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Heteroatom as a Promotor: Synthesis of Polyfunctionalized Benzenes and Naphthalenes

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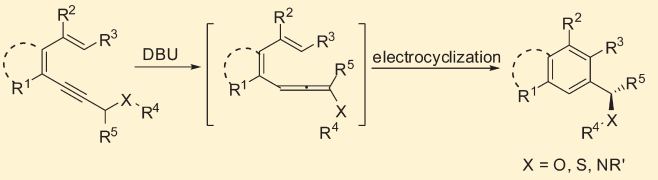
Supporting Information

ABSTRACT: Construction of a new benzene via the electrocyclization of diene−allene is an efficient protocol to access polysubstituted benzenes from simple, readily available starting materials. In this paper, we present a comprehensive study of a heteroatom-promoted propargyl−allenyl isomerization and electrocyclization for the facile and efficient synthesis of polyfunctionalized benzenes and naphthalenes. As a result of the readily accessible starting materials, simple operation, and mild conditions, this reaction should be an appealing strategy in organic synthesis.



INTRODUCTION

The benzenoid aromatic compounds are arguably the most ubiquitous class in nature and the laboratory. Generally, there are only two ways to prepare them: direct functionalization to benzene or construction of a new benzene. Direct functionalization to benzene, because of the effect of the substituent(s), might encounter difficulty in some cases. Thus, construction of a new benzene remains an efficient protocol to access polysubstituted benzenes from simple, readily available starting materials.

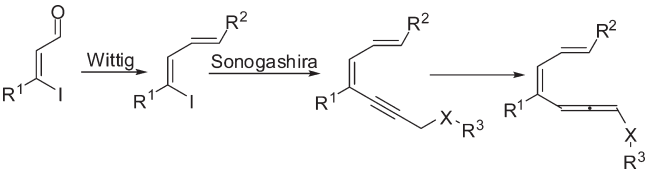
The 6π-electrocyclization could offer the skeleton of a benzene ring, and the electrocyclization of diene−allenes could construct a benzene ring due to the unstable properties of the cyclization product isotoluene.[1−3] However, building suitable diene−allenes may become the main challenge for developing facile and efficient synthetic methods. A good solution is propargyl−allenyl isomerization, which means only readily available propargyl dienes are used as the substrates (Scheme 1).

In a preliminary communication, we reported sulfur-assisted propargyl−allenyl isomerizations and electrocyclizations for the synthesis of polyfunctionalized benzenes and naphthalenes.[4] On the basis of our previous understanding of the propargyl−allenyl isomerization[5−12] and the enediyne−alleneyne isomerization,[13−17] we wish to report the full details of heteroatom (O, N, and S)-promoted propargyl−allenyl isomerization and electrocyclization, which may offer convenient protocols to various polysubstituted benzenes.

RESULTS AND DISCUSSION

Reasonably, the oxygen-promoted propargyl−allenyl isomerizations and electrocyclizations were first investigated. The difference between sulfur and oxygen is that the latter could increase the acidity of the adjacent methylene group less than the former. Thus, we chose DBU as the base instead of triethylamine.

Scheme 1. Synthesis of the Substrates



Luckily, upon treatment of (2*E*,4*Z*)-ethyl 5-phenyl-8-(*p*-tolyloxy) octa-2,4-dien-6-ynoate (**1a**) with 1.2 equiv of DBU in acetonitrile at 50 °C for 6 h, the expected product, ethyl 3-(*p*-tolyloxymethyl)biphenyl-4-carboxylate (**2a**), was obtained in 91% yield (Table 1, entry 1). The amide analogue of **1a**, (2*E*,4*Z*)-*N*-methyl-*N*,5-diphenyl-8-(*p*-tolyloxy)octa-2,4-dien-6-ynamide (**1b**), could proceed with similar isomerization and electrocyclization to give *N*-methyl-*N*-phenyl-3-(*p*-tolyloxymethyl)biphenyl-4-carboxamide (**2b**) in 77% yield (entry 2). Notably, the electron-withdrawing groups (ester, acyl, or amide group) of **1**, which could increase the acidity of the methylene group adjacent to the oxygen atom and shorten the reaction time, can be replaced by a phenyl group, although the result is rather sluggish (entry 6).

The result from the entry 6 of Table 1 showed that the electron-withdrawing groups in substrates are as essential as we thought in the preliminary communication.[4] Without the electron-withdrawing group, the propargyl−allenyl isomerization and electrocyclization might still be possible in the presence of DBU with the assistance of heating. Treatment of (*Z*)-phenyl (4-phenylhepta-4,6-dien-2-ynyl)sulfane (**3a**) in acetonitrile at 65 °C for 6 h gave (biphenyl-3-ylmethyl)(phenyl)sulfane (**4a**) in 82% yield (Table 2, entry 1), and a series of thioprop-1-ynyl dienes offered satisfactory results (Table 2).

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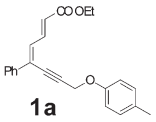
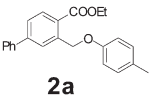
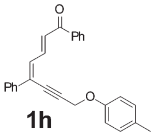
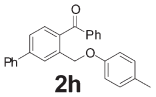
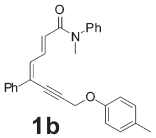
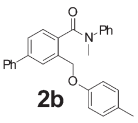
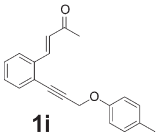
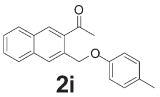
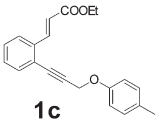
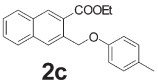
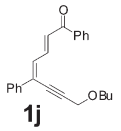
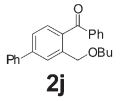
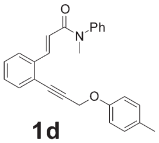
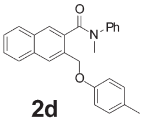
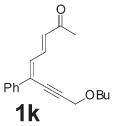
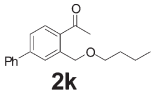
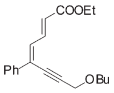
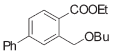
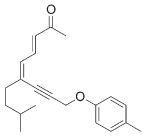
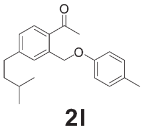
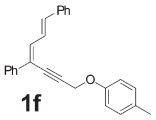
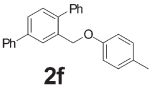
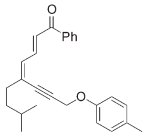
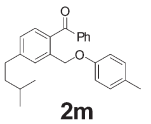
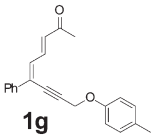
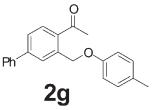
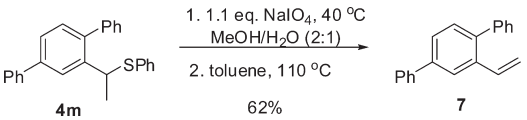
Table 1. Oxygen-Promoted Propargyl-Allenyl Isomerization and Electrocyclization [a]

entry	substrate	product	T/°C	t/h	yield	entry	substrate	product	T/°C	t/h	yield
1	 1a	 2a	50	6	91%	8	 1h	 2h	50	6	68%
2	 1b	 2b	60	12	77%	9	 1i	 2i	reflux	24	55%
3	 1c	 2c	reflux	24	58%	10	 1j	 2j	60	12	60%
4	 1d	 2d	reflux	24	62%	11	 1k	 2k	60	12	61%
5	 1e	 2e	60	12	83%	12	 1l	 2l	60	6	77%
6	 1f	 2f	reflux	24	55%	13	 1m	 2m	40	6	55%
7	 1g	 2g	50	6	70%						

[a] Substrate **1a** (0.5 mmol) and base (1.0 mmol) in acetonitrile (3 mL) under a N_2 atmosphere.

