JOC The Journal of Organic Chemistry

Note

One-Pot Reaction of Carboxylic Acids and Ynol Ethers for The Synthesis of #-Keto Esters

Linwei Zeng, Zhencheng Lai, and Sunliang Cui

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.8b02715 • Publication Date (Web): 19 Nov 2018

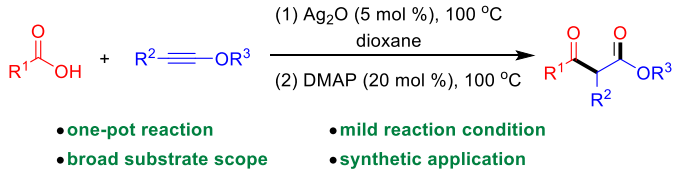
ACS Publications

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

One-Pot Reaction of Carboxylic Acids and Ynol Ethers for The Synthesis of β-Keto Esters

Linwei Zeng, Zhencheng Lai, and Sunliang Cui*

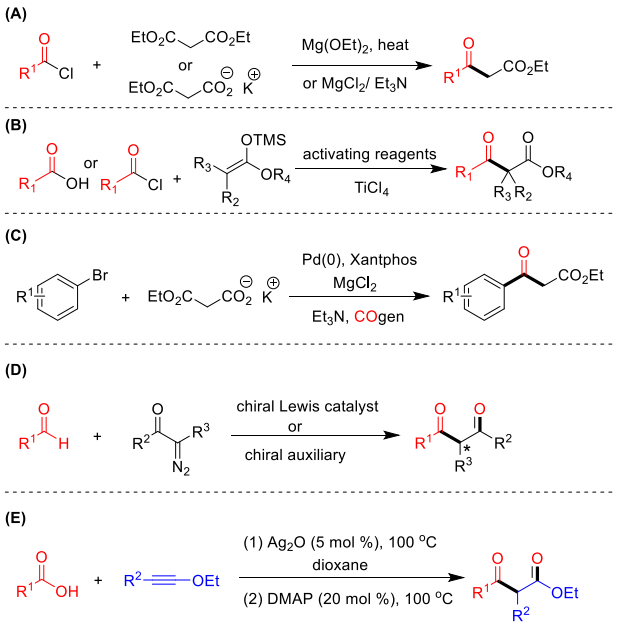
Institute of Drug Discovery and Design, College of Pharmaceutical Sciences, Zhejiang University, Hangzhou 310058, China



ABSTRACT: A one-pot reaction of carboxylic acids and ynol ethers for the synthesis of β-keto esters has been developed. Under promotion of Ag_2O, various carboxylic acids and ynol ethers could transform to α-acyloxy enol esters, which undergoes a following DMAP-catalyzed rearrangement to deliver β-keto esters rapidly. This method provides a direct approach to β-keto esters from carboxylic acids without any pre-activation. The protocol features mild reaction condition, broad substrate scope and the products could be transformed to an array of compounds.

β-Keto esters are type of fundamental and versatile building blocks in organic synthesis, and have been widely used in the synthesis of various heterocycles, pharmaceuticals and natural products.[1,2] Therefore, the syntheses of β-keto esters have received considerable attention.[3] The Claisen condensation is recognized as a fundamental C-C bond forming reaction in organic syntheses, and it is the most popular method for the synthesis of β-keto esters.[4] However, this reaction suffers from the need of a stoichiometric amount of a strong base and uncontrollable cross-condensation between two esters.[5] Other traditional method, Blaise reaction, which synthesize β-keto esters from nitriles and α-halo esters in the presence of Zn, remains limitation because of its expensive stating materials and narrow substrate scope.[6] A direct approach to β-keto esters involves the acylation of diethyl malonate and the sequential hydrolysis/decarboxylation,[7] and this method has the disadvantage of diacylation and retro-condensations. Meanwhile, a modified method has been developed by Wemple and co-workers.[8] They used monoethyl potassium malonate and acyl chloride as reagents under promotion of $MgCl_2$ and Et_3N, and the acylation/decarboxylation domino process would furnish the β-keto esters in good yields (Scheme 1A). In 2006, Tanabe and co-workers disclosed a nice synthesis of β-keto esters from silyl enol ethers and activated carboxylic acid derivatives under the promotion of $TiCl_4$ (Scheme 1B).[9] Recently, Taaning and Skrydstrup reported a palladium-catalyzed carboxylative coupling of aryl halides with monoester potassium malonates (Scheme 1C).[10] In addition, Maruoka and Feng have independently established the chiral synthesis of β-keto esters either using chiral auxiliary or chiral Lewis catalyst (Scheme 1D).[11] In spite of these advances,

Scheme 1. Synthesis of β-Keto Esters



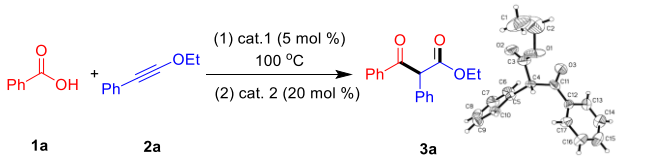
the general and direct transformation of carboxylic acids to β-keto esters without any pre-activation remains challenge and interesting.

Ynol ethers are type of unique alkynes with carbon–carbon triple bonds attached to the oxygen atom and exhibit dual nucleophilic and electrophilic properties.[12,13] Over the past two decades, ynol ethers haven been widely used as useful tools in organic chemistry because of their potential to form transient ketenium ions, thus, an array of reactions involving ynol ethers have been reported.[14] Recently, Zhu and coworkers reported that the carboxylic

acids could undergo addition to ynol ethers in the presence of Ag_2O catalyst,[15,16] and our group applied this in the multicomponent synthesis of tetrahydroisoquinolines.[17] During our research interests of ynamides and ynol ethers,[18] we assumed that the structure of *in situ* generated α-acyloxy enol esters intermediates are very similar to indolyl acetate,[19] which might undergo rearrangement to deliver β-keto esters and constitute a direct approach toward β-keto esters. Herein we would like to report a one-pot reaction of carboxylic acids and ynol ethers for the synthesis of β-keto esters (Scheme 1E).

We commenced our study by investigating benzoic acid **1a** and ynol ether **2a**. Initially, we carried out the reaction by mixing **1a**, **2a** and 5 mol % Ag_2O in dioxane at 100 °C to deliver α-acyloxy enol ester intermediate, and then added the Lewis base catalyst to test the rearrangement. When PPh_3 was added as catalyst (20 mol % amount), the rearrangement did not occur and the α-acyloxy enol ester intermediate was recovered (Table 1, entry 1). The utilization of PBu_3 gave the same result and there was not any new product formation (entry 2). Meanwhile, the employment of amine type catalysts such as DBU, DABCO and quinoline, was also found ineffective to initiate the desired rearrangement process. To our delight, the addition of DMAP was found effective to yield a rearrangement product **3a** in 87% yield (entry 6). The standard analysis identified the product to be β-keto ester, which is inconsistent with ^{1}HNMR, ^{13}CNMR and MS. Moreover, the X-ray analysis confirmed the structure.[20] At this stage, we tried to use some other catalysts to replace Ag_2O to trigger this reaction. The use of different silver salts such as AgOTf, $AgBF_4$ and Ag_2CO_3 was found to be inferior, and the product was formed in decreased yields (entry 7-9), while other metal salts such as $Cu(OTf)_2$ and PPh_3AuCl were not optimal due to the suppression of α-acyloxy enol ester intermediate formation in the first step (entry 10-11). When the reaction temperature was decreased to 80 °C, the reaction gave a comparable 85% yield (entry 12). When the reaction was conducted at room temperature, the yield of **3a** was lowered to 72% (entry 13). The survey of solvents showed that DCE, DMF, toluene and THF were not optimal and gave the product in slightly lower yields (entries 14-17), while the utilization of CH_3CN would completely suppress this rearrangement (entry 18). Besides, the addition of equivalent amount of DMAP did not show significant improvement of the yield, which suggested that the rearrangement is a catalytic process (entry 19). Furthermore, a 5 mmol scale reaction was also conducted to prove the scalability (entry 20).

