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Cascade Reactions of Aromatic Aldehydes with Electron-Deficient Acetylenes: Regioselective Construction of Diverse Aromatic Ring Systems

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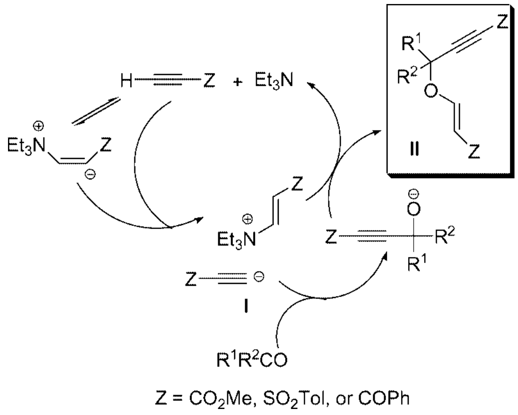
A new triethylamine-catalyzed cascade reaction of aromatic aldehydes with terminal conjugated acetylenes has been developed. This serial multiple bond forming process furnishes diverse polycyclic aromatic hydrocarbons including naphthalenes, phenanthrenes, benzofurans, and tetrahydronaphtho[2,3-*b*]furans. The chemical outcome of the process depends on the reaction temperature and can therefore be tailored selectively by an appropriate choice of experimental conditions. The resulting tetrahydronaphthofurans can be aromatized further to give strongly fluorescent naphtho[2,3-*b*]furans (fluorescent quantum yield, Φ_f, up to 0.94) in a one-pot procedure. Furthermore, polysubstituted furans are obtained when the reaction is performed in the presence of dialkyl acetylenedicarboxylates. These cascade processes exhibit high bond-forming efficiency and high regioselectivity.

Introduction

The development of new strategies that can dramatically increase the level of structural complexity remains a preeminent goal and a great challenge in modern organic chemistry, both from the academic and industrial points of view. Towards this end, cascade or domino reactions that allow molecular complexity to be created by the facile formation of several new covalent bonds in a one-pot transformation have received considerable attention due to their high efficiency in the synthesis of complex organic building blocks from easily available starting materials.[1–4] Unlike the usual stepwise bond formation towards a target molecule, the most important attribute of cascade or domino processes is the inherent formation of several bonds in one operation without isolating the intermediates, changing the reaction conditions, or adding further reagents. This methodology minimizes waste generation and the need for excessive handling and is therefore very suitable for the total synthesis of natural products.[5]

The use of alkynylides as carbon nucleophiles for the formation of C–C bonds is valuable in organic synthesis. However, the use of stoichiometric or substoichiometric amounts of strong bases for their generation is often incompatible with the use of electrophilic partners.[6] Even the mild method employing in situ catalytic activation of acetylene to form reactive zinc acetylides and their subsequent addition to nitrones, imines, and aldehydes to give propargylic hydroxylamines, amines, and alcohols, respectively,[7] fails when applied to terminal conjugated acetylenes because of the known tendency of these compounds to form self-addition oligomers under strongly basic conditions. On the other hand, catalytic generation of these reactive, conjugated acetylides **I** by Michael addition of a tertiary amine to terminal conjugated alkynoates, as shown in Scheme 1, enables formation of enol-protected functionalized propargylic alcohols **II**, which then react with an aldehyde or an activated ketone in a domino process to give 1,3-dioxolanes, 1,3-oxazolidines, or pyrroles.[8] We have recently developed a new and interesting triethylamine-catalyzed cascade process of aromatic aldehydes with terminal conjugated acetylenes. As reported previously in a communication,[9] this reaction furnishes diverse polycyclic aromatic hydrocarbons



Scheme 1. Domino process of terminal conjugated acetylenes with aldehydes or ketones.

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including naphthalenes, phenanthrenes, benzofurans and tetrahydronaphtho[2,3-*b*]furans. Here, we report full details on the application of this cascade reaction, as well as its extension to a three-component reaction of aromatic aldehydes with terminal conjugated acetylenes and dialkyl acetylenedicarboxylates.

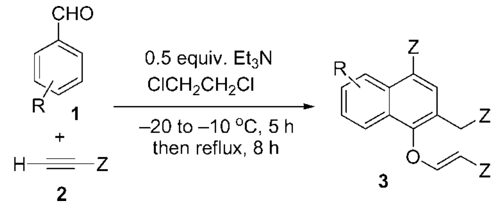
Results and Discussion

Triethylamine-Catalyzed Cascade Reaction of Aromatic Aldehydes and Propiolates

Recently, García-Tellado et al.[8c,8d] have reported a triethylamine-catalyzed reaction of aliphatic aldehydes with methyl propiolate, which affords either enol-protected functionalized propargylic alcohols (at 0 °C) or 1,3-dioxolanes (at –78 °C). We have investigated the triethylamine-catalyzed reaction of aromatic aldehydes with terminal conjugated acetylenes. However, we surprisingly found that benzaldehydes **1** (0.67 equiv.) combine with propiolates **2** (1.0 equiv.) in the presence of a catalytic amount of triethylamine (0.5 equiv.) to give the naphthalene derivative **3** in 45–66% yield when the reaction is carried out in $ClCH_2CH_2Cl$ at –20 to –10 °C for 5 h and then at reflux for 8 h (Table 1). When the reaction was performed in CH_2Cl_2 at –20 to –10 °C for 5 h and then at 25 °C for 8 h, products **4** and **5** were isolated in 56–71% total yields instead of **3** (Table 2). When the latter reaction was quenched at –40 °C with dilute HCl, 2,3,9,9a-tetrahydronaphtho[2,3-*b*]furans **6** were obtained in 63–66% yield (Table 3). Thus, triethylamine alone is able to catalyze the formation of up to five new C–C bonds and two C–O bonds in one operation. In all cases, no (*Z*) isomers of the products were detected.

It is noteworthy that asymmetric benzaldehydes **1i** and **1j** furnished only the less crowded naphthalenes **3i** (Table 1, Entry 9) and **3j** (Table 1, Entry 10) or **4g** and **5g** (Table 2,

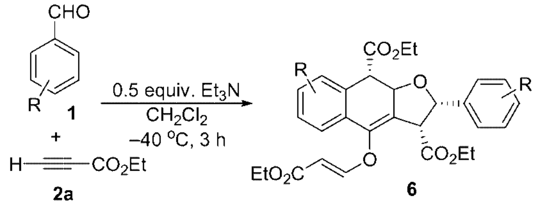
Table 1. Triethylamine-catalyzed synthesis of polysubstituted naphthalenes **3**.



