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Metal-Catalyzed Formation of 1,3-Cyclohexadienes: A Catalyst-Dependent Reaction

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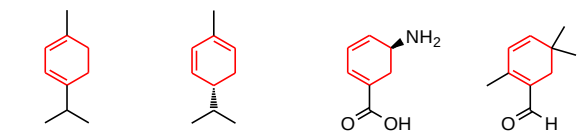
A metal-dependent and complementary catalytic method to synthesize the cyclohexadienes has been developed. When gold or indium salts were used as catalysts, 1,3-cyclohexadiene (1,3-CHD) could be obtained; when $Cu(OTf)_2$ was used as the catalyst, however, another isomer 2,4-cyclohexadiene (2,4-CHD) was furnished instead.

Introduction

1,3-Cyclohexadiene (1,3-CHD) is the core structure of many naturally occurring and biologically active substances, such as α-Terpinene,[1] α-Phellandrene,[2] Gabaculine[3] and Safranal[4] (Scheme 1). Among them, both α-Terpinene and α-Phellandrene are monoterpenoids, which are the raw materials of many flavor and fragrance.[1,2] Gabaculine, a naturally occurring neurotoxin which was first isolated from the bacteria Streptomyces toyacaensis, is a potent and irreversible GABA transaminase inhibitor.[3] For Safranal, it is the main constituent responsible for the aroma of saffron.[4] However, due to the easy rearrangement of the double bonds and difficulties in isolation of the isomers of CHD, it would be a great challenge to selectively and efficiently synthetize 1,3-CHD and its isomers in organic chemistry.



Scheme 1

To this end, we would like to report a metal-dependent method to selectively synthesize the isomers of CHD from the intermediate **B**, which was generated through metal-catalyzed reaction of enynals and alkenes (Scheme 2).[6]

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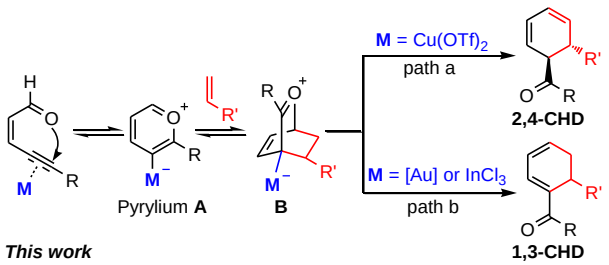


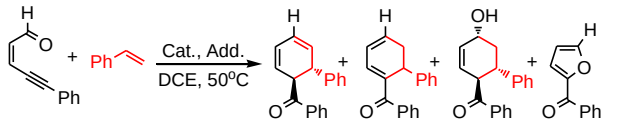
Scheme 2 Metal-catalyzed 1,3-cyclohexadiene.

Results and discussion

Initial efforts were made to systematically investigate different metal catalysts for the reaction of enynal **1a** with styrene **2a** in DCE at 50 °C (Table 1). It was found that this reaction is highly catalyst-dependent, four cyclic-products **3a-6a** could be afforded selectively when different metal salts were applied. For example, 1,3-cyclohexadiene **3a** could be obtained in 45% yield when $Cu(OTf)_2$ was employed (entry 1). The low yield could be attributed to the isomerization of the starting material **1a**, as *trans*-**1a** was detected after reaction. When NHC-AuCl/Selectfluor[6,7] and $InCl_3$ were used as the catalysts[8] instead, another cyclohexadiene **4a**, which is the isomer of **3a**, could be obtained in 80% and 79% yields, respectively (entries 2-3). The salts of ZnI_2, $AgSbF_6$ and AgF could also be served as the catalysts of choice. In these cases, cyclohexenol **5a** was furnished in 58-74% yields (entries 4-6). It is supposed that trace amount of adventitious water in the system could mediate the reactions. Intriguingly, the catalysts of $CuCl_2{\cdot}2H_2O$ and $AgNO_3$ afforded the furyl ketone **6a** in 61% and 67% yields, respectively (entries 7-8).

As shown in Table 1, the reaction is highly dependent on the catalysts. The conditions of entries 1-3 could lead to the 1,3-CHD **3a** and **4a** selectively. Although gold and indium showed similar reaction results in producing 1,3-CHD **4a**, however, the indium showed better reaction scope and reproducibility to

Table 1. Optimization of Reaction Conditions.[a]



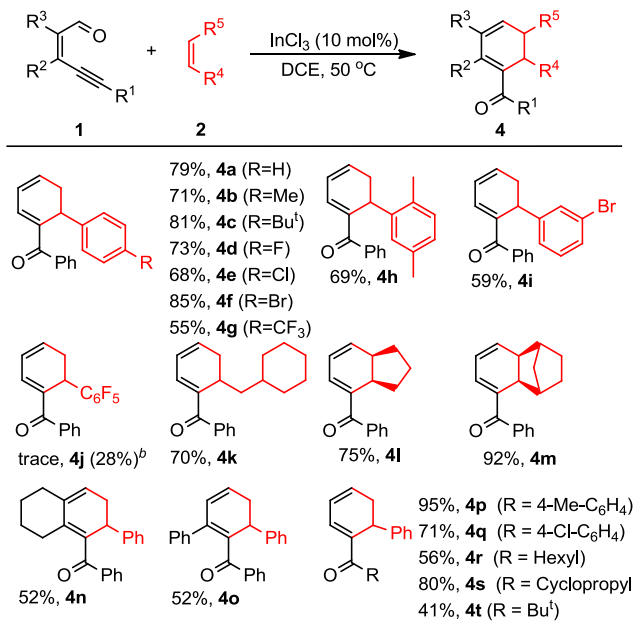
1a 2a 3a 4a 5a 6a

Entry	Cat.	Add.	3a	4a	5a	6a	Conv.
1[b]	$Cu(OTf)_2$	-	45%	-	-	-	> 99%
2[c,d]	IMes-AuCl	Selectfluor	-	80%	-	-	> 99%
3	$InCl_3$	-	-	79%	-	-	> 99%
4	ZnI_2	-	-	-	64%	-	> 99%
5	$AgSbF_6$	-	-	-	74%	-	> 99%
6	AgF	-	-	-	58%	-	> 99%
7	$CuCl_2 \cdot 2H_2O$	-	-	-	-	61%	> 99%
8	$AgNO_3$	-	-	-	-	67%	> 99%

[a] Unless otherwise noted, the reactions were performed in DCE at 50 °C for 24h using 10 mol% catalyst under N_2, **1/2** = 1:3. [**1**] = 0.25 M; The yield refers to isolated yield. IMes: 1,3-dimesityl-imidazol-2-ylidene; The stereochemistry of products **3a** and **5a** were determined by noe spectrum; [b] trans-**1a** could be detected (32 %) after reaction; [c] 80 °C; [d] 5 mol% IMes-AuCl, 15 mol% Selectfluor.

prepare 1,3-CHD **4a** in most cases (see SI). Therefore, the substrate scope was then examined with $InCl_3$ as catalyst. As summarized in Table 2, the catalytic process could be successfully applied to various enynals **1** and alkenes **2**. For example, in addition to styrene **2a**, different styrene derivatives could be effectively reacted with enynal **1a** as well (Table 2, **4a-4j**). The reaction was not very sensitive to the electronic properties and steric hindrance of the alkenes. For example, for the alkyl- or halogen-substituted styrene derivatives, the yields were typically higher than 60% (**4a-4i**).The electron-deficient 4-CF_3-styrene and bulky 2,5-dimethyl styrene gave the products **4g** and **4h** in 55% and 69%, both of which was slightly lower than their analogues **4a-4c**. However, for the extremely electron-deficient 2,3,4,5,6-pentafluorostyrene, only trace

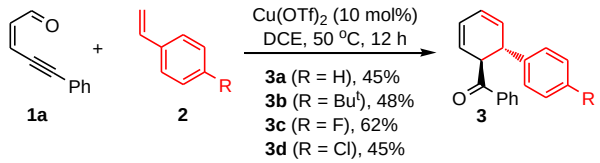
Table 2. Substrate Scopes.[a]



[a] The reaction was performed at 50 °C for 24 h using 10 mol % cat. under N_2; **1**:**2** = 1:3; [**1**] = 0.25 M, isolated yield. [b] 5 mol% IMes-AuCl and15 mol% Selectfluor was used instead.

