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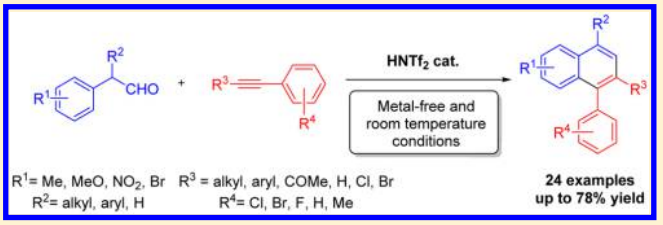
$HNTf_2$-Catalyzed Regioselective Preparation of Polysubstituted Naphthalene Derivatives Through Alkyne−Aldehyde Coupling

Sudipta Ponra, Maxime R. Vitale,* Véronique Michelet,* and Virginie Ratovelomanana-Vidal*

PSL Research University, Chimie ParisTech - CNRS, Institut de Recherche de Chimie Paris, 75005, Paris, France

Supporting Information

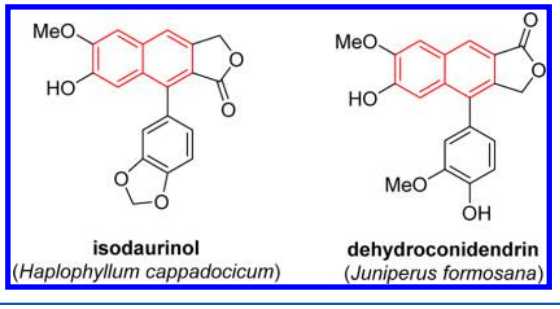
ABSTRACT: We report herein the preparation of polysubstituted naphthalene derivatives by the original Brønsted-acid-catalyzed benzannulation reaction of phenylacetaldehydes with alkynes. This reaction, which was usually performed with Lewis acids under thermal activation, is efficiently promoted by 15 mol % of triflimide ($HNTf_2$) at room temperature under metal-free and mild reaction conditions and leads with a perfect regioselectivity to a wide variety of diversely functionalized naphthalenes in 41−78% yield. A catalytic cycle is proposed together with some further applications of this catalytic system in the related benzannulation transformations of epoxide and acetal derivatives.



INTRODUCTION

Substituted naphthalene derivatives are an important class of compounds that possesses widespread applications. They are found in numerous optical and electronic materials[1] and constitute the core of many biologically relevant molecules including the vast family of arylnaphthalene lignans (Scheme 1).[2]

Scheme 1. Representative Examples of Arylnaphthalene Lignans



Accordingly, many efforts have been devoted to their regioselective synthesis in past decades, the contribution of catalysis to this field being particularly remarkable.[3] Among the different strategies examined so far, the catalyzed construction of the second aromatic ring of the naphthalene core through the incorporation of a two-carbon alkyne unit and following a formal [4 + 2] process is undeniably straightforward.[4−9] Such kind of catalytic transformation typically includes Larock's palladium(0)-catalyzed cyclizations of vinyl/aryl iodides or triflates (Scheme 2, eq 1) and the benzannulation reactions of 2-alkynylbenzaldehydes under π-Lewis-acid metal catalysis originally described by Asao and Yamamoto (Scheme 2, eq 2).[4,5] Alternatively, the regioselective synthesis of naphthalene derivatives may also arise from the condensation of phenylacetaldehydes with alkynes (Scheme 2, eq 3). Whereas this efficient benzannulation reaction was successfully realized by using $TiCl_4$ or $FeCl_3$ in stoichiometric quantities,[10] Li and Balamurugan independently reported the use of more expensive $GaCl_3$ or $AuCl_3/AgSbF_6$ catalytic systems.[6,7] In the restricted case of terminal phenylacetylenes, boron trifluoride etherate complex was also described as an appropriate catalyst.[8] Notably, all these last methods are based on the use of Lewis-acid mediators, and to the best of our knowledge, the use of simple Brønsted-acid catalyst has not yet been reported. In this context, we report herein that triflimide ($HNTf_2$) is an efficient organocatalyst for the benzannulation of phenylacetaldehyde derivatives with alkynes.[11] This metal-free reaction proceeds at room temperature and leads, under mild reaction conditions, to a wide variety of highly substituted naphthalene compounds with perfect regioselectivity (Scheme 2, eq 4).

RESULTS AND DISCUSSION

In the course of our studies concerning the α-alkenylation of aldehydes with alkynes under synergistic catalysis,[12] we discovered that 20 mol % of indium(III) chloride in 1,2-dichloroethane (DCE) at 100 °C partially promoted the benzannulation reaction of 2-phenylpropionaldehyde **1** with 2 equiv of 1-phenyl-1-propyne **2** (Table 1, entry 1). In these conditions after 5 h, naphthalene **3** was formed with encouraging 74% GC yield and with total regioselectivity, which prompted us to further study this transformation (Table 1). Under milder reaction conditions, at room temperature for 24 h, we still observed some reactivity with indium(III) chloride (Table 1, entry 2). However, better reaction rates and GC yields were obtained when indium(III) bromide, indium(III) trifluoromethanesulfonate, and indium(III) triflimidate

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Scheme 2. Catalytic Formal [4 + 2] Benzannulation Approaches to Naphthalenes with Alkynes

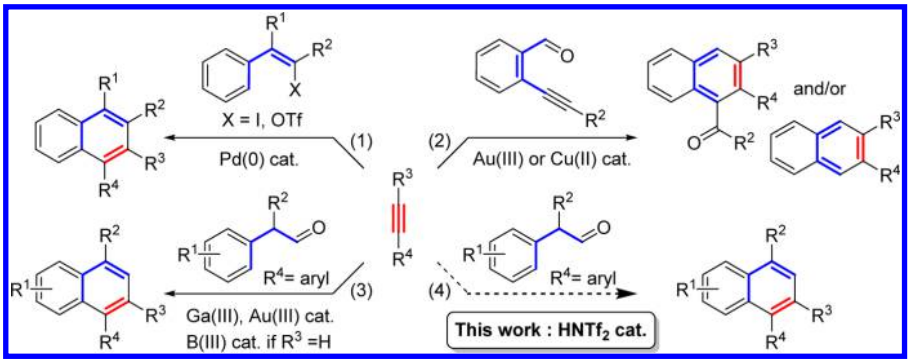
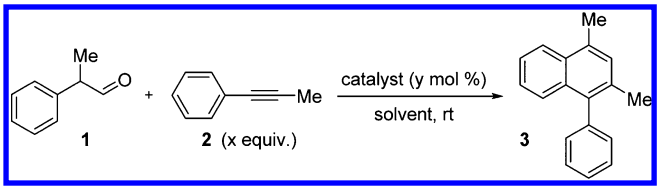


