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PII: S0040-4020(18)31165-7

DOI: 10.1016/j.tet.2018.09.054

Reference: TET 29826

To appear in: *Tetrahedron*

Received Date: 28 July 2018

Revised Date: 13 September 2018

Accepted Date: 28 September 2018

Please cite this article as: Li Z, He J, Chen X, Cheng Y, Yang J, Controllable single- or double-oxa-Michael addition of ynones with alcohols: Synthesis of 3-alkoxyprop-2-en-1-ones and 3,3-dialkoxypropan-1-ones, *Tetrahedron* (2018), doi: https://doi.org/10.1016/j.tet.2018.09.054.

Controllable Single- or Double-oxa-Michael Addition of Ynones with Alcohols: Synthesis of 3-Alkoxyprop-2-en-1-ones and 3,3-Dialkoxypropan-1-ones

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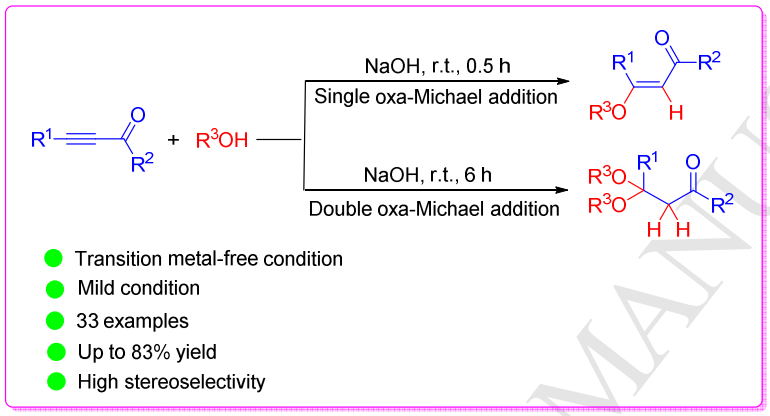


Abstract: Single- or double-oxa-Michael addition of ynones with various alcohols was achieved at room temperature. (*E*)-3-Alkoxyprop-2-en-1-ones and 3,3-dialkoxypropan-1-ones were efficiently synthesized by time-controlling approach. This protocol has advantages of wide range of substrates, no transition metal catalyst, mild condition, high yield and high stereoselectivity.

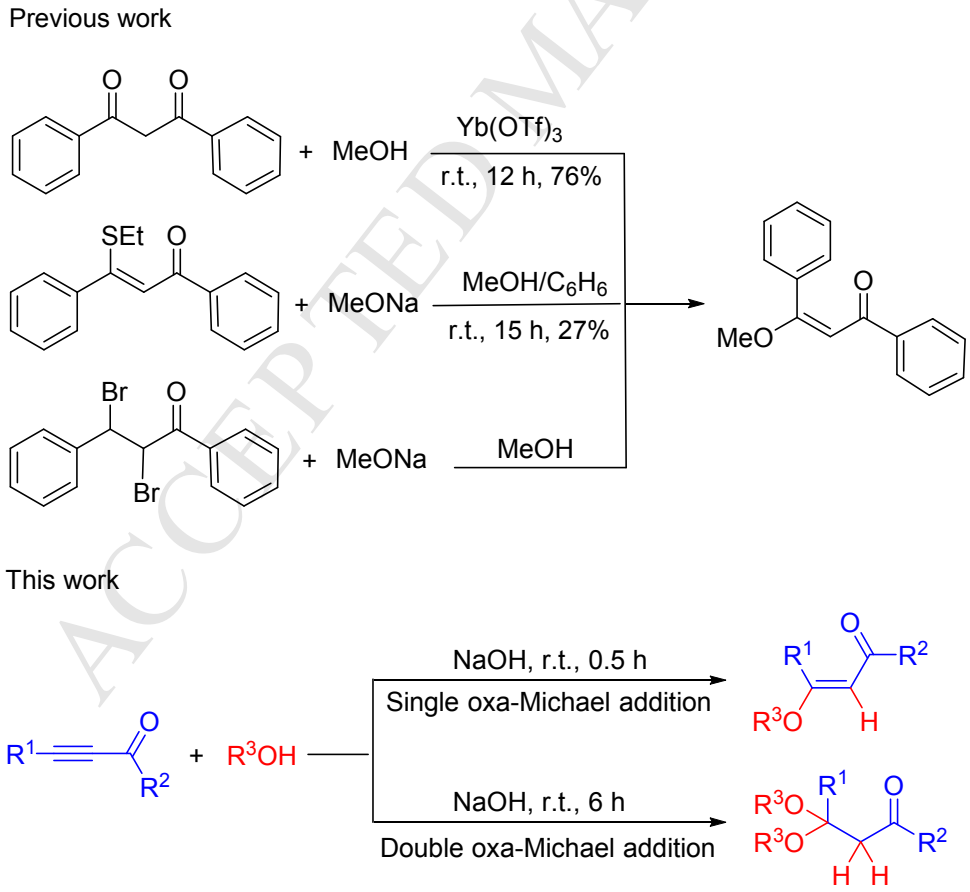
Keywords: ynone, alcohol, oxa-Michael addition, (*E*)-3-alkoxyprop-2-en-1-one, 3,3-dialkoxypropan-1-one

1. Introduction

3-Alkoxyprop-2-en-1-ones as important building blocks in organic synthesis have attracted much attention, which can be used as versatile intermediates for the construction of various fine chemicals.[1] Numerous methods have been developed for the formation of 3-alkoxyprop-2-en-1-ones in literatures (Scheme 1). For example, the

typical methods for the preparation of 3-methoxyprop-2-en-1-one include i) the ytterbium triflate catalyzed reaction of β-diketone with methanol;[2] ii) the substitution reaction of 2-ethylthio-1-alkenyl ketone with sodium methoxide in methanol and benzene;[3] iii) the reaction of α,β-dibromoketone with sodium methoxide in methanol.[4] In addition, some other methods also reported for analogues of 3-methoxyprop-2-en-1-one.[5] However, these methods often suffer from major or minor limitations, such as drastic reaction conditions, low yields, tedious work-up procedures and co-occurrence of several side reactions. Therefore, the development of more efficient routes which use more suitable materials is still desirable.

3,3-Dialkoxypropan-1-ones as precursors of β-diketones may play an important role in organic synthesis. However, the reports related to their preparations are very scarce. Therefore the exploration for the efficient synthetic methods is quite necessary.



