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Iodide-Catalyzed Halocyclization/Cycloaddition/Elimination Cascade Reaction

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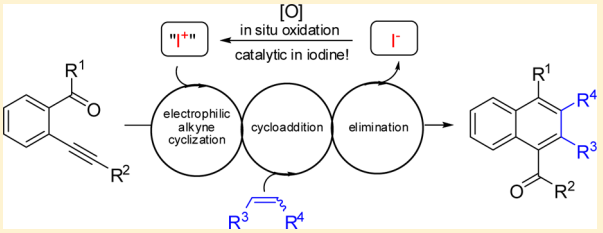
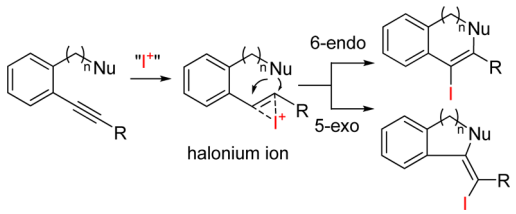
Supporting Information

ABSTRACT: An iodocyclization reaction of *o*-alkynylphenyl carboxaldehydes is reported that is truly catalytic with respect to the electrophilic iodine source. With a combination of tetrabutylammonium iodide (TBAI), Oxone as non-nucleophilic and easy to handle co-oxidant, and fluorinated protic solvents, highly substituted 1-naphthalenones could be prepared in high yields of up to 91%.



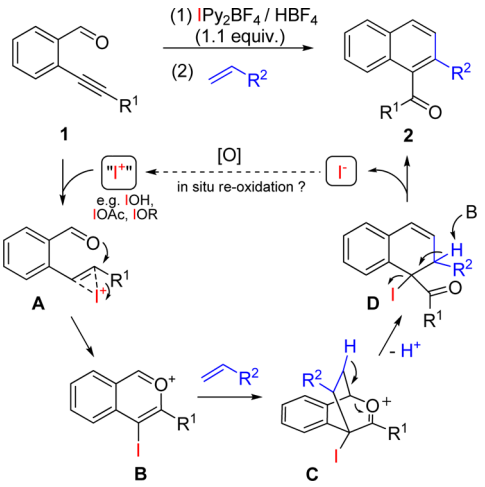
The electrophilic iodine-induced cyclization of *ortho*-substituted arylalkynes is a powerful method for the construction of benzannulated carbo- and heterocycles.[1] The electrophilic iodine atom activates the alkyne through formation of an iodonium ion that is attacked by carbon-,[2] nitrogen-,[3] oxygen-,[4] sulfur-,[5] or selenium-containing nucleophiles[6] to give a highly functionalized carbo- or heterocycle (Scheme 1). As electrophilic iodine sources mostly NIS, IPy_2BF_4 (Barluenga's reagent), ICl, or I_2 are utilized. These alkyne-based halocyclization reactions are useful and metal-free alternatives to gold-catalyzed alkyne cyclizations.[7] However, their major drawback is still the need for stoichiometric amounts of the halogen source. Of course, if the iodine atom is supposed to be part of the final reaction product, as it is in many cases, the use of stoichiometric amounts of these iodination reagents is mandatory. However, one could in principle imagine halocyclization-based cascade reactions, where the iodinated intermediate reacts further under loss of iodide, for example, through a subsequent substitution or elimination process. In this case, only catalytic amounts of an iodide source would be necessary if a co-oxidant is present in the reaction mixture.

Scheme 1. Electrophilic Halogen-Induced Cyclization of Arylalkynes through a Halonium Ion Intermediate



In 2006, Barluenga and co-workers reported the reaction of *o*-alkynylarenecarboxaldehydes **1** with stoichiometric amounts of IPy_2BF_4 (Scheme 2).[4g] In this reaction, a benzo[*c*]pyrillium ion **B** is formed through intramolecular ring closure of the iodonium ion **A**. In a consecutive step, in situ formed **B** is trapped by an alkene. A cycloaddition yields intermediate **C** and subsequently **D**, which readily eliminates an iodide anion to give the desired 2-substituted 1-naphthalenone **2**. Similar substituted naphthalenones could so far only be observed by Au(III)-catalyzed benzannulations between *o*-alkynylbenzaldehydes and alkynes.[8a,b] However, since in this transformation the iodine atom is not part of the final product this transformation could be conducted much more efficient with only catalytic amounts of an iodine source, if the electrophilic iodine atom can be recovered in situ by oxidation.

