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Advanced Synthesis & Catalysis

Effective [3+1+1+1] Cycloaddition to Six-Membered Carbocycle Based on DMSO as Dual Carbon Synthon

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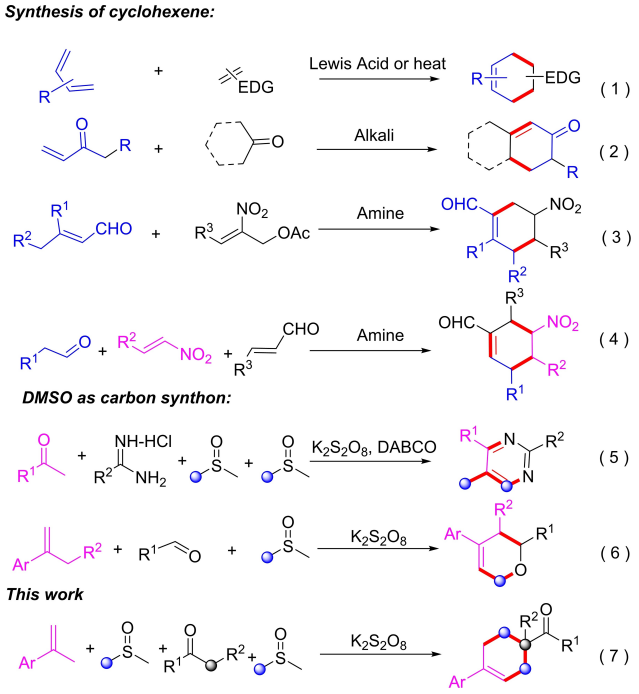
Abstract: A [3+1+1+1] cycloaddition was developed among 2-arylpropene, ketone and DMSO in the presence of $K_2S_2O_8$. 2-arylpropene provides three carbons, ketone offers one carbon, and DMSO as dual carbon donor contributes two carbons to the six-membered carbocycle. It gave the cyclohexene motif and spirocyclohexene skeleton. Four C–C bonds formed in this process. Both propylene and ketone could be well tolerated and give the corresponding cyclohexene or spirocyclohexene motif in useful yields. Based on the controlled experiments, a possible mechanism was proposed.

Keywords: Dual-carbon donor; Cycloaddition; Six-membered carbocycle; DMSO; Spirocyclohexene

Introduction

Six-membered carbocycle compounds are common in numerous natural products, such as cyclic terpenes, steroids, statins, and even alkaloids.[1] The development of efficient methods to construct six-membered carbocycle has attracted considerable attention. In the past years, many strategies have been developed to construct this scaffold. The classic strategy is the [4+2] cycloaddition reactions. They are [4+2] cycloaddition between 1, 3-butadiene and alkene and [4+2] cycloaddition between α, β-unsaturated ketone and cyclic ketone respectively. In the [4+2] cycloaddition between 1, 3-butadiene and alkene (Scheme 1, eqn. 1),[2] 1, 3-butadiene offers four carbons, and alkene offers two carbons to the carbocycle. After further development, this cycloaddition has been recognized as one of the cornerstone reactions in modern organic chemistry. In the [4+2] cycloaddition between α, β-unsaturated ketone and cyclic ketone (Scheme 1, eqn. 2),[1,3] α, β-unsaturated ketone contribute four carbons and the cyclic ketone contribute two carbons to the carbocycle. This process used two ketones to construct six-membered carbocycle containing α, β-unsaturated ketone, and avoided the using of 1, 3-butadienes. α, β-unsaturated carbonyl compounds can form iminium ions with lower LUMO energy in the presence of amine catalyst, which has led to their widespread use in cycloaddition reactions.[4,5] In 2016, Chen and his cooperators reported a [3+3] protocol to construct six-membered carbocycle by the cross coupling of α, β-unsaturated aldehyde and 2-nitropropylene catalyzed by amine (Scheme 1, eqn. 3).[5] This protocol construct polysubstituted cyclohexene framework, and there is no need for cyclic ketone. α, β-unsaturated aldehyde and 2-nitro-propylene each provide three carbons to the carbocycle. With multicomponent reactions attracting more attention due to their step economy,[6] [2+2+2] cycloaddition based on multicomponent reactions to construct six-membered carbocycle using α, β-unsaturated aldehyde and nitro alkene has also been reported.[7] A typical example is [2+2+2] cycloaddition among β-nitro styrene, α, β-unsaturated aldehyde and substituted aldehyde (Scheme 1, eqn. 4).[7a] This cycloaddition used three starting materials to afford the cyclohexene framework in one pot without isolation of intermediate. These strategies provide simple routes to construct six-membered carbocycle. Despite these advancements, there is still a demand for the development of a direct strategy to construct six-membered carbocycle.

As an active pharmaceutical ingredient and a compound storage medium in the pharmaceutical industry, DMSO has also been considered as a reagent



Scheme 1. Synthesis of Six-membered Carbocycle and DMSO as Carbon Synthon.

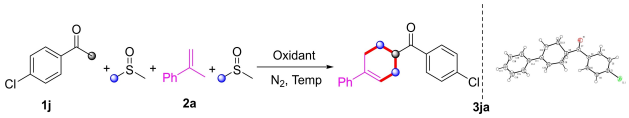
in chemical reactions.[8] Generally, DMSO was widely employed as a single carbon synthon such as methyl (<C-CH_3), methylene (–CH_2-, =CH_2), methine (=CH).[8,9] However, there are few examples about applications of DMSO as a dual carbon synthon in cycloaddition process. In 2018, Wu and his co-operators reported DMSO as dual carbon synthon to 5-methyl pyrimidine (Scheme 1, eqn. 5).[9] In their work, one of the DMSO contributes a carbon to the pyrimidine, and the other one served as methyl group. Our group has exploited a [3+2+1] cycloaddition between 2-arylpropene, aldehyde and DMSO, and the product is 3, 6-dihydro-2*H*-pyran (Scheme 1, eqn. 6).[10] Here, we wish to report the first [3+1+1+1] cycloaddition process among 2-arylpropene, ketone and DMSO that DMSO serves as dual-carbon block contributed two carbons to the six-membered carbocycle (Scheme 1, eqn. 7). 2-arylpropene provides three carbons; ketone offers one carbon, and DMSO as dual carbon donor to construct the six-membered carbocycle. Four C–C bonds formed in this process. To our best knowledge, this is the first synthesis of the six-membered carbocycle by the [3+1+1+1] cycloaddition reaction, and the first example with DMSO as dual-carbon synthon to give the cyclohexene motif.

Results and Discussion

The [3+1+1+1] cycloaddition among 1-(4-chlorophenyl)ethan-1-one (**1 j**), 2-phenyl-propene (**2 a**) and DMSO at 140 °C in the presence of $K_2S_2O_8$ gave the product **3 ja** at 67% yield (Table 1, entry 6), its exact structure was unambiguously determined by the X-ray crystallography.[11] The addition of alkali reduces the yield of the reaction even to 0 (Table 1, entries 1–4). Meantime, lowering or increasing the temperature, the reaction yields decreased (Table 1, entries 5, 7). When $K_2S_2O_8$ was replayed by $Na_2S_2O_8$, KHS_2O_8, $(NH_4)_2S_2O_8$ and TBHP, the reaction was weakened or didn't happen (Table 1, entries 8–11). DMSO is necessary for the cross-coupling reaction. When DMSO was replayed by DMF or toluene, the reaction could not take place (Table 1, entry 12).

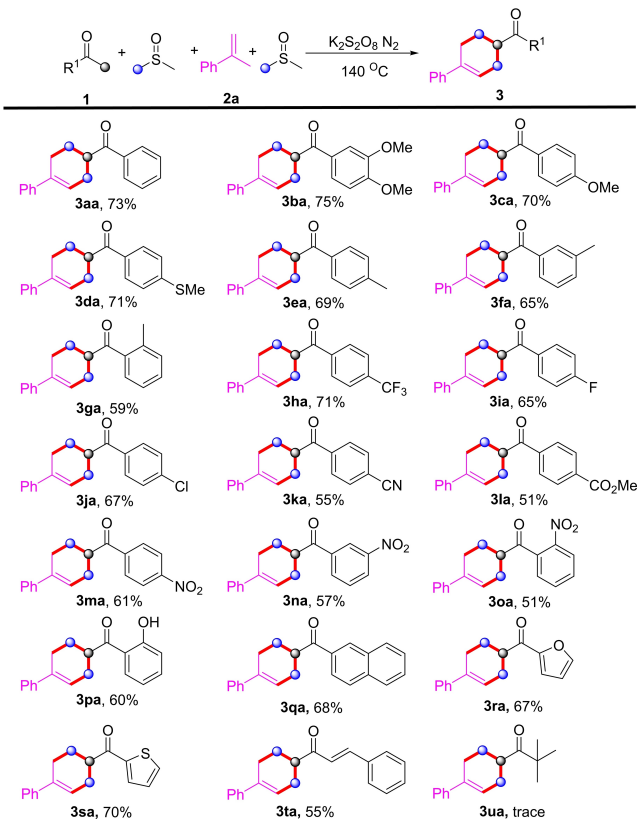
With the optimized reaction conditions in hand (Table 1, entry 6), the scope of nucleophilic methyl ketones was evaluated firstly. As shown in the Scheme 2, multifarious methyl ketones including those with functional groups are appropriate for this process. The acetophenones containing both electron-rich and electron-deficient at different positions of the aryl rings could react with 2-phenyl-propene and DMSO, producing the corresponding products in good yields. Thus, substrates bearing hydrogen, alkyl, alkoxy, and methylthio groups at the benzene ring served well in this reaction (**3 aa**–**3 ga**). The acetophenone derivatives with electron-withdrawing groups like trifluoromethyl (**1 h**), halo (**1 i** and **1 j**), nitrile (**1 k**), ester (**1 l**) and nitro (**1 m**–**1 o**) groups were also found to be reactive, furnishing the expected products in good yields (**3 ha**–**3 oa**).

