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# Heterobimetallic Pd−Sn Catalysis: Michael Addition Reaction with C-, N-, O-, and S-Nucleophiles and in Situ Diagnostics

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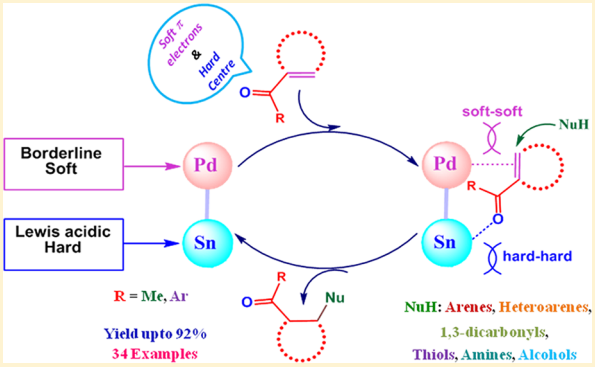
Supporting Information

**ABSTRACT:** An efficient Michael addition reaction of differently substituted enones with carbon, sulfur, oxygen, and nitrogen nucleophiles has been achieved by a new heterobimetallic "Pd−Sn" catalyst system. The nature of the catalytically relevant species and their interactions with the enone moiety has been examined by spectroscopy. The effect of ligand and the coordination mode of enone with "Pd−Sn" heterobimetallic system have been investigated by kinetics and DFT studies. A straightforward application of this methodology is shown in the synthesis of 1,4-oxathiepane core.




## INTRODUCTION

Activation of an organic functionality by two different types of catalytic centers, main group (Lewis acids) and transition metals, is an important theme of research in modern organic reactions.[1] The relative ability of the metals (both main group and transition) to make a $\sigma$- or a $\pi$-complex with appropriate substrates is useful in making the choice of catalysts for the desired transformations, especially in cases where bi- or polyfunctional substrates are involved. Over the past decade, multimetallic catalysis has received much attention since during substrate activation and coupling steps in the catalytic cycle the synergistic functions of more than one active centers in the catalyst can enhance the catalytic activity and selectivity.[2] Irrespective of their types, multimetallic catalysts offer superior results in terms of efficiency and selectivity relative to the individuals. In this regard, heterobimetallic catalysis constitutes an important subarea within the broader domain of multimetallic catalysis. In cooperative intramolecular heterobimetallic catalysis, the two different metals are linked together by a metal−metal bond or via a ligand and directly or indirectly the two metals participate in substrate activation.[2f,3,4] Electrophile and nucleophile can be also activated separately by different metal complexes as in cooperative dual metal catalysis.[5,6] Additionally, dual metal reagents are used to provide a more active species in situ for substrate activation.[6a,b,7] In continuation of our research program in bimetallic catalysis involving a transition-metal partner and tin as a main group metal partner, we present here a new bimetallic (Pd/Sn) catalyst system for the activation of enone toward Michael addition with a large spectrum of nucleophiles.[4,6]

Michael addition reaction is widely recognized as one of the most important C−C, C−O, C−N, and C−S bond-forming reactions, and the resulting products are of wide importance.[8] Various acids/base,[9] transition-metal salts,[9q,10] and organocatalysts[9q,11] are known to promote the reaction. Besides this, various homo- or heterobimetallic catalytic systems efficiently catalyzes the Michael reaction.[3a,5d,7b,12] In an early demonstration, Shibasaki and co-workers achieved a highly efficient Michael addition of 2-hydroxy-1,5-methoxyacetophenone to $\alpha,\beta$-unsaturated ketones promoted by a bimetallic oxo-bridged $Zn^{II}/Zn^{II}$ homobimetallic catalyst built on a binol scaffold.[12b] Subsequently, the group has demonstrated the catalytic use of oxo-bridged heterobimetallic assemblies built using rare-earth and alkali metal combination in asymmetric aza-Michael reaction. Mechanistic studies further established that the reaction proceeds via a novel Lewis acid−Lewis acid cooperative mechanism.[3a] Yet another achievement by the group is the use of homo- and heterobimetallic $TM_2$ catalysts (TM is transition metal) built on a Schiff-base scaffold for various asymmetric Michael reactions.[12a,e] Lee et al. showed the utility of a novel tetranuclear $Zn^{II}/Fe^{III}$ heterobimetallic catalyst in mediating the thia-Michael addition of thiophenols to $\alpha,\beta$-unsaturated enones.[12c] Jautze and Peters designed ferrocene-bridged $Pd^{II}/Pd^{II}$ heterobimetallic catalysts for the asymmetric Michael reaction between substituted cyanoacetates and vinyl ketones.[12d] The authors suggested a cooperative intramolecular bimetallic mechanism involving activation of substrates at both

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the $Pd^{II}$ sites. Gao et al. have demonstrated that a dual reagent combination of $FeCl_3$ and $PdCl_2$ in acetylacetonate can efficiently mediate the Michael addition of indoles to chalcones.[7b] In situ mass spectral studies confirmed the formation of a bimetallic Fe−Pd species in the reaction. It may be mentioned here that Jacobsen and co-workers pioneered the concept of dual-role catalyst using a combination of two reagent system to generate the active catalyst for conjugate addition to $\alpha,\beta$-unsaturated imides.[5d]

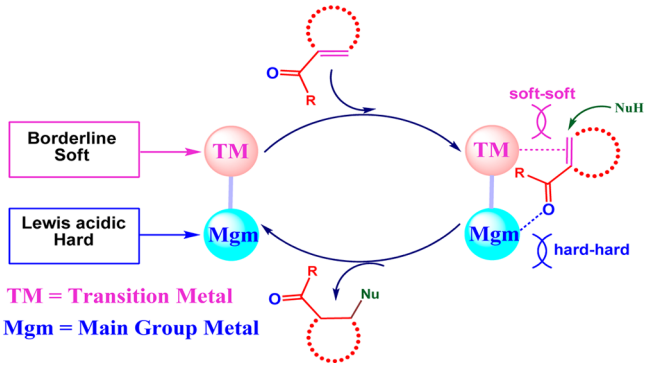
Although numerous advances have been made in catalytic Michael addition reaction, there exists a wide scope to develop catalytic system capable of forming C−C and C−Z (Z = heteroatom) bonds directly via Michael reaction with wide range of substrate scopes. In this context the catalyst loading (>5 mol %) and the use of additives are of concern in some of the reported catalytic Michael addition reaction.[9b−f,11g−j,13] For example, Ramachary et al. employed bifunctional amine (30 mol %) as organocatalyst with acid additive (30 mol %) for the direct addition of a variety of alcohols to enones.[13g] Xu et al. achieved the Michael reactions of chalcones with active methylene compounds using 15 mol % of $FeCl_3$.[9d] 1,4-Conjugated addition of indoles/thiols to $\alpha,\beta$-unsaturated ketones mediated by a catalytic amount (10 mol %) of $InBr_3$ was reported by Umani-Ronchi et al.[9e] In the present work, we were interested to test the principle of cooperative catalysis in the Michael reaction using a new heterobimetallic "Pd−Sn" catalyst to establish the scope of its reactivity and finally to make initial attempts to understand the nature of substrate activation.

## RESULTS AND DISCUSSION

In general, a borderline soft transition metal (TM) center is well-known to form a $\pi$-complex with soft functional groups like an alkene or an alkyne. On the other hand, a hard Lewis acid (LA) center prefers $\sigma$-complexation with C═Y, where Y is generally a hard center (O, N).[1] Since an enone has two binding sites (soft double bond and relatively hard keto oxygen atom), they can be concurrently activated across a hetero-bimetallic system having a TM and a Lewis acidic (LA) center. Thus, the combination of a hard, electrophilic, and Lewis acidic metal center with a borderline soft transition metal center may potentially lead to novel bimetallic reactivity and enhance the efficiency in Michael reaction of enones with various nucleophiles (Scheme 1).

The above idea inspired us to check the reactivity of enone against various nucleophiles in the presence of heterobimetallic systems containing Pd as TM and Sn as Lewis acid partner. The heterobimetallic Pd−Sn catalysts (**A1**−**A5**) have been synthesized via the insertion reaction of $SnCl_2$ across $PdCl_2(MeCN)_2$ in the presence of ligand in acetone−dichloromethane (Scheme 2).[14,6c]

**Scheme 1. Proposed Bimetallic Model for the Activation of Enone**




**Scheme 2. Preparation of Complexes**

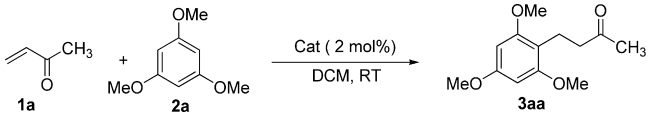
$(MeCN)_2PdCl_2 + SnCl_2 + L\text{–}L \xrightarrow[RT]{CH_2Cl_2/acetone}$ (L-L)PdClSnCl$_3$ or (L-L)Pd(SnCl$_3$)$_2$

L-L = COD (**A1**), NBD (**A2**) CHD (**A3**) $PPh_3$ (**A4**) for (L-L)PdClSnCl$_3$

L-L =DPPE (**A5**) for (L-L)Pd(SnCl$_3$)$_2$

Initially, we had chosen the model reaction between methyl vinyl ketone (MVK) **1a** and 1,3,5-trimethoxy benzene **2a** in the presence of various "Pd−Sn" heterobimetallic complexes as catalyst (2 mol %) in dichloromethane (DCM) at room temperature (Table 1).