Table 1. Reaction Optimization[a]

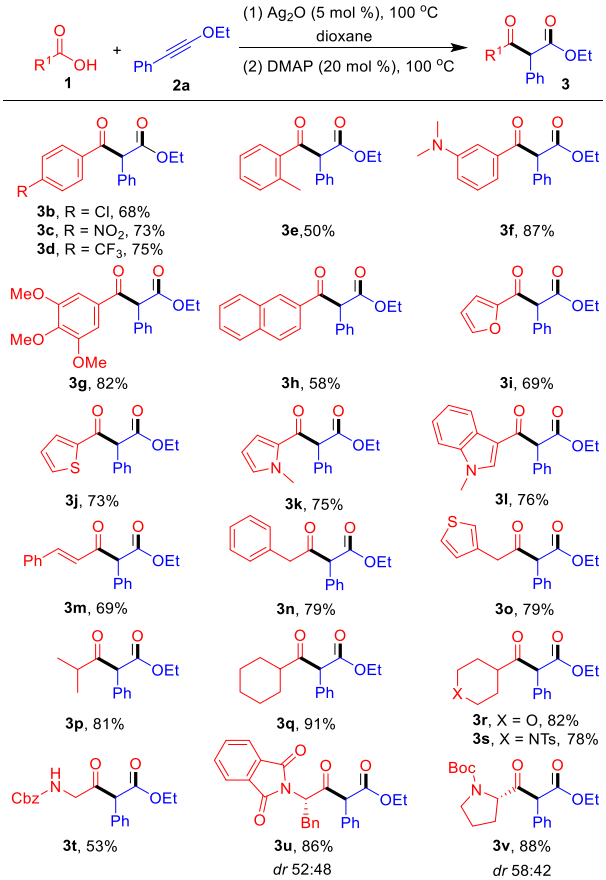


entry	cat. 1	cat. 2	temp. (°C)	solvent	yield (%)
1	Ag_2O	PPh_3	100	dioxane	0
2	Ag_2O	PBu_3	100	dioxane	0
3	Ag_2O	DBU	100	dioxane	0
4	Ag_2O	DABCO	100	dioxane	0
5	Ag_2O	quinoline	100	dioxane	0
6	Ag_2O	DMAP	100	dioxane	87
7	AgOTf	DMAP	100	dioxane	64
8	$AgBF_4$	DMAP	100	dioxane	76
9	Ag_2CO_3	DMAP	100	dioxane	78
10	$Cu(OTf)_2$	DMAP	100	dioxane	trace
11	PPh_3AuCl	DMAP	100	dioxane	trace
12	Ag_2O	DMAP	80	dioxane	85
13	Ag_2O	DMAP	rt	dioxane	72
14	Ag_2O	DMAP	100	DCE	64
15	Ag_2O	DMAP	100	DMF	47
16	Ag_2O	DMAP	100	toluene	72
17	Ag_2O	DMAP	100	THF	62
18	Ag_2O	DMAP	100	CH_3CN	0
19[b]	Ag_2O	DMAP	100	dioxane	86
20[c]	Ag_2O	DMAP	100	dioxane	83

[a] Reaction conditions: **1a** (0.28 mmol), **2a** (0.25 mmol) and Ag_2O (5 mol %) were added to dioxane (2 mL) and heated at 100 °C for 3 h, then the catalyst (20 mol %) were added and kept at the corresponding temperature. [b] DMAP (0.25 mmol) was used. [c] 5 mmol scale.

With the optimized reaction condition in hand, we next tested the substrate scope. As shown in Table 2, a variety of carboxylic acids were subjected to this one-pot

Table 2. Scope of Carboxylic Acids[a]

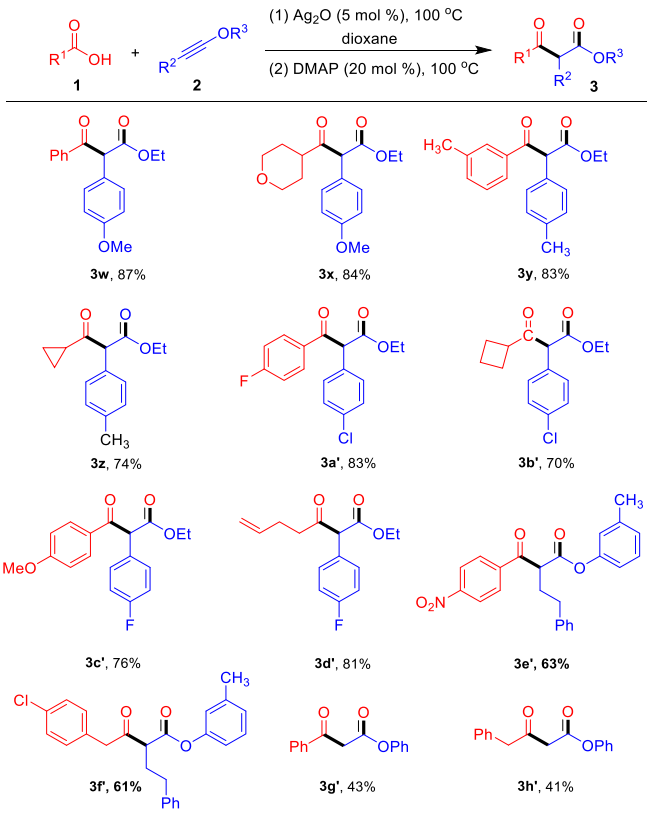


[a] Reaction conditions: **1** (0.28 mmol), **2a** (0.25 mmol) and Ag_2O (5 mol %) were added to dioxane (2 mL) and heated at 100 °C for 3 h, then DMAP (20 mol %) in dioxane (0.5 mL) was added and the solution was kept at 100 °C for another 3 h.

reaction. The substituted benzoic acids, including the *ortho*-, *meta*-, and *para*- substitution, could undergo this process smoothly to deliver the β-keto esters in moderate to good yields (**3b**-**3g**). And the functional groups like chloro, nitro, trifluoromethyl, *N, N*-dimethylamino, methoxy, could be well tolerable. In addition, the heterocyclic carboxylic acids with the moiety of naphthyl, furan, thiophene, pyrrole and indole, could be applicable for direct transformation to the β-keto ester products (**3h**-**3l**). The cinnamic acid could also participate in reaction smoothly to provide the product **3m** in 69% yield. Meanwhile, when the aliphatic carboxylic acids were used, including phenylacetic acid, thiophene-3-acetic acid, isobutyric acid, cyclohexanecarboxylic acid, the process could deliver the corresponding products in good to excellent yields (**3n**-**3q**). Moreover, the saturated heterocyclic carboxylic acids including the moiety of tetrahydropyran and piperidine, were also found applicable. Interestingly, the amino acids such as the protected glycine, *L*-phenylalanine and *L*- proline could engage in this process to deliver the products smoothly (**3t**-**3v**), and the *dr* values of the newly formed stereocenter ranged from 52:48 to 58:42. Considering the readily availability of carboxylic acid, this method provided a direct approach to β-keto esters in simple operation. It should be noted that this protocol excludes any preactivation, thus broadening the substrate scope and improving functional groups compatibility.

