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Synthesis of 2-Phenylnaphthalenes through Gold-Catalyzed Dimerization via a Highly Selective Carbon Nucleophile Pathway

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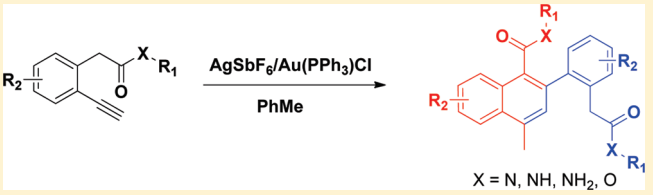
Supporting Information

ABSTRACT: A protocol for the facile synthesis of 2-phenylnaphthalene has been developed. The benzyl carbon acts as a nucleophilic center in the presence of the amide nitrogen and acetate oxygen, affording the selective formation of a naphthalene scaffold through the dimerization of the reactants.



INTRODUCTION

In recent years, there has been tremendous growth in the number of gold-catalyzed reactions reported.[1] In particular, gold salts have been proven to be soft, carbophilic Lewis acids for the electrophilic activation of alkynes. Thus, gold complexes are efficient in promoting a number of nucleophilic addition reactions to form various carbon−heteroatom bonds.[2,3] However, nucleophilic addition reactions using carbon nucleophiles such as electron-rich arenes and 1,3-dicarbonyl compounds are still reported occasionally.[4] In such reactions, the nucleophilicity of the oxygen or nitrogen is usually superior to that of the carbon nucleophiles, and the reactions usually proceed through a C−O or C−N bond formation pathway. Therefore, the highly selective gold-catalyzed addition of carbon nucleophiles to alkynes remains a challenge in modern organometallic catalysis.[5]

It has been our long-term goal to develop a novel and convenient method for the synthesis of potentially useful heterocycles using transition-metal catalysts.[6] We have previously reported a regiocontrolled intramolecular addition, in which the carbonyl oxygen acts as the nucleophile.[7] In another case, in a regioselective intramolecular hydroamidation process following the 7-*endo-dig* pathway, the amide NH acts as the nucleophile.[8] Hashmi et al. described a gold-catalyzed dimerization of *o*-alkynylbenzyl alcohols and a gold-catalyzed desymmetrisation of symmetrical substrates.[9] In this paper, we report an unexpected gold-catalyzed dimerization in which the benzyl carbon of the α-aryl acetamide or α-aryl acetate compounds acts as the nucleophile. Products formed via the benzyl carbon nucleophilic pathway were obtained with high selectivity in the presence of carbonyl oxygen and amide nitrogen atoms.

RESULTS AND DISCUSSION

The reaction conditions for the formation of dimerized 2-phenylnaphthalene were optimized using different catalysts, various reaction temperatures, solvents, and reaction times. *N*-Butyl-2-(2-ethynylphenyl)acetamide (**1a**) was chosen as the model substrate. The results are shown in Table 1, from which it can be seen that no reaction occurred when the gold salt alone was used as the catalyst (entries 1 and 2, Table 1). A trace amount of **2a** was observed when the reaction was carried out in the presence of $AuCl_3/AgSbF_6$ as the catalyst (entry 3, Table 1).The reaction proceeded to completion when using $AgOTf/Au(PPh_3)Cl$ or $AgSbF_6/Au(PPh_3)Cl$ as the catalyst, affording **2a** in 61% or 63% yield, respectively (entries 4 and 5, Table 1). Subsequently, it was found that the optimum temperature for this reaction was 70 °C with argon protection (entries 6−8, Table 1). Different solvents were screened, and polar solvents such as DMSO, $DMSO/H_2O$, and THF were shown to be ineffective. Nonpolar solvents such as dichloromethane performed better, and anhydrous toluene was found to be the most effective (entries 9−12, Table 1).

The structure of **2a** was confirmed by ^1H NMR and ^{13}C NMR spectroscopy, mass spectrometry, and X-ray crystallography.[10]

As shown in Scheme 1, there are three possible nucleophilic centers in the substrate: the amide nitrogen, carbonyl oxygen, and benzyl carbon. Therefore, the reaction could occur through different routes. Intramolecular nucleophilic attack of the amide nitrogen would give product **A1** or **A2** (path A), whereas intramolecular addition of the carbonyl group would give product **B1** or **B2** (path B). **C1** or **C2** could be obtained if the reaction were to proceed through the intramolecular addition of the benzyl carbon. In fact, we observed an unexpected dimerization of the reactant, giving rise to product **D** (path D). There are two possible reasons for this surprising result: (1) dual activation of the carbonyl and benzyl groups in the substrate enhances the nucleophilicity of the benzyl carbon, and (2) the conjugated π system of the dimerized product is thermodynamically favorable.[11] Both these factors would result in the benzyl carbon being more nucleophilic than the amide nitrogen and the carbonyl oxygen.

Using the optimized reaction conditions, we went on to examine the scope of the substrate for this reaction. This chemistry

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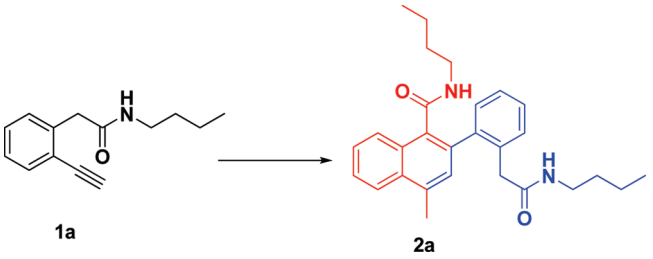
was first probed by varying the R_1 group: the reaction proceeded satisfactorily whether R_1 was a nonsubstituted amide (entry 2, Table 2), a monosubstituted alkyl amide (entries 1 and 3, Table 2), or a disubstituted alkyl amide (entry 4, Table 2). When the R_1 group was an aryl amide, it was found that the dimerization yield depended on the substituents. When R_1 was an electron-donating aryl amide, the reaction proceeded well and the corresponding product **2f** was obtained in 83% yield (entry 6, Table 2). However, for an electron-withdrawing aryl amide, only a moderate yield was obtained (entry 7, Table 2). No product was obtained when R_1 was a heteroaryl amide (entry 8, Table 2). The dimerization also proceeded successfully when the substrate contained an ester group, giving **2i** in 72% yield (entry 9, Table 2).

Next, we studied the reaction scope by varying the substituents on the benzene ring of the reactant. As shown in Table 3, we obtained the desired products in high yields when the aromatic ring was substituted with electron-donating groups such as MeO (entries 1−3, Table 3) and Me (entry 4, Table 3) as well as weakly electron-withdrawing groups such as halide atoms (entry 6, Table 3). In comparison, only a trace amount of product was obtained when R_2 was a strongly electron-withdrawing substituent such as $-CF_3$ (entry 5, Table 3).