**Table 1. Catalyst Screening**[a]




| entry | complex | time (h) | yield of **3aa**[b] (%) |
|---|---|---|---|
| 1 | **Pd(COD)ClSnCl$_3$ (A1)** | **1** | **75** |
| 2 | Pd(PPh$_3$)$_2$ClSnCl$_3$ (**A4**) | 12 | trace |
| 3 | Pd(dppe)(SnCl$_3$)$_2$ (**A5**) | 12 | trace |

[a]A mixture of **2a** (0.25 mmol), **1a** (0.5 mmol), and catalyst (2 mol %) in 2 mL of DCM was stirred at room temperature (30 °C). [b]$^1$H NMR yield using triphenylmethane as external standard.

The above studies indicated that with respect to catalytic efficiency, only catalyst **A1** bearing a diene ligand (COD) was promising. The inactivity of other complexes may be due to the lack of a coordination site for MVK activation. For a better look on the effect of ligand on catalyst efficiency, we carried out a kinetic study in the presence of "Pd−Sn" catalysts (Figure 1, for details see the Supporting Information).[15] From the pseudo-first-order rate data (vide $^1$H NMR, Figure 1), we noted the

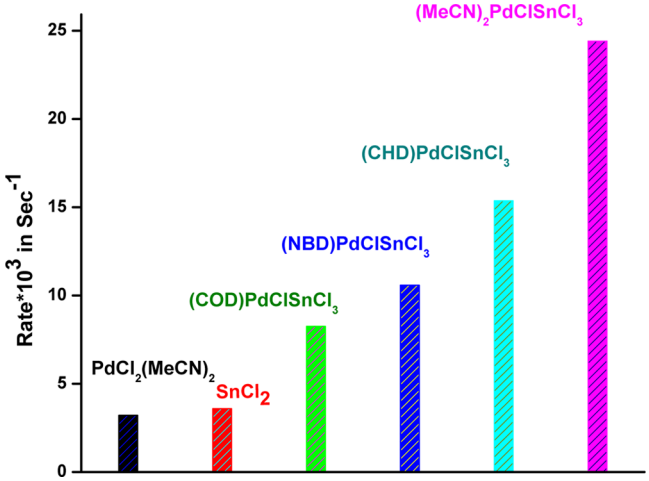



**Figure 1.** Comparative reactivity pseudo-first-order rate plot for different catalysts.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following: (a) a combination of catalytic amounts of $PdCl_2(MeCN)_2$ and $SnCl_2$ showed highest activity; (b) individually $PdCl_2(MeCN)_2$ and $SnCl_2$ were least reactive; (c) catalysts bearing the diene ligands showed reactivity order as CHD > NBD > COD.

The highest reactivity of a combination of $PdCl_2(MeCN)_2$ and $SnCl_2$ encouraged us to look for the active species of this catalytic system. Toward this end, UV−vis study was carried out in DCM/acetonitrile solvent. Upon addition of $SnCl_2$ (1 equiv) to $PdCl_2(MeCN)_2$ (1 equiv), the initial yellow color changed to reddish-orange. The corresponding spectrum was in sharp contrast to that of $PdCl_2(MeCN)_2$ indicating the formation of a new species (Figure 2). Addition of 1,5-

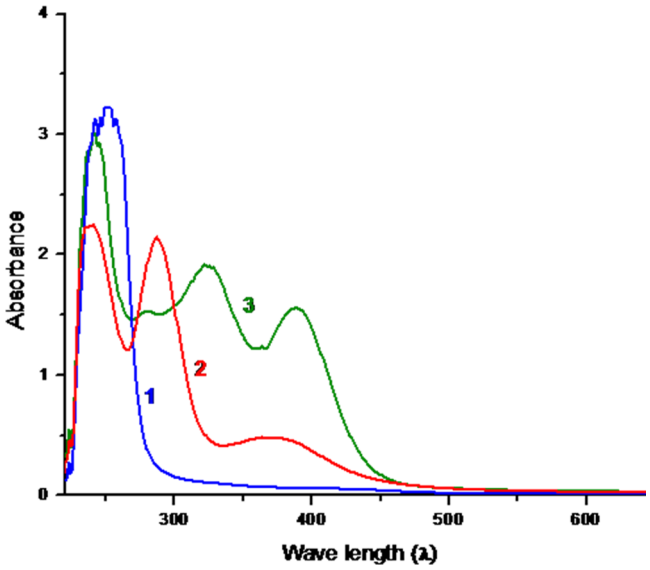
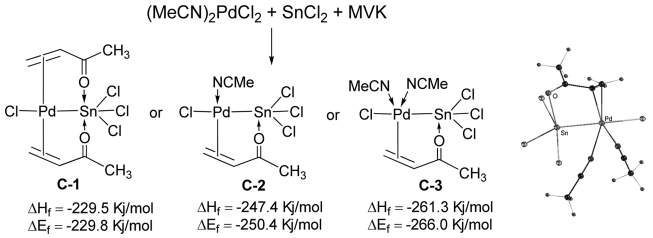



**Figure 2.** UV−vis spectrum of (1) $PdCl_2(MeCN)_2$; (2) a mixture of $PdCl_2(MeCN)_2$ and $SnCl_2$ (1:1); (3) a mixture of $PdCl_2(MeCN)_2$, $SnCl_2$, and COD (1:1:1). The inset shows the molecular structure of $PdCl(COD)SnCl_3$ **A1**.

cyclooctadiene (COD) to this solution generated the complex $PdCl(COD)SnCl_3$ **A1** (Figure 2). It is therefore apparent that the combination of $PdCl_2(MeCN)_2$ and $SnCl_2$ leads to the in situ generation of $(MeCN)_2PdCl(SnCl_3)$ **A6**, which we believe is the catalytically active species.

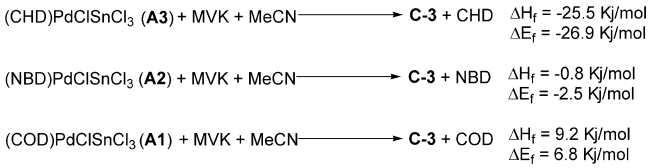
We also carried out in situ $^{13}C$ NMR experiments to understand the binding of enone to complex **A6**. The $^{13}C$ NMR spectrum of a 1:1:1 mixture of $PdCl_2(MeCN)_2$, $SnCl_2$, and **1b** in $CDCl_3$/acetonitrile at room temperature revealed that upon binding to the Pd−Sn motif the carbonyl carbon and the double bond carbons of enone **1b** were downfield shifted as compared to free **1b**.[16] A similar observation was made in the case of binding of chalcone **1i** to Pd−Sn (Supporting Information). The above results establish the activation of the enone moiety by the bimetallic assembly. However, the relative extent of such activation at each of the metal centers cannot be predicted with the given data. Therefore, we wished to derive further insight on the nature of enone−activation across the Pd−Sn motif from DFT studies. MVK was chosen as the representative enone for these studies. The energetically most stable structure of the MVK-coordinated Pd−Sn complex was determined from complex formation energy in terms of $\Delta H_f$ and $\Delta E_f$ with zero-point energies (ZPE) and thermal corrections at 298 K.[17] All of the calculations have been performed at the B3LYP/LANL2DZ, 6-31G* level of theory. The study revealed that complex **C-3** is more stable than **C-2** and **C-1** (Scheme 3).

**Scheme 3. Relative Complex Formation Energy of Active Complex between "Pd−Sn" and MVK**




We also looked into the ease of formation of intermediate **C-3** from the corresponding precursor complexes (diene)-$PdClSnCl_3$ (**A1**−**A3**). The calculated enthalpy of formation ($\Delta H_f$) and formation energy in terms of electronic energy shown below indicates that the ease of displacement of a diene ligand from the corresponding complexes by MVK follows the order CHD > NBD > COD (Scheme 4).[18]

**Scheme 4. Formation Energy for the Reaction of "Pd−Sn" Complex A1−A3, MVK, and MeCN**




This trend correlates well with the experimentally determined comparative efficacy of the catalysts in the model reaction (**A3** > **A2** > **A1**; Figure 1).

Equipped with the preliminary understanding on bond activation as described above, we proposed examination of the scope and optimization of the reaction conditions of the bimetallic "Pd−Sn" catalyst. For this purpose we had chosen the relatively slow reaction between MVK **1a** with 2-methylthiophene **2c**. From solvent screening, acetonitrile was judged as the best solvent for the "Pd−Sn"-catalyzed Michael addition reaction over DCE, $C_6H_6$, or hexane (Table 2). The optimum catalyst loading was found to be 2 mol %. Reduction of catalyst loading from 2 to 1 mol % drastically reduced the yield of the reaction (entry 5, Table 2).

The scope of the present bimetallic Pd−Sn-catalyzed C−C and C−heteroatom bond forming Michael addition reaction of enones is illustrated in Tables 3 and 4. The generality of the reaction was successfully tested in the case of various enones (**1a**−**e**,**k**,**l**) with electron-rich arenes (**2a**,**b**) and heteroarenes (**2c**−**h**) as the nucleophiles under the optimized conditions and at room temperature (30 °C) (Chart 1). In most cases, the corresponding hydroarylated products were obtained in moderate to excellent yields (Table 3, entries 1−12). In all cases, only monoadduct product was obtained with the exception of entry 4. Notably, in the case of free indole, the reactions were completely C3-selective, with no N-alkyl product being formed (Table 3, entries 5, 8, 10, and 11). One may note that the hydroarylation reaction failed with arenes such as anisole or toluene. Next, we extended the scope of the reaction by employing cyclic, symmetrical, and


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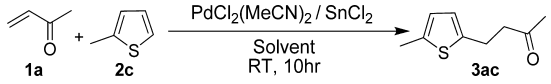
**Table 2. Solvent Screening and Optimization**[a]



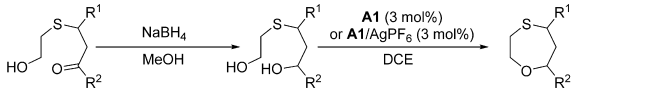

| entry | solvent | yield of **3ac**[b] (%) |
|---|---|---|
| 1 | **MeCN** | **87** |
| 2 | DCE | 65 |
| 3 | benzene | 37 |
| 4 | hexane | 35 |
| 5[c] | MeCN | 40 |

[a]Reaction conditions: **1a** (0.25 mmol), **2c** (0.75 mmol), 2 mol % of $PdCl_2(MeCN)_2$, and 2 mol % of $SnCl_2$ in solvent (1 mL) at room temperature (30 °C). [b]$^1H$ NMR yield using triphenylmethane as external standard. [c]1 mol % of $PdCl_2(MeCN)_2$ and 1 mol % of $SnCl_2$ was used.

unsymmetrical 1,3-dicarbonyls (**2i–l**) as the nucleophile for carbon–carbon bond formation (Table 3, entries 13–17).