Table 1. Optimization of the Aldehyde−Alkyne Benzannulation Reaction



entry	catalyst	*y*	*x*	solvent	*t* (h)	conv. (%)[a]	yield (%)[a]
1[b]	$InCl_3$	20	2	DCE	5	90	74
2	$InCl_3$	20	2	DCE	24	56	33
3	$InBr_3$	20	2	DCE	24	80	60
4	$In(OTf)_3$	20	2	DCE	24	>95	68
5	$In(NTf_2)_3$	20	2	DCE	8	>95	85
6	$HNTf_2$	20	2	DCE	8	>95	84
7	TfOH	20	2	DCE	8	73	59
8	MsOH	20	2	DCE	8	26	3
9	$HNTf_2$	20	2.5	DCE	8	>95	85
10	$HNTf_2$	20	1.5	DCE	8	>95	86, [70][c]
11	$HNTf_2$	20	1	DCE	8	87	77
12	$HNTf_2$	15	1.5	DCE	13	>95	85, [70][c]
13	$HNTf_2$	10	1.5	DCE	24	84	73
14	$HNTf_2$	5	1.5	DCE	24	83	64
15	$HNTf_2$	15	1.5	CH_2Cl_2	13	95	78
16	$HNTf_2$	15	1.5	toluene	10	60	38
17	$HNTf_2$	15	1.5	Et_2O	10	40	3
18	$HNTf_2$	15	1.5	hexane	10	94	71

[a]Determined by GC analysis using tridecane as internal standard. [b]Performed at 100 °C. [c]Yield.

were employed (Table 1, entries 3−5). In this last case, we were pleased to observe almost complete conversion after only 8 h and 85% GC yield of naphthalene **3** (Table 1, entry 5). Unexpectedly and gratifyingly, a control experiment using 20 mol % of triflimide ($HNTf_2$) led to comparable results, thus indicating for the first time that this transformation could also be efficiently catalyzed by simple Brønsted acids (Table 1, entry 6). Comparatively, the use of trifluoromethanesulfonic (TfOH) and methanesulfonic (MsOH) acids led to limited reactivity (Table 1, entries 7 and 8). Further optimization studies including the variation of the quantity of alkyne and the catalytic charge of $HNTf_2$ allowed us to determine that 1.5 equiv of alkyne in the presence of 15 mol % catalyst was optimum to promote the desired transformation (Table 1, entries 9−14). Under these metal-free conditions, after 13 h at room temperature, naphthalene **3** was obtained in 70% isolated yield (Table 1, entry 12), which compares favorably to the result obtained by Li et al. in the presence of 13 mol % of $GaCl_3$ in refluxing dichloromethane during 24 h (70% yield).[6] Other solvents such as dichloromethane, toluene, diethyl ether, or hexane did not give better results (Table 1, entries 15−18).

With these optimized reaction conditions in hand, we then studied the scope of this Brønsted-acid-catalyzed benzannulation reaction. The influence of the carbonyl reactant was first examined by submitting 1-phenyl-1-propyne **2** to various phenylacetaldehydes **4a−i** (Scheme 3).

This benzannulation reaction well tolerated the use of phenylacetaldehydes bearing electron-donating groups at the 4 position of their aromatic moiety. Accordingly, naphthalene **5a** and **5b** were obtained in 70% and 62%, respectively. Moreover, the 4-nitro- and 4-bromo-substituted phenylacetaldehydes **4c** and **4d** reacted well, which indicated that electron-withdrawing groups on the aromatic ring were also compatible with this catalytic benzannulation process. Steric hindrance at the 2 position of the phenyl ring did not significantly hamper this method. Indeed, the reaction of 4-bromo- and 2-bromo-phenyl propionaldehydes **4d** and **4e** yielded the corresponding naphthalenes **5d** and **5e** with similar yields. The *α* substitution

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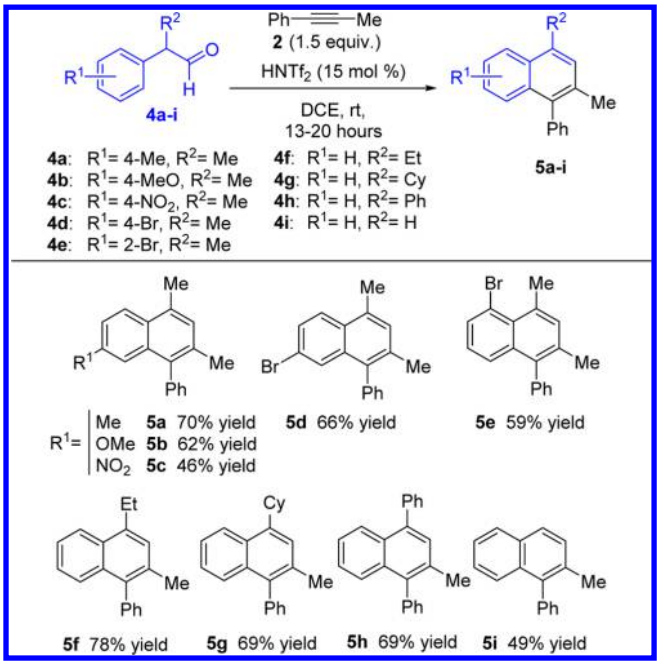
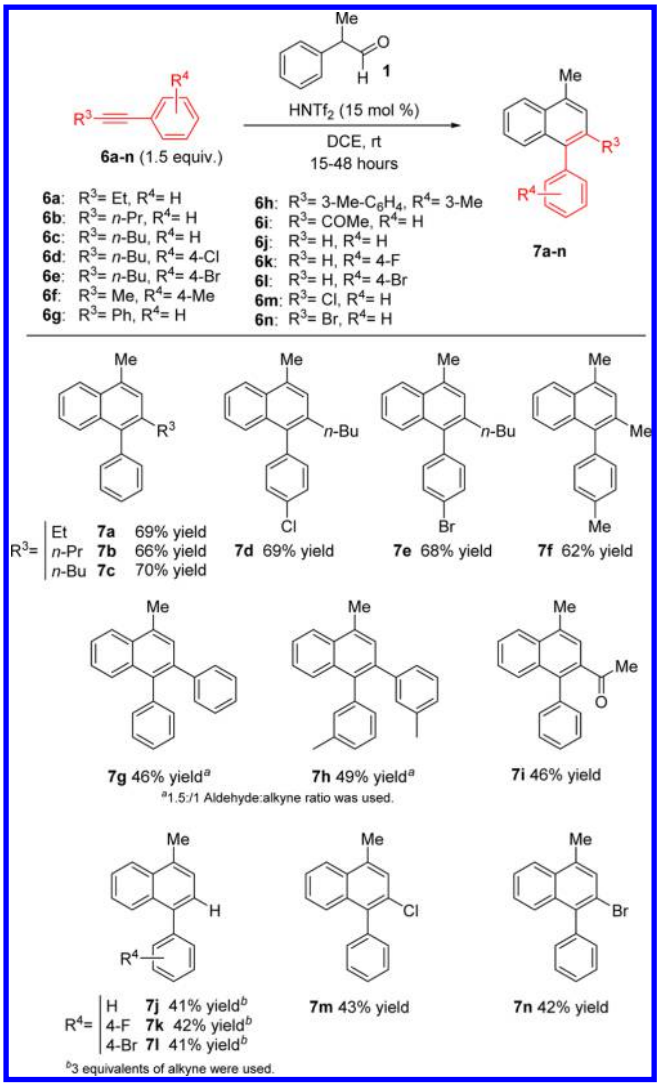
Scheme 3. Aldehyde Scope for the $HNTf_2$-Catalyzed Benzannulation Reaction