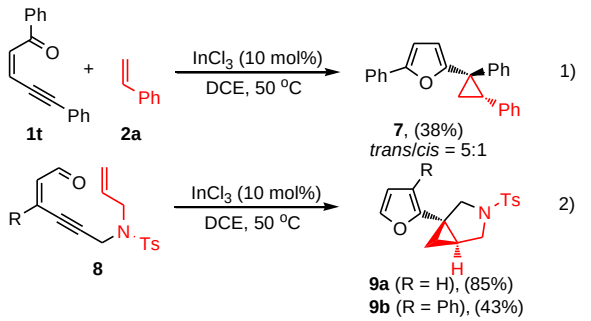
product **4j** was detected. However, the combination of IMes-AuCl/Selectfluor could enable the formation of **4j** in 28% yield. In addition to the styrene derivatives, the aliphatic alkenes could be served as good substrates as well and it could give the desired 1,3-CHDs **4k-4m** with yields ranging from 70% to 92%. Besides enynal **1a**, different derivatives could also react with styrene. For example, the enynals having substituents on the C=C double bonds gave the products in moderate yields (**4n**, **4o**). For the enynals with different substituents (electron-donating, electron-withdrawing, and alkyl groups) on the C≡C triple bonds, the reactions proceeded smoothly as well, furnishing the desired products **4p-4t** with yields ranging from 41% to 95%.

Having established the indium-catalyzed reaction of enynals and alkenes as a reliable and efficient synthetic process to construct the 1,3-CHD **4**, Our attention was then turned to the $Cu(OTf)_2$-catalyzed formation of 2,4-CHD **3**. With enynal **1a** as the standard substrate, the reactions functioned well for different styrene derivatives giving the desired 2,4-CHDs **3a-3d** in moderate yields (Scheme 3). It is worth to note that all the products **3** are formed in *trans*-isomer.



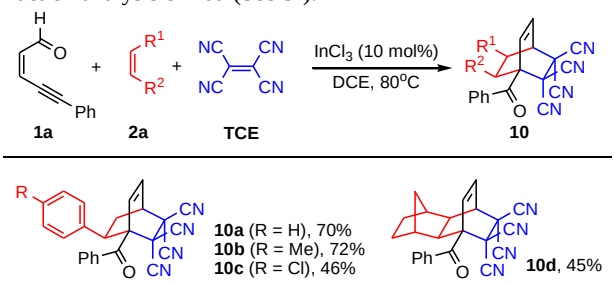
Scheme 3 $Cu(OTf)_2$-Catalyzed Reaction of **1a** with **2**.

Interestingly, when enynone **1t** and the intramolecular substrate enynal **8** were subjected to the same reaction conditions in Table 2, the cyclopropanation products **7** and **9** could be obtained instead in moderate to good yields (Scheme 4). These results could be attributed to the formation of carbene intermediate.



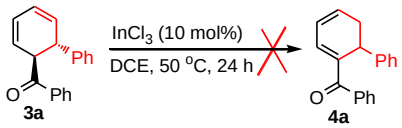
Scheme 4 $InCl_3$-Catalyzed Cyclopropanation of enynals.

Furthermore, when an electron-deficient dienophile (tetracyanoethylene, **TCE**) was added to trap the 1,3-cyclohexadiene **4**, the reaction occurred in one-pot, three-component manner, affording the bridged product **10** (Scheme 5). The structure and stereochemistry of the products were further confirmed by the X-ray diffraction analysis of **10a** (See SI).



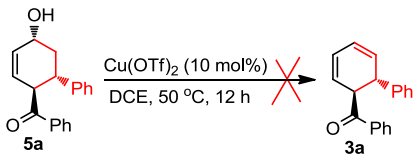
Scheme 5 Three-Component Reaction.

It seems that 1,3-CHD **4** is more stable than its isomer **3**, as the C=C double bond in the former molecule is conjugated with the carbonyl group.[9] One may expect that the formation of product **4** would come from the metal-catalyzed isomerization of its isomer **3**. To elucidate the potential relationship between **3** and **4**, a controlled reaction was then conducted. As shown in Scheme 6, 2,4-CHD **3a** remained unchanged upon treatment by $InCl_3$ in DCE at 50 °C for 24h, which indicated that the formation of **4a** did not come from the isomerization of **3a**, but directly from the catalytic process.



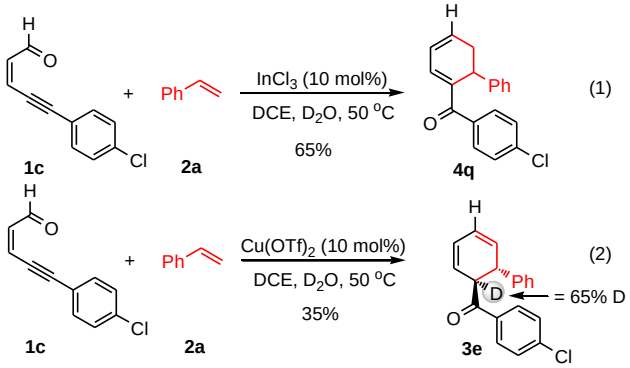
Scheme 6 The control reaction.

Furthermore, the controlled experiment also indicated that 2,4-CHD **3** did not come from the dehydration of cyclohexenol **5**. For example, cyclohexenol **5a** remained unchanged upon treatment by $Cu(OTf)_2$ in DCE at 50 °C for 12h. Therefore, the formation of **3a** should not come from the dehydration of **5a** (Scheme 7).



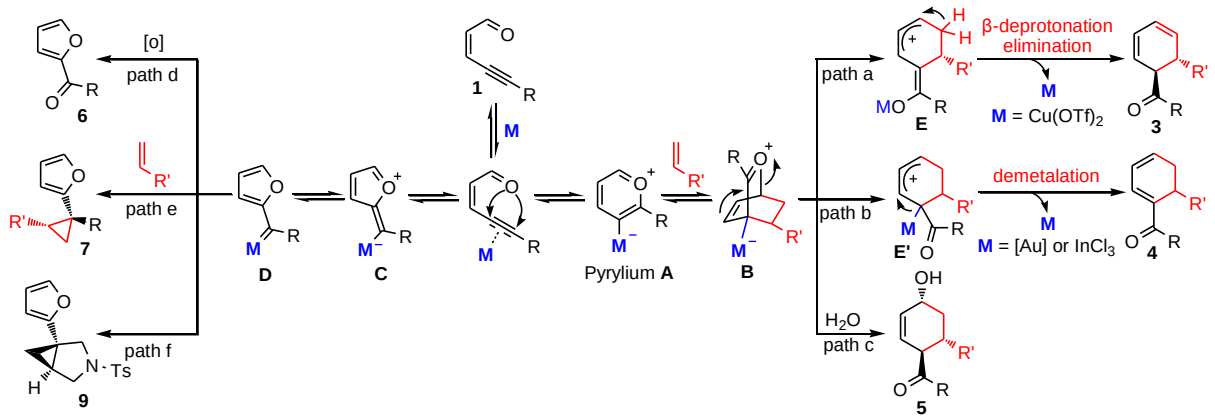
Scheme 7 The control reaction.