Scheme 1 Preparation of 3-alkoxyprop-2-en-1-ones and 3,3-dialkoxypropan-1-ones

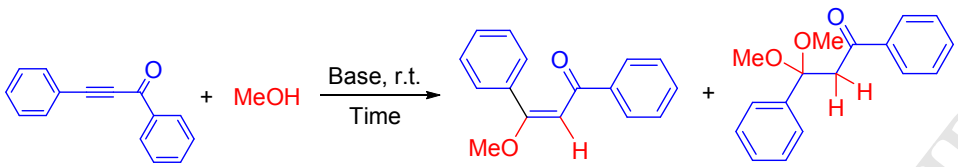
In this paper, we report an efficient method to controllably synthesize (*E*)-3-alkoxyprop-2-en-1-ones and 3,3-dialkoxypropan-1-ones through single- or double-oxa-Michael addition of ynones with various alcohols at room temperature under transition metal-free and mild condition.

2. Results and Discussion

Initially, the reaction of 1,3-diphenylprop-2-yn-1-one (**1a**) with methanol, which was used as both reactant and solvent, as a model reaction was attempted at room temperature, but no any products were observed (Table **1**, entry **1**). Then 1 equiv of *t*-BuOLi as a base was added. After the mixture was stirred at room temperature for 0.5 h, two kinds of products were isolated, which were identified as (*E*)-3-methoxy-1,3-diphenylprop-2-en-1-one (**2a**) as a major product in 69% and 3,3-dimethoxy-1,3-diphenylpropan-1-one (**3a**) as a minor product in 12% (Table **1**, entry **2**). The similar result was also obtained using MeONa as a base (Table **1**, entry **3**). The stereochemical structure of **2a** was determined according to literature reports.[1, 5a] No *Z*- isomer was observed. This implied that this reaction showed high stereoselectivity for *E*- structure. In order to further improve the yield and selectivity of **2a** or **3a**, the bases and reaction time were optimized. It was found that some inorganic bases (Na_2CO_3, $NaHCO_3$ and K_2CO_3) and organic bases (DMAP, Et_3N, DBU and DABCO) gave the desired products **2a** and **3a** in low yield (Table **1**, entries 4−6 and 9−12). In contrast, KOH and NaOH as bases could give **2a** in high yield after the mixture was stirred for 0.5 h at room temperature (Table **1**, entries 7, 8). The best yield was obtained using NaOH as a base (Table **1**, entry **8**). Reaction time played an important role in the reaction. When the reaction time was prolonged in the presence of NaOH, the yield of **3a** could be greatly improved (Table **1**, entry 13). When the reaction mixture was stirred at room temperature for 6 h, **3a** as a major product could be obtained in 82%. Meanwhile the yield for **2a** as a minor product could be greatly minimized (Table **1**, entry 14). This result implied that the reaction selectivity for products **2a** and **3a** could be realized by simply controlling reaction time. In addition,

the yield of **3a** at elevated temperature (65 °C) could not further improve (Table 1, entry 15).

Table 1 Optimization of reaction conditions[a]



1a **2a** **3a**

Entry	Base	Time (h)	Yield (%)[b]	
			2a	**3a**
1	None	0.5	0	0
2	*t*-BuOLi	0.5	69	12
3	MeONa	0.5	63	12
4	Na_2CO_3	0.5	11	3
5	$NaHCO_3$	0.5	8	5
6	K_2CO_3	0.5	9	4
7	KOH	0.5	72	10
8	NaOH	0.5	78	15
9	DMAP	0.5	12	6
10	Et_3N	0.5	17	4
11	DBU	0.5	11	4
12	DABCO	0.5	13	5
13	NaOH	2	10	79
14	NaOH	6	8	82
15[c]	NaOH	6	9	80

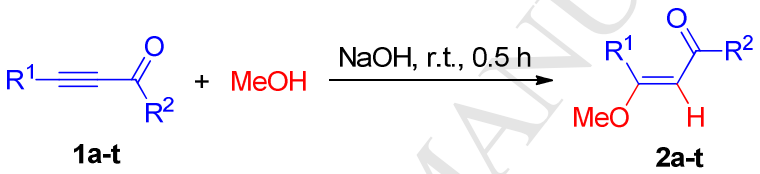
[a] Reaction conditions: ynone **1a** (0.5 mmol), MeOH (2 mL) and base (0.5 mmol) at room temperature for appropriate time.

[b] Isolated yield.

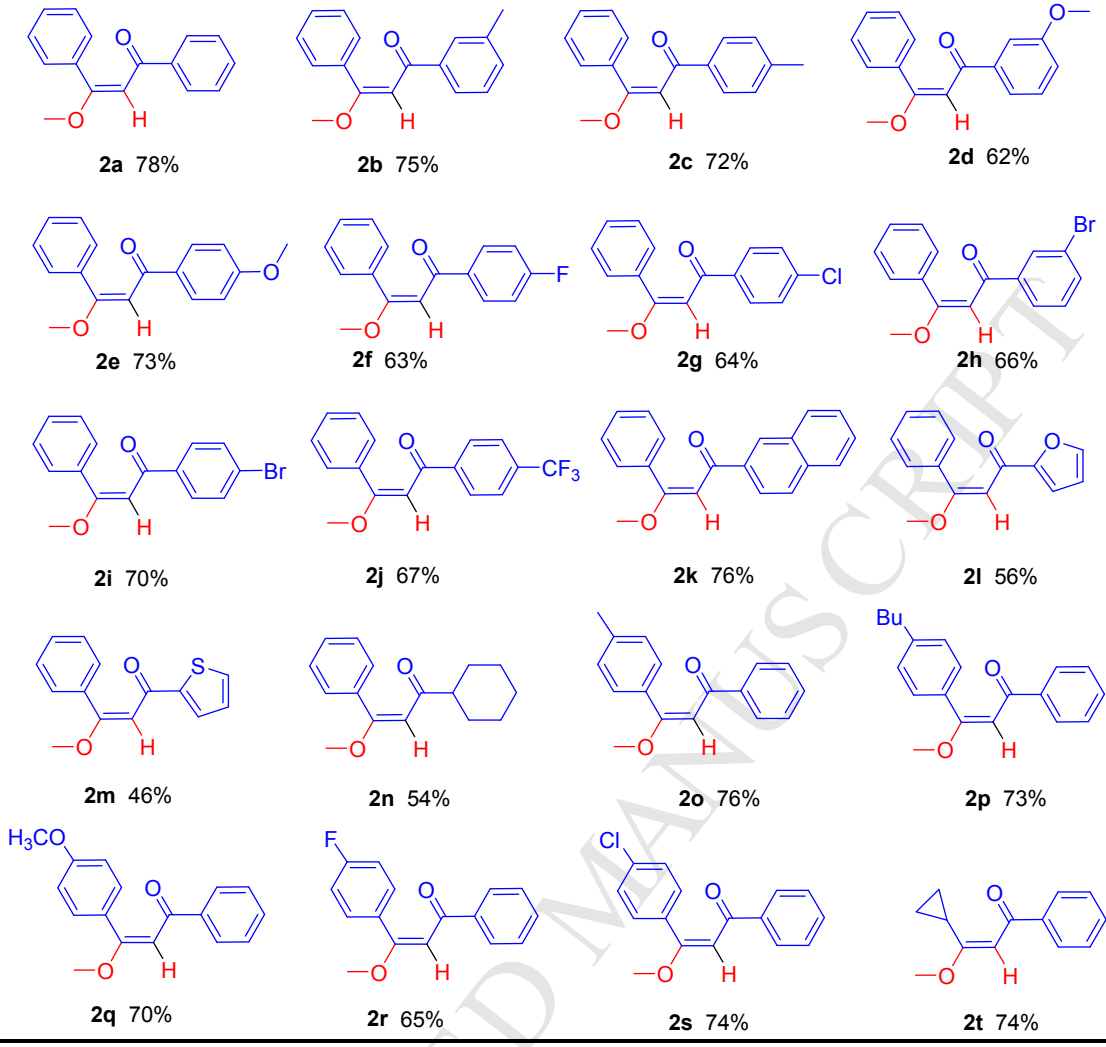
[c] At 65 °C.