Scheme 4. Alkyne Scope for the $HNTf_2$-Catalyzed Benzannulation Reaction



of the aldehyde group could also be successfully modified since 2-ethyl-, 2-cyclohexyl-, and 2-phenyl-substituted phenylacetaldehydes **4f–h** allowed the formation of naphthalenes **5f–h** in good yields ranging from 69% to 78%. Furthermore, the α substitution on the aldehyde partner was not essential as the reaction of phenylacetaldehyde **4i** afforded the expected naphthalene **5i** with a slight diminution of yield. It is worth noting that in all cases only one regioisomer was obtained.

We next studied the influence of the alkyne partner in the catalytic benzannulation reaction of 2-phenylpropionaldehyde **1** (Scheme 4). We were satisfied to observe that 2-phenyl-2-propyne could be successfully replaced by alkynes possessing a longer alkyl chain. Indeed, under the optimized reaction conditions, 1-phenyl-but-1-yne **6a**, 1-phenyl-pent-1-yne **6b**, and 1-phenyl-hex-1-yne **6c** yielded the corresponding naphthalene compounds **7a–c** in good 66–70% yield. In the related aryl–alkyl alkyne family, substitution of the aromatic ring was examined. The reaction of 4-chloro-, 4-bromo-, and 4-methyl-substituted alkynes **6d–f** afforded the desired products **7d–f** with comparable good results (62–69% yield). Diaryl-substituted alkynes were also prone to react under these mild catalytic conditions. In these cases, longer reaction times were needed and a reversed aldehyde/alkyne ratio was found to be successful to easily separate the desired product from the starting alkyne. The benzannulation of symmetrical alkynes **6g** and **6h** led to naphthalenes **7g** and **7h** in 46% and 49% yield, respectively. The effectiveness of this catalytic reaction was further demonstrated by reacting 4-phenyl-but-3-yn-2-one **6i**, which afforded the corresponding 2-acetyl-substituted naphthalene **7i** in moderate 46% isolated yield. To the best of our knowledge, this represents the first example based on the use of an alkyne deactivated by an electron-withdrawing group in related aldehyde–alkyne benzannulation processes. Similarly to the $GaCl_3$-catalyzed transformation developed by Li et al.,[6] we observed inferior reactivity for phenylacetylene **6j**. Modifying the reaction conditions by increasing the amount of alkyne to 3 equivalents allowed the formation of 4-methyl-1-phenyl-naphthalene **7j** in 41% yield. Under the corresponding reaction conditions, the 4-fluoro- and 4-bromo-phenylacetylenes afforded naphthalenes **7k** and **7l** with similar results. Gratifyingly, this protocol could also be extended to the use of halogen-substituted phenylacetylenes **6m** and **6n**, which were scarcely employed in related benzannulation reactions.[8] The corresponding 2-chloro- and 2-bromo-substituted aromatic compounds **7m** and **7n** were obtained in useful 43% and 42% yields, respectively. Noteworthy, these 2-halo-naphthalene derivatives might serve as valuable building blocks in well-established palladium cross-coupling reactions.[13] Under the reaction conditions reported herein, terminal and internal aliphatic alkynes such as hex-1-yne and oct-3-yne reacted sluggishly with 2-phenylpropionaldehyde, which emphasized the key stabilizing role of the aromatic moiety of the phenylacetylenes that were employed.

To further demonstrate the efficiency of this $HNTf_2$-catalyzed aldehyde–alkyne benzannulation process, we performed a gram-scale control experiment under open air reaction conditions. Pleasingly, starting from 2-phenylpropionaldehyde **1** and 1-phenyl-1-propyne **2**, the reaction worked perfectly well and led to naphthalene **3** in almost identical yield (Scheme 5). Accordingly, this Brønsted-acid-catalyzed benzan-

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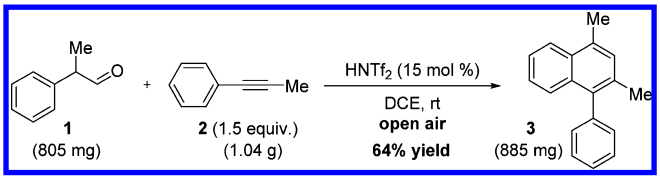
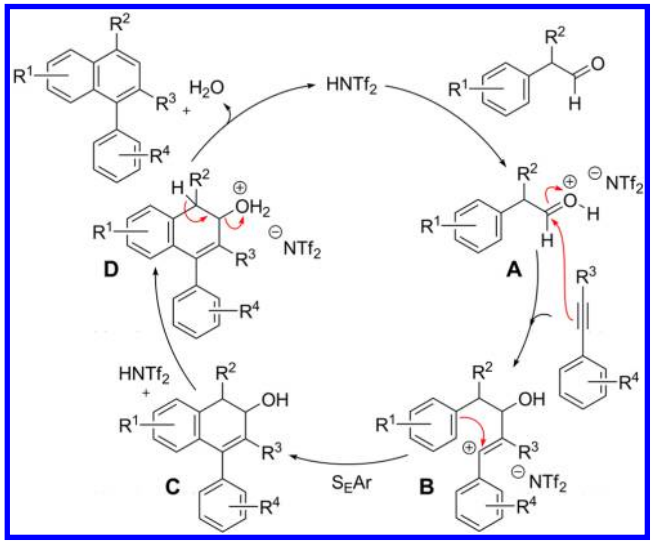
Scheme 5. Gram-Scale $HNTf_2$-Catalyzed Benzannulation under Open Air Reaction Conditions



nulation reaction was demonstrated to be a particularly robust solution for the larger scale production of naphthalene derivatives in mild and easy to setup reaction conditions.

On the basis of the above experimental results and literature,[6−8] we propose the following catalytic cycle for this Brønsted-acid-catalyzed benzannulation reaction (Scheme 6).

