First Partially Intramolecular Palladium-Catalyzed [2+2+2] Cycloaddition of Benzyne: Application to the Synthesis of Benzo[*b*]fluorenones

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The palladium(0)-catalyzed reaction of benzyne with suitably functionalized benzodiynes to afford benzo[*b*]fluorenones is described. The outcome of the reaction is affected by the steric and electronic properties of the diynes and proved to be regioselective when an unsymmetrically substituted aryne is used. This work represents the first example of a partially intramolecular [2+2+2] cycloaddition involving arynes.

Introduction

Intramolecular — or *partially* intramolecular — versions of cycloaddition reactions are extremely useful tools in the synthesis of polycyclic molecules, since they provide methods for the construction of several rings in a single step, with a concomitant increase in molecular complexity. In particular, with regard to the transition metal mediated [2+2+2] cycloaddition reactions of alkynes,[1] partially intramolecular variants have allowed the (otherwise difficult) control of the chemoselectivity and the regiochemistry of such transformations, as well as the participation of alkenes or nitriles as reaction partners.

Recently, we reported the intermolecular palladium-catalyzed cocyclotrimerization of arynes with alkynes[2−4] and, following our first reports, other groups have described metal-catalyzed cycloadditions of arynes.[5,6] Despite the excellent control of the chemoselectivity achieved in those reactions, the fact that they are "purely" intermolecular clearly limits their scope for synthetic applications. As a continuation of our research project we envisioned the development of partially intramolecular versions of the palladium-catalyzed [2+2+2] cycloadditions involving arynes, which have the potential to allow the construction of complex polycyclic systems. In this paper we describe our initial efforts in this field and, in particular, the application of the palladium-catalyzed cocyclotrimerization of benzyne with diynes in the synthesis of benzo[*b*]fluorenones, which constitute the polycyclic skeleton of the antitumor antibiotics kinamycins.[7]

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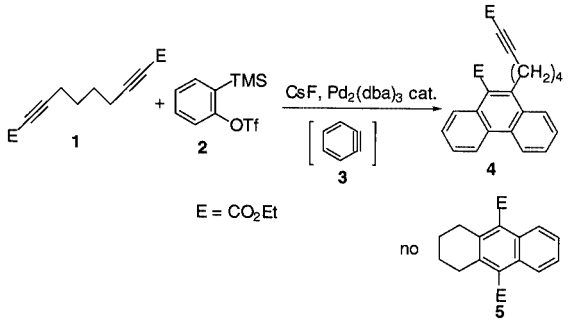
Results and Discussion

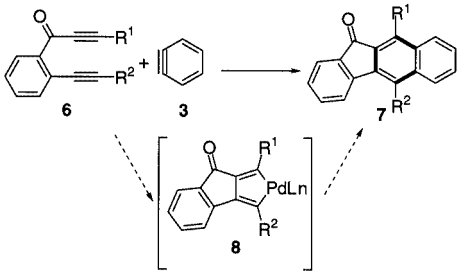
The requisite for a partially intramolecular cyclotrimerization is that two of the three cycloaddition partners are linked in the same molecule. When considering the cocycloaddition between arynes and alkynes, the simplest scenario for a partially intramolecular transformation would involve the reaction of a molecule containing two alkyne moieties (a diyne) with an external aryne. A literature precedent describing the stoichiometric reaction of a nickel−benzyne complex with 1,7-octadiyne[8] led us initially to investigate a catalytic version of this reaction. Our previous work on intermolecular Pd^0-catalyzed cocycloadditions of arynes with alkynes had shown that, because of the extremely high reactivity of arynes,[9] efficient cycloaddition involving two alkyne moieties and one molecule of aryne was possible only when a highly activated alkyne was used and $Pd_2(dba)_3$ acted as a catalyst. In these cases we postulated the initial formation of a palladacyclopentadiene, by oxidative coupling of two alkynes, as an intermediate in the catalytic cycle.[2,10] With this information in mind we prepared diyne **1**,[11] which contains two electron-withdrawing ethoxycarbonyl groups as substituents on the alkynes, and assessed its reaction with benzyne (**3**), generated from 2-(trimethylsilyl)phenyl triflate (**2**),[12] in the presence of 5 mol % $Pd_2(dba)_3$ (Scheme 1). The major product isolated from this reaction was compound **4**, which resulted from the intermolecular cocycloaddition between two molecules of benzyne and one of the alkyne moieties of the diyne. The expected tetrahydroanthracene **5**, which should be formed by a partially intramolecular reaction between **1** and **3**, was not detected, probably because of electronic and/or conformational factors precluding the generation of the required palladacyclic intermediate.

Next we decided to investigate a different model diyne with a higher degree of conformational restrictions and containing at least one highly electrophilic alkyne. In this



Scheme 1

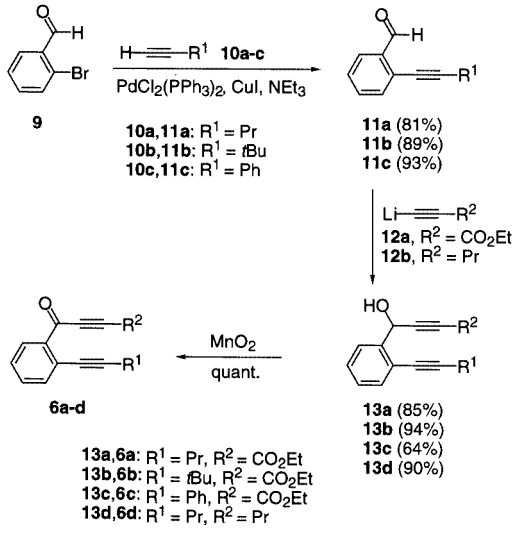
sense, we envisioned as potential candidates benzodiynes **6**, which upon [2+2+2] cycloaddition with benzyne should afford benzo[*b*]fluorenones **7** (Scheme 2). We reasoned that in this case, after initial coordination of one of the alkyne units (electron-deficient) in **6** to the metal atom, entropic factors should favor the formation of a palladacycle of type **8**, which should subsequently react with benzyne to afford the desired cycloaddition product **7**.