Based on the aforementioned findings, a series of reactions of ynones with alcohols were examined for the single oxa-Michael addition at room temperature for 0.5 h using NaOH as a base. The reactions of ynones **1a-t** with methanol could proceed smoothly and produce corresponding (*E*)-3-methoxyprop-2-en-1ones **2a**–**t** in satisfactory yield (Table 2). The products were isolated only as *E*-isomers. It was found that ynones bearing aromatic rings, heteroaromatic rings (furanyl and thienyl), and cycloalkyls (cyclopropyl and cyclohexyl) could participate in single oxa-Michael addition to give the corresponding products in good to high yield.

Table 2 Scope of single oxa-Michael addition of ynones **1a-t** with methanol for the synthesis of **2a-t**[a]



1a-t **2a-t**

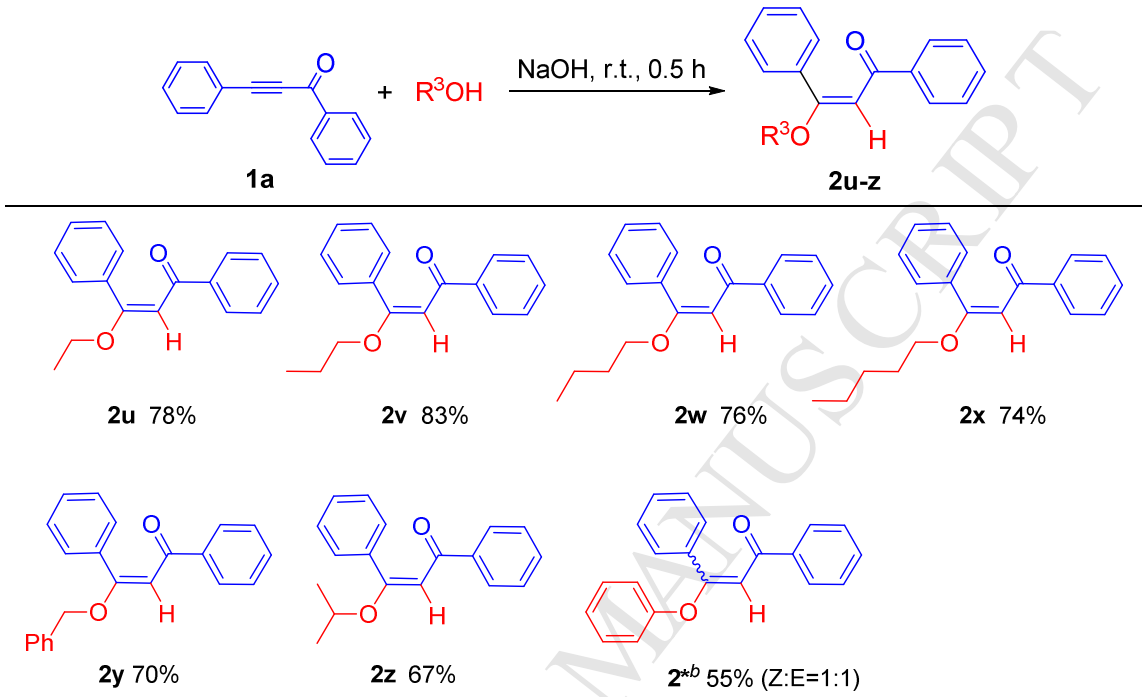


[a] Reaction conditions: ynones **1a-t** (0.5 mmol), MeOH (2 mL) and NaOH (0.5 mmol) at room temperature for 0.5 h.

In addition, the reactions of ynone **1a** with various alcohols were also examined for the single oxa-Michael addition at room temperature for 0.5 h using NaOH as a base (Table 3). The $C_{2\text{-}5}$ alcohols could participate in the reactions with no obvious carbon chain effect for the yield of products (**2u-z**). Benzyl alcohol could also give the corresponding product in satisfactory yield (**2y**). Although isopropanol could afford the corresponding product **2z** in good yield, tertiary butanol could not undergo the oxa-Michael addition probably because of the large steric hindrance. In addition, it is worthy to mention that when phenol as analogue of alcohols was used to react with **1a** in acetonitrile, *Z*-, *E*- configuration products (*Z*/*E* = 1:1) with a mixed yield of 55% were obtained with no stereoselectivity (**2***). This result may be caused by the

mandatory usage of different solvent media.

Table 3 Scope of single oxa-Michael addition of ynone **1a** with various alcohols for the synthesis of **2u-z**[a]

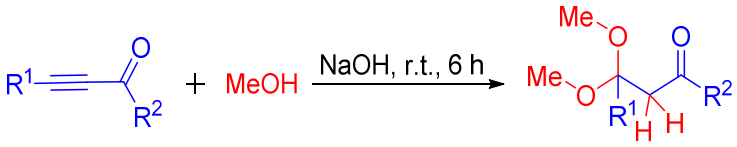


[a] Reaction conditions: ynone **1a** (0.5 mmol), alcohol (2 mL), and NaOH (0.5 mmol) at room temperature for 0.5 h. [b] Phenol (0.5 mmol) in MeCN (2 mL) medium.

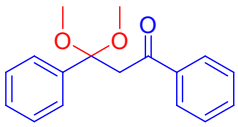
Double oxa-Michael addition of ynones with methanol to synthesize 3,3-dimethoxypropan-1-ones could be carried out at room temperature for 6 h using NaOH as a base (Table 4). Ynones bearing aromatic rings and aromatic heterocyclic ring (furanyl) could react with methanol to give the double oxa-Michael addition products in high yield with no obvious differences (**3a-f**). However, when ethanol was used as an alcohol to react with ynone **1a**, only trace amount of the corresponding double oxa-Michael addition product was observed at elevated temperature (60 ^{o}C). This result may be caused by the large steric hindrance due to the increase of carbon chain of alcohols.