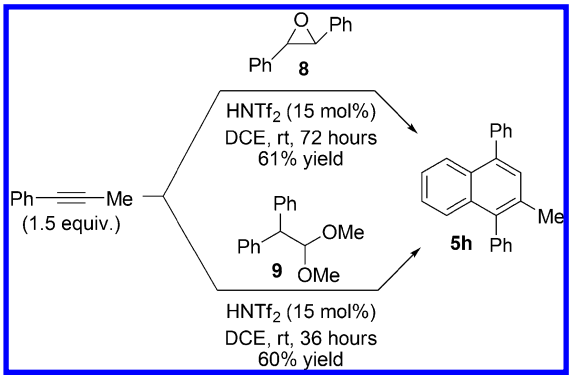
Scheme 6. Reaction Mechanism Proposal



The initial protonation of the aldehyde oxygen atom with $HNTf_2$, favored by the high acidity of this Brønsted acid,[11] would lead to an oxocarbenium ion **A** whose high electrophilicity would trigger the regioselective nucleophilic attack of the alkyne partner. The resulting vinylic carbocation **B**, stabilized by the aromatic ring which is present in its α position,[14] would then undergo an intramolecular electrophilic aromatic substitution with the proximal phenyl ring leading to a dihydro-β-naphtol **C**. In a last step, the Brønsted-acid-mediated elimination of a water molecule would account for the formation of the naphthalene product together with the regeneration of the catalyst. The superiority of $HNTf_2$ compared to other Brønsted acids might then be rationalized by the fact that its counteranion NTf_2^- displays a negligible nucleophilicity which may hamper competitive deactivation pathways such as the quenching of the transitory vinylic carbocation.[7a]

Finally, with this mechanistic proposition in mind, we envisioned that this Brønsted-acid-catalyzed benzannulation reaction could rationally be extended to the use of epoxides or acetals.[15] Indeed, under protic reaction conditions the Meinwald rearrangement of epoxides and α elimination of acetals are believed to form transitory oxocarbenium ions.[16] To assess this hypothesis, we performed some preliminary experiments in which *trans*-stilbene oxide **8** and dimethyl-acetal **9** were submitted to 1.5 equiv of 1-phenyl-1-propyne in the presence of 15 mol % $HNTf_2$ in DCE at room temperature (Scheme 7).

Scheme 7. Benzannulation Approaches to Naphthalenes with Epoxides and Dimethylacetals



Pleasingly, in both cases the desired naphthalene **5h** was obtained in 60−61% yield. Therefore, our Brønsted-acid catalytic approach to naphthalenes with phenylacetaldehydes may also find some interesting applications in the related benzannulation reactions of styrene oxides and 2-aryl-acetals.

CONCLUSION

In the course of this study, we demonstrated that triflimide ($HNTf_2$) is an efficient Brønsted-acid catalyst for benzannulation reaction of phenylacetaldehyde derivatives with aryl−alkynes at room temperature. Noteworthy, in all cases only one naphthalene isomer is obtained, which implies a total regioselectivity for this formal [4 + 2] process. This novel protocol clearly distinguishes itself from already reported catalytic systems, which are mostly based on the use of metal Lewis acids and often require thermal activation. A study of the scope of this reaction has been realized which has allowed us to access to a wide variety of polysubstituted naphthalene compounds in fair to good yields and to suggest a catalytic cycle for this transformation. The mild reaction conditions tolerate the use of diversely functionalized aldehydes as well as internal and terminal aromatic alkynes. Further studies aiming at broadening the scope of this $HNTf_2$-catalyzed benzannulation methodology to the use of styrene oxides and 2-aryl-acetals are currently underway and will be reported in due course.

EXPERIMENTAL SECTION

All reactions were performed under argon atmosphere. 1,2-Dichloroethane was distilled from CaH_2. All products were purified by flash chromatography using silica gel (230−400 mesh). ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ with chemical shifts reported relative to the residual $CHCl_3$ peak for ^1H NMR (7.26 ppm) or the central peak of $CDCl_3$ for ^{13}C NMR (77.16 ppm). HRMS data for new compounds were obtained using an atmospheric pressure photoionization source (APPI) coupled to a LTQ-Orbitrap high-resolution detector. Unless otherwise noted, all reagents were ordered and used without further purification. Aldehydes **4a−i** were synthesized by using a literature procedure,[17] and their NMR analytical data matched those previously reported.[17,18] Alkynes **6d−f** and **6h** were prepared according to literature procedures, and their NMR analytical data matched those previously reported.[19,20] Halogenated alkynes **6m** and **6n** were synthesized according to the literature.[21]

General Procedure for the Benzannulation Reaction. In a screw cap vial under argon atmosphere were sequentially added the

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aldehyde, epoxide, or acetal (1.0 mmol, 1 equiv), the alkyne (1.5 mmol, 1.5 equiv), 1,2-dichloroethane (1 mL), and $HNTf_2$ (42 mg, 0.15 mmol, 0.15 equiv). The resulting mixture was stirred at room temperature until TLC analysis showed completion of the reaction (vide infra). The reaction mixture was then diluted with dichloromethane (5 mL) and water (15 mL) and transferred to a separating funnel. The aqueous phase was extracted with dichloromethane (3 × 15 mL), and the combined organic extracts were washed by water (2 × 40 mL) and brine (40 mL) before being dried over $MgSO_4$. After filtration and evaporation of the solvents under reduced pressure, the crude material was purified by flash column chromatography on silica gel to afford the desired naphthalene. In specific cases, this first purification step was followed by a bulb to bulb distillation under reduced pressure in order to remove residual alkyne.

2,4-Dimethyl-1-phenylnaphthalene (3). Starting from 2-phenylpropionaldehyde **1** (134 mg, 1.0 mmol) and 1-phenyl-1-propyne **2** (174 mg, 1.5 mmol) and following the general procedure, after 13 h of reaction the crude material was purified by flash column chromatography on silica gel using cyclohexane as eluent. The desired naphthalene **3** was obtained as a white solid (162 mg, 70% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.01 (d, J = 8.2 Hz, 1H), 7.54−7.39 (m, 5H), 7.37−7.30 (m, 1H), 7.30−7.24 (m, 3H), 2.73 (d, J = 0.7 Hz, 3H), 2.21 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 139.7, 136.2, 132.8 (2C), 132.1, 130.7, 129.9, 129.0, 127.9, 126.5, 126.4, 125.1, 124.2, 123.5, 20.3, 18.9. These analytical data are in accordance with the literature.[6]

2,4,7-Trimethyl-1-phenylnaphthalene (5a). Starting from 2-(*p*-tolyl)-propanal **4a** (148 mg, 1.0 mmol) and 1-phenyl-1-propyne **2** (174 mg, 1.5 mmol) and following the general procedure, after 16 h of reaction the crude material was purified by flash column chromatography on silica gel using petroleum ether as eluent. The desired naphthalene **5a** was obtained as a colorless oil (173 mg, 70% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02 (d, J = 8.5 Hz, 1H), 7.68−7.50 (m, 3H), 7.44−7.30 (m, 5H), 2.82 (s, 3H), 2.49 (s, 3H), 2.31 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 140.3, 136.1, 135.2, 133.3 (2C), 132.9, 130.5, 129.4, 128.7, 128.5, 126.9 (2C), 125.9, 124.0, 21.9, 20.9, 19.5. HRMS (APPI) m/z: $[M]^{+\bullet}$ calcd for $C_{19}H_{18}$ 246.1403, found 246.1409.