Scheme 2. Oxidation and Pyrolytic Elimination of 4m



Then our attention was diverted to nitrogen. Amines might provide more choices for the functionalization of the products than ethers or sulfanes. We chose (2*E*,4*Z*)-ethyl 8-(methyl(phenyl)amino)-5-phenylocta-2,4-dien-6-ynoate (**5a**) as the starting material and obtained ethyl 3-((methyl(phenyl)amino)methyl)biphenyl-4-carboxylate (**6a**) in 78% yield after heating for 6 h (Table 3, entry 1). However, we recovered just the starting material if the ester group was replaced by hydrogen or a phenyl group. For increasing the acidity of the methylene group adjacent to the nitrogen atom, we introduced an electron-withdrawing group on the nitrogen and chose (*Z*)-*N*-(4-phenylhepta-4,6-dien-2-ynyl)-*N*-*p*-tolylacetamide (**5b**) as the substrate. Fortunately, we obtained *N*-(biphenyl-3-ylmethyl)-*N*-*p*-tolylacetamide (**6b**) in good yield (entry 2). It is noteworthy that the introduction of the electron-withdrawing group on the nitrogen not only improves the reaction itself but also affords a useful way to get functionalized amine derivatives (Table 3).

As mentioned, the heteroatoms, which triggered the propargyl–allenyl isomerization in the substrates, are also a very useful part of the products prepared by the above protocols and could be used as a convenient chemical handle for preparing other compounds. We treated **4m** with $NaIO_4$ in aqueous methanol then heated it in toluene at 110 °C for an oxidation/pyrolytic elimination, and 4-phenyl-2-vinylbiphenyl (**7**) was isolated in 62% yield (Scheme 2).

We treated **6j** in HCl/MeOH at 110 °C and obtained 2-(4-chlorophenyl)-5-phenylisoindolin-1-one (**8**) in almost quantitative yield (Scheme 3). Isoindolin-1-one derivatives, which exhibit a variety of biological activities, are known as an important class applied widely in pharmaceutical fields.[18−20]

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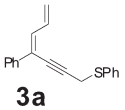
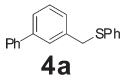
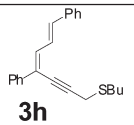
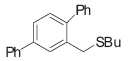
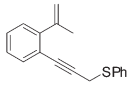
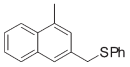
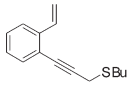
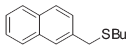
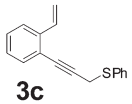
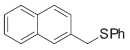
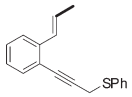
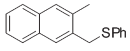
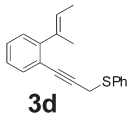
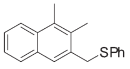
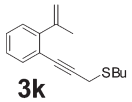
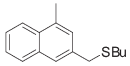
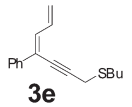
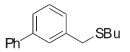
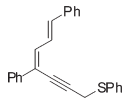
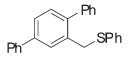
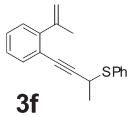
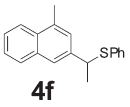
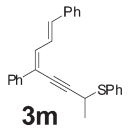
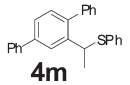
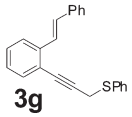
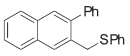
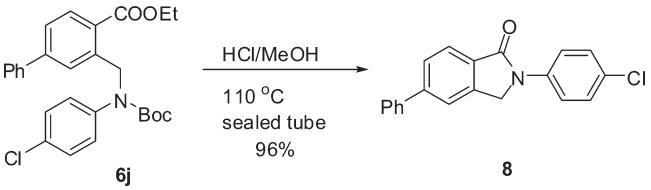
Table 2. Sulfur-Promoted Propargyl−Allenyl Isomerization and Electrocyclization[a]

entry	substrate	product	T/°C	t/h	yield	entry	substrate	product	T/°C	t/h	yield
1	 **3a**	 **4a**	50	6	82%	8	 **3h**	 **4h**	50	6	72%
2	 **3b**	 **4b**	50	6	80%	9	 **3i**	 **4i**	60	12	87%
3	 **3c**	 **4c**	50	6	80%	10	 **3j**	 **4j**	50	6	80%
4	 **3d**	 **4d**	50	12	63%	11	 **3k**	 **4k**	60	12	85%
5	 **3e**	 **4e**	50	6	83%	12	 **3l**	 **4l**	30	3	88%
6	 **3f**	 **4f**	50	12	75%	13	 **3m**	 **4m**	30	3	84%
7	 **3g**	 **4g**	50	6	70%						

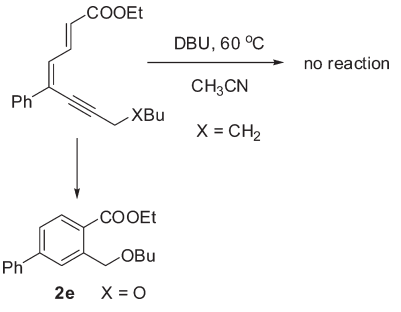
[a] Substrate **3a** (0.5 mmol) and base (1.0 mmol) in acetonitrile (3 mL) under a N_2 atmosphere.

Scheme 3. Acidolysis and Cyclization of 6j



6j **8**

Scheme 4. Plausible Mechanism



2e X = O

There are two plausible pathways for this reaction: electrocyclization of diene−allenes or electrocyclization of diene−alkyne (Bergman and Myers−Saito-type cyclization). Thus, we prepared (2*Z*,4*E*)-ethyl 5-phenyltrideca-2,4-dien-6-ynoate (**9**), which could be thought of as a C-analogue of **1e** for replacing the heteroatom by carbon, and conducted the reaction under the same conditions. Only the starting materials were recovered, illustrating that the heteroatom might play a role in promoting the reaction (Scheme 4).

We then synthesized **3m** deuterated on the methenyl group adjacent to the sulfur atom and conducted the reaction under the same conditions. The methenyl group of **4m** was protonated, and the deuterium moved to the new benzene ring, demonstrating that a propargyl−allene isomerization and aromatization of the intermediate isotoluene occurred (Scheme 5).

CONCLUSION

In summary, we have presented here a comprehensive study of the heteroatom-promoted propargyl−allenyl isomerizations and electrocyclizations for the facile and efficient synthesis of polyfunctionalized benzenes and naphthalenes. As a result of the readily accessible starting materials, simple operation, and mild conditions, this reaction should be an appealing strategy in organic synthesis. Further studies on the synthetic application are currently ongoing.

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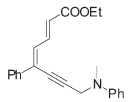
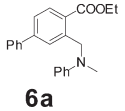
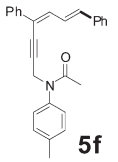
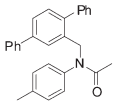
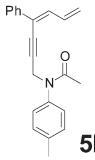
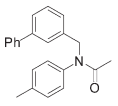
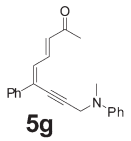
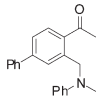
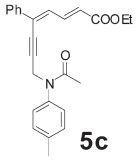
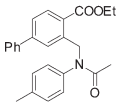
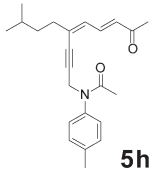
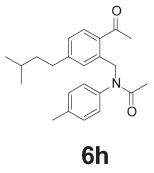
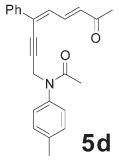
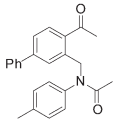
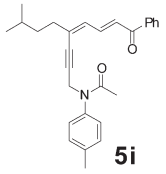
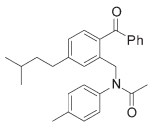
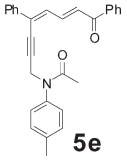
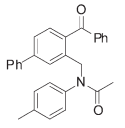
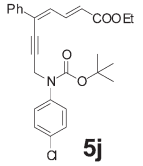
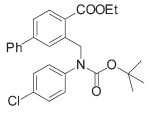
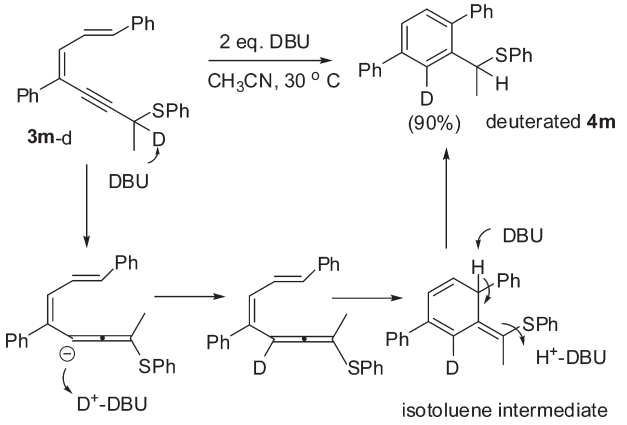
Table 3. Nitrogen-Promoted Propargyl−Allenyl Isomerization and Electrocyclization[a]