To gain more information about the reaction mechanism, additional D_2O was added in the reaction of **1c** and styrene. The olefinic carbon atom in product **4q** did not have the deuterium label. Instead, 65 % incorporation of deuterium was found at the position of the alkyl group of **3e** (Scheme 8).



Scheme 8 Deuterium-labeling experiments.

A plausible mechanism was then proposed in Scheme 9 based on the above controlled reaction results. The coordination of the triple bond of enynal **1** to [M] enhanced the electrophilicity of alkyne, and the subsequent nucleophilic attack of the carbonyl oxygen to the electron-deficient alkyne would form the 6-*endo*-dig- intermediate pyrylium[10] **A** or 5-*exo*-dig-intermediate **C**. A Diels-Alder reaction between pyrylium **A** and alkene **2** was followed to furnish the intermediate **B**. From the intermediate **B**, three different ways occurred. The break of C-O bond could lead to the enolate allyl cation **E** (path a, M = $Cu(OTf)_2$) or the allyl cation **E'** with C-M being intact (path b, M = [Au] or $InCl_3$). *β*-Deprotonation elimination of **E** or demetalation of **E'** selectively afforded to the isomers of 1,3-cyclohexadienes **3** and **4**. In addition, the intermediate **B** could also be trapped by the adventitious H_2O to give the cyclohexenol **5** (path c). The 5-*exo*-dig-intermediate **C** is equilibrium with furan carbene **D**. The carbine intermediate **D** can be oxidized into furyl ketone **6** (path d) or trapped by C=C to form furyl cyclopropanes **7** (path e) or **9** (path f). We believed that the formation of intermediates **A**-**D** are reversible and competitive with each other. The metals/catalysts could control the reaction pathway, thus furnished different products.



Scheme 9 Proposed Mechanism.

Conclusions

In summary, a metal-dependent and complementary catalytic method to synthesize the cyclohexadienes has been developed. When gold or indium was used as the catalyst, 1,3-cyclohexadiene (1,3-CHD) could be obtained. While $Cu(OTf)_2$ was applied as the catalyst, however, another isomer 2,4-cyclohexadiene (2,4-CHD) was furnished instead. In addition to cyclohexadienes **3** and **4**, cyclohexenol **5**, furyl ketone **6**, furyl cyclopropanes **7** or **9** could be selectively formed as well. We believe such metal-dependent reaction mechanism would render useful information to the organometallic chemists in understanding the catalytic behavior of different transition metals.

Experimental

General information

Unless specified, all reactions were carried out under an inert atmosphere of dry N_2 in Schlenk tube, solvents were purified by standard method. ^1H, ^{13}C, ^{19}F NMR spectra were recorded on a Bruker AVANCE 400 spectrometer (400 MHz for ^1H; 100 MHz for ^{13}C; 376 MHz for ^{19}F), ^1H NMR and ^{13}C NMR chemical shifts were determined relative to internal standard TMS at δ 0.0 and ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ as external standard. Chemical shifts (δ) are reported in ppm, and coupling constants (*J*) are in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d =doublet, t = triplet, q = quartet, m = multiplet, br = broad. Infrared (IR) spectra are recorded on a Nicolet 210 spectrophotometer. All reagents were used as received from commercial sources, unless specified otherwise, or prepared as described in the literature.

General procedure for copper -catalyzed tandem reaction of enynals with olefins

To a dichloroethane (DCE, 2 ml) suspension of $Cu(OTf)_2$ (10.8 mg, 0.03 mmol) in Schlenk tube with a magnetic bar under a nitrogen atmosphere was added olefin (**2**, 0.6 mmol) and enynals (**1**, 0.3 mmol), the reaction was stirred at 50 ^oC unless being noted. The reaction was monitored by TLC, then the solvent was evaporated under reduced pressure and the residue was purified by flash chromatography on silica gel (Hex/EtOAc = 20/1) to afford the product **3**.

(1,2-Dihydro-[1,1'-biphenyl]-2-yl)(phenyl)methanone (3a). Pale yellow oil; yield: 45% (35 mg); R_f = 0.38; IR (KBr) ν_{max} 3056.49, 2957.19, 2858.46, 1686.72, 1596.71, 1537.84, 1386.63, 1210.16, 947.53, 702.17; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.79 (d, *J* = 7.3 Hz, 2H), 7.45 (t, *J* = 6.8 Hz, 1H), 7.34 (t, *J* = 7.3 Hz, 2H), 7.25 (d, *J* = 6.9 Hz, 2H), 7.22 – 7.17 (m, 2H), 7.13 (d, *J* = 6.6 Hz, 1H), 5.98 (s, 2H), 5.82 (d, *J* = 8.2 Hz, 1H), 5.54 (d, *J* = 7.6 Hz, 1H), 4.35 (d, *J* = 8.6 Hz, 1H), 4.27 (d, *J* = 9.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 198.82, 144.12, 135.91, 133.07, 130.61, 128.69, 128.64, 128.24, 126.81, 125.14, 122.30, 121.86, 50.47, 40.88; HRMS (EI) calcd for $C_{19}H_{14}O$ $[M\text{-}H_2]^+$: 258.1045, Found: 258.1043.

(4'-(Tert-butyl)-1,2-dihydro-[1,1'-biphenyl]-2-yl)(phenyl)methanone (3b). Brown yellow oil; yield: 48% (45 mg); R_f = 0.36; IR (KBr) ν_{max} 3057.07, 2958.49, 2855.18, 1692.35, 1596.86, 1517.61, 1223.71, 932.67, 815.21, 708.78; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.79 (d, *J* = 7.4 Hz, 2H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.17 (t, *J* = 6.1 Hz, 2H), 5.97 (dd, *J* = 14.5, 6.6 Hz, 2H), 5.83 (dd, *J* = 8.7, 3.8 Hz, 1H), 5.54 (dd, *J* = 8.6, 4.1 Hz, 1H), 4.38 – 4.29 (m, 1H), 4.26 – 4.18 (m, 1H), 1.21 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 198.90, 149.58, 140.93, 136.06, 132.92, 130.74, 128.63, 128.61, 127.77, 125.49, 125.14, 122.06, 121.89, 50.47, 40.37, 34.40, 29.70; HRMS (EI) calcd for $C_{23}H_{24}O$ [M]: 316.1827, Found: 316.1831.

(4'-Fluoro-1,2-dihydro-[1,1'-biphenyl]-2-yl)(phenyl)methanone (3c). Pale yellow oil; yield: 62% (51 mg); R_f = 0.33; IR (KBr) ν_{max} 3049.15, 2928.07, 2854.30, 1661.55, 1596.03, 1443.43, 1250.46, 953.71, 724.50, 697.93; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.79 (d, *J* = 7.9 Hz, 2H), 7.47 (t, *J* = 7.3 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.21 (dd, *J* = 7.9, 6.3 Hz, 2H), 6.88 (t, *J* = 8.5 Hz, 2H), 6.07 – 5.91 (m, 2H), 5.85 – 5.74 (m, 1H), 5.61 – 5.48 (m, 1H), 4.36 – 4.20 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 198.73, 161.75 (d, $J_{C\text{-}F}$= 243.0Hz), 139.88, 135.90, 133.12, 130.55, 129.72 (d, $J_{C\text{-}F}$= 7.9Hz), 128.64 (d, $J_{C\text{-}F}$= 12.1Hz), 125.07, 122.50, 121.89, 115.44, 115.23, 50.70, 40.24; ^{19}F NMR (376 MHz, $CDCl_3$) *δ* -116.27; HRMS (EI) calcd for $C_{19}H_{13}FO$ $[M\text{-}H_2]^+$: 276.0950, Found: 276.0954.