Scheme 2. Electrophilic Halogen-Induced Cyclization of *o*-Alkynylarenecarboxaldehydes[4g]



The in situ oxidation of iodide salts to electrophilic iodine species such as (hypo)iodites and their subsequent use as environmental benign catalysts in oxidative C−C and C−X bond-forming reactions has been investigated intensively

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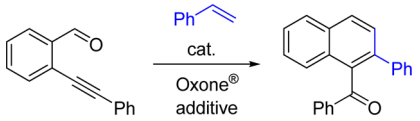
Table 1. Optimization Studies[a]



1a **2a**

entry	cat (mol %)	additive (equiv)	solvent	T (°C)	time (h)	yield of **2a** (%)
1	TBAI (10)	AcOH (3)	MeCN	70	72	29
2	TBAI (10)		MeCN	70	72	traces
3	TBAI (20)	AcOH (3)	MeCN	70	72	31
4	TBAI (20)	AcOH (3)	MePh	70	72	0
5	TBAI (20)	AcOH (3)	DCM	rt	72	0
6	TBAI (20)	AcOH (3)	DMF	70	72	0
7	TBAI (20)	AcOH (3)	TFE	70	2	72
8	KI (20)	AcOH (3)	TFE	70	21	65
9	I_2 (20)	AcOH (3)	TFE	70	21	49
10	I_2 (120)	AcOH (3)	TFE	70	3	12
11	TBABr (20)	AcOH (3)	TFE	70	72	0
12	TBAI (20)		TFE	70	21	64
13	TBAI (20)	NaOAc (3)	TFE	70	12	64
14	TBAI (20)	TFA (1)	TFE	70	12	23
15	TBAI (20)	$HBF_4{\cdot}OEt_2$ (1)	TFE	70	12	traces
16	TBAI (20)	CSA (3)	TFE	70	12	22
17	TBAI (20)	AcOH (3)	HFIP	50	15	24
18	**TBAI (20)**		**HFIP**	**50**	**3**	**91**

[a]General reaction conditions: 0.1 mmol of **1a**, 0.2 mmol (2 equiv) of styrene, catalyst, additive, and 0.15 mmol (1.5 equiv) of Oxone in 1 mL of solvent. [b]0.3 mmol (3 equiv) of Oxone. [c]Isolated yield after flash column chromatography.

recently.[9,10] In this context, our group has developed a direct oxidative amination protocol for benzo[*d*]oxazoles using simple tetrabutylammonium iodide (TBAI) and aqueous solutions of *tert*-butyl hydroperoxide (TBHP) or hydrogen peroxide as co-oxidants.[11] In this paper, we report the first application of (hypo)iodite catalysis in Barluenga's iodocyclization/cyclo-addition/elimination cascade reaction.[12,13]

TBHP, which was intensively used as co-oxidant in previous (hypo)iodite catalyzed reactions, seemed to be a nonsuitable co-oxidant due to the nucleophilic properties of the emerging *t*-BuO^- anion which could undergo undesired nucleophilic addition to the benzo[*c*]pyrilium intermediate **B**. Therefore, a co-oxidant was needed that, after its reduction, yields a non-nucleophilic anion. Here, Oxone ($KHSO_5/KHSO_4/K_2SO_4$) was chosen as an alternative because of the non-nucleophilic character of the resulting KSO_4^- anion. Furthermore, Oxone is, just as TBHP, cheap and easy to handle.[14] In a first experiment, we were pleased to find that with Oxone in acetonitrile and acetic acid as an additive the desired 1-naphthalenone **2a** could be isolated, although in only 29% yield (Table 1, entry 1). Without an acid additive only traces of **2a** could be observed (entry 2). Increasing catalyst loading from 10 to 20 mol % increased the yield of **2a** slightly to 31% (entry 3). In aromatic and chlorinated solvents as well as in other polar aprotic solvents such as DMF, the reaction did not proceed at all (entry 4−6).

However we were pleased to find that in TFE (2,2,2-trifluoroethanol) yields increased significantly to 72% (entry 7).

Other iodine sources were not as effective as TBAI, and with the corresponding bromine salt (TBABr) no reaction was observed at all (entries 8−11). Next, we tested the influence of the additive. In TFE we found that the reaction gave **2a** still in good yields even without addition of acetic acid. Addition of NaOAc was also effective (entries 12 and 13). With stronger Brønsted acids such as TFA, CSA, or HBF_4, yields dropped significantly to 22−23% (entries 14−16). Finally we tested HFIP (1,1,1,3,3,3-hexafluoro-2-propanol) as an alternative fluorinated protic solvent. When AcOH was added to the reaction mixture the yield was significantly lower compared to TFE (24%, entry 17). However, due to the remarkable low pK_a of HFIP (9.3) we thought an acidic additive might be unnecessary, and therefore, we repeated the experiment, this time without an additional Brønsted acid. To our great delight, we observed that the reaction was very clean and **2a** could be isolated in excellent yields of 91% (entry 18). We propose that the significant influence of the solvent and/or acetic acid might be the result of stable in situ formed hypoiodite species such as AcOI or $(CF_3)_2HCOI$.