Table 1. Optimization of Reaction Conditions.[a]

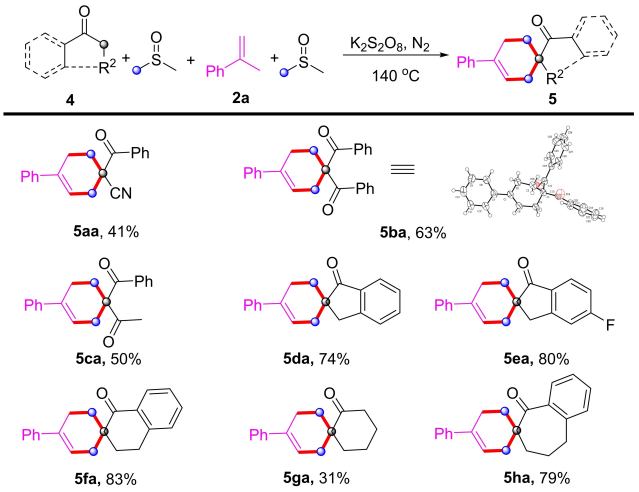


Entry	Oxidant	Base	Temp °C	Yield %[b]
1	$K_2S_2O_8$	DABCO	140	trace
2	$K_2S_2O_8$	Et_3N	140	45
3	$K_2S_2O_8$	Na_2OAc	140	trace
4	$K_2S_2O_8$	K_2CO_3	140	trace
5	$K_2S_2O_8$		120	61
6	***$K_2S_2O_8$***		***140***	***67***
7	$K_2S_2O_8$		160	35
8	$(NH_4)_2S_2O_8$		140	trace
9	$Na_2S_2O_8$		140	65
10	KHS_2O_8		140	31
11	DTBP		140	0
12[c]	$K_2S_2O_8$		140	0

[a] Reaction conditions: 1-(4-chlorophenyl)ethan-1-one (**1 j**, 0.5 mmol), oxidant (1.0 mmol), 2-phenyl-propene (**2 a**, 1.0 mmol), and DMSO (2 mL) under N_2 for 24 h.
[b] GC yield using 1,4-dichlorobenzene as an internal standard.
[c] DMSO replaced by DMF.



Scheme 2. Scope of Methyl Ketone.[a,b] [a] Reaction condition: ketone (**1**, 0.5 mmol), 2-phenyl-propene (**2a**, 1.0 mmol), DMSO (2 mL) and $K_2S_2O_8$ (1.0 mmol) under N_2 at 140 °C for 24 h. [b] Isolated yield.



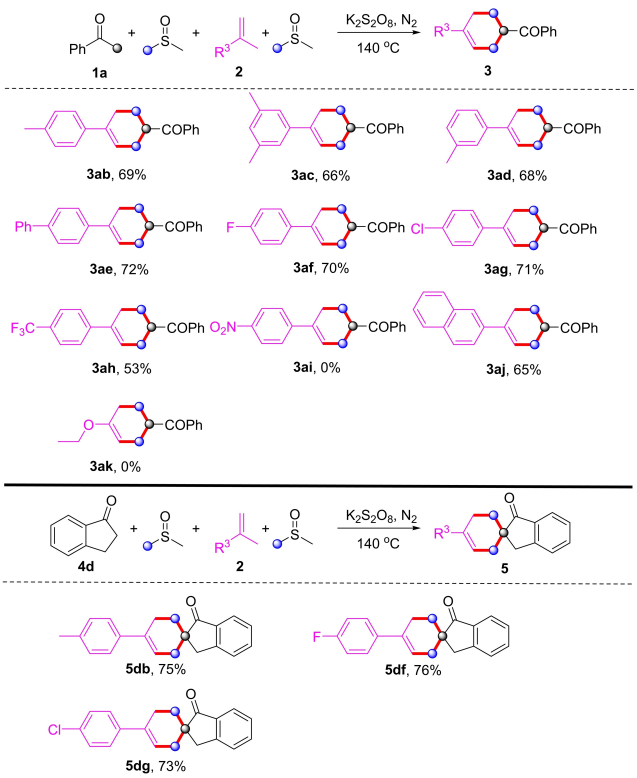
Scheme 3. Scope of Substituted Methyl Ketones.[a,b] [a] Reaction condition: ketone (**4**, 0.5 mmol), 2-phenyl-propene (**2a**, 1.0 mmol), DMSO (2 mL) and $K_2S_2O_8$ (1.0 mmol) under N_2 at 140 °C for 24 h. [b] Isolated yield.

To our delight, the hydroxyl group (**1p**) could be tolerated in this route at good yield. It is worth noting that the π-extended 1-(naphthalen-2-yl)ethan-1-one, and heterocyclic 1-(furan-2-yl)ethan-1-one and 1-(thiophen-2-yl)ethan-1-one underwent this cycloaddition to give the desired products **3qa**, **3ra** and **3sa** in 68%, 67% and 70%. At the same time, alkenyl methyl ketone like cinnamyl awarded the homologous product (**3ta**) in 55%. Nevertheless, the alkyl ethano-1-nes like 3, 3, 3-trimethylbutan-2-one did not work in the present reaction system (**3ua**).

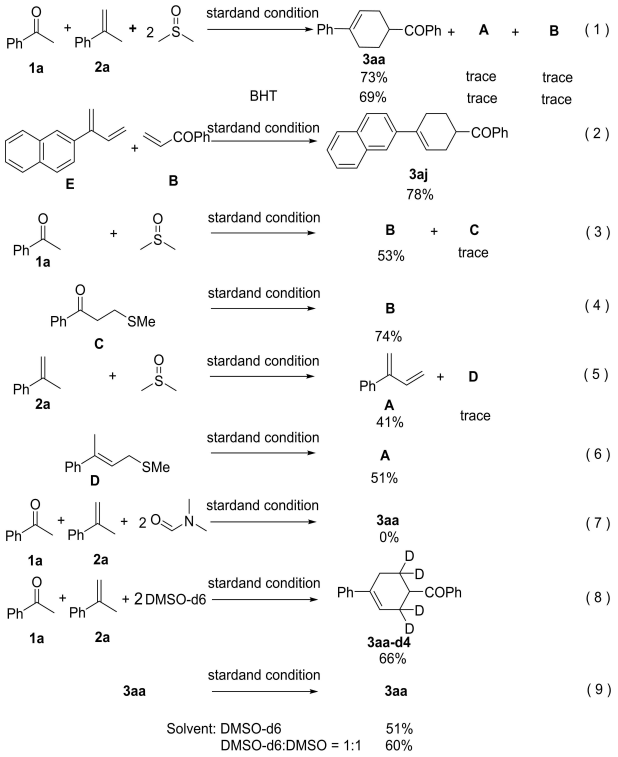
At the same time, this process could tolerate an all-carbon quaternary center.[12] When methyl ketone was replaced by α-substituted methyl ketone, then all-carbon quaternary center was formed under the standard reaction condition (Scheme 3). Some groups for instance nitrile, acetyl and benzoyl groups were discovered to be reactive, affording the estimated commodity in moderate rate (**5aa**–**5ca**). The exact structure of **5ba** was unambiguously determined by the X-ray crystallography.[13]

Spirocyclic compounds are widely found in various natural products as the fundamental skeleton.[14] Among them, the spirocyclohexenes represent an important class of organic compounds in the field of organic chemistry, which show a diverse range of biological activities, such as anti-inflammatory, antibiotic, analgesic, anticancer, and cytotoxic activity.[15] This cycloaddition strategy could well be used to construct different spirocyclohexene skeleton containing an all-carbon quaternary center with good yield (Scheme 3). For example, this route could give −1-phenylspiro[cyclohex[6]ene-4,2′-inden]-1′(3′H)-one (**5da**) and its branch (**5ea**). At the same time, 1-phenyl-3′,4′-dihydro-1′H- spiro[cyclohex[6]ene-4,2′-naphthalen]-1′-one (**5fa**) and 1′- phenyl-8,9-dihydro-spiro[benzo[7]annulene-6,4′-cyclohex[6]en]-5(7H)-one (**5ha**) also could be gained by this cross coupling reaction. It is worth noting that cyclohexanone (**4g**) also could give the homologous molecule (**5ga**). These facts reflected its potential application value of this reaction in the field of drugs.