To gain insight into the mechanism of the reaction, we carried out labeling studies using deuterated starting materials or solvents, and the results are shown in Scheme 2. The reaction of [D3]-**1a** in deuterated benzene under the optimized conditions afforded [D6]-**2a** (eq 1). The hydrogen atoms in the newly formed benzene and in the methyl group were deuterated. This indicates that one molecule of **1a** offers its benzyl carbon, two phenyl carbons, and one acetylenyl carbon, while another molecule of **1a** provides its two acetylenyl carbons to form the new benzene. [D3]-**1a** in benzene gave the same result, and **1a** in deuterated benzene gave the nondeuterated product showing that the solvent did not participate in the reaction (eqs 2 and 3). We then conducted the reaction of **1a** with an excess of a terminal alkyne, and fortunately, product *N*-butyl-4-methyl-2-phenyl-1-naphthamide was obtained in 66% yield (eq 4). A crossover experiment of deuterated and undeuterated substrates was also performed (eqs 5 and 6). The hydrogen atoms in the newly formed methyl group were deuterated when deuterated **1a** was used. In contrast, the hydrogen atom in the newly formed benzene was deuterated when deuterated phenylacetylene was used. We speculate that in the dimerization reaction, one of the deuterated methyl hydrogen atoms originated from the terminal alkynyl hydrogen and the other two came from the benzyl hydrogen atoms. The deuterated hydrogen in the newly formed benzene came from the terminal hydrogen in the alkyne of the other molecule of **1a**.

In accordance with our labeling studies, we propose a mechanism accounting for the formation of product **2**, as depicted in

Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst	condition	yield[b] (%)
1	$Au(PPh_3)Cl$	100 °C, PhMe, 5 h	trace[c]
2	$NaAuCl_4$	100 °C, PhMe, 5 h	0[d]
3	$AgSbF_6/AuCl_3$[e]	70 °C, PhMe, 8 h	trace
4	$AgOTf/Au(PPh_3)Cl$	100 °C, PhMe, 5 h	61
5	$AgSbF_6/Au(PPh_3)Cl$	100 °C, PhMe, 5 h	63
6	$AgSbF_6/Au(PPh_3)Cl$	80 °C, PhMe, 5 h	73
7	$AgSbF_6/Au(PPh_3)Cl$	70 °C, PhMe, 8 h	81/70[f]
8	$AgSbF_6/Au(PPh_3)Cl$	25 °C, PhMe, 24 h	trace
9	$AgSbF_6/Au(PPh_3)Cl$	80 °C, DMSO, 24 h	0[c]
10	$AgSbF_6/Au(PPh_3)Cl$	80 °C, DMSO/H_2O, 24 h	0[c]
11	$AgSbF_6/Au(PPh_3)Cl$	80 °C, THF, 16 h	trace[c]
12	$AgSbF_6/Au(PPh_3)Cl$	80 °C, CH_2Cl_2, 16 h	65

[a] Reactions were performed under Ar with 10 mol % of the catalyst. [b] Yields of isolated products. [c] **1a** was recovered. [d] Complicated reaction mixture but no **2a**. [e] 15 mol % of $AgSbF_6$ and 5 mol % of $AuCl_3$. [f] Reaction performed without argon protection.

Scheme 1. Possible Reaction Pathways of *N*-Butyl-2-(2-ethynylphenyl)acetamide

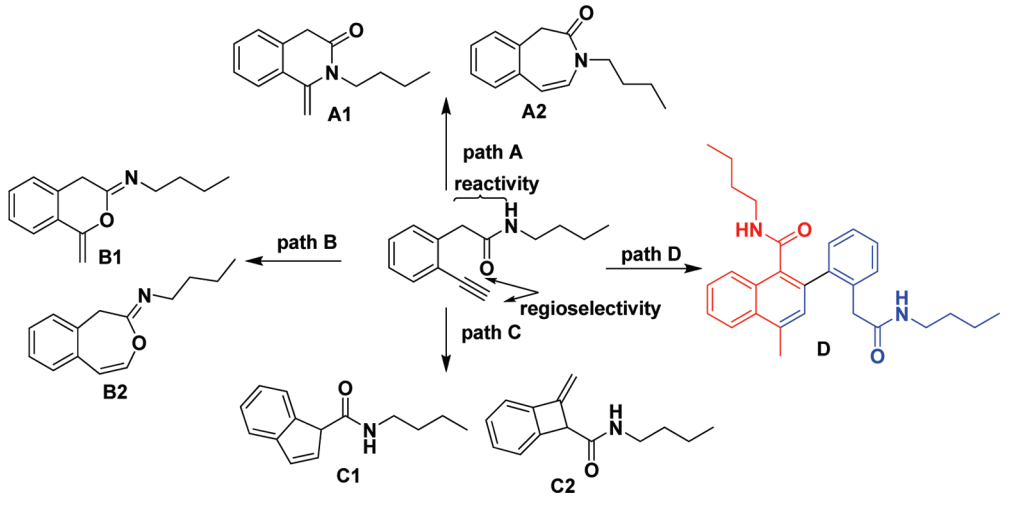


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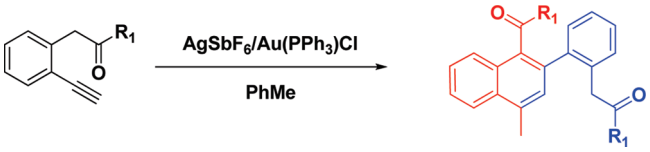
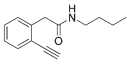
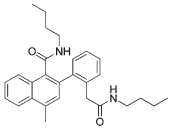
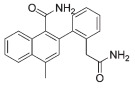
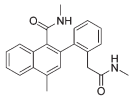
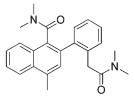
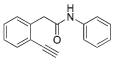
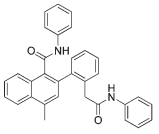
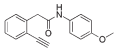
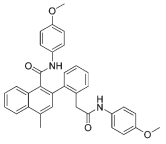
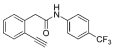
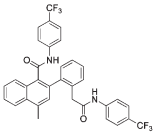
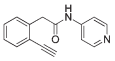
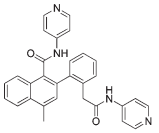
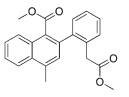
Table 2. Reaction Scope of the Dimerization to Synthesize Substituted 2-Phenylnaphthalene[a]



entry	substrate **1**	product **2**		yield (%)[b]
1			**2a**	81
2			**2b**	78
3			**2c**	80
4			**2d**	84
5			**2e**	77
6			**2f**	83
7			**2g**	42[c]
8			**2h**	0[d]
9			**2i**	72

[a] The reaction was performed with $AgSbF_6$ (10 mol %) and $Au(PPh_3)Cl$ (10 mol %) in anhydrous toluene under Ar protection at 70 °C unless otherwise noted. [b] Yields of isolated products. [c] The reaction was carried out for 1 h at 60 °C. [d] **1h** was recovered.