Entry	R	Z	Product	Yield [%][a]
1	H (**1a**)	CO_2Et (**2a**)	**3a**	45
2	2-Me (**1b**)	CO_2Me (**2b**)	**3b**	53
3	4-Me (**1c**)	**2a**	**3c**	66
4	4-Et (**1d**)	**2b**	**3d**	65
5	4-Ph (**1e**)	**2a**	**3e**	63
6	4-MeO (**1f**)	**2b**	**3f**	60
7	4-$PhCH_2O$ (**1g**)	**2a**	**3g**	56
8	4-TsO (**1h**)	**2a**	**3h**	56
9	3,4-dimethyl (**1i**)	**2a**	**3i**	52
10	3,4-OCH_2O- (**1j**)	**2a**	**3j**	57

[a] Isolated yield refers to propiolate.

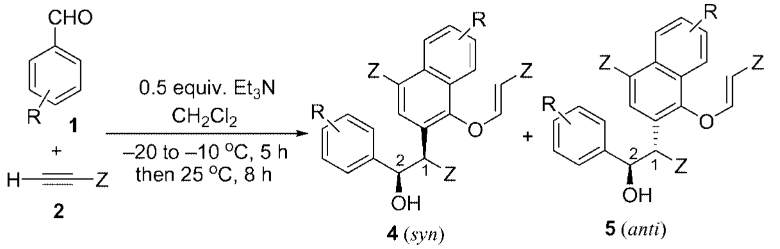
Table 3. Triethylamine-catalyzed synthesis of tetrahydronaphtho[2,3-*b*]furans **6**.



Entry	R	Product	Yield [%][a]
1	**1a**	**6a**	63
2	**1c**	**6b**	65
3	**1d**	**6c**	66
4	4-*t*Bu (**1m**)	**6d**	55

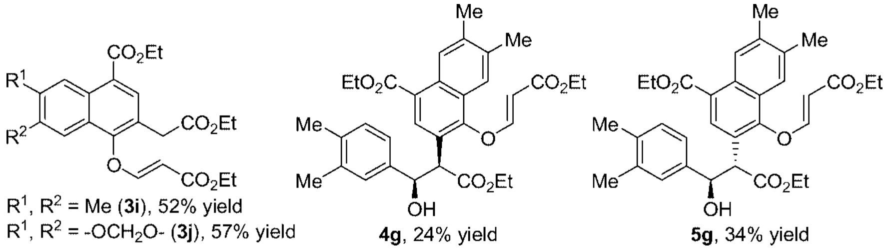
[a] Isolated yield refers to propiolate.

Table 2. Triethylamine-catalyzed synthesis of polysubstituted naphthalenes **4** and **5**.



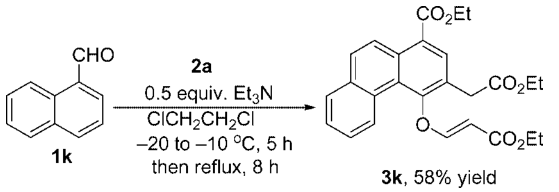
Entry	R	Z	Product (Yield [%])[a]	
1	**1a**	**2a**	**4a** (21)	**5a** (35)
2	**1c**	**2a**	**4b** (28)	**5b** (40)
3	**1d**	**2b**	**4c** (29)	**5c** (42)
4	**1e**	**2a**	**4d** (27)	**5d** (43)
5	**1f**	**2b**	**4e** (26)	**5e** (37)
6	**1g**	**2a**	**4f** (27)	**5f** (38)
7	**1i**	**2a**	**4g** (24)	**5g** (34)

[a] Isolated yield refers to propiolate.



Scheme 2. The structure of products **3i**, **3j**, **4g**, and **5g**.

Entry 7), presumably because of steric reasons (see Scheme 2). We also found that 1-naphthaldehyde (**1k**) affords the phenanthrene derivative **3k** in 58% yield (Scheme 3), and that furan-2-carbaldehyde (**1l**) gives the benzofuran derivative **3l** (53% yield) (Scheme 4, route A), or **4h** (30% yield) and **5h** (21% yield) (Scheme 4, route B), respectively. The *syn* and *anti* configurations of the products **4** and **5** were assigned from NMR evidence, namely $J_{H1,H2}$.[10] The structure of **6b** was unambiguously established by X-ray crystallographic analysis (Figure 1).[11]



Scheme 3. Cascade reaction of 1-naphthaldehyde (**1k**) with **2a**.

We subsequently performed analogous reactions with electron-deficient benzaldehydes such as 4-bromobenzaldehyde and other terminal alkynes such as 3-butyn-2-one and ethynyl *p*-tolyl sulfone, but did not observe any of the corresponding naphthalene or tetrahydronaphtho[2,3-*b*]furan derivatives.

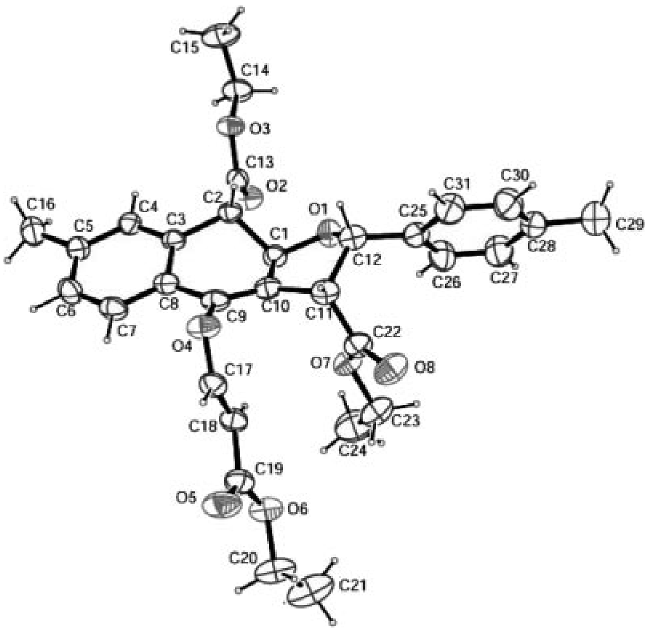
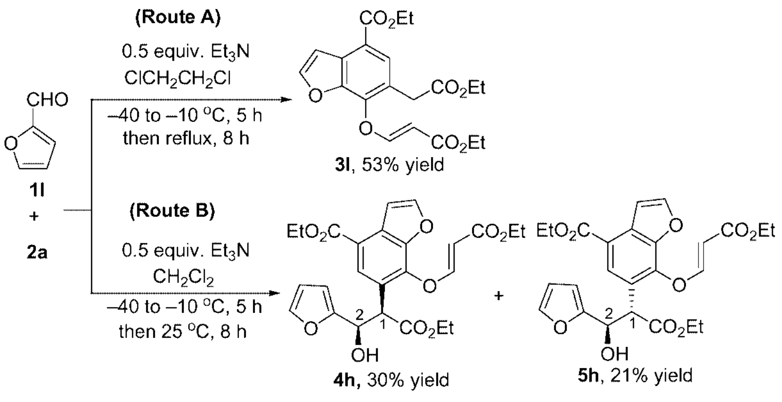


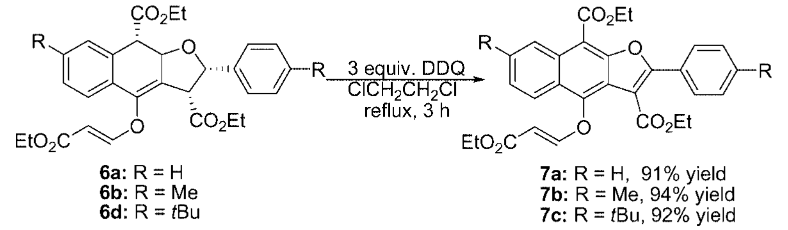
Figure 1. X-ray structure of **3a**.