entry	substrate	product	T/°C	t/h	yield	entry	substrate	product	T/°C	t/h	yield
1	 5a	 6a	60	6	78%	6	 5f	 6f	60	6	92%
2	 5b	 6b	reflux	12	91%	7	 5g	 6g	50	6	58%
3	 5c	 6c	50	6	91%	8	 5h	 6h	50	3	96%
4	 5d	 6d	40	6	95%	9	 5i	 6i	50	3	73%
5	 5e	 6e	40	6	90%	10	 5j	 6j	40	3	88%

[a] Substrate **5a** (0.5 mmol) and base (1.0 mmol) in acetonitrile (3 mL) under a N_2 atmosphere.

Scheme 5. Control Experiment



EXPERIMENTAL SECTION

Ethyl 3-(*p*-Tolyloxymethyl)biphenyl-4-carboxylate (2a). To a solution of 0.5 mmol of **1a** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 50 °C. The reaction was monitored by TLC until completion (6 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 40/1) of the reaction mixture afforded 158 mg of **2a**: yield 91%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14−8.12 (d, J = 8.0 Hz, 1H), 8.04−8.03 (m, 1H), 7.65−7.63 (m, 2H), 7.61−7.59 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 1H), 7.49−7.45 (m, 2H), 7.42−7.38 (m, 1H), 7.12−7.10 (d, J = 8.0 Hz, 2H), 6.98−6.95 (m, 2H), 5.55 (s, 2H), 4.43−4.37 (q, J = 7.2 Hz, 2H), 2.31 (s, 3H), 1.43−1.39 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.1, 157.0, 145.4, 140.6, 140.3, 131.6, 130.4, 130.2, 129.1, 128.4, 127.6, 127.0, 126.4, 126.0, 115.1, 68.7, 61.3, 20.8, 14.6; IR (neat, cm^{-1}) 2984, 1712, 1509, 1245, 755; HRMS calcd for $C_{23}H_{22}O_3$ 346.1569, found 346.1560.

***N*-Methyl-*N*-phenyl-3-(*p*-tolyloxymethyl)biphenyl-4-carboxamide (2b).** To a solution of 0.5 mmol of **1b** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 60 °C. The reaction was monitored by TLC until completion (12 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 7/1) of the reaction mixture afforded 157 mg of **2b**: yield 77%; ^{1}H NMR (500 MHz, DMSO-d_6, 80 °C) δ 7.73 (s, 1H), 7.60−7.59 (d, J = 7.5 Hz, 2H), 7.44−7.41(m, 3H), 7.36−7.33(t, J = 7.5 Hz, 1H), 7.30−7.21(m, 5H), 7.16−7.11(m, 3H), 6.95−6.94 (d, J = 9.0 Hz, 2H), 5.21 (s, 2H), 3.36 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (DMSO-d_6, 125 MHz, 80 °C) δ 168.5, 156.1, 143.4, 140.0, 138.7, 134.9, 134.7, 129.4, 128.8, 128.5, 128.4, 127.9, 127.3, 126.3, 126.2, 126.1, 126.0, 124.9, 114.5, 67.5, 37.1, 19.6; IR (neat, cm^{-1})

dx.doi.org/10.1021/jo2004555 |J. Org. Chem. 2011, 76, 4582–4590

2921, 1638, 1373, 1233, 695; HRMS calcd for $C_{28}H_{25}NO_2$ 407.1885, found 407.1893.

Ethyl 3-(*p*-Tolyloxymethyl)-2-naphthoate (2c). To a solution of 0.5 mmol of **1c** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at reflux. The reaction was monitored by TLC until completion (24 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 30/1) of the reaction mixture afforded 93 mg of **2c**: yield 58%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.17 (s, 1H), 7.96−7.94 (d, J = 8.0 Hz, 1H), 7.90−7.88 (d, J = 8.0 Hz, 1H), 7.62−7.53 (m, 2H), 7.15−7.13 (d, J = 8.0 Hz, 2H), 7.01−6.99 (d, J = 8.4 Hz, 2H), 5.61 (s, 2H), 4.47−4.42 (q, J = 7.2 Hz, 2H), 2.33 (s, 3H), 1.47−1.43 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.4, 157.0, 135.2, 135.1, 132.6, 131.9, 130.4, 130.2, 129.0, 128.6, 128.1, 127.0, 126.9, 126.6, 115.1, 69.0, 61.4, 20.8, 14.6; IR (neat, cm^{-1}) 2978, 1704, 1512, 1240, 805; HRMS calcd for $C_{21}H_{20}O_3$ 320.1412, found 320.1411.

***N*-Methyl-*N*-phenyl-3-(*p*-tolyloxymethyl)-2-naphthamide (2d).** To a solution of 0.5 mmol of **1d** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at reflux. The reaction was monitored by TLC until completion (24 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 7/1) of the reaction mixture afforded 118 mg of **2d**: yield 62%; ^{1}H NMR (500 MHz, DMSO-d_6, 80 °C) δ 7.96 (s, 1H), 7.85−7.84 (d, J = 8.5 Hz, 1H), 7.74−7.72 (d, J = 7.5 Hz, 1H), 7.67 (s, 1H), 7.51−7.45 (m, 2H), 7.34−7.32 (d, J = 7.5, 2H), 7.23−7.20 (t, J = 7.8 Hz, 2H), 7.13−7.11 (d, J = 8.0 Hz, 2H), 7.09−7.06 (t, J = 7.5 Hz, 1H), 6.98−6.95 (m, 2H), 5.30 (s, 2H), 3.38 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (DMSO-d_6, 125 MHz, 80 °C) δ 168.6, 156.2, 143.7, 133.3, 131.9, 131.8, 131.1, 129.4, 128.8, 128.4, 127.2, 127.2, 127.1, 126.9, 126.6, 126.2, 126.2, 125.9, 114.5, 78.7, 67.8, 19.6; IR (neat, cm^{-1}) 2920, 1665, 1506, 1251, 691; HRMS calcd for $C_{26}H_{23}NO_2$ 381.1729, found 381.1731.

Ethyl 3-(Butoxymethyl)biphenyl-4-carboxylate (2e). To a solution of 0.5 mmol of **1e** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 60 °C. The reaction was monitored by TLC until completion (12 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 30/1) of the reaction mixture afforded 130 mg of **2e**: yield 83%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06−8.04 (d, J = 8.0 Hz, 1H), 7.97−7.96 (m, 1H), 7.69−7.66 (m, 2H), 7.58−7.56 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1H), 7.51−7.47 (m, 2H), 7.43−7.39 (m, 1H), 4.99 (s, 2H), 4.43−4.38 (q, J = 7.2 Hz, 2H), 3.64−3.61 (t, J = 6.6 Hz, 2H), 1.73−1.66 (m, 2H), 1.50−1.42 (m, 5H), 0.99−0.96 (t, J = 7.4 Hz, 3H); ^{13}C NMR($CDCl_3$, 100 MHz) δ 166.9, 144.7, 141.8, 140.2, 131.0, 128.8, 127.9, 127.2, 126.9, 126.0, 125.2, 70.8, 70.6, 60.7, 31.8, 19.4, 14.2, 13.9; IR (neat, cm^{-1}) 2958, 1711, 1254, 1079, 755; HRMS calcd for $C_{20}H_{24}O_3$ 312.1725, found 312.1717.