Attracted by the direct C–C bond formation via Michael addition reaction, we next examined the reactivity of the "Pd–Sn" catalyst in C–heteroatom bond formation with representative S-, N-, and O-nucleophiles under similar reaction conditions. Generally sulfur-containing compounds are potential catalyst poisons because of their strong coordinating properties.[19] However, the addition to various enones was accomplished smoothly at room temperature with both aromatic and aliphatic thiols (Table 4, entries 1–8). With an aliphatic bifunctional nucleophile like 2-mercaptoethanol, selective C–S bond formation took place (entries 4 and 8). Similarly, in the case of 2-mercaptophenol **2q**, exclusive C–S bond formation was observed resulting in the formation of **3fq** (Table 4, entry 3). Aromatic amines also showed moderate to good reactivity with differently substituted $\alpha,\beta$-unsaturated ketones (Table 4, entries 9, 10, 13–15). Weak nucleophilic substrates such as acetanilides or sulfonamides were inert toward the transformation. Similar reactions with aliphatic amines and *O*-nucleophiles were briefly examined and the desired products were obtained in excellent yields (Table 4, entries 11, 12, 16, and 17). The structures of **3ca** and **3cp** were established by X-ray crystallographic analysis (Supporting Information). Here, it is also noted that our attempt to activate other $\alpha,\beta$-unsaturated systems like unsaturated aldehydes, esters, or cyanides was not successful with the present bimetallic catalyst system.

**Scheme 5. Synthesis of 1,4-Oxathiepane Cores**




Next, a brief study was undertaken employing the present reaction for the synthesis of less commonly studied 1,4-oxathiepane core (Scheme 5). Here, the Michael product was reduced by $NaBH_4$, and then corresponding cyclization was carried out by 3 mol % of catalyst $PdCl(COD)SnCl_3$ **C1** or **C1**/$AgPF_6$ for the preparation of substituted 1,4-oxathiepane **4a** and **4b** (for details, see the Experimental Section).[4c,6c]

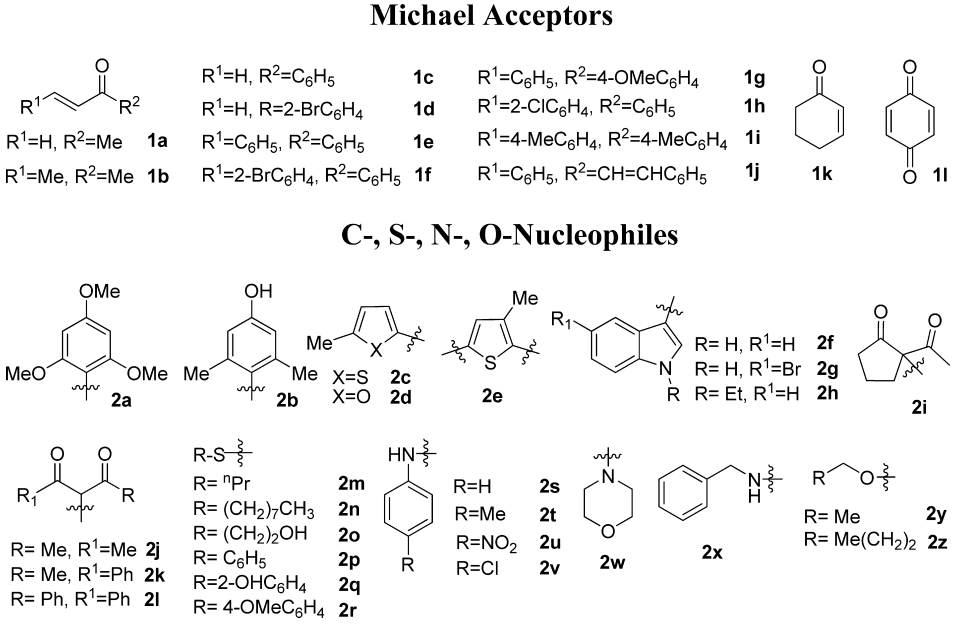
## CONCLUSION

We have developed a new heterobimetallic "Pd–Sn" catalyst system to activate enones for the effective construction of direct C–C and C–heteroatom bond with a wide range of nucleophiles via Michael addition reaction. Spectroscopic and theoretical investigations provided initial insight in to the nature of activation of enone by the catalyst.

## EXPERIMENTAL SECTION

**General Methods.** All preparations and manipulations were performed under a dry, oxygen-free, argon atmosphere. All solvents used for the synthesis, were dried and distilled by standard methods. Precoated silica gel $60F_{254}$ was used for thin-layer chromatography,

**Chart 1. Electrophiles and Nucleophiles Employed in the Michael Addition Reaction**




[a]The position of substitution is indicated by the truncated bond.


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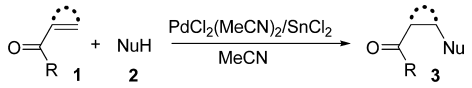
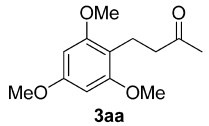
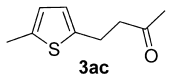
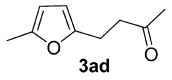
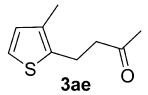
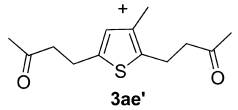
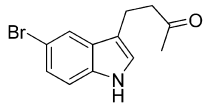
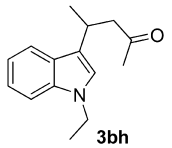
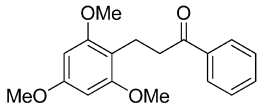
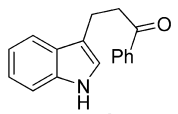
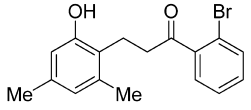
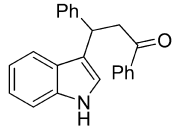
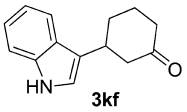
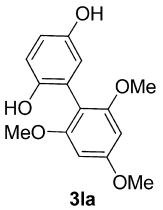
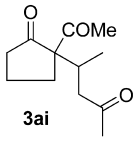
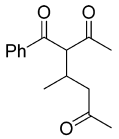
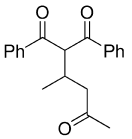
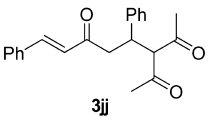
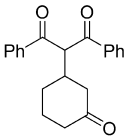
**Table 3. Michael Addition of Various Michael Acceptors 1 with C-Nucleophiles 2**[a]




| Entry | Substrates | Time (h) | Product | Yield of 3[b] (%) |
|---|---|---|---|---|
| 1 | **1a**+**2a** | 2 |  **3aa** | 92 |
| 2[c] | **1a**+**2c** | 10 |  **3ac** | 87 |
| 3[c] | **1a**+**2d** | 12 |  **3ad** | 76 |
| 4[c] | **1a**+**2e** | 12 |  **3ae** +  **3ae'** | 69 + 15 |
| 5 | **1a**+**2g** | 2 |  **3ag** | 90 |
| 6 | **1b**+**2h** | 2 |  **3bh** | 84 |
| 7 | **1c**+**2a** | 10 |  **3ca** | 80 |
| 8 | **1c**+**2f** | 6 |  **3cf** | 85 |
| 9[d,f] | **1d**+**2b** | 10 |  **3db** | 60 |
| 10 | **1e**+**2f** | 12 |  **3ef** | 50 |


dx.doi.org/10.1021/jo302643v | J. Org. Chem. 2013, 78, 2430−2442

**Table 3. continued**

| Entry | Substrates | Time (h) | Product | Yield of **3**[b] (%) |
|---|---|---|---|---|
| 11[d,e] | **1k**+**2f** | 12 |  **3kf** | 61 |
| 12[d,e,f] | **1l**+**2a** | 16 |  **3la** | 30 |
| 13[e] | **1a**+**2i** | 8 |  **3ai** | 35 |
| 14 | **1b**+**2k** | 22 |  **3bk** | 45 |
| 15 | **1b**+**2l** | 20 |  **3bl** | 48 |
| 16[c,f] | **1j**+**2j** | 20 |  **3jj** | 60 |
| 17[d,e] | **1k**+**2l** | 12 |  **3kl** | 55 |

[a]All of the reactions were carried out in acetonitrile at room temperature with 1.2 equiv of Michael acceptor, 1 equiv of NuH, 2 mol % of $SnCl_2$, and 2 mol % of $PdCl_2(MeCN)_2$ unless otherwise stated. [b]Except entries **2**–**4** where $^1H$ NMR yield was calculated using triphenylmethane as external standard; all others are isolated yield. [c]Carried out with 1 equiv of Michael acceptor and 3 equiv of NuH. [d]Carried out at 60 °C. [e]Carried out with 2.5 equiv of Michael acceptor and 1 equiv of NuH. [f]Carried out with 5 mol % of $SnCl_2$ and 5 mol % of $PdCl_2(MeCN)_2$.

and silica gel 100–200 mesh was used for column chromatography. $PdCl_2$, 1,5-cyclooctadiene, and other reagents were purchased from common commercial sources and were used without further purification. Dry $SnCl_2$ were prepared from commercially available $SnCl_2{,}2H_2O$. $^1H$ (200, 400 MHz) and $^{13}C$ (54.6, 100 MHz) NMR spectra were recorded on 200 and 400 MHz spectrometers. $^1H$ chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuterochloroform: $\delta$ 7.26 ppm). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, dd = double doublet, m = multiplet), coupling constant (Hz). $^{13}C$ chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: $\delta$ 77.0 ppm). The X-ray diffraction intensity data were collected at 293 K using a CCD diffractometer. UV–vis spectra were recorded using spectrophotometric grade solvent. High-resolution mass spectra were recorded with a mass spectrometer (TOF) in positive ion mode. All of the melting points are uncorrected. Elemental analyses were performed on a CHNS/O analyzer. IR (4000–500 $cm^{-1}$; using KBr pellet) spectra were obtained using an FTIR spectrometer.