Numerous biologically significant natural products and pharmaceuticals as well as optical and electronic materials contain a naphthalene unit.[12] Traditionally, access to polysubstituted naphthalenes is based on the stepwise introduction of substituents by electrophilic substitution. More recent routes for the synthesis of naphthalenes include Fischer (carbene)metal annulation (Dötz reaction)[13] andmetal-catalyzed cyclization.[14] Compared with these published works, our approach is of higher bond-forming efficiency and higher economy because up to six bonds (4 C–C bonds and 2 C–O bonds) are formed in one operation. Furthermore, this domino reaction is metal-free and the substrates are simple and readily available.

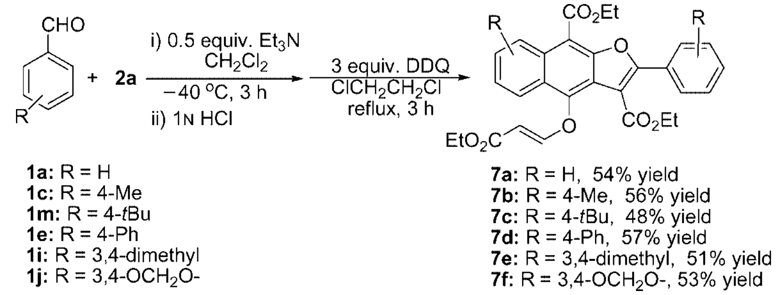
We applied our method to synthesize substituted naphthofurans, which are important structural units in numerous biologically significant natural products and pharmaceuticals[15] as well as optical materials. 2,3,9,9a-Tetra-



Scheme 4. Cascade reactions of furan-2-carbaldehyde (**1l**) with **2a**.



Scheme 5. Synthesis of naphthofuran derivatives **7** from **6**.



Scheme 6. Synthesis of naphthofuran derivatives **7** from **1** and **2**.

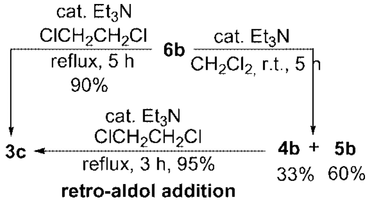
hydronaphtho[2,3-*b*]furans **6** were aromatized with DDQ to give naphtho[2,3-*b*]furans **7** in excellent yields (Scheme 5). In this way, naphthofuran structures were constructed in two steps from simple aromatic aldehydes **1** and propiolates **2**. A one-pot procedure without isolation of the tetrahydronaphtho[2,3-*b*]furan was also developed for the synthesis of naphthofuran derivatives (Scheme 6). The yields of naphthofurans **7** are comparable to those obtained by the two-step procedure.

We surprisingly found that the synthesized naphthofuran derivatives exhibit very strong fluorescence. Data for two representatives, **7d** and **7f**, are summarized in Table 4. Their maximum emission wavelengths appear between 396 and 446 nm with fluorescent quantum yields, Φ_f, of 0.54–0.94 relative to a 9,10-diphenylanthrane standard. In addition to potential applications of these substituted naphthofurans (e.g., as organic light-emitting diodes), they are also of interest because further conversion into diverse derivatives is possible.

Table 4. Fluorescent spectroscopic data for compounds **7d** and **7f**.

		Cyclohexane	CH_2Cl_2	MeOH
7d	λ_{em} [nm]	441	446	443
	Φ_f	0.94	0.54	0.57
7f	λ_{em} [nm]	396	411	436
	Φ_f	0.94	0.64	0.60

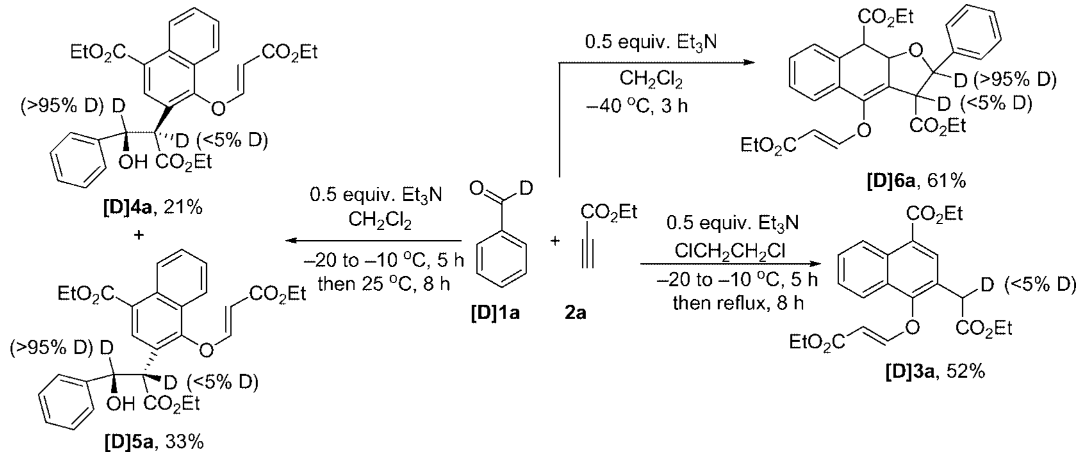
To understand the mechanism of our domino process, we examined the relationship between products **3**–**6**. We found that compound **6b** can be transformed into naphthalene **3c** (90%) and 4-methylbenzaldehyde (**1c**) by refluxing with triethylamine in $ClCH_2CH_2Cl$, while **4b** (33%) and **5b** (60%) were obtained upon stirring a mixture of **6b** and triethylamine in CH_2Cl_2 at room temperature (Scheme 7). On the other hand, refluxing of **4b** and **5b** in the presence of triethylamine in $ClCH_2CH_2Cl$ also yielded **3c** (95%) and **1c** (Scheme 8). However, **4b**, **5b**, and **6b** are stable even at refluxing temperature in the absence of triethylamine. These results indicate that compound **3** is formed by a retro-aldol reaction from **4** or **5**, which, in turn, are generated from **6**.