To expand the application of this methodology, the substrate scope was further examined employing the optimal conditions for 2-substituted-propene (Scheme 4). Firstly, the electronic effect on the phenyl ring was investigated. The result showed that substrates electron-donating groups such as methyl (**2b**, **2c**, **2d**) could afford the homologous cyclohexene in good yield. The 2-phenyl-propene derivatives with electron-withdrawing groups like phenyl (**2e**), halo (**2f** and **2g**) could also produce the corresponding products. Meantime, the CF_3 group could also found to be reactive, and obtain the target product (**3ah**). Whereas, 1-nitro-4-(prop-1-en-2-yl)benzene (**2i**) gave target molecule 0% yield (**3ai**). This 2-substituted-propene was oxidized to 1-(4-nitrophenyl)ethan-1-one due to the strong electron-withdrawing effect of NO_2 group. In the meantime, the π-extended 2-allylnaphthalene



Scheme 4. Scope of 2-substituted-propene.[a,b] [a] Reaction condition: ketone (**1a** or **5d**, 0.5 mmol), 2-substituted-propene (**2**, 1.0 mmol), DMSO (2 mL) and $K_2S_2O_8$ (1.0 mmol) under N_2 at 140 °C for 24 h. [b] Isolated yield.

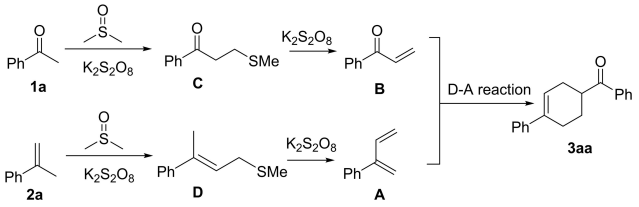


Scheme 5. Controlled Experiments.

generated products **3aj** with 65% yield. When we attempted to replace benzene with ethoxyl group (**3ak**), the corresponding molecules was not available. Moreover, the 2-phenylpropene with substituents such as methyl (**2b**), halo (**2f** and **2g**) on the benzene ring could also react with 2, 3-dihydro-1*H*-inden-1-one (**4d**), and give the corresponding spirocyclohexenes (**5db**, **5df** and **5dg**).

To gain insight into the reaction mechanism, some control experiments were investigated. The reactions manifested normally in the presence of radical inhibitors, 2, 6-ditert-butyl-4-methylphenol (BHT) (Scheme 5, eqn. (1)), producing the desired product **3aa** in 71% yields, which might rule out a radical process in this transformation. In these processes, two intermediates **A** and **B** were found by GC-MS; meanwhile, under the standard reaction condition, conjugated diene **E** could be transformed into **3aj** with **B** (Scheme 5, eqn. (2)). Hereby, we deduced that this reaction underwent a course of Diels- Alder reaction. To furthermore explore the pathway of **A** and **B**, several independent experiments were used. In the trials of **2a**, **A** and **D** were detected by GC-MS (Scheme 5, eqn. (5)).[10] Meanwhile, **D** could be converted to **A** under the standard condition (Scheme 5, eqn. (6)).[10] On the other hand, intermediates **B** and **C** were discovered as well (Scheme 5, eqn. (3)). **B** could be synthesized by **C** (Scheme 5, eqn. (4)).[16] Meantime, when DMSO was replaced by DMF, the cycloaddition could not be performed (Scheme 5, eqn. (7)). When DMSO was replaced by DMSO-d6, **3aa**-d4 could be obtained with 66% yield (Scheme 5, eqn. (8)). At the same time, when product **3aa** was added in the solvent (DMSO-d6 or DMSO-d6: DMSO = 1:1) under standard condition, the GC-MS spectra showed no product of hydrogen-deuterium exchange (Scheme 5, eqn. (9)). These facts testified that DMSO provided two carbons for the cyclohexene framework.

On the basis of above facts and previous literature,[2,10,16,17] we believe that the reaction proceeds along the pathway presented in Scheme 6. The reaction began with the coupling of **1a** and DMSO to give **C** in the presence of $K_2S_2O_8$. Meanwhile, **2a** couples with DMSO to give **D**. Then, **C** and **D** went through demethylthiolation to grant **A** and **B** in the presence of



Scheme 6. Possible Mechanism.

$K_2S_2O_8$. Lastly, Diels-Alder process took place between **B** and **A** to grant the final product **3 aa**.

Conclusion

In summary, an efficient [3 + 1 + 1 + 1] cycloaddition based on DMSO as dual-carbon synthon to synthesis of six-membered carbocycle was developed among 2-arylpropene, ketone and DMSO in the presence of $K_2S_2O_8$. This is the first synthesis of the six- membered carbocycle by the [3 + 1 + 1 + 1] cycloaddition reaction, and the first example with DMSO as dual-carbon synthon to give the cyclohexene motif. 2-arylpropene provides three carbon atoms; ketone offers one carbon, and DMSO as dual carbon donor to construct the six-membered carbocycle. This process allows the simultaneous construction of four C–C bonds, and the product is cyclohexene skeleton. Meanwhile, it could construct spirocyclic compound, which reflected its potential application value in the field of drugs. 39 examples were developed. Based on the controlled experiments, a possible mechanism has been proposed.

Experimental Section

General Information

Except noted otherwise, all reactions were carried out in Schlenk tubes. Reagents and solvents were obtained from commercial sources and used without further purification. The ^1H and ^{13}C spectra were recorded on a Brucker ADVANCE III spectrometer at 400 MHz and 100 MHz, and chemical shifts were reported in parts per million (ppm). Flash column chromatography was performed using silica gel of 300–400 μm. The GC-MS results were recorded on a GC-MS QP2010 equipmment, GC analysis was performed on GC 2010 Plus. The electron ionization (EI) and electrospray ionization (ESI) method was used for HRMS measurement, and the mass analyzer type is TOF for EI and ESI. The HRMS (EI) was recorded on an Esquire 3000 plus instrument, and the HRMS (ESI) was recorded on an Agilent 6210 ESI/TOF MS.

General Procedure

In a Schlenk tube of 25 mL, $K_2S_2O_8$ (1.0 mmol, 270 mg), DMSO (2 mL) were added. After attiring for one minute, ketone (**1**, 0.5 mmol), 2-substituted-propylene (**2**, 1.0 mmol) were added. The mixture was stirred at 140 °C for 24 h under N_2 atmosphere. After completion of the reaction, the resulting solution was cooled to room temperature; then it was diluted with ethyl acetate (6 mL), washed with water (6 mL), extracted with ethyl acetate (6 × 3 mL), and dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel to give the desired product final product.

Spectra Data of the Products

phenyl(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl) methanone (3 aa)

Prepared according to the general procedure to afford colorless oil in 73% yield, 95.6 mg. **^1H NMR** (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.6 Hz, 2H), 7.60–7.55 (m, 1H), 7.48 (t, J = 7.4 Hz, 2H), 7.40 (d, J = 7.6 Hz, 2H), 7.32 (t, J = 7.3 Hz, 2H), 7.23 (d, J = 8.3 Hz, 1H), 6.18 (s, 1H), 3.60 (s, 1H), 2.59 (s, 2H), 2.49 (dd, J = 34.5, 14.1 Hz, 2H), 2.18 (d, J = 12.0 Hz, 1H), 1.88 (ddd, J = 21.3, 12.2, 8.9 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.32, 141.75, 136.29, 133.03, 128.74, 128.37, 128.34, 126.92, 125.08, 123.14, 41.31, 28.76, 27.21, 26.29. **HRMS** (**EI**): calcd for $C_{19}H_{18}O$: 262.1358, found: 262.1356.

3,4-dimethoxyphenyl)(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)methanone (3 ba)

Prepared according to the general procedure to afford white solid in 75% yield, 120.7 mg, and melting point: 125.1–126.7 °C. **^1H NMR** (400 MHz, CDCl3) δ 7.66 (d, J = 8.4 Hz, 1H), 7.60 (d, J = 1.5 Hz, 1H), 7.43 (d, J = 7.7 Hz, 2H), 7.35 (t, J = 7.6 Hz, 2H), 7.28 (s, 1H), 6.93 (d, J = 8.4 Hz, 1H), 6.21 (d, J = 4.2 Hz, 1H), 3.98 (s, 3H), 3.97 (s, 3H), 3.64–3.53 (m, 1H), 2.64–2.60 (m, 2H), 2.52 (ddd, J = 42.4, 12.1, 3.8 Hz, 2H), 2.22–2.14 (m, 1H), 1.92 (ddd, J = 16.9, 10.5, 5.9 Hz, 1H). **^{13}C NMR** (101 MHz, CDCl3) δ 201.93, 153.26, 149.23, 141.74, 136.23, 129.43, 128.31, 126.88, 125.03, 123.25, 122.76, 110.58, 110.03, 56.10, 56.02, 40.82, 29.08, 27.24, 26.54. **HRMS** (**ESI**): calcd for $C_{21}H_{23}O_3$ [M + H]: 323.1647, found: 323.1649.

