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Cyclopropane Cycloaddition

$Sc(OTf)_3$-Catalyzed Diastereoselective Formal [3+2] Cycloaddition Reactions of Alkynylcyclopropane Ketones with Electron-Rich Aromatic Aldehydes To Yield 2,5-*trans*-Tetrahydrofurans

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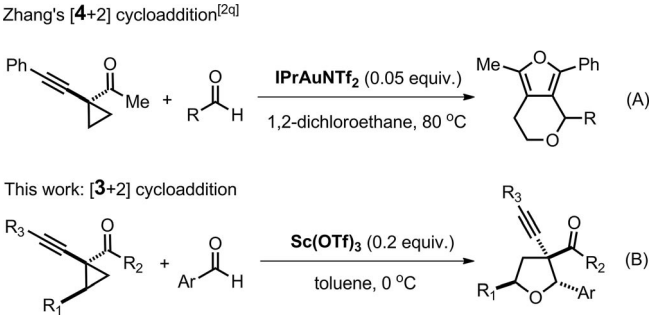
Abstract: In contast to the general [4+2] cycloaddition reactions of alkynylcyclopropane ketones reported in the literature, we report herein a $Sc(OTf)_3$-catalyzed formal intermolecular [3+2] cycloaddition reaction of alkynylcyclopropane ketones with electron-rich aromatic aldehydes. 2,3,3,5-Tetrasubstituted tetrahydrofurans were obtained by this method, and the tetrahydrofuran skeleton was diastereoselectively constructed with a 2,5-*trans* configuration. This is also quite different to the 2,5-*cis* configuration usually obtained from typical [3+2] cycloaddition reactions of most donor–acceptor cyclopropanes. Additionally, the cycloadducts were subjected to a domino carbopalladation/C–H activation/C–C bond-formation process for the highly efficient construction of polycyclic skeletons.

Introduction

Various types of cycloaddition reactions of donor–acceptor cyclopropanes have been developed for the construction of structurally diverse cyclic skeletons and they have been widely applied in organic synthesis.[1] Since being introduced by Zhang and Schmalz,[2j] the alkynylcyclopropane (ACP) ketone has recently proved to be a versatile building block in organic synthesis.[2] As a novel type of donor–acceptor cyclopropane, the ACP ketone has also attracted attention in recent years for its novel cycloaddition reactions.[2k–2q] Zhang et al. reported a novel $IPrAuNTf_2$-cataylzed intermolecular [4+2] cycloaddition of the ACP ketone with carbonyls to afford furan-fused dihydropyrans in which the ACP ketone served as a 1,4-dipole (Scheme 1, A).[2q] In our recent research on the intramolecular cross-cycloaddition reactions of ACP ketones with carbonyls,[2k] we found that under catalysis by $Sc(OTf)_3$ an intermolecular [3+2] cycloaddition took place in which the ACP ketone acted as a 1,3-dipole (Scheme 1, B). Additionally, examples of ACP ketones as C_3 synthons are quite limited. Besides our intramolecular [3+2] example,[2k] the only other report refers to the [3+3] cycloaddition with nitrones reported by Zhang et al.[2n] It was also noted that this cycloaddition stereoselectively afforded the 2,5-*trans*-tetrahydrofuran skeleton.[3] This 2,5-*trans* stereoselectivity is quite different to that observed for the reactions of cyclopropane 1,1-diesters with aldehydes reported by Johnson and co-workers.[4] Few 2,5-*trans*-tetrahydrofurans from the reactions of donor–acceptor cyclopropanes with aldehydes have been described.[5] Therefore we have explored this reaction and we report herein our recent results on the intermolecular [3+2] cycloaddition reactions of ACP ketones.



Scheme 1. Two different types of cycloaddition reactions of ACP ketones with aldehydes.

Results and Discussion

The reaction of ACP ketone **1a** and 3,4-dimethoxybenzaldehyde (**2a**) was initially performed and the results are summarized in Table 1. Several solvents were screened and when the reaction was conducted in 1,2-dichloroethane (DCE) at 40 °C under catalysis by $Sc(OTf)_3$ (0.2 equiv.) a mixture of three diastereoisomers, **3aa**, **4aa**, and **5aa**, was obtained in a ratio of 0.68:0.12:1 (Table 1, entry 1). The 2,5-*cis* isomers (**4aa** and **5aa**) were the major species, similarly to the case of cyclopropane 1,1-dies-

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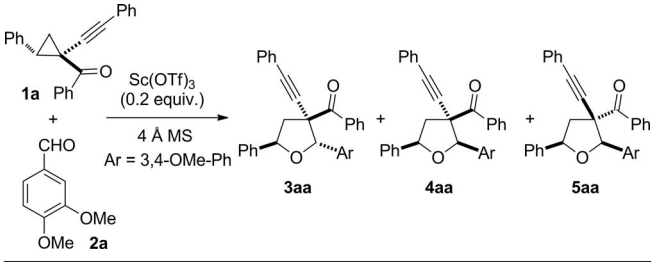
ters.[4] The structures of **3aa** and **4aa** were unambiguously confirmed by NMR, HRMS, and X-ray crystal analysis.[6] To our surprise, when the solvent was switched to toluene, the diastereoselectivity of the three isomers changed to 1:0.17:0.17, with **3aa** as the major isomer (Table 1, entry 3). We found that the reaction also proceeded smoothly at 0 °C with a better diastereoselectivity, with only a trace of **5aa** observed (Table 1, entry 8).[7] This condition was selected as optimal for further research. At a lower temperature (–20 °C), the reaction gave a mixture of **3aa** and **4aa** (1:1.23), the latter being the major isomer (Table 1, entry 9). These results (Table 1, entries 3, 8, and 9) suggest that **4aa** is a kinetic product and **3aa** and **5aa** are thermodynamic products.

Table 1. Optimization of reaction conditions.[a]



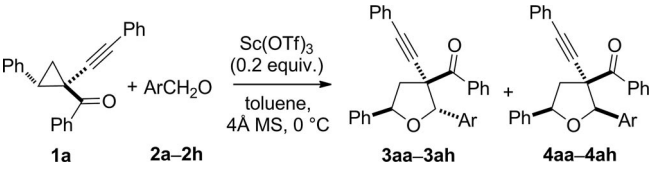
Entry	Solvent	*T* [°C]	**3aa**[b]	**4aa**[b]	**5aa**[b]
1	DCE	40	0.68	0.12	1
2	DCM	40	0.93	0.14	1
3	toluene	40	1	0.17	0.17
4	THF[c]	40	–	–	–
5	CH_3CN[c]	40	–	–	–
6	CH_3NO_2[c]	40	–	–	–
7	benzene	40	1	0.15	0.71
8	toluene[d]	0	1	0.17	trace
9	toluene[e]	–20	1	1.23	0

[a] Reagents and conditions: **1a** (0.06 mmol), **2a** (1.5 equiv.), $Sc(OTf)_3$ (0.2 equiv.), solvent (2 mL), 4 Å molecular sieves, 2 h. [b] Ratio was determined by ^1H NMR analysis of the reaction mixture. [c] No reaction. [d] 5.0 equiv. of **2a** was added and the reaction mixture was stirred for 4 h. [e] 0.4 equiv. of $Sc(OTf)_3$ and 10.0 equiv. of **2a** were added and the reaction mixture was stirred overnight; about 60 % of **1a** was consumed.

The scope of the aldehydes was explored next and the results are summarized in Table 2. Several alkoxybenzaldehydes reacted smoothly and gave good-to-excellent yields and diastereoselectivities (Table 2, entries 1–6). The reaction of thiophene-2-carbaldehyde (**2g**) also worked well at room temperature (Table 2, entry 7). However, the reaction of 4-(dimethylamino)benzaldehyde (**2h**) failed and gave a yellow precipitate instead of the desired product (Table 2, entry 8). We also tried several other types of aldehydes/ketones. Unfortunately, benzaldehyde, electron-deficient aromatic aldehydes, and aliphatic aldehydes/ketones were not suitable for this reaction.

We then screened the scope of ACP ketones **1** (Table 3). When the donor group R^1 on the cyclopropane ring was phenyl, electron-deficient 4-ClPh, or weakly electron-rich 4-*t*BuPh, the reactions proceeded smoothly (Table 3, entries 1–3). However, when R^1 was the strongly electron-rich 4-MeOPh, a rearrangement cyclization occurred to give dihydrofuran product **7** instead of the cycloaddition product (Table 3, entry 4). This might be due to the activated C–C bond in the cyclopropane ring.

Table 2. Scope of aldehydes in the $Sc(OTf)_3$-catalyzed [3+2] cycloaddition of **1a**.[a]



1a **2a–2h** **3aa–3ah** **4aa–4ah**

Entry	**2** (equiv.)	Ar	Yield [%][b]	*dr*[c] (**3**/**4**)
1	**2a** (5.0)	3,4-$(OMe)_2$Ph	82	5.5:1
2	**2b** (5.0)	3,4-OCH_2OPh	79	7.2:1
3	**2c** (5.0)	4-BnOPh	90	5.9:1
4	**2d** (10.0)	4-MeOPh[d,e]	95	5.9:1
5	**2e** (5.0)	4-EtOPh[d]	93	5.0:1
6	**2f** (10.0)	2-MeOPh[d]	75	3.3:1
7	**2g** (10.0)	2-thienyl[d,f]	88	5.0:1
8	**2h** (5.0)	4-Me_2NPh	n.r.[g]	–

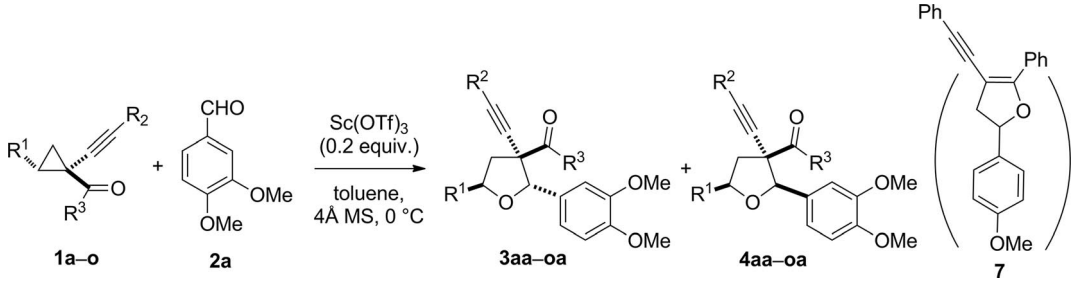
[a] Reagents and conditions: **1a** (0.3 mmol), **2**, molecular sieves (4 Å, 100 mg), toluene (10 mL), stirring overnight, 0 °C. [b] Isolated combined yield. [c] Ratio determined by ^1H NMR analysis of the reaction mixture. [d] 0.3 equiv. of $Sc(OTf)_3$ was used. [e] 10 equiv. of **2** was used. [f] Reaction was carried out at ambient temperature (20–25 °C). [g] n.r.: no reaction, a yellow precipitate appeared instead.

Such a ring-opening rearrangement has often been observed in cyclopropane ketones.[8] When R^1 was the weak carbocation-stabilizing group *n*-propyl (substrate **1e**), the reaction was very sluggish and gave a complex mixture of products when the temperature was increased (Table 3, entry 5). The electronic nature of substituent R^2 on the alkyne moiety seemed to have less influence on the reactivity (Table 3, entries 6–10). There was no distinct difference between two substrates with an electron-poor (**1f**) or electron-rich (**1g**) phenyl group (Table 3, entries 6 and 7). Trimethylsilyl-substituted (**1h**) and unsubstituted (**1i**) substrates also worked well under catalysis by $Sc(OTf)_3$ (Table 3, entries 8 and 9). Substrate **1j** also reacted smoothly, the terminal cyclopropane ring having no influence on the reaction (Table 3, entry 10). Substituent R^3 had a significant influence on the diastereoselectivity. Substrates with an electron-poor (**1k**) or electron-rich (**1l**) phenyl group or a thienyl group (**1m**) behaved normally (Table 3, entries 11–13). However, when R^3 was an alkyl group, both the reactivity and stereoselectivity were quite different from those observed with the aromatic substituents. When R^3 was *n*Bu (**1n**), the diastereoselectivity decreased significantly (Table 3, entry 14), and when R^3 was the bulky *t*Bu group (**1o**), the reaction gave a complex mixture at reflux instead of the desired products (Table 3, entry 15). These results imply that both the electronic and steric properties of R^3 have a significant influence on the reactivity and stereoselectivity of the reaction.