On the other hand, the scope of ynol ethers was also tested. As shown in Table 3, the *para*-methoxyphenyl, *para*-methylphenyl, *para*-chlorophenyl, *para*-fluorophenyl

Table 3. Scope of Ynol Ethers[a]

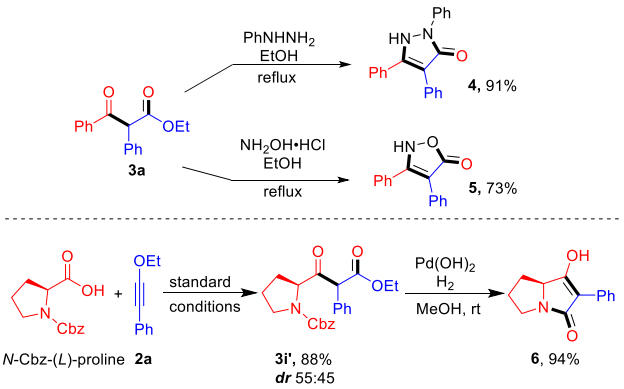


[a] Reaction conditions: **1** (0.28 mmol), **2** (0.25 mmol) and Ag_2O (5 mol %) were added to dioxane (2 mL) and heated at 100 °C for 3 h, then DMAP (20 mol %) in dioxane (0.5 mL) was added and the solution was kept at 100 °C for another 3 h.

substituted ynol ethers were all amenable in this process to undergo addition/rearrangement with carboxylic acids to deliver the β-keto esters in good yields (**3w**-**3d'**). And the moiety of pyran, cyclopropyl, *para*-fluorophenyl, cyclobutyl and alkene were amenable in the process. Respecting to the alkyl substituted internal ynol ethers, the phenylethyl and ethyl substituted substrates could undergo the one-pot addition/rearrangement with 4-nitrobenzoic acid and 4-chlorophenylacetic acid respectively to furnish the products in moderate yields (**3e'** and **3f'**). In addition, the terminal ynol ether was also applicable in this process to deliver the β-keto ester products in moderate yields (**3g'** and **3h'**).

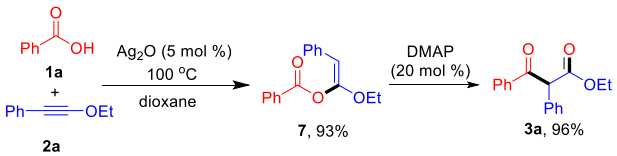
To demonstrate the synthetic utility, a diversification was carried out (Scheme 2). For example, the cyclization of compound **3a** with phenyl hydrazine and hydroxylamine would deliver the heterocyclic 1,2-dihydro-3*H*-pyrazol-3-one **4** and isoxazol-5(2*H*)-one **5** in good yields. Furthermore, the *N*-Cbz protected *L*-proline would engage in this one-pot reaction with ynol ether **2a** to deliver **3i'** with 55:45 *dr* value, and the following $Pd(OH)_2$-catalyzed hydrogenation would remove Cbz group to constitute cyclization and isomerization for accessing **6**.

Scheme 2. Diversifications of β-Keto Esters



Meanwhile, control reaction was conducted to probe the reaction mechanism. As shown in Scheme 3, **1a** and **2a** were coupled in the presence of Ag_2O to deliver α-acyloxy enol ester intermediate **7**. **7** was isolated and then treated with 20 mol % DMAP. Indeed, the β-keto ester **3a** could be afforded in 96% yield. This reaction showed that the one-pot reaction includes the successive addition/rearrangement process.

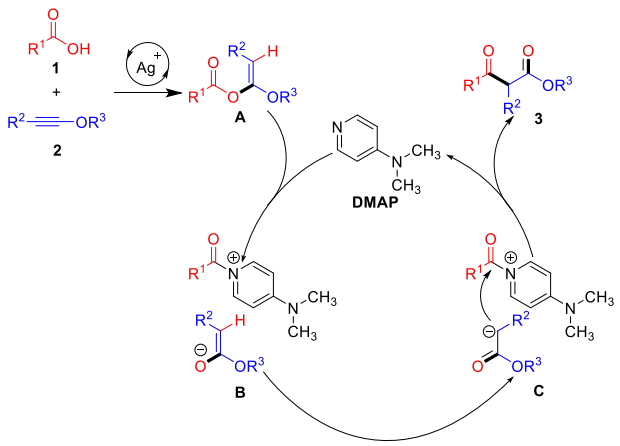
Scheme 3. Control Reaction



Based on these results and the literatures[11-15], a plausible reaction mechanism for this one-pot reaction was proposed in Scheme 4. Initially, the carboxylic acids **1** would undergo addition with the ynol ethers **2** to give the α-acyloxy enol ester **A** under promotion of Ag_2O. The α-acyloxy enol ester is reactive and could be attacked by DMAP to form zwitterionic complex **B**, and the following isomerization of enol ether anion to ester species **C**. The next addition of carbon anion to acyl pyridium would deliver β-keto esters **3** and regenerate DMAP. Thus the Ag_2O-catalyzed addition of carboxylic acids to ynol ethers and

the following DMAP-catalyzed rearrangement constitute the one-pot reaction for the synthesis of β-keto esters.

Scheme 4. Proposed Reaction Mechanism



In summary, a one-pot reaction of carboxylic acids and ynol ethers for accessing β-keto esters has been developed. This method provides a direct transformation of carboxylic acids to β-keto esters without any pre-activation. This protocol is featured with broad substrate scope and sufficient structural diversity. Furthermore, the products could be diversified to an array of compounds.

EXPERIMENTAL SECTION

General Information. Column chromatography was performed over silica gel (200–300mesh). Melting points were measured with X–4 micro melting point apparatus. HRMS were performed on Waters GCT premier time of flight mass spectrometer (EI). ^{1}H NMR spectra and ^{13}C NMR spectra were recorded on a *Bruker AV-600* spectrometer or a WNMR-I-400 spectrometer in DMSO-d_6 or chloroform-*d* (contain internal TMS). For DMSO-d_6, chemical shifts of ^{1}H NMR spectra were reported in ppm with the DMSO signal at 2.500 ppm as a standard and chemical shifts of ^{13}C NMR spectra were reported in ppm with the DMSO signal at 39.52 ppm as a standard. For $CDCl_3$, chemical shifts of ^{1}H NMR spectra were reported in ppm with the internal TMS signal at 0 ppm as a standard and chemical shifts of ^{13}C NMR spectra were reported in ppm with the chloroform signal at 77.16 ppm as a standard. [21] The data is being reported as (s = singlet, d = doublet, t = triplet, q = quartet, dd = double doublet, dt = double of triplet, m = multiplet or unresolved, br = broad singlet, coupling constant(s) in Hz, integration). High temperature NMR experiment was conducted on a WNMR-I-400 spectrometer at 60 °C in DMSO-d_6. Solvents and reagents were commercial available and used without further purification unless otherwise noted. Anhydrous solvents were purified according to standard methods.