Table 4 Scope of double oxa-Michael addition of ynones with alcohols for the

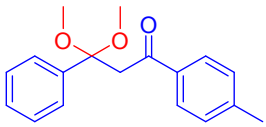
synthesis of **3a-f**[a]



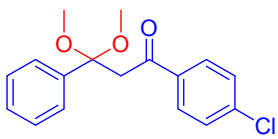
3a-f



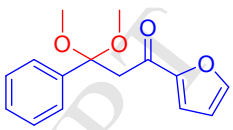
3a 82%



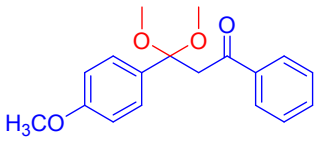
3b 80%



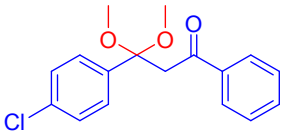
3c 76%



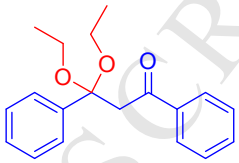
3d 78%



3e 75%



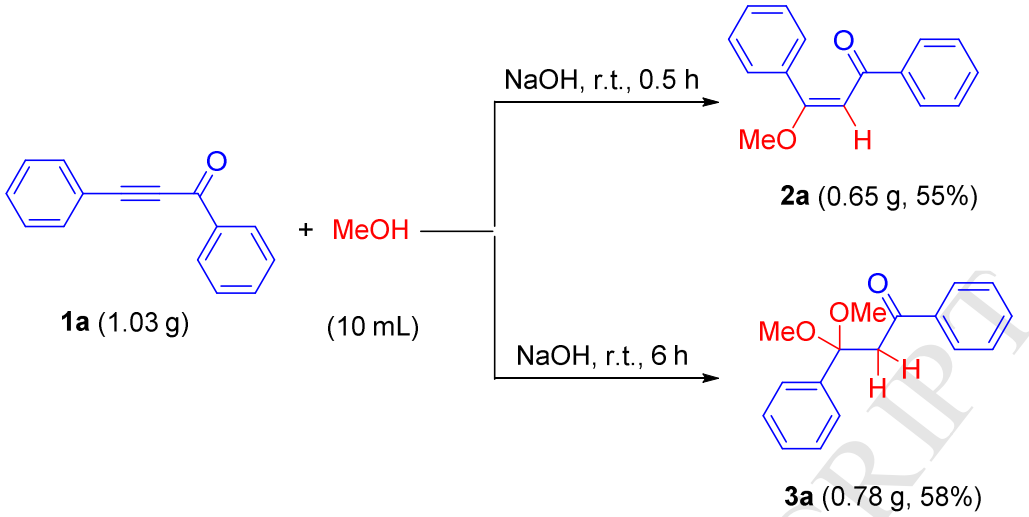
3f 75%



Trace[b]

[a] Reaction conditions: ynone (0.5 mmol), alcohol (2 mL) and NaOH (0.5 mmol) at room temperature for 6 h. [b] At 60 °C for 8 h.

It is worthy to mention that the controlled synthesis of **2a** and **3a** could also be performed on gram-scale and give the corresponding products in good yield (Scheme 2). The reaction of 1.03 g of **1a** with 10 mL of methanol in the presence of 0.20 g of NaOH was performed at room temperature for 0.5 h to give **2a** in 55% yield (0.65 g) isolated yield. If the reaction was prolonged to 6 h, **3a** was obtained in 58% yield (0.78 g). The success of this gram scale reaction further showed the potency of optimized condition for the bulk processes.



Scheme 2 Gram-scale synthesis of **2a** and **3a**

3. Conclusions

Single- or double-oxa-Michael addition of ynones with various alcohols at room temperature has developed. (*E*)-3-Alkoxyprop-2-en-1-ones and 3,3-dialkoxypropan-1-ones were efficiently synthesized by time-controlling approach. This protocol has advantages of wide range of substrates, no transition metal catalyst, mild condition, high yield and high stereoselectivity, providing a practical and versatile method for the synthesis of a wide range of 3-alkoxyenones and 3,3-dialkoxyketones.

4. Experimental

4.1. General Information

^{1}H NMR and ^{13}C NMR spectra were recorded on a Mercury-600 MB instrument using DMSO-d_6 as solvent and Me_4Si as internal standard. Elemental analyses were performed on a Vario El Elemental Analysis instrument. Melting points were observed in an electrothermal melting point apparatus. Ynones were synthesized according to literature method.[6]

*4.2. Typical procedure for synthesis of 3-alkoxyprop-2-en-1-ones **2a-z***

The mixture of ynones (0.5 mmol), alcohol (2 mL) and sodium hydroxide (0.5 mmol) was stirred at room temperature for 0.5 h. The reaction progress was monitored by TLC. After the completion of the reaction, the mixture was extracted with ethyl acetate (3×10 mL), and the liquor was washed with saturated brine (3×10 mL). The resulting organic phase was dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was isolated by column chromatography using petroleum ether and ethyl acetate (v/v 8:1) as eluent to give pure product. The analytical data for products are given below.

*4.2.1. (E)-3-Methoxy-1,3-diphenylprop-2-en-1-one (**2a**)*

Yellow oil (92 mg, 78%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.90 (dd, J = 8.3, 1.4 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.48 – 7.42 (m, 2H), 7.40 – 7.28 (m, 4H), 6.38 (s, 1H), 3.92 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 189.47, 171.00, 139.62, 135.99, 132.66, 129.92, 129.22, 128.86, 128.39, 128.12, 98.75, 57.32. Anal. Calcd. For $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.58; H, 5.94.

*4.2.2. (E)-3-Methoxy-3-phenyl-1-(m-tolyl)prop-2-en-1-one (**2b**)*

Yellow oil (94 mg, 75%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.72 (d, J = 1.6 Hz, 2H), 7.38 – 7.29 (m, 7H), 6.37 (s, 1H), 3.91 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 189.62, 170.80, 139.62, 138.16, 136.04, 133.25, 129.88, 129.20, 128.90, 128.75, 128.10, 125.63, 98.91, 57.29, 21.33. Anal. Calcd. For $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 80.98; H, 6.36.