With these optimized reaction conditions in hand, we next elucidated the substrate scope of the iodocyclization/cyclo-addition/elimination cascade reaction. First, we reacted various *o*-alkynylphenyl carboxaldehydes **1** with styrene (Table 2). Electron-rich *o*-alkynylaryl aldehydes such as **1b** could be transformed into the corresponding 1-naphthalenone **2b** in 82% yield. Remarkably, no significant iodination of the arene was observed.[15] Furthermore, various alkyl-substituted alkynyl derivatives **1c−f** were tested. All gave the corresponding 1-napthalenones **2c−f** in good yields between 60% and 81% after short reaction times. The *t*-Bu-substituted alkyne **1g** gave **2g** in 85% yield. An alkynyl ester was tolerated as well giving **2h** in 30% yield. With example **2i** we could surprisingly show that even *o*-alkynyl substituted acetophenones gave the cyclized 1-naphthalenone in 53% yield after 5 h. Here no significant Oxone-mediated oxidation of the ketone to the corresponding dioxirane was observed.

However nitrogen-containing heterocycles, such as nicotinaldehyde are not tolerated, most likely due to an undesired *N*-oxidation.

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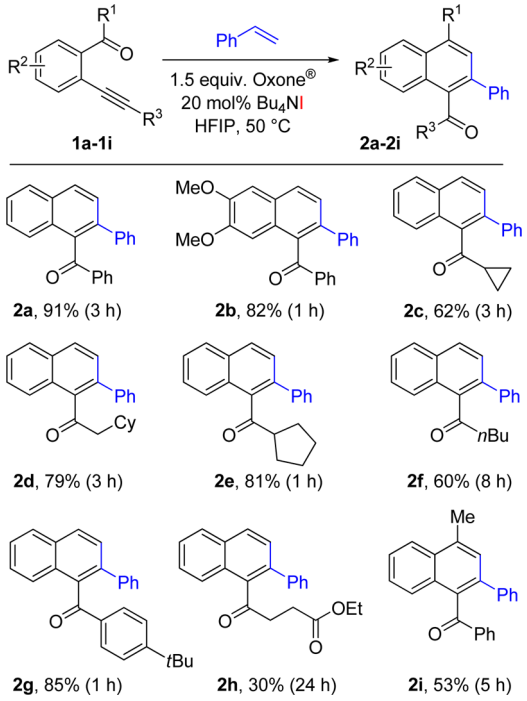
Table 2. Reaction of Various *o*-Alkynylarenecarboxaldehydes and -ketones 1 with Styrene[a]



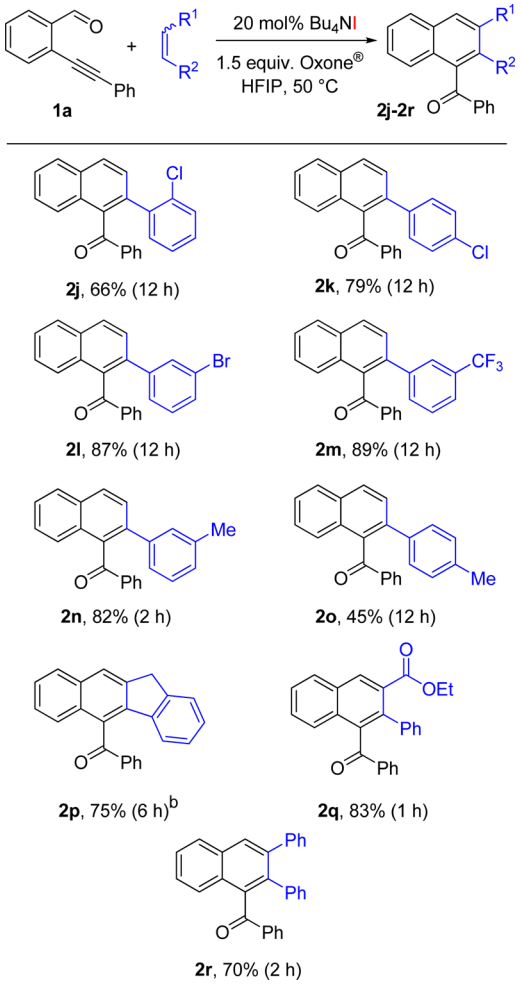
[a]General reaction conditions: 0.1 mmol of **1a**, 0.2 mmol (2 equiv) of styrene, TBAI, and Oxone in 1 mL of 1,1,1,3,3,3-hexafluoro-2-propanol. The given equivalents are related to **1**.

Next we elaborated the influence of various alkenes on the reaction with **1a** (Table 3). A variety of halogen-substituted styrenes (2-Cl, 4-Cl, and 3-Br) could be reacted with **1a** giving the desired products **2j–l** in 66–87% yield. 3-CF_3-substituted styrene gave **2m** in 89% yield.