(4'-Chloro-1,2-dihydro-[1,1'-biphenyl]-2-yl)(phenyl)methanone (3d). Brown yellow oil; yield: 45% (39 mg); R_f = 0.35; IR (KBr) ν_{max} 3042.12, 2921.44, 2854.81, 1660.30, 1528.62, 1401.66, 1384.31, 1105.97, 699.84, 619.39; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.79 (d, *J* = 7.3 Hz, 2H), 7.47 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.20 – 7.14 (m, 4H), 6.06 – 5.95 (m, 2H), 5.77 (dd, *J* = 10.1, 2.7 Hz, 1H), 5.59 – 5.49 (m, 1H), 4.33 – 4.22 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 198.48, 142.67, 135.82, 133.14, 132.53, 130.21, 129.63, 128.71, 128.68, 128.58, 125.06, 122.66, 121.86, 50.51, 40.31; HRMS(EI)calcd for $C_{19}H_{13}ClO$ $[M\text{-}H_2]^+$: 292.0655, Found: 292.0657.

(4-Chlorophenyl)(2-deuterio-1,2-dihydro-[1,1'-biphenyl]-2-yl)methanone (3e). Pale yellow oil; yield: 35%(23 mg); R_f = 0.33 (Hex/EtOAc = 20/1); IR (KBr) ν_{max} 3054.27, 2918.95, 2850.03, 1679.28, 1588.17, 1489.53, 1384.00, 1109.57, 701.39, 618.86; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.3 Hz, 3H), 7.22 (s, 6H), 7.14 (d, *J* = 7.5 Hz, 2H), 6.00 (t, *J* = 9.2 Hz, 2H), 5.83 (s, 1H), 5.50 (d, *J* = 9.0 Hz, 1H), 4.28 (s, 0.3H), 4.22 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.82, 143.88, 139.50, 134.31, 131.04, 130.61, 129.99, 128.96, 128.64, 128.16, 126.88, 126.06, 125.38, 122.31, 121.49, 50.54, 41.10; HRMS (EI)calcd for $C_{19}H_{14}DClO$ $[M]^+$: 295.0874, Found: 295.0877.

General procedure for Indium-catalyzed tandem reaction of enynals with olefins

To a dichloroethane (DCE, 2 ml) suspension of $InCl_3$ (6.5 mg, 0.03 mmol) in schlenk tube with a magnetic bar under a nitrogen atmosphere was added olefin (**2**, 0.9 mmol) and enynals (**1**, 0.3 mmol), the reaction was stirred at 50 ℃ unless being noted. The reaction was monitored by TLC, then the solvent was evaporated under reduced pressure and the residue was purified by flash chromatography on silica gel (Hex/EtOAc = 20/1) to afford the product **4**.

(1,6-Dihydro-[1,1'-biphenyl]-2-yl)(phenyl)methanone (4a)[11]**.** Pale yellow oil; yield: 79% (61 mg); R_f = 0.33; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.54 (d, *J* = 7.5 Hz, 2H), 7.40 (d, *J* = 6.9 Hz, 1H), 7.34 (d, *J* = 7.5 Hz, 2H), 7.25 (d, *J* = 7.5 Hz, 2H), 7.19 – 7.15 (m, 2H), 7.11 (d, *J* = 7.3 Hz, 1H), 6.73 (d, *J* = 5.0 Hz, 1H), 6.14 – 6.01 (m, 2H), 4.30 – 4.20 (m, 1H), 2.86 (dd, *J* = 18.6, 10.4 Hz, 1H), 2.65 – 2.55 (m,1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 196.86, 143.17, 138.71, 137.48, 137.07, 133.01, 132.07, 131.41, 129.05, 128.43, 128.11, 127.23, 126.59, 123.84, 35.34, 32.03.

(4'-Methyl-1,6-dihydro-[1,1'-biphenyl]-2-yl)(phenyl)methanone (4b). Pale yellow oil; yield: 71% (58 mg); R_f = 0.30; IR (KBr) ν_{max} 3035.60, 2922.95, 2860.17, 1639.78, 1564.76, 1508.48, 1271.00, 812.09, 742.08, 702.71; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.68 (d, *J* = 7.4 Hz, 2H), 7.53 (t, *J* = 7.3 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 2H), 7.27 (d, *J* = 7.9 Hz, 2H), 7.12 (d, *J* = 7.7 Hz, 2H), 6.85 (d, *J* = 5.1 Hz, 1H), 6.25 – 6.12 (m, 2H), 4.35 (d, *J* = 8.7 Hz, 1H), 2.97 (dd, *J* = 18.5, 10.3 Hz, 1H), 2.71 (ddd, *J* = 18.5, 4.9, 2.7 Hz, 1H),2.34(s,3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 196.88, 140.16, 138.79, 137.69, 136.93, 136.10, 133.02, 131.40, 129.17, 129.09, 128.12, 127.15, 123.87, 35.01, 32.17, 21.06; HRMS (EI) calcd for $C_{20}H_{18}O$ [M]: 274.1358, Found: 274.1360.

(4'-(Tert-butyl)-1,6-dihydro-[1,1'-biphenyl]-2-yl)(phenyl)methanone (4c). Yellow oil; yield: 81% (76 mg); R_f = 0.32; IR (KBr) ν_{max} 3058.13, 2959.27, 2856.56, 1723.10, 1567.19, 1455.90, 1404.68, 1269.77, 1018.41, 705.42; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.55 (d, *J* = 7.2 Hz, 2H), 7.41 (t, *J* = 7.3 Hz, 1H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.22

– 7.14 (m, 4H), 6.73 (d, *J* = 5.2 Hz, 1H), 6.13 – 6.00 (m, 2H), 4.23 (dd, *J* = 10.2, 2.5 Hz, 1H), 2.89 – 2.77 (m, 1H), 2.61 (ddd, *J* = 18.5, 5.2, 2.7 Hz, 1H), 1.20 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.92, 149.20, 139.94, 138.81, 137.62, 137.04, 133.14, 131.34, 129.09, 128.08, 126.84, 125.30, 123.82, 34.66, 34.35, 32.01, 31.38; HRMS (EI) calcd for $C_{23}H_{22}O$ [M-H_2]$^+$: 314.1671, Found: 314.1668.

(4'-Fluoro-1,6-dihydro-[1,1'-biphenyl]-2-yl)(phenyl)methanone (4d). Pale yellow oil; yield: 73% (60 mg); R_f = 0.35; IR (KBr) ν_{max} 3054.37, 2923.59, 2857.00, 1634.52, 1505.76, 1269.07, 1229.19, 1163.58, 830.49, 705.44; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.1 Hz, 2H), 7.41 (t, *J* = 6.9 Hz, 1H), 7.33 (t, *J* = 7.1 Hz, 2H), 7.20 (s, 2H), 6.85 (t, *J* = 8.2 Hz, 2H), 6.74 (d, *J* = 4.1 Hz, 1H), 6.08 (d, *J* = 11.2 Hz, 2H), 4.21 (d, *J* = 10.1 Hz, 1H), 2.84 (dd, *J* = 18.2, 10.4 Hz, 1H), 2.55 (d, *J* = 18.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.79, 161.70 (d, J_{C-F} = 242.6Hz), 138.89, 138.59, 137.35, 137.19, 132.97, 131.52, 129.02, 128.68 (d, J_{C-F} = 7.8Hz), 128.18, 123.93, 115.20 (d, J_{C-F} = 21.3Hz), 34.67, 32.09; ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.67; HRMS (EI) calcd for $C_{19}H_{15}FO$ [M]: 278.1107, Found: 278.1106 .