**Computational Methods.** The ground-state geometry optimizations of all of the probable complexes were performed using GAUSSIAN 03[20] at the B3LYP level of theory. We employed LANL2DZ effective core potential (ECP) for Pd and Sn, and all other atoms were treated with the 6-31G(d) basis set. Geometries of all species studied were fully optimized, and they were characterized as


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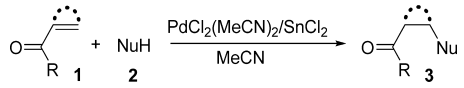
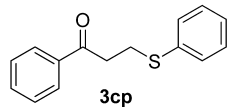
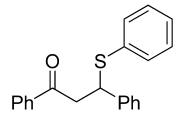
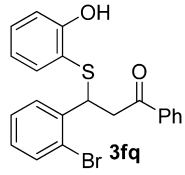
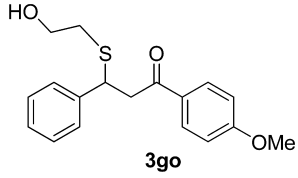
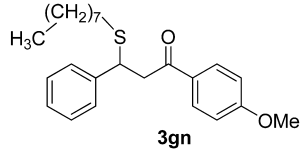
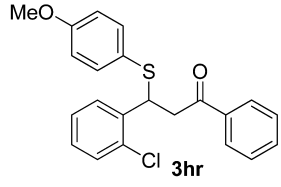
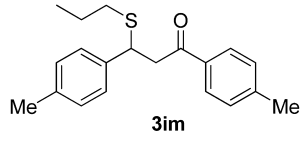
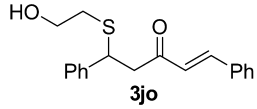
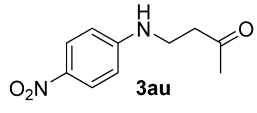
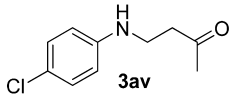
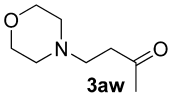
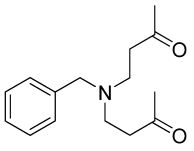
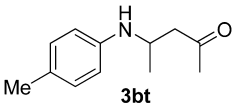
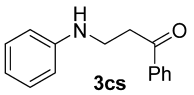
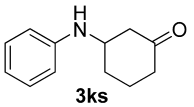
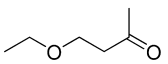
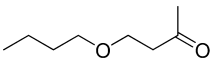
**Table 4. Michael Addition of Various Michael Acceptors 1 with Heteroatom−Nucleophiles 2[a]**




| Entry | Substrates | Time (h) | Product | Yield of 3[b] (%) |
|---|---|---|---|---|
| 1 | **1c+2p** | 0.5 |  **3cp** | 85 |
| 2 | **1e+2p** | 12 |  **3ep** | 90 |
| 3 | **1f+2q** | 12 |  **3fq** | 70 |
| 4 | **1g+2o** | 6 |  **3go** | 81 |
| 5 | **1g+2n** | 10 |  **3gn** | 82 |
| 6 | **1h+2r** | 3 |  **3hr** | 88 |
| 7 | **1i+2m** | 8 |  **3im** | 70 |
| 8 | **1j+2o** | 12 |  **3jo** | 60 |
| 9[c] | **1a+2u** | 12 |  **3au** | 76 |


dx.doi.org/10.1021/jo302643v | J. Org. Chem. 2013, 78, 2430−2442

**Table 4. continued**

| Entry | Substrates | Time (h) | Product | Yield of **3**[b] (%) |
|---|---|---|---|---|
| 10 | **1a+2v** | 12 |  **3av** | 70 |
| 11 | **1a+2w** | 1 |  **3aw** | 85 |
| 12[c] | **1a+2x** | 1 |  **3ax** | 80 |
| 13 | **1b+2t** | 12 |  **3bt** | 60 |
| 14 | **1c+2s** | 2 |  **3cs** | 81 |
| 15 | **1k+2s** | 10 |  **3ks** | 30 |
| 16[d] | **1a+2y** | 6 |  **3ay** | 90 |
| 17[d] | **1a+2z** | 6 |  **3az** | 83 |

[a]All of the reactions were carried out in acetonitrile at room temperature with 1.2 equiv of Michael acceptor, 1 equiv of NuH, 2 mol % of $SnCl_2$, and 2 mol % of $PdCl_2(MeCN)_2$ unless otherwise stated. [b]Except entries **16** and **17** where $^1H$ NMR yield was calculated using triphenylmethane as external standard; all others are isolated yield. [c]Carried out with 2.5 equiv of Michael acceptor and 1 equiv of NuH, [d]NuH was used as a solvent.

true intermediates on the potential energy surface by the absence of imaginary frequencies, after frequency calculation on the optimized geometries. Zero-point energies (ZPE) and thermal corrections at 298 K were calculated by using the frequencies computed at the same level of theory. The formation energies in the form of $\Delta H_f$ and $\Delta E_f$ have been calculated from the energy difference between product and reactant from their corresponding enthalpy, electronic energy, and free energy differences.

**Starting Materials.** $PdCl_2(MeCN)_2$ was prepared following the literature methods.[21] The enones, namely, **1c**[22a] and **1d**,[22b] were prepared and confirmed according to the literature procedure. Another set of enones, for example, **1e−j** were also prepared according to a reported procedure.[23a] The spectral data of **1e**,[23b] **1f**,[23c] **1g**,[23b] **1h**,[23d] **1i**,[23e] and **1j**[23a] were in excellent agreement with the reported data.

**Syntheses and Characterization of Complexes.**[14,6c] *[Pd(COD)Cl(SnCl$_3$)] (**A1**).* The 1,5-cyclooctadiene (55.1 mg, 0.51 mmol) was dissolved in $CH_2Cl_2$ (10 mL) by stirring with a magnetic stirrer, and a solution of $SnCl_2$ (95 mg, 0.5 mmol) in 0.5 mL of $Me_2CO$ was added, giving a milky suspension. Then solid $PdCl_2(MeCN)_2$ (130 mg, 0.50 mmol) was added to this suspension, and stirring was continued for 10 min. Freshly distilled petroleum ether (30 mL) was added to the mixture, and stirring was continued for another 10 min. The precipitate was separated by filtration, washed with petroleum ether, and dried in vacuum to give **A1** as a yellow solid (201 mg, 85%). $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ 6.31 (br, s, 4H), 2.89−2.95 (m, 4H), 2.50−2.62 (m, 4H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 116.6, 30.9. DEPT 135: 116.6, 30.9. UV−vis (DCM): ($\lambda_{max}$, nm): 325, 390. Anal. Calcd for $C_8H_{12}Cl_4PdSn$: C, 20.22; H, 2.55. Found: C, 20.31; H, 2.48.

$[PdCl(PPh_3)_2(SnCl_3)]$ (**A4**) was prepared according to the above procedure by using 2 equiv of triphenylphosphine ligand with respect to $SnCl_2$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.68−7.73 (m, 12H), 7.36−7.49 (m, 18H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 135, 134.98, 134.92, 130.4, 128.1, 128, 127.9. $^{31}P$ NMR ($CDCl_3$ + DCM): $\delta$ 27.32. Anal. Calcd for $C_{36}H_{30}Cl_4P_2PdSn$: C, 48.50; H, 3.39. Found: C, 48.27; H, 3.28.

Similarly, $[Pd(dppe)(SnCl_3)_2]$ (**A5**) was prepared by using 2 equiv of $SnCl_2$ with respect to ligand dppe or $PdCl_2(MeCN)_2$. Anal. Calcd for $C_{26}H_{24}Cl_6P_2PdSn_2$: C, 32.70; H, 2.53. Found: C, 32.53; H, 2.67.

**Typical Procedure for the Michael Addition of 1,3,5-Trimethoxybenzene 2a to Methyl Vinyl Ketone 1a Using Pd/Sn Catalyst.** A 10 mL Schlenk flask equipped with a magnetic bar was charged with $[PdCl_2(MeCN)_2]$ (2.60 mg, 0.01 mmol), $SnCl_2$ (1.90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mg, 0.01 mmol), methyl vinyl ketone **1a** (42 mg, 0.6 mmol), and dry acetonitrile (2 mL) under an argon atmosphere. Then 1,3,5-trimethoxybenzene **2a** (84 mg, 0.5 mmol) was added, and the reaction was allowed to continue at room temperature (30 °C). Following completion of the reaction, solvent was removed under reduced pressure, and the mixture was subjected to column chromatography over silica gel (100−200 mesh, eluent: petroleum ether 60−80 °C/ethylacetate 4:1 v/v) to afford a corresponding product **3aa** as a colorless solid in 92% isolated yield.