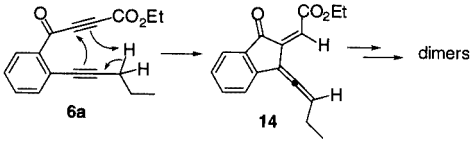
Scheme 2

Several diynes **6** with different steric and electronic properties were prepared according to the reaction sequence shown in Scheme 3. Sonogashira coupling[13] of alkynes **10a**−**c** with 2-bromobenzaldehyde (**9**) afforded the corresponding 2-alkynylbenzaldehydes **11a**−**c**, which upon reaction with the lithium acetylide **12a**, derived from ethyl propiolate, gave alcohols **13a**−**c** in good to excellent yields. Oxidation of **13a**−**c** with MnO_2 led to the quantitative isolation of the corresponding ketones **6a**−**c**. Although we had reasoned that the presence of at least one highly electron-deficient alkyne in **6** should be a prerequisite for a successful reaction, we also prepared **6d**, with an alkyl group as R^1, in order to check this premise.[14] Compound **6d** was prepared in a similar way to **6a**−**c** and the reactions proved equally efficient (Scheme 3).

Compounds **6a**−**c**, with $R^2 = CO_2Et$, proved too labile when stored at room temperature and it was necessary to prepare these materials just prior to use from the corresponding stable alcohols **13**. Interestingly, we observed that **6a** was transformed, upon standing at room temperature for 7 h, into a more-polar yellow product whose structure was assigned on the basis of its ^1H NMR spectrum as vinylallene **14**. The formation of this compound can be explained in terms of an intramolecular ene reaction on benzodiynone **6a** (Scheme 4). This compound, which incorporates a highly reactive diene system, finally evolved to a mixture of dimers of **6a**. As expected, ketone **6b** (R^1 = *t*Bu), which lacks propargylic hydrogen atoms and therefore cannot decompose through the previously proposed pathway, was found to be considerably more stable.

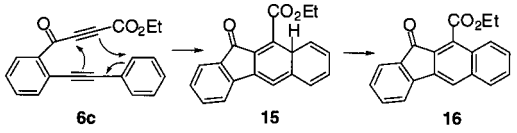


Scheme 3



Scheme 4

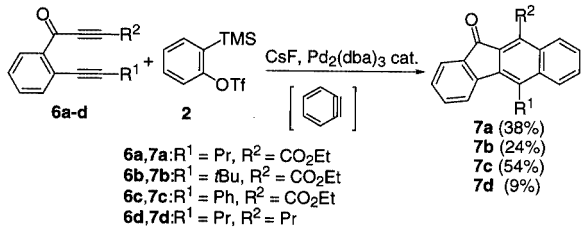
It is worth noting also that diyne **6c** (R^1 = Ph) is slowly transformed into a mixture of products in which the major compound (over 60%) was benzo[*b*]fluorenone **16**, which is probably formed by a formal intramolecular [4+2] cycloaddition via the cyclic allene **15** (Scheme 5).[15]



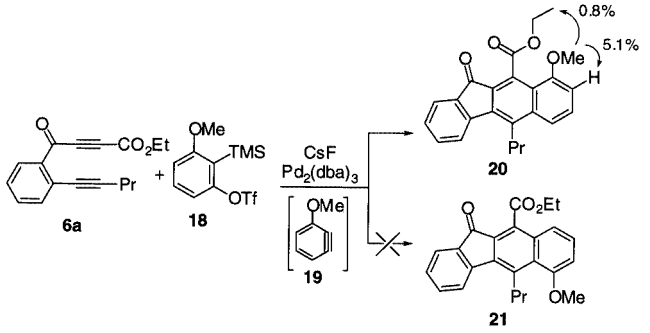
Scheme 5

With diynes **6** in hand, we proceeded to study their reaction with benzyne, generated from 2-(trimethylsilyl)phenyl triflate (**2**),[12] in the presence of a Pd^0 complex (Scheme 6). The catalyst of choice was $Pd_2(dba)_3$, which according to our previous work on the intermolecular version of this reaction should favor the chemoselective cocycloaddition of two molecules of alkyne with one molecule of aryne.[2,3] Satisfyingly, the reaction catalyzed by $Pd_2(dba)_3$ between crude **6a**, prepared immediately before use from alcohol **13a** as described above, and benzyne afforded the desired benzofluorenone **7a** in a moderate 38% yield,[16] together with minor amounts of triphenylene (9%) and other products de-

rived from the decomposition of **6a** through the ene reaction outlined in Scheme 4.