(4'-Chloro-1,6-dihydro-[1,1'-biphenyl]-2-yl)(phenyl)methanone (4e). Pale yellow oil; yield: 68% (59 mg); R_f = 0.35; IR (KBr) $\nu_{max.}$ 3075.12, 2924.85, 2850.42, 1731.58, 1560.59, 1487.96, 1274.70, 1034.23, 928.91, 702.59; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.5 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.16 (q, *J* = 8.5 Hz, 4H), 6.75 (d, *J* = 5.3 Hz, 1H), 6.14 – 6.02 (m, 2H), 4.20 (dd, *J* = 10.3, 2.5 Hz, 1H), 2.85 (dd, *J* = 18.6, 10.3 Hz, 1H), 2.55 (ddd, *J* = 18.6, 5.4, 2.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.69, 141.68, 138.52, 137.27, 137.07, 132.91, 132.29, 131.52, 128.99, 128.61, 128.55, 128.17, 123.94, 34.91, 31.91; HRMS (EI) calcd for $C_{19}H_{15}ClO$ [M]: 294.0811, Found: 294.0810.

(4'-Bromo-1,6-dihydro-[1,1'-biphenyl]-2-yl)(phenyl)methanone (4f). Yellow oil; yield: 85% (86 mg); R_f = 0.36; IR (KBr) ν_{max} 3056.78, 2924.64, 2858.43, 1719.93, 1656.25, 1589.77, 1483.95, 1271.98, 1070.10, 704.30; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.5 Hz, 2H), 7.42 (t, *J* = 7.2 Hz, 1H), 7.31 (dd, *J* = 19.7, 7.7 Hz, 4H), 7.12 (d, *J* = 7.9 Hz, 2H), 6.75 (d, *J* = 5.1 Hz, 1H), 6.08 (d, *J* = 11.5 Hz, 2H), 4.18 (d, *J* = 9.7 Hz, 1H), 2.85 (dd, *J* = 18.3, 10.3 Hz, 1H), 2.54 (d, *J* = 18.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.64, 142.23, 138.51, 137.29, 136.99, 132.89, 131.52, 131.51, 129.02, 128.99, 128.18, 123.96, 120.39, 35.00, 31.85; HRMS (EI) calcd for $C_{19}H_{15}BrO$ [M]: 338.0306, Found: 338.0301.

Phenyl(4'-(trifluoromethyl)-1,6-dihydro-[1,1'-biphenyl]-2-yl)-methanone (4g). Pale yellow oil; yield: 55% (54 mg); R_f = 0.31; IR (KBr) ν_{max} 3061.76, 2924.22, 2848.49, 1726.27, 1565.95, 1452.10, 1324.47, 1274.43, 1121.20, 702.98; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.5 Hz, 2H), 7.44 (d, *J* = 7.8 Hz, 3H), 7.35 (d, *J* = 7.1 Hz, 4H), 6.81 (d, *J* = 5.2 Hz, 1H), 6.25 – 5.98 (m, 2H), 4.28 (d, *J* = 9.9 Hz, 1H), 2.88 (dd, *J* = 18.5, 10.4 Hz, 1H), 2.57 (d, *J* = 18.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.56, 147.23, 138.39, 137.75, 136.62, 132.92, 131.61, 129.00, 128.22, 127.56, 125.42 (m, J_{C-F} = 3.8Hz), 124.06, 35.51, 31.83, 22.13; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.37; HRMS (EI) calcd for $C_{20}H_{15}F_3O$ [M]: 328.1075, Found: 328.1079.

(2',5'-Dimethyl-1,6-dihydro-[1,1'-biphenyl]-2-yl)(phenyl)methanone (4h). Brown yellow oil; yield: 69% (59 mg); R_f = 0.32; IR (KBr) ν_{max} 3051.19, 2921.71, 2856.98, 1725.05, 1566.51, 1451.59, 1272.30, 929.16, 733.08, 701.74; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d,*J* = 7.4 Hz, 2H), 7.43 – 7.37 (m, 1H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.02 – 6.92 (m, 2H), 6.81 (d, *J* = 6.0 Hz, 2H), 6.10 (s, 1H), 5.97 (d, *J* = 4.2 Hz, 1H), 4.43 (dd, *J* = 11.1, 2.9 Hz, 1H), 2.82 (dd, *J* = 18.3, 11.4 Hz, 1H), 2.40 (d, *J* = 19.0 Hz, 1H), 2.35 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.71, 140.84, 138.71, 137.93, 137.24, 135.03, 132.63, 132.00, 131.36, 130.67, 129.02, 128.09, 127.19, 127.15, 123.60, 31.44, 31.14, 21.25, 19.26; HRMS (EI) calcd for $C_{20}H_{18}O$ [M]: 288.1514, Found: 288.1516.

(3'-Bromo-1,6-dihydro-[1,1'-biphenyl]-2-yl)(phenyl)methanone (4i). Pale yellow oil; yield: 59% (60 mg); R_f = 0.32; IR (KBr) $\nu_{max.}$ 3055.73, 2922.94, 2854.50, 1631.83, 1560.93, 1460.08, 1271.60, 1068.59, 735.47, 695.80; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.50 (m, 2H), 7.43 (dd, *J* = 13.0, 5.5 Hz, 1H), 7.35 (dd, *J* = 14.6, 7.0 Hz, 3H), 7.24 (d, *J* = 7.9 Hz, 1H), 7.18 – 7.14 (m, 1H), 7.04 (t, *J* = 7.8 Hz, 1H), 6.78 (d, *J* = 5.4 Hz, 1H), 6.21 – 5.97 (m, 2H), 4.20 (dd, *J* = 10.3, 2.5 Hz, 1H), 2.85 (ddt, *J* = 18.3, 10.3, 2.6 Hz, 1H), 2.56 (ddd, *J* = 18.6, 5.6, 2.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.55, 145.51, 138.51, 137.60, 136.69, 132.92, 131.52, 130.26, 130.02, 129.74, 129.00, 128.19, 126.00, 124.01, 122.50, 35.19, 31.90; HRMS (EI) calcd for $C_{19}H_{15}BrO$ [M]: 338.0306; Found: 338.0309.

(2',3',4',5',6'-Pentafluoro-1,6-dihydro-[1,1'-biphenyl]-2-yl)(phenyl)methanone (4j). Brown yellow oil; yield: 28% (29 mg); R_f = 0.29; IR (KBr) ν_{max} 3056.28, 2924.44, 2864.21, 1642.90, 1501.48, 1401.21, 1274.77, 1126.44, 705.11, 619.38; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.4 Hz, 2H), 7.46 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 2H), 6.63 (d, *J* = 3.8 Hz, 1H), 6.25 – 6.16 (m, 1H), 6.16 – 6.07 (m, 1H), 4.50 (dd, *J* = 14.3, 10.4 Hz, 1H), 2.69 – 2.45 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.78, 137.37, 136.86, 135.83, 132.76, 132.20, 129.42, 128.29, 123.78, 30.25, 30.05; ^{19}F NMR (376 MHz, $CDCl_3$) δ -141.16, -141.18, -141.21, -141.23, -157.59, -157.65, -157.70, -162.51, -162.53, -162.57, -162.58, -162.62, -162.64; HRMS (EI) calcd for $C_{19}H_{11}F_5O$ [M]: 350.0730, Found: 350.0735.

(6-(Cyclohexylmethyl)cyclohexa-1,3-dien-1-yl)(phenyl)methanone (4k). Pale yellow oil; yield: 70% (59 mg); R_f = 0.32; IR (KBr) $\nu_{max.}$ 3057.48, 2922.03, 2851.58, 1663.01, 1588.05, 1449.13, 1266.32, 1072.80, 928.32, 705.01; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.6 Hz, 2H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.34 (t, *J* = 7.2 Hz, 2H), 6.46 (d, *J* = 4.4 Hz, 1H), 6.01 (s, 2H), 3.06 (s, 1H), 2.44 – 2.28 (m, 2H), 1.76 (d, *J* = 12.8 Hz, 1H), 1.68 – 1.49 (m, 5H), 1.37 – 1.25 (m, 2H), 1.18 – 1.00 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.29, 140.50, 139.02, 136.07, 132.91, 131.22, 129.01, 128.04, 123.57, 38.43, 34.81, 34.20, 32.64, 27.78, 26.66, 26.61, 26.42, 26.29; HRMS (EI) calcd for C20H24O [M]: 280.1827, Found: 280.1825.