**Product Data.** *4-(2,4,6-Trimethoxyphenyl)butan-2-one (**3aa**).*[10h] Colorless solid (109.5 mg, 92%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 2.14 (s, 3H), 2.51−2.58 (m, 2H), 2.79−2.87 (m, 2H), 3.77 (s, 6H), 3.79 (s, 3H), 6.11 (s, 2H). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 17.5, 29.5, 43.6, 55.3, 55.6, 90.5, 109.6, 158.7, 159.6, 209.6.

*4-(5-Methylthiophene-2-yl)butan-2-one (**3ac**).*[24] Pale yellow oil (73 mg, 87%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 2.15 (s, 3H), 2.42 (s, 3H), 2.78 (t, 2H, $J$ = 7.4 Hz), 3.02 (t, 2H, $J$ = 7.4 Hz), 6.52−6.57 (m, 2H). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 15.2, 24.1, 30.0, 45.2, 124.2, 124.7, 137.7, 141.3, 207.3.

*4-(5-Methylfuran-2-yl)butan-2-one (**3ad**).*[25] Yellow oil (57.7 mg, 76%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 2.18 (s, 3H), 2.26 (s, 3H), 2.73−2.92 (m, 4H), 5.83−5.88 (m, 2H). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 13.4. 22.3, 29.8, 41.9, 105.7, 105.8, 150.5, 152.6, 207.4.

*4-(3-Methylthiophene-2-yl)butan-2-one (**3ae**).* Colorless oil (58 mg, 69%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 2.19 (s, 3H), 2.21 (s, 3H), 2.80 (t, 2H, $J$ = 7.6 Hz), 3.04 (t, 2H, $J$ = 7.6 Hz), 6.81 (d, 1H, $J$ = 5.0 Hz), 7.05 (d, 1H, $J$ = 5.0 Hz). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 13.7, 22.0, 30.2, 45.0, 121.5, 130.2, 133.2, 136.7, 207.6. DEPT 135: $\delta$ 13.7, 22.0, 30.2, 45.0, 121.5, 130.2. IR (KBr, cm$^{-1}$): 2923, 1717, 1363, 1162, 707. Anal. Calcd for $C_9H_{12}OS$: C, 64.25; H, 7.19. Found: C, 64.46; H, 7.27.

*4,4′-(3-Methylthiophene-2,5-diyl)dibutan-2-one (**3ae′**).* Colorless oil (18 mg, 15%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 2.09 (s, 3H), 2.18 (s, 6H), 2.71−2.79 (m, 4H), 2.90−3.04 (m, 4H), 6.48 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 13.7, 22.0, 24.1, 30.23, 30.24, 45.0, 45.3, 127.8, 132.8, 134.6, 139.5, 207.6, 207.8. DEPT 135: $\delta$ 13.7, 22.0, 24.1, 30.23, 30.24, 45.0, 45.3, 127.8. IR (KBr, cm$^{-1}$): 2921, 1714, 1363, 1162. Anal. Calcd for $C_{13}H_{18}O_2S$: C, 65.51; H, 7.61. Found: C, 65.17; H, 7.49.

*4-(5-Bromo-1H-indol-3-yl)butan-2-one (**3ag**).*[26] Colorless solid (120 mg, 90%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 2.18 (s, 3H), 2.85 (t, 2H, $J$ = 7.0 Hz), 3.02 (t, 2H, $J$ = 7.0 Hz), 6.99 (s, 1H), 7.20−7.32 (m, 2H), 7.74 (s, 1H), 8.34 (br s, 1H). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 19.2, 30.2, 44.0, 112.6, 112.8, 114.8, 121.3, 123.0, 124.8, 129.1, 135.0, 209.0.

*4-(1-Ethyl-1H-indol-3-yl)pentan-2-one (**3bh**).* Colorless oil (96 mg, 84%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 1.43−1.52 (m, 6H), 2.14 (s, 3H), 2.75 (dd, 1H, $J$ = 8.2, 16.0 Hz), 2.99 (dd, 1H, $J$ = 5.8, 16.0 Hz), 3.61−3.78 (m, 1H), 4.15 (q, 2H, $J$ = 7.2 Hz), 6.95 (s, 1H), 7.12−7.39 (m, 3H), 7.71 (d, 1H, $J$ = 7.8 Hz). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 15.5, 21.5, 27.1, 30.4, 40.8, 51.7, 109.5, 118.7, 119.4, 119.6, 121.5, 123.3, 126.9, 136.3, 208.7. DEPT 135: $\delta$ 15.5, 21.5, 27.1, 30.4, 40.8, 51.7, 109.5, 118.7, 119.4, 121.5, 123.3. IR (KBr, cm$^{-1}$): 2971, 2931, 1712, 1462, 1356, 1156, 1013, 740. Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.76; H, 8.42; N, 6.02.

*1-Phenyl-3-(2,4,6-trimethoxyphenyl)propan-1-one (**3ca**).* Colorless solid (120 mg, 80%). Mp: 80−82 °C. $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 2.95−3.16 (m, 4H), 3.78 (s, 6H), 3.82 (s, 3H), 6.14 (s, 2H), 7.41−7.55 (m, 3H), 8.02 (d, 2H, $J$ = 6.8 Hz). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 18.5, 38.9, 55.6, 55.8, 90.7, 110.0, 128.4, 128.6, 132.9, 137.3, 159.0, 159.8, 201. DEPT 135: $\delta$ 18.5, 38.9, 55.6, 55.8, 90.7, 128.4, 128.6, 132.9. IR (KBr, cm$^{-1}$): 2939, 1683, 1598, 1457, 1204, 1157, 1119, 811, 692. Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 72.21; H, 6.79.

*3-(1H-Indol-3-yl)-1-phenylpropan-1-one (**3cf**).*[26] Colorless solid (106 mg, 85%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 3.23−3.31 (m, 2H), 3.38−3.47 (m, 2H), 7.03 (d, 1H, $J$ = 2.0 Hz), 7.15−7.29 (m, 2H), 7.35−7.62 (m, 4H), 7.68 (d, 1H, $J$ = 7.0 Hz), 8.00 (d, 2H, $J$ = 7.0 Hz), 8.14 (br s, 1H). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 19.8, 39.4, 111.3, 115.4, 118.8, 119.4, 121.7, 122.1, 127.3, 128.1, 128.7, 133.1, 136.4, 137.1, 200.2.

*1-(2-Bromophenyl)-3-(4-hydroxy-2,6-dimethylphenyl)propan-1-one (**3db**).* Colorless solid (100 mg, 60%). Mp: 62−63 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 2.27 (s, 6H), 2.95−3.06 (m, 4H), 4.88 (br s, 1H), 6.51 (s, 2H), 7.26−7.37 (m, 3H), 7.60 (d, 1H, $J$ = 7.6 Hz). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 19.8, 23.2, 42.1, 114.9, 118.5, 127.4, 128.1, 129.5, 131.5, 133.5, 137.6, 141.7, 153.4, 204.1. DEPT 135: $\delta$ 19.8, 23.2, 42.1, 114.9, 127.4, 128.1, 131.5, 133.5. IR (KBr, cm$^{-1}$): 3422, 1700, 1595, 1465, 1309, 1140, 1025, 757. Anal. Calcd for $C_{17}H_{17}BrO_2$: C, 61.28; H, 5.14. Found: C, 61.12; H, 5.33.

*3-(1H-Indol-3-yl)-1,3-diphenylpropan-1-one (**3ef**).*[11h] Colorless solid (81.2 mg, 50%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 3.67−3.90 (m, 2H), 5.09 (t, 1H, $J$ = 7.2 Hz), 6.97−7.06 (m, 2H), 7.12−7.55 (m, 11H), 7.95 (d, 2H, $J$ = 7.2 Hz), 8.01 (br s, 1H). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 38.4, 45.4, 111.3, 119.4, 119.5, 119.7, 121.6, 122.3, 126.5, 126.8, 128.0, 128.3, 128.6, 128.7, 133.2, 136.8, 137.3, 144.4, 198.8.

*3-(1H-Indol-3-yl)cyclohexanone (**3kf**).*[11h] Colorless oil (65 mg, 61%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 1.78−2.09 (m, 3H), 2.22−2.49 (m, 3H), 2.57−2.70 (m, 1H), 2.76−2.87 (m, 1H), 3.39−3.53 (m, 1H), 6.97 (d, 1H, $J$ = 2.0 Hz), 7.09−7.26 (m, 2H), 7.37 (d, 1H, $J$ = 7.4 Hz), 7.64 (d, 1H, $J$ = 7.6 Hz), 8.13 (br s, 1H). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 24.9, 31.7, 36.0, 41.6, 48.1, 111.4, 119.0, 119.4, 119.7, 120.4, 122.2, 126.2, 136.5, 212.0.

*2′,4′,6′-Trimethoxybiphenyl-2,5-diol (**3la**).* Pink solid (41 mg, 30%). Mp: 208−210 °C. $^1$H NMR (200 MHz, DMSO-$d_6$): $\delta$ 3.60 (s, 6H), 3.78 (s, 3H), 6.22 (s, 2H), 6.29 (d, 1H, $J$ = 2.8 Hz), 6.42−6.58 (m, 2H), 7.94 (br s, 1H), 8.43 (br s, 1H). $^{13}$C NMR (54.6 MHz, DMSO-$d_6$ + $CDCl_3$): $\delta$ 55.6, 56.0, 91.5, 109.4, 114.5, 116.0, 119.4, 122.6, 148.5, 149.5, 158.7, 160.6. IR (KBr, cm$^{-1}$): 3430, 1468, 1203, 752. Anal. Calcd for $C_{15}H_{16}O_5$: C, 65.21; H, 5.84. Found: C, 65.55; H, 5.75.