3-Methylstyrene also reacted smoothly to give **2n** in 82% yield. However, with 4-methylstyrene as dienophile yields dropped significantly to 45% (**2o**). In general, highly electron-rich methoxy-substituted styrenes gave rather complex reaction mixtures. Here, only traces of the desired product could be observed. However, indene gave **2p** in 75% yield, and ethyl cinnamate gave the 3-carboxylated 1-naphthalenone **2q** in 83% yield. Stilbene gave naphthalenone **2r** in 70% yield. Alkenes that do not contain an aryl substituent, such as cyclohexene, do not give the desired 1-naphthalenones. Interestingly, undesired oxidation products such as epoxides or carboxylic acids could not be observed in significant amounts. Furthermore, it is worth mentioning that no undesired iodine-containing starting materials were observed in significant amounts. This undesired halogenation is one of the major side reactions in halocyclizations in which stoichiometric amounts of the electrophilic iodine source must be used.

In summary, we have developed the first truly catalytic iodonium-mediated benzannulation protocol. The key to the success of this efficient iodine-catalyzed transformation was the use of fluorinated protic solvents, in particular, HFIP and Oxone as the co-oxidant. With only 20 mol % of TBAI, a variety of highly functionalized 1-naphthalenones could be isolated in excellent yields of up to 91%. On the basis of this novel catalytic procedure, many other truly catalytic iodonium-initiated cyclization/elimination cascades should be possible.

Table 3. Reaction of Various Alkenes with 2-(Phenylethynyl)benzaldehyde 1a[a]



[a]General reaction conditions: 0.1 mmol of **1a**, 0.2 mmol (2 equiv) of dienophile, TBAI, and Oxone in 1 mL of 1,1,1,3,3,3-hexafluoro-2-propanol. [b]0.3 mmol (3 equiv) of 1*H*-indene was added dropwise over 6 h. The given equivalents are related to **1a**.

EXPERIMENTAL SECTION

^{1}H NMR spectra were recorded on a 400 MHz instrument. Chemical shifts for ^{1}H NMR were reported as δ (parts per million) relative to the signal of $CHCl_3$ at 7.26(s) ppm. Chemical shifts for ^{13}C NMR were reported as δ (parts per million) relative to the $CDCl_3$ triplet at 77.0 ppm. The following abbreviations were used to describe splitting patterns: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constants *J* are given in Hz. Mass spectra were recorded using the EI or FAB method. High-resolution mass spectra were recorded using the ESI method with a FT-ICR mass analyzer.

Unless otherwise stated, all chemicals were used as received from a commercial supplier. Solvents for flash column and thin-layer chromatography including cyclohexane, ethyl acetate, toluene, and diethyl ether were distilled prior to use. Thin-layer chromatography was performed on fluorescence indicator marked precoated silica gel 60 plates and visualized by either UV light (254 nm/366 nm) or stains of 2,4-dinitrophenylhydrazine or potassium permanganate. Flash column chromatography was performed on silica gel (0.040–0.063 mm). For air- or moisture-sensitive reactions, standard Schlenk techniques were applied under an argon atmosphere.

Compounds **1a–i** were prepared following the procedure reported by Larock and co-workers.[16a] To a solution of the appropriate 2-bromobenzaldehyde (2.00 mmol, 1.0 equiv) and alkyne (2.40 mmol, 1.2 equiv) in Et_3N (8 mL) was added $(PPh_3)_2PdCl_2$ (2 mol %) under

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an argon atmosphere. After being stirred for 5 min at rt, CuI (1 mol %) was added, and the resulting dark solution was heated to 50 °C until TLC analysis indicated complete consumption of the starting material. The reaction mixture was diluted with water and extracted with DCM (3 ×). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel to afford **1a−i**. The resulting compounds **1a−c,e−g,i** were in accordance with the known literature data.[16]

2-(3-Cyclohexylprop-1-ynyl)benzaldehyde (1d). Yield: 191 mg (42%); brown liquid; toluene/cyclohexane (1:20). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 10.55 (d, $^4J_{HH}$ = 0.8 Hz, 1H), 7.88 (dt, $^3J_{HH}$ = 7.7 Hz, $^4J_{HH}$ = 0.9 Hz, 1H), 7.52−7.49 (m, 2H), 7.41−7.35 (m, 1H), 2.38 (d, $^3J_{HH}$ = 6.6 Hz, 2H), 1.89−1.85 (m, 2H), 1.78−1.73 (m, 2H), 1.71−1.55 (m, 2H), 1.34−1.03 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 192.2, 136.0, 133.7, 133.3, 128.0, 127.8, 126.9, 97.1, 77.2, 37.4, 32.8, 27.4, 26.2, 26.1. HRMS (ESI): calcd for $C_{16}H_{19}O$ m/z 227.143042, found 227.142894.