*4.2.3. (E)-3-Methoxy-3-phenyl-1-(p-tolyl)prop-2-en-1-one (**2c**)*

Yellow oil (90 mg, 72%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.82 (d, J = 8.2 Hz, 2H), 7.38 – 7.29 (m, 5H), 7.25 (d, J = 7.5 Hz, 2H), 6.37 (s, 1H), 3.90 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 189.01, 170.55, 142.90, 137.03, 136.07, 129.84, 129.43, 129.19, 128.54, 128.10, 98.67, 57.22, 21.51. Anal. Calcd. For $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 80.85; H, 6.41.

*4.2.4. (E)-3-Methoxy-1-(3-methoxyphenyl)-3-phenylprop-2-en-1-one (**2d**)*

Yellow oil (83 mg, 62%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.53 (d, J = 7.7 Hz, 1H), 7.40 – 7.29 (m, 7H), 7.11 (dd, J = 8.1, 2.8 Hz, 1H), 6.36 (s, 1H), 3.91 (s, 3H), 3.77 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 189.13, 171.13, 159.74, 141.12, 136.01,

130.00, 129.92, 129.20, 128.11, 120.91, 118.63, 113.08, 98.78, 57.35, 55.68. Anal. Calcd. For $C_{17}H_{16}O_3$: C, 76.10; H, 6.01; Found: C, 76.05; H, 6.03.

*4.2.5. (E)-3-Methoxy-1-(4-methoxyphenyl)-3-phenylprop-2-en-1-one (**2e**)*

Yellow oil (97 mg, 73%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.90 (d, J = 8.8 Hz, 2H), 7.38 – 7.29 (m, 5H), 6.97 (d, J = 8.8 Hz, 2H), 6.35 (s, 1H), 3.89 (s, 3H), 3.80 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 188.14, 169.97, 162.97, 136.15, 132.32, 130.67, 129.76, 129.17, 128.08, 114.07, 98.69, 57.15, 55.89. Anal. Calcd. For $C_{17}H_{16}O_3$: C, 76.10; H, 6.01; Found: C, 76.17; H, 6.00.

*4.2.6. (E)-1-(4-Fluorophenyl)-3-methoxy-3-phenylprop-2-en-1-one (**2f**)*

Yellow oil (80 mg, 63%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.00 – 7.95 (m, 2H), 7.39 – 7.35 (m, 1H), 7.34 – 7.29 (m, 4H), 7.28 – 7.23 (m, 2H), 6.37 (s, 1H), 3.92 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 187.62, 170.69, 164.39 (d, J = 250.0 Hz), 135.71 (d, J = 2.6 Hz), 135.42, 130.77 (q, J = 8.4 Hz), 129.45, 128.70, 127.62, 115.25 (d, J = 21.7 Hz), 98.10, 56.87. Anal. Calcd. For $C_{16}H_{13}FO_2$: C, 74.99; H, 5.11; Found: C, 75.06; H, 5.09.

*4.2.7. (E)-1-(4-Chlorophenyl)-3-methoxy-3-phenylprop-2-en-1-one (**2g**)*

Yellow oil (87 mg, 64%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.91 (d, J = 8.5 Hz, 2H), 7.50 (d, J = 8.5 Hz, 2H), 7.39 – 7.35 (m, 1H), 7.32 (dd, J = 7.6, 1.5 Hz, 4H), 6.36 (s, 1H), 3.92 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 188.32, 171.58, 138.29, 137.50, 135.86, 130.33, 130.03, 129.23, 128.91, 128.15, 98.49, 57.45. Anal. Calcd. For $C_{16}H_{13}ClO_2$: C, 70.46; H, 4.80; Found: C, 70.40; H, 4.81.

*4.2.8. (E)-1-(3-Bromophenyl)-3-methoxy-3-phenylprop-2-en-1-one (**2h**)*

Yellow oil (100 mg, 66%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.00 (t, J = 1.8 Hz, 1H), 7.89 (dt, J = 7.8, 1.3 Hz, 1H), 7.72 (ddd, J = 7.9, 2.0, 1.0 Hz, 1H), 7.42 – 7.35 (m, 2H), 7.35 – 7.29 (m, 4H), 6.36 (s, 1H), 3.93 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 188.12, 172.05, 141.72, 135.84, 135.21, 131.08, 130.96, 130.10, 129.23, 128.17, 127.43, 122.35, 98.52, 57.60. Anal. Calcd. For $C_{16}H_{13}BrO_2$: C, 60.59; H, 4.13; Found: C, 60.64; H, 4.11.

*4.2.9. (E)-1-(4-Bromophenyl)-3-methoxy-3-phenylprop-2-en-1-one (**2i**)*

Yellow oil (110 mg, 70%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.83 (d, J = 8.5 Hz, 2H), 7.64 (d, J = 8.5 Hz, 2H), 7.41 – 7.35 (m, 1H), 7.35 – 7.29 (m, 4H), 6.35 (s, 1H), 3.92 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 188.47, 171.61, 138.63, 135.85, 131.87, 130.48, 130.04, 129.23, 128.16, 126.59, 98.45, 57.46. Anal. Calcd. For $C_{16}H_{13}ClO_2$: C, 60.59; H, 4.13; Found: C, 60.54; H, 4.14.

*4.2.10. (E)-3-Methoxy-3-phenyl-1-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (**2j**)*

Yellow oil (102 mg, 67%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.05 (d, J = 7.9 Hz, 2H), 7.79 (d, J = 8.2 Hz, 2H), 7.40 – 7.29 (m, 5H), 6.40 (s, 1H), 3.94 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 188.17, 171.82, 142.59, 135.19, 131.66, 131.45, 129.67, 128.78, 128.71, 127.68, 125.28 (q, J = 3.0 Hz), 98.21, 57.09. Anal. Calcd. For $C_{17}H_{13}F_3O_2$: C, 66.67; H, 4.28; Found: C, 66.72; H, 4.26.

*4.2.11. (E)-3-Methoxy-1-(naphthalen-2-yl)-3-phenylprop-2-en-1-one (**2k**)*

Yellow oil (109 mg, 76%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.64 (s, 1H), 8.09 (d, J = 8.0 Hz, 1H), 7.97 – 7.90 (m, 3H), 7.64 – 7.56 (m, 2H), 7.40 – 7.33 (m, 3H), 7.31 (t, J = 7.1 Hz, 2H), 6.56 (s, 1H), 3.98 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 189.45, 170.93, 136.89, 136.07, 135.10, 132.67, 129.91, 129.82, 129.79, 129.24, 128.59, 128.46, 128.14, 128.02, 127.15, 124.54, 98.96, 57.41. Anal. Calcd. For $C_{20}H_{16}O_2$: C, 83.31; H, 5.59; Found: C, 83.23; H, 5.62.