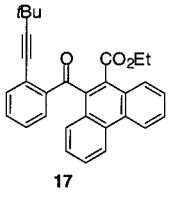


Scheme 6



Scheme 7

The reaction of the more stable ketone **6b** (R^1 = *t*Bu) under similar reaction conditions gave the benzofluorenone **7b** in a lower yield (24%), with the major product of the reaction being the substituted phenanthrene **17** (38%), which results from the [2+2+2] cycloaddition of two molecules of benzyne with the more electrophilic alkyne unit in **6b**.[17] We attribute this result to the presence of the bulky *tert*-butyl group, which probably disfavors the coordination of the second alkyne moiety to the metal atom and makes the formation of a metallacyclic intermediate of type **8** more difficult. The best result obtained in our study involved the reaction of ketone **6c**, which is less labile than **6a** and contains a smaller R^1 group (R^1 = Ph) than **6b**. Reaction of **6c** with benzyne in the presence of 5 mol % $Pd_2(dba)_3$ afforded the corresponding benzofluorenone **7c** in 54% yield. As expected, the reaction of compound **6d** (R^1 = R^2 = Pr) failed, affording only a 9% yield of the desired cocycloaddition product **7d** and confirming our predictions regarding the electronic requirements of the diynes (see above).



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Finally, we carried out the reaction of ketone **6a** with 3-methoxybenzyne (**19**), generated from triflate **18**, in order to gain an insight into the regioselectivity of the process when an unsymmetrically substituted aryne acts as a reaction partner. Reaction of **6a** with **18** under the reaction conditions previously described afforded benzofluorenone **20** as the only cocycloaddition product in 43% yield. The structure of the product was established on the basis of NOE and COSY experiments: irradiation of the OCH_3 group (δ = 3.94 ppm) afforded a positive difference NOE to 8-H (δ = 6.88 ppm, 5.1%) and to the terminal CH_3 unit of the ethoxyl group (δ = 1.48 ppm, 0.8%), which had been assigned previously with the help of a homonuclear ^1H-^1H COSY spectrum. The other possible regioisomer **21** was not detected in the reaction mixture (Scheme 7).

In summary, we report a novel approach to the benzo[*b*]fluorenone nucleus by palladium-catalyzed cycloaddition of benzyne to a suitably functionalized diyne. The outcome of the reaction is affected by the steric and electronic properties of the diyne and, when an unsymmetrically substituted aryne was used, the reaction proved to be regioselective. Although the moderate yields obtained limit the general applicability of the reaction for preparative purposes, the major interest of this work arises from the fact that it represents the first example of a partially intramolecular [2+2+2] cyclotrimerization involving arynes. Work is in progress aimed at the rational design of novel cycloaddition partners and the application of this methodology to the synthesis of other bioactive polycyclic compounds.

Experimental Section

General: All reactions were performed under argon. Solvents were dried by distillation from a drying agent: Et_2O and THF from Na/benzophenone; CH_3CN from CaH_2. TMSCl and NEt_3 were distilled from CaH_2 prior to use. Reported melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 250.13 and 62.83 MHz, respectively. LR and HR mass spectra were recorded using EI (70 eV) or FAB techniques. TLC was performed on Merck silica gel 60 F_{254}; chromatograms were visualized with UV light (254 and 360 nm), phosphomolybdic acid, and/or *p*-anisaldehyde. Column chromatography was performed on Merck silica gel 60 (ASTM 230−400 mesh). 2-(Trimethylsilyl)phenyl trifluoromethanesulfonate (**2**) and 3-methoxy-2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**18**) were prepared according to a recently published procedure developed in our laboratories.[12] $Pd_2(dba)_3{\cdot}CHCl_3$ and $PdCl_2(PPh_3)_2$ were purchased from Strem; other commercial reagents were purchased from Aldrich Chemical Co. and were all used without further purification.

2-(1-Pentynyl)benzaldehyde (11a): $PdCl_2(PPh_3)_2$ (0.215 g, 0.31 mmol) and CuI (0.097 g, 0.51 mmol) were added to a solution of 2-bromobenzaldehyde (**9**, 1.877 g, 10.15 mmol), 1-pentyne (**10a**, 1.35 mL, 13.77 mmol), and NEt_3 (2.8 mL, 20.40 mmol) in THF (20 mL). The mixture was heated under reflux for 3 h under argon. The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography (SiO_2; Et_2O/hexane, 2:98) to yield **11a**[18] (1.421 g, 81%) as a yellow oil. ^1H NMR ($CDCl_3$, 25 °C): δ = 1.07 (t, *J* = 7.3 Hz, 3 H, $CH_2CH_2CH_3$), 1.68 (m, 2 H, $CH_2CH_2CH_3$), 2.47 (t, *J* = 7.0 Hz, 2 H, $CH_2CH_2CH_3$), 7.38 (m, 1 H, ArH), 7.51−7.53 (m, 2 H, ArH), 7.89 (d, *J* = 7.7 Hz, 1 H, ArH), 10.55 (d, *J* = 0.8 Hz, 1 H, CHO) ppm. ^{13}C NMR DEPT

($CDCl_3$, 25 °C): δ = 13.2 (CH_3), 21.1 (CH_2), 21.6 (CH_2), 76.1 (C), 97.6 (C), 126.4 (CH), 127.5 (CH), 132.9 (CH), 133.3 (CH), 135.5 (C), 191.5 (CO) ppm.

2-(3,3-Dimethyl-1-butynyl)benzaldehyde (11b): $PdCl_2(PPh_3)_2$ (0.268 g, 0.38 mmol) and CuI (0.121 g, 0.63 mmol) were added to a solution of 2-bromobenzaldehyde (**9**, 2.35 g, 12.70 mmol), 3,3-dimethyl-1-butyne (**10b**, 1.9 mL, 15.24 mmol), and NEt_3 (3.5 mL, 25.40 mmol) in THF (24 mL). The mixture was heated under reflux for 3 h under argon. The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography (SiO_2; Et_2O/hexane, 1:99) to yield **11b**[18] (2.103 g, 89%) as a yellow oil. ^1H NMR ($CDCl_3$, 25 °C): δ = 1.35 (s, 9 H, *t*Bu), 7.36 (m, 1 H, ArH), 7.46−7.54 (m, 2 H, ArH), 7.88 (d, *J* = 7.8 Hz, 1 H, ArH), 10.53 (s, 1 H, CHO) ppm.