(4-methoxyphenyl)(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)methanone (3 ca)

Prepared according to the general procedure to afford white solid in 70% yield, 102.2 mg, and melting point: 176.1–177.9 °C. **^1H NMR** (400 MHz, $CDCl_3$) δ 8.00 (d, J = 8.8 Hz, 2H), 7.41 (d, J = 7.4 Hz, 2H), 7.33 (t, J = 7.6 Hz, 2H), 7.23 (d, J = 7.3 Hz, 1H), 6.97 (d, J = 8.8 Hz, 2H), 6.19 (d, J = 4.2 Hz, 1H), 3.88 (s, 3H), 3.56 (ddd, J = 12.0, 6.6, 3.8 Hz, 1H), 2.63–2.57 (m, 2H), 2.57–2.35 (m, 2H), 2.21–2.11 (m, 1H), 1.89 (tt, J = 13.1, 8.6 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.85, 163.44, 141.78, 136.23, 130.61, 129.26, 128.30, 126.86, 125.05, 123.28, 113.85, 55.50, 40.95, 28.92, 27.26, 26.43. **HRMS** (**EI**): calcd for $C_{20}H_{20}O_2$: 292.1463, found: 292.1465.

(4-(methylthio)phenyl)(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)methanone (3 da)

Prepared according to the general procedure to afford white solid in 71% yield, 109.3 mg, and melting point: 149.3–151.1 °C. **^1H NMR** (400 MHz, $CDCl_3$) δ 7.92 (d, J = 7.8 Hz, 2H), 7.41 (d, J = 7.5 Hz, 2H), 7.34 (d, J = 7.3 Hz, 2H), 7.30 (d, J = 8.7 Hz, 2H), 7.23 (d, J = 7.4 Hz, 1H), 6.18 (s, 1H), 3.55 (t, J = 10.7 Hz, 1H), 2.59 (s, 2H), 2.53 (s, 3H), 2.43 (d, J = 17.7 Hz, 2H), 2.16 (d, J = 12.5 Hz, 1H), 1.87 (dd, J = 20.2, 11.5 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.30, 145.77, 141.74, 136.27, 132.52, 128.79, 128.32, 126.90, 125.15, 125.06, 123.16, 41.09, 28.81, 27.21, 26.34, 14.82. **HRMS** (**ESI**): calcd for $C_{20}H_{21}OS$ [M + H]: 309.1313, found: 309.1314.

(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)(p–tolyl) methanone (3 ea)

Prepared according to the general procedure to afford white solid in 69% yield, 95.2 mg, and melting point: 110.9–112.5 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.7 Hz, 2H), 7.41 (d, J = 7.5 Hz, 2H), 7.34 (d, J = 7.3 Hz, 2H), 7.29 (d, J = 7.8 Hz, 2H), 7.23 (d, J = 7.2 Hz, 1H), 6.19 (s, 1H), 3.57 (d, J = 10.3 Hz, 1H), 2.59 (s, 2H), 2.57–2.44 (m, 2H), 2.43 (s, 3H), 2.17 (d, J = 12.9 Hz, 1H), 1.93–1.83 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.94, 143.78, 141.77, 136.24, 133.76, 129.39, 128.47, 128.29, 126.86, 125.05, 123.22, 41.16, 28.81, 27.22, 26.33, 21.64. **HRMS** (**EI**): calcd for $C_{20}H_{20}O$: 276.1514, found: 276.1510.

(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)(m–tolyl) methanone (3 fa)

Prepared according to the general procedure to afford colorless oil in 65% yield, 89.7 mg. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.0 Hz, 2H), 7.40 (dd, J = 13.0, 7.1 Hz, 4H), 7.33 (t, J = 7.5 Hz, 2H), 7.24 (d, J = 8.5 Hz, 1H), 6.18 (s, 1H), 3.58 (d, J = 9.7 H z, 1H), 2.60 (d, J = 5.0 Hz, 2H), 2.57–2.44 (m, 2H), 2.43 (s, 3H), 2.18 (d, J = 12.3 Hz, 1H), 1.89 (dt, J = 29.7, 10.5 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.58, 141.78, 138.54, 136.34, 133.78, 128.88, 128.59, 128.33, 126.91, 125.56, 125.08, 123.19, 41.33, 28.83, 27.22, 26.29, 21.46. **HRMS** (**ESI**): calcd for $C_{20}H_{21}O$ [M + H]: 277.1592, found: 277.1591.

(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)(o–tolyl) methanone (3 ga)

Prepared according to the general procedure to afford colorless oil in 59% yield, 81.4 mg. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 (d, J = 7.8 Hz, 1H), 7.38 (d, J = 7.9 Hz, 3H), 7.34 (d, J = 5.4 Hz, 1H), 7.30 (d, J = 7.5 Hz, 2H), 7.27 (s, 1H), 7.22 (d, J = 7.5 Hz, 1H), 6.14 (s, 1H), 3.39 (s, 1H), 2.56 (d, J = 11.8 Hz, 2H), 2.49 (s, 2H), 2.45 (s, 3H), 2.15 (d, J = 14.4 Hz, 1H), 1.83 (dt, J = 18.3, 11.4 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.83, 141.77, 138.45, 137.62, 136.36, 131.76, 130.81, 128.32, 127.61, 126.91, 125.65, 125.07, 123.03, 44.40, 28.18, 27.13, 25.61, 20.84. **HRMS** (**ESI**): calcd for $C_{20}H_{21}O$ [M + H]: 277.1592, found: 277.1598.

(2, 3, 4, 5-tetrahydro-[1,1′-biphenyl]-4-yl)(4-(trifluoromethyl)phenyl)methanone (3 ha)

Prepared according to the general procedure to afford white solid in 71% yield, 117.2 mg, and melting point: 83.4–85.0 °C. **^{1}H NMR** (400 MHz, CDCl3) δ 8.12 (d, J = 7.9 Hz, 1H), 7.79 (d, J = 7.9 Hz, 1H), 7.43 (d, J = 7.5 Hz, 1H), 7.36 (t, J = 7.4 Hz, 1H), 7.28 (t, J = 7.2 Hz, 1H), 6.20 (s, 1H), 3.62 (s, 1H), 2.63 (s, 1H), 2.57 (d, J = 10.2 Hz, 1H), 2.49 (d, J = 17.8 Hz, 1H), 2.22 (d, J = 11.9 Hz, 1H), 2.06–1.83 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.22, 141.57, 139.08, 136.41, 134.31 (d, J = 32.7 Hz), 128.64, 128.33, 127.00, 125.80, 125.76, 125.06, 122.67, 41.69, 28.51, 27.08, 26.07. **HRMS** (**ESI**): calcd for $C_{20}H_{18}F_3O$ [M + H]: 331.1310, found: 331.1309.

(4-fluorophenyl)(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)methanone (3 ia)

Prepared according to the general procedure to afford white solid in 65% yield, 91.0 mg, and melting point:92.5–94.2 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06–8.00 (m, 2H), 7.40 (d, J = 7.5 Hz, 2H), 7.33 (t, J = 7.4 Hz, 2H), 7.24 (d, J = 7.8 Hz, 1H), 7.16 (t, J = 8.2 Hz, 2H), 6.18 (s, 1H), 3.54 (d, J = 9.8 Hz, 1H), 2.59 (s, 2H), 2.58 −2.39 (m, 2H), 2.17 (d, J = 12.4 Hz, 1H), 1.88 (dt, J = 12.2, 9.0 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.67, 141.65, 136.31, 130.96, 128.32, 126.94, 125.05, 122.96, 115.91, 115.70, 41.26, 28.73, 27.15, 26.25. **HRMS** (**ESI**): calcd for $C_{19}H_{18}FO$ [M + H]: 281.1342, found: 281.1339.

(4-chlorophenyl)(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)methanone (3 ja)

Prepared according to the general procedure to afford white solid in 67% yield, 99.1 mg, and melting point: 137.5–139.2 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 (d, J = 7.9 Hz, 2H), 7.46 (d, J = 8.0 Hz, 2H), 7.40 (d, J = 7.6 Hz, 2H), 7.33 (t, J = 7.5 Hz, 2H), 7.24 (d, J = 7.5 Hz, 1H), 6.17 (s, 1H), 3.54 (t, J = 10.7 Hz, 1H), 2.59 (d, J = 3.1 Hz, 2H), 2.48 (dd, J = 33.7, 14.1 Hz, 2H), 2.16 (d, J = 13.0 Hz, 1H), 1.94–1.81 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.07, 141.64, 139.45, 136.34, 134.56, 129.79, 129.05, 128.34, 126.97, 125.06, 122.90, 41.33, 28.68, 27.14, 26.20. **HRMS** (**ESI**): calcd for $C_{19}H_{18}ClO$ [M + H]: 297.1046, found: 297.1043.