*4.2.12. (E)-1-(Furan-2-yl)-3-methoxy-3-phenylprop-2-en-1-one (**2l**)*

Yellow oil (64 mg, 56%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.89 (dd, J = 1.8, 0.8 Hz, 1H), 7.44 – 7.30 (m, 6H), 6.66 (dd, J = 3.5, 1.7 Hz, 1H), 6.29 (s, 1H), 3.89 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 176.76, 171.23, 154.03, 147.18, 135.79, 130.03, 129.23, 128.03, 117.03, 112.79, 97.44, 57.35. Anal. Calcd. For $C_{14}H_{12}O_3$: C, 73.67; H, 5.30; Found: C, 73.59; H, 5.32.

*4.2.13. (E)-3-Methoxy-3-phenyl-1-(thiophen-2-yl)prop-2-en-1-one (**2m**)*

Yellow oil (56 mg, 46%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.01 (dd, J = 3.8, 1.2 Hz, 1H), 7.87 (dd, J = 5.0, 1.1 Hz, 1H), 7.41 – 7.32 (m, 5H), 7.19 (q, J = 4.9, 3.8 Hz, 1H), 6.41 (s, 1H), 3.92 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 181.40, 171.08, 147.45, 135.87, 134.18, 132.07, 129.97, 129.22, 128.86, 128.05, 97.86, 57.44. Anal. Calcd. For $C_{14}H_{12}O_2S$: C, 68.83; H, 4.95; Found: C, 68.78; H, 4.96.

*4.2.14. (E)-1-Cyclohexyl-3-methoxy-3-phenylprop-2-en-1-one (**2n**)*

Yellow oil (65 mg, 54%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.38 (t, *J* = 7.2 Hz, 1H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.28 (dd, *J* = 8.3, 1.5 Hz, 2H), 5.77 (s, 1H), 3.76 (s, 3H), 2.29 (m, *J* = 11.0, 3.5 Hz, 1H), 1.77 – 1.64 (m, 4H), 1.22 – 1.11 (m, 6H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 201.11, 169.31, 135.97, 129.81, 129.09, 128.05, 128.04, 100.70, 56.92, 50.80, 28.99, 25.97, 25.75. Anal. Calcd. For $C_{16}H_{20}O_2$: C, 78.65; H, 8.25; Found: C, 78.58; H, 8.28.

*4.2.15. (E)-3-Methoxy-1-phenyl-3-(p-tolyl)prop-2-en-1-one (**2o**)*

Yellow oil (95 mg, 76%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.91 (dd, *J* = 8.2, 1.3 Hz, 2H), 7.54 (t, *J* = 7.3 Hz, 1H), 7.47 – 7.43 (m, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 7.12 (d, *J* = 7.6 Hz, 2H), 6.34 (s, 1H), 3.90 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 189.44, 171.08, 139.76, 139.66, 133.02, 132.58, 129.25, 128.85, 128.66, 128.36, 98.44, 57.21, 21.37. Anal. Calcd. For $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 80.88; H, 6.40.

*4.2.16. (E)-3-(4-butylphenyl)-3-methoxy-1-phenylprop-2-en-1-one (**2p**)*

Yellow oil (107 mg, 73%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.90 (dd, *J* = 8.2, 1.2 Hz, 2H), 7.52 (t, *J* = 7.3 Hz, 1H), 7.45 – 7.41 (m, 2H), 7.26 (d, *J* = 8.2 Hz, 2H), 7.11 (d, *J* = 8.2 Hz, 2H), 6.33 (s, 1H), 3.89 (s, 3H), 2.54 (t, *J* = 7.7 Hz, 2H), 1.51 (p, *J* = 7.6 Hz, 2H), 1.26 (h, *J* = 7.4 Hz, 2H), 0.86 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 189.55, 171.11, 144.49, 139.74, 133.20, 132.52, 129.29, 128.79, 128.38, 127.96, 98.46, 57.20, 35.12, 33.34, 22.16, 14.18. Anal. Calcd. For $C_{20}H_{22}O_2$: C, 81.60; H, 7.53; Found: C, 81.54; H, 7.56.

*4.2.17. (E)-3-methoxy-3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one (**2q**)*

Yellow oil (93 mg, 70%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.89 (d, *J* = 7.3 Hz, 2H), 7.53 (t, *J* = 7.3 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.32 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 6.30 (s, 1H), 3.89 (s, 3H), 3.74 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 189.41, 170.92, 160.86, 139.87, 132.53, 131.08, 128.84, 128.34, 127.83, 113.45, 97.93, 57.19, 55.62. Anal. Calcd. For $C_{17}H_{16}O_3$: C, 76.10; H, 6.01; Found: C, 76.05; H, 6.03.

*4.2.18. (E)-3-(4-fluorophenyl)-3-methoxy-1-phenylprop-2-en-1-one (**2r**)*

Yellow oil (83 mg, 65%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.91 (d, J = 6.9 Hz, 2H), 7.54 (t, J = 7.3 Hz, 1H), 7.45 (t, J = 7.7 Hz, 2H), 7.41 (dd, J = 8.8, 5.4 Hz, 2H), 7.14 (t, J = 8.9 Hz, 2H), 6.40 (s, 1H), 3.91 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 189.32, 170.04, 163.14 (d, J = 245.3 Hz), 139.57, 132.71, 132.31 (d, J = 3.3 Hz), 131.69 (d, J = 8.5 Hz), 128.88, 128.40, 115.09 (d, J = 21.7 Hz), 98.73, 57.39. Anal. Calcd. For $C_{16}H_{13}FO_2$: C, 74.99; H, 5.11; Found: C, 75.06; H, 5.09.

*4.2.19. (E)-3-(4-Chlorophenyl)-3-methoxy-1-phenylprop-2-en-1-one (**2s**)*

Yellow oil (97 mg, 72%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.92 (dd, J = 8.3, 1.3 Hz, 2H), 7.56 (t, J = 7.3 Hz, 1H), 7.49 – 7.44 (m, 2H), 7.42 – 7.32 (m, 4H), 6.44 (s, 1H), 3.92 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 188.73, 169.32, 138.95, 134.33, 134.11, 132.29, 130.60, 128.40, 127.90, 127.74, 98.50, 56.98. Anal. Calcd. For $C_{16}H_{13}ClO_2$: C, 70.46; H, 4.80; Found: C, 70.50; H, 4.78.