7-Methoxy-2,4-dimethyl-1-phenylnaphthalene (5b). Starting from 2-(4-methoxyphenyl)propanal **4b** (164 mg, 1.0 mmol) and 1-phenyl-1-propyne **2** (174 mg, 1.5 mmol) and following the general procedure, after 20 h of reaction the crude material was purified by flash column chromatography on silica gel using cyclohexane as eluent. The desired naphthalene **5b** was obtained as a pale yellow oil (161 mg, 62% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02 (d, J = 9.1 Hz, 1H), 7.57 (m, 3H), 7.43−7.35 (m, 2H), 7.27−7.20 (m, 2H), 6.88 (d, J = 2.6 Hz, 1H), 3.77 (s, 3H), 2.79 (s, 3H), 2.30 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 157.4, 140.3, 135.7, 134.5, 133.5, 133.4, 130.4, 128.6, 127.5, 127.0, 126.6, 125.7, 116.6, 105.9, 55.1, 20.9, 19.5. HRMS (APPI) m/z: $[M]^{+\bullet}$ calcd for $C_{19}H_{18}O$ 262.1352, found 262.1354.

2,4-Dimethyl-7-nitro-1-phenylnaphthalene (5c). Starting from 2-(4-nitrophenyl)-propanal **4c** (70 mg, 0.39 mmol) and 1-phenyl-1-propyne **2** (70 mg, 0.59 mmol) and following the general procedure, after 13 h of reaction the crude material was purified by flash column chromatography on silica gel using cyclohexane:ethyl acetate (98:2) as eluent. The desired naphthalene **5c** was obtained as a pale yellow solid (50 mg, 46% yield); mp 120−122 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.37 (d, J = 2.3 Hz, 1H), 8.19 (dd, J = 9.2, 2.3 Hz, 1H), 8.09 (d, J = 9.2 Hz, 1H), 7.59−7.43 (m, 4H), 7.29−7.20 (m, 2H), 2.76 (d, J = 0.7 Hz, 3H), 2.24 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 145.5, 138.9, 138.3, 135.5, 133.8, 133.4, 132.4, 130.3, 128.9, 128.3, 127.9, 125.8, 123.6, 118.1, 20.9, 19.5. HRMS (APPI) m/z: $[M]^{+\bullet}$ calcd for $C_{18}H_{15}NO_2$ 277.1097, found 277.1101.

7-Bromo-2,4-dimethyl-1-phenylnaphthalene (5d). Starting from 2-(4-bromophenyl)-propanal **4d** (213 mg, 1.0 mmol) and 1-phenyl-1-propyne **2** (174 mg, 1.5 mmol) and following the general procedure, after 20 h of reaction the crude material was purified by flash column chromatography on silica gel using cyclohexane as eluent. The desired naphthalene **5d** was obtained as a pale yellow solid (203 mg, 66% yield); mp 87−89 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.85 (d, J = 8.8 Hz, 1H), 7.55−7.43 (m, 5H), 7.28 (s, 1H), 7.24−7.21 (m, 2H), 2.69 (d, J = 0.7 Hz, 3H), 2.18 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 139.2, 136.0, 134.5, 134.2, 133.5, 130.3, 130.0, 129.7, 128.8, 128.7, 128.0, 127.3, 125.9, 120.2, 20.9, 19.4. HRMS (APPI) m/z: $[M]^{+\bullet}$ calcd for $C_{18}H_{15}Br$ 310.0352, found 310.0356.

5-Bromo-2,4-dimethyl-1-phenylnaphthalene (5e). Starting from 2-(2-bromophenyl)-propanal **4e** (106 mg, 0.50 mmol) and 1-phenyl-1-propyne **2** (87 mg, 0.75 mmol) and following the general procedure, after 16 h of reaction the crude material was purified by flash column chromatography on silica gel using cyclohexane as eluent. The desired naphthalene **5e** was obtained as a low melting point white solid (92 mg, 59% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.78 (dd, J = 7.4, 1.3 Hz, 1H), 7.57−7.39 (m, 4H), 7.34 (s, 1H), 7.27−7.20 (m, 2H), 7.06 (dd, J = 8.5, 7.4 Hz, 1H), 3.18 (d, J = 0.7 Hz, 3H), 2.19 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 140.3, 137.7, 136.3, 134.4, 133.9, 133.7, 132.4, 130.3, 129.9, 128.7, 127.5, 127.2, 125.4, 120.2, 26.5, 20.6. HRMS (APPI) m/z: $[M]^{+\bullet}$ calcd for $C_{18}H_{15}Br$ 310.0352, found 310.0357.

4-Ethyl-2-methyl-1-phenylnaphthalene (5f). Starting from 2-phenylbutanal **4f** (148 mg, 1.0 mmol) and 1-phenyl-1-propyne **2** (174 mg, 1.5 mmol) and following the general procedure, after 13 h of reaction the crude material was purified by flash column chromatography on silica gel using petroleum ether as eluent. The desired naphthalene **5f** was obtained as a white solid (192 mg, 78% yield); mp 75−77 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.19 (d, J = 8.4 Hz, 1H), 7.66−7.50 (m, 5H), 7.49−7.36 (m, 4H), 3.26 (q, J = 7.5 Hz, 2H), 2.35 (s, 3H), 1.57 (t, J = 7.5 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 140.2, 139.4, 136.6, 133.5, 132.9, 130.5, 130.3, 128.5, 127.9, 127.1, 127.0, 125.5, 124.7, 123.7, 26.0, 21.0, 15.3. HRMS (APPI) m/z: $[M]^{+\bullet}$ calcd for $C_{19}H_{18}$ 246.1403, found 246.1407.