4-(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-carbonyl) benzonitrile (3 ka)

Prepared according to the general procedure to afford white solid in 55% yield, 78.9 mg, and melting point: 181.3–182.9 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (d, J = 7.8 Hz, 2H), 7.80 (d, J = 7.8 Hz, 2H), 7.40 (d, J = 7.5 Hz, 2H), 7.33 (t, J = 7.3 Hz, 2H), 7.25 (d, J = 9.0 Hz, 1H), 6.17 (s, 1H), 3.55 (d, J = 9.5 Hz, 1H), 2.61 (s, 2H), 2.49 (dd, J = 30.1, 14.0 Hz, 2H), 2.18 (d, J = 12.0 Hz, 1H), 1.96–1.82 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.89, 141.48, 139.35, 136.43, 132.64, 128.76, 128.37, 127.08, 125.07, 122.52, 117.98, 116.29, 41.69, 28.45, 27.02, 26.01. **HRMS** (**ESI**): calcd for $C_{20}H_{18}NO$ [M + H]: 288.1388, found: 283.1381.

methyl 4-(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-carbonyl)benzoate (3 la)

Prepared according to the general procedure to afford white solid in 51% yield, 81.6 mg, and melting point: 165.5–167.2 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.15 (d, J = 7.9 Hz, 2H), 8.04 (d, J = 7.9 Hz, 2H), 7.41 (d, J = 7.6 Hz, 2H), 7.33 (t, J = 7.4 Hz, 2H), 7.23 (s, 1H), 6.18 (s, 1H), 3.96 (s, 3H), 3.60 (s, 1H), 2.60 (s, 2H), 2.50 (dd, J = 28.9, 14.1 Hz, 2H), 2.19 (d, J = 13.4 Hz, 1H), 1.89 (dt, J = 21.0, 10.6 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.79, 166.25, 141.61, 139.61, 136.36, 133.79, 129.95, 128.28, 126.97, 125.06, 122.81, 52.48, 41.70, 28.56, 27.11, 26.11. **HRMS** (**ESI**): calcd for $C_{21}H_{21}O_3$ [M + H]: 321.1491, found: 321.1497.

(4-nitrophenyl)(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)methanone (3ma)

Prepared according to the general procedure to afford yellow solid in 61% yield, 93.6 mg, and melting point: 184.3–185.9 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.40–8.33 (m, 2H), 8.20–8.12 (m, 2H), 7.46–7.39 (m, 2H), 7.36 (dd, J = 10.2, 4.8 Hz, 2H), 7.28 (s, 1H), 6.23–6.16 (m, 1H), 3.62 (tdd, J = 8.0, 5.4, 2.7 Hz, 1H), 2.67–2.61 (m, 2H), 2.60–2.44 (m, 2H), 2.26–2.18 (m, 1H), 1.98–1.87 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.69, 150.28, 141.45, 140.87, 136.46, 129.33, 128.36, 127.08, 125.06, 123.98, 122.44, 41.96, 28.42, 27.01, 25.98. **HRMS** (**EI**): calcd for $C_{19}H_{17}NO_3$: 307.1208, found: 307.1215.

(3-nitrophenyl)(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)methanone (3na)

Prepared according to the general procedure to afford yellow oil in 57% yield, 87.5 mg. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.42 (d, J = 8.1 Hz, 1H), 8.31 (d, J = 7.7 Hz, 1H), 7.70 (t, J = 7.9 Hz, 1H), 7.40 (d, J = 7.6 Hz, 2H), 7.33 (t, J = 7.4 Hz, 2H), 7.24 (d, J = 8.2 Hz, 1H), 6.16 (s, 1H), 3.62 (dd, J = 17.7, 6.0 Hz, 1H), 2.61 (s, 2H), 2.51 (dd, J = 27.3, 13.9 Hz, 2H), 2.19 (d, J = 13.7 Hz, 1H), 1.98–1.85 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.01, 148.60, 141.49, 137.56, 136.47, 133.97, 130.06, 128.38, 127.33, 127.08, 125.09, 123.20, 122.48, 41.61, 28.52, 27.01, 26.05. **HRMS** (**ESI**): calcd for $C_{19}H_{18}NO_3$ [M + H]: 308.1287, found: 308.1284.

(2-nitrophenyl)(2,3,4,5-tetrahydro-[1,1'-biphenyl]-4-yl)methanone (3oa)

Prepared according to the general procedure to afford yellow oil in 51% yield, 78.3 mg. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.1 Hz, 1H), 7.75 (t, J = 7.2 Hz, 1H), 7.63 (t, J = 7.8 Hz, 1H), 7.41 (d, J = 7.4 Hz, 1H), 7.36–7.28 (m, 4H), 7.22 (d, J = 6.8 Hz, 1H), 6.11 (s, 1H), 3.02 (d, J = 10.2 Hz, 1H), 2.71–2.55 (m, 2H), 2.54–2.40 (m, 2H), 2.22 (d, J = 13.0 Hz, 1H), 1.95–1.81 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 205.58, 145.78, 141.62, 137.69, 136.38, 134.33, 130.48, 128.31, 128.02, 126.97, 125.09, 124.58, 122.60, 46.62, 28.17, 27.13, 25.57. **HRMS** (**ESI**): calcd for $C_{19}H_{18}NO_3$ [M + H]: 308.1287, found: 308.1286.

(2-hydroxyphenyl)(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)methanone (3pa)

Prepared according to the general procedure to afford colorless oil in 60% yield, 83.4 mg. **^{1}H NMR** (400 MHz, CDCl3) δ 12.51 (s, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.48 (t, J = 7.7 Hz, 1H), 7.40 (d, J = 7.4 Hz, 2H), 7.33 (t, J = 7.3 Hz, 2H), 7.23 (d, J = 6.6 Hz, 1H), 7.01 (d, J = 8.4 Hz, 1H), 6.91 (t, J = 7.5 Hz, 1H), 6.17 (s, 1H), 3.69–3.55 (m, 1H), 2.61 (s, 2H), 2.58–2.40 (m, 2H), 2.17 (d, J = 13.7 Hz, 1H), 1.93 (dd, J = 15.5, 7.2 Hz, 1H). **^{13}C NMR** (101 MHz, CDCl3) δ 209.53, 163.17, 141.57, 136.43, 136.36, 129.87, 128.37, 127.03, 125.08, 122.77, 118.94, 118.88, 118.45, 40.94, 28.91, 27.13, 26.47. **HRMS** (**ESI**): calcd for $C_{19}H_{19}O_2$ [M + H]: 279.1385, found: 279.1383.

naphthalen-2-yl(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)methanone (3qa)

Prepared according to the general procedure to afford white solid in 68% yield, 106.1 mg, and melting point: 117.3–118.8 °C. **^{1}H NMR** (400 MHz, CDCl3) δ 8.52 (s, 1H), 8.07 (d, J = 8.6 Hz, 1H), 7.99 (d, J = 7.9 Hz, 1H), 7.92 (dd, J = 13.2, 8.5 Hz, 2H), 7.59 (dt, J = 14.8, 7.0 Hz, 2H), 7.44 (d, J = 7.6 Hz, 2H), 7.35 (t, J = 7.3 Hz, 2H), 7.24 (s, 1H), 6.22 (s, 1H), 3.78 (s, 1H), 2.65 (s, 2H), 2.56 (dd, J = 27.1, 14.2 Hz, 2H), 2.25 (d, J = 12.5 Hz, 1H), 2.01–1.90 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.33, 141.77, 136.34, 135.63, 133.64, 132.69, 129.87, 129.66, 128.66, 128.52, 128.40, 127.85, 126.99, 126.86, 125.12, 124.34, 123.21, 41.39, 29.01, 27.26, 26.43. **HRMS** (**ESI**): calcd for $C_{23}H_{21}O$ [M + H]: 313.1592, found: 313.1596.

furan-2-yl(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl) methanone (3ra)

Prepared according to the general procedure to afford white solid in 67% yield, 84.5 mg, and melting point: 80.6–82.4 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.44 (d, J = 7.6 Hz, 2H), 7.36 (t, J = 7.6 Hz, 2H), 7.30–7.27 (m, 2H), 6.60 (dd, J = 3.4, 1.5 Hz, 1H), 6.21 (d, J = 4.6 Hz, 1H), 3.43 (tdd, J = 9.5, 5.4, 2.6 Hz, 1H), 2.64 (d, J = 3.0 Hz, 2H), 2.61–2.42 (m, 2H), 2.21 (dd, J = 11.4, 3.4 Hz, 1H), 2.00–1.87 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.33, 152.37, 146.38, 141.75, 136.24, 128.30, 126.89, 125.06, 122.94, 117.31, 112.24, 42.04, 28.18, 27.17, 25.91. **HRMS** (**EI**): calcd for $C_{17}H_{16}O_2$: 252.1150, found: 252.1149.