*2-Acetyl-2-(4-oxopentan-2-yl)cyclopentanone (**3ai**).* Colorless oil (36.7 mg, 35%). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 0.83 (d, 3H, $J$ = 6.4 Hz), 1.61−1.76 (m, 2H), 1.87−1.97 (m, 1H), 2.09−2.14 (m, 6H), 2.19 (s, 3H), 2.24−2.32 (m, 1H), 2.50−2.58 (m, 1H), 3.01−3.08 (m, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 15.7, 19.4, 25.6, 25.7, 30.4, 32.5, 39.6, 46.1, 73.4, 204.2, 206.5, 215.5. DEPT 135: $\delta$ 15.7, 19.4, 25.6, 25.7, 30.4, 32.5, 39.6, 46.1. IR (KBr, cm$^{-1}$): 2970, 1734, 1701, 1362, 1149, 1120. Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.29; H, 8.76.

*3-Benzoyl-4-methylheptane-2,6-dione (**3bk**).* Colorless oil (55 mg, 45%). The two diastereomers were obtained, and their ratio (1:1) was determined by $^1$H NMR analysis. $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 0.88 (d, 3H, $J$ = 6.8 Hz), 0.93 (d, 3H, $J$ = 6.8 Hz), 2.03 (s, 3H), 2.05 (s, 3H), 2.06 (s, 3H), 2.07 (s, 3H), 2.19−2.60 (m, 4H), 2.85−3.03 (m, 2H), 4.50 (d, 1H, $J$ = 2.6 Hz), 4.54 (d, 1H, $J$ = 2.2 Hz), 7.38−7.58 (m, 6H), 7.89−7.98 (m, 4H). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 17.4, 18.3, 28.3, 28.8, 29.7, 29.9, 30.3, 30.5, 47.5, 47.8, 67.3, 67.5, 128.6, 128.8, 128.9, 133.9, 136.7, 137.1, 196.3, 203.9, 207.6. IR (KBr, cm$^{-1}$): 1640, 1260, 1019, 799. Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.87; H, 7.51.

*2-Benzoyl-3-methyl-1-phenylhexane-1,5-dione (**3bl**).* Colorless oil (74 mg, 48%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 1.08 (d, 3H, $J$ = 7.0 Hz), 2.10 (s, 3H), 2.57 (dd, 1H, $J$ = 7.0, 17.6 Hz), 2.81 (dd, 1H, $J$ = 5.2, 17.6 Hz), 3.00−3.13 (m, 1H), 5.60 (d, 1H, $J$ = 6.8 Hz), 7.40−7.59 (m, 6H), 7.94−8.04 (m, 4H). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 18.0, 30.6, 30.7, 47.9, 59.9, 128.8, 128.9, 129.1, 133.7, 133.8, 136.7, 137.1, 196.2, 196.3, 208.7. IR (KBr, cm$^{-1}$): 1699, 1671, 1263, 1215, 758, 690. Anal. Calcd for $C_{20}H_{20}O_3$: C, 77.90; H, 6.54. Found: C, 77.63; H, 6.68.

*(E)-3-Acetyl-4,8-diphenyloct-7-ene-2,6-dione (**3jj**).*[27] Colorless solid (100 mg, 60%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 1.88 (s, 3H), 2.16 (s, 3H), 2.82−3.06 (m, 2H), 4.08−4.19 (m, 1H), 4.30 (d, 1H, $J$ = 11.0 Hz), 6.55 (d, 1H, $J$ = 16.2 Hz), 7.17−7.47 (m, 11H). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 29.8, 29.9, 41.4, 45.2, 74.2, 126.0, 127.4, 128.1, 128.3, 128.8, 128.9, 130.6, 134.3, 140.3, 143.2, 197.6, 202.9, 203.3.

*2-(3-Oxocyclohexyl)-1,3-diphenylpropane-1,3-dione (**3kl**).*[28] Colorless oil (88 mg, 55%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 1.47−1.68 (m, 2H), 1.86−2.03 (m, 2H), 2.13−2.41 (m, 4H), 2.96−3.06 (m, 1H),


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5.23 (d, 1H, $J$ = 8.4 Hz), 7.34−7.53 (m, 6H), 7.89−7.97 (m, 4H). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 24.8, 29.5, 39.5, 41.2, 45.9, 62.3, 128.6, 128.9, 133.8, 136.5, 194.4, 194.6, 209.7.

*1-Phenyl-3-(phenylthio)propan-1-one (**3cp**).* Colorless solid (103 mg, 85%). Mp: 72−74 °C. $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 3.27−3.31 (m, 4H), 7.16−7.56 (m, 8H), 7.89−7.94 (m, 2H). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 27.9, 38.4, 126.3, 128.1, 128.7, 129.1, 129.4, 133.4, 135.9, 136.5, 198.1. DEPT 135: $\delta$ 27.9, 38.4, 126.3, 128.1, 128.7, 129.1, 129.4, 133.4. IR (KBr, cm$^{-1}$): 1684, 1355, 1181, 974, 743, 727, 688. Anal. Calcd for $C_{15}H_{14}OS$: C, 74.34; H, 5.82. Found: C, 74.49; H, 5.77.

*1,3-Diphenyl-3-(phenylthio)propan-1-one (**3ep**).*[9e,11c] Colorless solid (143 mg, 90%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 3.55−3.71 (m, 2H), 5.01 (t, 1H, $J$ = 7.0 Hz), 7.20−7.51 (m, 13H), 7.88 (d, 2H, $J$ = 7.2 Hz). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 45.0, 48.5, 127.7, 127.8, 128.1, 128.3, 128.7, 128.9, 129.1, 133.0, 133.5, 134.6, 137.0, 141.5, 197.2.

*3-(2-Bromophenyl)-3-(2-hydroxyphenylthio)-1-phenylpropan-1-one (**3fq**).* Colorless solid (144 mg, 70%). Mp: 61−63 °C. $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 3.51−3.75 (m, 2H), 5.16 (t, 1H, $J$ = 7.4 Hz), 6.74 (t, 1H, $J$ = 7.4 Hz), 6.98−7.63 (m, 10H), 7.91 (d, 2H, $J$ = 7.8 Hz). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 43.3, 47.4, 115.4, 116.4, 120.2, 124.4, 127.7, 128.2, 128.8, 129.0, 132.1, 133.2, 133.7, 136.3, 137.1, 139.9, 158.4, 196.8. DEPT 135: $\delta$ 43.3, 47.4, 115.4, 120.2, 127.7, 128.2, 128.8, 129.0, 132.1, 133.2, 133.7, 137.1. IR (KBr, cm$^{-1}$): 3384, 1683, 1469, 1448, 1203, 1024, 752, 688. Anal. Calcd for $C_{21}H_{17}BrO_2S$: C, 61.02; H, 4.15. Found: C, 61.39; H, 4.06.

*3-(2-Hydroxyethylthio)-1-(4-methoxyphenyl)-3-phenylpropan-1-one (**3go**).* Colorless solid (128 mg, 81%). Mp: 80−82 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 2.55 (t, 2H, $J$ = 6.0 Hz), 3.39−3.55 (m, 2H), 3.59−3.73 (m, 2H), 3.83 (s, 3H), 4.58 (t, 1H, $J$ = 7.2 Hz), 6.90 (d, 2H, $J$ = 8.8 Hz), 7.20−7.32 (m, 3H), 7.41 (d, 2H, $J$ = 7.6 Hz), 7.90 (d, 2H, $J$ = 8.8 Hz). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 34.6, 44.0, 45.0, 55.6, 60.7, 113.8, 127.5, 127.8, 128.7, 129.8, 130.5, 142.3, 163.8, 195.6. DEPT 135: $\delta$ 34.6, 44.0, 45.0, 55.6, 60.7, 113.8, 127.5, 127.8, 128.7, 130.5. IR (KBr, cm$^{-1}$): 3420, 1666, 1604, 1420, 1259, 1173, 1063, 703. Anal. Calcd for $C_{19}H_{20}O_2S$: C, 73.04; H, 6.45. Found: C, 73.32; H, 6.57. Anal. Calcd for $C_{18}H_{20}O_3S$: C, 68.33; H, 6.37. Found: C, 68.69; H, 6.49.

*1-(4-Methoxyphenyl)-3-(octylthio)-3-phenylpropan-1-one (**3gn**).* Yellow solid (157 mg, 82%). Mp: 58−60 °C. $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 0.79 (t, 3H, $J$ = 7.0 Hz), 1.14 (br s, 10H), 1.35−1.42 (m, 2H), 2.10−2.37 (m, 2H), 3.40 (d, 2H, $J$ = 7.0 Hz), 3.79 (s, 3H), 4.47 (t, 1H, $J$ = 7.0 Hz), 6.83 (d, 2H, $J$ = 7.0 Hz), 7.13−7.37 (m, 5H), 7.83 (d, 2H, $J$ = 7.0 Hz). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 14.1, 22.7, 28.9, 29.2, 29.3, 31.6, 31.8, 44.6, 45.1, 55.5, 113.8, 127.2, 127.9, 128.5, 130.0, 130.5, 142.5, 163.6, 195.6. DEPT 135: $\delta$ 14.1, 22.7, 28.9, 29.2, 29.3, 31.6, 31.8, 44.6, 45.1, 55.5, 113.8, 127.2, 127.9, 128.5, 130.5. IR (KBr, cm$^{-1}$): 2919, 2848, 1670, 1600, 1257, 1172, 697. Anal. Calcd for $C_{24}H_{32}O_2S$: C, 74.95; H, 8.39. Found: C, 75.19; H, 8.28.