Phenyl(2,3,3a,7a-tetrahydro-1H-inden-4-yl)methanone (4l). Pale yellow oil; yield: 75% (50 mg); R_f = 0.38; IR (KBr) ν_{max} 2957.05, 2925.60, 2852.12, 1640.62, 1561.97, 1447.15, 1383.94, 1104.89, 701.34, 619.20; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.52 (m, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.34 (t, *J* = 7.4 Hz, 2H), 6.44 – 6.38 (m, 1H), 5.85 (dd, *J* = 3.3, 1.8 Hz, 2H), 3.08 (dt, *J* = 11.3, 8.9 Hz, 1H), 2.99 – 2.89 (m, 1H), 2.18 (ddd, *J* = 12.1, 7.2, 3.5 Hz, 1H), 2.09 (dt, *J* = 14.0, 7.8 Hz, 1H), 1.61 (ddd, *J* = 12.4, 9.9, 6.2 Hz, 1H), 1.49 – 1.41 (m, 2H), 1.39 – 1.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.94, 139.20, 139.12, 139.03, 134.53, 131.19, 128.96, 128.04, 120.72, 38.74, 36.12, 34.42, 34.37, 22.98; HRMS (EI) calcd for $C_{16}H_{16}O$ [M]: 224.1201, Found: 224.1202.

(1,2,3,4,4a,8a-Hexahydro-1,4-methanonaphthalen-5-yl)(phenyl)methanone (4m). Pale yellow oil; yield: 92% (69 mg); R_f = 0.30; IR (KBr) ν_{max} 3054.12, 2952.00, 2873.57, 1641.71, 1569.84, 1451.32, 1265.82, 928.55, 729.37, 702.49; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.51 (m, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.33 (t, *J* = 7.4 Hz, 2H), 6.24 (d, *J* = 5.9 Hz, 1H), 5.78 (dd, *J* = 9.5, 4.2 Hz, 1H), 5.68 (ddd, *J* = 9.5, 5.9, 1.7 Hz, 1H), 3.11 (d, *J* = 12.3 Hz, 1H), 2.66 (dd, *J* = 12.2, 3.2 Hz, 1H), 2.11 (d, *J* = 8.0 Hz, 2H), 1.70 (d, *J* = 9.7 Hz, 1H), 1.55

– 1.47 (m, 3H), 1.43 – 1.38 (m, 1H), 1.24 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.27, 139.27, 136.61, 136.39, 135.50, 131.28, 128.91, 128.05, 120.85, 45.60, 45.55, 44.88, 41.21, 34.81, 30.67, 30.36; HRMS (EI) calcd for $C_{18}H_{18}O$ [M]: 250.1358, Found: 250.1359.

Phenyl(2-phenyl-2,3,5,6,7,8-hexahydronaphthalen-1-yl)methanone (4n). Yellow oil; yield: 52% (49 mg); R_f = 0.36; IR (KBr) ν_{max} 3026.36, 2926.19, 2857.48, 1668.87, 1597.36, 1384.34, 1242.73, 1096.58, 700.51, 618.42; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 7.6 Hz, 2H), 7.40 (t, J = 7.3 Hz, 1H), 7.30 (t, J= 7.5 Hz, 2H), 7.14 – 7.08 (m, 4H), 7.03 (d, J = 6.5 Hz, 1H), 5.75 (s, 1H), 3.89 (s, 1H), 2.43 – 2.27 (m, 2H), 2.20 (d, J = 15.1 Hz, 1H), 2.15 – 2.02 (m, 4H), 1.80 (dt, J = 11.3, 5.3 Hz, 1H), 1.67 – 1.55 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.86, 142.96, 137.86, 136.55, 133.63, 133.07, 132.68, 129.01, 128.62, 128.44, 128.10, 126.29, 44.32, 31.66, 28.68, 27.49, 25.87, 23.02; HRMS (EI) calcd for $C_{23}H_{23}O$ $[M+H]^+$: 315.1743, Found: 315.1734.

(1',6'-dihydro-[1,1':3',1''-terphenyl]-2'-yl)(phenyl)methanone (4o). Yellow oil; yield: 52% (52 mg); R_f = 0.33; IR (KBr) ν_{max} 3058.80, 2924.45, 2851.59, 1642.72, 1578.39, 1492.40, 1238.46, 1073.31, 736.70, 698.22; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 7.9 Hz, 2H), 7.28 (d, J = 7.6 Hz, 2H), 7.18 – 7.06 (m, 7H), 6.98 (t, J = 7.3 Hz, 4H), 6.25 (d, J = 9.7 Hz, 1H), 6.09 – 5.98 (m, 1H), 4.11 (dd, J = 9.6, 5.2 Hz, 1H), 2.98 – 2.85 (m, 1H), 2.63 (dt, J = 18.1, 5.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.84, 142.83, 139.68, 139.35, 137.84, 134.31, 131.89, 129.11, 129.07, 128.42, 128.33, 128.03, 127.75, 127.68, 127.67, 126.72, 41.17, 31.64; HRMS (MALDI/DHB) calcd for $C_{25}H_{21}O$ $[M+H]^+$: 337.1586 ±0.002, Found: 337.15869.

(1,6-Dihydro-[1,1'-biphenyl]-2-yl)(p-tolyl)methanone (4p). Pale yellow oil; yield: 95% (78 mg); R_f = 0.33; IR (KBr) ν_{max} 3050.66, 2924.10, 2858.77, 1639.84, 1565.86, 1449.24, 1270.24, 1178.22, 742.54, 704.81; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.0 Hz, 2H), 7.24 (s, 1H), 7.13 (dt, J = 16.8, 7.9 Hz, 6H), 6.71 (d, J = 5.3 Hz, 1H), 6.11 – 5.98 (m, 2H), 4.23 (dd, J = 10.3, 2.9 Hz, 1H), 2.85 (ddd, J = 15.7, 9.0, 5.2 Hz, 1H), 2.58 (ddd, J = 18.5, 5.3, 3.1 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.63, 143.29, 142.07, 137.65, 136.30, 135.92, 132.61, 129.30, 128.80, 128.41, 127.25, 126.54, 123.83, 35.58, 32.03, 21.53; HRMS (EI) calcd for $C_{20}H_{18}O$ [M]: 274.1358, Found: 274.1362.

(4-Chlorophenyl)(1,6-dihydro-[1,1'-biphenyl]-2-yl)methanone (4q). White solid (m.p.83℃); yield: 71% (62 mg); R_f = 0.35; IR (KBr) ν_{max} 3056.43, 2920.63, 2856.42, 1682.32, 1583.12, 1481.11, 1396.18, 1099.04, 751.11, 615.01; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.2 Hz, 2H), 7.22 (d, J = 7.3 Hz, 2H), 7.16 (t, J = 7.3 Hz, 2H), 7.12 – 7.07 (m, 1H), 6.69 (d, J = 4.3 Hz, 1H), 6.07 (s, 2H), 4.21 (d, J = 8.5 Hz, 1H), 2.84 (dd, J = 18.6, 10.4 Hz, 1H), 2.59 (d, J = 18.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.52, 143.10, 137.76, 137.36, 136.98, 136.94, 133.35, 130.49, 128.50, 128.45, 127.19, 126.69, 123.73, 35.47, 32.01; HRMS (EI) calcd for $C_{19}H_{15}ClO$ [M]: 294.0811, Found: 294.0813.