4-Phenyl-2-(*p*-tolyloxymethyl)biphenyl (2f). To a solution of 0.5 mmol of **1f** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at reflux. The reaction was monitored by TLC until completion (24 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 60/1) of the reaction mixture afforded 97 mg of **2f**: yield 55%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.65−7.61 (m, 3H), 7.46−7.38 (m, 7H), 7.36−7.33 (m, 2H), 7.05−7.03 (d, J = 8.0 Hz, 2H), 6.80−6.78 (d, J = 8.4 Hz, 2H), 4.96 (s, 2H), 2.26(s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.5, 140.8, 140.6, 140.5, 140.2, 134.7, 130.6, 130.1, 129.8, 129.2, 128.8, 128.3, 128.2, 127.4, 127.3, 127.2, 126.7, 114.8, 68.3, 20.4; IR (neat, cm^{-1}) 3029, 2923, 1509, 1233, 697; HRMS calcd for $C_{26}H_{22}O$ 350.1671, found 350.1676.

1-(3-(*p*-Tolyloxymethyl)biphenyl-4-yl)ethanone (2g). To a solution of 0.5 mmol of **1g** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 50 °C. The reaction was monitored by TLC until completion (6 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 15/1) of the reaction mixture afforded 111 mg of **2g**: yield 70%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.95−7.93 (d, J = 8.0 Hz, 1H), 7.66−7.62 (t, J = 8.4 Hz, 3H), 7.50−7.47 (t, J = 7.6 Hz, 2H), 7.43−7.40 (m, 1H), 7.13−7.11 (d, J = 8.4 Hz, 2H), 6.97−6.95 (d, J = 8.4 Hz, 2H), 5.49 (s, 2H), 2.68 (s, 3H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 200.4, 156.6, 145.0, 139.9, 139.8, 133.9, 130.7, 130.2, 129.9, 128.9, 128.2, 127.3, 126.2, 125.5, 114.8, 68.6, 28.8, 20.5; IR (neat, cm^{-1}) 2923, 1665, 1508, 1245, 768; HRMS calcd for $C_{22}H_{20}O_2$ 316.1463, found 316.1466.

Phenyl(3-(*p*-tolyloxymethyl)biphenyl-4-yl)methanone (2h). To a solution of 0.5 mmol of **1h** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 50 °C. The reaction was monitored by TLC until completion (6 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 20/1) of the reaction mixture afforded 129 mg of **2h**: yield 68%; ^{1}H NMR(400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.87−7.86 (d, J = 7.2 Hz, 2H), 7.68−7.66 (d, J = 7.2 Hz, 2H), 7.62−7.59 (m, 2H), 7.53−7.46 (m, 5H), 7.43−7.39 (m, 1H), 7.04−7.01 (d, J = 8.4 Hz, 2H), 6.77−6.75 (d, J = 8.4 Hz, 2H), 5.28 (s, 2H), 2.26 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 197.5, 156.4, 143.7, 140.1, 138.2, 137.8, 135.9, 133.1, 130.2, 130.2, 129.8, 128.9, 128.4, 128.0, 127.3, 127.1, 125.6, 114.7, 67.8, 20.5; IR (neat, cm^{-1}) 2924, 1647, 1510, 1239, 698; HRMS calcd for $C_{27}H_{22}O_2$ 378.1620, found 378.1629.

1-(3-(*p*-Tolyloxymethyl)naphthalen-2-yl)ethanone (2i). To a solution of 0.5 mmol of **1i** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at reflux. The reaction was monitored by TLC until completion (24 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 15/1) of the reaction mixture afforded 80 mg of **2i**: yield 55%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 8.18 (s, 1H), 7.94−7.92 (d, J = 7.6 Hz, 1H), 7.88−7.86 (d, J = 8.0 Hz, 1H), 7.62−7.53 (m, 2H), 7.11−7.09 (d, J = 8.4 Hz, 2H), 6.96−6.94 (d, J = 8.4 Hz, 2H), 5.53 (s, 2H), 2.76 (s, 3H), 2.30 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 200.8, 156.7, 134.8, 134.6, 134.0, 131.6, 131.5, 130.2, 130.0, 128.7, 128.6, 127.9, 126.9, 126.8, 114.9, 68.8, 28.8, 20.5; IR (neat, cm^{-1}) 2923, 1666, 1509, 1267, 748; HRMS calcd for $C_{20}H_{18}O_2$ 290.1307, found 290.1308.

(3-(Butoxymethyl)biphenyl-4-yl)(phenyl)methanone (2j). To a solution of 0.5 mmol of **1j** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 60 °C. The reaction was monitored by TLC until completion (12 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 30/1) of the reaction mixture afforded 103 mg of **2j**: yield 60%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88−7.85 (m, 2H), 7.82 (b, 1H), 7.68−7.66 (m, 2H), 7.63−7.56 (m, 2H), 7.51−7.45 (m, 5H), 7.43−7.39 (m, 1H), 4.68 (s, 2H), 3.41−3.38 (t, J = 6.6 Hz, 2H), 1.48−1.41 (m, 2H), 1.29−1.22 (m, 2H), 0.84−0.80 (t, J = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 197.7, 143.3, 140.3, 139.3, 137.8, 136.4, 133.0, 130.1, 129.6, 128.9, 128.3, 127.9, 127.3, 127.1, 125.4, 70.8, 70.5, 31.6, 19.2, 13.9; IR (neat, cm^{-1}) 3029, 2927, 1662, 1313, 698; HRMS calcd for $C_{24}H_{24}O_2$ 344.1776, found 344.1782.

1-(3-(Butoxymethyl)biphenyl-4-yl)ethanone (2k). To a solution of 0.5 mmol of **1k** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 60 °C. The reaction was monitored by TLC until completion (12 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 20/1) of the reaction mixture afforded 86 mg of **2k**: yield 61%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.85−7.83 (d, J = 8.0 Hz, 1H), 7.67−7.65 (d, J = 7.6 Hz, 2H), 7.59−7.57 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1H), 7.50−7.47 (t, J = 7.4 Hz, 2H), 7.43−7.39 (t, J = 7.4 Hz, 1H), 4.89 (s, 2H), 3.61−3.58 (t, J = 6.6 Hz, 2H), 2.64 (s, 3H), 1.71−1.64 (m, 2H), 1.48−1.42 (m, 2H), 0.98−0.94 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 200.9, 144.6, 141.0, 140.1, 134.7, 130.2, 128.9, 128.1, 127.3, 126.4, 125.3, 71.0, 31.9, 29.1, 19.5, 14.0; IR (neat, cm^{-1}) 2957, 1675, 1253, 1098, 764; HRMS calcd for $C_{19}H_{22}O_2$ 282.1620, found 282.1625.

1-(4-Isopentyl-2-(*p*-tolyloxymethyl)phenyl)ethanone (2l). To a solution of 0.5 mmol of **1l** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 60 °C. The reaction was monitored by TLC until completion (6 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 25/1) of the reaction

mixture afforded 120 mg of **2l**: yield 77%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81−7.79 (d, J = 7.6 Hz, 1H), 7.67 (s, 1H), 7.23−7.21 (d, J = 8.0, 1H), 7.12−7.10 (d, J = 8.4 Hz, 2H), 6.95−6.93 (d, J = 8.4 Hz, 2H), 5.43 (s, 2H), 2.72−2.68 (t, J = 7.6 Hz, 2H), 2.63 (s, 3H), 2.32 (s, 3H), 1.61−1.51 (m, 3H), 0.96−0.95 (d, J = 6.4 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 200.5, 156.7, 148.3, 139.3, 132.8, 130.5, 130.1, 129.9, 127.6, 126.9, 114.9, 68.7, 40.3, 34.0, 28.8, 27.7, 22.5, 20.5; IR (neat, cm^{-1}) 2955, 1675, 1510, 1240, 813; HRMS calcd for $C_{21}H_{26}O_2$ 310.1933, found 310.1926.