Typical procedure for one-pot synthesis of β-keto esters. To an oven-dried schlenk tube was added benzoic acid **1a** (34.5 mg, 0.28 mmol) and Ag_2O (2.9 mg, 0.0125 mmol), then evacuated and purged with Argon three times. (Ethoxyethynyl)benzene **2a** (36.5 mg, 0.25 mmol) was dissolved in anhydrous dioxane (2 mL) and added by a syringe. The mixture was stirred at 100 °C in an oil bath until the starting material was fully converted to α-acyloxy enol ester intermediate, then 4-dimethylaminopyridine (DMAP) (6 mg, 0.05 mmol) was dissolved in anhydrous dioxane (0.5 mL) and added. The reaction was allowed to proceed at this temperature under stirring until it was completed. Solvent was removed under vacuum and the residue was purified by silica gel column chromatography using ethyl acetate/petroleum ether (v/v, 1:20) as eluent to give ethyl 3-oxo-2,3-diphenylpropanoate **3a** (59 mg, 87% yield) as a white solid.

*Ethyl 3-oxo-2,3-diphenylpropanoate (**3a**)*. White solid, (58 mg, 87% yield), m. p. 69.8-71.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$, isomers seen, ratio = 95/5) δ 13.64 (s, 0.05H), 7.96 (d, *J* = 7.4 Hz, 1.9H), 7.57 – 7.50 (m, 0.95H), 7.47 – 7.27 (m, 6.65H), 7.24 – 7.07 (m, 0.50H), 5.61 (s, 0.95H), 4.32 – 4.13 (m, 2H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.09 – 7.99 (m, 2H), 7.66 – 7.60 (m, 1H), 7.54 – 7.47 (m, 2H), 7.44 – 7.39 (m, 2H), 7.36 – 7.32 (m, 2H), 7.30 – 7.23 (m, 1H), 6.20 (s, 1H), 4.31 – 3.96 (m, 2H), 1.15 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 194.1, 169.0, 135.1, 133.9, 133.4, 129.7, 129.0, 128.9, 128.6, 127.8, 61.1, 58.9, 14.0; HRMS (EI) *m/z* calcd for $C_{17}H_{16}O_3$ [M]$^+$: 268.1099; Found: 268.1091.

*Ethyl 3-(4-chlorophenyl)-3-oxo-2-phenylpropanoate (**3b**)*. White solid, (51 mg, 68% yield), m. p. 77.8-79.5 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.07 – 8.00 (m, 2H), 7.64 – 7.54 (m, 2H), 7.41 – 7.37 (m, 2H), 7.37 – 7.33 (m, 2H), 7.31 – 7.27 (m, 1H), 6.19 (s, 1H), 4.21 – 4.06 (m, 2H), 1.15 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 193.2, 168.8, 139.0, 133.8, 133.2, 130.8, 129.7, 129.2, 128.7, 128.0, 61.2, 59.0, 14.0; HRMS (EI) Calcd for $C_{17}H_{15}ClO_3$ [M]$^+$:302.0710; Found: 302.0713.

*Ethyl 3-(4-nitrophenyl)-3-oxo-2-phenylpropanoate (**3c**)*. Yellow oil, (57 mg, 73% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.35 – 8.30 (m, 2H), 8.26 – 8.22 (m, 2H), 7.42 – 7.25 (m, 5H), 6.29 (s, 1H), 4.20 – 4.07 (m, 2H), 1.15 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 193.4, 168.6, 150.2, 139.8, 132.8, 130.2, 129.7, 128.8, 128.1, 124.1, 61.4, 59.4, 14.0; HRMS (EI) *m/z* calcd for $C_{17}H_{15}NO_5$ [M]$^+$: 313.0950; Found: 313.0957.

*Ethyl 3-oxo-2-phenyl-3-(4-(trifluoromethyl)phenyl)propanoate (**3d**)*. Colourless oil, (63 mg, 75% yield). ^{1}H NMR (600 MHz, DMSO) δ 8.21 (d, *J* = 8.4 Hz, 2H), 7.90 (d, *J* = 8.4 Hz, 2H), 7.42 – 7.38 (m, 2H), 7.38 – 7.34 (m, 2H), 7.32 – 7.27 (m, 1H), 6.27 (s, 1H), 4.18 – 4.09 (m, 2H), 1.14 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO) δ 193.7, 168.7, 138.4, 133.1 (q, *J* = 32.2 Hz), 132.9, 129.7, 129.6, 128.7, 128.0, 126.0(q, *J* = 3.5 Hz), 123.6(q, *J* = 272.8 Hz), 61.3, 59.3, 13.9; HRMS (EI) *m/z* calcd for $C_{18}H_{15}F_3O_3$ [M]$^+$: 336.0973; Found: 336.0969.

*Ethyl 3-oxo-2-phenyl-3-(o-tolyl)propanoate (**3e**)*. Colourless oil, (35 mg, 50% yield). ^{1}H NMR (600 MHz, DMSO-d_6, isomers seen, ratio = 87/13) δ 13.28 (s, 0.13H), 7.93 (d, *J* = 7.8 Hz, 0.87H), 7.43 – 6.96 (m, 8.13H), 6.03 (s, 0.87H), 4.22 (q, *J* = 7.2 Hz, 0.26H), 4.16 – 4.05 (m, 1.74H), 2.36 (s, 2.61H), 2.22 (s, 0.39H), 1.15 (t, *J* = 7.2 Hz, 0.39H), 1.12 (t, *J* = 7.2 Hz, 2.61H);^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6, isomers seen) δ 197.4, 172.5, 168.9, 138.2, 136.3, 135.2, 134.6, 134.1, 133.3, 132.0, 131.8, 131.3, 129.9, 129.7, 129.1, 129.0, 128.9, 128.6, 127.8, 127.5, 126.6, 126.0, 125.2, 105.8, 61.4, 61.1, 20.7, 19.2, 14.1, 14.0; HRMS (EI) *m/z* calcd for $C_{18}H_{18}O_3$ [M]$^+$: 282.1256; Found: 282.1263.

*Ethyl 3-(3-(dimethylamino)phenyl)-3-oxo-2-phenylpropanoate (**3f**)*. Yellow oil, (67 mg, 87% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.43 – 7.38 (m, 2H), 7.36 – 7.25 (m, 5H), 7.25 – 7.22 (m, 1H), 6.95 (dd, J_1 = 8.4 Hz, J_2 = 1.8 Hz, 1H), 6.16 (s, 1H), 4.30 – 3.87 (m, 2H), 2.90 (s, 6H), 1.16 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ

194.6, 169.2, 150.5, 135.7, 133.8, 129.7, 129.4, 128.6, 127.8, 117.5, 116.7, 111.8, 61.1, 59.1, 40.0, 14.1; HRMS (EI) *m/z* calcd for $C_{19}H_{21}NO_3$ $[M]^+$: 311.1521; Found: 311.1524.