1-(1,6-Dihydro-[1,1'-biphenyl]-2-yl)heptan-1-one (4r). Pale yellow oil; yield: 56% (45 mg); R_f = 0.35; IR (KBr) ν_{max} 2958.92, 2926.43, 2856.19, 1659.59, 1565.79, 1493.39, 1275.19, 1182.05, 751.25, 697.83; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (d, J = 3.7 Hz, 4H), 7.06 (d, J = 5.5 Hz, 2H), 6.15 – 6.06 (m, 1H), 6.04 – 5.95 (m, 1H), 4.07 (d, J = 10.2 Hz, 1H), 2.75 (dd, J = 18.3, 10.4 Hz, 1H), 2.53 (dt, J = 18.5, 6.6 Hz, 3H), 1.51 – 1.43 (m, 2H), 1.16 (s, 6H), 0.78 (t, J = 6.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.57, 143.02, 137.63, 133.06, 132.90, 128.29, 127.24, 126.48, 123.93, 77.38, 77.06, 76.74, 37.37, 34.35, 32.05, 31.66, 29.02, 24.86, 22.52, 14.05; HRMS (EI) calcd for $C_{16}H_{16}O$ [M]: 269.1905, Found: 269.1900.

Cyclopropyl(1,6-dihydro-[1,1'-biphenyl]-2-yl)methanone (4s). Pale yellow oil; yield: 80% (54 mg); R_f = 0.32; IR (KBr) ν_{max} 3068.52, 2920.54, 2854.64, 1733.21, 1555.45, 1457.14, 1263.94, 1207.13, 1023.88, 741.92; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, J = 5.5 Hz, 1H), 7.17 – 7.14 (m, 3H), 7.11 – 7.06 (m, 1H), 6.14 (ddd, J = 8.9, 5.5, 3.1 Hz, 1H), 6.07 – 5.93 (m, 1H), 4.08 (dd, J = 10.2, 1.6 Hz, 1H), 2.82 – 2.70 (m, 1H), 2.51 (ddd, J = 18.4, 6.0, 1.4 Hz, 1H), 2.34 – 2.25 (m, 1H), 0.96 – 0.87 (m, 2H), 0.78 – 0.69 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.78, 142.94, 138.26, 133.04, 132.75, 128.32, 127.24, 126.46, 124.08, 34.83, 32.14, 16.01, 10.81, 10.54; HRMS (EI) calcd for $C_{16}H_{16}O$ [M]: 224.1201, Found: 224.1197.

1-(1,6-Dihydro-[1,1'-biphenyl]-2-yl)-2,2-dimethylpro-pan-1-one. (4t). Pale yellow oil; yield: 41% (30 mg); R_f = 0.35; IR (KBr) ν_{max} 2958.58, 2924.85, 2851.36, 1647.09, 1564.74, 1453.18, 1268.55, 1147.64, 749.96, 701.09; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, J = 3.7 Hz, 4H), 7.19 (d, J = 4.2 Hz, 1H), 7.09 (d, J = 5.4 Hz, 1H), 6.18 (s, 1H), 6.01 (s, 1H), 4.14 (d, J = 9.9 Hz, 1H), 2.85 (dd, J = 17.8, 10.0 Hz, 1H), 2.58 (d, J = 18.2 Hz, 1H), 1.26 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.85, 142.17, 134.98, 130.31, 130.03, 127.23, 126.24, 125.35, 122.60, 76.31, 76.00, 75.68, 42.80, 35.30, 31.11, 27.63; HRMS (EI) calcd for $C_{17}H_{20}NaO$ $[M+Na]^+$: 263.1412, Found: 263.1406.

(5-Hydroxy-1,2,5,6-tetrahydro-[1,1'-biphenyl]-2-yl)(phenyl)methanone (5a). Pale yellow oil; yield: 73% (61 mg); R_f = 0.23 (Hex/EtOAc = 5/1); IR (KBr) ν_{max} 3604.83, 3027.12, 2921.47, 2848.98, 1685.77, 1597.62, 1493.23, 1284.34, 959.84, 698.81; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 7.9 Hz, 2H), 7.42 (t, J = 7.3 Hz, 1H), 7.29 (t, J = 7.6 Hz, 2H), 7.16 (t, J = 9.2 Hz, 4H), 7.05 (t, J = 6.8 Hz, 1H), 6.03 (dd, J = 6.3, 3.5 Hz, 1H), 5.78 (d, J = 9.9 Hz, 1H), 4.27 (d, J = 8.9 Hz, 1H), 4.21 (d, J = 3.0 Hz, 1H), 3.55 (dd, J = 16.3, 8.1 Hz, 1H), 2.06 (dd, J = 7.7, 3.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.50, 143.88, 136.31, 133.18, 130.68, 128.61, 128.50, 128.15, 127.55, 126.60, 63.73, 51.14, 37.68, 37.18; HRMS (EI) calcd for $C_{19}H_{18}NaO_2$ $[M+Na]^+$: 301.1204, Found: 301.1199.

1,2-diphenylcyclopropyl)-5-phenylfuran (7). Pale yellow oli; yield: 38% (38 mg); dr (Z:E) = 84:16; R_f = 0.4 (Hex/EtOAc = 50/1); IR (KBr) ν_{max} 2957.38, 2923.42, 2850.31, 1461.67, 1385.26, 1277.84, 913.14, 746.40, 697.89, 632.96; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 7.6 Hz, 2H), 7.30 (t, J = 7.5 Hz, 2H), 7.18 – 7.14 (m, 1H), 7.10 (s, 5H), 6.98 (t, J = 8.1 Hz, 3H), 6.76 (d, J = 7.4 Hz, 2H), 6.45 – 6.40 (m, 1H), 5.69 – 5.64 (m, 1H), 3.00 (t, J = 7.7 Hz, 1H), 2.06 (dd, J = 8.7, 5.6 Hz, 1H), 1.91 (t, J = 5.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.50, 152.46, 143.82, 138.04, 131.61, 131.03, 128.48, 128.42, 128.20, 127.83, 126.75, 126.60, 126.23, 123.49, 110.78, 105.50, 77.37, 77.05, 76.73, 32.89, 32.67, 19.53; HRMS (EI) calcd for $C_{25}H_{20}NaO_2$[M+Na]$^+$: 359.1412, Found: 359.1406.

Procedure for intramolecular reaction of tethered alkenyl enynals

To a dichloroethane (DCE, 2 ml) suspension of $InCl_3$ (6.3 mg, 0.03 mmol) in schlenk tube with a magnetic bar under a nitrogen atmosphere was added olefin (**8**, 0.3 mmol). the reaction was stirred at 50 ℃ unless being noted. The reaction was monitored by TLC, then the solvent was evaporated under reduced pressure and the residue was purified by flash chromatography on silica gel (Hex/EtOAc = 5/1) to afford the product **9**.

1-(Furan-2-yl)-3-tosyl-3-azabicyclo[3.1.0]hexane (9a). Brown yellow solid (m.p.89℃); yield: 85% (80 mg); R_f = 0.34; IR (KBr) ν_{max} 3056.45, 2922.68, 2851.24, 1734.39, 1598.32, 1462.51, 1349.00, 1165.19, 1101.18, 740.74; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.0 Hz, 2H), 7.27 (d, J = 7.9 Hz, 2H), 7.15 (s, 1H), 6.19 (s, 1H), 5.90 (d, J = 2.8 Hz, 1H), 3.69 (d, J = 9.0 Hz, 1H), 3.54 (d, J = 9.3 Hz, 1H), 3.25 (d, J = 9.0 Hz, 1H), 3.12 (dd, J = 9.2, 3.6 Hz, 1H), 2.37 (s, 3H), 1.69 (dt, J = 8.1, 4.2 Hz, 1H), 1.14 – 1.08 (m, 1H), 0.97 (t, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.45, 143.66, 141.11, 133.42, 129.73, 127.59, 110.40, 104.91, 51.23, 49.80, 25.70, 24.19, 21.55, 14.75; HRMS (EI) calcd for $C_{16}H_{17}NO_3S$ [M]: 303.0929, Found: 303.0925.