(4-Isopentyl-2-(*p*-tolyloxymethyl)phenyl)(phenyl)methanone (2m). To a solution of 0.5 mmol of **1m** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 40 °C. The reaction was monitored by TLC until completion (6 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 40/1) of the reaction mixture afforded 103 mg of **2m**: yield 55%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83−7.81 (d, J = 7.6 Hz, 2H), 7.61−7.56 (m, 2H), 7.48−7.44 (t, J = 7.4 Hz, 2H), 7.38−7.36 (d, J = 8.0 Hz, 1H), 7.21−7.19 (d, J = 7.6 Hz, 1H), 7.04−7.02 (d, J = 8.4 Hz, 2H), 6.76−6.74 (d, J = 8.8 Hz, 2H), 5.22 (s, 2H), 2.74−7.70 (t, J = 7.8 Hz, 2H), 2.27 (s, 3H), 1.65−1.54 (m, 3H), 0.98−0.97 (d, J = 6.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 197.8, 156.4, 146.6, 138.0, 137.7, 134.5, 132.9, 130.1, 129.9, 129.8, 128.4, 128.3, 126.8, 114.7, 67.9, 40.5, 33.9, 27.7, 22.5, 20.5; IR (neat, cm^{-1}) 2955, 1659, 1510, 1237, 702; HRMS calcd for $C_{26}H_{28}O_2$ 372.2089, found 372.2092.

(Biphenyl-3-ylmethyl)(phenyl)sulfane (4a). To a solution of 0.5 mmol of **3a** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 50 °C. The reaction was monitored by TLC until completion (6 h). After evaporation, chromatography on silica gel (hexane) of the reaction mixture afforded 113 mg of **4a**: yield 82%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57−7.55 (d, J = 8.0 Hz, 2H), 7.51−7.48 (m, 2H), 7.46−7.43 (t, J = 7.4 Hz, 2H), 7.40−7.34 (m, 4H), 7.31−7.27 (m, 3H), 7.24−7.20 (m, 1H), 4.19 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 141.7, 141.2, 138.3, 136.6, 130.4, 129.2, 129.2, 129.0, 128.0, 127.6, 127.4, 126.8, 126.3, 39.5; MS (m/z) 276 (M, 38), 167 (M − 109, 100); IR (neat, cm^{-1}) 3057, 2922, 1579, 1477, 692; HRMS calcd for $C_{19}H_{16}S$ 276.0973, found 276.0965.

((4-Methylnaphthalen-2-yl)methyl)(phenyl)sulfane (4b). To a solution of 0.5 mmol of **3b** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 50 °C. The reaction was monitored by TLC until completion (6 h). After evaporation, chromatography on silica gel (hexane) of the reaction mixture afforded 106 mg of **4b**: yield 80%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03−8.01 (m, 1H), 7.83−7.81 (m, 1H), 7.62 (s, 1H), 7.57−7.51 (m, 2H), 7.43−7.39 (m, 3H), 7.33−7.29 (m, 2H), 7.26−7.22 (m, 1H), 4.30 (s, 2H), 2.73 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.6, 134.8, 134.4, 133.5, 131.9, 129.8, 128.9, 128.4, 127.7, 126.4, 126.3, 125.9, 125.7, 124.0, 39.4, 19.3; MS (m/z) 264 (M, 82), 155 (M − 109, 100); IR (neat, cm^{-1}) 3056, 2920, 1691, 1477, 738; HRMS calcd for $C_{18}H_{16}S$ 264.0973, found 264.0964.

(Naphthalen-2-ylmethyl)(phenyl)sulfane (4c). To a solution of 0.5 mmol of **3c** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 50 °C. The reaction was monitored by TLC until completion (6 h). After evaporation, chromatography on silica gel (hexane) of the reaction mixture afforded 100 mg of **4c**: yield 80%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85−7.81 (m, 2H), 7.79−7.77 (m, 1H), 7.71 (s, 1H), 7.51−7.47 (m, 3H), 7.37−7.36 (m, 2H), 7.29−7.25 (m, 2H), 7.22−7.19 (m, 1H), 4.30 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.3, 134.9, 133.3, 132.6, 130.0, 128.8, 128.3, 127.7, 127.6, 127.4, 127.0, 126.4, 126.1, 125.8, 39.4; MS (m/z) 250 (M, 35), 141 (M − 109, 100); IR (neat, cm^{-1}) 3054, 2921, 1579, 1477, 754; HRMS calcd for $C_{17}H_{14}S$ 250.0816, found 250.0818.

((3,4-Dimethylnaphthalen-2-yl)methyl)(phenyl)sulfane (4d). To a solution of 0.5 mmol of **3d** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 50 °C. The reaction was monitored by TLC until completion (12 h). After evaporation, chromatography on silica gel (hexane) of the reaction mixture afforded 88 mg of **4d**: yield 63%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03−8.01 (d, J = 8.0 Hz, 1H), 7.70−7.68 (d, J = 8.0 Hz, 1H), 7.51−7.46 (m, 2H), 7.42−7.36 (m, 3H), 7.30−7.25 (m, 2H), 7.23−7.19 (m, 1H), 4.30 (s, 2H), 2.65 (s, 3H), 2.55 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.0, 133.7, 132.7, 132.6, 132.5, 132.0, 130.5, 129.1, 128.4, 127.3, 126.7, 126.0, 125.1, 124.1, 39.4, 16.3, 15.3; MS (m/z) 278 (M, 25), 169 (M − 109, 100); IR (neat, cm^{-1}) 3050, 2921, 1580, 1477, 735; HRMS calcd for $C_{19}H_{18}S$ 278.1129, found 278.1126.

(Biphenyl-3-ylmethyl)(butyl)sulfane (4e). To a solution of 0.5 mmol of **3e** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 50 °C. The reaction was monitored by TLC until completion (6 h). After evaporation, chromatography on silica gel (hexane) of the reaction mixture afforded 106 mg of **4e**: yield 83%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62−7.60 (m, 2H), 7.56 (s, 1H), 7.49−7.43 (m, 3H), 7.41−7.34 (m, 2H), 7.32−7.30 (m, 1H), 3.78 (s, 2H), 2.49−2.45 (t, J = 7.6 Hz, 2H), 1.60−1.54 (m, 2H), 1.42−1.37 (m, 2H), 0.92−0.88 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 141.7, 141.3, 139.5, 129.1, 129.0, 128.0, 127.9, 127.6, 127.4, 126.0, 36.7, 31.6, 31.5, 22.2, 13.9; MS (m/z) 256 (M, 80), 167 (M − 89, 100); IR (neat, cm^{-1}) 3031, 2924, 1699, 1456, 755, 698; HRMS calcd for $C_{17}H_{20}S$ 256.1286, found 256.1280.

(1-(4-Methylnaphthalen-2-yl)ethyl)(phenyl)sulfane (4f). To a solution of 0.5 mmol of **3f** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 50 °C. The reaction was monitored by TLC until completion (12 h). After evaporation, chromatography on silica gel (hexane) of the reaction mixture afforded 104 mg of **4f**: yield 75%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01−7.99 (m, 1H), 7.81−7.79 (m, 1H), 7.56−7.55 (m, 1H), 7.54−7.48 (m, 2H), 7.44 (s, 1H), 7.39−7.36 (m, 2H), 7.27−7.22 (m, 3H), 4.55−4.49 (q, J = 7.1 Hz, 1H), 2.73 (s, 3H), 1.77−1.76 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 140.4, 135.5, 135.0, 133.7, 132.7, 132.3, 129.0, 128.7, 127.4, 126.6, 126.1, 125.9, 124.5, 124.2, 48.5, 22.6, 19.7; MS (m/z) 278 (M, 20), 169 (M − 109, 100); IR (neat, cm^{-1}) 3056, 2968, 1601, 1441, 744; HRMS calcd for $C_{19}H_{18}S$ 278.1129, found 278.1128.