To further understand the reaction mechanism, we separated **3aa**, **4ca**, and **5aa** and treated them with $Sc(OTf)_3$ independently (Scheme 2). We found that the reactions of **3aa** and **5aa** at 40 °C gave similar results; the three diastereoisomers **3aa**, **4aa**, and **5aa** were obtained and in a similar ratio. The reaction of **4ca** at 0 °C gave a mixture of **3ca** and **4ca**, with **3ca** the major isomer.

We suggest the plausible mechanism shown in Scheme 3. The 2,5-*cis* isomer **4** was obtained in the first stage, which is

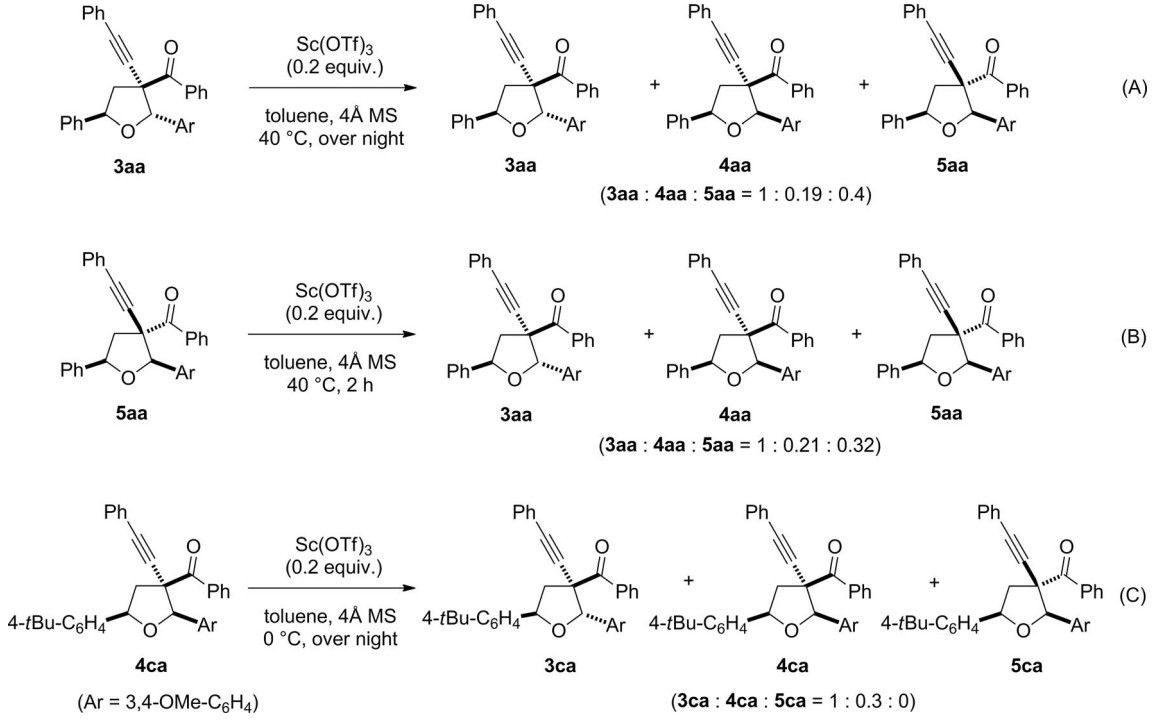
Table 3. Scope of ACP ketones in the $Sc(OTf)_3$-catalyzed [3+2] cycloaddition of **2a**.[a]



1a–o 2a 3aa–oa 4aa–oa 7

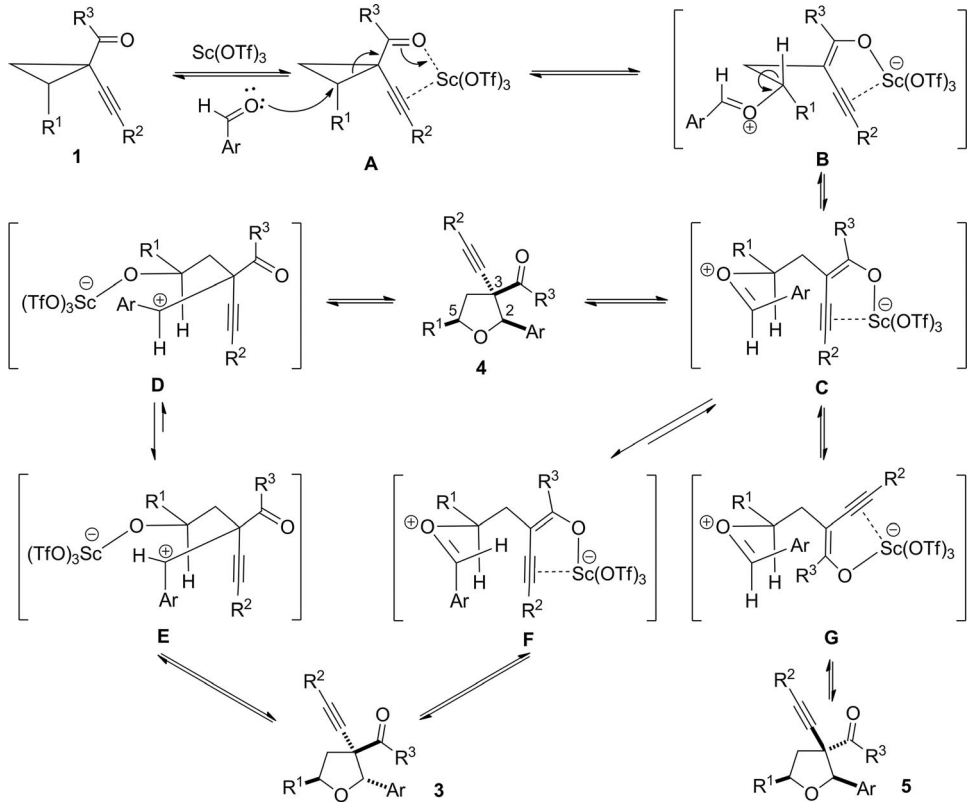
Entry	1	R^1	R^2	R^3	Yield [%][b]	dr[c] (3/4)
1	**1a**	Ph	Ph	Ph	82	5.5:1
2	**1b**	4-ClPh[d]	Ph	Ph	92	5.3:1
3	**1c**	4-*t*BuPh	Ph	Ph	85	4.9:1
4	**1d**	4-MeOPh	Ph	Ph	–[e]	–
5	**1e**	*n*Pr	Ph	Me	n.r.[f]	–
6	**1f**	Ph	4-ClPh	Ph	83	4.9:1
7	**1g**	Ph	3,4-$(MeO)_2$Ph	Ph	90	5.3:1
8	**1h**	Ph	Me_3Si	Ph	88	4.3:1
9	**1i**	Ph	H	Ph	90	3.8:1
10	**1j**	Ph	cyclopropyl	Ph	75	5.7:1
11	**1k**	Ph	Ph	4-ClPh	83	4.9:1
12	**1l**	Ph	Ph	4-MeOPh	82	5.3:1
13	**1m**	Ph	Ph	2-thienyl	95	6.2:1
14	**1n**	Ph	Ph	*n*Bu[g]	90	1.7:1
15	**1o**	Ph	Ph	*t*Bu	n.r.[f]	–

[a] Reagents and conditions: **1a** (0.3 mmol), **2** (5.0 equiv.), 4 Å molecular sieves (100 mg), toluene (8 mL), stirring for 4 h, 0 °C. [b] Isolated combined yield. [c] Ratio determined by ^1H NMR analysis of the reaction mixture. [d] 10.0 equiv. of **2a** was used. [e] Compound **7** was obtained instead in 92 % yield. [f] n.r.: no reaction; the reaction gave a complex mixture of products when heated at reflux. [g] Reaction was carried out at 40 °C.



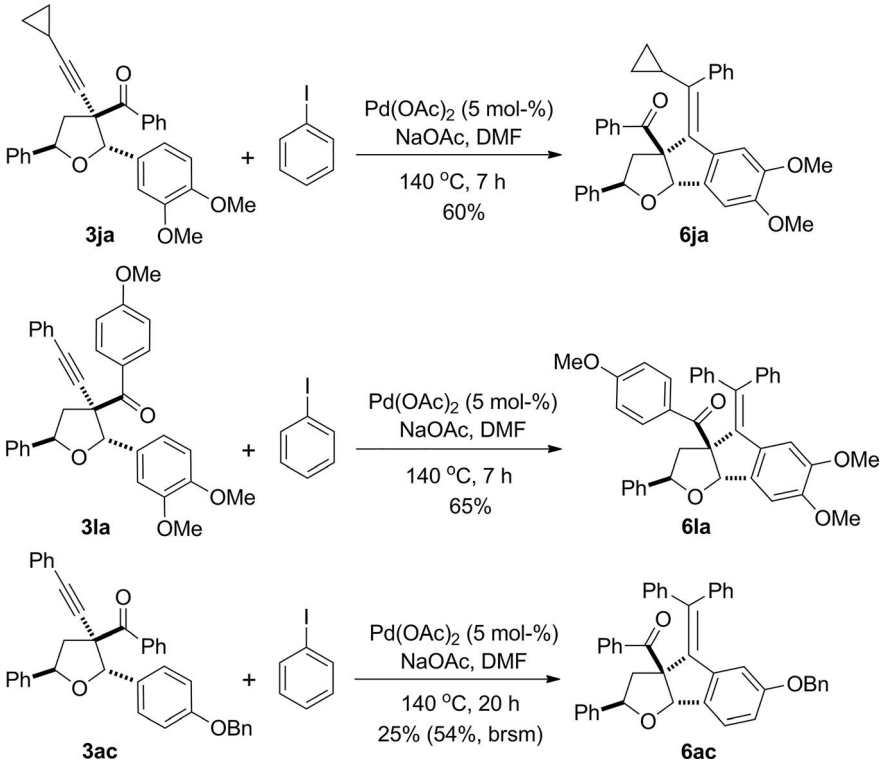
Scheme 2.

similar to that reported by Johnson and co-workers for the [3+2] cycloaddition of cyclopropane 1,1-diesters.[4] The relative stereochemistry at C3 was not affected and the carbonyl group at C3 and the phenyl group at C5 show a *cis* relationship. In the second stage, the C2–C3 or O-C2 bond in isomer **4** are cleaved under the reaction conditions (thermal and Lewis acid) to give



Scheme 3. Plausible mechanism for the intermolecular [3+2] cycloaddition of ACP ketones.

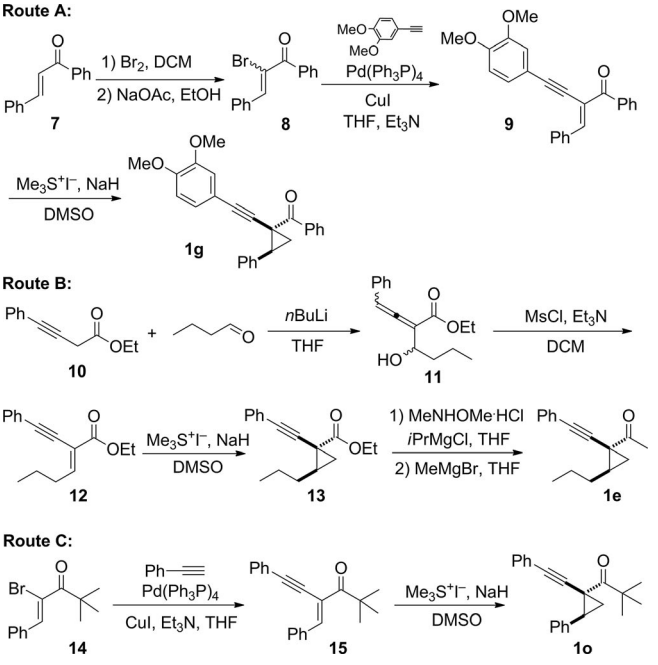
zwitterionic intermediate **C** or **D**. This is attributed to the push–pull principle of the strong donor Ar group at C2 and the two acceptors (alkoxy and carbonyl). Reconnection of the C2–C3 or O-C2 bond occurs to give isomer **3**, **4**, or **5**. Replacing the phenyl R^3 group by an alkyl group (**1n**) causes reduced diastereoselectivity as a result of the lower steric hindrance. The



Scheme 4. Domino intermolecular carbopalladation/C–H activation/C–C bond-forming reactions of cycloadducts **3**.

failure of **1o** to react may be attributed to the bulky *t*Bu group, which makes the formation of the C2–C3 bond in the first [3+2] stage more difficult. The weaker electron-donating propyl group (R^1) prevented the reaction of **1e**. This proposed mechanism is somewhat in accordance with those reported for cyclopropane 1,1-diesters in the literature.[4a,5c,9]

The cycloadducts obtained in this work, with the adjacent 3-alkynyl and 2-phenyl groups in *cis* positions, provide a good opportunity for the efficient construction of polycyclic skeletons. Zhu and co-workers have developed a domino intermolecular carbopalladation/C–H activation/C–C bond-forming process to construct oxindoles.[10] We successfully applied a similar strategy to the cycloadducts **3**. Thus, under catalysis by $Pd(OAc)_2$, **3ja** and iodobenzene were heated at 140 °C in DMF to afford the desired product **6ja** in 60 % yield (Scheme 4). Under similar conditions, **6la** and **6ac** were also obtained from **3la** and **3ac**, respectively. The structure of **6ja** was unambiguously confirmed by X-ray crystal analysis.[6]



Conclusions

We have developed a strategy for the $Sc(OTf)_3$-catalyzed [3+2] cycloaddition of alkynylcyclopropane ketones with electron-rich aromatic aldehydes. 2,5-*trans*-Configurated tetrahydrofurans containing a quaternary carbon center were smoothly synthesized in high-to-excellent yields with good diastereoselectivities. The cycloadducts were subjected to a domino carbopalladation/C–H activation/C–C bond-formation process for a highly efficient construction of polycyclic skeletons.