Ethyl 5-(2-Formylphenyl)pent-4-ynoate (1h). Yield: 207 mg (45%); yellow oil; EtOAc/cyclohexane (1:10); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 10.49 (d, $^4J_{HH}$ = 0.8 Hz, 1H), 7.89−7.87 (m, 1H), 7.53−7.47 (m, 2H), 7.41−7.37 (m, 1H), 4.19 (q, $^3J_{HH}$ = 7.1 Hz, 2H), 2.80 (t, $^3J_{HH}$ = 7.2 Hz, 2H), 2.65 (t, $^3J_{HH}$ = 7.0 Hz, 2H), 1.27 (t, $^3J_{HH}$ = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 191.9, 171.6, 136.1, 133.6, 133.3, 128.2, 127.2, 127.0, 95.7, 76.9, 60.8, 33.3, 15.6, 14.2. HRMS (ESI): calcd for $C_{14}H_{14}O_3Na$ m/z 253.083515, found 253.083394.

General Procedure for the Preparation of the 1-Naphthalenone Derivatives (Tables 2 and 3). A solution of the corresponding 2-alkynylbenzaldehyde **1** (0.10 mmol, 1 equiv), the appropriate alkene (0.20 mmol, 2 equiv), and TBAI (7.40 mg, 0.02 mmol, 20 mol %) in HFIP (1 mL) was heated to 50 °C, before Oxone (92.3 mg, 0.15 mmol, 1.5 equiv) was added. The resulting inhomogeneous mixture was stirred at 50 °C until the starting material was completely converted. The reaction mixture was allowed to cool to rt and then treated with saturated aqueous solutions of $Na_2S_2O_3$ and $NaHCO_3$. The aqueous phase was extracted with EtOAc (3×), and the combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel to afford **2a−r**.

*Phenyl(2-phenylnaphthalen-1-yl)methanone (**2a**).* Yield: 28.1 mg (91%); white solidified oil; toluene/cyclohexane (1:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.02 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 7.95 (d, $^3J_{HH}$ = 8.0 Hz, 1H), 7.73 (d, $^3J_{HH}$ = 8.6 Hz, 1H), 7.63−7.60 (m, 2H), 7.58 (d, $^3J_{HH}$ = 8.5 Hz, 1H), 7.55−7.50 (m, 1H), 7.48−7.44 (m, 1H), 7.41−7.37 (m, 1H), 7.36−7.33 (m, 2H), 7.25−7.20 (m, 4H), 7.19−7.15 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 199.6, 140.2, 137.9, 137.4, 135.7, 133.2, 132.4, 130.7, 129.6, 129.5 (2×), 128.3, 128.2, 128.1, 127.6, 127.4, 127.2, 126.3, 125.5. MS (EI): m/z = 308.2 $[M]^+$.[4b]

*(2,3-Dimethoxy-6-phenylnaphthalen-5-yl)(phenyl)methanone (**2b**).* Yield: 30.2 mg (82%); light yellow solidified oil; EtOAc/cyclohexane (1:5). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.86 (d, $^3J_{HH}$ = 8.3 Hz, 1H), 7.60−7.57 (m, 2H), 7.42 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 7.39−7.35 (m, 1H), 7.32−7.29 (m, 2H), 7.23−7.11 (m, 6H), 7.04 (s, 1H), 4.03 (s, 3H), 3.81 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 200.2, 150.4, 149.7, 140.6, 138.1, 136.3, 134.1, 133.0, 129.4, 128.5, 128.1 (2×), 127.9, 127.1, 126.3, 125.8, 106.4, 104.1, 55.9, 55.8. MS (FAB) m/z = 369.2 $[M + H]^+$.[8a]

*Cyclopropyl(2-phenylnaphthalen-1-yl)methanone (**2c**).* Yield: 16.9 mg (62%); colorless oil; EtOAc/cyclohexane (1:25). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.95 (d, $^3J_{HH}$ = 8.5 Hz, 1H), 7.92−7.87 (m, 2H), 7.57−7.51 (m, 3H), 7.51−7.37 (m, 5H), 1.90−1.84 (m, 1H), 1.14−1.11 (m, 2H), 0.74−0.69 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 209.1, 140.6, 138.8, 136.7, 132.6, 129.7, 129.4, 129.2, 128.4, 128.1, 127.7, 127.6, 127.3, 126.2, 125.3, 24.7, 13.1. HRMS (ESI): calcd for $C_{20}H_{16}ONa$ m/z 295.109336, found 295.109561.

*2-Cyclohexyl-1-(2-phenylnaphthalen-1-yl)ethanone (**2d**).* Yield: 25.9 mg (79%); light yellow solidified oil; EtOAc/cyclohexane (1:70). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.94−7.88 (m, 2H), 7.84−7.80 (m, 1H), 7.57−7.50 (m, 3H), 7.47−7.37 (m, 5H), 2.19 (d, $^3J_{HH}$ = 6.4 Hz, 2H), 1.86−1.75 (m, 1H), 1.57−1.51 (m, 5H), 1.25−1.14 (m, 2H), 1.07−0.99 (m, 1H), 0.67−0.57 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 209.1, 140.3, 138.5, 135.9, 132.5, 129.6, 129.1 (2×), 128.6, 128.2, 127.8, 127.5, 127.3, 126.2, 124.8, 52.7, 33.0, 32.8, 26.1, 26.0. HRMS (ESI): calcd for $C_{24}H_{24}ONa$ m/z 351.171936, found 351.172170.