*3-(2-Chlorophenyl)-3-(4-methoxyphenylthio)-1-phenylpropan-1-one (**3hr**).* Colorless oil (168 mg, 88%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 3.61 (d, 2H, $J$ = 7.2 Hz), 3.72 (s, 3H), 5.29 (t, 1H, $J$ = 7.2 Hz), 6.47 (d, 2H, $J$ = 8.8 Hz), 7.08−7.14 (m, 2H), 7.23−7.55 (m, 7H), 7.87 (d, 2H, $J$ = 8.8 Hz). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 43.7, 45.4, 55.3, 114.4, 123.6, 126.8, 128.1, 128.3, 128.4, 128.7, 129.8, 133.3, 133.9, 136.5, 138.7, 160.0, 196.6. IR (KBr, cm$^{-1}$): 2924, 1684, 1591, 1490, 1246, 1030, 752, 688. Anal. Calcd for $C_{22}H_{19}ClO_2S$: C, 69.01; H, 5.00. Found: C, 69.22; H, 5.09.

*3-Propylsulfanyl-1,3-di-p-tolylpropan-1-one (**3im**).* Yellow solid (109 mg, 70%). Mp: 49−51 °C. $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 0.89 (t, 3H, $J$ = 7.2 Hz), 1.43−1.61 (m, 2H), 2.19−2.33 (m, 2H), 2.25 (s, 3H), 2.37 (s, 3H), 3.48 (d, 2H, $J$ = 7.0 Hz), 4.52 (t, 1H, $J$ = 7.2 Hz), 7.09 (d, 2H, $J$ = 8.0 Hz), 7.21 (d, 2H, $J$ = 8.0 Hz), 7.29 (d, 2H, $J$ = 8.0 Hz), 7.81 (d, 2H, $J$ = 8.0 Hz). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 13.7, 21.3, 21.8, 22.8, 33.7, 44.3, 45.6, 127.9, 128.5, 129.4, 129.5, 134.7, 136.9, 139.5, 144.2, 196.9. IR (KBr, cm$^{-1}$): 2961, 2922, 1684, 1607, 1180, 811. Anal. Calcd for $C_{20}H_{24}OS$: C, 76.88; H, 7.74. Found: C, 76.53; H, 7.87.

*(E)-5-(2-hydroxyethylthio)-1,5-diphenylpent-1-en-3-one (**3jo**).* Colorless solid (94 mg, 60%). Mp: 104−106 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 2.58 (t, 2H, $J$ = 6.0 Hz), 2.86 (br s, 1H), 3.18−3.32 (m, 2H), 3.62−3.75 (m, 2H), 4.54 (t, 1H, $J$ = 7.2 Hz), 6.71 (d, 1H, $J$ = 16.0 Hz), 7.09−7.54 (m, 11H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 34.4, 43.9, 47.4, 60.7, 125.8, 127.5, 127.7, 128.4, 128.7, 128.9, 130.7, 134.2, 141.9, 143.5, 196.9. DEPT 135: $\delta$ 34.4, 43.9, 47.4, 60.7, 125.8, 127.5, 127.7, 128.4, 128.7, 128.9, 130.7, 143.5. IR (KBr, cm$^{-1}$): 1653, 1609, 1449, 1338, 1072, 750, 699. Anal. Calcd for $C_{19}H_{20}O_2S$: C, 73.04; H, 6.45. Found: C, 73.32; H, 6.57.

*4-(4-Nitrophenylamino)butan-2-one (**3au**).*[29] Yellow solid (79 mg, 76%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 2.13 (s, 3H), 2.74 (t, 2H, $J$ = 6.0 Hz), 3.44 (t, 2H, $J$ = 6.0 Hz), 6.46 (d, 2H, $J$ = 9.2 Hz), 7.97 (d, 2H, $J$ = 9.2 Hz). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 30.2, 37.6, 42.1, 111.0, 126.4, 137.8, 153.1, 207.5.

*4-(4-Chlorophenylamino)butan-2-one (**3av**).*[30] Colorless solid (69 mg, 70%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 2.14 (s, 3H), 2.71 (t, 2H, $J$ = 6.0 Hz), 3.34 (t, 2H, $J$ = 6.0 Hz), 3.94 (br s, 1H), 6.50 (d, 2H, $J$ = 8.0 Hz), 7.09 (d, 2H, $J$ = 8. Hz). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 30.3, 38.5, 42.3, 114.2, 122.1, 129.1, 146.2, 207.9.

*4-Morpholinobutan-2-one (**3aw**).*[30] Yellow oil (66.7 mg, 85%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 2.15 (s, 3H), 2.46 (t, 4H, $J$ = 4.6 Hz), 2.66 (s, 4H), 3.69 (t, 4H, $J$ = 4.6 Hz). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 30.1, 40.7, 53.0, 53.5, 66.7, 207.4.

*4,4′-(Benzylazanediyl)dibutan-2-one (**3ax**).* Colorless oil (99 mg, 80%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 2.08 (s, 6H), 2.57 (t, 4H, $J$ = 6.6 Hz), 2.74 (t, 4H, $J$ = 6.6 Hz), 3.54 (s, 2H),.7.22−7.32 (m, 5H). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 30.3, 41.6, 48.7, 58.9, 127.3, 128.4. 128.9, 139.0, 208.4. Anal. Calcd for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56; N, 5.66. Found: C, 73.12; H, 8.47; N, 5.73.

*4-(p-Tolylamino)pentan-2-one (**3bt**).* Colorless oil (57 mg, 60%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 1.28 (d, 3H, $J$ = 6.4 Hz), 2.19 (s, 3H), 2.28 (s, 3H), 2.56 (dd, 1H, $J$ = 7.2, 16.4 Hz), 2.79 (dd, 1H, $J$ = 5.0, 16.4 Hz), 3.29 (br s, 1H), 3.89−4.02 (m, 1H), 6.58 (d, 2H, $J$ = 8.0 Hz), 7.03 (d, 2H, $J$ = 8.0 Hz). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 20.5, 20.9, 30.9, 45.8, 49.8, 114.0, 127.1, 130.0, 144.6, 208.2. DEPT 135: $\delta$ 20.5, 20.9, 30.9, 45.8, 49.8, 114.0, 130.0. IR (KBr, cm$^{-1}$): 3393, 2918, 1706, 1146, 808. HRMS (ESI) calcd for $C_{12}H_{17}NO + H^+$ 192.1388, found 192.1387. Anal. Calcd for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.61; H, 8.84; N, 7.27.

*1-Phenyl-3-(phenylamino)propan-1-one (**3cs**).*[31] Yellow solid (91 mg, 81%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 3.29 (t, 2H, $J$ = 6.0 Hz), 3.63 (t, 2H, $J$ = 6.0 Hz), 6.65−6.77 (m, 3H), 7.20 (d, 2H, $J$ = 7.8 Hz), 7.42−7.58 (m, 3H), 7.93−7.98 (m, 2H). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 37.7, 38.8, 113.1, 117.7, 128.1, 128.7, 129.3, 133.3, 136.7, 147.7, 199.3.

*3-(Phenylamino)cyclohexanone (**3ks**).*[32] Yellow oil (28.3 mg, 30%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 1.64−1.78 (m, 2H), 1.99−2.39 (m, 5H), 2.81 (dd, 1H, $J$ = 3.2 Hz), 3.70−3.81 (m, 1H), 6.57 (t, 2H, $J$ = 8.4 Hz), 6.70 (t, 1H, $J$ = 7.2 Hz), 7.12−7.24 (m, 2H). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 22.1, 31.1, 41.1, 48.5, 52.3, 113.3, 117.9, 129.4, 146.3, 209.6.

*4-Ethoxybutan-2-one (**3ay**).*[33] Colorless oil (52 mg, 90%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 1.12 (t, 3H, $J$ = 7.0 Hz), 2.13 (s, 3H), 2.63 (t, 2H, $J$ = 6.2 Hz), 3.43 (q, 2H, $J$ = 7.0 Hz), 3.65 (t, 2H, $J$ = 6.2 Hz). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 14.9, 30.3, 43.7, 65.3, 66.4, 207.8.

*4-Butoxybutan-2-one (**3az**).*[33] Pale yellow oil (60 mg, 83%). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 0.89 (t, 3H, $J$ = 7.2 Hz), 1.24−1.38 (m, 2H), 1.48−1.56 (m, 2H), 2.17 (s, 3H), 2.67 (t, 2H, $J$ = 6.4 Hz), 3.41 (t, 2H, $J$ = 6.4 Hz), 3.66 (t, 2H, $J$ = 6.4 Hz). $^{13}$C NMR (54.6 MHz, $CDCl_3$): $\delta$ 13.8, 19.3, 30.4, 31.6, 43.8, 65.7, 70.9, 207.4.

*Procedure for the Synthesis of **4a**.*[34] Reduction of (*E*)-5-(2-hydroxyethylthio)-1,5-diphenylpent-1-en-3-one **3jo** (156 mg, 0.5 mmol) was carried out with sodium borohydride (38 mg, 1 mmol) in methanol (1 mL) for 1 h at 0−10 °C. After completion of the reaction, distilled water (10 mL) was added and then the solution was extracted with ethyl acetate. The organic layer was dried over $Na_2SO_4$ and evaporated under vacuum. Compound (*E*)-5-(2-hydroxyethylth-


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io)-1,5-diphenylpent-1-en-3-ol **4a** was obtained in 88% yield after column purification.