*Ethyl 3-oxo-2-phenyl-3-(3,4,5-trimethoxyphenyl)propanoate (**3g**)*. Colourless oil, (73 mg, 82% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.44 (d, J = 7.2 Hz, 2H), 7.38 – 7.32 (m, 4H), 7.30 – 7.26 (m, 1H), 6.29 (s, 1H), 4.15 (q, J = 7.2 Hz, 2H), 3.81 (s, 6H), 3.71 (s, 3H), 1.18 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 192.9, 169.1, 152.8, 142.3, 133.8, 130.1, 129.7, 128.6, 127.8, 106.6, 61.1, 60.2, 58.7, 56.1, 14.1; HRMS (EI) *m/z* calcd for $C_{20}H_{22}O_6$ $[M]^+$: 358.1416; Found: 358.1419.

*Ethyl 3-(naphthalen-2-yl)-3-oxo-2-phenylpropanoate (**3h**)*. Colourless oil, (46 mg, 58% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.83 (s, 1H), 8.09 (d, J = 8.4 Hz, 1H), 8.03 – 7.98 (m, 2H), 7.96 (d, J = 8.4 Hz, 1H), 7.69 – 7.64 (m, 1H), 7.64 – 7.60 (m, 1H), 7.53 – 7.48 (m, 2H), 7.38 – 7.32 (m, 2H), 7.29 – 7.24 (m, 1H), 6.38 (s, 1H), 4.31 – 3.98 (m, 2H), 1.15 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 194.1, 169.0, 135.2, 133.5, 132.5, 132.1, 131.3, 129.8, 129.7, 129.3, 128.7, 128.6, 127.9, 127.8, 127.3, 124.0, 61.2, 58.9, 14.0; HRMS (EI) *m/z* calcd for $C_{21}H_{18}O_3$ $[M]^+$: 318.1256; Found: 318.1239.

*Ethyl 3-(furan-2-yl)-3-oxo-2-phenylpropanoate (**3i**)*. Colourless oil, (44 mg, 69% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.05 (d, J = 0.6 Hz, 1H), 7.69 (d, J = 3.6 Hz, 1H), 7.45 – 7.41 (m, 2H), 7.38 – 7.34 (m, 2H), 7.33 – 7.29 (m, 1H), 6.75 (dd, J_1 = 3.6 Hz, J_2 = 1.8 Hz, 1H), 5.81 (s, 1H), 4.48 – 3.96 (m, 2H), 1.15 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 181.7, 168.4, 150.6, 149.2, 133.2, 129.6, 128.5, 128.0, 121.0, 113.1, 61.3, 58.8, 14.0; HRMS (EI) *m/z* calcd for $C_{15}H_{14}O_4$ $[M]^+$: 258.0892; Found: 258.0877.

*Ethyl 3-oxo-2-phenyl-3-(thiophen-2-yl)propanoate (**3j**)*. White solid, (50 mg, 73% yield), m. p. 63.8-65.4 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.14 (dd, J_1 = 3.6 Hz, J_2 = 0.6 Hz, 1H), 8.07 (dd, J_1 = 4.8 Hz, J_2 = 0.6 Hz, 1H), 7.50 – 7.44 (m, 2H), 7.40 – 7.33 (m, 2H), 7.32 – 7.28 (m, 1H), 7.25 (dd, J_1 = 4.8 Hz, J_2 = 4.2 Hz, 1H), 6.06 (s, 1H), 4.14 (q, J = 7.2 Hz, 2H), 1.16 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 186.9, 168.5, 142.3, 136.8, 135.3, 133.5, 129.6, 129.1, 128.6, 128.0, 61.3, 59.3, 14.0; HRMS (EI) *m/z* calcd for $C_{15}H_{14}O_3S$ $[M]^+$: 274.0664; Found: 274.0671.

*Ethyl 3-(1-methyl-1H-pyrrol-2-yl)-3-oxo-2-phenylpropanoate (**3k**)*. White solid, (51 mg, 75% yield), m. p. 61.2-63.0 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.55 – 7.43 (m, 2H), 7.36 – 7.30 (m, 3H), 7.29 – 7.24 (m, 1H), 7.21 – 7.14 (m, 1H), 6.13 (dd, J_1 = 4.2 Hz, J_2 = 2.4 Hz, 1H), 5.79 (s, 1H), 4.16 – 4.03 (m, 2H), 3.81 (s, 3H), 1.16 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 183.6, 169.1, 134.7, 133.3, 129.5, 129.0, 128.3, 127.6, 121.6, 108.5, 61.0., 59.3, 37.2, 14.1; HRMS (EI) *m/z* calcd for $C_{16}H_{17}NO_3$ $[M]^+$: 271.1208; Found: 271.1212.

*Ethyl 3-(1-methyl-1H-indol-3-yl)-3-oxo-2-phenylpropanoate (**3l**)*. Colourless oil, (61 mg, 76% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.60 (s, 1H), 8.16 (d, J = 7.8 Hz, 1H), 7.58 – 7.50 (m, 3H), 7.35 – 7.31 (m, 2H), 7.30 – 7.22 (m, 3H), 5.78 (s, 1H), 4.19 – 4.06 (m, 2H), 3.86 (s, 3H), 1.16 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 187.7, 169.1, 139.0, 137.5, 134.8, 129.5, 128.3, 127.5, 126.0, 123.4, 122.7, 121.4, 114.0, 111.0, 60.9, 59.8, 33.5, 14.1; HRMS (EI) *m/z* calcd for $C_{20}H_{19}NO_3$ $[M]^+$: 321.1365; Found: 321.1371.

*Ethyl (E)-3-oxo-2,5-diphenylpent-4-enoate (**3m**)*. Light-yellow solid, (50 mg, 69% yield), m. p. 84.8-86.2 °C. ^{1}H NMR (600 MHz, DMSO-d_6, isomers seen, ratio = 56/44) δ 13.09 (s, 0.44H), 7.74 (d, J = 16.2 Hz, 0.56H), 7.69 – 7.65 (m, 1H), 7.50 – 7.16 (m, 10.44H), 6.93 (d, J = 16.2 Hz, 0.56H), 6.38 (d, J = 15.6 Hz, 0.44H), 5.57 (s, 0.56H), 4.22 – 4.10 (m, 2H), 1.18 (t, J = 7.2 Hz, 1.68H), 1.13 (t, J = 7.2Hz, 1.32H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6, isomers seen) δ 193.3, 172.5, 168.8, 166.0, 144.4, 136.9, 135.0, 134.0, 133.6, 133.2, 131.7, 131.1, 129.8, 129.7, 129.14, 129.11, 128.8, 128.6, 128.2, 127.9, 127.54, 127.51, 124.9, 119.8, 105.8, 61.3, 61.08, 61.05, 14.09, 14.08; HRMS (EI) *m/z* calcd for $C_{19}H_{18}O_3$ $[M]^+$: 294.1256; Found: 294.1267.

*Ethyl 3-oxo-2,4-diphenylbutanoate (**3n**)*. Colourless oil, (56 mg, 79% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.40 – 7.37 (m, 2H), 7.36 – 7.31 (m, 3H), 7.30 – 7.26 (m, 2H), 7.25 – 7.21 (m, 1H), 7.10 – 7.05 (m, 2H), 5.25 (s, 1H), 4.16 – 4.07 (m, 2H), 3.90 (d, J = 16.8 Hz, 1H), 3.79 (d, J = 16.8 Hz, 1H), 1.16 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 201.6, 168.4, 133.9, 132.9, 129.8, 129.7, 128.6, 128.3, 128.0, 126.8, 63.2, 61.2, 47.9, 14.0; HRMS (EI) *m/z* calcd for $C_{18}H_{18}O_3$ $[M]^+$: 282.1256; Found: 282.1259.