Scheme 3. The dimerization is initiated through activation of the terminal alkyne moiety of **1** by the $AgSbF_6/Au(PPh_3)Cl$ catalyst system[12] to form the Au−alkyne π-complex **A**. A subsequent attack by the benzyl carbon atom on the activated terminal alkyne of another molecule of **1** leads to the intermediate **C**;[13] this is followed by intramolecular cyclization to give intermediate **D**.[14] Then, with double-bond transfer, the final product **2** is produced and the catalyst is regenerated. This proposed mechanism is consistent with the results of our labeling studies.

CONCLUSION

In conclusion, we have demonstrated a simple gold-catalyzed protocol for the synthesis of substituted 2-phenylnaphthalene derivatives, which are the scaffold of a marketed acne treatment medicine adapalene (differin), and can be frequently found in pharmaceuticals, natural products, and agrochemicals.[15] The unexpected dimerization gave high yields when the R_1 group was an alkyl amide, an electron-donating aryl amide, or an ester. The reaction was also tolerant to an aromatic ring with electron-donating substituents. In this reaction, the benzyl carbon in the substrates of α-arylacetamides or α-arylacetates acted as a nucleophilic center, which has not been reported previously. The nucleophilic carbon selectively afforded a naphthalene scaffold in the presence of amide nitrogen and acetate oxygen atoms through the dimerization of the reactants. This means that the gold catalyst could be used with a wider range of reactants to form novel carbon−carbon bonds. Further studies of this reaction and the application of this methodology are underway.

EXPERIMENTAL SECTION

Typical Procedures for the Synthesis of *N*-Butyl-2-(2-ethynylphenyl)acetamide (1a). $SOCl_2$ (10 mL) was added to 2-iodophenylacetic acid (262 mg, 1.0 mmol), and the solution was refluxed for 2 h. Excess $SOCl_2$ was removed under vacuum. The residue was dissolved in CH_2Cl_2 (5.0 mL), and 1-butylamine (73 mg, 1.0 mmol) was added. The reaction mixture was stirred for 2 h. The solvent was removed under reduced pressure. The crude product was dissolved in Et_3N (5.0 mL), and then (trimethylsilyl) acetylene (117.6 mg, 1.2 mmol), $Pd(PPh_3)_2Cl_2$ (70.2 mg, 0.1 mmol), and CuI (1.9 mg, 0.01 mmol) were added. The resulting mixture was heated under Ar protection at 70 °C. The reaction was monitored by TLC. After the starting materials were completely consumed, the solvent was removed under reduced pressure, and the residue was purified by a flash column chromatography (petroleum ether/ethyl acetate = 4/1, v/v, as an eluent) to yield *N*-butyl-2-(2-((trimethylsilyl)ethynyl)phenyl)acetamide in 90% yield. Then it was dissolved in 1:1 $MeOH/CH_2Cl_2$ (8 mL), and K_2CO_3 was added (552 mg, 4.0 mmol). After being stirred at room temperature for 2 h, the reaction mixture was quenched with water (10 mL) and then extracted with ethyl acetate (30 mL). The organic layer was isolated, washed with brine, and dried over $MgSO_4$. Filtration to remove $MgSO_4$ followed by concentration under vacuum afforded **1a** as a white solid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.54 (d, J = 7.2 Hz, 1H), 7.36−7.29 (m, 2H), 7.24 (d, J = 7.2 Hz, 1H), 5.52 (br s, 1H), 3.76 (s, 2H), 3.33 (s, 1H), 3.19 (q, J = 6.6 Hz, 2H), 1.46−1.36 (m, 2H), 1.32−1.20 (m, 2H), 0.87 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 137.7, 133.0, 129.9, 129.4, 127.2, 121.9, 81.8, 81.8, 42.4, 39.3, 31.4, 19.9, 13.6; ESI-MS m/z $[M + H]^+$ 216.1; HRMS (ESI) calcd for $C_{14}H_{17}NONa$ $[M + Na]^+$ 238.1208, found 238.1217.

2-(2-Ethynylphenyl)acetamide (1b): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.60 (d, J = 8.1 Hz, 1H), 7.37−7.29 (m, 2H), 7.20−7.15 (m, 1H), 5.54 (br s, 2H), 3.74 (s, 2H), 3.22 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.5, 135.8, 132.8, 129.9, 129.0, 127.4, 122.5, 81.9, 81.4, 39.4; ESI-MS m/z $[M + H]^+$ 160.1; HRMS (ESI) calcd for $C_{10}H_9NONa$ $[M + Na]^+$ 182.0582, found 182.0578.

2-(2-Ethynylphenyl)-*N*-methylacetamide (1c): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.53 (d, J = 7.2 Hz, 1H), 7.36−7.33 (m, 2H), 7.29−7.25 (m, 1H), 5.50 (br s, 1H), 3.76 (s, 2H), 3.33 (s, 1H), 2.76 (d, J = 4.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9, 137.5, 133.1, 130.1, 129.5, 127.4, 122.1, 82.0, 81.7, 42.3, 26.5; ESI-MS m/z $[M + H]^+$

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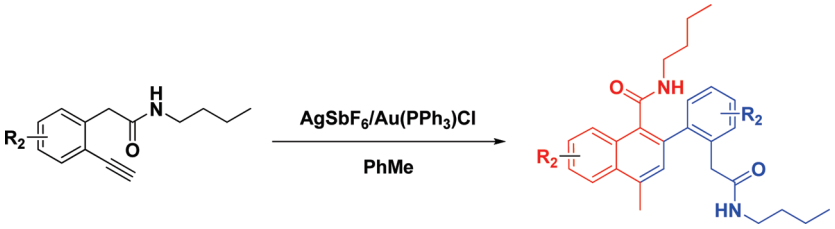
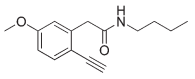
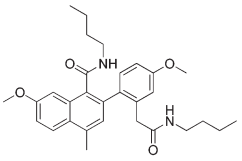
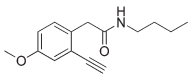
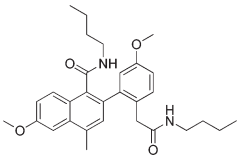
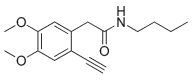
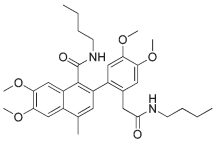
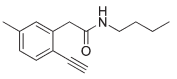
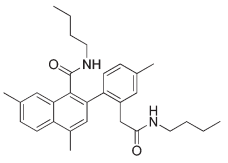
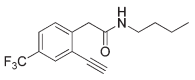
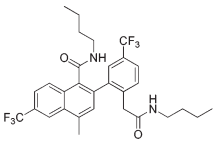
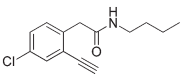
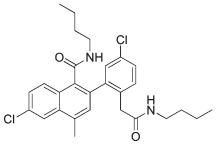
Table 3. Reaction Scope of the Dimerization to Synthesize Substituted 2-Phenylnaphthalene[a]



entry	substrate **1**	product **2**	yield (%)[b]
1		 **2j**	77
2		 **2k**	82
3		 **2l**	80
4		 **2m**	78
5		 **2n**	trace[c]
6		 **2o**	70

[a] The reaction was performed with $AgSbF_6$ (10 mol %) and $Au(PPh_3)Cl$ (10 mol %) in anhydrous toluene under Ar protection at 70 °C unless otherwise noted. [b] Yields of isolated products. [c] Complicated reaction mixture.