Experimental Section

General: Unless otherwise noted, all commercial materials were used without purification. Flash column chromatography was performed on silica gel (200–300 mesh) by using petroleum/ethyl acetate as eluting solvents. TLC was performed on silica gel GF254 plates and visualized by UV light (254 nm) or $KMnO_4$. NMR (400 MHz for ^1H and 101 MHz for ^{13}C) spectra were recorded in $CDCl_3$ unless otherwise indicated at ambient temperature. The chemical shifts (δ) are given in ppm and were measured with solvents as references (for $CDCl_3$, ^1H: δ = 7.26 ppm; ^{13}C NMR, δ = 77.1 ppm). IR spectra were recorded as a film on KBr. Melting points were obtained with an apparatus. High-resolution mass spectra were recorded with a MALDI-TOF resource.

ACP ketones **1a**,[2o] **1b**,[2l] **1f**,[2l] **1j**,[2o] **1k**.[2l] and **1n**[2p] were prepared according to the literature and their data are the same as reported. ACP ketones **1c**, **1d**, **1g**, **1h**, **1i**, **1l**, and **1m** were synthesized following the general route A,[2p] **1e** was synthesized following route B,[2k] and **1o** was synthesized following route C[11,2p] (see below).

Diastereoisomeric ratios were determined by ^1H NMR analysis of the crude products. NMR spectroscopic data for the major and minor diastereoisomers have been reported in most cases. In some cases the two diastereomers were inseparable, in these circumstances the NMR spectroscopic data for the mixture of two diastereoisomers or only the major diastereoisomer have been reported.

Typical Procedure for Synthesis of ACP Ketone 1g (Route A): Bromine (5.11 g, 31.9 mmol, 1.2 equiv.) was added dropwise to a solution of chalcone **7** (5.50 g, 26.6 mmol, 1.0 equiv.) in DCM (40 mL) at 0 °C. The mixture was stirred for 30 min at the same temperature before quenching by the addition of a saturated $Na_2S_2O_3$ solution (50 mL). The aqueous phase was separated and extracted with DCM (50 mL × 3). The organic phases were combined and washed with brine. After drying with $MgSO_4$, the solvent was removed under vacuum. The residue was dissolved in EtOH (40 mL), then NaOAc (3.28 g, 31.9 mmol, 1.2 equiv.) was added, and the mixture was heated at reflux for 4 h. After cooling to room temperature, the solvent was removed under vacuum and water (100 mL) was added. The aqueous phase was extracted with DCM (50 mL × 3). The organic phases were combined and washed with brine. After drying with $MgSO_4$, the solvent was removed under vacuum, and the crude product was purified by flash chromatography (PE/EA, 100:1) to give **8** (8.48 g, 90 %) as a mixture of *Z*/*E* isomers. The data for **8** were the same as reported in the literature.

$[Pd(Ph_3P)_4]$ (162.9 mg, 0.141 mmol, 0.05 equiv.) and CuI (53.7 mg, 0.282 mmol, 0.1 equiv.) were added to a solution of **8** (810 mg, 2.82 mmol, 1.0 equiv.) in THF (4.0 mL) and Et_3N (4.0 mL) under Ar. The reaction mixture was flushed with Ar (3 ×) and 4-ethynyl-1,2-dimethoxybenzene (549 mg, 3.38 mmol, 1.2 equiv.) was added by syringe. The mixture was stirred for 4 h until TLC indicated completion of the reaction. The mixture was diluted with EtOAc (50 mL), washed with 1 N HCl and brine, and dried with $MgSO_4$. After removing the solvent under vacuum, the crude product was purified by flash chromatography (PE/EA, 10:1) to give (*E*)-2-benzylidene-4-(3,4-dimethoxyphenyl)-1-phenylbut-3-yn-1-one (**9**; 697.8 mg, 67 %) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 6.7 Hz, 2 H), 8.00 (d, *J* = 7.5 Hz, 2 H), 7.61–7.54 (m, 2 H), 7.50–7.44 (m, 5 H), 7.03 (d, *J* = 8.2 Hz, 1 H), 6.88–6.79 (m, 2 H), 3.89 (s, 3 H), 3.85 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.8, 150.2, 148.9, 144.5, 137.5, 135.1, 132.6, 130.6, 130.5, 129.0, 128.7, 128.2, 125.0, 121.3, 115.2, 114.1, 111.2, 101.3, 86.2, 56.1, 56.1 ppm.

NaH (60 % in mineral oil, 79.6 mg, 1.99 mmol, 1.05 equiv.) was added to a solution of trimethylsulfoxonium iodide (437.9 mg, 1.99 mmol, 1.05 equiv.) in DMSO (7 mL). The mixture was stirred for

30 min until the solution turned clear, then **9** (697.8 mg, 1.89 mmol, 1.00 equiv.) was added, and the mixture was stirred at room temperature until TLC indicated completion of the reaction. Water (30 mL) and EtOAc (30 mL) were added and the aqueous phase was separated and extracted with EtOAc (30 mL × 2). The organic phases were combined and washed with brine. After drying with $MgSO_4$, the solvent was removed under vacuum, and the crude product was purified by flash chromatography (PE/EA, 20:1) to give {1-[(3,4-dimethoxyphenyl)ethynyl]-2-phenylcyclopropyl}(phenyl)methanone (**1g**; 556.6 mg, 77 %) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10–8.08 (m, 2 H), 7.55–7.52 (m, 1 H), 7.46–7.33 (m, 7 H), 6.67–6.60 (m, 2 H), 6.42 (s, 1 H), 3.82 (s, 3 H), 3.75 (s, 3 H), 3.03 (t, *J* = 8.3 Hz, 1 H), 2.51 (dd, *J* = 8.7, 4.5 Hz, 1 H), 1.96 (dd, *J* = 7.9, 4.5 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 197.0, 149.1, 148.3, 132.6, 129.3, 128.9, 128.1, 128.0, 127.3, 124.3, 115.3, 114.0, 110.7, 86.6, 84.8, 55.9, 55.8, 38.0, 32.1, 23.6 ppm. IR (KBr): $\tilde{\nu}$ = 2930, 1674, 1513, 1256, 1136, 1025 cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{23}O_3$ [M + H]$^+$ 383.1642; found 383.1640.

Compounds **1c**, **1d**, **1h**, **1i**, **1l**, and **1m** were also prepared according to route A.

{2-[4-(*tert*-Butyl)phenyl]-1-(phenylethynyl)cyclopropyl}(phenyl)methanone (1c): Yield 83 %; yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94–7.89 (m, 2 H), 7.36–7.32 (m, 1 H), 7.27–7.22 (m, 4 H), 7.15–7.13 (m, 2 H), 7.01–6.92 (m, 3 H), 6.77–6.73 (m, 2 H), 2.87 (t, *J* = 8.4 Hz, 1 H), 2.34 (dd, *J* = 9.0, 4.6 Hz, 1 H), 1.78 (dd, *J* = 7.8, 4.6 Hz, 1 H), 1.19 (s, 9 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 197.0, 150.3, 137.0, 133.0, 132.6, 131.2, 129.3, 128.5, 128.0, 128.0, 127.8, 125.1, 123.2, 88.7, 84.7, 38.3, 34.6, 32.1, 31.5, 23.8 ppm. IR (KBr): $\tilde{\nu}$ = 2963, 2868, 1674, 1597, 1490, 1446, 1366, 1265, 996, 838, 756, 692 cm^{-1}. HRMS (ESI): calcd. for $C_{28}H_{27}O$ [M + H]$^+$ 379. 2056; found 379.2063.

[2-(4-Methoxyphenyl)-1-(phenylethynyl)cyclopropyl](phenyl)methanone (1d): Yield 75 %; yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10–8.04 (m, 2 H), 7.57–7.51 (m, 1 H), 7.45–7.42 (m, 2 H), 7.32–7.30 (m, 2 H), 7.21–7.14 (m, 3 H), 7.04–7.03 (m, 2 H), 6.95–6.93 (m, 2 H), 3.84 (s, 3 H), 2.97 (t, *J* = 8.5 Hz, 1 H), 2.53 (dd, *J* = 9.1, 4.7 Hz, 1 H), 1.90 (dd, *J* = 7.9, 4.7 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 197.0, 159.0, 136.9, 132.6, 131.2, 129.8, 129.3, 128.1, 128.0, 127.9, 123.2, 114.0, 113.6, 88.5, 84.9, 55.4, 38.2, 32.2, 23.8 ppm. IR (KBr): $\tilde{\nu}$ = 3060, 3004, 1671, 1610, 1516, 1446, 1251, 1178, 1035, 1005, 833, 756, 692 cm^{-1}. HRMS (ESI): calcd. for $C_{25}H_{20}O_2$ [M + Na]$^+$ 375.1356; found 375.1360.

Phenyl{2-phenyl-1-[(trimethylsilyl)ethynyl]cyclopropyl}methanone (1h): Yield 92 %; colorless solid, m.p. 65–67 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 7.7 Hz, 2 H), 7.55–7.51 (m, 1 H), 7.36 (dq, *J* = 25.8, 7.6 Hz, 6 H), 2.91 (t, *J* = 8.4 Hz, 1 H), 2.44 (dd, *J* = 9.0, 4.6 Hz, 1 H), 1.86 (dd, *J* = 7.8, 4.6 Hz, 1 H), –0.09 (s, 9 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 196.7, 136.7, 135.7, 132.6, 129.5, 128.8, 128.0, 127.8, 127.3, 104.5, 90.2, 38.5, 32.4, 23.6, –0.5 ppm. IR (KBr): $\tilde{\nu}$ = 2958, 2163, 1669, 1597, 1268, 1249, 1031, 865, 843 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{23}OSi$ [M + H]$^+$ 319.1513; found 319.1514.

(1-Ethynyl-2-phenylcyclopropyl)(phenyl)methanone (1i): Yield 82 %; light-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04–7.99 (m, 2 H), 7.57–7.53 (m, 1 H), 7.46–7.37 (m, 4 H), 7.36–7.33 (m, 3 H), 2.89 (t, *J* = 8.5 Hz, 1 H), 2.44 (dd, *J* = 9.1, 4.8 Hz, 1 H), 2.05 (s, 1 H), 1.87 (dd, *J* = 7.9, 4.8 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 196.4, 136.4, 135.4, 132.8, 129.3, 128.7, 128.2, 128.1, 127.5, 82.1, 73.5, 37.2, 31.2, 22.5 ppm. IR (KBr): $\tilde{\nu}$ = 3705, 3289, 1675, 1449, 1264, 1173, 694 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{15}O$ [M + H]$^+$ 247.1117; found 247.1119.

(4-Methoxyphenyl)[2-phenyl-1-(phenylethynyl)cyclopropyl]methanone (1l): Yield 86 %; light-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (d, *J* = 8.6 Hz, 2 H), 7.45–7.34 (m, 5 H), 7.22–7.18 (m, 3 H), 7.07–7.05 (m, 2 H), 6.94 (d, *J* = 8.6 Hz, 2 H), 3.86 (s, 3 H), 2.99 (t, *J* = 8.4 Hz, 1 H), 2.52 (dd, *J* = 8.9, 4.7 Hz, 1 H), 1.94 (dd, *J* = 7.5, 4.9 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.5, 163.2, 136.0, 131.8, 131.2, 129.3, 128.7, 128.1, 127.8, 127.3, 123.1, 113.3, 88.6, 84.6, 55.4, 37.1, 31.7, 22.8 ppm. IR (KBr): $\tilde{\nu}$ = 2839, 1667, 1600, 1256, 1174, 1030, 846, 756 cm^{-1}. HRMS (ESI): calcd. for $C_{25}H_{21}O_2$ [M + H]$^+$ 353.1536; found 353.1538.