2-(2-Phenyl-1-ethynyl)benzaldehyde (11c): $PdCl_2(PPh_3)_2$ (0.084 g, 0.12 mmol) and CuI (0.038 g, 0.20 mmol) were added to a solution of 2-bromobenzaldehyde (**9**, 0.740 g, 4.00 mmol), phenylacetylene (**10c**, 0.527 mL, 4.80 mmol), and NEt_3 (1.1 mL, 8.00 mmol) in THF (8 mL). The mixture was heated under reflux for 3 h under argon. The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography (SiO_2; Et_2O/hexane, 2:98) to yield **11c**[18] (0.763 g, 93%) as a yellow oil. ^1H NMR ($CDCl_3$, 25 °C): δ = 7.41−7.36 (m, 4 H, ArH), 7.47−7.66 (m, 4 H, ArH), 7.85 (dd, *J* = 7.7, 0.9 Hz, 1 H, ArH), 10.65 (s, 1 H, CHO) ppm. ^{13}C NMR DEPT ($CDCl_3$, 25 °C): δ = 84.7 (alkyne C), 96.2 (alkyne C), 122.1 (C), 126.6 (C), 127.0 (CH), 128.3 (CH), 128.4 (CH), 128.9 (CH), 131.5 (CH), 133.0 (CH), 133.6 (CH), 135.5 (C), 191.4 (CHO) ppm. MS: *m*/*z* (%) = 206 (100), 176 (47), 152 (28).

Ethyl 4-Hydroxy-4-[2-(1-pentynyl)phenyl]-2-butynoate (13a): *n*BuLi (1.73 mL, 2.04 M in hexanes, 3.53 mmol) was added dropwise to a solution of ethyl propiolate (0.34 mL, 3.36 mmol) in THF (20 mL) at −78 °C. Immediately, a solution of **11a** (0.551 g, 3.20 mmol) in THF (5 mL) was added and the resulting mixture was warmed to room temp. and stirred for 12 h. 10% aq. NH_4Cl (15 mL) was added, the organic layer was separated, and the aqueous layer was extracted with Et_2O (2 × 15 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (SiO_2; Et_2O/hexane, 2:8) to yield **13a** (0.733 g, 85%) as a colorless oil. ^1H NMR ($CDCl_3$, 25 °C): δ = 1.07 (t, *J* = 7.3 Hz, 3 H, CH_3), 1.31 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.67 (m, 2 H, $CH_2CH_2CH_3$), 2.46 (t, *J* = 7.0 Hz, 2 H, $CH_2CH_2CH_3$), 2.84 (d, *J* = 6.6 Hz, 1 H, CHOH), 4.24 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 5.91 (d, *J* = 6.6 Hz, 1 H, CHO*H*), 7.28−7.37 (m, 2 H, ArH), 7.44 (dd, *J* = 7.1, 2.0 Hz, 1 H, ArH), 7.57 (d, *J* = 8.0 Hz, 1 H, ArH) ppm.^{13}C NMR DEPT ($CDCl_3$, 25 °C): δ = 13.3 (CH_3), 13.6 (CH_3), 21.2 (CH_2), 21.7 (CH_2), 61.9 (OCH_2), 62.2 (CHOH), 77.4 (alkyne C), 76.7 (alkyne C), 86.2 (alkyne C), 96.5 (alkyne C), 121.9 (C), 126.2 (CH), 127.9 (CH), 128.2 (CH), 132.1 (CH), 139.8 (C), 153.3 (ester CO) ppm. MS: *m*/*z* (%) = 270 (1), 255 (9), 241 (13), 208 (100). HRMS for $C_{16}H_{15}O_3$, calcd: 255.1021; found 255.1034.

Ethyl 4-[2-(3,3-Dimethyl-1-butynyl)phenyl]-4-hydroxy-2-butynoate (13b): According to the experimental procedure described above for the synthesis of **13a**, a solution of ethyl propiolate (0.591 mL, 3.36 mmol) in THF (30 mL) was treated with *n*BuLi (3.00 mL, 2.04 M in hexanes, 6.14 mmol) and a solution of **11b** (1.037 g, 5.58 mmol) in THF (10 mL). The residue obtained after workup was purified by flash chromatography (SiO_2; Et_2O/hexane, 1:9) to yield **13b** (1.50 g, 94%) as a colorless oil. ^1H NMR ($CDCl_3$, 25 °C): δ = 1.30 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 1.36 (s, 9 H, *t*Bu), 3.01 (d, *J* = 7.1 Hz, 1 H, CHOH), 4.23 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 5.82 (d, *J* = 6.9 Hz, 1 H, CHO*H*), 7.27−7.34 (m, 2 H, ArH), 7.42 (dd, *J* = 7.2, 2.3 Hz, 1 H, ArH), 7.51 (dd, *J* = 6.7, 2.3 Hz, 1 H, ArH) ppm.^{13}C NMR DEPT ($CDCl_3$, 25 °C): δ = 13.8 (ethyl CH_3), 28.1 (*t*Bu C), 30.6 (*t*Bu CH_3), 62.0 (CH_2), 62.8 (CHOH), 76.1 (alkyne C), 76.9 (alkyne C), 86.1 (alkyne C), 105.1 (alkyne C), 121.8 (C), 126.3 (CH), 128.0 (CH), 128.3 (CH), 132.2 (CH), 140.0 (C), 153.3 (ester CO) ppm. MS, *m*/*z* (%) = 284 (3), 269 (7), 256 (10), 223 (58), 195 (100). HRMS for $C_{18}H_{20}O_3$, calcd: 284.1413; found 284.1414.