(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)(thiophen-2-yl)methanone (3sa)

Prepared according to the general procedure to afford white solid in 70% yield, 93.8 mg, and melting point: 64.7–66.5 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.66 (d, J = 4.3 Hz, 1H), 7.41 (d, J = 7.4 Hz, 2H), 7.33 (t, J = 7.4 Hz, 2H), 7.24 (d, J = 6.9 Hz, 1H), 7.16 (d, J = 3.9 Hz, 1H), 6.18 (d, J = 3.1 Hz, 1H), 3.44 (dd, J = 14.7, 9.7 Hz, 1H), 2.61 (d, J = 3.9 Hz, 2H), 2.59–2.36 (m, 2H), 2.21 (d, J = 13.3 Hz, 1H), 2.01–1.87 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.26, 143.81, 141.70, 136.26, 133.74, 131.76, 128.34, 128.19, 126.94, 125.07, 122.97, 43.09, 28.94, 27.20, 26.59. **HRMS** (**ESI**): calcd for $C_{17}H_{17}OS$ [M + H]: 269.1000, found: 269.1005.

3-phenyl-1-(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl) prop-2-en-1-one (3ta)

Prepared according to the general procedure to afford white solid in 55% yield, 79.2 mg, and melting point: 111.1–112.0 °C. **^{1}H NMR** (400 MHz, CDCl3) δ 7.67 (d, J = 16.0 Hz, 1H), 7.59 (d, J = 3.0 Hz, 2H), 7.41 (d, J = 6.1 Hz, 5H), 7.33 (t, J = 7.4 Hz, 2H), 7.24 (d, J = 7.4 Hz, 1H), 6.90 (d, J = 16.0 Hz, 1H), 6.18 (s, 1H), 3.08–2.97 (m, 1H), 2.59 (s, 2H), 2.49 (d, J = 11.7 Hz, 2H), 2.20 (d, J = 12.8 Hz, 1H), 1.90–1.78 (m, 1H). **^{13}C NMR** (101 MHz, CDCl3) δ 202.54, 142.79, 141.77, 136.35, 134.65, 130.50, 128.98, 128.37, 128.32, 126.90, 125.07, 124.64, 122.97, 44.83, 27.98, 27.16, 25.61. **HRMS** (**ESI**): calcd for $C_{21}H_{21}O$ [M + H]: 289.1592, found: 289.1595.

4-benzoyl-2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-carbonitrile (5 aa)

Prepared according to the general procedure to afford white solid in 41% yield, 58.9 mg, and melting point: 138.2–139.9 °C.**^{1}H NMR** (400 MHz, CDCl3) δ 8.20 (d, *J*=7.6 Hz, 2H), 7.64 (t, *J*=7.3 Hz, 1H), 7.53 (t, *J*=7.4 Hz, 2H), 7.41 (d, *J*=7.6 Hz, 2H), 7.35 (t, *J*=7.3 Hz, 2H), 7.29 (d, *J*=6.9 Hz, 1H), 6.09 (s, 1H), 2.92 (s, 2H), 2.88 (s, 1H), 2.66 (d, *J*=14.9 Hz, 1H), 2.54 (d, *J*=12.6 Hz, 1H), 2.27 (td, *J*=12.1, 5.0 Hz, 1H). **^{13}C NMR** (101 MHz, CDCl3) δ 193.50, 140.51, 136.78, 134.03, 133.91, 129.36, 128.80, 128.44, 127.54, 125.23, 120.69, 118.97, 44.59, 33.97, 30.10, 24.63. **HRMS** (**EI**): calcd for $C_{20}H_{17}NO$: 287.1310, found: 287.1311.

(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4,4-diyl)bis(phenylmethanone) (5 ba)

Prepared according to the general procedure to afford white solid in 63% yield, 115.3 mg, and melting point: 128.9–130.3 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 (d, *J*=7.7 Hz, 4H), 7.45 (t, *J*=7.3 Hz, 2H), 7.34 (t, *J*=7.5 Hz, 6H), 7.28 (t, *J*=7.4 Hz, 2H), 7.20 (t, *J*=7.1 Hz, 1H), 6.16 (s, 1H), 2.92 (s, 2H), 2.62 (t, *J*=6.1 Hz, 2H), 2.34 (s, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 198.91, 141.07, 136.02, 135.01, 133.14, 129.14, 128.72, 128.27, 126.92, 125.00, 121.36, 62.56, 33.83, 30.10, 23.91. **HRMS** (**ESI**): calcd for $C_{26}H_{23}O_2$ [M+H]: 367.1698, found: 367.1697.

1-(4-benzoyl-2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)ethan-1-one (5 ca)

Prepared according to the general procedure to afford white solid in 50% yield, 76.1 mg, and melting point: 92.9–94.7 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J*=7.7 Hz, 2H), 7.55 (t, *J*=7.3 Hz, 1H), 7.43 (t, *J*=7.5 Hz, 2H), 7.31 (dd, *J*=12.6, 7.5 Hz, 4H), 7.21 (t, *J*=6.9 Hz, 1H), 6.09 (s, 1H), 2.81 (dd, *J*=47.4, 17.5 Hz, 2H), 2.56–2.48 (m, 1H), 2.37 (s, 2H), 2.37–2.29 (m, 1H), 2.19 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.12, 198.48, 141.02, 136.09, 135.51, 132.99, 128.71, 128.66, 128.25, 126.99, 125.00, 121.11, 64.40, 31.54, 28.38, 26.59, 24.23. **HRMS** (**ESI**): calcd for $C_{21}H_{21}O_2$ [M+H]: 305.1542, found: 305.1543.

1-phenylspiro[cyclohex[6]ene-4,2′-inden]-1′(3′H)-one (5 da)

Prepared according to the general procedure to afford white solid in 74% yield, 101.4 mg, and melting point: 159.1–160.8 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J*=7.6 Hz, 1H), 7.59 (t, *J*=7.4 Hz, 1H), 7.43 (d, *J*=8.0 Hz, 3H), 7.39 (d, *J*=7.4 Hz, 1H), 7.33 (t, *J*=7.5 Hz, 2H), 7.23 (d, *J*=6.7 Hz, 1H), 6.20 (d, *J*=4.5 Hz, 1H), 3.11 (d, *J*=17.3 Hz, 1H), 2.96 (d, *J*=17.3 Hz, 1H), 2.63 (dd, *J*=26.5, 11.9 Hz, 3H), 2.05 (dt, *J*=15.1, 5.6 Hz, 2H), 1.72–1.66 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 211.07, 152.80, 141.52, 136.05, 135.90, 134.95, 128.36, 127.52, 127.02, 126.74, 125.06, 124.36, 122.55, 48.17, 39.10, 35.08, 29.30, 24.86. **HRMS** (**ESI**): calcd for $C_{20}H_{19}O$ [M+H]: 275.1436, found: 275.1438.

5′-fluoro-1-phenylspiro[cyclohex[6]ene-4,2′-inden]-1′(3′H)-one (5 ea)

Prepared according to the general procedure to afford white solid in 80% yield, 116.8 mg, and melting point: 160.7–162.6 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87–7.75 (m, 1H), 7.43 (d, *J*=7.5 Hz, 2H), 7.34 (t, *J*=7.3 Hz, 2H), 7.25 (d, *J*=6.7 Hz, 1H), 7.09 (t, *J*=8.8 Hz, 2H), 6.20 (d, *J*=4.3 Hz, 1H), 3.11 (d, *J*=17.5 Hz, 1H), 2.96 (d, *J*=17.5 Hz, 1H), 2.74–2.53 (m, 3H), 2.15–1.98 (m, 2H), 1.70 (dd, *J*=13.4, 3.4 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 209.12, 168.70, 155.66 (d, *J*=10.0 Hz), 141.40, 136.08, 132.25, 128.38, 127.09, 126.64 (d, *J*=10.5 Hz), 125.05, 122.32, 115.86 (d, *J*=23.8 Hz), 113.32 (d, *J*=22.1 Hz), 48.54, 39.00, 35.04, 29.27, 24.76. **HRMS** (**ESI**): calcd for $C_{20}H_{18}FO$ [M+H]: 293.1342, found: 293.1345.