[2-Phenyl-1-(phenylethynyl)cyclopropyl](thiophen-2-yl)methanone (1m): Yield 70 %; light-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.34 (dd, *J* = 3.9, 1.1 Hz, 1 H), 7.57 (dd, *J* = 5.0, 1.1 Hz, 1 H), 7.32–7.22 (m, 5 H), 7.18–7.11 (m, 3 H), 7.05–7.00 (m, 3 H), 3.08 (t, *J* = 8.5 Hz, 1 H), 2.42 (dd, *J* = 9.1, 4.5 Hz, 1 H), 1.89 (dd, *J* = 8.0, 4.5 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 187.9, 142.9, 135.9, 134.6, 134.2, 131.4, 129.0, 128.3, 128.2, 128.1, 128.0, 127.4, 123.0, 88.4, 85.1, 39.3, 31.8, 25.6 ppm. IR (KBr): $\tilde{\nu}$ = 3060, 2924, 1639, 1492, 1411, 1354, 1263, 777, 755, 724 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{16}OS$ [M + Na]$^+$ 351.0814; found 351.0818.

Synthesis of ACP Ketone 1e (Route B): *n*BuLi (1.6 M in hexane, 12.0 mL, 1.2 equiv.) was added dropwise to a solution of ethyl 4-phenylbut-3-ynoate (**10**; 3.00 g, 15.94 mmol, 1.0 equiv.) in dry THF (40 mL) at –78 °C. The mixture was stirred at the same temperature for 0.5 h before butyraldehyde (1.38 g, 19.13 mmol, 1.2 equiv.) in dry THF (10 mL) was added dropwise. The mixture was stirred at –78 °C and the reaction was monitored by TLC. Upon completion, the reaction was quenched with saturated NH_4Cl solution and the aqueous phase was separated and extracted with EtOAc (30 mL × 2). The organic phases were combined and washed with brine. After drying with $MgSO_4$, the solvent was removed under vacuum, and the crude product was purified by flash chromatography (PE/EA, 40:1–20:1) to give **11** (1.50 g, 36 %) as a yellow oil.

MsCl (0.79 g, 6.92 mmol, 1.2 equiv.) in DCM (10 mL) was added dropwise to a solution of **11** (1.50 g, 5.76 mmol, 1.0 equiv.) and Et_3N (1.75 g, 17.28 mmol, 3.0 equiv.) in DCM (35 mL) at –10 °C, the mixture was stirred at the same temperature and the reaction was monitored by TLC. Upon completion, the reaction was quenched with water and the aqueous phase was separated and extracted with DCM (20 mL × 2). The organic phases were combined and washed with brine. After drying with $MgSO_4$, the solvent was removed under vacuum, and the crude product was purified by flash chromatography (PE/EA, 20:1) to give **12** (663.6 mg, 48 %) as a light-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53–7.47 (m, 2 H), 7.37–7.30 (m, 3 H), 7.28–7.24 (m, 1 H), 4.28 (dd, *J* = 14.2, 7.1 Hz, 2 H), 2.50 (dd, *J* = 14.9, 7.5 Hz, 2 H), 1.62–1.51 (m, 2 H), 1.35 (t, *J* = 7.1 Hz, 3 H), 1.03–0.96 (t, *J* = 7.4 Hz, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.9, 153.2, 131.7, 128.5, 128.4, 123.2, 117.5, 95.9, 83.2, 61.4, 33.0, 21.6, 14.3, 14.0 ppm.

NaH (60 % in mineral oil, 131.6 mg, 3.29 mmol, 1.2 equiv.) was added to a solution of trimethylsulfoxonium iodide (723.6 mg, 3.29 mmol, 1.2 equiv.) in DMSO (20 mL), the mixture was stirred for 30 min until the solution turned clear, then **12** (663.6 mg, 2.74 mmol, 1.0 equiv.) was added, and the mixture was stirred at room temperature until TLC indicated completion of the reaction. Water (30 mL) and EtOAc (30 mL) were added and the aqueous phase was separated and extracted with EtOAc (30 mL × 2). The organic phases were combined and washed with brine. After drying with $MgSO_4$, the solvent was removed under vacuum, and the crude product was purified by flash chromatography (PE/EA, 40:1) to give ethyl 1-(phenylethynyl)-2-propylcyclopropanecarboxylate (**13**; 671.8 mg, 96 %) as a pale-yellow oil.

Isopropylmagnesium chloride (1.0 M in THF, 7.9 mL, 3.0 equiv.) was added dropwise to a solution of ethyl 1-(phenylethynyl)-2-propylcy-

clopropanecarboxylate (**13**; 671.8 mg, 2.62 mmol, 1.0 equiv.) and *N*,*O*-dimethylhydroxylamine hydrochloride (383.3 mg, 3.93 mmol, 1.5 equiv.) in dry THF (16 mL) at –20 °C. The reaction mixture was stirred at the same temperature for a further 15 min, then water (20 mL) was added to quench the reaction. The aqueous phase was separated and extracted with EtOAc (20 mL × 3), the combined organic layers were washed with water and brine, and dried with $MgSO_4$. The solvent was removed under vacuum and the residue was then added to a flask filled with dry THF (20 mL) under Ar. Methylmagnesium bromide (3 M in diethyl ether, 1.3 mL, 1.5 equiv.) was added dropwise at 0 °C. The mixture was stirred for an additional 2 h and water (20 mL) was added to quench the reaction. The aqueous phase was separated and extracted with EtOAc (20 mL × 3), and the combined organic layers were washed with water and brine, and dried with $MgSO_4$. After removing the solvent under vacuum, the crude product was purified by flash chromatography (PE/EA, 80:1) to give 1-[1-(phenylethynyl)-2-propylcyclopropyl]ethanone (**1e**; 350.0 mg, 59 %) as a light-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.43 (m, 2 H), 7.33–7.31 (m, 3 H), 2.55 (s, 3 H), 1.84 (dd, *J* = 8.7, 3.2 Hz, 1 H), 1.78–1.74 (m, 1 H), 1.67–1.44 (m, 4 H), 1.11 (dd, *J* = 7.3, 3.2 Hz, 1 H), 0.98 (t, *J* = 7.2 Hz, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 205.9, 131.6, 128.3, 128.0, 123.4, 88.3, 82.8, 34.8, 32.4, 29.9, 29.5, 29.0, 22.1, 13.9 ppm. IR (KBr): $\tilde{\nu}$ = 2959, 2930, 1700, 1491, 1356, 755, 690 cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{19}O$ $[M + H]^+$ 227.1430; found 227.1433.

Synthesis of ACP Ketone 1o (Route C): $[Pd(Ph_3P)_4]$ (123.6 mg, 0.107 mmol, 0.05 equiv.) and CuI (40.8 mg, 0.214 mmol, 0.1 equiv.) were added to a solution of (*Z*)-2-bromo-4,4-dimethyl-1-phenylpent-1-en-3-one (**14**, synthesized according to ref.[11]; 571.9 mg, 2.14 mmol, 1.0 equiv.) in THF (4.0 mL) and Et_3N (4.0 mL) under Ar. The reaction mixture was flushed with Ar (3 ×) and phenylacetylene (262.3 mg, 2.57 mmol, 1.2 equiv.) was added by syringe. The mixture was stirred at room temperature until TLC indicated completion of the reaction. The mixture was diluted with EtOAc (50 mL), washed with 1 N HCl and brine, and dried with $MgSO_4$. After removing the solvent under vacuum, the crude product was purified by flash chromatography (PE/EA, 100:1) to give (*E*)-4-benzylidene-2,2-dimethyl-6-phenylhex-5-yn-3-one (**15**; 429 mg. 70 %) as a pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 7.1 Hz, 2 H), 7.51 (s, 1 H), 7.39–7.09 (m, 8 H), 1.33 (s, 9 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 204.2, 144.7, 135.1, 131.1, 130.4, 130.2, 128.9, 128.7, 128.5, 123.0, 120.0, 100.2, 87.4, 44.7, 27.2 ppm.

NaH (60 % in mineral oil, 59.5 mg, 1.49 mmol, 1.0 equiv.) was added to a solution of trimethylsulfoxonium iodide (327.4 mg, 1.49 mmol, 1.0 equiv.) in DMSO (6 mL). The mixture was stirred for 30 min until the solution turned clear, then **15** (429.0 mg, 1.49 mmol, 1.0 equiv.) was added, and the mixture was stirred at room temperature until TLC indicated completion of the reaction. Water (15 mL) and EtOAc (10 mL) were added and the aqueous phase was separated and extracted with EtOAc (10 mL × 2), The organic phases were combined and washed with brine. After drying with $MgSO_4$, the solvent was removed under vacuum, and the crude product was purified by flash chromatography (PE/EA, 100:1) to give 2,2-dimethyl-1-[2-phenyl-1-(phenylethynyl)cyclopropyl]propan-1-one (**1o**; 384.4 mg, 85 %) as a light-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26–7.20 (m, 2 H), 7.19–7.16 (m, 3 H), 7.11–7.04 (m, 3 H), 6.97–6.92 (m, 2 H), 2.78 (t, *J* = 8.4 Hz, 1 H), 2.16 (dd, *J* = 8.9, 4.2 Hz, 1 H), 1.67 (dd, *J* = 7.8, 4.2 Hz, 1 H), 1.33 (s, 9 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 209.5, 136.1, 131.1, 129.1, 128.2, 128.0, 127.9, 127.2, 123.3, 89.0, 84.4, 45.4, 39.6, 30.5, 26.7, 25.7 ppm. IR (KBr): $\tilde{\nu}$ = 3412, 2969, 1684, 1598, 1184, 1103, 1063, 754, 692 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{23}O$ $[M + H]^+$ 303.1743; found 303.1746.

General Procedure for the [3+2] Cycloaddition Reactions of ACP Ketones with Aldehydes: $Sc(OTf)_3$ (0.06 mmol, 0.2 equiv.) was added to a solution of ACP ketone **1** (0.3 mmol, 1 equiv.) and aldehyde **2** (1.5 mmol, 5 equiv.) in toluene (8 mL) at 0 °C. The reaction mixture was stirred at 0 °C and monitored by TLC. Upon completion, the reaction mixture was passed through a small plug of silica, eluting with Et_2O (20 mL), and the solvent was removed under vacuum. The crude mixture was purified by flash chromatography to give the pure products. For the cases in which the products were inseparable from excess aldehyde, the excess aldehyde was oxidized by using Montanari's modified Pinnick oxidation.[12] The resulting mixture was dissolved in CH_3CN (4 mL) and H_2O (6 mL) and then NaH_2PO_4 (100 mg) and 30 % H_2O_2 (0.15 mL, 1.32 mmol, 4.4 equiv.) were added. Following the addition of $NaClO_2$ (1.8 mmol, 6.0 equiv.), the reaction mixture was stirred overnight. Upon completion, the reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with a saturated $NaHCO_3$ solution and brine. After drying with $MgSO_4$, the solvent was removed under vacuum, and the crude products were purified by flash chromatography to give the pure products. In some cases, the two diastereoisomers were separated by preparative TLC.

[2-(3,4-Dimethoxyphenyl)-5-phenyl-3-(phenylethynyl)tetrahydrofuran-3-yl](phenyl)methanone (3aa): Yellow oil; yield (with **4aa**): 117.5 mg (82 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 7.9 Hz, 2 H), 7.50–7.48 (m, 2 H), 7.41–7.34 (m, 4 H), 7.32–7.20 (m, 8 H), 7.18–7.13 (m, 1 H), 6.84 (d, *J* = 8.3 Hz, 1 H), 5.94 (s, 1 H), 5.76 (dd, *J* = 10.0, 5.9 Hz, 1 H), 3.89 (s, 3 H), 3.77 (s, 3 H), 3.19 (dd, *J* = 12.4, 5.9 Hz, 1 H), 2.83 (dd, *J* = 12.4, 10.0 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.9, 148.8, 148.2, 142.1, 135.7, 133.1, 131.3, 130.9, 129.8, 128.6, 128.5, 128.4, 128.0, 127.8, 125.7, 122.6, 120.3, 110.8, 110.2, 91.1, 87.9, 86.5, 80.2, 60.3, 55.9, 55.7, 49.6 ppm. IR (KBr): $\tilde{\nu}$ = 2972, 1678, 1596, 1516, 1491, 1266, 1236, 1028, 757, 693 cm^{-1}. HRMS (ESI): calcd. for $C_{33}H_{29}O_4$ $[M + H]^+$ 489.2060; found 489.2052.