*4.2.20. (E)-3-cyclopropyl-3-methoxy-1-phenylprop-2-en-1-one (**2t**)*

Yellow solid (75 mg, 74%). M.p. 92 ^{o}C. ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.94 (dd, J = 8.3, 1.4 Hz, 2H), 7.54 (t, J = 7.3 Hz, 1H), 7.47 (t, J = 7.5 Hz, 2H), 6.31 (s, 1H), 3.71 (s, 3H), 3.40 (tt, J = 8.3, 5.0 Hz, 1H), 0.94 – 0.90 (m, 2H), 0.85 – 0.82 (m, 2H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 189.39, 176.97, 140.82, 132.20, 128.85, 127.91, 96.33, 56.34, 12.65, 8.19. Anal. Calcd. For $C_{13}H_{14}O_2$: C, 77.20; H, 6.98; Found: C, 77.14; H, 7.00.

*4.2.21. (E)-3-Ethoxy-1,3-diphenylprop-2-en-1-one (**2u**)*

Yellow oil (98 mg, 78%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.89 (dd, J = 8.3, 1.3 Hz, 2H), 7.53 (t, J = 7.3 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 7.38 – 7.29 (m, 5H), 6.36 (s, 1H), 4.17 (q, J = 7.0 Hz, 2H), 1.36 (t, J = 7.0 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 189.46, 170.26, 139.70, 136.19, 132.58, 129.84, 129.25, 128.84, 128.36, 128.08, 99.09, 65.52, 14.59. Anal. Calcd. For $C_{17}H_{16}O_2$: C, 80.93; H, 6.39; Found: C, 80.97; H, 6.38.

*4.2.22. (E)-1,3-diphenyl-3-propoxyprop-2-en-1-one (**2v**)*

Yellow oil (110 mg, 83%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.89 (dd, J = 8.3, 1.3 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.44 (dd, J = 8.3, 7.2 Hz, 2H), 7.40 – 7.29 (m, 5H), 6.36 (s, 1H), 4.09 (t, J = 6.4 Hz, 2H), 1.80 – 1.73 (m, 2H), 0.99 (t, J = 7.4 Hz, 3H).

^{13}C NMR (150 MHz, DMSO-d_6): δ 189.45, 170.35, 139.67, 136.18, 132.60, 129.90, 129.22, 128.84, 128.36, 128.12, 99.09, 71.19, 22.12, 10.90. Anal. Calcd. For $C_{18}H_{18}O_2$: C, 81.17; H, 6.81; Found: C, 81.22; H, 6.78.

*4.2.23. (E)-3-Butoxy-1,3-diphenylprop-2-en-1-one (**2w**)*

Yellow oil (106 mg, 76%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.89 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.47 – 7.42 (m, 2H), 7.39 – 7.28 (m, 5H), 6.37 (s, 1H), 4.12 (t, *J* = 6.4 Hz, 2H), 1.75 – 1.70 (m, 2H), 1.44 (m, 2H), 0.93 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 189.46, 170.37, 139.69, 136.20, 132.58, 129.87, 129.21, 128.83, 128.37, 128.11, 99.09, 69.45, 30.77, 19.25, 14.08. Anal. Calcd. For $C_{19}H_{20}O_2$: C, 81.40; H, 7.19; Found: C, 81.33; H, 7.22.

*4.2.24. (E)-3-(pentyloxy)-1,3-diphenylprop-2-en-1-one (**2x**)*

Yellow oil (108 mg, 74%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.89 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.38 – 7.29 (m, 5H), 6.36 (s, 1H), 4.11 (t, *J* = 6.4 Hz, 2H), 1.77 – 1.72 (m, 2H), 1.43 – 1.37 (m, 2H), 1.36 – 1.31 (m, 2H), 0.88 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 189.44, 170.36, 139.69, 136.20, 132.58, 129.87, 129.21, 128.83, 128.36, 128.12, 99.09, 69.73, 28.38, 28.17, 22.24, 14.29. Anal. Calcd. For $C_{20}H_{22}O_2$: C, 81.60; H, 7.53; Found: C, 81.55; H, 7.55.

*4.2.25. (E)-3-(Benzyloxy)-1,3-diphenylprop-2-en-1-one (**2y**)*

Yellow solid (108 mg, 70%). M.p. 94 ^{o}C. ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.89 (dd, *J* = 8.2, 1.3 Hz, 2H), 7.54 (t, *J* = 7.3 Hz, 1H), 7.50 (d, *J* = 6.8 Hz, 2H), 7.48 – 7.29 (m, 10H), 6.53 (s, 1H), 5.26 (s, 2H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 189.51, 169.61, 139.57, 136.41, 135.95, 132.72, 129.98, 129.33, 129.00, 128.87, 128.62, 128.48, 128.42, 128.17, 100.08, 71.43. Anal. Calcd. For $C_{22}H_{18}O_2$: C, 84.05; H, 5.77; Found: C, 83.97; H, 5.79.

*4.2.26. (E)-3-Isopropoxy-1,3-diphenylprop-2-en-1-one (**2z**)*

Yellow solid (89 mg, 67%). M.p. 80 ^{o}C. ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.86 (dd, *J* = 8.2, 1.2 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.45 (t, 2H), 7.37 – 7.33 (m, 1H), 7.33 – 7.28 (m, 4H), 6.38 (s, 1H), 4.83 (m, 1H), 1.34 (d, *J* = 6.0 Hz, 6H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 189.52, 169.12, 139.78, 136.55, 132.52, 129.75, 129.28, 128.84,

128.31, 128.07, 99.64, 71.70, 21.82. Anal. Calcd. For $C_{18}H_{18}O_2$: C, 81.17; H, 6.81; Found: C, 81.23; H, 6.78.

*4.3. Typical procedure for synthesis of 3-phenoxy-1,3-diphenylprop-2-en-1-one (**2***)*

The mixture of ynone **1a** (0.5 mmol), phenol (0.5 mmol) and sodium hydroxide (0.5 mmol) in 2 mL of acetonitrile was stirred at room temperature for 0.5 h. The reaction progress was monitored by TLC. After the completion of the reaction, the mixture was extracted with ethyl acetate (3×10 mL), and the liquor was washed with saturated brine (3×10 mL). The resulting organic phase was dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was isolated by column chromatography using petroleum ether and ethyl acetate (v/v 8:1) as eluent to give pure product. The analytical data for products are given below.

*4.3.1. (Z)-3-Phenoxy-1,3-diphenylprop-2-en-1-one (**2***-Z)*

Yellow oil (19 mg, 23%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.68 (d, *J* = 7.5 Hz, 2H), 7.56 – 7.44 (m, 6H), 7.39 (t, *J* = 7.6 Hz, 3H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.30 (d, *J* = 7.8 Hz, 2H), 7.24 (t, *J* = 8.0 Hz, 1H), 6.12 (s, 1H).^{13}C NMR (150 MHz, DMSO-d_6): δ 190.00, 168.63, 154.45, 138.85, 134.07, 133.06, 130.72, 130.61, 129.76, 129.01, 128.37, 128.27, 125.91, 121.31, 105.53. Anal. Calcd. For $C_{21}H_{16}O_2$: C, 83.98; H, 5.37; Found: C, 84.05; H, 5.35.