1-phenyl-3′,4′-dihydro-1′H-spiro[cyclohex[6]ene-4,2′-naphthalen]-1′-one (5 fa)

Prepared according to the general procedure to afford colorless oil in 83% yield, 119.6 mg. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (d, *J*=7.7 Hz, 1H), 7.37 (d, *J*=7.4 Hz, 1H), 7.33 (d, *J*=7.5 Hz, 2H), 7.23 (s, 3H), 7.15 (d, *J*=7.0 Hz, 2H), 6.08 (s, 1H), 2.96 (dd, *J*=9.4, 5.6 Hz, 1H), 2.82 (dd, *J*=21.4, 18.7 Hz, 2H), 2.45 (s, 2H), 2.06–1.81 (m, 5H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.43, 143.23, 141.52, 134.74, 133.16, 131.81, 128.73, 128.33, 128.11, 126.87, 126.71, 124.98, 122.39, 43.07, 32.50, 30.34, 28.00, 25.24, 24.45. **HRMS** (**ESI**): calcd for $C_{21}H_{21}O$ [M+H]: 289.1592, found: 289.1595.

9-phenylspiro[5.5]undec-8-en-1-one (5 ga)

Prepared according to the general procedure to afford yellow oil in 31% yield, 37.2 mg. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 (d, *J*=7.8 Hz, 2H), 7.29 (t, *J*=7.4 Hz, 2H), 7.21 (t, *J*=7.1 Hz, 1H), 6.07 (s, 1H), 2.52 (dd, *J*=16.8, 10.7 Hz, 2H), 2.41 (dd, *J*=18.8, 7.0 Hz, 3H), 2.12–2.05 (m, 2H), 1.88–1.71 (m, 7H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 215.34, 141.55, 135.04, 128.22, 126.75, 124.94, 122.10, 47.01, 38.55, 36.62, 33.23, 29.66, 27.91, 24.05, 20.96. **HRMS** (**ESI**): calcd for $C_{17}H_{21}O$ [M+H]: 241.1492, found: 241.1490.

1′-phenyl-8,9-dihydrospiro[benzo[7]annulene-6,4′-cyclohex[6]en]-5(7H)-one (5 ha)

Prepared according to the general procedure to afford colorless oil in 79% yield, 119.3 mg. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 (d, *J*=7.8 Hz, 2H), 7.35–7.30 (m, 3H), 7.22 (t, *J*=7.2 Hz, 3H), 7.15 (d, *J*=7.4 Hz, 1H), 6.06 (s, 1H), 2.93–2.83 (m, 2H), 2.71 (d, *J*=18.0 Hz, 1H), 2.49 (dd, *J*=47.8, 17.8 Hz, 2H), 2.22–2.10 (m, 2H), 1.97 (dd, *J*=14.3, 6.5 Hz, 2H), 1.83 (ddd, *J*=19.4, 12.5, 6.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 213.68, 141.56, 141.43, 137.17, 135.76, 130.30, 128.72, 128.28, 126.98, 126.88, 126.44, 125.00, 122.19, 48.47, 35.68, 34.66, 34.10, 30.24, 24.58, 23.23. **HRMS** (**ESI**): calcd for $C_{22}H_{23}O$ [M+H]: 303.1749, found: 303.1752.

(4′-methyl-2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)(phenyl)methanone (3 ab)

Prepared according to the general procedure to afford white solid in 69% yield, 95.3 mg. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.6 Hz, 2H), 7.58 (t, *J* = 7.1 Hz, 1H), 7.49 (t, *J* = 7.3 Hz, 2H), 7.30 (d, *J* = 7.3 Hz, 2H), 7.14 (d, *J* = 7.6 Hz, 2H), 6.14 (d, *J* = 1.9 Hz, 1H), 3.67–3.52 (m, 1H), 2.58 (s, 2H), 2.48 (dd, *J* = 32.4, 14.1 Hz, 2H), 2.34 (s, 3H), 2.17 (d, *J* = 11.2 Hz, 1H), 1.93–1.83 (m, 1H). **^{13}C NMR** (101 MHz, CDCl3) δ 203.40, 138.89, 136.57, 136.34, 136.09, 132.98, 129.01, 128.71, 128.35, 124.93, 122.26, 41.37, 28.76, 27.24, 26.29, 21.07. **HRMS** (**ESI**): calcd for $C_{20}H_{21}O$ [M + H]: 277.1592, found: 277.1594.

(3′,5′-dimethyl-2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)(phenyl)methanone (3 ac)

Prepared according to the general procedure to afford yellow oil in 66% yield, 95.7 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.4 Hz, 2H), 7.59 (d, *J* = 7.2 Hz, 1H), 7.51 (t, *J* = 7.3 Hz, 2H), 7.06 (s, 2H), 6.93 (s, 1H), 6.17 (s, 1H), 3.62 (s, 1H), 2.61 (s, 2H), 2.59–2.47 (m, 2H), 2.35 (s, 6H), 2.17 (d, *J* = 9.3 Hz, 1H), 1.96–1.85 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.34 (s), 141.89 (s), 137.71 (s), 136.53 (s), 136.37 (s), 132.98 (s), 128.72 (s), 128.59 (s), 128.36 (s), 123.10 (s), 122.77 (s), 41.40 (s), 28.79 (s), 27.41 (s), 26.35 (s), 21.45 (s). **HRMS** (**EI**): called for $C_{21}H_{22}O$: 290.1671, found: 290.1672.

(3′-methyl-2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)(phenyl)methanone (3 ad)

Prepared according to the general procedure to afford yellow oil in 68% yield, 93.8 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.4 Hz, 2H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.50 (t, *J* = 7.3 Hz, 2H), 7.23 (d, *J* = 6.0 Hz, 3H), 7.08 (d, *J* = 5.0 Hz, 1H), 6.17 (s, 1H), 3.62 (d, *J* = 9.8 Hz, 1H), 2.60 (s, 2H), 2.50 (dd, *J* = 33.8, 14.0 Hz, 2H), 2.38 (s, 3H), 2.19 (d, *J* = 12.9 Hz, 1H), 1.89 (dd, *J* = 14.2, 6.3 Hz, 1H). 13 C NMR (101 MHz, $CDCl_3$) δ 203.31, 141.79, 137.78, 136.41, 136.34, 132.97, 128.71, 128.34, 128.21, 127.66, 125.91, 122.93, 122.21, 41.35, 28.76, 27.30, 26.31, 21.56. **HRMS** (**EI**): called for $C_{20}H_{20}O$: 276.1514, found: 276.1515

phenyl(2,3,4,5-tetrahydro-[1,1′:4′,1″-terphenyl]-4-yl) methanone (3 ae)

Prepared according to the general procedure to afford white solid in 72% yield, 121.7 mg, and melting point: 150.7–152.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.7 Hz, 2H), 7.60 (dd, *J* = 14.5, 7.5 Hz, 5H), 7.50 (t, *J* = 7.4 Hz, 4H), 7.45 (t, *J* = 7.3 Hz, 2H), 7.34 (t, *J* = 7.3 Hz, 1H), 6.26 (s, 1H), 3.64 (d, *J* = 12.1 Hz, 1H), 2.64 (d, *J* = 5.2 Hz, 2H), 2.53 (dd, *J* = 34.4, 14.0 Hz, 2H), 2.21 (d, *J* = 12.9 Hz, 1H), 1.91 (dd, *J* = 15.0, 7.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.25, 140.80, 140.62, 139.66, 136.32, 135.79, 133.00, 128.77, 128.72, 128.35, 127.20, 126.99, 126.94, 125.41, 123.23, 41.31, 28.80, 27.15, 26.29. **HRMS** (**EI**): called for $C_{25}H_{22}O$: 338.1671, found: 338.1672

(4′-fluoro-2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)(phenyl)methanone (3 af)

Prepared according to the general procedure to afford white solid in 70% yield, 98.0 mg. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.3 Hz, 2H), 7.61–7.56 (m, 1H), 7.49 (t, *J* = 7.4 Hz, 2H), 7.39–7.33 (m, 2H), 7.01 (t, *J* = 8.0 Hz, 2H), 6.12 (s, 1H), 3.61 (d, *J* = 7.7 Hz, 1H), 2.57 (t, *J* = 11.9 Hz, 2H), 2.47 (t, *J* = 18.1 Hz, 2H), 2.18 (d, *J* = 13.6 Hz, 1H), 1.94–1.82 (m, 1H). **^{13}C NMR** (101 MHz, CDCl3) δ 203.20, 161.98 (d, J = 245.7 Hz), 137.86, 136.25, 135.35, 133.05, 128.74, 128.35, 126.57 (d, J = 7.8 Hz), 123.03, 115.07 (d, J = 21.2 Hz), 41.17, 28.66, 27.31, 26.21. **HRMS** (**ESI**): calcd for $C_{19}H_{18}FO$ [M + H]: 281.1342, found: 281.1346.