[2-(3,4-Dimethoxyphenyl)-5-phenyl-3-(phenylethynyl)tetrahydrofuran-3-yl](phenyl)methanone (4aa): Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92–7.90 (m, 2 H), 7.55–7.51 (m, 2 H), 7.37–7.31 (m, 5 H), 7.30–7.17 (m, 7 H), 6.71 (dd, *J* = 8.3, 1.8 Hz, 1 H), 6.57 (d, *J* = 1.8 Hz, 1 H), 6.51 (d, *J* = 8.3 Hz, 1 H), 5.61 (s, 1 H), 5.46 (dd, *J* = 11.0, 5.2 Hz, 1 H), 3.67 (s, 3 H), 3.50 (s, 3 H), 3.17 (dd, *J* = 12.6, 11.0 Hz, 1 H), 2.68 (dd, *J* = 12.6, 5.2 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.7, 148.9, 148.3, 140.6, 136.1, 132.6, 131.5, 130.4, 130.0, 128.6, 128.6, 128.5, 127.9, 127.6, 126.4, 122.8, 120.6, 111.3, 110.6, 91.8, 90.7, 87.6, 80.2, 59.1, 55.8, 55.6, 45.8 ppm. IR (KBr): $\tilde{\nu}$ = 2929, 1681, 1597, 1517, 1413, 1264, 1239, 1161, 1028, 758, 694 cm^{-1}. HRMS (ESI): calcd. for $C_{33}H_{29}O_4$ $[M + H]^+$ 489.2060; found 489.2056.

[2-(3,4-Dimethoxyphenyl)-5-phenyl-3-(phenylethynyl)tetrahydrofuran-3-yl](phenyl)methanone (5aa): Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01–7.96 (m, 2 H), 7.45–7.40 (m, 2 H), 7.38–7.33 (m, 1 H), 7.28–7.21 (m, 4 H), 7.10–7.00 (m, 6 H), 6.90–6.84 (m, 2 H), 6.70 (d, *J* = 8.3 Hz, 1 H), 5.50 (s, 1 H), 4.96 (t, *J* = 7.9 Hz, 1 H), 3.72 (s, 3 H), 3.61 (s, 3 H), 3.18 (dd, *J* = 12.8, 7.4 Hz, 1 H), 2.63 (dd, *J* = 12.8, 8.4 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 196.5, 148.9, 148.3, 141.2, 135.0, 133.3, 131.2, 130.2, 128.6, 128.3, 128.3, 128.1, 127.9, 126.4, 120.8, 111.4, 110.4, 100.0, 90.5, 90.0, 89.7, 86.4, 79.6, 58.8, 56.0, 55.8, 49.1 ppm. IR (KBr): $\tilde{\nu}$ = 2950, 1678, 1597, 1516, 1447, 1263, 1236, 1029, 757, 693 cm^{-1}. HRMS (ESI): calcd. for $C_{33}H_{29}O_4$ $[M + H]^+$ 489.2060; found 489.2057.

[2-(Benzo[*d*][1,3]dioxol-5-yl)-5-phenyl-3-(phenylethynyl)tetrahydrofuran-3-yl](phenyl)methanone (3ab): Yellow oil; yield (with **4ab**): 80.5 mg (79 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09–8.02 (m, 2 H), 7.45–7.41 (m, 1 H), 7.39–7.24 (ddd, *J* = 23.0, 15.5, 7.5 Hz, 6 H), 7.23–7.14 (m, 7 H), 7.03 (dd, *J* = 8.1, 1.2 Hz, 1 H), 6.70 (d, *J* = 8.1 Hz,

1 H), 5.89 (s, 1 H), 5.85 (s, 2 H), 5.63 (dd, *J* = 10.0, 5.8 Hz, 1 H), 3.11 (dd, *J* = 12.3, 5.8 Hz, 1 H), 2.64 (dd, *J* = 12.3, 10.0 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.7, 147.3, 147.1, 141.9, 135.6, 133.2, 132.6, 131.3, 129.8, 128.6, 128.5, 128.3, 128.1, 127.8, 125.7, 122.7, 121.3, 108.5, 107.5, 100.9, 91.3, 87.7, 86.1, 80.3, 60.2, 49.6 ppm. IR (KBr): $\tilde{\nu}$ = 3414, 1721, 1490, 1445, 1239, 1039, 934, 757, 694 cm^{-1}. HRMS (ESI): calcd. for $C_{32}H_{25}O_4$ [M + H]$^+$ 473.1747; found 473.1738.

[2-(Benzo[*d*][1,3]dioxol-5-yl)-5-phenyl-3-(phenylethynyl)tetrahydrofuran-3-yl](phenyl)methanone (4ab): Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 7.7 Hz, 2 H), 7.53–7.47 (m, 2 H), 7.41–7.11 (m, 11 H), 6.65–6.60 (m, 2 H), 6.43–6.38 (m, 1 H), 5.71 (s, 2 H), 5.50 (s, 1 H), 5.36 (dd, *J* = 10.6, 5.3 Hz, 1 H), 3.13 (dd, *J* = 12.7, 10.6 Hz, 1 H), 2.65 (dd, *J* = 12.7, 5.3 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.1, 147.6, 147.4, 140.3, 136.1, 132.5, 131.6, 131.5, 129.9, 128.6, 128.6, 128.5, 128.0, 127.6, 126.5, 122.7, 122.1, 108.4, 107.7, 101.0, 91.9, 91.0, 87.5, 80.3, 59.0, 46.6 ppm. IR (KBr): $\tilde{\nu}$ = 2895, 1680, 1489, 1446, 1248, 1039, 757, 693 cm^{-1}. HRMS (ESI): calcd. for $C_{32}H_{24}O_4$ [M + Na]$^+$ 495.1567; found 495.1569.

{2-[4-(Benzyloxy)phenyl]-5-phenyl-3-(phenylethynyl)tetrahydrofuran-3-yl}(phenyl)methanone (3ac): Yellow oil; yield (with **4ac**): 142.4 mg (90 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 7.8 Hz, 2 H), 7.50 (d, *J* = 8.6 Hz, 2 H), 7.37–7.06 (m, 18 H), 6.85 (d, *J* = 8.6 Hz, 2 H), 5.86 (s, 1 H), 5.61 (dd, *J* = 10.1, 5.9 Hz, 1 H), 4.93 (s, 2 H), 3.07 (dd, *J* = 12.2, 5.9 Hz, 1 H), 2.65 (dd, *J* = 12.2, 10.1 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.7, 158.6, 142.2, 137.1, 135.6, 133.1, 131.3, 131.0, 129.8, 129.1, 128.6, 128.4, 128.3, 128.0, 127.9, 127.7, 127.4, 125.7, 122.7, 114.0, 91.1, 87.8, 86.2, 80.1, 69.9, 60.1, 49.5 ppm. IR (KBr): $\tilde{\nu}$ = 3062, 1679, 1611, 1511, 1450, 1239, 1173, 757, 695 cm^{-1}. HRMS (ESI): calcd. for $C_{38}H_{31}O_3$ [M + H]$^+$ 535.2268; found 535.2262.

[2-(4-Methoxyphenyl)-5-phenyl-3-(phenylethynyl)tetrahydrofuran-3-yl](phenyl)methanone (3ad): Yellow oil; yield (with **4ad**): 72.2 mg (95 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05–7.95 (m, 2 H), 7.53–7.47 (m, 2 H), 7.36–7.30 (m, 3 H), 7.26–7.17 (m, 4 H), 7.17–7.08 (m, 6 H), 6.81–6.74 (m, 2 H), 5.86 (s, 1 H), 5.61 (dd, *J* = 9.2, 6.2 Hz, 1 H), 3.64 (s, 3 H), 3.07 (dd, *J* = 12.3, 5.8 Hz, 1 H), 2.66 (dd, *J* = 12.3, 9.2 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.8, 159.5, 142.2, 135.7, 133.1, 131.3, 130.8, 129.8, 129.1, 128.6, 128.5, 128.3, 128.0, 127.7, 125.8, 122.7, 113.1, 91.1, 87.9, 86.3, 80.2, 60.2, 55.3, 49.6 ppm. IR (KBr): $\tilde{\nu}$ = 2927, 1679, 1611, 1513, 1446, 1248, 1173, 757, 694 cm^{-1}. HRMS (ESI): calcd. for $C_{32}H_{27}O_3$ [M + H]$^+$ 459.1955; found 459.1954.

[2-(4-Ethoxyphenyl)-5-phenyl-3-(phenylethynyl)tetrahydrofuran-3-yl](phenyl)methanone (3ae): Yellow oil; yield (with **4ae**): 136.2 mg (93 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10–8.04 (m, 2 H), 7.57 (d, *J* = 8.7 Hz, 2 H), 7.52–7.44 (m, 3 H), 7.39–7.32 (m, 4 H), 7.29–7.20 (m, 6 H), 6.87 (d, *J* = 8.7 Hz, 2 H), 5.94 (s, 1 H), 5.72 (dd, *J* = 10.0, 5.9 Hz, 1 H), 4.02 (q, *J* = 7.0 Hz, 2 H), 3.17 (dd, *J* = 12.4, 5.9 Hz, 1 H), 2.79 (dd, *J* = 12.4, 10.0 Hz, 1 H), 1.40 (t, *J* = 7.0 Hz, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.9, 158.9, 142.2, 135.8, 133.1, 131.4, 130.5, 129.8, 129.1, 128.6, 128.5, 128.3, 128.0, 127.7, 125.8, 122.8, 113.7, 91.1, 87.9, 86.4, 80.2, 63.5, 60.2, 49.6, 14.9 ppm. IR (KBr): $\tilde{\nu}$ = 3416, 1679, 1613, 1512, 1396, 1243, 1173, 1047, 757, 694 cm^{-1}. HRMS (ESI): calcd. for $C_{33}H_{29}O_3$ [M + H]$^+$ 473.2111; found 473.2107.

[2-(2-Methoxyphenyl)-5-phenyl-3-(phenylethynyl)tetrahydrofuran-3-yl](phenyl)methanone (3af): Yellow oil; yield (with **4af**): 106.8 mg (75 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82–7.76 (m, 3 H), 7.46–7.42 (m, 2 H), 7.36–7.12 (m, 11 H), 7.05–6.97 (m, 3 H), 6.60 (d, *J* = 8.1 Hz, 1 H), 6.00 (s, 1 H), 5.56 (dd, *J* = 10.3, 5.1 Hz, 1 H), 3.15 (s, 3 H), 3.07 (t, *J* = 11.4 Hz, 1 H), 2.83 (dd, *J* = 12.0, 5.1 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 196.1, 156.4, 141.8, 136.7, 132.3, 131.3, 129.5, 128.9, 128.6, 128.2, 127.8, 127.6, 127.5, 126.1, 123.0, 120.2, 109.4, 90.2, 89.1, 83.6, 80.8, 60.3, 54.2, 50.6 ppm. IR (KBr): $\tilde{\nu}$ = 3060, 1678, 1598, 1491, 1461, 1246, 1050, 1028, 756, 694 cm^{-1}. HRMS (ESI): calcd. for $C_{32}H_{27}O_3$ [M + H]$^+$ 459.1955; found 459.1947.

Phenyl[5-phenyl-3-(phenylethynyl)-2-(thiophen-2-yl)tetrahydrofuran-3-yl]methanone (3ag): Yellow oil; yield (with **4ag**): 110.3 mg (88 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19–8.14 (m, 2 H), 7.51–7.45 (m, 1 H), 7.40–7.17 (m, 13 H), 6.94 (dd, *J* = 3.9, 0.4 Hz, 1 H), 6.74 (d, *J* = 3.9 Hz, 1 H), 6.07 (s, 1 H), 5.62 (dd, *J* = 10.0, 6.0 Hz, 1 H), 3.16 (dd, *J* = 12.5, 6.0 Hz, 1 H), 2.55 (dd, *J* = 12.5, 10.0 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.8, 141.4, 140.7, 135.1, 133.5, 131.5, 129.9, 129.5, 128.7, 128.7, 128.6, 128.4, 128.3, 128.0, 125.7, 125.4, 125.2, 91.2, 86.7, 83.1, 59.7, 48.8 ppm. IR (KBr): $\tilde{\nu}$ = 3032, 1678, 1597, 1400, 1182, 757, 695 cm^{-1}. HRMS (ESI): calcd. for $C_{29}H_{23}O_2S$ [M + H]$^+$ 435.1413; found 435.1405.