*Ethyl 3-oxo-2-phenyl-4-(thiophen-3-yl)butanoate (**3o**)*. Colourless oil, (57 mg, 79% yield). ^{1}H NMR (600 MHz, DMSO-d_6, isomers seen, ratio = 92/8) δ 13.11 (s, 0.08H), 7.47 (dd, J_1 = 4.8 Hz, J_2 = 3.0 Hz, 0.08H), 7.45 (dd, J_1 = 4.8 Hz, J_2 = 3.0 Hz, 0.92H), 7.41 – 6.82 (m, 7H), 5.23 (s, 0.92H), 4.20 – 4.05 (m, 2H), 3.92 (d, J = 17.4 Hz, 0.92H), 3.86 (s, 0.16H), 3.81 (d, J = 17.4 Hz, 0.92H), 1.16 (t, J = 7.2 Hz, 1.76H), 1.09 (t, J = 7.2 Hz, 0.24H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6, major isomer seen) δ 201.2, 168.4, 133.5, 132.9, 129.6, 129.0, 128.6, 128.0, 126.0, 123.7, 63.0, 61.2, 42.5, 14.0; HRMS (EI) *m/z* calcd for $C_{16}H_{16}O_3S$ $[M]^+$: 288.0820; Found:288.0813.

*Ethyl 4-methyl-3-oxo-2-phenylpentanoate (**3p**)*. Colourless oil, (47 mg, 81% yield). ^{1}H NMR (600 MHz, DMSO-d_6, isomers seen, ratio = 94/6) δ 13.22 (s, 0.06H), 7.46 – 7.11 (m, 5H), 5.34 (s, 0.94H), 4.25 – 4.02 (m, 2H), 2.71 (hept, J = 6.6 Hz, 0.94H), 2.55 – 2.51 (m, 0.06H), 1.16 (t, J = 7.2 Hz, 2.82H), 1.08 (t, 0.18H), 1.05 (d, J = 6.6 Hz, 2.82H), 1.00 (d, J = 7.2 Hz, 0.36H), 0.90 (d, J = 6.6 Hz, 2.82H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6, major isomer seen) δ 207.7, 168.6, 133.1, 129.6, 128.5, 127.9, 61.5, 61.1, 39.8, 18.4, 18.0, 14.0; HRMS (EI) *m/z* calcd for $C_{14}H_{18}O_3$ $[M]^+$: 234.1256; Found:234.1261.

*Ethyl 3-cyclohexyl-3-oxo-2-phenylpropanoate (**3q**)*. Colourless oil, (62 mg, 91% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.41 – 7.26 (m, 5H), 5.32 (s, 1H), 4.19 – 4.02 (m, 2H), 2.49 – 2.45 (m, 1H), 1.92 – 1.83 (m, 1H), 1.73 – 1.64 (m, 1H), 1.63 – 1.52 (m, 3H), 1.27 – 1.17 (m, 3H), 1.15 (t, J = 7.2 Hz, 3H), 1.13 – 1.05 (m, 2H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 206.7, 168.6, 133.1, 129.7, 128.5, 127.9, 61.5, 61.0, 49.5, 28.2, 27.9, 25.3, 25.1, 24.8, 14.0; HRMS (EI) *m/z* calcd for $C_{17}H_{22}O_3$ $[M]^+$: 274.1569; Found:274.1573.

*Ethyl 3-oxo-2-phenyl-3-(tetrahydro-2H-pyran-4-yl)propanoate (**3r**)*. Colourless oil, (56 mg, 82% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.45 – 7.26 (m, 5H), 5.38 (s, 1H), 4.18 – 4.03 (m, 2H), 3.87 – 3.81 (m, 1H), 3.79 – 3.75 (m, 1H), 3.28 (td, J_1 = 11.4 Hz, J_2 = 2.4 Hz, 1H), 3.22 (td, J_1 = 11.4 Hz, J_2 = 2.4 Hz, 1H), 2.76 (tt, J_1 = 11.4 Hz, J_2 = 3.6 Hz, 1H), 1.83 – 1.76 (m, 1H), 1.54 – 1.35 (m, 3H), 1.16 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 205.5, 168.5, 132.9, 129.7, 128.6, 127.9, 66.2, 66.0, 61.2, 61.1, 46.5, 28.1, 27.8, 14.0; HRMS (EI) *m/z* calcd for $C_{16}H_{20}O_4$ $[M]^+$: 276.1362; Found:276.1367.

Ethyl 3-oxo-2-phenyl-3-(1-tosylpiperidin-4-

*yl)propanoate (**3s**)*. Colourless oil, (83 mg, 78% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.59 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.4 Hz, 2H), 7.35 – 7.28 (m, 3H), 7.28 – 7.25 (m, 2H), 5.29 (s, 1H), 4.16 – 3.95 (m, 2H), 3.56 – 3.51 (m, 1H), 3.49 – 3.44 (m, 1H), 2.55 – 2.51 (m, 1H), 2.39 (s, 3H), 2.26 (td, J_1 = 11.4 Hz, J_2 = 2.4 Hz, 1H), 2.19 (td, J_1 = 11.4 Hz, J_2 = 2.4 Hz, 1H), 1.96 – 1.89 (m, 1H), 1.68 – 1.62 (m, 1H), 1.51 – 1.35 (m, 2H), 1.12 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 205.5, 168.4, 143.7, 132.7, 132.4, 129.9, 129.6, 128.6, 128.0, 127.6, 61.4, 61.2, 46.1, 45.2, 45.1, 26.9, 26.6, 21.1, 14.0; HRMS (EI) *m/z* calcd for $C_{23}H_{27}NO_5S$ [M]$^+$: 429.1610; Found:429.1615.

*Ethyl 4-(((benzyloxy)carbonyl)amino)-3-oxo-2-phenylbutanoate (**3t**)*. Colourless oil, (47 mg, 53% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.60 (t, J = 6.0 Hz, 1H), 7.39 – 7.29 (m, 10H), 5.23 (s, 1H), 5.01 (s, 2H), 4.15 – 4.08 (m, 2H), 4.05 (dd, J_1 = 18.6 Hz, J_2 = 6.0 Hz, 1H), 3.91 (dd, J_1 = 18.6 Hz, J_2 = 6.0 Hz, 1H), 1.17 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 200.5, 168.2, 156.4, 137.0, 132.8, 129.6, 128.6, 128.5, 128.0, 127.9, 127.8, 65.6, 61.3, 60.4, 49.5, 14.0; HRMS (EI) *m/z* calcd for $C_{20}H_{21}NO_5$ [M]$^+$: 355.1420; Found:355.1435.