*Cyclopentyl(2-phenylnaphthalen-1-yl)methanone (**2e**).* Yield: 24.3 mg (81%); light yellow oil; EtOAc/cyclohexane (1:70). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.94 (d, $^3J_{HH}$ = 8.3 Hz, 1H), 7.92−7.88 (m, 1H), 7.85−7.81 (m, 1H), 7.57−7.50 (m, 3H), 7.49−7.37 (m, 5H), 2.72−2.64 (m, 1H), 1.75−1.70 (m, 2H), 1.66−1.59 (m, 2H), 1.43−1.27 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 212.5, 140.5, 138.8, 136.2, 132.5, 129.6 (2×), 129.3, 128.7, 128.1, 127.8, 127.5, 127.3, 126.2, 125.2, 53.6, 29.5, 26.0. HRMS (ESI): calcd for $C_{22}H_{20}ONa$ m/z 323.140636, found 323.140649.

*1-(2-Phenylnaphthalen-1-yl)pentan-1-one (**2f**).* Yield: 17.3 mg (60%); light yellow oil; EtOAc/cyclohexane (1:70). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.94 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 7.92−7.89 (m, 1H), 7.83−7.80 (m, 1H), 7.57−7.51 (m, 3H), 7.47−7.38 (m, 5H), 2.28 (t, $^3J_{HH}$ = 7.4 Hz, 2H), 1.47−1.40 (m, 2H), 1.13−1.04 (m, 2H), 0.70 (t, $^3J_{HH}$ = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 210.0, 140.4, 138.5, 135.9, 132.5, 129.4, 129.2, 128.7, 128.2, 127.9, 127.4, 127.3, 126.3, 124.9, 119.6, 44.9, 25.7, 22.0, 13.6. MS (FAB): m/z = 289.1 $[M + H]^+$.[4b]

*(4-tert-Butylphenyl)(2-phenylnaphthalen-1-yl)methanone (**2g**).* Yield: 31.0 mg (85%); light yellow solidified oil; EtOAc/cyclohexane (1:30). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.00 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 7.93 (d, $^3J_{HH}$ = 8.1 Hz, 1H), 7.71 (d, $^3J_{HH}$ = 8.5 Hz, 1H), 7.58−7.55 (m, 3H), 7.53−7.49 (m, 1H), 7.46−7.42 (m, 1H), 7.39−7.36 (m, 2H), 7.26−7.15 (m, 5H), 1.24 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 199.2, 156.9, 140.3, 137.2, 136.0, 135.4, 132.4, 130.6, 129.6, 129.5, 129.2, 128.1 (2×), 127.7, 127.3, 127.1, 126.2, 125.7, 125.2, 35.0, 30.9. HRMS (ESI): calcd for $C_{27}H_{24}ONa$ m/z 387.171936, found 387.172144.

*Ethyl 4-Oxo-4-(2-phenylnaphthalen-1-yl)butanoate (**2h**).* Yield: 10.1 mg (30%); light yellow solidified oil; EtOAc/cyclohexane (1:15). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.95 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 7.92−7.89 (m, 1H), 7.86−7.84 (m, 1H), 7.58−7.51 (m, 3H), 7.48−7.38 (m, 5H), 4.11 (q, $^3J_{HH}$ = 7.1 Hz, 2H), 2.61 (t, $^3J_{HH}$ = 6.6 Hz, 2H), 2.43 (t, $^3J_{HH}$ = 6.6 Hz, 2H), 1.24 (t, $^3J_{HH}$ = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 207.7, 172.5, 140.2, 137.6, 135.9, 132.5, 129.5, 129.3, 129.2, 128.8, 128.1, 128.0, 127.5, 127.3, 126.4, 124.9, 60.6, 39.8, 28.3, 14.1. HRMS (ESI): calcd for $C_{22}H_{20}O_3Na$ m/z 355.130466, found 355.130460.

*(1-Methyl-3-phenylnaphthalen-4-yl)(phenyl)methanone (**2i**).* Yield: 17.2 mg (53%); colorless solidified oil; EtOAc/cyclohexane (1:25). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.10 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 7.75 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 7.63−7.60 (m, 2H), 7.58−7.54 (m, 1H), 7.48−7.43 (m, 1H), 7.43 (d, $^4J_{HH}$ = 0.7 Hz, 1H), 7.40−7.32 (m, 3H), 7.25−7.13 (m, 5H), 2.81 (d, $^4J_{HH}$ = 0.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 199.9, 140.3, 138.2, 137.1, 136.0, 134.1, 133.1, 131.6, 130.8, 129.6, 129.4, 128.3, 128.2, 128.1, 127.3, 126.8, 126.2, 126.1, 124.3, 19.7. MS (FAB): m/z = 323.2 $[M + H]^+$.[8a]