Phenyl((3-phenylnaphthalen-2-yl)methyl)sulfane (4g). To a solution of 0.5 mmol of **3g** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 50 °C. The reaction was monitored by TLC until completion (6 h). After evaporation, chromatography on silica gel (hexane) of the reaction mixture afforded 114 mg of **4g**: yield 70%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.85−7.83 (m, 1H), 7.82−7.79 (m, 1H), 7.76 (s, 1H), 7.53−7.43 (m, 7H), 7.24−7.23 (m, 4H), 7.22−7.19 (m, 1H), 4.24 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 141.1, 140.7, 136.8, 133.2, 132.9, 132.8, 130.5, 129.8, 129.4, 129.2, 129.0, 128.5, 127.9, 127.7, 127.5, 126.7, 126.5, 126.4, 37.8; MS (m/z) 326 (M, 15), 217 (M − 109, 66); IR (neat, cm^{-1}) 3054, 2923, 1699, 1480, 1439, 739, 696; HRMS calcd for $C_{23}H_{18}S$ 326.1129, found 326.1131.

Butyl((4-phenyllbiphenyl-2-yl)methyl)sulfane (4h). To a solution of 0.5 mmol of **3h** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 50 °C. The reaction was monitored by TLC until completion (6 h). After evaporation, chromatography on silica gel (hexane) of the reaction mixture afforded 120 mg of **4h**: yield 72%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.70−7.69 (m, 2H), 7.58−7.55 (m, 1H), 7.52−7.46 (m, 6H), 7.44−7.36 (m, 3H), 3.79 (s, 2H), 2.48−2.44 (t, J = 7.2 Hz, 2H), 1.49−1.46 (m, 2H), 1.39−1.34 (m, 2H), 0.91−0.87 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 141.3, 141.1, 140.9, 140.6, 136.6, 130.9, 129.7, 129.1, 129.0, 128.4, 127.6, 127.4, 127.4, 125.8, 34.3, 32.3, 31.7, 22.2, 13.9; MS (m/z) 332 (M, 10), 243 (M − 89, 40); IR (neat, cm^{-1}) 3026, 2924, 1601, 1476, 697; HRMS calcd for $C_{23}H_{24}S$ 332.1599, found 332.1602.

Butyl(naphthalen-2-ylmethyl)sulfane (4i). To a solution of 0.5 mmol of **3i** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 60 °C. The reaction was monitored by TLC until completion (12 h). After evaporation, chromatography on silica gel

(hexane) of the reaction mixture afforded 100 mg of **4i**: yield 87%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86−7.82 (m, 2H), 7.74 (s, 1H), 7.55−7.47 (m, 3H), 3.90 (s, 2H), 2.49−2.45 (t, J = 7.6 Hz, 2H), 1.64−1.57 (m, 2H), 1.46−1.39 (m, 2H), 0.94−0.90 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.3, 133.6, 132.8, 128.6, 127.9, 127.9, 127.4, 126.4, 126.0, 36.8, 31.6, 31.3, 22.3, 13.9; MS (m/z) 230 (M, 95), 141 (M − 89, 100); IR (neat, cm^{-1}) 3053, 2925, 1632, 1459, 748; HRMS calcd for $C_{15}H_{18}S$ 230.1129, found 230.1133.

((3-Methylnaphthalen-2-yl)methyl)(phenyl)sulfane (4j). To a solution of 0.5 mmol of **3j** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 50 °C. The reaction was monitored by TLC until completion (6 h). After evaporation, chromatography on silica gel (hexane) of the reaction mixture afforded 106 mg of **4j**: yield 80%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78−7.77 (d, J = 7.2 Hz, 1H), 7.73−7.71 (d, J = 7.2 Hz, 1H), 7.68 (s, 1H), 7.61 (s, 1H), 7.47−7.37 (m, 4H), 7.32−7.24 (m, 3H), 4.29 (s, 2H), 2.62 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.7, 135.0, 134.1, 133.3, 132.3, 130.8, 129.1, 128.8, 128.7, 127.6, 127.1, 126.9, 126.1, 125.5, 38.2, 19.9; MS (m/z) 264 (M, 35), 155 (M − 109, 100); IR (neat, cm^{-1}) 3026, 2922, 1698, 1480, 737; HRMS calcd for $C_{18}H_{16}S$ 264.0973, found 264.0979.

Butyl((4-methylnaphthalen-2-yl)methyl)sulfane (4k). To a solution of 0.5 mmol of **3k** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 60 °C. The reaction was monitored by TLC until completion (12 h). After evaporation, chromatography on silica gel (hexane) of the reaction mixture afforded 104 mg of **4k**: yield 85%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98−7.95 (m, 1H), 7.81−7.79 (m, 1H), 7.55 (s, 1H), 7.50−7.47 (m, 2H), 7.34 (s, 1H), 3.83 (s, 2H), 2.69 (s, 3H), 2.45−2.41 (t, J = 7.4 Hz, 2H), 1.59−1.53 (m, 2H), 1.41−1.35 (m, 2H), 0.90−0.87 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 135.8, 135.1, 133.7, 132.0, 128.5, 128.0, 126.1, 125.9, 125.8, 124.2, 36.8, 31.6, 31.2, 22.3, 19.6, 13.9; MS (m/z) 244 (M, 95), 155 (M − 89, 100); IR (neat, cm^{-1}) 3030, 2926, 1602, 1464, 747; HRMS calcd for $C_{16}H_{20}S$ 244.1286, found 244.1288.

((4-Phenylbiphenyl-2-yl)methyl)(phenyl)sulfane (4l). To a solution of 0.5 mmol of **3l** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 30 °C. The reaction was monitored by TLC until completion (3 h). After evaporation, chromatography on silica gel (hexane) of the reaction mixture afforded 155 mg of **4l**: yield 88%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70−7.69 (m, 1H), 7.63−7.61 (d, J = 7.6 Hz, 2H), 7.60−7.57 (dd, J = 8 Hz, 1H), 7.51−7.47 (m, 6H), 7.44−7.37 (m, 3H), 7.32−7.23 (m, 5H), 4.19 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 141.4, 140.8, 140.8, 140.6, 136.7, 135.3, 131.0, 130.6, 129.6, 129.3, 129.2, 129.1, 128.6, 127.7, 127.6, 127.4, 126.8, 126.2, 37.5; MS (m/z) 352 (M, 15), 243 (M − 109, 62); IR (neat, cm^{-1}) 3056, 2924, 1579, 1476, 694; HRMS calcd for $C_{25}H_{20}S$ 352.1286, found 352.1291.

(1-(4-Phenylbiphenyl-2-yl)ethyl)(phenyl)sulfane (4m). To a solution of 0.5 mmol of **3m** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 30 °C. The reaction was monitored by TLC until completion (3 h). After evaporation, chromatography on silica gel (hexane) of the reaction mixture afforded 154 mg of **4m**: yield 84%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92−7.91 (m, 1H), 7.70−7.68 (m, 2H), 7.54−7.49 (m, 3H), 7.45−7.41 (m, 4H), 7.33−7.31 (m, 2H), 7.27−7.26 (m, 1H), 7.21 (s, 5H), 4.61−4.55 (q, J = 7.1 Hz, 1H), 1.65−1.63 (d, J = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 141.3, 141.1, 141.0, 140.5, 135.4, 133.0, 130.6, 129.6, 129.1, 129.0, 128.8, 128.4, 127.7, 127.5, 127.4, 126.4, 125.8, 44.3, 23.3; MS (m/z) 366 (M, 10), 257 (M − 109, 100); IR (neat, cm^{-1}) 3056, 2922, 1579, 1475, 694; HRMS calcd for $C_{26}H_{22}S$ 366.1442, found 366.1449.