4-Cyclohexyl-2-methyl-1-phenylnaphthalene (5g). Starting from 2-cyclohexyl-2-phenylacetaldehyde **4g** (202 mg, 1.0 mmol) and 1-phenyl-1-propyne **2** (174 mg, 1.5 mmol) and following the general procedure, after 14 h of reaction the crude material was purified by flash column chromatography on silica gel using petroleum ether as eluent. The desired naphthalene **5g** was obtained as a white solid (209 mg, 69% yield); mp 151−153 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.27 (d, J = 8.5 Hz, 1H), 7.66−7.49 (m, 5H), 7.48−7.35 (m, 4H), 3.60−3.39 (m, 1H), 2.36 (s, 3H), 2.23 (t, J = 10.1 Hz, 2H), 2.15−1.91 (m, 3H), 1.86−1.62 (m, 4H), 1.60−1.39 (m, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 142.9, 140.3, 136.4, 133.5, 132.8, 130.5, 129.9, 128.5, 127.2, 127.0, 125.3 (2C), 124.6, 123.1, 39.3, 34.4, 27.5, 26.8, 21.2. HRMS (APPI) m/z: $[M]^{+\bullet}$ calcd for $C_{23}H_{24}$ 300.1872, found 300.1876.

2-Methyl-1,4-diphenylnaphthalene (5h). Starting from 2,2-diphenylacetaldehyde **4h** (196 mg, 1.0 mmol) and 1-phenyl-1-propyne **2** (174 mg, 1.5 mmol) and following the general procedure, after 16 h of reaction the crude material was purified by flash column chromatography on silica gel using cyclohexane as eluent. The desired naphthalene **5h** was obtained as a white solid (202 mg, 69% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.11−8.01 (m, 1H), 7.72−7.54 (m, 9H), 7.53 (s, 1H), 7.46 (m, 4H), 2.41 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 141.0, 140.0, 139.6, 137.9, 133.4, 132.8, 130.4, 130.3 (2C), 129.8, 128.6, 128.4, 127.3, 127.2, 126.7, 126.0, 125.8, 125.0, 21.0. These analytical data are in accordance with the literature.[22]

2-Methyl-1-phenylnaphthalene (5i). Starting from phenylacetaldehyde **4i** (120 mg, 1.0 mmol) and 1-phenyl-1-propyne **2** (174 mg, 1.5 mmol) and following the general procedure, after 16 h of reaction the crude material was purified by flash column chromatography on silica gel using cyclohexane as eluent. The desired naphthalene **5i** was obtained as a low melting point white solid (106 mg, 49% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.94 (d, J = 8.1 Hz, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.64−7.34 (m, 9H), 2.35 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 139.9, 138.3, 133.2, 133.1, 132.1, 130.3, 128.7, 128.5, 127.9, 127.4, 127.1, 126.3, 125.9, 124.9, 21.0. These analytical data are in accordance with the literature.[6]

2-Ethyl-4-methyl-1-phenylnaphthalene (7a). Starting from 2-phenylpropionaldehyde **1** (134 mg, 1.0 mmol) and 1-phenyl-but-1-yne **6a** (195 mg, 1.5 mmol) and following the general procedure, after 15 h of reaction the crude material was purified by flash column

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chromatography on silica gel using cyclohexane as eluent. The desired naphthalene **7a** was obtained as a pale yellow solid (170 mg, 69% yield); mp 63−65 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00 (d, J = 8.3 Hz, 1H), 7.53−7.38 (m, 4H), 7.37−7.23 (m, 5H), 2.74 (d, J = 0.8 Hz, 3H), 2.50 (q, J = 7.6 Hz, 2H), 1.11 (t, J = 7.6 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 139.9, 139.1, 136.1, 133.8, 133.4, 131.2, 130.7, 128.3, 128.1, 127.2, 127.0, 125.6, 124.8, 124.0, 27.1, 19.7, 16.2. HRMS (APPI) m/z: $[M]^{+\bullet}$ calcd for $C_{19}H_{18}$ 246.1403, found 246.1407.

4-Methyl-1-phenyl-2-(*n*-propyl)-naphthalene (7b). Starting from 2-phenylpropionaldehyde **1** (134 mg, 1.0 mmol) and 1-phenyl-pent-1-yne **6b** (216 mg, 1.5 mmol) and following the general procedure, after 15 h of reaction the crude material was purified by flash column chromatography on silica gel using cyclohexane as eluent followed by bulb to bulb distillation at 100 °C/0.3 Torr during 1 h in order to remove traces of starting alkyne. The desired naphthalene **7b** was obtained as a low melting point white solid (172 mg, 66% yield).^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00 (d, J = 8.3 Hz, 1H), 7.52−7.37 (m, 4H), 7.37−7.23 (m, 5H), 2.73 (d, J = 0.8 Hz, 3H), 2.51−2.41 (m, 2H), 1.62−1.47 (m, 2H), 0.82 (t, J = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 139.9, 137.5, 136.5, 133.5, 133.4, 131.2, 130.8, 128.6, 128.3, 127.2, 127.0, 125.5, 124.8, 124.0, 35.9, 24.9, 19.7, 14.3. These analytical data are in accordance with the literature.[6]

2-(*n*-Butyl)-4-methyl-1-phenylnaphthalene (7c). Starting from 2-phenylpropionaldehyde **1** (134 mg, 1.0 mmol) and 1-phenyl-hex-1-yne **6c** (237 mg, 1.5 mmol) and following the general procedure, after 15 h of reaction the crude material was purified by flash column chromatography on silica gel using cyclohexane as eluent followed bulb to bulb distillation of residual alkyne at 100 °C/0.3 Torr during 1 h. The desired naphthalene **7c** was obtained as a low melting point pale yellow solid (192 mg, 70% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99 (d, J = 8.3 Hz, 1H), 7.52−7.38 (m, 4H), 7.37−7.23 (m, 5H), 2.73 (d, J = 0.8 Hz, 3H), 2.53−2.43 (m, 2H), 1.54−1.43 (m, 2H), 1.29−1.14 (m, 2H), 0.79 (t, J = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 139.9, 137.8, 136.4, 133.5, 133.4, 131.2, 130.8, 128.6, 128.3, 127.2, 127.0, 125.6, 124.8, 124.0, 34.0, 33.6, 22.8, 19.7, 14.0. HRMS (APPI) m/z: $[M]^{+\bullet}$ calcd for $C_{21}H_{22}$ 274.1716, found 274.1724.