Ethyl 4-Hydroxy-4-[2-(2-phenyl-1-ethynyl)phenyl]-2-butynoate (13c): According to the experimental procedure described above for the synthesis of **13a**, a solution of ethyl propiolate (0.307 mL, 3.04 mmol) in THF (15 mL) was treated with *n*BuLi (1.316 mL, 2.38 M in hexanes, 3.13 mmol) and a solution of **11c** (0.597 g, 2.90 mmol) in THF (5 mL). The residue obtained after workup was purified by flash chromatography (SiO_2; Et_2O/hexane, 5:95) to yield **13c** (0.568 g, 64%) as a colorless oil. ^1H NMR ($CDCl_3$, 25 °C): δ = 1.29 (t, *J* = 7.2 Hz, 3 H, OCH_2CH_3), 2.82 (d, *J* = 6.5 Hz, 1 H, CHOH), 4.23 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 6.01 (d, *J* = 6.4 Hz, 1 H, CHO*H*), 7.36−7.42 (m, 5 H, ArH), 7.56−7.60 (m, 3 H, ArH), 7.65 (d, *J* = 7.7 Hz, 1 H, ArH) ppm. ^{13}C NMR DEPT ($CDCl_3$, 25 °C): δ = 13.9 (CH_3), 62.2 (CH_2), 62.8 (CHOH), 77.4 (alkyne C), 85.8 (alkyne C), 86.0 (alkyne C), 95.4 (alkyne C), 121.4 (C), 122.5 (C), 126.8 (CH), 128.3 (CH), 128.7 (CH), 128.9 (CH), 131.6 (CH), 132.5 (CH), 140.0 (C), 153.3 (ester CO) ppm. MS: *m*/*z* (%) = 304 (1), 289 (7), 276 (13), 231 (70), 202 (100).

1-[2-(1-Pentynyl)phenyl]-2-hexyn-1-ol (13d): *n*BuLi (1.01 mL, 2.38 M in hexanes, 2.40 mmol) was added dropwise to a solution of 1-pentyne (**10a**, 0.218 mL, 2.22 mmol) in THF (15 mL) at −78 °C. The resulting solution was stirred for 10 min at −78 °C and then a solution of **11d** (0.332 g, 1.93 mmol) in THF (5 mL) was added. The resulting mixture was warmed to room temp. and stirred for 12 h. 10% aq. NH_4Cl (15 mL) was added, the organic layer was separated and the aqueous layer was extracted with Et_2O (2 × 15 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (SiO_2; Et_2O/hexane, 8:92) to yield **13d** (0.415 g, 90%) as a colorless oil. ^1H NMR ($CDCl_3$, 25 °C): δ = 0.99 (t, *J* = 7.3 Hz, 3 H, $CH_2CH_2CH_3$), 1.07 (t, *J* = 7.3 Hz, 3 H, $CH_2CH_2CH_3$), 1.49−1.70 (m, 4 H, $CH_2CH_2CH_3$), 2.25 (dt, *J* = 7.1, 2.0 Hz, 2 H, $CH_2CH_2CH_3$), 2.44 (t, *J* = 7.0 Hz, 2 H, $CH_2CH_2CH_3$), 2.67 (d, *J* = 4.8 Hz, 1 H, CHOH), 5.84 (br. s, 1 H, CHO*H*), 7.21−7.35 (m, 2 H, ArH), 7.41 (dd, *J* = 7.2, 1.6 Hz, 1 H, ArH), 7.67 (d, *J* = 7.5 Hz, 1 H, ArH) ppm.^{13}C NMR DEPT ($CDCl_3$, 25 °C): δ = 13.5 (CH_3), 13.6 (CH_3), 20.8 (CH_2), 21.5 (CH_2), 22.0 (CH_2), 22.1 (CH_2), 63.4 (CHOH), 78.1 (alkyne C), 79.3 (alkyne C), 87.2 (alkyne C), 95.9 (alkyne C), 122.0 (C), 126.5 (CH), 127.9 (CH), 128.0 (CH), 132.4 (CH), 142.6 (C) ppm. MS: *m*/*z* (%) = 240 (4), 225 (4), 211 (48), 197 (100). HRMS for $C_{17}H_{20}O$, calcd: 240.1514; found 240.1521.

General Procedure for the Synthesis of Benzo[*b*]fluoren-11-ones 7: MnO_2 (300−400 mol %) was added in portions to a solution of alcohol **13** (approx. 0.50 mmol) in Et_2O (10 mL). The resulting suspension was stirred at room temp. for 5−60 min, filtered through Celite, and concentrated under reduced pressure to yield the corresponding ketone **6**. The resulting product was dissolved in CH_3CN (approx. 5 mL) and to this solution was added 2-(trimethylsilyl)-phenyl trifluoromethanesulfonate (**3**, 50 mol %), $Pd_2(dba)_3$·(5 mol %), and CsF (100 mol %). The mixture was stirred under argon at room temp. for 12 h. The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography to yield the corresponding benzofluorenone **7**.