Ethyl 3-((Methyl(phenyl)amino)methyl)biphenyl-4-carboxylate (6a). To a solution of 0.5 mmol of **5a** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 60 °C. The reaction was monitored by TLC until completion (6 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 20/1) of the reaction mixture afforded 135 mg of **6a**: yield 78%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16−8.14 (d, J = 8.0 Hz, 1H), 7.59−7.56 (m, 2H), 7.53−7.51 (m, 2H), 7.44−7.40 (m, 2H), 7.38−7.34 (m, 1H), 7.27−7.23 (t, J = 7.8, 2H), 6.77−6.73 (m, 3H), 5.02 (s, 2H), 4.45−4.40 (q, J = 7.1 Hz, 2H), 3.12 (s, 3H), 1.47−1.44 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.5, 150.0, 145.4, 142.2, 140.4, 132.1, 129.4, 129.1, 128.3, 127.8, 127.5, 126.0, 125.5, 116.8, 112.4, 61.2, 56.6, 39.0, 14.7; IR (neat, cm^{-1}) 2896, 1713, 1506, 1253, 745; HRMS calcd for $C_{23}H_{23}NO_2$ 345.1729, found 345.1735.

***N*-(Biphenyl-3-ylmethyl)-*N*-*p*-tolylacetamide (6b).** To a solution of 0.5 mmol of **5b** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at reflux. The reaction was monitored by TLC until completion (12 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 5/1) of the reaction mixture afforded 144 mg of **6b**: yield 91%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53−7.51 (m, 2H), 7.47−7.45 (d, J = 7.6 Hz, 1H), 7.42−7.38 (m, 3H), 7.35−7.30 (m, 2H), 7.20−7.17 (d, J = 7.6 Hz, 1H), 7.12−7.10 (d, J = 8.0 Hz, 2H), 6.90−6.87 (d, J = 8.4 Hz, 2H), 4.93 (s, 2H), 2.33 (s, 3H), 1.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.6, 141.2, 141.0, 140.3, 138.2, 137.8, 130.2, 128.8, 128.7, 128.0, 127.8, 127.6, 127.3, 127.2, 126.1, 52.9, 22.7, 21.1; IR (neat, cm^{-1}) 3030, 2925, 1653, 1389, 908, 728; HRMS calcd for $C_{22}H_{21}NO$ 315.1623, found 315.1631.

Ethyl 3-((*N*-*p*-Tolylacetamido)methyl)biphenyl-4-carboxylate (6c). To a solution of 0.5 mmol of **5c** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 50 °C. The reaction was monitored by TLC until completion (6 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 5/1) of the reaction mixture afforded 176 mg of **6c**: yield 91%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91−7.89 (d, J = 8.0 Hz, 1H), 7.73 (s, 1H), 7.60−7.58 (d, J = 8.0 Hz, 2H), 7.50−7.43 (m, 3H), 7.39−7.36 (m, 1H), 7.11−7.09 (d, J = 8.0 Hz, 2H), 6.96−6.94 (d, J = 8.0 Hz, 2H), 5.42 (s, 2H), 4.21−4.15 (q, J = 7.1 Hz, 2H), 2.30 (s, 3H), 1.92 (s, 3H), 1.31−1.28 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.9, 167.1, 144.7, 140.6, 140.0, 139.3, 137.7, 131.1, 130.1, 128.9, 128.6, 128.1, 128.1, 127.7, 127.3, 125.5, 60.9, 50.6, 22.7, 21.0, 14.2; IR (neat, cm^{-1}) 2981, 1710, 1655, 1254, 730; HRMS calcd for $C_{25}H_{25}NO_3$: 387.1834, found 387.1839.

***N*-((4-Acetylbiphenyl-3-yl)methyl)-*N*-*p*-tolylacetamide (6d).** To a solution of 0.5 mmol of **5d** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 40 °C. The reaction was monitored by TLC until completion (6 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 3/1) of the reaction mixture afforded 170 mg of **6d**: yield 95%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80−7.79 (m, 1H), 7.73−7.71 (d, J = 8.0 Hz, 1H), 7.64−7.62 (m, 2H), 7.55−7.53 (dd, J = 8.0 Hz, 1H), 7.51−7.47 (m, 2H), 7.43−7.40 (m, 1H), 7.15−7.13 (d, J = 8.0 Hz, 2H), 7.00−6.98 (d, J = 8.0 Hz, 2H), 5.34 (s, 2H), 2.42 (s, 3H), 2.34 (s, 3H), 1.95 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 201.1, 170.8, 144.4, 140.7, 139.9, 138.4, 137.7, 136.3, 130.2, 129.9, 129.0, 128.2, 128.0, 127.7, 127.3, 125.4, 50.6, 29.2, 22.7, 21.0; IR (neat, cm^{-1}) 3032, 1654, 1512, 1251, 727; HRMS calcd for $C_{24}H_{23}NO_2$ 357.1729, found 357.1724.

***N*-((4-Benzoylbiphenyl-3-yl)methyl)-*N*-*p*-tolylacetamide (6e).** To a solution of 0.5 mmol of **5e** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 40 °C. The reaction was monitored by TLC until completion (6 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 3/1) of the reaction mixture afforded 189 mg of **6e**: yield 90%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.64−7.62 (d, J = 7.2 Hz, 2H), 7.54−7.45 (m, 6H), 7.41−7.39 (d, J = 7.2 Hz, 1H), 7.36−7.32 (t, J = 7.8 Hz, 2H), 7.30−7.28 (d, J = 8.4 Hz, 1H), 6.95−6.93 (d, J = 8.4, Hz, 2H), 6.81−6.79 (d, J = 8.4 Hz, 2H), 5.18 (s, 2H), 2.20 (s, 3H), 1.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 197.3, 170.7, 143.5, 140.0, 139.8, 138.0, 137.6, 137.5, 137.2, 132.9, 130.2, 130.1, 129.6, 129.0, 128.8, 128.1, 128.0, 127.7, 127.3, 125.0, 48.9, 22.6, 21.0; IR (neat, cm^{-1}) 3032, 1654, 1282, 909, 728; HRMS calcd for $C_{29}H_{25}NO_2$ 419.1885, found 419.1882.

***N*-((4-Methylbiphenyl-2-yl)methyl)-*N*-*p*-tolylacetamide (6f).** To a solution of 0.5 mmol of **5f** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 60 °C. The reaction was monitored by TLC until completion (6 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 5/1) of the reaction mixture afforded 180 mg of **6f**: yield 92%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81−7.80 (m, 1H), 7.68−7.66 (d, J = 7.6 Hz, 2H), 7.53−7.46 (m, 3H), 7.40−7.36 (t, J = 7.4 Hz, 1H), 7.29−7.27 (m, 3H), 7.21−7.19 (d, J = 8.0 Hz, 1H), 7.05−7.03 (d, J = 8.0 Hz, 2H), 6.94−6.91 (m, 2H), 6.76−6.74 (d, J = 8.4 Hz, 2H), 4.99 (s, 2H), 2.33 (s, 3H), 1.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.7, 141.1, 140.7, 140.4, 140.3, 140.0, 137.6, 135.5, 130.3, 130.0, 129.2, 128.9, 127.9, 127.8, 127.6, 127.4, 127.2, 126.9, 125.7, 49.3, 22.6, 21.1; IR (neat, cm^{-1}) 3029, 1652, 1477, 1388, 729; HRMS calcd for $C_{28}H_{25}NO$ 391.1936, found 391.1947.