174.1; HRMS (ESI) calcd for $C_{11}H_{11}NONa$ $[M + Na]^+$ 196.0738, found 196.0728.

2-(2-Ethynylphenyl)-*N*,*N*-dimethylacetamide (1d): ^1H NMR ($CDCl_3$, 300 MHz): δ 7.50 (d, J = 5.7 Hz, 1H), 7.33−7.31 (m, 2H), 7.23−7.21 (m, 1H), 3.91 (s, 2H), 3.29 (s, 1H), 3.01 (s, 3H), 2.98 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 137.7, 132.7, 129.1, 128.8, 126.6, 121.7, 81.9, 81.4, 38.8, 37.5, 35.5; ESI-MS m/z $[M + H]^+$ 188.1; HRMS (ESI) calcd for $C_{12}H_{13}NONa$ $[M + Na]^+$ 210.0895, found 210.0878.

2-(2-Ethynylphenyl)-*N*-phenylacetamide (1e): ^1H NMR ($CDCl_3$, 300 MHz) δ 7.59 (d, J = 7.2 Hz, 1H), 7.45−7.37 (m, 5H), 7.34−7.28 (m, 2H), 7.11−7.06 (m, 1H), 3.93 (s, 2H), 3.44 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.4, 137.8, 137.2, 133.2, 130.0, 129.7, 128.9, 127.6, 124.3, 121.8, 119.8, 82.2, 82.1, 43.5; ESI-MS m/z $[M + H]^+$ 236.1; HRMS (ESI) calcd for $C_{16}H_{13}NONa$ $[M + Na]^+$ 258.0895, found 258.0874.

2-(2-Ethynylphenyl)-*N*-(4-methoxyphenyl)acetamide (1f): ^1H NMR ($CDCl_3$, 300 MHz) δ 7.58 (d, J = 7.5 Hz, 1H), 7.43 (d, J = 7.5 Hz, 1H), 7.38−7.29 (m, 4H), 6.82 (d, J = 7.8 Hz, 2H), 5.30 (br s, 1H), 3.91 (s, 2H), 3.77 (s, 3H), 3.41 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.3, 156.4, 137.3, 133.2, 130.8, 130.0, 129.6, 127.5, 121.9, 121.8, 114.0, 82.2, 82.0, 55.4, 43.2; ESI-MS m/z $[M + H]^+$ 266.1; HRMS (ESI) calcd for $C_{17}H_{15}NO_2Na$ $[M + Na]^+$ 288.1000, found 288.1008.

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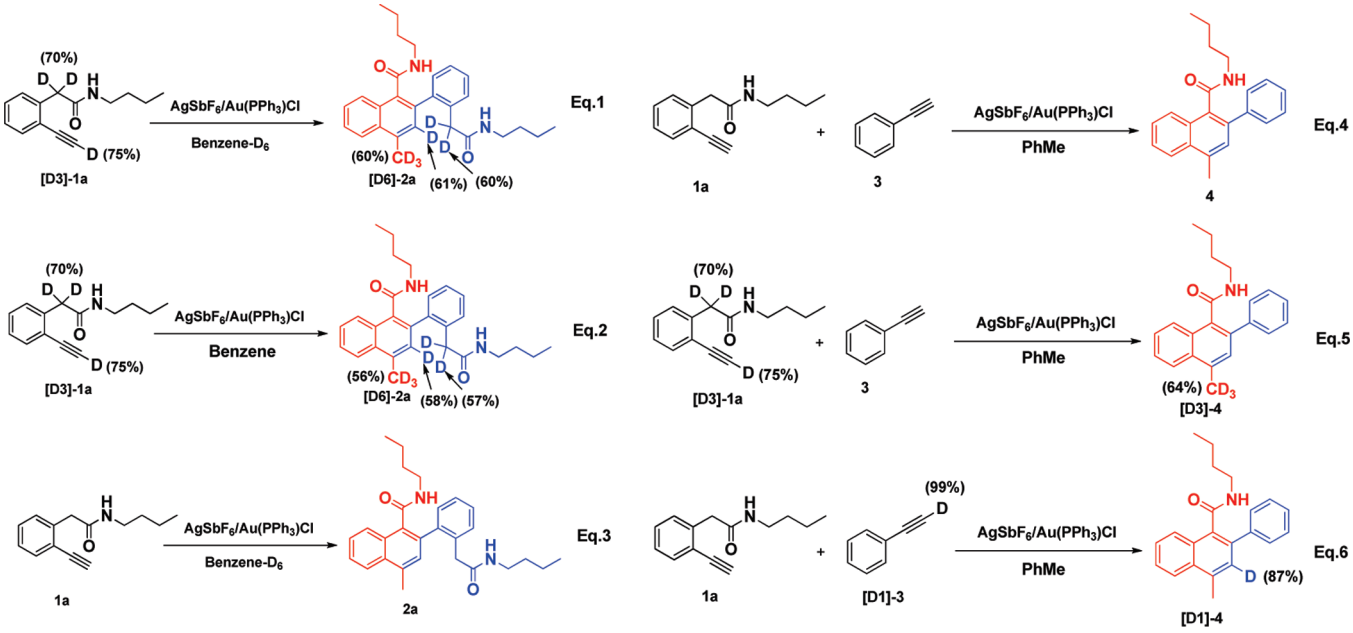
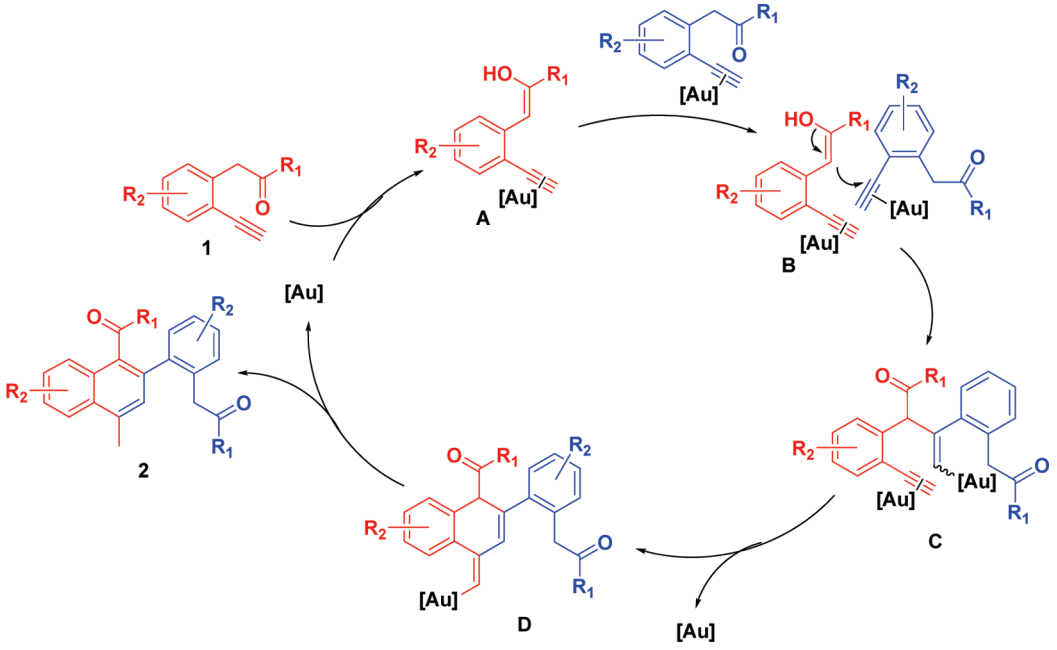
Scheme 2. Labeling Studies