1-(3-Phenylfuran-2-yl)-3-tosyl-3-azabicyclo[3.1.0]hexane (9b). Brown yellow solid (m.p.124℃); yield: 43% (49 mg); R_f = 0.30; IR (KBr) ν_{max} 2955.99, 2919.67, 2848.53, 1737.17, 1564.40, 1446.96, 1346.64, 1162.84, 745.48, 700.54; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 7.9 Hz, 2H), 7.26 (d, J = 7.9 Hz, 2H), 7.20 (s, 6H), 6.39 (s, 1H), 3.72 (d, J = 9.2 Hz, 1H), 3.54 (d, J = 9.3 Hz, 1H), 3.15 (dd, J = 9.3, 3.7 Hz, 1H), 3.10 (d, J = 9.2 Hz, 1H), 2.39 (s, 3H), 1.63 (dt, J = 8.1, 4.0 Hz, 1H), 1.02 (t, J = 4.8 Hz, 1H), 0.92 – 0.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.61, 143.63, 141.15, 133.02, 132.91, 129.71, 128.38, 127.90, 127.64, 126.95, 123.73, 111.65, 52.62, 49.89, 24.48, 24.31, 21.58, 15.09; HRMS (EI) calcd for $C_{22}H_{21}NO_3S$ [M]: 379.1242, Found: 379.1246.

General procedure for Indium-catalyzed tandem reaction of enynals with olefins and tetracyanoethylene

To a dichloroethane (DCE, 2 ml) suspension of $InCl_3$ (6.3 mg, 0.03 mmol) in schlenk tube with a magnetic bar under a nitrogen atmosphere, was added olefin (**2**, 0.9 mmol) and enynals (**1**, 0.3 mmol) and tetracyanoethylene (0.6 mmol), the reaction was stirred at 80 ℃ unless being noted. The reaction was monitored by TLC, then the solvent was evaporated under reduced pressure and the residue was purified by flash chromatography on silica gel (Hex/EtOAc = 5/1) to afford the product **10**.

1-Benzoyl-7-phenylbicyclo[2.2.2]oct-5-ene-2,2,3,3-tetracarbonitrile (10a). CCDC Number 1014190, Brown yellow solid (m.p.159 ℃); yield: 70% (81 mg); R_f = 0.30; IR (KBr) ν_{max} 3057.09, 2925.18, 2856.70, 2232.62, 1715.02, 1620.45, 1380.52, 1096.28, 701.68, 620.75; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (t, J = 7.4 Hz, 1H), 7.18 (d, J = 4.6 Hz, 3H), 7.10 (t, J = 7.8 Hz, 2H), 7.06 – 6.99 (m, 2H), 6.98 – 6.91 (m, 1H), 6.80 (d, J = 8.5 Hz, 1H), 6.67 (d, J = 7.6 Hz, 2H), 4.05 (dd, J = 9.7, 5.0 Hz, 1H), 3.86 – 3.72 (m, 1H), 2.84 (dd, J = 14.3, 10.7 Hz, 1H), 2.19 – 2.07 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.21, 138.25, 135.92, 134.54, 132.54, 132.07, 129.60, 129.28, 128.97, 128.28, 127.94, 111.64, 111.31, 111.27, 111.18, 61.30, 47.22, 45.95, 43.17, 40.80, 28.61; HRMS (EI) calcd for $C_{25}H_{17}ON_4$ [M+H]$^+$: 389.1397, Found: 389.1386.

1-Benzoyl-7-(p-tolyl)bicyclo[2.2.2]oct-5-ene-2,2,3,3-tetracarbonitrile (10b). Brown solid (m.p.162 ℃); yield: 72% (87 mg); R_f = 0.28; IR (KBr) ν_{max} 3037.09, 2919.97, 2858.13, 2225.52, 1745.70, 1630.45, 1384.52, 1096.80, 700.68, 618.31; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (t, J = 7.3 Hz, 1H), 7.11 (t, J = 7.6 Hz, 2H), 6.98 (d, J = 7.8 Hz, 2H), 6.92 (dd, J = 13.2, 7.9 Hz, 3H), 6.78 (d, J = 8.6 Hz, 1H), 6.69 (d, J = 7.9 Hz, 2H), 4.02 (dd, J = 9.6, 5.0 Hz, 1H), 3.78 (s, 1H), 2.82 (dd, J = 15.1, 9.9 Hz, 1H), 2.20 (s, 3H), 2.13 – 2.05 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.30, 139.03, 135.94, 135.16, 134.43, 132.50, 132.12, 129.87, 129.43, 128.21, 128.08, 111.67, 111.33, 111.29, 111.23, 61.37, 47.16, 45.95, 42.83, 40.82, 28.60, 20.93; HRMS (EI) calcd for $C_{26}H_{19}ON_4$ [M+H]$^+$: 403.1546, Found: 403.1553.

1-Benzoyl-7-(4-chlorophenyl)bicyclo[2.2.2]oct-5-ene-2,2,3,3-tetracarbonitrile (10c). Brown solid (m.p.167 ℃); yield: 46% (58 mg); R_f = 0.25; IR (KBr) ν_{max} 3040.58, 2935.20, 2859.07, 2228.41, 1760.13, 1642.45, 1388.52, 1099.57, 702.26, 619.82; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (t, J = 7.4 Hz, 1H), 7.32 – 7.23 (m, 4H), 7.06 (d, J = 8.1 Hz, 3H), 6.94 (d, J = 8.6 Hz, 1H), 6.87 (d, J = 7.8 Hz, 2H), 4.12 (dd, J = 9.8, 5.1 Hz, 1H), 3.90 (s, 1H), 2.95 (dd, J = 14.5, 10.0 Hz, 1H), 2.21 – 2.08 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.62, 136.74, 135.69, 135.18, 134.77, 132.88, 131.91, 130.84, 129.38, 128.46, 128.02, 111.51, 111.18, 111.14, 110.99, 61.09, 47.20, 45.83, 42.53, 40.67, 28.79; HRMS (EI) calcd for $C_{25}H_{16}ON_4Cl$ [M+H]$^+$: 423.1007, Found: 423.0995.

1-Benzoyl-1,4,4a,5,6,7,8,8a-octahydro-1,4-ethano-5,8-methanonaphthalene-10,10,11,11-tetracarbonitrile (10d). Brown yellow solid (m.p.150 ℃); yield: 45% (51 mg); R_f = 0.30; IR (KBr) ν_{max} 3031.51, 2964.92, 2878.06, 2225.50, 1668.95, 1596.01, 1383.62, 1094.63, 785.28, 618.12; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.0 Hz, 2H), 7.62 (t, J = 7.3 Hz, 1H), 7.50 (t, J = 7.7 Hz, 2H), 6.92 (d, J = 8.5 Hz, 1H), 6.75 – 6.65 (m, 1H), 3.72 (d, J = 6.2 Hz, 1H), 2.55 (d, J = 8.4 Hz, 1H), 2.43 (d, J = 8.3 Hz, 1H), 2.28 (d, J = 11.6 Hz, 2H), 2.07 (d, J = 10.7 Hz, 1H), 1.57 – 1.50 (m, 1H), 1.48 – 1.41 (m, 1H), 1.29 (dd, J = 16.8, 9.9 Hz, 1H), 1.03 (d, J = 10.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.92, 134.42, 134.40, 133.67, 131.88, 130.22, 129.02, 111.69, 111.52, 111.41, 111.37, 61.33, 47.41, 47.02, 46.58, 43.82, 41.70, 41.04, 40.92, 34.59, 30.82, 30.60; HRMS (EI) calcd for $C_{24}H_{19}ON_4$ [M+H]$^+$: 379.1553, Found: 379.1543.

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