Phenyl[5-phenyl-3-(phenylethynyl)-2-(thiophen-2-yl)tetrahydrofuran-3-yl]methanone (4ag): Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 7.5 Hz, 2 H), 7.62–7.58 (m, 2 H), 7.51–7.47 (m, 1 H), 7.44–7.30 (m, 10 H), 7.12–7.08 (m, 1 H), 6.67–6.62 (m, 2 H), 6.11 (s, 1 H), 5.58 (dd, *J* = 11.3, 4.5 Hz, 1 H), 3.21 (dd, *J* = 12.8, 11.3 Hz, 1 H), 2.75 (dd, *J* = 12.8, 4.6 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.5, 141.7, 140.1, 135.7, 132.9, 131.6, 129.9, 128.8, 128.5, 128.5, 128.0, 127.9, 127.2, 126.5, 126.1, 122.5, 90.8, 88.0, 85.6, 80.6, 59.3, 44.9 ppm. IR (KBr): $\tilde{\nu}$ = 3415, 1681, 1639, 1619, 1240, 756, 693 cm^{-1}. HRMS (ESI): calcd. for $C_{29}H_{23}O_2S$ [M + H]$^+$ 435.1413; found 435.1405.

[5-(4-Chlorophenyl)-2-(3,4-dimethoxyphenyl)-3-(phenylethynyl)tetrahydrofuran-3-yl](phenyl)methanone (3ba): Yellow oil; yield (with **4ba**): 104.4 mg (92 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 7.7 Hz, 2 H), 7.39 (t, *J* = 7.3 Hz, 1 H), 7.22–7.31 (m, 6 H), 7.20–7.10 (m, 6 H), 7.04 (d, *J* = 8.2 Hz, 1 H), 6.73 (d, *J* = 8.2 Hz, 1 H), 5.79 (s, 1 H), 5.63 (dd, *J* = 9.6, 6.0 Hz, 1 H), 3.77 (s, 3 H), 3.66 (s, 3 H), 3.07 (dd, *J* = 12.4, 6.0 Hz, 1 H), 2.68 (dd, *J* = 12.4, 9.6 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.7, 148.9, 148.3, 140.6, 135.6, 133.3, 133.1, 131.2, 130.6, 129.7, 128.7, 128.6, 128.3, 127.9, 127.0, 122.5, 120.3, 110.8, 110.3, 91.2, 87.7, 86.6, 79.4, 60.2, 55.9, 55.7, 49.3 ppm. IR (KBr): $\tilde{\nu}$ = 2998, 1679, 1596, 1515, 1491, 1265, 1236, 1028, 757, 691 cm^{-1}. HRMS (ESI): calcd. for $C_{33}H_{27}ClO_4$ [M + Na]$^+$ 545.1490; found 545.1493.

[5-(4-Chlorophenyl)-2-(3,4-dimethoxyphenyl)-3-(phenylethynyl)tetrahydrofuran-3-yl](phenyl)methanone (4ba): Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91–7.85 (m, 2 H), 7.48–7.46 (m, 2 H), 7.36–7.30 (m, 5 H), 7.30–7.19 (m, 6 H), 6.70 (dd, *J* = 8.3, 1.9 Hz, 1 H), 6.54–6.52 (m, 2 H), 5.59 (s, 1 H), 5.42 (dd, *J* = 10.8, 5.4 Hz, 1 H), 3.68 (s, 3 H), 3.50 (s, 3 H), 3.10 (dd, *J* = 12.6, 10.8 Hz, 1 H), 2.68 (dd, *J* = 12.6, 5.4 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.7, 148.9, 148.2, 139.2, 136.0, 133.6, 132.6, 131.5, 130.1, 129.9, 128.7, 128.5, 127.7, 127.6, 122.6, 120.5, 111.2, 110.6, 91.5, 90.8, 87.7, 79.4, 59.0, 55.8, 55.6, 45.9 ppm. IR (KBr): $\tilde{\nu}$ = 2999, 1680, 1597, 1517, 1492, 1264, 1239, 1161, 1028, 757, 692 cm^{-1}. HRMS (ESI): calcd. for $C_{33}H_{27}ClO_4$ [M + Na]$^+$ 545.1490; found 545.1495.

{5-[4-(*tert*-Butyl)phenyl]-2-(3,4-dimethoxyphenyl)-3-(phenylethynyl)tetrahydrofuran-3-yl}(phenyl)methanone (3ca): Yellow oil; yield (with **4ca**): 111.4 mg (85 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 8.0 Hz, 2 H), 7.38 (t, *J* = 7.4 Hz, 1 H), 7.33–7.29 (m, 4 H), 7.28–7.24 (m, 2 H), 7.20–7.09 (m, 6 H), 7.07–7.02 (m, 1 H), 6.72 (d, *J* = 8.3 Hz, 1 H), 5.84 (s, 1 H), 5.63 (dd, *J* = 10.0, 5.9 Hz, 1 H), 3.77 (s, 3 H), 3.66 (s, 3 H), 3.07 (dd, *J* = 12.4, 5.9 Hz, 1 H), 2.74 (dd, *J* = 12.4, 10.0 Hz, 1 H), 1.22 (s, 9 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 196.0, 150.7, 148.7, 148.2, 138.9, 135.7, 133.0, 131.3, 131.1, 129.7, 128.5, 128.3, 127.9, 125.5, 125.5, 122.6, 120.2, 110.7, 110.1, 90.9, 88.0, 86.3, 80.0, 60.3, 55.9, 55.7, 49.4, 34.5, 31.4 ppm. IR (KBr): $\tilde{\nu}$ = 2961,

1679, 1596, 1515, 1492, 1463, 1267, 1236, 1028, 758, 692 cm^{-1}. HRMS (ESI): calcd. for $C_{37}H_{36}O_4$ $[M + Na]^+$ 567.2506; found 567.2499.

{5-[4-(*tert*-Butyl)phenyl]-2-(3,4-dimethoxyphenyl)-3-(phenylethynyl)tetrahydrofuran-3-yl}(phenyl)methanone (4ca): Yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, J = 7.7 Hz, 2 H), 7.56–7.51 (m, 2 H), 7.46–7.36 (m, 5 H), 7.34–7.24 (m, 5 H), 6.77 (dd, J = 8.3, 1.6 Hz, 1 H), 6.63 (d, J = 1.6 Hz, 1 H), 6.56 (d, J = 8.3 Hz, 1 H), 5.65 (s, 1 H), 5.49 (dd, J = 10.9, 5.2 Hz, 1 H), 3.72 (s, 3 H), 3.56 (s, 3 H), 3.26 (dd, J = 12.7, 10.9 Hz, 1 H), 2.71 (dd, J = 12.7, 5.2 Hz, 1 H), 1.33 (s, 9 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.8, 150.9, 148.8, 148.2, 137.4, 136.2, 132.5, 131.5, 130.5, 130.0, 128.6, 128.5, 127.6, 126.3, 125.5, 122.8, 120.6, 111.3, 110.5, 92.0, 90.7, 87.5, 80.1, 59.1, 55.8, 55.6, 45.6, 34.7, 31.5 ppm. IR (KBr): $\tilde{\nu}$ = 2960, 1681, 1597, 1517, 1491, 1265, 1240, 1161, 1028, 757, 693 cm^{-1}. HRMS (ESI): calcd. for $C_{37}H_{36}O_4$ $[M + Na]^+$ 567.2506; found 567.2512.

2-(4-Methoxyphenyl)-5-phenyl-4-(phenylethynyl)-2,3-dihydrofuran (7): Yellow oil; yield 98.3 mg (92 %). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.10–8.04 (m, 2 H), 7.46–7.09 (m, 9 H), 6.82 (d, J = 8.8 Hz, 2 H), 5.58 (dd, J = 10.4, 8.8 Hz, 1 H), 3.71 (s, 3 H), 3.38 (dd, J = 15.1, 10.4 Hz, 1 H), 2.99 (dd, J = 15.1, 8.8 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 159.5, 157.8, 134.1, 131.1, 130.4, 129.3, 128.4, 128.2, 127.8, 127.3, 126.6, 124.1, 114.1, 95.2, 91.5, 85.9, 81.9, 55.4, 43.2 ppm. IR (KBr): $\tilde{\nu}$ = 2932, 2198, 1598, 1514, 1248, 1029, 757, 692 cm^{-1}. HRMS (ESI): calcd. for $C_{25}H_{20}O_2$ $[M + Na]^+$ 375.1356; found 375.1358.

{3-[(4-Chlorophenyl)ethynyl]-2-(3,4-dimethoxyphenyl)-5-phenyltetrahydrofuran-3-yl}(phenyl)methanone (3fa): Yellow oil; yield (with **4fa**) 151.9 mg (83 %). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.95 (d, J = 7.5 Hz, 2 H), 7.45–7.35 (m, 3 H), 7.30–7.26 (m, 4 H), 7.23–7.11 (m, 4 H), 7.06–7.02 (m, 3 H), 6.74 (d, J = 8.3 Hz, 1 H), 5.85 (s, 1 H), 5.64 (dd, J = 10.2, 5.9 Hz, 1 H), 3.79 (s, 3 H), 3.69 (s, 3 H), 3.09 (dd, J = 12.4, 6.0 Hz, 1 H), 2.72 (dd, J = 12.4, 10.2 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.7, 148.8, 148.3, 142.0, 135.7, 134.6, 133.2, 132.5, 130.9, 129.7, 128.7, 128.6, 128.0, 127.8, 125.7, 121.1, 120.2, 110.8, 110.2, 90.0, 89.0, 86.5, 80.2, 60.3, 56.0, 55.8, 49.5 ppm. IR (KBr): $\tilde{\nu}$ = 2935, 1680, 1595, 1515, 1490, 1266, 1236, 1160, 1139, 1090, 1028 cm^{-1}. HRMS (ESI): calcd. for $C_{33}H_{28}ClO_4$ $[M + H]^+$ 523.1671; found 523.1665.

{3-[(4-Chlorophenyl)ethynyl]-2-(3,4-dimethoxyphenyl)-5-phenyltetrahydrofuran-3-yl}(phenyl)methanone (4fa): Yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.86 (m, 2 H), 7.55–7.51 (m, 2 H), 7.37–7.33 (m, 3 H), 7.30–7.19 (m, 7 H), 6.70 (dd, J = 8.3, 1.8 Hz, 1 H), 6.56 (d, J = 1.8 Hz, 1 H), 6.51 (d, J = 8.3 Hz, 1 H), 5.60 (s, 1 H), 5.44 (dd, J = 11.0, 5.2 Hz, 1 H), 3.67 (s, 3 H), 3.49 (s, 3 H), 3.17 (dd, J = 12.7, 11.0 Hz, 1 H), 2.67 (dd, J = 12.7, 5.2 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.4, 148.9, 148.2, 140.4, 136.0, 134.7, 132.7, 132.7, 130.3, 129.9, 128.8, 128.6, 127.9, 127.6, 126.3, 121.2, 120.6, 111.2, 110.5, 92.8, 90.6, 86.5, 80.1, 59.0, 55.8, 55.6, 45.6 ppm. IR (KBr): $\tilde{\nu}$ = 3000, 2956, 1681, 1596, 1517, 1490, 1265, 1240, 1161, 1028, 701 cm^{-1}. HRMS (ESI): calcd. for $C_{33}H_{28}ClO_4$ $[M + H]^+$ 523.1671; found 523.1668.

{2-(3,4-Dimethoxyphenyl)-3-[(3,4-dimethoxyphenyl)ethynyl]-5-phenyltetrahydrofuran-3-yl}(phenyl)methanone (3ga): Yellow oil, inseparable from the minor isomer **4ga**; yield (with **4ga**): 96.7 mg (90 %). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, J = 8.2 Hz, 2 H), 7.54–7.46 (m, 3 H), 7.45–7.25 (m, 7 H), 7.20 (d, J = 8.4 Hz, 1 H), 6.90–6.83 (m, 2 H), 6.63 (t, J = 3.7 Hz, 1 H), 6.01 (s, 1 H), 5.79 (dd, J = 9.9, 5.8 Hz, 1 H), 3.87–3.80 (m, 12 H), 3.22 (dd, J = 12.3, 5.8 Hz, 1 H), 2.82–2.77 (m, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.8, 149.6, 148.6, 148.5, 148.2, 142.0, 135.7, 132.9, 131.3, 129.7, 128.5, 128.4, 127.8, 127.6, 126.2, 125.6, 124.3, 120.1, 114.7, 113.9, 110.9, 110.9, 110.2, 91.1, 86.2, 80.1, 60.2, 55.8, 55.7, 55.7, 49.3 ppm. IR (KBr): $\tilde{\nu}$ = 2934, 1681, 1515, 1268, 1241, 1138, 1026 cm^{-1}. HRMS (ESI): calcd. for $C_{35}H_{33}O_6$ $[M + H]^+$ 549.2272; found 549.2266.