Scheme 3. Proposed Mechanism for the Dimerization of 1 to 2



2-(2-Ethynylphenyl)-*N*-(4-(trifluoromethyl)phenyl)acetamide (1g): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.61−7.52 (m, 5H), 7.43−7.34 (m, 2H), 7.31 (dd, J = 7.2 Hz, 1.8 Hz, 1H), 5.31 (s, 1H), 3.95 (s, 2H), 3.45 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.6, 140.8, 136.7, 133.4, 130.1, 129.9, 128.5, 127.8, 126.2, 126.2, 121.8, 119.3, 82.4, 82.1, 43.6; ESI-MS m/z $[M + H]^+$ 303.9; HRMS (ESI) calcd for $C_{17}H_{12}NOF_3Na$ $[M + Na]^+$ 326.0769, found 326.0778.

2-(2-Ethynylphenyl)-*N*-(pyridin-4-yl)acetamide (1h): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.63 (br s, 1H), 8.42 (d, J = 6.3 Hz, 2H), 7.54 (d, J = 7.5 Hz, 1H), 7.45 (d, J = 6.3 Hz, 2H), 7.35 (m, 2H), 7.27 (dd, J = 7.5 Hz, 2.1 Hz, 1H), 3.92 (s, 2H), 3.38 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.6, 150.1, 145.5, 136.5, 133.1, 129.9, 129.5, 127.5, 121.9, 113.7, 82.2, 81.9, 43.0; ESI-MS m/z $[M + H]^+$ 237.0; HRMS (ESI) calcd for $C_{15}H_{13}N_2O$ $[M + H]^+$ 237.1028, found 237.1044.

Methyl 2-(2-ethynylphenyl)acetate (1i): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.52 (d, J = 7.5 Hz, 1H), 7.35−7.30 (m, 2H), 7.27 (d, J = 7.8 Hz, 1H), 3.89 (s, 2H), 3.71 (s, 3H), 3.28 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.4, 136.5, 132.7, 129.7, 128.9, 127.1, 122.3, 81.5, 81.5, 52.0, 39.5; LRMS (EI) m/z 174 (M^+); HRMS (EI) m/z calcd for $C_{11}H_{10}O_2$ (M^+) 174.0681, found 174.0681.

***N*-Butyl-2-(2-ethynyl-5-methoxyphenyl)acetamide (1j):** ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.44 (d, J = 8.4 Hz, 1H), 6.87 (d,

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J = 2.7 Hz, 1H), 6.78 (dd, J = 8.4 Hz, 2.7 Hz, 1H), 5.62 (br s, 1H), 3.81 (s, 3H), 3.70 (s, 2H), 3.24 (s, 1H), 3.22−3.16 (m, 2H), 1.43−1.38 (m, 2H), 1.28−1.25 (m, 2H), 0.90−0.84 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 160.2, 139.5, 134.4, 115.1, 113.9, 113.4, 82.0, 80.4, 55.4, 42.8, 39.4, 31.5, 19.9, 13.7; ESI-MS m/z $[M + H]^+$ 246.1; HRMS (ESI) calcd for $C_{15}H_{19}NO_2Na$ $[M + Na]^+$ 268.1313, found 268.1309.

***N*-Butyl-2-(2-ethynyl-4-methoxyphenyl)acetamide (1k):** ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.21 (d, J = 8.4 Hz, 1H), 7.02 (d, J = 2.1 Hz, 1H), 6.88 (dd, J = 8.7 Hz, 2.7 Hz, 1H), 5.52 (br s, 1H), 3.78 (s, 3H), 3.66 (s, 2H), 3.29 (s, 1H), 3.21−3.15 (m, 2H), 1.41−1.34 (m, 2H), 1.28−1.21 (m, 2H), 0.88−0.82 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 158.4, 131.1, 129.8, 122.9, 117.6, 116.0, 81.7, 81.6, 55.3, 41.5, 39.3, 31.4, 19.9, 13.6; ESI-MS m/z $[M + H]^+$ 246.1; HRMS (ESI) calcd for $C_{15}H_{19}NO_2Na$ $[M + Na]^+$ 268.1313, found 268.1323.

***N*-Butyl-2-(2-ethynyl-4,5-dimethoxyphenyl)acetamide (1l):** ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.99 (s, 1H), 6.83 (s, 1H), 5.62 (br s, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.69 (s, 2H), 3.26 (s, 1H), 3.20 (q, J = 6.6 Hz, 2H), 1.49−1.37 (m, 2H), 1.36−1.21 (m, 2H), 0.88 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 150.1, 147.9, 131.4, 115.0, 113.6, 112.5, 82.2, 80.3, 56.0, 42.2, 39.4, 31.5, 20.0, 13.7; ESI-MS m/z $[M + H]^+$ 276.1; HRMS (ESI) calcd for $C_{16}H_{21}NO_3Na$ $[M + Na]^+$ 298.1419, found 298.1409.

***N*-Butyl-2-(2-ethynyl-5-methylphenyl)acetamide (1m):** ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.43 (d, J = 7.8 Hz, 1H), 7.17 (s, 1H), 7.08 (d, J = 7.8 Hz, 1H), 5.64 (br s, 1H), 3.71 (s, 2H), 3.30 (s, 1H), 3.24−3.18 (m, 2H), 2.36 (s, 3H), 1.45−1.40 (m, 2H), 1.32−1.27 (m, 2H), 0.91−0.86 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.2, 139.8, 137.6, 132.9, 130.7, 128.1, 118.8, 81.8, 81.1, 42.3, 39.4, 31.4, 21.4, 19.9, 13.6; ESI-MS m/z $[M + H]^+$ 230.1; HRMS (ESI) calcd for $C_{15}H_{19}NO$-Na $[M + Na]^+$ 252.1364, found 252.1370.