*(E)-5-(2-Hydroxyethylthio)-1,5-diphenylpent-1-en-3-ol (**4a**).* Colorless oil (138 mg, 88%); The two diastereomers was obtained and their ratio was determined by $^1$H NMR analysis; **4a**$^A$:**4a**$^B$ = 66:34. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 2.05−2.23 (m, 2H$^A$ + 2H$^B$), 2.46−2.56 (m, 2H$^A$ + 2H$^B$), 2.98 (br s, 2H$^A$ + 2H$^B$), 3.55−3.72 (m, 2H$^A$ + 2H$^B$), 4.09−4.15 (m, 1H$^A$ + 2H$^B$), 4.55 (q, 1H$^A$, $J$ = 7.2 Hz), 6.11−6.21 (m, 1H$^A$ + 1H$^B$), 6.46−6.55 (m, 1H$^A$ + 1H$^B$), 7.18−7.38 (m, 10H$^A$ + 10H$^B$). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 34.0, 34.1, 43.7, 43.9, 45.7, 45.8, 60.6, 60.8, 70.4, 70.5, 126.5, 126.6, 127.4, 127.5, 127.8, 128.1, 128.7, 128.8, 130.5, 130.9, 131.5, 131.8, 136.5, 136.6, 141.9, 142.9. DEPT 135: $\delta$ 34.0, 34.1, 43.7, 43.9, 45.7, 45.8, 60.6, 60.8, 70.4, 70.5, 126.5, 126.6, 127.4, 127.5, 127.8, 128.1, 128.7, 128.8, 130.5, 130.9, 131.5, 131.8. Anal. Calcd for $C_{19}H_{22}O_2S$: C, 72.57; H, 7.05. Found: C, 72.17; H, 6.88.

*Procedure for the Synthesis of **5a**.* A mixture of **4a** (78.5 mg, 0.25 mmol) and 3 mol % [Pd(COD)Cl($SnCl_3$)] in 2 mL of dry DCE was stirred at 90 °C for 6 h under an argon atmosphere. Then, the reaction mixture was evaporated and purified by column chromatography to give the corresponding 1,4-oxathiepane **5a** in 78% yield.

*(E)-5-Phenyl-7-styryl-1,4-oxathiepane (**5a**).* Colorless oil (57.7 mg, 78%). The two diastereomers was obtained and their ratio (1:1) was determined by $^1$H NMR analysis. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 2.40−2.51 (m, 4H), 2.74 (d, 1H, $J$ = 14.4 Hz), 2.91−2.97 (m, 1H), 3.04−3.21 (m, 2H), 3.83 (t, 1H, $J$ = 10.4 Hz), 4.05−4.13 (m, 3H), 4.24−4.33 (m, 2H), 4.51 (dd, 1H, $J$ = 2.4, 12.4 Hz), 4.86 (q, 1H, $J$ = 6.0 Hz), 6.22−6.29 (m, 2H), 6.62−6.68 (m, 2H), 7.22−7.42 (m, 20H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 34.5, 37.8, 46.3, 46.9, 50.60, 50.63, 69.1, 75.3, 77.7, 81.5, 126.60, 126.62, 127.0, 127.3, 127.5, 127.6, 127.7, 127.8, 128.7, 128.8, 128.9, 129.3, 129.7, 130.3, 130.4, 136.9, 137.0, 142.6, 143.3. DEPT 135: $\delta$ 34.5, 37.8, 46.3, 46.9, 50.60, 50.63, 69.1, 75.3, 77.7, 81.5, 126.60, 126.62, 127.0, 127.3, 127.5, 127.6, 127.7, 127.8, 128.7, 128.8, 128.9, 129.3, 129.7, 130.3, 130.4. IR (KBr, cm$^{-1}$): 3025, 2923, 1599, 1493, 1450, 967, 748, 697. HRMS (ESI): calcd for $C_{19}H_{20}OS$ + $H^+$ 297.1313, found 297.1305. Anal. Calcd for $C_{19}H_{20}OS$: C, 76.98; H, 6.80. Found: C, 76.63; H, 6.89.

*Procedure for the Synthesis of **4b**.* Reduction of 3-(2-hydroxyethylthio)-1-(4-methoxyphenyl)-3-phenylpropan-1-one **3go** (158 mg, 0.5 mmol) was carried out with sodium borohydride (76 mg, 2 mmol) in methanol (1 mL) for 3 h at 30 °C. After completion of the reaction, distilled water (10 mL) was added and then the solution extracted with ethyl acetate. The organic layer was dried over $Na_2SO_4$ and evaporated under vacuum. Compound 3-(2-hydroxyethylthio)-1-(4-methoxyphenyl)-3-phenylpropan-1-ol **4b** was obtained in 90% yield after column purification.

*3-(2-Hydroxyethylthio)-1-(4-methoxyphenyl)-3-phenylpropan-1-ol (**4b**).* Colorless oil (143 mg, 90%). The two diastereomers was obtained and their ratio was determined by $^1$H NMR analysis; **4b**$^A$:**4b**$^B$ = 62:38. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 2.10−2.50 (m, 6H$^A$ + 6H$^B$), 3.49−3.62 (m, 2H$^A$ + 2H$^B$), 3.77 (3H$^B$), 3.79 (s, 3H$^A$), 3.95−4.05 (m, 1H$^A$ + 1H$^B$), 4.42−4.45 (m, 1H$^B$), 4.82−4.86 (m, 1H$^A$), 6.82−6.87 (m, 2H$^A$ + 2H$^B$), 7.16−7.34 (m, 7H$^A$ + 7H$^B$). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 34.2, 34.3, 45.6, 45.7, 46.2, 46.3, 55.5, 60.7, 60.9, 71.6, 71.7, 114.1, 114.2, 127.2, 127.51, 127.54, 127.6, 127.9, 128.2, 128.8, 128.9, 136.2, 136.5, 142.1, 142.9, 159.3, 159.4. DEPT 135: $\delta$ 34.2, 34.3, 45.6, 45.7, 46.2, 46.3, 55.5, 60.7, 60.9, 71.6, 71.7, 114.1, 114.2, 127.2, 127.51, 127.54, 127.6, 127.9, 128.2, 128.8, 128.9. IR (KBr, cm$^{-1}$): 3419, 2926, 1508, 1244, 1030, 832, 701. Anal. Calcd for $C_{18}H_{22}O_3S$: C, 67.89; H, 6.96. Found: C, 68.16; H, 6.73.

*Procedure for the Synthesis of **5b**.* A mixture of **4b** (79.5 mg, 0.25 mmol), 3 mol % of [Pd(COD)Cl($SnCl_3$)], and 3 mol % of $AgPF_6$ in 2 mL of dry DCE was stirred at 90 °C for 30 min under an argon atmosphere. Then, the reaction mixture was evaporated and purified by column chromatography to give the corresponding 1,4-oxathiepane **5b** in 72% yield.

*7-(4-Methoxyphenyl)-5-phenyl-1,4-oxathiepane (**5b**).* Colorless oil (54 mg, 72%). The two diastereomers was obtained and their ratio was determined by $^1$H NMR analysis; **5b**$^A$:**5b**$^B$ = 62:38. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 2.46−2.64 (m, 2H$^A$ + 2H$^B$), 2.76 (d, 1H$^A$, $J$ = 14.4 Hz), 2.98−3.02 (m, 1H$^B$), 3.09−3.25 (m, 1H$^A$ + 1H$^B$), 3.79 (s, 3H$^A$ + 3H$^B$), 3.82−3.89 (m, 2H$^B$), 4.02−4.15 (m, 1H$^A$ + 1H$^B$), 4.32 (dd, 1H$^A$, $J$ = 6.4, 10.4 Hz), 4.49−4.52 (m, 1H$^A$), 4.61 (d, 1H$^B$, $J$ = 10.4 Hz), 5.21 (dd, 1H$^A$, $J$ = 5.2, 9.6 Hz), 6.87 (d, 2H$^A$ + 2H$^B$, $J$ = 8.4 Hz), 7.22−7.41 (m, 7H$^A$ + 7H$^B$). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 34.4, 37.8, 48.1, 48.9, 50.9, 51.1, 55.5, 69.3, 75.5, 79.2, 82.9, 113.9, 126.9, 127.0, 127.2, 127.5, 127.6, 128.8, 128.9, 135.5, 135.7, 142.6, 143.3, 158.9, 159.0. DEPT $\delta$ 34.4, 37.8, 48.1, 48.9, 50.9, 51.1, 55.5, 69.3, 75.5, 79.2, 82.9, 113.9, 126.9, 127.0, 127.2, 127.5, 127.6, 128.8, 128.9. IR (KBr, cm$^{-1}$): 2926, 1636, 1508, 1246, 1100, 699. ESI-MS for $C_{18}H_{20}O_2S$ [M], [M + K]$^+$ = 339.10. Anal. Calcd for $C_{18}H_{20}O_2S$: C, 71.96; H, 6.71. Found: C, 71.61; H, 6.89.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

Experimental procedures, kinetics plot, UV−vis spectra, DFT study, spectra for all compounds, and X-ray crystallographic data for **3ca** and **3cP** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

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(15) [Pd(NBD)Cl($SnCl_3$)] (**A2**) and [Pd(CHD)Cl($SnCl_3$)] (**A3**) were prepared in situ.

(16) (a) To avoid unwanted polymerization of MVK (**1a**) in presence of $SnCl_2$ and $Pd(MeCN)_2$, (*E*)-pent-3-en-2-one (**1b**) was chosen to study the interaction. (b) No considerable amount of shift was observed in $^1H$ NMR spectrum for a 1:1:1 mixture of **1b** and $PdCl_2(MeCN)_2$ and $SnCl_2$ in $CDCl_3$/acetonitrile at room temperature.

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(18) Alternatively, the enone activation could take place with two units of Pd−Sn system. We thank one of the five reviewers for indicating this possibility. Calculations at a higher level of theory may resolve this issue.

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