Ethyl 11-Oxo-5-propyl-11*H*-benzo[*b*]fluorene-10-carboxylate (7a): According to the general procedure described above, alcohol **13a** (162 mg, 0.60 mmol) was treated with MnO_2 (1.57 g, 18.00 mmol) for 5 min to afford 4-[2-(1-pentynyl)phenyl]-4-oxo-2-butynoate (**6a**) as a yellow oil. The resulting product was treated with 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**2**, 0.073 mL, 0.30 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (16 mg, 0.015 mmol), [18]crown-6[19] (40 mg, 0.15 mmol), and CsF (114 mg, 0.75 mmol) in CH_3CN (6 mL). Workup and purification by flash chromatography (SiO_2; Et_2O/hexane, 3:97 then 1:9) afforded triphenylene (2 mg, 9%) and **7a** (39 mg, 38%) as a yellow solid. Data for **6a**: ^1H NMR ($CDCl_3$, 25 °C): δ = 1.07 (d, *J* = 7.3 Hz, 3 H, CH_3), 1.35 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.74−1.59 (m, 2 H, $CH_2CH_2CH_3$), 2.46 (t, *J* = 7.0 Hz, 2 H, $CH_2CH_2CH_3$), 4.32 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 7.39 (m, 1 H, ArH), 7.47−7.53 (m, 2 H, ArH), 8.01 (d, *J* = 7.6 Hz, 1 H, ArH) ppm. Data for **7a**: M.p. 135 °C. ^1H NMR ($CDCl_3$, 25 °C): δ = 1.20 (t, *J* = 7.3 Hz, 3 H, CH_3); 1.49 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.85−1.75 (m, 2 H, $CH_2CH_2CH_3$), 3.35−3.28 (m, 2 H, $CH_2CH_2CH_3$), 4.65 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 7.35 (t, *J* = 7.6 Hz, 1 H, ArH), 7.65−7.49 (m, 3 H, ArH), 7.86−7.76 (m, 3 H, ArH), 8.11 (d, *J* = 8.3 Hz, 1 H, ArH) ppm. ^{13}C NMR DEPT ($CDCl_3$, 25 °C): δ = 14.1 (CH_3), 14.5 (CH_3), 22.8 (CH_2), 30.3 (CH_2), 62.2 (benzylic CH_2), 124.2 (CH), 124.5 (CH), 124.8 (CH), 127.4 (CH), 127.6 (CH), 128.7 (CH), 129.2 (CH), 129.4 (C), 129.8 (C), 134.1 (C), 135.3 (CH), 136.1 (2C), 136.2 (2C), 145.1 (C), 167.9 (ester CO), 191.6 (CO) ppm. UV ($CHCl_3$): λ_{max} = 292 nm. MS: *m*/*z* (%) = 344 (87), 315 (100), 299 (30). HRMS for $C_{23}H_{20}O_3$: calcd. 344.1413; found 344.1415.

Ethyl 5-(3,3-Dimethyl-1-butynyl)-11-oxo-11*H*-benzo[*b*]fluorene-10-carboxylate (7b): According to the general procedure described above, alcohol **13b** (145 mg, 0.51 mmol) was treated with MnO_2 (1.78 g, 20.44 mmol) for 15 min to afford 4-[2-(3,3-dimethyl-1-butynyl)phenyl]-4-oxo-2-butynoate (**6b**) as a yellow oil. The resulting product was treated with 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**2**, 0.062 mL, 0.26 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (13 mg, 0.012 mmol), and CsF (97 mg, 0.64 mmol). Workup and purification by flash chromatography (SiO_2; Et_2O/hexane, 4:96) afforded **7b** (22 mg, 24%) and ethyl 10-[2-(3,3-dimethyl-1-butynyl)benzoyl]-phenanthrene-9-carboxylate (**17**, 21 mg, 38%) as yellow solids. Data for **6b**: ^1H NMR ($CDCl_3$, 25 °C): δ = 1.34 (s, 9 H, *t*Bu), 1.35 (t, *J* = 7.2 Hz, 3 H, OCH_2CH_3), 4.32 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 7.38 (m, 1 H, ArH), 7.50−7.52 (m, 2 H, ArH), 8.99 (d, *J* = 7.7 Hz, 1 H, ArH) ppm. MS: *m*/*z* (%) = 282 (17), 267 (100), 165 (89). Data for **7b**: M.p. 122 °C. ^1H NMR ($CDCl_3$, 25 °C): δ = 1.50 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 1.77 (s, 9 H, *t*Bu), 4.64 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 7.32 (d, *J* = 7.4 Hz, 1 H, ArH), 7.44−7.57 (m, 3 H, ArH), 7.73−7.78 (m, 2 H, ArH), 7.83 (d, *J* = 7.9 Hz, 1 H, ArH), 8.29 (dd, *J* = 7.5, 1.8 Hz, 1 H, ArH) ppm. ^{13}C NMR DEPT ($CDCl_3$, 25 °C): δ = 14.1 (ethyl CH_3), 32.7 (*tert*-butyl CH_3), 37.7 (*tert*-butyl C), 62.2 (CH_2), 124.2 (CH), 126.5 (CH), 126.6 (CH), 126.7 (CH), 127.8 (CH), 128.3 (CH), 128.4 (C), 128.8 (CH), 130.0 (C), 130.3 (C), 133.8 (CH), 135.6 (C), 136.9 (C), 137.5 (C), 147.1 (C), 148.0 (C), 168.0 (ester CO), 191.4 (CO) ppm. IR (film): $\tilde{\nu}$ = 1731, 1711 cm^{-1}. UV ($CHCl_3$): λ_{max} = 300, 257 nm. MS: *m*/*z* (%) = 358 (100), 343 (51), 315 (56). HRMS for $C_{24}H_{22}O_3$, calcd: 358.1569; found 358.1572. Data for **17**: M.p. 92 °C. ^1H NMR ($CDCl_3$, 25 °C): δ = 0.88 (s, 9 H, *t*Bu), 1.16 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 4.14 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 7.31 (d, *J* = 7.7 Hz, 1 H, ArH), 7.42−7.56 (m, 3 H, ArH), 7.64−7.79 (m, 4 H, ArH), 7.85 (d, *J* = 8.2 Hz, 1 H, ArH), 8.27 (d, *J* = 7.9 Hz, 1 H, ArH), 8.74 (d, *J* = 8.4 Hz, 1 H, ArH, H-4 or H-5), 8.75 (d, *J* = 7.8 Hz, 1 H, ArH, H-4 or H-5) ppm. ^{13}C NMR DEPT ($CDCl_3$), δ = 13.6 (ethyl CH_3), 27.8 (*tert*-butyl C), 30.2 (*tert*-butyl CH_3), 61.7 (CH_2), 77.7 (alkyne C), 105.4 (alkyne C), 122.7 (CH), 122.8 (CH), 124.5 (C), 126.7 (CH), 127.16 (CH), 127.21 (CH), 127.3 (CH), 127.5 (CH), 127.6 (C), 127.9 (CH), 128.1 (C), 128.2 (CH), 128.4 (C), 130.8 (C), 131.0 (CH), 131.1 (C), 132.1 (CH), 134.8 (CH), 137.9 (C), 138.9 (C), 167.5 (ester CO), 196.9 (CO) ppm. IR (film): $\tilde{\nu}$ = 1725, 1662 cm^{-1}. UV ($CHCl_3$): λ_{max} = 256 nm. MS: *m*/*z* (%) = 434 (36), 419 (100), 302 (57). HRMS for $C_{30}H_{26}O_3$: calcd. 434.1882; found 434.1869.

