.1 °C.

IR (KBr): 1748 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.49 (d, *J* = 5.0 Hz, 1 H), 7.33–7.30 (m, 1 H), 7.29–7.24 (m, 3 H), 7.24–7.22 (m, 1 H), 7.14 (d, *J* = 9.0 Hz, 1 H), 4.71 (t, *J* = 8.5 Hz, 1 H), 4.04 (t, *J* = 8.5 Hz, 1 H), 3.47 (m, 1 H), 3.03, 3.01 (dd, *J* = 7.5, 6.5 Hz, 1 H), 2.87, 2.84 (dd, *J* = 15.0, 15.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.8, 140.1, 135.9, 133.9, 130.5, 129.1, 127.9, 127.4, 127.3, 126.7, 124.1 71.0, 36.0, 32.8.

LRMS (EI, 70 eV): *m*/*z* (%) = 268 (M^+, 84), 223 (100), 209 (50), 165 (23).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{16}H_{12}O_2S$: 268.0558; found: 268.0554.

9-Phenyl-2-propyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindol-1-one (2r)
Yellow oil.

IR (KBr): 1675 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42–7.37 (m, 3 H), 7.27–7.21 (m, 4 H), 7.14 (t, *J* = 7.5 Hz, 1 H), 6.92 (d, *J* = 8.0 Hz, 1 H), 3.74–3.68 (m, 1 H), 3.37–3.32 (m, 1 H), 3.23 (d, *J* = 8.5 Hz, 1 H), 3.15–3.11 (m, 2 H), 3.06–3.02 (m, 1 H), 3.04, 2.82–2.79 (m, 1 H), 1.60–1.55 (m, 2 H), 0.89 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.6, 140.3, 136.6, 135.6, 135.4, 130.2, 129.7, 128.3, 128.2, 127.7, 127.7, 127.6, 60.4, 50.9, 34.0, 32.4, 20.6, 11.4.

LRMS (EI, 70 eV): *m*/*z* (%) = 304 (72), 303 (M^+, 100), 302 (27), 274 (74), 260 (47), 231 (57), 215 (30), 202 (54).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{21}H_{21}NO$: 303.1623; found: 303.1622.

2-Benzyl-9-phenyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindol-1-one (2s)
Yellow solid; mp 135.8–138.0 °C.

IR (KBr): 1674 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.45–7.33 (m, 3 H), 7.32–7.28 (m, 4 H), 7.28–7.20 (m, 5 H), 7.18–7.12 (m, 1 H), 6.93 (d, *J* = 7.5 Hz, 1 H), 4.65 (d, *J* = 14.5 Hz, 1 H), 4.37 (d, *J* = 15.0 Hz, 1 H), 3.60 (t, *J* = 9.0 Hz, 1 H), 3.12–3.02 (m, 1 H), 3.01–2.96 (m, 2 H), 2.78, 2.75 (dd, *J* = 5.0, 16.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.5, 141.0, 136.5 (2 C), 135.6, 135.4, 130.2, 129.2, 128.6, 128.4, 128.3, 128.2, 127.7, 127.6, 127.5, 126.9, 56.3, 47.0, 33.9, 32.2.

LRMS (EI, 70 eV): *m*/*z* (%) = 351 (M^+, 14), 351 (73), 350 (33), 349 (100), 258 (62), 245 (57), 215 (42), 202 (26), 91 (50).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{25}H_{21}NO$: 351.1623; found: 351.1620.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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