(4′-chloro-2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)(phenyl)methanone (3 ag)

Prepared according to the general procedure to afford white solid in 71% yield, 105.1 mg, and melting point: 111.7–113.2 °C. **^{1}H NMR** (400 MHz, CDCl3) δ 7.99 (d, *J* = 7.6 Hz, 2H), 7.58 (t, *J* = 7.2 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 6.18 (d, *J* = 2.6 Hz, 1H), 3.67–3.53 (m, 1H), 2.55 (s, 2H), 2.45 (d, *J* = 17.7 Hz, 2H), 2.18 (d, *J* = 12.8 Hz, 1H), 1.94–1.81 (m, 1H). **^{13}C NMR** (101 MHz, CDCl3) δ 203.10, 140.14, 136.23, 135.24, 133.06, 132.58, 128.75, 128.40, 128.34, 126.33, 123.73, 41.11, 28.66, 27.08, 26.17. **HRMS** (**ESI**): calcd for $C_{19}H_{18}ClO$ [M + H]: 297.1046, found: 297.1044.

phenyl(4′-(trifluoromethyl)-2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl)methanone (3 ah)

Prepared according to the general procedure to afford white solid in 53% yield, 87.5 mg, and melting point: 76.5–78.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.6 Hz, 2H), 7.62–7.56 (m, 3H), 7.49 (d, *J* = 7.4 Hz, 4H), 6.28 (s, 1H), 3.67–3.56 (m, 1H), 2.59 (s, 3H), 2.48 (d, *J* = 17.8 Hz, 1H), 2.21 (d, *J* = 12.9 Hz, 1H), 1.95–1.85 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.92, 145.17, 136.89–136.51 (m), 136.18, 135.32, 133.08, 128.75, 128.32, 125.40, 125.26, 125.22, 41.00, 28.64, 27.01, 26.12. **HRMS** (**EI**): calcd for $C_{20}H_{17}F_3O$: 330.1231, found: 330.1228.

(4-(naphthalen-2-yl)cyclohex-3-en-1-yl)(phenyl) methanone (3 aj)

Prepared according to the general procedure to afford white solid in 65% yield, 101.4 mg, and melting point; 89.2–90.8 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.2 Hz, 2H), 7.79 (t, *J* = 9.9 Hz, 4H), 7.57 (dd, *J* = 16.9, 7.9 Hz, 2H), 7.50–7.41 (m, 4H), 6.33 (s, 1H), 3.62 (t, *J* = 10.7 Hz, 1H), 2.70 (s, 2H), 2.66–2.39 (m, 2H), 2.27–2.16 (m, 1H), 1.99–1.85 (m, 1H). **^{13}C NMR** (101 MHz, CDCl3) δ 203.30, 138.86, 136.31, 136.03, 133.55, 133.08, 132.60, 128.78, 128.41, 128.14, 127.82, 127.58, 126.15, 125.63, 123.85, 123.77, 123.41, 41.36, 28.92, 27.20, 26.36. **HRMS** (**ESI**): calcd for $C_{23}H_{21}O$ [M + H]: 313.1592, found: 313.1589.

1-(p–tolyl)spiro[cyclohex[6]ene-4,2′-inden]-1′(3′H)-one (5db)

Prepared according to the general procedure to afford white solid in 75% yield, 108.0 mg, and melting point: 149.7–151.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J=7.6 Hz, 1H), 7.61 (t, J=7.4 Hz, 1H), 7.45 (d, J=7.6 Hz, 1H), 7.40 (t, J=7.4 Hz, 1H), 7.34 (d, J=7.6 Hz, 2H), 7.16 (d, J=7.7 Hz, 2H), 6.18 (d, J=4.2 Hz, 1H), 3.13 (d, J=17.3 Hz, 1H), 2.98 (d, J=17.3 Hz, 1H), 2.74–2.54 (m, 3H), 2.36 (s, 3H), 2.07 (ddd, J=23.3, 14.9, 5.1 Hz, 2H), 1.70 (dd, J=12.7, 4.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.14, 152.84, 138.67, 136.70, 135.93, 135.82, 134.92, 129.04, 127.49, 126.73, 124.91, 124.35, 121.68, 48.22, 39.08, 35.07, 29.30, 24.86, 21.09. **HRMS** (**EI**): calcd for $C_{21}H_{20}O$: 288.1514, found: 288.1516.

1-(4-fluorophenyl)spiro[cyclohex[6]ene-4,2′-inden]-1′(3′H)-one (5df)

Prepared according to the general procedure to afford brown solid in 76% yield, 110.9 mg, and melting point: 56.8–58.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J=7.6 Hz, 1H), 7.61 (t, J=7.4 Hz, 1H), 7.45 (d, J=7.6 Hz, 1H), 7.39 (t, J=6.9 Hz, 3H), 7.03 (t, J=8.3 Hz, 2H), 6.15 (d, J=3.6 Hz, 1H), 3.12 (d, J=17.3 Hz, 1H), 2.97 (d, J=17.2 Hz, 1H), 2.71–2.52 (m, 3H), 2.11–2.00 (m, 2H), 1.70 (dd, J=13.2, 2.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.92, 162.04 (d, J=245.9 Hz), 152.72, 137.63, 135.86, 135.14, 134.97, 127.55, 126.72, 126.57 (d, J=7.8 Hz), 124.38, 122.45, 115.10 (d, J=21.3 Hz), 48.05, 39.12, 35.00, 29.26, 25.02. **HRMS** (**EI**): calcd for $C_{20}H_{17}FO$: 292.1263, found: 292.1262.

1-(4-chlorophenyl)spiro[cyclohex[6]ene-4,2′-inden]-1′(3′H)-one (5dg)

Prepared according to the general procedure to afford white solid in 73% yield, 112.4 mg, and melting point: 178.8–180.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J=7.6 Hz, 1H), 7.61 (t, J=7.3 Hz, 1H), 7.45 (d, J=7.6 Hz, 1H), 7.41 (d, J=7.4 Hz, 1H), 7.36 (d, J=8.5 Hz, 2H), 7.30 (d, J=8.2 Hz, 2H), 6.20 (s, 1H), 3.12 (d, J=17.3 Hz, 1H), 2.96 (d, J=17.2 Hz, 1H), 2.73–2.51 (m, 3H), 2.13–1.99 (m, 2H), 1.70 (dd, J=13.2, 2.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.83, 152.69, 139.92, 135.83, 135.00, 132.69, 128.44, 127.57, 126.74, 126.33, 124.38, 123.18, 48.01, 39.13, 35.02, 29.23, 24.80. **HRMS** (**EI**): calcd for $C_{20}H_{17}ClO$: 308.0968, found: 308.0964.

phenyl(2,3,4,5-tetrahydro-[1,1′-biphenyl]-4-yl-3,3,5,5–d4)methanone (3aa–d4)

Prepared according to the general procedure to afford colorless oil in 66% yield, 87.8 mg. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (d, J=7.3 Hz, 2H), 7.60–7.56 (m, 1H), 7.49 (s, 2H), 7.41 (d, J=7.1 Hz, 2H), 7.33 (t, J=7.1 Hz, 2H), 7.25 (s, 1H), 6.18 (s, 1H), 3.58 (s, 1H), 2.59 (s, 2H).

1-phenylprop-2-en-1-one (B)[16]

Yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95 (d, J=7.7 Hz, 1H), 7.58 (t, J=7.3 Hz, 1H), 7.48 (t, J=7.5 Hz, 1H), 7.16 (dd, J=17.1, 10.6 Hz, 1H), 6.44 (d, J=17.1 Hz, 1H), 5.94 (d, J=10.6 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 191.10, 137.29, 133.02, 132.40, 130.24, 128.72, 128.64.

3-(methylthio)-1-phenylpropan-1-one (C)[16]

Yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, J=7.9 Hz, 2H), 7.57 (t, J=7.4 Hz, 1H), 7.47 (t, J=7.5 Hz, 2H), 3.29 (t, J=7.3 Hz, 2H), 2.91 (t, J=7.4 Hz, 2H), 2.16 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 198.43, 136.64, 133.28, 128.68, 128.04, 77.39, 77.08, 76.76, 38.64, 28.49, 15.94.

methyl(3-phenylbut-2-en-1-yl)sulfane (D)[10]

Yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41 (d, J=7.7 Hz, 2H), 7.32 (t, J=7.2 Hz, 2H), 7.25 (s, 1H), 5.86 (t, J=7.9 Hz, 1H), 3.32 (d, J=7.8 Hz, 2H), 2.08 (d, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.10, 137.73, 128.27, 127.12, 125.79, 123.69, 31.76, 15.91, 14.63.

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UPDATES

Effective [3 + 1 + 1 + 1] Cycloaddition to Six-Membered Carbocycle Based on DMSO as Dual Carbon Synthon

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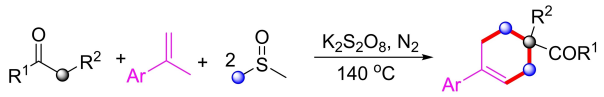

Multiple C-H Cross-Coupling *DMSO as dual carbon source and solvent*

Four C-C bonds formed *Efficient access to Six-membered carbocycle*