{2-(3,4-Dimethoxyphenyl)-5-phenyl-3-[(trimethylsilyl)ethynyl]tetrahydrofuran-3-yl}(phenyl)methanone (3ha): Yellow oil; yield (with **4ha**): 126.2 mg (88 %). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, J = 7.5 Hz, 2 H), 7.47–7.40 (m, 3 H), 7.34–7.28 (m, 4 H), 7.27–7.21 (m, 1 H), 7.11–7.09 (m, 2 H), 6.79 (d, J = 8.0 Hz, 1 H), 5.79 (s, 1 H), 5.62 (dd, J = 10.0, 5.8 Hz, 1 H), 3.84 (s, 3 H), 3.83 (s, 3 H), 3.03 (dd, J = 12.3, 5.9 Hz, 1 H), 2.68 (dd, J = 12.3, 10.2 Hz, 1 H), 0.00 (s, 9 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.9, 148.7, 148.1, 142.0, 135.6, 133.0, 131.0, 130.0, 128.6, 127.8, 127.7, 125.7, 120.1, 110.9, 110.3, 104.1, 96.5, 86.3, 80.1, 60.7, 56.0, 55.8, 49.6, 0.4 ppm. IR (KBr): $\tilde{\nu}$ = 2958, 2166, 1679, 1596, 1516, 1450, 1260, 1237, 1029, 846 cm^{-1}. HRMS (ESI): calcd. for $C_{30}H_{33}O_4Si$ $[M + H]^+$ 485.2143; found 485.2152.

{2-(3,4-Dimethoxyphenyl)-5-phenyl-3-[(trimethylsilyl)ethynyl]tetrahydrofuran-3-yl}(phenyl)methanone (4ha): Colorless solid, m.p.124–126 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.76–7.72 (m, 2 H), 7.42–7.40 (m, 2 H), 7.25–7.20 (m, 2 H), 7.17–7.13 (m, 1 H), 7.09–7.05 (m, 3 H), 6.57 (dd, J = 8.3, 1.8 Hz, 1 H), 6.42–6.38 (m, 2 H), 5.39 (s, 1 H), 5.27 (dd, J = 10.8, 5.3 Hz, 1 H), 3.56 (s, 3 H), 3.39 (s, 3 H), 2.95 (dd, J = 12.6, 11.0 Hz, 1 H), 2.48 (dd, J = 12.6, 5.3 Hz, 1 H), 0.00 (s, 9 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.6, 148.8, 148.1, 140.5, 136.1, 132.4, 130.4, 130.1, 128.5, 127.8, 127.4, 126.4, 120.4, 111.1, 110.5, 108.4, 92.6, 90.7, 80.1, 59.4, 55.8, 55.5, 45.7, –0.2 ppm. IR (KBr): $\tilde{\nu}$ = 2923, 1675, 1455, 1243, 1139, 1047, 1024, 841 cm^{-1}. HRMS (ESI): calcd. for $C_{30}H_{32}O_4Si$ $[M + Na]^+$ 507.1962; found 507.1961.

[2-(3,4-Dimethoxyphenyl)-3-ethynyl-5-phenyltetrahydrofuran-3-yl](phenyl)methanone (3ia): Yellow oil; yield (with **4ia**): 137.5 mg (90 %). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.93–7.87 (m, 2 H), 7.40–7.37 (m, 1 H), 7.35–7.33 (m, 2 H), 7.28–7.21 (m, 4 H), 7.20–7.11 (m, 2 H), 7.02 (dd, J = 8.3, 1.7 Hz, 1 H), 6.71 (d, J = 8.3 Hz, 1 H), 5.74 (s, 1 H), 5.59 (dd, J = 10.0, 5.9 Hz, 1 H), 3.77 (s, 3 H), 3.76 (s, 3 H), 3.02 (dd, J = 12.4, 6.0 Hz, 1 H), 2.66 (dd, J = 12.4, 10.1 Hz, 1 H), 2.48 (s, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.5, 148.7, 148.1, 141.9, 135.4, 133.1, 130.4, 129.8, 128.5, 127.9, 127.7, 125.6, 120.1, 110.9, 110.1, 86.1, 82.3, 79.8, 79.5, 59.6, 55.8, 55.8, 49.4 ppm. IR (KBr): $\tilde{\nu}$ = 3238, 2954, 1674, 1516, 1270, 1235, 1160, 1025, 750, 688 cm^{-1}. HRMS (ESI): calcd. for $C_{27}H_{24}O_4$ $[M + Na]^+$ 435.1567; found 435.1570.

[2-(3,4-Dimethoxyphenyl)-3-ethynyl-5-phenyltetrahydrofuran-3-yl](phenyl)methanone (4ia): Yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, J = 7.9 Hz, 2 H), 7.51–7.49 (m, 2 H), 7.35–7.31 (m, 3 H), 7.29–7.15 (m, 3 H), 6.68–6.66 (m, 1 H), 6.55–6.45 (m, 2 H), 5.54 (s, 1 H), 5.39 (dd, J = 10.9, 5.1 Hz, 1 H), 3.64 (s, 3 H), 3.49 (s, 3 H), 3.11 (dd, J = 12.7, 10.9 Hz, 1 H), 2.66 (s, 1 H), 2.60 (dd, J = 12.7, 5.1 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.0, 148.9, 148.2, 140.3, 135.7, 132.6, 130.2, 130.0, 128.5, 127.9, 127.6, 126.3, 120.6, 111.2, 110.5, 90.5, 86.6, 80.0, 76.0, 58.3, 55.8, 55.5, 45.7 ppm. IR (KBr): $\tilde{\nu}$ = 3284, 1681, 1517, 1463, 1262, 1240, 1141, 1027, 732 cm^{-1}. HRMS (ESI): calcd. for $C_{27}H_{24}O_4$ $[M + Na]^+$ 435.1567; found 435.1568.

[3-(Cyclopropylethynyl)-2-(3,4-dimethoxyphenyl)-5-phenyltetrahydrofuran-3-yl](phenyl)methanone (3ja): Colorless solid; yield (with **4ja**): 117.4 mg (75 %); m.p. 122–124 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.93–7.86 (m, 2 H), 7.40–7.30 (m, 3 H), 7.27–7.20 (m, 4 H), 7.17–7.11 (m, 1 H), 7.11–7.10 (m, 1 H), 6.98 (dd, J = 8.2, 1.2 Hz, 1 H), 6.71 (d, J = 8.3 Hz, 1 H), 5.72 (s, 1 H), 5.54 (dd, J = 10.0, 5.8 Hz, 1 H), 3.80 (s, 3 H), 3.77 (s, 3 H), 2.91 (dd, J = 12.2, 5.8 Hz, 1 H), 2.55 (dd, J = 12.2, 10.0 Hz, 1 H), 1.07–1.03 (m, 1 H), 0.60–0.50 (m, 2 H), 0.38–0.25 (m, 2 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ =

196.3, 148.5, 148.0, 142.1, 135.7, 132.8, 131.3, 129.7, 128.4, 127.7, 127.6, 125.6, 120.1, 110.9, 110.1, 94.6, 86.1, 79.9, 73.4, 59.6, 55.8, 55.7, 49.6, 7.9, 7.8, –0.3 ppm. IR (KBr): $\tilde{\nu}$ = 2907, 2238, 1677, 1596, 1515, 1450, 1265, 1236, 1160, 1140, 1029, 699 cm^{-1}. HRMS (ESI): calcd. for $C_{30}H_{28}O_4$ $[M + Na]^+$ 475.1880; found 475.1886.

[3-(Cyclopropylethynyl)-2-(3,4-dimethoxyphenyl)-5-phenyltetrahydrofuran-3-yl](phenyl)methanone (4ja): Yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, J = 7.6 Hz, 2 H), 7.51–7.48 (m, 2 H), 7.35–7.29 (m, 3 H), 7.28–7.16 (m, 3 H), 6.62 (dd, J = 8.2, 1.6 Hz, 1 H), 6.50–6.45 (m, 2 H), 5.45 (s, 1 H), 5.37 (dd, J = 11.0, 5.1 Hz, 1 H), 3.65 (s, 3 H), 3.47 (s, 3 H), 3.02 (dd, J = 12.6, 11.0 Hz, 1 H), 2.51 (dd, J = 12.6, 5.1 Hz, 1 H), 1.27–1.21 (m, 1 H), 0.75–0.66 (m, 2 H), 0.62–0.53 (m, 2 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.0, 148.7, 148.2, 140.8, 136.2, 132.3, 130.8, 130.0, 128.5, 127.7, 127.4, 126.3, 120.5, 111.3, 110.5, 91.1, 90.7, 80.0, 77.9, 58.6, 55.8, 55.5, 45.7, 8.2, 8.1, –0.1 ppm. IR (KBr): $\tilde{\nu}$ = 2975, 2243, 1680, 1516, 1261, 1110, 1025, 800, 734 cm^{-1}. HRMS (ESI): calcd. for $C_{30}H_{29}O_4$ $[M + H]^+$ 453.2060; found 453.2064.

(4-Chlorophenyl)[2-(3,4-dimethoxyphenyl)-5-phenyl-3-(phenylethynyl)tetrahydrofuran-3-yl]methanone (3ka): Yellow oil; yield (with **4ka**): 91.2 mg (83 %). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, J = 8.5 Hz, 2 H), 7.45–7.43 (m, 2 H), 7.39–7.17 (m, 11 H), 7.06 (d, J = 8.1 Hz, 1 H), 6.79 (d, J = 8.3 Hz, 1 H), 5.82 (s, 1 H), 5.71 (dd, J = 9.8, 5.9 Hz, 1 H), 3.85 (s, 3 H), 3.73 (s, 3 H), 3.10 (dd, J = 12.3, 5.9 Hz, 1 H), 2.83 (dd, J = 12.3, 9.8 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.8, 149.0, 148.4, 142.0, 139.6, 134.1, 131.3, 130.7, 128.7, 128.7, 128.5, 128.3, 127.8, 125.7, 122.4, 120.4, 110.9, 110.3, 91.4, 87.7, 86.7, 80.2, 60.4, 56.0, 55.8, 49.4 ppm. IR (KBr): $\tilde{\nu}$ = 2932, 1680, 1588, 1515, 1264, 1236, 1092, 1028, 804, 757, 696 cm^{-1}. HRMS (ESI): calcd. for $C_{33}H_{27}ClO_4$ $[M + H]^+$ 523.1671; found 523.1662.

[2-(3,4-Dimethoxyphenyl)-5-phenyl-3-(phenylethynyl)tetrahydrofuran-3-yl](4-methoxyphenyl)methanone (3la): Colorless oil; yield (with **4la**): 136.1 mg (82 %). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, J = 8.7 Hz, 2 H), 7.37–7.35 (m, 2 H), 7.25 (t, J = 7.5 Hz, 2 H), 7.18–7.10 (m, 7 H), 7.05 (d, J = 8.3 Hz, 1 H), 6.74–6.65 (m, 3 H), 5.81 (s, 1 H), 5.64 (dd, J = 10.0, 5.9 Hz, 1 H), 3.76 (s, 3 H), 3.69 (s, 3 H), 3.65 (s, 3 H), 3.05 (dd, J = 12.4, 5.9 Hz, 1 H), 2.72 (dd, J = 12.4, 10.0 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.7, 163.4, 148.7, 148.2, 142.1, 132.4, 131.2, 131.0, 128.5, 128.4, 128.3, 127.6, 125.7, 122.7, 120.4, 113.1, 110.9, 110.1, 90.8, 88.3, 86.3, 80.1, 59.9, 55.9, 55.7, 55.4, 49.5 ppm. IR (KBr): $\tilde{\nu}$ = 2934, 1670, 1598, 1513, 1258, 1172, 1028, 757, 696, 615 cm^{-1}. HRMS (ESI): calcd. for $C_{34}H_{30}O_5$ $[M + Na]^+$ 541.1985; found 541.1986.

[2-(3,4-Dimethoxyphenyl)-5-phenyl-3-(phenylethynyl)tetrahydrofuran-3-yl](4-methoxyphenyl)methanone (4la): Yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, J = 8.8 Hz, 2 H), 7.52 (d, J = 7.5 Hz, 2 H), 7.35–7.32 (m, 4 H), 7.28–7.22 (m, 3 H), 6.73–6.66 (m, 3 H), 6.57 (s, 1 H), 6.51 (d, J = 8.3 Hz, 1 H), 5.61 (s, 1 H), 5.47 (dd, J = 11.0, 5.0 Hz, 1 H), 3.74 (s, 3 H), 3.66 (s, 3 H), 3.51 (s, 3 H), 3.18 (dd, J = 12.7, 11.0 Hz, 1 H), 2.64 (dd, J = 12.7, 5.1 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 192.6, 163.1, 148.8, 148.2, 140.7, 132.5, 131.5, 130.7, 128.8, 128.5, 128.5, 127.8, 126.3, 122.8, 120.6, 112.8, 111.3, 110.5, 92.2, 90.7, 87.3, 80.1, 58.8, 55.8, 55.6, 55.5, 45.5 ppm. IR (KBr): $\tilde{\nu}$ = 2932, 1674, 1599, 1515, 1264, 1236, 1092, 1028, 804, 757, 696, 615 cm^{-1}. HRMS (ESI): calcd. for $C_{34}H_{30}O_5$ $[M + Na]^+$ 541.1985; found 541.1980.