1-(3-((Methyl(phenyl)amino)methyl)biphenyl-4-yl)-ethanone (6g). To a solution of 0.5 mmol of **5g** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 50 °C. The reaction was monitored by TLC until completion (6 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 10/1) of the reaction mixture afforded 92 mg of **6g**: yield 58%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96−7.94 (d, J = 8.0 Hz, 1H), 7.63−7.59 (m, 2H), 7.53−7.52 (d, J = 6.8 Hz, 2H), 7.45−7.41 (t, J = 7.4 Hz, 2H), 7.39−7.36 (m, 1H), 7.26−7.22 (m, 2H), 6.76−6.72 (m, 3H), 4.94 (s, 2H), 3.09 (s, 3H), 2.68 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 200.9, 149.7, 144.9, 141.4, 139.9, 134.9, 131.1, 129.1, 128.9, 128.1, 127.2, 126.1, 125.1, 116.6, 112.2, 56.6, 38.8, 29.2; IR (neat, cm^{-1}) 2921, 1665, 1506, 1251, 689; HRMS calcd for $C_{22}H_{21}NO$ 315.1623, found 315.1624.

***N*-(2-Acetyl-5-isopentylbenzyl)-*N*-*p*-tolylacetamide (6h).** To a solution of 0.5 mmol of **5h** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 50 °C. The reaction was monitored by TLC until completion (3 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 3/1) of the reaction mixture afforded 169 mg of **6h**: yield 96%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55−7.53 (d, J = 7.2 Hz, 1H), 7.34 (s, 1H), 7.11−7.09 (d, J = 8.0 Hz, 3H), 6.93−6.91 (d, J = 8.4 Hz, 2H), 5.25 (s, 2H), 2.67−2.63 (t, J = 8.0 Hz, 2H), 2.34 (s, 3H), 2.31 (s, 3H), 1.93 (s, 3H), 1.59−1.47 (m, 3H), 0.95−0.93 (d, J = 6.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 201.1, 170.7, 147.4, 140.6, 137.8, 137.6, 135.1, 130.1, 129.6, 129.4, 127.7, 126.7, 50.4, 40.3, 33.8, 29.0, 27.6, 22.7, 22.5, 21.0; IR (neat, cm^{-1}) 2971, 1673, 1648, 1384, 1052; HRMS calcd for $C_{23}H_{29}NO_2$ 351.2198, found 351.2191.

***N*-(2-Benzoyl-5-isopentylbenzyl)-*N*-*p*-tolylacetamide (6i).** To a solution of 0.5 mmol of **5i** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 50 °C. The reaction was monitored by TLC until completion (3 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 4/1) of the reaction mixture afforded 151 mg of **6i**. yield 73%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53−7.47 (m, 3H), 7.43 (s, 1H), 7.34−7.31 (t, J = 7.6 Hz, 2H), 7.14−7.12 (d, J = 8.0 Hz, 1H), 7.08−7.06 (d, J = 7.6 Hz, 1H), 6.94−6.92 (d, J = 8.0 Hz, 2H), 6.78−6.76 (d, J = 8.0 Hz, 2H), 5.12 (s, 2H), 2.69−2.65 (t, J = 7.8 Hz, 2H), 2.20 (s, 3H), 1.87 (s, 3H), 1.62−1.50 (m, 3H), 0.97−0.96 (d, J = 6.8 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 197.5, 170.6, 146.3, 139.7, 137.7, 137.5, 135.9, 132.6, 130.2, 130.2, 130.0, 129.3, 128.0, 127.7, 126.3, 48.6, 40.5, 33.8, 27.7, 22.6, 22.6, 21.0; IR (neat, cm^{-1}) 2955, 1657, 1604, 1270, 705; HRMS calcd for $C_{28}H_{31}NO_2$ 413.2355, found 413.2343.

Ethyl 3-((*tert*-Butoxycarbonyl(4-chlorophenyl)amino)methyl)biphenyl-4-carboxylate (6j). To a solution of 0.5 mmol of **5j** in 3 mL of acetonitrile was charged 1 mmol of DBU under a N_2 atmosphere at 40 °C. The reaction was monitored by TLC until completion (3 h). After evaporation, chromatography on silica gel (hexane/ethyl acetate 15/1) of the reaction mixture afforded 205 mg of **6j**: yield 88%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06−8.04 (d, J = 8.4 Hz, 1H), 7.70 (s, 1H), 7.60−7.54 (m, 3H), 7.47−7.44 (t, J = 7.2 Hz, 2H), 7.41−7.37 (t, J = 7.4 Hz, 1H), 7.25−7.19 (m, 4H), 5.34 (s, 2H), 4.36−4.31 (q, J = 7.2 Hz, 2H), 1.41−1.37 (m, 12H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 166.9, 154.5, 145.0, 141.6, 139.9, 131.6, 130.9, 129.0, 128.7, 128.2, 128.2, 127.3, 127.2, 126.8, 125.7, 125.3, 81.1, 61.0, 52.6, 28.2, 14.3; IR (neat, cm^{-1}) 2977, 1701, 1606, 1251, 756; HRMS calcd for $C_{27}H_{28}ClNO_4$ 465.1707, found 465.1713.

4-Methyl-2-vinylbiphenyl (7). To a solution of $NaIO_4$ (1.1 mmol) in water (6 mL) was added **4m** (1.0 mmol) in 12 mL of MeOH, followed by a heating at 40 °C for 18 h. After evaporation to remove MeOH, the reaction rescue (product, $NaIO_3$, and water) was diluted with 30 mL of water and extracted with EtOAc. The extracts were washed with water and dried over anhydrous Na_2SO_4. Evaporation of the EtOAc afforded directly the crude product for the next step. The solution of the crude product in 5 mL of toluene was heated at 110 °C for 3 h. Evaporation of toluene and chromatography on silica gel (eluent: petroleum ether) of the reaction mixture afforded the desired product **7** (159 mg, 62%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91−7.90 (m, 1H), 7.72−7.70 (d, J = 7.6 Hz, 2H), 7.62−7.59 (dd, J = 7.6 Hz, 1H), 7.53−7.48 (m, 3H), 7.46−7.39 (m, 6H), 6.86−6.79 (m, 1H), 5.85−5.80 (m, 1H), 5.30−5.27 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 140.9, 140.5, 140.4, 139.8, 136.1, 136.0, 130.6, 129.8, 128.8, 128.1, 127.4, 127.2, 127.1, 126.5, 124.6, 115.0; IR (neat, cm^{-1}) 3056, 1576, 1473, 911, 696; HRMS calcd for $C_{20}H_{16}$ 256.1252, found 256.1255.

2-(4-Chlorophenyl)-5-phenylisoindolin-1-one (8). A 20-mL tube was charged **6j** (0.5 mmol) and a saturated HCl/MeOH solution (5 mL). The tube was sealed and placed in an oil bath (110 °C) for 30 h at which time it was opened. After evaporation, the reaction mixture was washed with water (2 × 10 mL) to afford **8** (153 mg, 96%): mp 216−218 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98−7.96 (d, J = 7.2 Hz, 1H), 7.87−7.85 (d, J = 8.8 Hz, 2H), 7.74−7.71 (m, 2H), 7.65−7.63 (d, J = 7.6 Hz, 2H), 7.52−7.48 (t, J = 7.4 Hz, 2H), 7.44−7.38 (m, 3H), 4.92 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 163.8, 145.7, 140.6, 140.2, 138.1, 132.1, 129.6, 129.2, 129.0, 128.3, 127.9, 127.5, 124.5, 121.3, 120.5, 50.668; IR (neat, cm^{-1}) 2922, 1679, 1489, 1376, 692; HRMS calcd for $C_{20}H_{14}ClNO$ 319.0764, found 319.0766.

■ ASSOCIATED CONTENT

Supporting Information. Proton and carbon NMR spectra of products and experimental procedures for the synthesis of the substrates. This material is available free of charge via the Internet at http://pubs.acs.org.

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