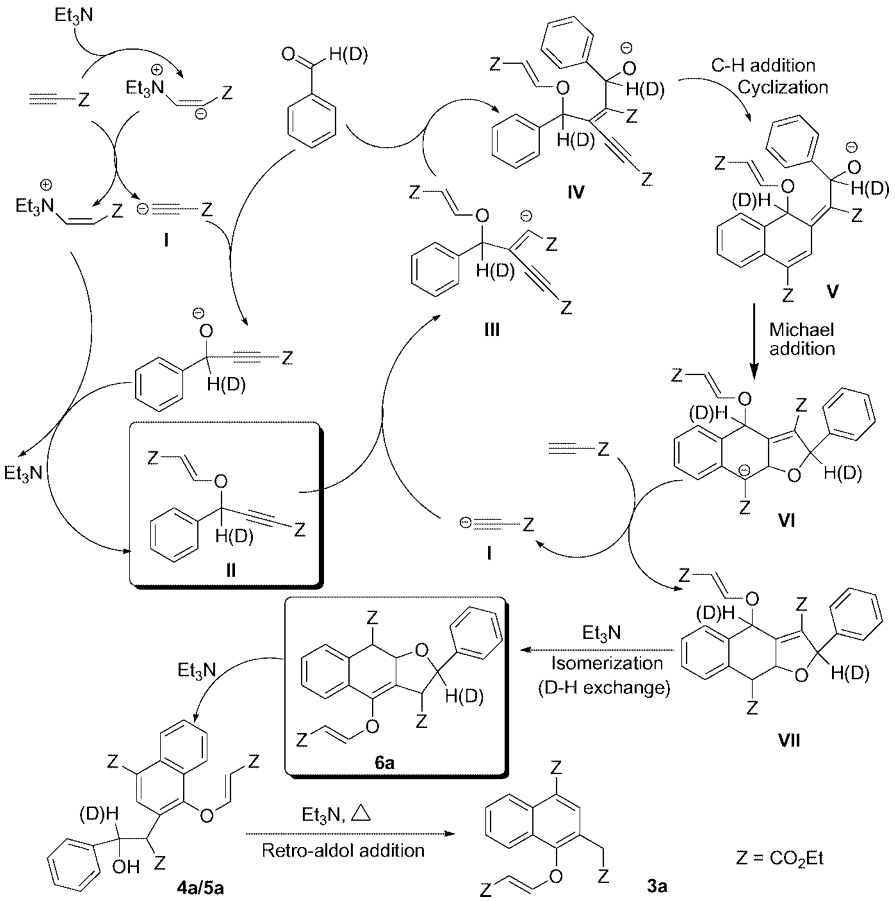
Scheme 7. Transformations between compounds **3**–**6**.

Further insight into the reaction mechanism was gained by conducting a deuterium-labeling experiment, i.e., the reaction of $C_6H_5C(O)D$ (**[D]1a**) (98% D) with **1b** (Scheme 9). The deuteriated products [D]**3a**, [D]**4a**, [D]**5a**, and [D]**6a** were isolated in 52%, 21%, 33%, and 61% yields, respectively.

Our results can be rationalized as shown in Scheme 9. In the first cascade, triethylamine serves as a nucleophilic trigger for the domino sequence to generate the enol-protected propargyl alcohol **II** according to García-Tellado's proposal.[8] In the second cascade, **II** undergoes a Michael-type addition with the acetylide **I** to produce anion **III**, which adds to benzaldehyde to form anion **IV**. Intramolecular hydroarylation of **IV**, followed by an intramolecular Michael



Scheme 8. Cascade reaction of $C_6H_5C(O)D$ ([D]**1a**) with **1b**.



Scheme 9. Possible mechanism for the domino reaction of aldehydes and propiolates.

addition, protonation, and a triethylamine-catalyzed isomerization, leads to tetrahydronaphtho[2,3-*b*]furan **6**. In the third cascade, the furan ring of **6** is opened by triethylamine to give a mixture of **4** and **5** at 25 °C. At higher temperature, further transformation into **3** by a retro-adol reaction ensues.

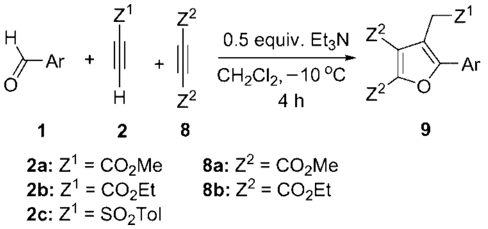
Triethylamine plays a key role in this cascade process. Our optimization experiments showed that the nature of the tertiary amine is critical for the success of the reaction. Thus, trioctylamine (TOA) exhibits a lower activity than triethylamine. The sterically demanding DIPEA is totally ineffective, as are DBU, DABCO, diethylamine, and pyridine.

Triethylamine-Catalyzed Domino Reaction of Aromatic Aldehydes with Electron-Deficient Acetylenes and Dialkyl Acetylenedicarboxylates

Previously, we and other groups have reported that dimethyl acetylenedicarboxylate (DMAD) reacts with nucleophiles in a Michael-type process.[16] Encouraged by our success with the triethylamine-catalyzed cascade reaction of aromatic aldehydes with propiolates, we further extended our reaction system by adding DMAD as one of the components. In a preliminary experiment, we found that equimolar amounts of benzaldehyde (**1a**), methyl propiolate (**2a**), and DMAD (**9a**) in the presence of Et_3N at –10 °C (optimum temperature) combined to afford the highly substituted furan derivative **9a** (Table 5, Entry 1). Further investigations indicated that the presence of a catalytic amount of Et_3N (0.5 equiv.) gives the best result. We also found that TOA has a similar catalytic activity to Et_3N but that DABCO, DBU, pyridine, DIPEA, and Et_2NH are ineffective.

After establishing the optimal reaction conditions, we examined a greater variety of aromatic aldehydes and electron-deficient acetylenes. Electron-rich benzaldehydes (Table 5, Entries 1–3 and 10–15) performed better than their electron-deficient counterparts (Table 5, Entries 4–6, 15, and 16), and heteroaryl aldehydes also gave good results (Table 5, Entries 7–9 and 17). In addition to propiolates **1a** and **1b**, ethynyl *p*-tolyl sulfone (**1c**) also yielded the furan derivative in 40% yield (Table 5, Entry 18). However, 3-butyn-2-one did not give the corresponding furan derivative. The structure of the polysubstituted furans **9** was unambiguously supported by an X-ray structure analysis of **9c** (Figure 2).[17]

Table 5. Cascade reaction of aromatic aldehydes with electron-deficient acetylenes.[a]