*2-(2-Chlorophenyl)naphthalen-1-yl)(phenyl)methanone (**2j**).* Yield: 22.7 mg (66%); yellow solidified oil; toluene/cyclohexane (1:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.98 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 7.95 (d, $^3J_{HH}$ = 8.2 Hz, 1H), 7.73 (d, $^3J_{HH}$ = 8.5 Hz, 1H), 7.63 (dd, $^3J_{HH}$ = 8.3, $^4J_{HH}$ = 1.3 Hz, 2H), 7.56−7.50 (m, 2H), 7.48−7.43 (m, 1H), 7.42−7.37 (m, 1H), 7.26−7.17 (m, 4H), 7.13−7.06 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 198.9, 138.0, 137.8, 136.7, 134.7, 133.3, 132.9, 132.7, 132.5, 130.7, 129.5, 129.4, 129.1, 128.6, 128.2, (2×), 128.0, 127.2, 126.6, 126.2, 125.6. MS (FAB): m/z = 343.1 $[M + H]^+$.[17a]

*2-(4-Chlorophenyl)naphthalen-1-yl)(phenyl)methanone (**2k**).* Yield: 27.0 mg (79%); yellow solidified oil; toluene/cyclohexane (2:3); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.00 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 7.93 (d, $^3J_{HH}$ = 8.1 Hz, 1H), 7.69 (d, $^3J_{HH}$ = 8.5 Hz, 1H), 7.62−7.59 (m, 2H), 7.54−7.40 (m, 4H), 7.29−7.17 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 199.4, 138.6, 137.7, 136.0, 135.8, 133.6, 133.5, 132.5,

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130.7, 130.6, 129.6, 129.5, 128.4 (2×), 128.2, 127.4, 127.2, 126.5, 125.6. MS (FAB): m/z = 343.1 $[M + H]^+$.[17a]

*2-(3-Bromophenyl)naphthalen-1-yl)(phenyl)methanone (**2l**).* Yield: 33.5 mg (87%); yellow oil; toluene/cyclohexane (2:3). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.03 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 7.95 (d, $^3J_{HH}$ = 8.1 Hz, 1H), 7.72 (d, $^3J_{HH}$ = 8.5 Hz, 1H), 7.63−7.61 (m, 2H), 7.56−7.52 (m, 2H), 7.50−7.41 (m, 3H), 7.32−7.25 (m, 4H), 7.08 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 199.2, 142.2, 137.9, 136.0, 135.7, 133.4, 132.6, 132.3, 130.6, 130.4, 129.7, 129.6, 129.5, 128.4, 128.2 (2×), 127.4, 127.1, 126.6, 125.6, 122.3. HRMS (ESI): calcd for $C_{23}H_{15}BrONa$ m/z 409.019849, found 409.019608.

*2-(3-(Trifluoromethyl)phenyl)naphthalen-1-yl)(phenyl)-methanone (**2m**).* Yield: 33.6 mg (89%); light yellow oil; toluene/cyclohexane (2:3). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.05 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 7.97 (d, $^3J_{HH}$ = 8.0 Hz, 1H), 7.76 (d, $^3J_{HH}$ = 8.5 Hz, 1H), 7.61−7.58 (m, 3H), 7.56−7.47 (m, 4H), 7.44−7.40 (m, 2H), 7.34 (t, $^3J_{HH}$ = 7.8 Hz, 1H), 7.25 (t, $^3J_{HH}$ = 7.8 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 199.3, 141.0, 137.9, 136.3, 135.8, 133.5, 132.7 (2×), 130.6, 130.5 (q, $^2J_{CF}$ = 32.3 Hz), 129.8, 129.5, 128.7, 128.4, 128.2, 127.5, 127.0, 126.7, 126.2 (q, $^3J_{CF}$ = 3.8 Hz), 125.6, 124.1 (q, $^3J_{CF}$ = 3.8 Hz), 123.8 (q, $^1J_{CF}$ = 272.4 Hz). HRMS (ESI): calcd for $C_{24}H_{15}F_3ONa$ m/z 399.096721, found 399.096576.

*Phenyl(2-m-tolylnaphthalen-1-yl)methanone (**2n**).* Yield: 26.4 mg (82%); yellow oil; Et_2O/cyclohexane (1:20). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.01 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 7.94 (d, $^3J_{HH}$ = 8.0 Hz, 1H), 7.74 (d, $^3J_{HH}$ = 8.6 Hz, 1H), 7.63 (dd, $^3J_{HH}$ = 8.3, $^4J_{HH}$ = 1.2 Hz, 2H), 7.58 (d, $^3J_{HH}$ = 8.5 Hz, 1H), 7.54−7.50 (m, 1H), 7.48−7.44 (m, 1H), 7.42−7.38 (m, 1H), 7.27−7.23 (m, 2H), 7.17−7.14 (m, 2H), 7.10 (t, $^3J_{HH}$ = 7.4 Hz, 1H), 6.98 (d, $^3J_{HH}$ = 7.4 Hz, 1H), 2.25 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 199.7, 140.1, 138.0, 137.7, 137.6, 135.6, 133.1, 132.4, 130.7, 130.2, 129.5, 129.4, 128.2, 128.1 (2×), 128.0, 127.6, 127.1, 126.5, 126.2, 125.5, 21.3. MS (FAB): m/z = 323.2 $[M + H]^+$.[17a]