Ethyl 5-Phenyl-11-oxo-11*H*-benzo[*b*]fluorene-10-carboxylate (7c): According to the general procedure described above, alcohol **13c** (135 mg, 0.44 mmol) was treated with MnO_2 (773 mg, 8.88 mmol) for 30 min to afford 4-[2-(2-phenyl-1-ethynyl)phenyl]-4-oxo-2-butynoate (**6c**) as a yellow oil. The resulting product was treated with 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**2**, 0.054 mL, 0.22 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (11.5 mg, 0.011 mmol), and CsF (68 mg, 0.44 mmol). Workup and purification by flash chromatography (SiO_2; Et_2O/hexane, 4:96) afforded **7c** (45 mg, 54%) as a yellow solid. Data for **6c**: ^1H NMR ($CDCl_3$, 25 °C): δ = 1.29 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 4.26 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 7.35−7.38 (m, 3 H, ArH), 7.47 (dt, *J* = 7.5, 1.3 Hz, 1 H, ArH), 7.56−7.69 (m, 4 H, ArH), 8.11 (d, *J* = 7.7 Hz, 1 H, ArH) ppm. ^{13}C NMR DEPT ($CDCl_3$, 25 °C): δ = 13.9 (CH_3), 62.9 (CH_2), 80.6 (alkyne C), 80.9 (alkyne C), 87.5 (alkyne C), 96.3 (alkyne C), 122.8 (C), 123.5 (C), 128.1 (CH), 128.3 (CH), 128.9 (CH), 131.9 (CH), 133.5 (CH), 134.5 (CH), 136.3 (C), 152.3 (ester CO), 175.3 (CO) ppm. MS, *m*/*z* = (%) = 302 (47), 257 (48), 230 (100), 200 (85). Data for **7c**: M.p. 177 °C. ^1H NMR ($CDCl_3$, 25 °C): δ = 1.53 (t, *J* = 7.2 Hz, 3 H, OCH_2CH_3), 4.69 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 6.29 (dd, *J* = 6.4, 1.7 Hz, 1 H, H-4), 7.16−7.23 (m, 2 H, ArH), 7.36−7.39 (m, 2 H, ArH), 7.45−7.54 (m, 3 H, ArH), 7.60−7.63 (m, 3 H, ArH), 7.71 (m, 1 H, ArH), 7.90 (dd, *J* = 7.6, 1.4 Hz, 1 H, ArH), ppm. ^{13}C NMR DEPT ($CDCl_3$, 25 °C): δ = 14.2 (CH_3), 62.3 (CH_2), 123.9 (CH), 124.3 (CH), 127.1 (CH), 127.4 (CH), 127.6 (CH), 128.46 (C), 128.53 (CH), 128.9 (CH), 129.2 (CH), 129.4 (CH), 129.5 (CH), 129.6 (C), 130.4 (C), 134.6 (C), 134.9 (CH), 135.7 (C), 136.0 (C), 136.7 (C), 137.0 (C), 144.7 (C), 167.6 (ester CO), 191.4 (CO) ppm. UV ($CHCl_3$): λ_{max} = 292 nm. MS: *m*/*z* (%) = 378 (66), 333 (42), 306 (54), 276 (100). HRMS for $C_{26}H_{18}O_3$: calcd. 378.1256; found 378.1260.