Entry	Z^1	Z^2	Ar	Product	Yield [%][b]
1	**2a**	**8a**	C_6H_5	**9a**	48
2	**2a**	**8a**	4-MeC_6H_4	**9b**	55
3	**2a**	**8a**	4-$BnOC_6H_4$	**9c**	61
4	**2a**	**8a**	4-ClC_6H_4	**9d**	41
5	**2a**	**8a**	4-BrC_6H_4	**9e**	42
6	**2a**	**8a**	4-$MeO_2CC_6H_4$	**9f**	44
7	**2a**	**8a**	furan-2-yl	**9g**	50
8	**2a**	**8a**	thiophene-2-yl	**9h**	48
9	**2a**	**8a**	thiophene-3-yl	**9i**	56
10	**2b**	**8a**	C_6H_5	**9j**	49
11	**2b**	**8a**	2-$MeOC_6H_4$	**9k**	58
12	**2b**	**8a**	4-MeC_6H_4	**9l**	55
13	**2b**	**8a**	3,4-$(OCH_2O)C_6H_3$	**9m**	49
14	**2b**	**8a**	3,4,5-$(MeO)_3C_6H_2$	**9n**	46
15	**2b**	**8a**	2-ClC_6H_4	**9o**	42
16	**2b**	**8a**	4-BrC_6H_4	**9p**	43
17	**2b**	**8a**	furan-2-yl	**9q**	50
18	**2c**	**8b**	4-PhC_6H_4	**9r**	40

[a] **1** (1 mmol), **2** (1 mmol), **3** (1.5 mmol), and Et_3N (0.5 mmol) in CH_2Cl_2 at –10 °C for 4 h. [b] Isolated yield based on starting aldehyde.

Furans are common substructures in a variety of biologically active natural compounds, synthetic intermediates, and pharmaceuticals.[18] Accordingly, the synthesis of furans has attracted much attention.[19] In general, substituted furans are accessed by ring derivatization or cyclization of acyclic precursors.[20] Numerous heteroannulation reactions, including metal-catalyzed ones, leading to substituted

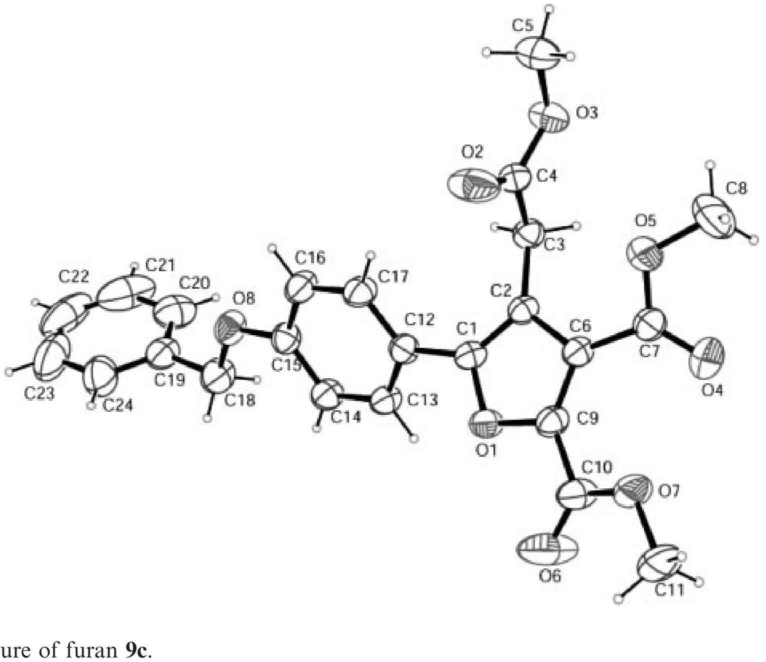
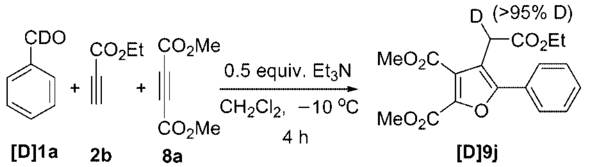


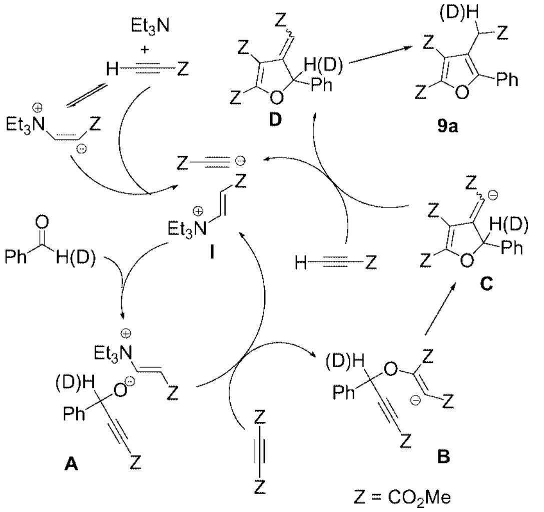
Figure 2. X-ray crystal structure of furan **9c**.

furans have been reported.[19,21] Our three-component domino reaction of aldehydes with electron-deficient acetylenes and dialkyl acetylenedicarboxylates represents a very mild, metal-free method for the preparation of substituted furans.

By performing an experiment with $C_6H_5C(O)D$ ([D]**1a**, 98% D) to generate the deuteriated furan [D]**9j** (>95% D; Scheme 10) we were able to formulate the reaction mechanism shown in Scheme 11. Triethylamine initiates the cascade sequence to form an ammonium acetylide salt **I**,[8] which quickly reacts with benzaldehyde to give an alkoxide **A** that adds to DMAD. Cyclization of the resulting **B** through an intramolecular Michael-type addition leads to anion **C**.[8c] Proton abstraction from a terminal acetylene gives 4,5-dihydrofuran **D**, which isomerizes to the corresponding furan derivative **9**.



Scheme 10. Cascade reaction of $C_6H_5C(O)D$ ([D]**1a**) with **2b** and DMAD.



Scheme 11. Possible mechanism for the cascade process of aldehydes with propiolates and DMAD.

Conclusions

We have demonstrated that triethylamine catalyzes the condensation of aromatic aldehydes with terminal conjugated acetylenes to furnish diverse polycyclic aromatic hydrocarbons including naphthalenes, phenanthrenes, benzofurans, and 2,3,9,9a-tetrahydronaphtho[2,3-*b*]furans. The chemical outcome of this serial multiple bond forming process depends on the reaction temperature, so it can be tailored selectively by the appropriate choice of experimental conditions. Polysubstituted furans are obtained when the reaction is performed in the presence of dialkyl acetylenedicarboxylates. These cascade processes exhibit high bond-forming efficiency and high regioselectivity. Furthermore, several examples are provided where the cascade products – tetrahydronaphthofurans – are further aromatized to strongly fluorescent naphtho[2,3-*b*]furans (fluorescent quantum yield up to 0.94) in a one-pot procedure. Current efforts are focused on the synthesis of some natural products and the development of new organic fluorescent materials (e.g. as organic light-emitting diodes) using these powerful reactions.