*Ethyl (4S)-4-(1,3-dioxoisoindolin-2-yl)-3-oxo-2,5-diphenylpentanoate (**3u**)*. Colourless oil, (95 mg, 86% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.86 – 7.75 (m, 4H), 7.35 – 7.22 (m, 5H), 7.15 – 6.99 (m, 5H), 5.37 (s, 1H), 5.26 (dd, J_1 = 11.4 Hz, J_2 = 4.8 Hz, 0.48H), 5.15 (dd, J_1 = 11.4 Hz, J_2 = 4.8 Hz, 0.52H), 4.05 (q, J = 7.2 Hz, 1.04H), 4.02 – 3.97 (m, 0.96H), 3.53 (dd, J_1 = 14.4 Hz, J_2 = 4.8 Hz, 0.48H), 3.44 (dd, J_1 = 14.4 Hz, J_2 = 4.8 Hz, 0.52H), 3.28 – 3.22 (m, 0.48H), 3.12 – 3.06 (m, 0.52H), 1.14 – 1.02 (m, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 198.8, 198.5, 167.9, 167.8, 167.1, 166.9, 136.8, 136.7, 134.98, 134.97, 132.5, 132.2, 130.784, 130.777, 129.6, 129.5, 128.80, 128.78, 128.6, 128.4, 128.3, 128.2, 128.0, 126.8, 126.7, 123.50, 123.47, 61.6, 61.3, 60.1, 59.9, 59.3, 58.9, 32.72, 32.66, 13.9, 13.8; HRMS (EI) *m/z* calcd for $C_{27}H_{23}NO_5$ [M]$^+$: 441.1576; Found:441.1569.

*Tert-butyl (2S)-2-(3-ethoxy-3-oxo-2-phenylpropanoyl)pyrrolidine-1-carboxylate (**3v**)*. Colourless oil, (80 mg, 88% yield). ^{1}H NMR (600 MHz, DMSO-d_6, 2 diastereoisomers and their rotamers seen, ratio = 41/17: 26/16) δ 7.48 – 7.28 (m, 5H), 5.30 (s, 0.41H), 5.26 (s, 0.17H), 5.21 (s, 0.16H), 5.17 (s, 0.26H), 4.45 (dd, J_1 = 9.6 Hz, J_2 = 3.0 Hz, 0.42H), 4.42 – 4.35 (m, 0.58H), 4.17 – 4.05 (m, 2H), 3.37 – 3.21 (m, 2H), 2.27 – 2.02 (m, 1H), 1.96 – 1.41 (m, 3H), 1.39 (s, 1.53H), 1.38 (s, 1.44H), 1.30 (s, 2.34H), 1.20 – 1.13 (m, 3H), 1.04 (s, 3.69H); ^{1}H NMR (400 MHz, DMSO-d_6, 60 °C, 2 diastereoisomers seen, ratio = 58/42) δ 7.50 – 7.26 (m, 5H), 5.22 (s, 0.58H), 5.15 (s, 0.42H), 4.52 – 4.33 (m, 1H), 4.19 – 4.08 (m, 2H), 3.44 – 3.22 (m, 2H), 2.35 – 1.47 (m, 4H), 1.41 – 1.02 (m, 12H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6, 2 diastereoisomers and their rotamers seen) δ 203.3, 203.2, 202.9, 202.4, 168.22, 168.18, 167.9, 167.8, 154.1, 153.7, 153.0, 132.7, 132.6, 132.5, 132.1, 129.9, 129.7, 129.6, 128.54, 128.46, 128.4, 128.12, 128.05, 127.9, 79.3, 79.2, 79.0, 78.7, 65.2, 65.1, 65.0, 64.6, 61.25, 61.23, 61.16, 60.55, 60.53, 60.3, 59.2, 46.8, 46.6, 46.5, 46.4, 30.1, 28.8, 28.7, 28.5, 28.12, 28.08, 27.8, 27.5, 24.0, 23.6, 23.1, 22.2, 13.99, 13.96, 13.95; HRMS (EI) *m/z* calcd for $C_{20}H_{27}NO_5$ [M]$^+$: 361.1889; Found:361.1877.

*Ethyl 2-(4-methoxyphenyl)-3-oxo-3-phenylpropanoate (**3w**)*. White solid, m. p. 68.8-70.9 °C, (65 mg, 87% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.02 (d, J = 7.8 Hz, 2H), 7.66 – 7.58 (m, 1H), 7.56 – 7.45 (m, 2H), 7.32 (d, J = 9.0 Hz, 2H), 6.90 (d, J = 7.8 Hz, 2H), 6.11 (s, 1H), 4.12 (q, J = 7.2 Hz, 2H), 3.70 (s, 3H), 1.15 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 194.4, 169.3, 158.9, 135.1, 133.9, 130.9, 129.0, 129.0, 125.3, 114.1, 61.1, 58.1, 55.1, 14.1; HRMS (EI) *m/z* calcd for $C_{18}H_{18}O_4$ [M]$^+$: 298.1205; Found:298.1211.

*Ethyl 2-(4-methoxyphenyl)-3-oxo-3-(tetrahydro-2H-pyran-4-yl)propanoate (**3x**)*. Colourless oil, (64 mg, 84% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.24 (d, J = 9.0 Hz, 2H), 6.91 (d, J = 9.0 Hz, 2H), 5.27 (s, 1H), 4.11 – 4.05 (m, 2H), 3.84 – 3.80 (m, 1H), 3.77 – 3.74 (m, 1H), 3.72 (s, 3H), 3.26 (td, J_1 = 11.4 Hz, J_2 = 2.4 Hz, 1H), 3.20 (td, J_1 = 11.4 Hz, J_2 = 2.4 Hz, 1H), 2.71 (tt, J_1 = 11.4 Hz, J_2 = 3.6 Hz, 1H), 1.81 – 1.74 (m, 1H), 1.49 – 1.34 (m, 3H), 1.14 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 205.8, 168.8, 159.0, 130.8, 124.8, 114.0, 66.3, 66.0, 61.0, 60.4, 55.1, 46.3, 28.2, 27.8, 14.0; HRMS (EI) *m/z* calcd for $C_{17}H_{22}O_5$ [M]$^+$: 306.1467; Found:306.1474.

*Ethyl 3-oxo-3-(m-tolyl)-2-(p-tolyl)propanoate (**3y**)*. White solid, (61 mg, 83% yield), m. p. 73.8-75.8 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.88 – 7.77 (m, 2H), 7.43 (d, J = 7.2 Hz, 1H), 7.40 – 7.33 (m, 1H), 7.27 (d, J = 8.4 Hz, 2H), 7.14 (d, J = 7.8 Hz, 2H), 6.10 (s, 1H), 4.18 – 4.07 (m, 2H), 2.33 (s, 3H), 2.24 (s, 3H), 1.15 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 194.3, 169.1, 138.5, 137.1, 135.2, 134.5, 130.4, 129.5, 129.2, 128.8, 126.3, 61.0, 58.5, 20.9, 20.7, 14.0; HRMS (EI) *m/z* calcd for $C_{19}H_{20}O_3$ [M]$^+$: 296.1412; Found:296.1422.

*Ethyl 3-cyclopropyl-3-oxo-2-(p-tolyl)propanoate (**3z**)*. Colourless oil, (45 mg, 74% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.22 (d, J = 7.8 Hz, 2H), 7.18 (d, J = 7.8 Hz, 2H), 5.21 (s, 1H), 4.11 (q, J = 7.2 Hz, 2H), 2.29 (s, 3H), 2.03 – 1.95 (m, 1H), 1.17 (t, J = 7.2 Hz, 3H), 0.94 – 0.87 (m, 2H), 0.85 – 0.79 (m, 2H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 204.3, 168.7, 137.2, 130.2, 129.6, 129.2, 63.7, 60.9, 20.8, 20.2, 14.0, 11.7, 11.6; HRMS (EI) *m/z* calcd for $C_{15}H_{18}O_3$ [M]$^+$: 246.1256; Found:246.1257.