5,10-Dipropyl-11*H*-benzo[*b*]fluorene-11-one (7d): According to the general procedure described above, alcohol **13d** (117 mg, 0.49 mmol) was treated with MnO_2 (1.7 g, 19.50 mmol) for 60 min to afford 1-[2-(1-pentynyl)phenyl]-2-hexyn-1-one (**6d**) as a yellow oil. The resulting product was treated with 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**2**, 0.059 mL, 0.24 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (13 mg, 0.012 mmol), and CsF (93 mg, 0.61 mmol). Work up and purification by flash chromatography (SiO_2; Et_2O/hexane, 2:98) afforded **7d** (7 mg, 9%) as a yellow solid. Data for **6d**: ^1H NMR ($CDCl_3$, 25 °C): δ = 1.05 (t, *J* = 7.3 Hz, 3 H, CH_3), 1.07 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.66 (m, 4 H, 2 × $CH_2CH_2CH_3$), 2.43 (t, *J* = 7.0 Hz, 2 H, $CH_2CH_2CH_3$), 2.45 (t, *J* = 7.0 Hz, 2 H, $CH_2CH_2CH_3$), 7.31−7.52 (m, 3 H, ArH), 8.05 (d, *J* = 7.6 Hz, 1 H, ArH) ppm. ^{13}C NMR DEPT ($CDCl_3$, 25 °C): δ = 13.4 (2 × CH_3), 21.0 (CH_2), 21.2 (CH_2), 21.7 (CH_2), 21.9 (CH_2), 79.2 (alkyne C), 80.7 (alkyne C), 96.2 (alkyne C), 96.5 (alkyne C), 123.4 (C), 126.9 (CH), 131.5 (CH), 131.9 (CH), 134.4 (CH), 138.1 (C), 177.7 (CO) ppm. MS: *m*/*z* (%) =238 (2), 223 (18), 210 (100). Data for **7d**: M.p. 118 °C. ^1H NMR ($CDCl_3$, 25 °C): δ = 1.12 (t, *J* = 7.3 Hz, 3 H, CH_3), 1.23 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.68−1.87 (m, 4 H, 2 × $CH_2CH_2CH_3$), 3.26−3.33 (m, 2 H, $CH_2CH_2CH_3$), 3.58−3.64 (m, 2 H, $CH_2CH_2CH_3$), 7.34 (t, *J* = 7.3 Hz, 1 H, ArH), 7.64−7.49 (m, 3 H, ArH), 7.78 (d, *J* = 6.8 Hz, 1 H, ArH), 7.79 (d,

J = 7.9 Hz, 1 H, ArH), 8.11 (d, J = 8.2 Hz, 1 H, ArH), 8.19 (d, J = 7.7 Hz, 1 H, ArH) ppm. ^{13}C NMR DEPT ($CDCl_3$, 25 °C): δ = 14.60 (CH_3), 14.61 (CH_3), 22.9 (CH_2), 24.3 (CH_2), 28.0 (CH_2), 30.4 (CH_2), 124.0 (CH), 124.1 (CH), 125.0 (CH), 126.4 (CH), 126.7 (CH), 128.2 (CH), 128.5 (C), 128.6 (CH), 133.1 (C), 133.4 (C), 134.7 (CH), 135.2 (C), 136.1 (C), 137.1 (C), 142.1 (C), 144.5 (C), 194.5 (CO) ppm. IR (film): $\tilde{\nu}$ = 1699 cm^{-1}. UV ($CHCl_3$): λ_{max} = 291 nm. MS: *m/z* (%) = 314 (59), 285 (51), 271 (100). HRMS for $C_{23}H_{22}O$: calcd. 314.1671; found 314.1668.

Ethyl 9-Methoxy-11-oxo-5-propyl-11*H*-benzo[*b*]fluorene-10-carboxylate (20): According to the general procedure described above, alcohol **13a** (162 mg, 0.60 mmol) was treated with MnO_2 (1.57 g, 18.00 mmol) for 5 min to afford **6a** as a yellow oil. The resulting product was treated with 3-methoxy-2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**18**, 98 mg, 0.30 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (16 mg, 0.015 mmol), [18]crown-6[19] (40 mg, 0.15 mmol), and CsF (114 mg, 0.75 mmol). Workup and purification by flash chromatography (SiO_2; Et_2O/hexane, 1:9 then 1:3) afforded **20** (48 mg, 43%). ^{1}H NMR ($CDCl_3$, 25 °C): δ = 1.18 (t, J = 7.3 Hz, 3 H, $CH_2CH_2CH_3$), 1.48 (t, J = 7.2 Hz, 3 H, OCH_2CH_3), 1.73−1.82 (m, 2 H, $CH_2CH_2CH_3$), 3.24−3.31 (m, 2 H, $CH_2CH_2CH_3$), 3.94 (s, 3 H, OCH_3), 4.52−4.52 (m, 2 H, OCH_2CH_3), 6.88 (d, J = 7.7 Hz, 1 H, H-8), 7.34 (t, J = 7.6 Hz, 1 H, H-2 ó H-3), 7.49−7.60 (m, 2 H, H-7 and H-1 to H-4), 7.69 (d, J = 8.3 Hz, 1 H, H-6), 7.75−7.79 (m, 2 H, ArH) ppm. ^{13}C NMR DEPT ($CDCl_3$, 25 °C): δ = 14.2 (CH_3), 14.5 (CH_3), 22.7 (propyl CH_2), 30.7 (propyl CH_2), 56.2 (OCH_3), 61.5 (ethyl CH_2), 107.1 (CH), 117.4 (CH), 121.4 (C), 124.1 (CH), 124.4 (CH), 127.4 (C), 128.4 (C), 128.7 (CH), 129.7 (CH), 134.9 (C), 135.1 (CH), 135.6 (C), 136.2 (C), 137.9 (C), 144.6 (C), 157.8 (C), 168.9 (ester CO), 191.6 (CO) ppm. IR (film): $\tilde{\nu}$ = 1717 cm^{-1}. UV ($CHCl_3$): λ_{max} = 292 nm. MS: *m/z* (%) = 374 (100), 345 (40), 329 (73).

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