Experimental Section

General Methods: All reactions were carried out under nitrogen in oven-dried glassware. The progress of all reactions was monitored by TLC. Starting materials and reagents were purchased from commercial suppliers and used without further purification, except the following: CH_2Cl_2, $ClCH_2CH_2Cl$, and triethylamine were distilled from CaH_2; hexane and ethyl acetate used in chromatography were distilled prior to use. Silica gel (230–400 mesh) was used for flash chromatography. ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded with a Bruker Avance DMX 500 apparatus. Low-resolution mass spectra were recorded with a Bruker esquire3000plus_01073 spectrometer and high-resolution spectra with an FT-ICR-MS Apex III apparatus using the ESI technique. IR spectra were obtained with a Nicolet Nexus 470 FT-IR spectrometer. Melting points were measured with a Yanaco micro melting point apparatus. UV absorption spectra were recorded with a UV-2450 Shimadzu UV/Visible spectrophotometer. Fluorescence spectra were obtained with an RF-5301PC Shimadzu spectrofluorophotometer.

General Procedure for the Synthesis of Naphthalene Derivatives 3: A solution of triethylamine (1.5 mmol) in $ClCH_2CH_2Cl$ (5 mL) was added dropwise to a solution of an aromatic aldehyde **1** (2 mmol) and propiolate **2** (3 mmol) in $ClCH_2CH_2Cl$ (10 mL) under N_2 at –20 °C. The mixture was stirred at –20 to –10 °C for 5 h and then refluxed for 8 h. After cooling to room temperature, the mixture was washed with brine two times and the organic layer was dried with anhydrous sodium sulfate. Concentrating the organic layer under reduced pressure gave a residue, which was purified by column chromatography on silica gel with hexane/ethyl acetate (1:5) to afford pure **3**.

Naphthalene 3a: Yield: 189 mg (45%), pale-yellow oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 8.96 (d, J = 8.6 Hz, 1 H), 8.17 (s, 1 H), 7.92 (d, J = 8.4 Hz, 1 H), 7.84 (d, J = 12.5 Hz, 1 H), 7.64 (m, 1 H), 7.59 (m, 1 H), 5.13 (d, J = 12.5 Hz, 1 H), 4.48 (q, J = 7.2 Hz, 2 H), 4.17 (q, J = 7.2 Hz, 2 H), 4.13 (q, J = 7.1 Hz, 2 H), 3.8 (s, 2 H), 1.47 (t, J = 7.1 Hz, 3 H), 1.24 (t, J = 7.2 Hz, 3 H), 1.22 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.4, 166.9, 166.8, 160.8, 151.8, 133.1, 132.6, 128.5, 127.5, 126.5, 126.1, 122.2, 101.6, 61.5, 60.4, 35.7, 14.6, 14.4, 14.3 ppm. IR (film): $\tilde{\nu}$ = 2982, 1738, 1716, 1633, 1573, 1508, 1367, 1247, 1122, 1032, 792 cm^{-1}. MS (ESI): *m*/*z* 423.0 $[M + Na]^+$. HRMS (ESI): calcd. for $C_{22}H_{24}O_7$ $[M + Na]^+$ 423.1414; found 423.1415.

Naphthalene 3b: Yield: 197 mg (53%), colorless oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 8.73 (d, J = 8.7 Hz, 1 H), 8.07 (s, 1 H), 7.71 (d, J = 12.5 Hz, 1 H), 7.50 (m, 1 H), 7.35 (d, J = 7.0 Hz, 1 H), 5.03 (d, J = 12.5 Hz, 1 H), 4.00 (s, 3 H), 3.75 (s, 2 H), 3.71 (s, 3 H), 3.67 (s, 3 H), 2.79 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.0, 167.7, 167.3, 161.0, 153.1, 133.9, 133.6, 132.7, 131.1, 128.2, 127.1, 124.6, 123.0, 101.4, 52.7, 52.6, 51.6, 35.8, 24.6 ppm. IR (film): $\tilde{\nu}$ = 2953, 1739, 1717, 1644, 1631, 1576, 1436, 1321, 1243, 1133, 966, 818 cm^{-1}. MS (ESI): *m/z* 395.1 [M + Na]$^+$. HRMS (ESI): calcd. for $C_{20}H_{20}O_7$ [M + Na]$^+$ 395.1101; found 395.1098.

General Procedure for the Synthesis of Naphthalene Derivatives 4 and 5: A solution of triethylamine (1.5 mmol) in CH_2Cl_2 (5 mL) was added dropwise to a solution of aromatic benzaldehydes **1** (2 mmol) and propiolates **2** (3 mmol) in CH_2Cl_2 (10 mL) under N_2 at –20 °C. The reaction mixture was stirred at –20 to –10 °C for 5 h and then at 25 °C for 8 h. After cooling to room temperature, the mixture was washed with brine two times and the organic layer was dried with anhydrous sodium sulfate. Concentration of the organic layer under reduced pressure gave an oily residue, which was purified by column chromatography on silica gel with hexane/ethyl acetate (1:5) to afford pure **4** and **5**, respectively.

Naphthalene 4a: Yield: 106 mg (21%), pale-yellow gum. ^1H NMR (500 MHz, $CDCl_3$): δ = 8.94 (d, J = 8.7 Hz, 1 H), 8.46 (s, 1 H), 7.85 (d, J = 8.4 Hz, 1 H), 7.61 (m, 3 H), 7.26 (m, 5 H), 5.50 (dd, J_1 = 2.3, J_2 = 6.5 Hz, 1 H), 5.20 (d, J = 12.4 Hz, 1 H), 4.51 (m, 2 H), 4.40 (d, J = 6.6 Hz, 1 H), 4.13 (m, 2 H), 4.05 (m, 2 H), 2.79 (d, J = 2.6 Hz, 1 H), 1.49 (t, J = 7.1 Hz, 3 H), 1.23 (t, J = 7.1 Hz, 3 H), 1.07 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.9, 167.1, 167.0, 161.2, 152.7, 140.9, 132.5, 131.2, 128.62, 128.58, 128.4, 127.4, 126.9, 126.7, 126.5, 126.0, 123.2, 122.6, 101.9, 74.7, 61.64, 61.60, 60.3, 51.9, 14.6, 14.5, 14.0 ppm. IR (KBr): $\tilde{\nu}$ = 3483, 2981, 1716, 1630, 1572, 1508, 1367, 1248, 1156, 1123, 1031, 766, 701 cm^{-1}. MS (ESI): *m/z* 524.0 [M + NH_4]$^+$. HRMS (ESI): calcd. for $C_{29}H_{30}O_8$ [M + Na]$^+$ 529.1833; found 529.1846.