***N*-Butyl-2-(2-ethynyl-4-(trifluoromethyl)phenyl)acetamide (1n):** ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.78 (s, 1H), 7.59 (d, J = 7.8 Hz, 1H), 7.51 (d, J = 7.8 Hz, 1H), 5.57 (br s, 1H), 3.78 (s, 2H), 3.41 (s, 1H), 3.23 (q, J = 6.6 Hz, 2H), 1.47−1.36 (m, 2H), 1,35−1.25 (m, 2H), 0.89 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.1, 141.5, 130.5, 129.8, 129.6, 125.9, 124.8, 122.7, 83.2, 80.6, 42.2, 39.5, 31.5, 19.9, 13.6; ESI-MS m/z $[M + H]^+$ 284.1; HRMS (ESI) calcd for $C_{15}H_{16}NOF_3Na$ $[M + Na]^+$ 306.1082, found 306.1079.

***N*-Butyl-2-(4-chloro-2-ethynylphenyl)acetamide (1o):** ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43 (d, J = 1.8 Hz, 1H), 7.39 (d, J = 8.1 Hz, 1H), 7.20 (dd, J = 8.4 Hz, 2.1 Hz, 1H), 5.36 (br s, 1H), 3.51 (s, 2H), 3.39 (s, 1H), 3.26−3.20 (m, 2H), 1.45−1.39 (m, 2H), 1.32−1.25 (m, 2H), 0.92−0.87 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 134.6, 133.4, 133.2, 130.8, 129.7, 121.8, 82.8, 43.0, 39.5, 31.5, 20.0, 13.7; ESI-MS m/z $[M + H]^+$ 250.1; HRMS (ESI) calcd for $C_{14}H_{16}NOClNa$ $[M + Na]^+$ 272.0818, found 272.0823.

General Procedure for the Synthesis of *N*-Butyl-2-(2-(2-(butylamino)-2-oxoethyl)phenyl)-4-methyl-1-naphthamide (2a). To a solution of **1a** (0.2 mmol) in 2 mL of anhydrous toluene was added $AgSbF_6$ (10 mol %)/$Au(PPh_3)Cl$ (10 mol %). The reaction mixture was heated at 70 °C in a sealed tube under argon protection for 8 h. After the reaction was cooled to ambient temperature, the solvent was evaporated under reduced pressure, and the residue was purified by a flash column chromatography to give **2a** as a white solid (PE/EA = 4:1) in 81% yield: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.11−8.09 (m, 1H), 8.01−7.99 (m, 1H), 7.55−7.53 (m, 2H), 7.34−7.27 (m, 4H), 7.13 (s, 1H), 6.04 (br s, 1H), 3.69 (d, J = 11.1 Hz, 1H), 3.34 (d, J = 11.1 Hz, 1H), 3.23−3.11 (m, 2H), 2.88−2.87 (m, 2H), 2.69 (s, 3H), 1.72 (br s, 1H), 1.11−1.00 (m, 8H), 0.78−0.70 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.2, 169.0, 140.6, 135.0, 134.7, 133.8, 133.2, 131.8, 130.8, 130.1, 129.9, 128.0, 127.6, 127.1, 126.8, 126.7, 126.2, 123.9, 41.2, 39.4, 39.3, 31.1, 30.9, 19.9, 19.8, 19.6, 13.8, 13.6; ESI-MS m/z $[M + H]^+$ 431.3; HRMS (ESI) calcd for $C_{28}H_{34}N_2O_2Na$ $[M + Na]^+$ 453.2518, found 453.2505.

2-(2-(2-Amino-2-oxoethyl)phenyl)-4-methyl-1-naphthamide (2b). Compound **2b** was obtained as a white solid after purification by flash chromatography (PE/EA = 1:1) in 78% yield: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.09−7.96 (m, 2H), 7.61−7.58 (m, 2H), 7.39−7.28 (m, 4H), 7.22 (s, 1H), 4.96 (br s, 2H), 3.81 (d, J = 15.6 Hz, 1H), 3.47 (d, J = 15.0 Hz, 1H), 2.72 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.2, 169.3, 140.7, 136.8, 136.3, 132.3, 131.6, 130.8, 130.0, 129.9, 129.5, 128.2, 128.1, 127.1, 126.7, 126.3, 125.8, 124.3, 39.7, 19.6; ESI-MS m/z $[M + H]^+$ 319.1; HRMS (ESI) calcd for $C_{20}H_{18}N_2O_2Na$ $[M + Na]^+$ 341.1266, found 341.1265.

***N*,4-Dimethyl-2-(2-(2-(methylamino)-2-oxoethyl)phenyl)-1-naphthamide (2c).** Compound **2c** was obtained as a white solid after purification by flash chromatography (PE/EA = 2:1) in 80% yield: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.12−8.00 (m, 2H), 7.58−7.53 (m, 2H), 7.32−7.32 (m, 4H), 7.13 (s, 1H), 6.10 (br s, 1H), 3.70 (d, J = 14.7 Hz, 1H), 3.37 (d, J = 15.6 Hz, 1H), 2.70 (s, 3H), 2.69 (d, J = 4.8 Hz, 3H), 2.51 (d, J = 5.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.1, 169.9, 140.7, 135.3, 135.0, 133.6, 132.9, 131.8, 130.7, 130.1, 129.6, 128.1, 127.7, 127.1, 126.9, 126.6, 126.3, 124.0, 40.8, 26.4, 26.3, 19.6; ESI-MS m/z $[M + H]^+$ 347.1; HRMS (ESI) calcd for $C_{22}H_{22}$-N_2O_2Na $[M + Na]^+$ 369.1579, found 369.1591.

2-(2-(2-(Dimethylamino)-2-oxoethyl)phenyl)-*N*,*N*,4-trimethyl-1-naphthamide (2d). Compound **2d** was obtained as a white solid after purification by flash chromatography (PE/EA = 2:1) in 84% yield: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.08−8.04 (m, 1H), 7.73−7.70 (m, 1H), 7.59−7.55 (m, 2H), 7.36−7.29 (m, 4H), 7.18 (s, 1H), 3.79 (d, J = 16.2 Hz, 1H), 3.54 (d, J = 15.9 Hz, 1H), 2.93 (s, 3H), 2.82 (s, 3H), 2.74 (s, 3H), 2.70 (s, 3H), 2.64 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.7, 169.9, 139.9, 136.0, 135.1, 134.8, 131.7, 129.9, 129.5, 129.3, 128.7, 128.1, 128.0, 127.0, 126.2, 125.9, 125.5, 124.4, 40.9, 38.3, 37.5, 35.3, 34.2, 19.3; ESI-MS m/z $[M + H]^+$ 375.1; HRMS (ESI) calcd for $C_{24}H_{26}N_2O_2Na$ $[M + Na]^+$ 397.1892, found 397.1905.