2-(*n*-Butyl)-1-(4-chlorophenyl)-4-methylnaphthalene (7d). Starting from 2-phenylpropionaldehyde **1** (134 mg, 1.0 mmol) and 1-chloro-4-(hex-1-ynyl)benzene **6d** (289 mg, 1.5 mmol) and following the general procedure, after 15 h of reaction the crude material was purified by flash column chromatography on silica gel using petroleum ether as eluent followed by bulb to bulb distillation of residual alkyne at 100 °C/0.3 Torr during 1 h. The desired naphthalene **7d** was obtained as a white solid (212 mg, 69% yield); mp 79−81 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.01 (dt, J = 8.4, 1.0 Hz, 1H), 7.50−7.41 (m, 3H), 7.36−7.28 (m, 3H), 7.24−7.16 (m, 2H), 2.74 (d, J = 0.9 Hz, 3H), 2.52−2.41 (m, 2H), 1.56−1.42 (m, 2H), 1.33−1.14 (m, 2H), 0.82 (t, J = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 138.3, 137.9, 135.0, 134.0, 133.2, 133.0, 132.2, 131.2, 128.5 (2C), 126.9, 125.7, 124.9, 124.1, 34.0, 33.6, 22.8, 19.7, 14.1. HRMS (APPI) m/z: $[M]^{+\bullet}$ calcd for $C_{21}H_{21}Cl$ 308.1326, found 308.1330.

1-(4-Bromophenyl)-2-(*n*-butyl)-4-methylnaphthalene (7e). Starting from 2-phenylpropionaldehyde **1** (134 mg, 1.0 mmol) and 1-bromo-4-(hex-1-ynyl)benzene **6e** (356 mg, 1.5 mmol) and following the general procedure, after 15 h of reaction the crude material was purified by flash column chromatography on silica gel using petroleum ether as eluent followed by bulb to bulb distillation of residual alkyne at 100 °C/0.3 Torr during 1 h. The desired naphthalene **7e** was obtained as a white solid (238 mg, 68% yield); mp 83−85 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00 (dt, J = 8.4 Hz, 1.1 Hz, 1H), 7.66−7.57 (m, 2H), 7.54−7.39 (m, 1H), 7.36−7.32 (m, 2H), 7.29 (s, 1H), 7.19−7.11 (m, 2H), 2.74 (d, J = 0.6 Hz, 3H), 2.52−2.43 (m, 2H), 1.57−1.41 (m, 2H), 1.31−1.17 (m, 2H), 0.82 (t, J = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 138.8, 137.8, 134.9, 134.0, 133.1, 132.5, 131.5, 131.2, 128.5, 126.8, 125.7, 124.9, 124.1, 121.2, 34.0, 33.6, 22.8, 19.7, 14.1. MS (EI) m/z 352 (80) $[M]^{+\bullet}$, 273 (5) $[M - Br]^+$, 230 (100) $[M - C_3H_7 - Br]^{+\bullet}$.

2,4-Dimethyl-1-(*p*-tolyl)-naphthalene (7f). Starting from 2-phenylpropionaldehyde **1** (134 mg, 1.0 mmol) and 1-methyl-4-(prop-1-ynyl)benzene **6f** (195 mg, 1.5 mmol) and following the general procedure, after 15 h of reaction the crude material was purified by flash column chromatography on silica gel using petroleum ether as eluent followed by bulb to bulb distillation of residual alkyne at 100 °C/0.3 Torr during 1 h. The desired naphthalene **7f** was obtained as a low melting point white solid (153 mg, 62% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.12 (d, J = 8.2 Hz, 1H), 7.66−7.52 (m, 2H), 7.50−7.36 (m, 4H), 7.33−7.25 (m, 2H), 2.84 (s, 3H), 2.59 (s, 3H), 2.35 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 137.1, 136.7, 136.5, 133.4, 133.3, 132.9, 131.2, 130.4, 129.6, 129.2, 127.0, 125.5, 124.7, 124.0, 21.4, 20.9, 19.5. HRMS (APPI) m/z: $[M]^{+\bullet}$ calcd for $C_{19}H_{18}$ 246.1403, found 246.1408.

4-Methyl-1,2-diphenylnaphthalene (7g). Starting from 2-phenylpropionaldehyde **1** (201 mg, 1.5 mmol) and diphenylacetylene **6g** (178 mg, 1.0 mmol) and following the general procedure, after 48 h of reaction the crude material was purified by flash column chromatography on silica gel using petroleum ether as eluent. The desired naphthalene **7g** was obtained as a white solid (134 mg, 46% yield); mp 141−143 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.28−8.18 (m, 1H), 7.89 (d, J = 8.5 Hz, 1H), 7.68 (ddd, J = 8.4, 6.8, 1.4 Hz, 1H), 7.64−7.60 (m, 1H), 7.56 (ddd, J = 8.3, 6.7, 1.3 Hz, 1H), 7.49−7.23 (m, 10H), 2.94 (d, J = 1.0 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 142.2, 139.3, 138.1, 136.1, 133.9, 132.9, 132.0, 131.8, 130.2, 129.2, 127.9, 127.7, 127.6, 126.7, 126.3, 126.0, 125.7, 124.2, 19.7. HRMS (APPI) m/z: $[M]^{+\bullet}$ calcd for $C_{23}H_{18}$ 294.14031352, found 294.1407. These analytical data are in accordance with the literature.[10a]

4-Methyl-1,2-di(*m*-tolyl)-naphthalene (7h). Starting from 2-phenylpropionaldehyde **1** (201 mg, 1.5 mmol) and 1,2-di(*m*-tolyl)-ethyne **6h** (206 mg, 1.0 mmol) and following the general procedure, after 48 h of reaction the crude material was purified by flash column chromatography on silica gel using petroleum ether as eluent. The desired naphthalene **7h** was obtained as a white solid (158 mg, 49% yield); mp 106−108 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.16−8.08 (m, 1H), 7.82−7.74 (m, 1H), 7.58 (ddd, J = 8.3, 6.8, 1.4 Hz, 1H), 7.51 (d, J = 1.1 Hz, 1H), 7.47 (ddd, J = 8.3, 6.7, 1.4 Hz, 1H), 7.24 (t, J = 7.5 Hz, 1H), 7.17−6.96 (m, 7H), 2.84 (d, J = 1.0 Hz, 3H), 2.36 (s, 3H), 2.31 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 142.2, 139.3, 138.1, 137.2, 137.1, 136.3, 133.6, 133.0, 132.5, 132.0, 131.0 (2C), 129.3, 128.8, 127.7, 127.5, 127.4, 127.3, 126.9, 125.9, 125.6, 124.1, 21.6, 21.5, 19.7. HRMS (APPI) m/z: $[M]^{+\bullet}$ calcd for $C_{25}H_{22}$ 322.1716, found 322.1721.