Naphthalene 5a: Yield: 177 mg (35%), colorless gum. ^1H NMR (500 MHz, $CDCl_3$): δ = 8.90 (d, J = 8.7 Hz, 1 H), 8.21 (s, 1 H), 7.76 (d, J = 8.3 Hz, 1 H), 7.60 (m, 1 H), 7.51 (m, 1 H), 7.46 (d, J = 12.4 Hz, 1 H), 7.13 (m, 5 H), 5.36 (dd, J_1 = 3.7, J_2 = 9.1 Hz, 1 H), 5.09 (d, J = 12.4 Hz, 1 H), 4.50 (q, J = 7.1 Hz, 2 H), 4.38 (q, J = 9.1 Hz, 1 H), 4.19 (m, 4 H), 3.57 (d, J = 3.8 Hz, 1 H), 1.49 (t, J = 7.1 Hz, 3 H), 1.25 (t, J = 7.1 Hz, 3 H), 1.19 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.9, 166.82, 166.80, 160.9, 151.8, 140.2, 132.4, 130.6, 128.7, 128.5, 128.4, 127.5, 126.9, 126.8, 126.5, 126.1, 123.6, 122.5, 102.1, 75.7, 61.9, 61.7, 60.4, 52.8, 14.6, 14.5, 14.1 ppm. IR (KBr): $\tilde{\nu}$ = 3483, 2981, 1716, 1632, 1572, 1508, 1367, 1248, 1155, 1122, 1034, 790, 701, 542 cm^{-1}. MS (ESI): *m/z* 507.0 [M + H]$^+$. HRMS (ESI): calcd. for $C_{29}H_{30}O_8$ [M + Na]$^+$ 529.1833; found 529.1835.

General Procedure for the Synthesis of 2,3,9,9a-Tetrahydronaphtho[2,3-*b*]furans 6: A solution of triethylamine (1.5 mmol) in CH_2Cl_2 (5 mL) was added dropwise to a solution of an aromatic aldehyde **1** (2 mmol) and propiolate **2** (3 mmol) in CH_2Cl_2 (10 mL) under N_2 at –50 °C. The reaction mixture was stirred at –40 °C for 3 h, then 1 N hydrochloric acid (1.5 mL) was added to quench the reaction. The solution was washed with brine, dried with anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with hexane/ethyl acetate (1:5) as eluent to afford pure **6**.

2,3,9,9a-Tetrahydronaphtho[2,3-*b*]furan 6a: Yield: 319 mg (63%), colorless crystals; m.p. 128–130 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.60 (d, J = 12.4 Hz, 1 H), 7.36 (d, J = 7.3 Hz, 2 H), 7.28 (m, 6 H), 7.13 (m, 1 H), 5.78 (dd, J_1 = 1.2, J_2 = 13.3 Hz, 1 H), 5.57 (d, J = 6.2 Hz, 1 H), 5.44 (d, J = 12.4 Hz, 1 H), 4.39 (m, 2 H), 4.12 (m, 2 H), 4.04 (m, 2 H), 3.71 (m, 2 H), 1.3 (t, J = 7.1 Hz, 3 H), 1.22 (t, J = 7.1 Hz, 3 H), 0.83 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.3, 168.8, 166.8, 159.5, 142.4, 137.4, 131.9, 129.7, 129.3, 128.4, 128.3, 126.9, 126.4, 125.1, 123.1, 101.6, 85.1, 80.9, 61.7, 61.3, 60.4, 52.6, 52.1, 14.54, 14.48, 13.8 ppm. IR (KBr): $\tilde{\nu}$ = 2981, 2938, 1739, 1719, 1642, 1452, 1373, 1321, 1275, 1189, 1119, 1035, 962, 747, 702, 594 cm^{-1}. MS (ESI): *m/z* 529.0 [M + Na]$^+$. HRMS (ESI): calcd. for $C_{29}H_{30}O_8$ [M + Na]$^+$ 529.1833; found 529.1809.

2,3,9,9a-Tetrahydronaphtho[2,3-*b*]furan 6b: Yield: 347 mg (65%), colorless crystals; m.p. 152–153 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.60 (d, J = 12.3 Hz, 1 H), 7.25 (d, J = 7.4 Hz, 2 H), 7.11 (m, 4 H), 6.92 (s, 1 H), 5.73 (d, J = 13.2 Hz, 1 H), 5.53 (d, J = 6.0 Hz, 1 H), 5.42 (d, J = 12.4 Hz, 1 H), 4.39 (m, 2 H), 4.12 (m, 2 H), 4.02 (d, J = 13.2 Hz, 1 H), 3.97 (d, J = 5.9 Hz, 1 H), 3.74 (m, 2 H), 2.32 (s, 3 H), 2.30 (s, 3 H), 1.38 (t, J = 7.0 Hz, 3 H), 1.23 (t, J = 7.0 Hz, 3 H), 0.87 (t, J = 7.3 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.6, 169.0, 167.0, 159.7, 142.4, 139.9, 138.1, 134.4, 132.0, 129.0, 128.9, 127.8, 126.7, 126.3, 124.2, 123.1, 101.5, 85.1, 81.0, 61.7, 61.2, 60.4, 52.7, 52.2, 21.8, 21.4, 14.6, 14.5, 13.9 ppm. IR (KBr): $\tilde{\nu}$ = 2985, 1741, 1709, 1627, 1370, 1315, 1223, 1174, 1136, 1124, 1032, 835, 798 cm^{-1}. MS (ESI): *m/z* 557.3 [M + Na]$^+$. HRMS (ESI): calcd. for $C_{31}H_{34}O_8$ [M + Na]$^+$ 557.2146; found 557.2142.

General Procedure for the Aromatization of 6 to 7: A solution of **6** (1 mmol) and DDQ (681 mg, 3 mmol) in $ClCH_2CH_2Cl$ (15 mL) was refluxed for 3 h. After cooling to room temperature, the solution was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography with hexane/ethyl acetate (1:5) as eluent to give pure **7**.

Naphtho[2,3-*b*]furan 7a: Yield: 457 mg (91%), pale-yellow solid; m.p. 78–80 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.72 (d, J = 8.7 Hz, 1 H), 8.10 (d, J = 8.5 Hz, 1 H), 7.96 (m, 2 H), 7.91 (d, J = 12.5 Hz, 1 H), 7.66 (m, 1 H), 7.55 (m, 4 H), 5.15 (d, J = 12.5 Hz, 1 H), 4.64 (q, J = 7.2 Hz, 2 H), 4.42 (q, J = 7.2 Hz, 2 H), 4.13 (q, J = 7.1 Hz, 2 H), 1.56 (t, J = 7.1 Hz, 3 H), 1.35 (t, J = 7.2 Hz, 3 H), 1.22 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.9, 165.3, 164.0, 161.5, 159.5, 152.6, 144.8, 131.1, 130.7, 128.83, 128.78, 128.7, 128.2, 125.9, 125.8, 124.1, 122.0, 119.3, 109.3, 108.1, 101.4, 102.2, 61.9, 60.4, 14.8, 14.5, 14.2 ppm. IR (KBr): $\tilde{\nu}$ = 2983, 2940, 1732, 1713, 1651, 1585, 1508, 1375, 1315, 1286, 1229, 1126, 1050, 944, 838, 771, 685 cm^{-1}. MS (ESI): *m/z* 525.0 [M + Na]$^+$. HRMS (ESI): calcd. for $C_{29}H_{26}O_8$ [M + Na]$^+$ 525.1520; found 525.1505.