4-Methyl-2-(2-(2-oxo-2-(phenylamino)ethyl)phenyl)-*N*-phenyl-1-naphthamide (2e). Compound **2e** was obtained as a white solid after purification by flash chromatography (PE/EA = 4:1) in 77% yield: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.91 (br s, 1H), 8.22 (d, J = 6.3 Hz, 1H), 8.04 (d, J = 6.3 Hz, 1H), 7.94 (br s, 1H), 7.60−7.57 (m, 2H), 7.41−7.27 (m, 8H), 7.26−7.14 (m, 5H), 7.09−6.98 (m, 2H), 3.96 (d, J = 15.3 Hz, 1H), 3.57 (d, J = 15.3 Hz, 1H), 2.74 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.9, 167.7, 140.3, 137.9, 137.7, 136.0, 135.1, 132.6, 131.9, 130.6, 130.1, 129.8, 128.7, 128.4, 127.6, 127.5, 127.2, 126.5, 126.3, 124.4, 124.2, 120.6, 119.8, 42.0, 19.7; ESI-MS m/z $[M + H]^+$ 470.9; HRMS (ESI) calcd for $C_{32}H_{26}N_2O_2Na$ $[M + Na]^+$ 493.1892, found 493.1888.

***N*-(4-Methoxyphenyl)-2-(2-(2-(4-methoxyphenylamino)-2-oxoethyl)phenyl)-4-methyl-1-naphthamide (2f).** Compound **2f** was obtained as a white solid after purification by flash chromatography (PE/EA = 4:1) in 83% yield: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.85 (br s, 1H), 8.21 (m, 1H), 8.04 (m, 1H), 7.81 (br s, 1H), 7.72 (m, 1H), 7.71−7.42 (m, 4H), 7.27−7.11 (m, 6H), 6.77−6.73 (m, 2H), 6.69−6.60 (m, 2H), 3.94 (d, J = 15.0 Hz, 1H), 3.75 (s, 3H), 3.72 (s, 3H), 3.55 (d, J = 15.0 Hz, 1H), 2.74 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.7, 167.5, 156.5, 156.2, 140.4, 135.9, 135.1, 134.1, 133.3, 132.8, 132.0, 131.0, 130.9, 130.7, 130.2, 129.9, 129.0, 128.8, 128.2, 127.6, 127.1, 126.5, 125.3, 124.2, 122.5, 121.7, 55.4, 41.8, 19.7; ESI-MS m/z $[M + H]^+$ 531.0; HRMS (ESI) calcd for $C_{34}H_{30}N_2O_4Na$ $[M + Na]^+$ 553.2103, found 553.2105.

4-Methyl-2-(2-(2-oxo-2-(4-(trifluoromethyl)phenylamino)ethyl)phenyl)-*N*-(4-(trifluoromethyl)phenyl)-1-naphthamide (2g). Compound **2g** was obtained as a yellow solid after purification by flash chromatography (PE/EA = 4:1) in 42% yield: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.13 (br s, 1H), 8.17 (br s, 1H), 8.03−8.02 (m, 2H), 7.74−7.71 (m, 3H), 7.60−7.26 (m, 12H), 4.03 (d, J = 16.2 Hz, 1H), 3.66 (d, J = 16.2 Hz, 1H), 2.75 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 167.9, 141.1, 140.2, 136.4, 134.2, 134.0, 132.8, 132.3, 132.0,

130.9, 129.8, 129.3, 129.2, 128.8, 128.6, 128.5, 128.1, 127.8, 127.5, 126.7, 125.9, 124.2, 120.0, 119.6, 119.3, 42.0, 19.7; ESI-MS m/z $[M + H]^+$ 607.0; HRMS (ESI) calcd for $C_{34}H_{24}F_6N_2O_2Na$ $[M + Na]^+$ 629.1640, found 629.1642.

Methyl 2-(2-(2-Methoxy-2-oxoethyl)phenyl)-4-methyl-1-naphthoate (2i). Compound **2i** was obtained as oil after purification by flash chromatography (PE/EA = 8:1) in 72% yield: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.09−8.05 (m, 1H), 7.99−7.96 (m, 1H), 7.61−7.58 (m, 2H), 7.39−7.29 (m, 3H), 7.26−7.21 (m, 2H), 3.69 (s, 1H), 3.60 (s, 3H), 3.54 (s, 3H), 3.52 (s, 1H), 2.73 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.2, 169.3, 140.6, 136.9, 136.3, 132.3, 131.6, 130.9, 130.0, 129.9, 129.5, 128.2, 128.0, 127.1, 126.7, 126.3, 125.8, 124.3, 51.8, 51.8, 38.6, 19.6; ESI-MS m/z $[M + H]^+$ 348.8; HRMS (ESI) calcd for $C_{22}H_{20}O_4Na$ $[M + Na]^+$ 371.1259, found 371.1273.

***N*-Butyl-2-(2-(2-(butylamino)-2-oxoethyl)-4-methoxyphenyl)-7-methoxy-4-methyl-1-naphthamide (2j).** Compound **2j** was obtained as a white solid after purification by flash chromatography (PE/EA = 2:1) in 77% yield: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.89 (d, J = 9 Hz, 1H), 7.38 (d, J = 3 Hz, 1H), 7.26−7.24 (m, 1H), 7.22−7.16 (m, 1H), 6.96 (s, 1H), 6.88 (d, J = 2.7 Hz, 1H), 6.83 (dd, J = 8.1 Hz, 2.7 Hz, 1H), 5.29 (br s, 1H), 3.90 (s, 3H), 3.82 (s, 3H), 3.69 (d, J = 14.7 Hz, 1H), 3.29 (d, J = 14.7 Hz, 1H), 3.20−3.09 (m, 2H), 2.93−2.87 (m, 2H), 2.64 (s, 3H), 1.10−1.05 (m, 8H), 0.80−0.71 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.1, 169.4, 159.2, 158.2, 135.3, 134.9, 134.5, 133.2, 132.9, 132.2, 131.0, 127.2, 126.0, 125.6, 118.7, 115.5, 112.4, 104.7, 55.4, 55.3, 41.5, 39.4, 39.3, 31.2, 31.1, 20.0, 19.8, 19.6, 13.8, 13.6; ESI-MS m/z $[M + H]^+$ 491.2; HRMS (ESI) calcd for $C_{30}H_{38}N_2O_4Na$ $[M + Na]^+$ 513.2729, found 513.2727.

***N*-Butyl-2-(2-(2-(butylamino)-2-oxoethyl)-5-methoxyphenyl)-6-methoxy-4-methyl-1-naphthamide (2k).** Compound **2k** was obtained as a white solid after purification by flash chromatography (PE/EA = 2:1) in 82% yield: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.04 (d, J = 9.6 Hz, 1H), 7.46−7.42 (m, 2H), 7.23−7.19 (m, 2H), 7.11 (s, 1H), 6.90−6.87 (m, 1H), 5.77 (br s, 1H), 3.95 (s, 3H), 3.77 (s, 3H), 3.64 (d, J = 14.7 Hz, 1H), 3.28 (d, J = 14.7 Hz, 1H), 3.12−3.06 (m, 2H), 2.92−2.86 (m, 2H), 2.64 (s, 3H), 1.12−1.02 (m, 8H), 0.80−0.73 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.6, 169.1, 158.4, 157.9, 141.8, 133.7, 133.3, 132.5, 131.2, 129.9, 128.4, 128.0, 126.1, 125.3, 118.7, 114.9, 114.2, 102.9, 55.4, 55.3, 40.5, 39.5, 39.3, 31.2, 31.0, 19.9, 19.8, 19.8, 13.8, 13.6; ESI-MS m/z $[M + H]^+$ 491.2; HRMS (ESI) calcd for $C_{30}H_{38}N_2O_4Na$ $[M + Na]^+$ 513.2729, found 513.2749.