*Phenyl(2-p-tolylnaphthalen-1-yl)methanone (**2o**).* Yield: 14.6 mg (45%); yellow oil; Et_2O/cyclohexane (1:40). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.00 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 7.93 (d, $^3J_{HH}$ = 8.0 Hz, 1H), 7.71−7.69 (m, 1H), 7.65−7.62 (m, 2H), 7.56 (d, $^3J_{HH}$ = 8.5 Hz, 1H), 7.53−7.49 (m, 1H), 7.46−7.39 (m, 2H), 7.27−7.23 (m, 4H), 7.03 (d, $^3J_{HH}$ = 7.8 Hz, 2H), 2.26 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 199.8, 137.9, 137.4, 137.3, 137.1, 135.5, 133.2, 132.3, 130.7, 129.6, 129.4, 129.3, 129.0, 128.3, 128.1, 127.8, 127.1, 126.2, 125.5, 21.1. MS (FAB): m/z = 323.2 $[M + H]^+$.[17b]

*(11H-Benzo[b]fluoren-5-yl)(phenyl)methanone (**2p**).* For compound **2p**, 3 equiv of 1*H*-indene was applied and added dropwise to the hot solution over a period of 6 h. Yield: 24.1 mg (75%); colorless solidified oil; toluene/cyclohexane (1:2). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.07 (s, 1H), 7.96 (d, $^3J_{HH}$ = 7.4 Hz, 2H), 7.92 (d, $^3J_{HH}$ = 8.2 Hz, 1H), 7.62−7.54 (m, 3H), 7.50−7.35 (m, 5H), 7.30−7.26 (m, 1H), 7.16 (t, $^3J_{HH}$ = 7.5 Hz, 1H), 4.15 (s, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 200.0, 144.3, 141.0, 139.3, 137.3, 136.8, 134.1, 132.5, 130.4, 130.2, 130.0, 129.0, 128.1, 127.8, 127.1, 126.2, 125.8, 125.4, 125.2, 124.4, 123.5, 36.3. HRMS (ESI): calcd for $C_{24}H_{16}ONa$: m/z 343.109336, found 343.109670.

*Ethyl (4-Benzoyl-3-phenyl)2-naphthalenecarboxylate (**2q**).* Yield: 31.6 mg (83%); yellow solidified oil; Et_2O/cyclohexane (1:10). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.51 (s, 1H), 8.04−8.02 (m, 1H), 7.67 (dd, $^3J_{HH}$ = 8.3, $^4J_{HH}$ = 1.2 Hz, 1H), 7.60−7.56 (m, 1H), 7.55−7.51 (m, 3H), 7.43−7.38 (m, 1H), 7.37−7.27 (m, 1H), 7.26−7.17 (m, 3H), 7.15−7.11 (m, 1H), 7.09−6.81 (m, 1H), 4.05 (q, $^3J_{HH}$ = 7.1 Hz, 2H), 0.93 (t, $^3J_{HH}$ = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 198.6, 168.1, 138.3, 138.1, 137.8, 135.7, 133.3, 131.5, 131.4, 130.0, 129.4, 129.1, 129.0, 128.2, 127.2, 127.1, 125.4, 61.1, 13.5. MS (FAB): m/z = 381.1 $[M + H]^+$.[17c]

*Phenyl(2,3-diphenylnaphthalen-1-yl)methanone (**2r**).* Yield: 26.9 mg (70%); yellow solidified oil; toluene/cyclohexane (1:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.03 (s, 1H), 7.97 (d, $^3J_{HH}$ = 8.2 Hz, 1H), 7.70 (dd, $^3J_{HH}$ = 8.4, $^4J_{HH}$ = 0.7 Hz, 1H), 7.59−7.53 (m, 3H), 7.48−7.44 (m, 1H), 7.41−7.30 (m, 2H), 7.25−7.12 (m, 9H), 6.98−6.95 (m, 1H), 6.82−6.58 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 199.5, 140.7, 139.4, 138.2, 138.0, 137.6, 136.4, 133.0, 132.6, 130.3, 130.0, 129.8, 129.4, 128.2, 128.1, 127.7, 127.1, 126.8, 126.7, 126.6, 125.4. HRMS (ESI): calcd for $C_{29}H_{20}ONa$ m/z 407.140636, found 407.140410.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra of *o*-alkynyl carboxaldehydes **1d** and **1h** and of all 1-naphthalenones (**2a−r**). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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