General Procedure for the One-Pot Synthesis of 7: A solution of triethylamine (1.5 mmol) in CH_2Cl_2 (5 mL) was added dropwise to a mixture of benzaldehyde (2 mmol) and ethyl propiolate (3 mmol) in CH_2Cl_2 (10 mL) under N_2 at –50 °C. The reaction mixture was stirred at –40 °C for 3 h, then 1 N hydrochloric acid (1.5 mL) was added to quench the reaction. The solution was washed with brine, dried with anhydrous sodium sulfate, and concentrated under reduced pressure. The residue and DDQ (1.26 g, 6 mmol) were dissolved in $ClCH_2CH_2Cl$ (20 mL) and refluxed for 3 h. After cooling to room temperature, the solution was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography with hexane/ethyl acetate (1:5) as eluent to give pure **7**.

Naphtho[2,3-*b*]furan 7d: Yield: 373 mg (57%), yellow solid; m.p. 116–117 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.00 (s, 1 H), 8.17 (d, J = 8.8 Hz, 1 H), 8.07 (d, J = 8.0 Hz, 2 H), 7.94 (d, J = 12.8 Hz, 1 H), 7.85 (d, J = 8.8 Hz, 1 H), 7.78 (m, 4 H), 7.69 (d, J = 7.6 Hz, 2 H), 7.52 (m, 4 H), 7.43 (m, 2 H), 5.21 (d, J = 12.4 Hz, 1 H), 4.68 (q, J = 6.8 Hz, 2 H), 4.46 (q, J = 6.8 Hz, 2 H), 4.15 (q, J = 6.8 Hz, 2 H), 1.60 (t, J = 7.2 Hz, 3 H), 1.40 (t, J = 7.2 Hz, 3 H), 1.23 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.0, 165.4, 164.1, 161.5, 159.3, 153.2, 144.8, 143.8, 140.80, 140.77, 140.1, 131.2, 129.2, 129.1, 128.3, 128.2, 127.8, 127.6, 127.5, 127.4, 125.8, 123.7, 123.4, 122.6, 119.4, 109.3, 108.2, 101.5, 62.2, 61.9, 603.4, 14.8, 14.5, 14.3 ppm. IR (KBr): $\tilde{\nu}$ = 2985, 2926, 1732, 1713, 1649, 1318, 1235, 1214, 1127, 767, 695 cm^{-1}. MS (ESI): *m/z* 676.9 [M + Na]$^+$. HRMS (ESI): calcd. for $C_{41}H_{34}O_8$ [M + Na]$^+$ 677.2146; found 677.2149.

General Procedure for the Synthesis of Polysubstituted Furans 9: Triethylamine (0.5 mmol) was added dropwise to a solution of an arenecarbaldehyde **1** (1 mmol), electron-deficient acetylene **2** (1 mmol), and acetylenedicarboxylate **8** (1.5 mmol) in CH_2Cl_2 (5 mL) at –10 °C under N_2 for 30 min. The resulting mixture was stirred at this temperature for 4 h and then diluted with CH_2Cl_2 (15 mL), washed twice with brine, and dried with anhydrous sodium sulfate. The solvent was evaporated in vacuo, and the residue was chromatographed on silica gel with ethyl acetate/hexane (1:4) to afford pure substituted furan **9**.

Furan 9a: Yield: 159 mg (48 %), yellow solid; m.p. 73–75 °C. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 7.64 (d, *J* = 7.04 Hz, 2 H), 7.45 (m, 3 H), 3.93 (s, 3 H), 3.92 (s, 3 H), 3.77 (s, 2 H), 3.72 (s, 3 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ = 170.9, 163.6, 158.4, 154.1, 142.1, 129.7, 129.1, 128.8, 127.6, 126.1, 115.3, 52.63, 52.57, 52.5, 30.4 ppm. IR (KBr): $\tilde{\nu}$ = 2957, 1736, 1728, 1720, 1553, 1448, 1206, 1088, 768, 687 cm^{-1}. MS (ESI): *m/z* 355.1 [M + Na]$^+$. HRMS (ESI): calcd. for $C_{17}H_{16}O_7$ [M + Na]$^+$ 355.0788; found 355.0773.

Furan 9b: Yield: 190 mg (55 %), white solid; m.p. 70–73 °C. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 7.55 (d, *J* = 8.0 Hz, 2 H), 7.29 (d, *J* = 7.84 Hz, 2 H), 3.944 (s, 3 H), 3.936 (s, 3 H), 3.7 (s, 2 H), 3.74 (s, 3 H), 2.42 (s, 3 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 171.0, 163.7, 158.5, 154.4, 141.8, 140.0, 129.8, 127.5, 126.2, 126.0, 114.8, 52.7, 52.6, 52.5, 30.4, 21.6 ppm. IR (KBr): $\tilde{\nu}$ = 2956, 1735, 1728, 1719, 1573, 1507, 1437, 1357, 1270, 1205, 108, 813, 767 cm^{-1}. MS (ESI): *m/z* 369.1 [M + Na]$^+$. HRMS (ESI): calcd. for $C_{18}H_{18}O_7$ [M + Na]$^+$ 369.0945; found 369.0938.

Furan 9c: Yield: 267 mg (61 %), yellow solid; m.p. 115–116 °C. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 7.59 (d, *J* = 8.23 Hz, 2 H), 7.43 (m, 4 H), 7.36 (m, 1 H), 7.06 (d, *J* = 8.24 Hz, 2 H), 5.12 (s, 2 H), 3.93 (s, 6 H), 3.74 (s, 2 H), 3.73 (s, 3 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ = 171.1, 163.8, 160.0, 158.5, 154.3, 141.6, 136.6, 129.2, 128.9, 128.4, 127.7, 126.3, 121.7, 115.5, 114.3, 70.3, 52.7, 52.59, 52.58, 30.5 ppm. IR (KBr): $\tilde{\nu}$ = 2947, 1746, 1736, 1719, 1603, 1503, 1434, 1348, 1251, 1164, 1083, 834, 755 cm^{-1}. MS (ESI): *m/z* 461.1 [M + Na]$^+$. HRMS (ESI): calcd. for $C_{24}H_{22}O_8$ [M + Na]$^+$ 461.1207; found 461.1185.

Supporting Information (see footnote on the first page of this article): Reaction condition optimization and experimental procedures. Spectroscopic data for all products. UV/Vis absorption and fluorescence spectra for compounds **7d** and **7f**.

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