[2-(3,4-Dimethoxyphenyl)-5-phenyl-3-(phenylethynyl)tetrahydrofuran-3-yl](thiophen-2-yl)methanone (3ma): Yellow oil; yield (with **4ma**): 169.1 mg (95 %). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, J = 3.6 Hz, 1 H), 7.42 (d, J = 4.8 Hz, 1 H), 7.36–7.30 (m, 2 H), 7.25–7.05 (m, 9 H), 6.98 (d, J = 8.0 Hz, 1 H), 6.84 (t, J = 4.4 Hz, 1 H), 6.67 (d, J = 8.3 Hz, 1 H), 5.69 (s, 1 H), 5.61 (dd, J = 10.1, 5.9 Hz, 1 H), 3.71 (s, 3 H), 3.59 (s, 3 H), 2.97 (dd, J = 12.4, 5.9 Hz, 1 H), 2.78 (dd, J = 12.4, 10.1 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 187.7, 148.7, 148.0, 141.9, 141.8, 134.9, 134.7, 131.2, 130.5, 128.5, 128.4, 128.3, 127.7, 127.6, 125.6, 122.3, 120.1, 110.6, 110.0, 90.7, 87.9, 86.3, 80.0, 60.3, 55.7, 55.5, 49.2 ppm. IR (KBr): $\tilde{\nu}$ = 3001, 1655, 1515, 1411, 1265, 1161, 1140, 1028, 912, 758, 731, 697 cm^{-1}. HRMS (ESI): calcd. for $C_{31}H_{26}O_4S$ $[M + Na]^+$ 517.1444; found 517.1446.

[2-(3,4-Dimethoxyphenyl)-5-phenyl-3-(phenylethynyl)tetrahydrofuran-3-yl](thiophen-2-yl)methanone (4ma): Yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.96 (dd, J = 3.9, 0.9 Hz, 1 H), 7.64 (d, J = 7.3 Hz, 2 H), 7.53–7.48 (m, 2 H), 7.47–7.33 (m, 7 H), 6.91 (dd, J = 4.8, 4.1 Hz, 1 H), 6.84 (dd, J = 8.3, 1.8 Hz, 1 H), 6.69 (d, J = 1.8 Hz, 1 H), 6.62 (d, J = 8.3 Hz, 1 H), 5.55 (s, 1 H), 5.45 (dd, J = 10.4, 5.9 Hz, 1 H), 3.76 (s, 3 H), 3.65 (s, 3 H), 3.30 (dd, J = 12.7, 10.5 Hz, 1 H), 2.73 (dd, J = 12.8, 5.9 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 187.6, 148.9, 148.3, 143.1, 140.4, 134.5, 133.9, 131.6, 129.7, 128.8, 128.6, 128.0, 127.4, 126.6, 122.7, 120.3, 110.8, 110.5, 91.7, 91.6, 87.3, 80.5, 59.1, 55.9, 55.7, 45.5 ppm. IR (KBr): $\tilde{\nu}$ = 2928, 1655, 1597, 1516, 1411, 1262, 1240, 1139, 1027, 780, 757, 730 cm^{-1}. HRMS (ESI): calcd. for $C_{31}H_{26}O_4S$ $[M + Na]^+$ 517.1444; found 517.1448.

1-[2-(3,4-Dimethoxyphenyl)-5-phenyl-3-(phenylethynyl)tetrahydrofuran-3-yl]pentan-1-one (3na): Yellow oil, inseparable from the minor isomer **4na**, **3na**/**4na** = 1:0.4; yield (with **4na**): 169.5 mg (90 %). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.57 (d, J = 7.8 Hz, 0.4 H), 7.45–7.39 (m, 1 H), 7.38–7.13 (m, 12.6 H), 7.06 (s, 1 H), 6.98–6.96 (m, 0.4 H), 6.91–6.81 (m, 1.4 H), 6.77–6.72 (m, 1.4 H), 5.53 (dd, J = 10.2, 6.0 Hz, 1 H), 5.48 (s, 1 H), 5.14 (s, 0.4 H), 5.09 (t, J = 8.2 Hz, 0.4 H), 3.79–3.77 (m, 5.4 H), 3.68 (s, 3 H), 2.94 (dd, J = 12.6, 9.7 Hz, 0.4 H), 2.78–2.70 (m, 1 H), 2.69–2.61 (m, 1.4 H), 2.58–2.42 (m, 2 H), 1.49–1.41 (m, 2 H), 1.25–1.12 (m, 2.8 H), 0.94–0.88 (m, 0.8 H), 0.77 (t, J = 7.2 Hz, 3 H), 0.61 (t, J = 7.2 Hz, 1.2 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 207.2, 207.1, 149.2, 148.8, 148.7, 148.4, 142.2, 140.4, 131.5, 131.5, 130.5, 128.6, 128.5, 128.5, 128.5, 128.4, 128.0, 127.7, 126.9, 125.7, 122.8, 122.6, 119.4, 119.3, 110.7, 110.2, 110.0, 109.9, 90.9, 90.5, 89.4, 87.4, 87.2, 85.8, 80.7, 80.4, 62.5, 59.7, 55.9, 55.8, 55.7, 48.6, 45.5, 41.5, 41.3, 25.7, 25.6, 22.2, 21.9, 13.9, 13.8 ppm. IR (KBr): $\tilde{\nu}$ = 2957, 1713, 1595, 1516, 1267, 1236, 1162, 1140, 1060, 1029, 758, 697 cm^{-1}. HRMS (ESI): calcd. for $C_{31}H_{33}O_4$ $[M + H]^+$ 469.2373; found 469.2373.

{4-[Cyclopropyl(phenyl)methylene]-6,7-dimethoxy-2-phenyl-3,3a,4,8b-tetrahydro-2*H*-indeno[1,2-*b*]furan-3a-yl}(phenyl)methanone (6ja): Methanone **3ja** (76.1 mg, 0.17 mmol) and iodobenzene (52.0 mg, 0.25 mmol) were added to DMF (2.0 mL), the reaction flask was flushed with Ar (3 ×), and then $Pd(OAc)_2$ (1.9 mg, 0.0085 mmol) and NaOAc (27.9 mg, 0.34 mmol) were added under Ar. The mixture was heated at 140 °C for 7 h until TLC showed the total consumption of **3ja**. After cooling to room temperature, water was added and the mixture was extracted with Et_2O (3 ×). The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc, 10:1) to give **6ja** (53.9 mg, 60 %) as a colorless solid, m.p. 211–212 °C, ^1H NMR (400 MHz, $CDCl_3$): δ = 7.63 (d, J = 7.7 Hz, 2 H), 7.37–7.22 (m, 5 H), 7.21–7.04 (m, 8 H), 7.00–6.95 (m, 1 H), 6.79 (s, 1 H), 6.34 (s, 1 H), 5.68 (s, 1 H), 5.19 (s, 1 H), 4.51 (dd, J = 10.8, 5.2 Hz, 1 H), 3.67 (s, 3 H), 3.49 (t, J = 11.8 Hz, 1 H), 3.11 (s, 3 H), 2.34 (dd, J = 12.4, 5.3 Hz, 1 H), 1.37 (m, 1 H), 0.31 (m, 1 H), 0.11 (m, 1 H), 0.01 (m, 1 H), –0.55 (m, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.8, 149.6, 141.4, 140.4, 137.5, 136.3, 135.9, 134.5, 134.3, 132.7, 130.1, 129.3, 129.0, 128.8, 128.7, 128.5, 128.0, 127.4, 126.8, 107.6, 106.1, 89.0, 79.3, 69.4, 55.9, 55.0, 45.5, 15.1, 4.8, 4.3 ppm. IR (KBr): $\tilde{\nu}$ = 1677, 1500, 1444,

1280, 1227, 695 cm^{-1}. HRMS (ESI): calcd. for $C_{36}H_{32}O_4$ $[M + Na]^+$ 551.2193; found 551.2196.

[4-(Diphenylmethylene)-6,7-dimethoxy-2-phenyl-3,3a,4,8b-tetrahydro-2*H*-indeno[1,2-*b*]furan-3a-yl](4-methoxyphenyl)methanone (6la): Methanone **3la** (106 mg, 0.2 mmol) and iodobenzene (61.2 mg, 0.3 mmol) were added to DMF (2.5 mL), the reaction flask was flushed with Ar (3 ×), and then $Pd(OAc)_2$ (2.2 mg, 0.01 mmol) and NaOAc (32.8 mg, 0.4 mmol) were added under Ar. The mixture was heated at 140 °C for 7 h until TLC showed total consumption of **3la**. After cooling to room temperature, water was added and the mixture was extracted with Et_2O (3 ×). The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc, 5:1) to give **6ja** (77.2 mg, 65 %) as a pale-yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.50 (d, J = 7.6 Hz, 2 H), 7.38–7.34 (m, 2 H), 7.32–7.14 (m, 8 H), 7.09–7.01 (m, 2 H), 6.95–6.90 (m, 3 H), 6.73 (d, J = 7.6 Hz, 2 H), 6.59 (d, J = 7.6 Hz, 2 H), 5.92 (s, 1 H), 5.90 (s, 1 H), 4.53 (t, J = 8.2 Hz, 1 H), 3.83 (s, 3 H), 3.78 (s, 3 H), 3.56 (dd, J = 12.8, 9.2 Hz, 1 H), 3.32 (s, 3 H), 2.50 (dd, J = 12.8, 7.2 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.3, 162.9, 150.6, 149.5, 144.2, 142.8, 141.5, 140.9, 135.6, 134.6, 133.2, 131.0, 129.8, 129.4, 129.4, 128.7, 128.6, 128.5, 128.0, 127.6, 127.4, 127.2, 112.9, 107.6, 106.9, 90.3, 80.0, 70.3, 56.1, 55.5, 55.2, 47.0 ppm. IR (KBr): $\tilde{\nu}$ = 1678, 1598, 1228, 697 cm^{-1}. HRMS (ESI): calcd. for $C_{40}H_{34}O_5$ $[M + Na]^+$ 617.2298; found 617.2300.

[6-(Benzyloxy)-4-(diphenylmethylene)-2-phenyl-3,3a,4,8b-tetrahydro-2*H*-indeno[1,2-*b*]furan-3a-yl](phenyl)methanone (6ac): Methanone **3ac** (80.1 mg, 0.15 mmol) and iodobenzene (61.2 mg, 0.3 mmol) were added to DMF (2.0 mL), the reaction flask was flushed with Ar (3 ×), and then $Pd(OAc)_2$ (3.4 mg, 0.015 mmol) and NaOAc (24.6 mg, 0.3 mmol) were added under Ar. The mixture was heated at 140 °C for 20 h. After cooling to room temperature, water was added and the mixture was extracted with Et_2O (3 ×). The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc, 20:1) to give unreacted **3ac** (43.0 mg) and **6ac** (22.8 mg, 54 % brsm) as a colorless solid, m.p. 191–192 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.51–7.46 (m, 2 H), 7.43–7.14 (m, 18 H), 7.05–6.98 (m, 2 H), 6.94–6.88 (m, 3 H), 6.53 (s, 1 H), 6.51 (s, 1 H), 6.03 (s, 1 H), 5.98 (s, 1 H), 4.57–4.47 (m, 3 H), 3.56 (dd, J = 12.6, 9.7 Hz, 1 H), 2.53 (dd, J = 12.6, 7.5 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 196.6, 159.3, 143.9, 142.5, 142.1, 141.4, 141.0, 137.2, 136.8, 135.3, 132.5, 129.7, 129.5, 129.4, 128.8, 128.7, 128.6, 128.5, 128.2, 128.1, 128.0, 127.7, 127.6, 127.5, 127.2, 126.8, 118.7, 109.6, 89.9, 80.0, 70.9, 69.5, 47.2 ppm. IR (KBr): $\tilde{\nu}$ = 1678, 1597, 1257, 1228, 733, 697 cm^{-1}. HRMS (ESI): calcd. for $C_{44}H_{34}O_3$ $[M + Na]^+$ 633.2400; found 633.2402.

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