*4.3.2. (E)-3-Phenoxy-1,3-diphenylprop-2-en-1-one (**2***-E)*

Yellow oil (18 mg, 22%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.97 (d, *J* = 7.5 Hz, 2H), 7.76 (dd, *J* = 7.6, 1.5 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.41 (q, *J* = 6.4 Hz, 3H), 7.35 (s, 1H), 7.20 (t, *J* = 7.9 Hz, 2H), 6.91 (t, *J* = 9.0 Hz, 3H).^{13}C NMR (150 MHz, DMSO-d_6): δ 188.95, 159.65, 157.18, 138.53, 134.27, 133.35, 131.11, 129.98, 129.28, 129.06, 128.66, 127.72, 122.67, 116.80, 111.85. Anal. Calcd. For $C_{21}H_{16}O_2$: C, 83.98; H, 5.37; Found: C, 83.92; H, 5.39.

*4.4. Typical procedure for synthesis of 3,3-dialkoxypropan-1-ones **3a-f***

The mixture of ynones (0.5 mmol), alcohol (2 mL) and sodium hydroxide (0.5 mmol) was stirred at room temperature for 6 h. The reaction progress was monitored by TLC. After the completion of the reaction, the mixture was extracted with ethyl acetate (3×10 mL), and the liquor was washed with saturated brine (3×10 mL). The

resulting organic phase was dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was isolated by column chromatography using petroleum ether and ethyl acetate (v/v 8:1) as eluent to give pure product. The analytical data for products are given below.

*4.4.1. (E)-3-Methoxy-1,3-diphenylprop-2-en-1-one (**3a**)*

Yellow oil (110 mg, 82%).^{1}H NMR (600 MHz, DMSO-d_6): δ 7.64 (dd, *J* = 8.0, 1.1 Hz, 2H), 7.46 (t, *J* = 7.4 Hz, 1H), 7.38 – 7.34 (m, 2H), 7.33 – 7.27 (m, 2H), 7.20 (t, *J* = 7.5 Hz, 2H), 7.14 (t, *J* = 7.3 Hz, 1H), 3.63 (s, 2H), 3.11 (s, 6H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 196.18, 140.43, 137.76, 133.07, 128.65, 128.36, 128.08, 127.29, 101.94, 48.88, 45.45. Anal. Calcd. For $C_{17}H_{18}O_3$: C, 75.53; H, 6.71; Found: C, 75.47; H, 6.74.

*4.4.2. 3,3-Dimethoxy-3-phenyl-1-(p-tolyl)propan-1-one (**3b**)*

Yellow solid (112 mg, 80%). M.p. 52 ^{o}C. ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.55 (d, *J* = 8.3 Hz, 2H), 7.38 – 7.34 (m, 2H), 7.21 (t, *J* = 7.4 Hz, 2H), 7.15 (t, *J* = 7.3 Hz, 1H), 7.11 (d, *J* = 7.9 Hz, 2H), 3.59 (s, 2H), 3.11 (s, 6H), 2.26 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 195.54, 143.38, 140.50, 135.33, 129.22, 128.52, 128.07, 128.04, 127.28, 101.98, 48.86, 45.29, 21.44. Anal. Calcd. For $C_{18}H_{20}O_3$: C, 76.03; H, 7.09; Found: C, 75.96; H, 7.12.

*4.4.3. 1-(4-Chlorophenyl)-3,3-dimethoxy-3-phenylpropan-1-one (**3c**)*

Yellow oil (115 mg, 76%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.63 (d, *J* = 8.5 Hz, 2H), 7.36 – 7.31 (m, 4H), 7.19 (t, *J* = 7.3 Hz, 2H), 7.14 (t, *J* = 7.2 Hz, 1H), 3.61 (s, 2H), 3.11 (s, 6H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 195.35, 140.25, 138.04, 136.37, 130.30, 128.69, 128.13, 127.25, 101.88, 48.91, 45.63. Anal. Calcd. For $C_{17}H_{17}ClO_3$: C, 67.00; H, 5.62; Found: C, 66.94; H, 5.64.

*4.4.4. 1-(Furan-2-yl)-3,3-dimethoxy-3-phenylpropan-1-one (**3d**)*

Yellow oil (101 mg, 78%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.73 (dd, *J* = 1.6, 0.6 Hz, 1H), 7.36 (dd, *J* = 8.2, 1.1 Hz, 2H), 7.23 (t, *J* = 7.5 Hz, 2H), 7.18 (t, *J* = 1.3 Hz, 1H), 7.07 (dd, *J* = 3.6, 0.6 Hz, 1H), 6.46 (dd, *J* = 3.6, 1.5 Hz, 1H), 3.41 (s, 2H), 3.12 (s, 6H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 183.66, 152.72, 148.03, 140.20, 128.17,

128.14, 127.20, 119.25, 112.62, 101.92, 48.93, 45.52. Anal. Calcd. For $C_{15}H_{16}O_4$: C, 69.22; H, 6.20; Found: C, 69.14; H, 6.22.

*4.4.5. 3,3-Dimethoxy-3-(p-tolyl)-1-phenylpropan-1-one (**3e**)*

Yellow oil (112 mg, 75%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.65 (d, *J* = 7.8 Hz, 2H), 7.46 (t, *J* = 7.3 Hz, 1H), 7.31 (t, *J* = 7.7 Hz, 2H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.00 (d, *J* = 8.0 Hz, 2H), 3.61 (s, 2H), 3.09 (s, 6H), 2.17 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 196.15, 137.78, 137.55, 137.15, 133.02, 128.65, 128.38, 127.22, 101.95, 48.77, 45.48, 21.01. Anal. Calcd. For $C_{18}H_{20}O_3$: C, 76.03; H, 7.09; Found: C, 76.11; H, 7.07.

*4.4.6. 3-(4-Chlorophenyl)-3,3-dimethoxy-1-phenylpropan-1-one (**3f**)*

Yellow oil (114 mg, 75%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.69 (d, *J* = 8.1 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.39 – 7.31 (m, 4H), 7.26 (d, *J* = 8.6 Hz, 2H), 3.67 (s, 2H), 3.09 (s, 6H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 196.04, 139.53, 137.60, 133.23, 132.83, 129.35, 128.74, 128.39, 128.07, 101.60, 48.89, 45.20. Anal. Calcd. For $C_{17}H_{17}ClO_3$: C, 67.00; H, 5.62; Found: C, 67.07; H, 5.60.

Acknowledgement

The authors thank the National Natural Science Foundation of China (21462038) for the financial support of this work.

Appendix A. Supplementary data

Supplementary data related to this article can be found.

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