***N*-Butyl-2-(2-(2-(butylamino)-2-oxoethyl)-4,5-dimethoxyphenyl)-6,7-dimethoxy-4-methyl-1-naphthamide (2l).** Compound **2l** was obtained as a white solid after purification by flash chromatography (PE/EA = 4:1) in 80% yield: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.45 (s, 1H), 7.40 (s, 1H), 7.20(s, 1H), 7.02(s, 1H), 6.89 (s, 1H), 6.85 (s, 1H), 6.82 (s, 1H), 4.04 (s, 3H), 3.99 (s, 3H), 3.91 (s, 3H), 3.83 (s, 3H), 3.74 (d, J = 15.3 Hz, 1H), 3.56−3.55 (m, 2H), 3.28 (d, J = 15.3 Hz, 1H), 2.96−2.91 (m, 2H), 2.64 (s, 3H), 1.18−1.05 (m, 8H), 0.81−0.72 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.6, 169.7, 149.9, 149.4, 148.3, 147.7, 133.5, 133.4, 130.9, 128.4, 127.8, 126.7, 125.0, 120.9, 115.8, 113.2, 112.8, 112.1, 56.0, 55.9, 55.9, 55.8, 40.9, 39.6, 39.3, 31.3, 31.1, 20.0, 19.9, 19.8, 13.7, 13.6; ESI-MS m/z $[M - H]^-$ 549.1; HRMS (ESI) calcd for $C_{32}H_{42}N_2O_6Na$ $[M + Na]^+$ 573.2941, found 573.2939.

***N*-Butyl-2-(2-(2-(butylamino)-2-oxoethyl)-4-methylphenyl)-4,7-dimethyl-1-naphthamide (2m).** Compound **2m** was obtained as a white solid after purification by flash chromatography (PE/EA = 4:1) in 78% yield: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.89 (d, J = 8.4 Hz, 1H), 7.84 (s, 1H), 7.37 (d, J = 8.7 Hz, 1H), 7.20 (d, J = 7.8 Hz, 1H), 7.16 (s, 1H), 7.09 (d, J = 8.4 Hz, 1H), 7.04 (s, 1H), 5.98 (br s, 1H), 3.64 (d, J = 15.0 Hz, 1H), 3.27 (d, J = 14.7 Hz, 1H), 3.16−3.10 (m, 2H), 2.90−2.88 (m, 2H), 2.66 (s, 3H), 2.50 (s, 3H), 2.36 (s, 3H), 1.13−1.01 (m, 8H), 0.79−0.70 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.3, 169.3, 137.7, 137.6, 136.6, 134.8, 133.1, 133.1, 130.9, 130.7, 130.0, 129.8, 128.4, 127.8, 127.0, 125.4, 123.8, 41.2, 39.4, 39.3, 31.1, 31.0, 21.8, 21.1, 19.9, 19.8, 19.6, 13.8, 13.6; ESI-MS m/z $[M + H]^+$ 459.2; HRMS (ESI) calcd for $C_{30}H_{38}N_2O_2Na$ $[M + Na]^+$ 481.2831, found 481.2816.

***N*-Butyl-2-(2-(2-(butylamino)-2-oxoethyl)-5-chlorophenyl)-6-chloro-4-methyl-1-naphthamide (2o).** Compound **2o** was obtained as a white solid after purification by flash chromatography (PE/EA = 1:1) in 70% yield: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.89 (d, J = 8.4 Hz, 1H), 7.40−7.28 (m, 3H), 7.25−7.19 (m, 2H), 7.05 (s, 1H), 5.97 (br s, 1H), 3.65 (d, J = 14.7 Hz, 1H), 3.27 (d, J = 14.7 Hz, 1H), 3.18−3.10 (m, 2H), 2.93−2.86 (m, 2H), 2.67 (s, 3H), 1.11−1.01 (m, 8H), 0.79−0.70 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.3, 169.3, 140.9, 137.8, 137.6, 136.7, 134.7, 133.2, 133.2, 131.0, 130.7, 130.2, 129.8, 128.3, 128.0, 127.0, 125.6, 123.8, 41.4, 39.5, 39.2, 31.2, 31.0, 20.0, 19.9, 19.7, 13.9, 13.6; ESI-MS m/z $[M + H]^+$ 499.2; HRMS (ESI) calcd for $C_{28}H_{32}N_2O_2Cl_2Na$ $[M + Na]^+$ 521.1739, found 521.1754.

Procedure for the Synthesis of Deuterated *N*-Butyl-2-(2-ethynylphenyl)acetamide. To a solution of 10 mol % of 1,5,7-triazabicyclo[4.4.0]dec-5-ene (5.5 mg, 0.04 mmol) in 3 mL of $CDCl_3$ was added **1a** (86 mg, 0.4 mmol). The reaction mixture was stirred at room temperature for 12 h and quenched with 1 N HCl (1 mL). The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4, and filtered. Filtrate was concentrated to afford deuterated **1a**.

Procedure for the Synthesis of *N*-Butyl-4-methyl-2-phenyl-1-naphthamide. To a solution of **1a** (0.2 mmol, 1 equiv) in 1 mL of anhydrous toluene and phenylacetylene (4.0 mmol, 20 equiv) was added $AgSbF_6$ (10 mol %)/$Au(PPh_3)Cl$ (10 mol %). The reaction mixture was heated at 70 °C in a sealed tube under argon protection for 8 h. After the reaction was cooled to ambient temperature, the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography to give **4** as a white solid (PE/EA = 4:1) in 66% yield: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.13−8.10 (m, 1H), 8.05−8.01 (m, 1H), 7.58−7.55 (m, 3H), 7.43−7.36 (m, 4H), 7.14 (s, 1H), 5.39 (br s, 1H), 3.27−3.20 (m, 2H), 2.74 (s, 3H), 1.20−1.13 (m, 2H), 1.03−0.96 (m, 2H), 0.76 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ169.5, 140.6, 136.0, 135.9, 132.2, 131.6, 130.4, 128.8, 128.4, 128.1, 127.7, 127.5, 126.9, 126.2, 124.1, 39.5, 31.0, 19.7, 19.6, 13.7; ESI-MS m/z $[M + H]^+$ 318.1; HRMS (ESI) calcd for $C_{22}H_{23}NONa$ $[M + Na]^+$ 340.1677, found 340.1696.

■ ASSOCIATED CONTENT

Supporting Information. Experimental procedures, X-ray structure of **2a**, NMR spectra, and characterization for all new materials. This material is available free of charge via the Internet at http://pubs.acs.org.

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