2-Acetyl-4-methyl-1-phenylnaphthalene (7i). Starting from 2-phenylpropionaldehyde **1** (134 mg, 1.0 mmol) and 4-phenylbut-3-yn-2-one **6i** (216 mg, 1.5 mmol) and following the general procedure, after 13 h of reaction the crude material was purified by flash column chromatography on silica gel using cyclohexane:ethyl acetate (98:2) as eluent followed by bulb to bulb distillation of residual alkyne at 100 °C/0.3 Torr during 1 h. The desired naphthalene **7i** was obtained as a low melting point pale yellow solid (120 mg, 46% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.06 (d, J = 8.4 Hz, 1H), 7.72 (ddd, J = 8.6, 1.4, 0.7 Hz, 1H), 7.60 (ddd, J = 8.3, 6.8, 1.4 Hz, 1H), 7.53−7.42 (m, 5H), 7.40−7.34 (m, 2H), 2.76 (d, J = 1.0 Hz, 3H), 1.92 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 205.2, 138.6, 137.8, 136.9, 134.5, 133.8, 132.1, 130.9, 128.6, 128.1, 128.0, 127.2, 126.4, 124.9, 124.2, 30.8, 19.6. HRMS (APPI) m/z: $[M + H]^+$ calcd for $C_{19}H_{16}O$ 261.1274, found 261.1274.

1-Methyl-4-phenylnaphthalene (7j). Starting from 2-phenylpropionaldehyde **1** (134 mg, 1.0 mmol) and phenylacetylene **6j** (306 mg, 3.0 mmol) and following the general procedure, after 21 h of reaction the crude material was purified by flash column chromatography on silica gel using petroleum ether as eluent. The desired naphthalene **7j** was obtained as a low melting point white solid (89 mg, 41% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.18−8.11 (m, 1H), 8.05−7.98 (m, 1H), 7.66−7.38 (m, 9H), 2.82 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 141.2, 138.8, 133.9, 132.9, 131.8, 130.3, 128.3, 127.2, 126.8 (2C), 126.3, 125.8 (2C), 124.5, 19.7. These analytical data are in accordance with the literature.[6]

1-(4-Fluorophenyl)-4-methylnaphthalene (7k). Starting from 2-phenylpropionaldehyde **1** (67 mg, 0.50 mmol) and 4-fluorophenylacetylene **6k** (180 mg, 1.5 mmol) and following the general procedure, after 21 h of reaction the crude material was purified by

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flash column chromatography on silica gel using petroleum ether as eluent. The desired naphthalene **7k** was obtained as a white solid (50 mg, 42% yield); mp 87−89 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.12 (ddd, J = 8.5, 1.5, 0.6 Hz, 1H), 7.92 (ddd, J = 8.4, 1.5, 0.6 Hz, 1H), 7.60 (ddd, J = 8.3, 6.8, 1.4 Hz, 1H), 7.54−7.44 (m, 3H), 7.42 (dd, J = 7.1, 1.0 Hz, 1H), 7.34 (d, J = 7.1 Hz, 1H), 7.27−7.16 (m, 2H), 2.80 (d, J = 0.9 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 162.3 (d, $^1J_{C-F}$ = 245.7 Hz), 137.7, 137.1, 137.0, 134.1, 132.9, 131.8 (d, $^3J_{C-F}$ = 7.8 Hz), 126.8, 126.5, 126.3, 125.9, 125.8, 124.6, 115.2 (d, $^2J_{C-F}$ = 21.1 Hz), 19.7. ^{19}F NMR (282 MHz, $CDCl_3$): δ −116.48 to −116.79 (m). HRMS (APPI) m/z: $[M]^{+\bullet}$ calcd for $C_{17}H_{13}F$ 236.0996, found 236.0998.

1-(4-Bromophenyl)-4-methylnaphthalene (7l). Starting from 2-phenylpropionaldehyde **1** (67 mg, 0.50 mmol) and 4-bromophenylacetylene **6l** (271 mg, 1.5 mmol) and following the general procedure, after 15 h of reaction the crude material was purified by flash column chromatography on silica gel using petroleum ether as eluent. The desired naphthalene **7l** was obtained as a white solid (61 mg, 41% yield); mp 129−131 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13−8.06 (m, 1H), 7.93−7.84 (m, 1H), 7.68−7.60 (m, 2H), 7.57 (ddd, J = 8.3, 6.7, 1.4 Hz, 1H), 7.47 (ddd, J = 8.3, 6.7, 1.4 Hz, 1H), 7.42−7.34 (m, 3H), 7.31 (d, J = 7.2 Hz, 1H), 2.77 (d, J = 1.0 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 140.0, 137.4, 134.4, 132.9, 132.0, 131.5 (2C), 126.7, 126.4, 126.3, 126.0, 125.9, 124.6, 121.4, 19.7. HRMS (APPI) m/z: $[M]^{+\bullet}$ calcd for $C_{17}H_{13}Br$ 296.0195, found 296.0199.

2-Chloro-4-methyl-1-phenylnaphthalene (7m). Starting from 2-phenylpropionaldehyde **1** (134 mg, 1.0 mmol) and 2-chloroethynylbenzene **6m** (205 mg, 1.5 mmol) and following the general procedure, after 20 h of reaction the crude material was purified by flash column chromatography on silica gel using petroleum ether as eluent. The desired naphthalene **7m** was obtained as a pale yellow solid (113 mg, 43% yield); mp 103−105 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.11−7.99 (m, 1H), 7.67−7.32 (m, 9H), 2.77 (d, J = 1.1 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 137.9, 135.8 (2C), 133.9, 131.4, 130.6 (2C), 130.4, 128.4, 127.8, 127.1, 126.6, 125.8, 124.3, 19.4. HRMS (APPI) m/z: $[M]^{+\bullet}$ calcd for $C_{17}H_{13}Cl$ 252.0700, found 252.0706.

2-Bromo-4-methyl-1-phenylnaphthalene (7n). Starting from 2-phenylpropionaldehyde **1** (134 mg, 1 mmol) and 2-bromoethynylbenzene **6n** (271 mg, 1.5 mmol) and following the general procedure, after 20 h of reaction the crude material was purified by flash column chromatography on silica gel using petroleum ether as eluent. The desired naphthalene **7n** was obtained as a pale orange solid (124 mg, 42% yield); mp 103−105 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.11−8.00 (m, 1H), 7.67−7.33 (m, 9H), 2.77 (d, J = 1.1 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 139.9, 138.2, 135.8, 134.0, 131.7, 130.4 (2C), 128.4, 127.8, 127.4, 126.6, 125.9, 124.3, 121.2, 19.3. HRMS (APPI) m/z: $[M]^{+\bullet}$ calcd for $C_{17}H_{13}Br$ 296.0195, found 296.0198.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H NMR and ^{13}C NMR spectra for all naphthalene derivatives. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: maxime.vitale@chimie-paristech.fr.

*E-mail: veronique.michelet@chimie-paristech.fr.

*E-mail: virginie.vidal@chimie-paristech.fr.

Notes

The authors declare no competing financial interest.

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