*Ethyl 2-(4-chlorophenyl)-3-(4-fluorophenyl)-3-oxopropanoate (**3a'**)*. Colourless oil, (66 mg, 83% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.17 – 8.07 (m, 2H), 7.45 – 7.40 (m, 4H), 7.39 – 7.32 (m, 2H), 6.25 (s, 1H), 4.24 – 4.05 (m, 2H), 1.14 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 192.6, 168.6, 165.5 (d, J = 253.6 Hz), 132.9, 132.3, 132.1 (d, J = 9.7 Hz), 131.7 (d, J = 2.7 Hz), 131.5, 128.7, 116.2 (d, J = 22.1 Hz), 61.4, 58.1, 14.0; HRMS (EI) *m/z* calcd for $C_{17}H_{14}ClFO_3$ [M]$^+$: 320.0616; Found:320.0619.

*Ethyl 2-(4-chlorophenyl)-3-cyclobutyl-3-oxopropanoate (**3b'**)*. Colourless oil, (49 mg, 70% yield). ^{1}H NMR (600 MHz, DMSO-d_6, isomers seen, ratio = 92/8) δ 13.34 (s, 0.08H), 7.43 (d, J = 8.4 Hz, 1.84H), 7.39 (d, J = 8.4 Hz, 0.16H), 7.35 (d, J = 8.4 Hz, 1.84H), 7.14 (d, J = 8.4 Hz, 0.16H), 5.17 (s, 0.92H), 4.32 – 3.96 (m, 2H), 3.56 – 3.29 (m, 1H), 2.19 – 1.78 (m, 5H), 1.72 – 1.61 (m, 1H), 1.17 (t, J = 7.2 Hz, 2.76H), 1.09 (t, J = 7.2 Hz, 0.24H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6, major isomer seen) δ 204.4, 168.3, 132.8, 132.0, 131.5, 128.5, 61.3, 60.6, 44.6, 24.5, 24.2, 17.1, 14.0; HRMS (EI) *m/z* calcd for $C_{15}H_{17}ClO_3$ [M]$^+$: 280.0866; Found:280.0874.

*Ethyl 2-(4-fluorophenyl)-3-(4-methoxyphenyl)-3-oxopropanoate (**3c'**)*. Colourless oil, (60 mg, 76% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.01 (d, J = 8.4 Hz, 2H), 7.52 – 7.39 (m, 2H), 7.21 – 7.14 (m, 2H), 7.03 (d, J = 8.4 Hz, 2H), 6.16 (s, 1H), 4.12 (q, J = 7.2 Hz, 2H), 3.81 (s, 3H), 1.15 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 192.5, 169.1, 163.8, 161.8 (d, J = 244.3 Hz), 131.7 (d, J = 8.2 Hz),

131.5, 130.0 (d, *J* = 2.9 Hz), 127.8, 115.5 (d, *J* = 21.4 Hz), 114.3, 61.2, 57.7, 55.8, 14.1; HRMS (EI) *m/z* calcd for $C_{18}H_{17}FO_4$ $[M]^+$: 316.1111; Found: 316.1123.

*Ethyl 2-(4-fluorophenyl)-3-oxohept-6-enoate (**3d'**)*. Colourless oil, (53 mg, 81% yield). ^1H NMR (600 MHz, DMSO-d_6, isomers seen, ratio = 93/7) δ 13.17 (s, 0.07H), 7.41 – 7.16 (m, 4H), 5.81 – 5.62 (m, 1H), 5.22 (s, 0.93H), 5.00 – 4.86 (m, 2H), 4.20 – 4.06 (m, 2H), 2.71 – 2.61 (m, 1H), 2.58 – 2.50 (m, 1H), 2.23 – 2.13 (m, 2H), 1.16 (t, *J* = 7.2 Hz, 2.79H), 1.08 (t, *J* = 7.2 Hz, 0.21H); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6, major isomer seen) δ 203.2, 168.5, 161.9 (d, *J* = 244.2 Hz), 137.0, 131.7 (d, *J* = 8.3 Hz), 129.3 (d, *J* = 3.0 Hz), 115.5 (d, *J* = 21.5 Hz), 115.4, 62.3, 61.2, 40.4, 27.1, 14.0; HRMS (EI) *m/z* calcd for $C_{15}H_{17}FO_3$ $[M]^+$: 264.1162; Found:264.1147.

*3-Tolyl 2-(4-nitrobenzoyl)-4-phenylbutanoate (**3e'**)*. Colourless oil, (63 mg, 63% yield). ^1H NMR (600 MHz, DMSO-d_6) δ 8.45 – 8.36 (m, 2H), 8.32 – 8.25 (m, 2H), 7.33 – 7.17 (m, 6H), 7.07 (d, *J* = 7.8 Hz, 1H), 6.85 – 6.77 (m, 2H), 5.02 (t, *J* = 7.2 Hz, 1H), 2.80 – 2.71 (m, 2H), 2.33 – 2.29 (m, 2H), 2.28 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ 194.7, 168.2, 150.3, 150.0, 140.8, 140.2, 139.5, 130.0, 129.3, 128.5, 128.4, 126.9, 126.2, 124.2, 121.7, 118.3, 53.1, 32.7, 30.1, 20.7; HRMS (EI) *m/z* calcd for $C_{24}H_{21}NO_5$ $[M]^+$: 403.1420; Found:403.1428.

*3-Tolyl 4-(4-chlorophenyl)-3-oxo-2-phenethylbutanoate (**3f'**)*. Colourless oil, (62 mg, 61% yield). ^1H NMR (600 MHz, DMSO-d_6) δ 7.38 (d, *J* = 8.4 Hz, 2H), 7.33 – 7.28 (m, 3H), 7.26 – 7.19 (m, 5H), 7.09 (d, *J* = 7.2 Hz, 1H), 6.97 – 6.84 (m, 2H), 4.10 – 4.00 (m, 3H), 2.71 – 2.61 (m, 2H), 2.31 (s, 3H), 2.28 – 2.13 (m, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ 202.6, 168.1, 150.1, 140.7, 139.4, 132.9, 131.8, 129.3, 128.5, 128.4, 128.30, 128.29, 126.9, 126.2, 121.9, 118.5, 57.0, 47.3, 32.8, 29.4, 20.8; HRMS (EI) *m/z* calcd for $C_{25}H_{23}ClO_3$ $[M]^+$: 406.1336; Found:406.1342.

*Phenyl 3-oxo-3-phenylpropanoate (**3g'**)*. Colourless oil, (26 mg, 43% yield). ^1H NMR (400 MHz, $CDCl_3$, isomers seen, ratio = 73/27) δ 12.33 (s, 0.27H), 8.01 (d, *J* = 7.6 Hz, 1.46H), 7.84 (d, *J* = 7.6 Hz, 0.54H), 7.68 – 7.05 (m, 8H), 5.92 (s, 0.27H), 4.24 (s, 1.46H); ^1H NMR (600 MHz, DMSO-d_6, isomers seen, ratio = 91/9) δ 12.21 (s, 0.09H), 8.04 (d, *J* = 7.2 Hz, 1.82H), 7.95 (d, *J* = 7.2 Hz, 0.18H), 7.74 – 7.51 (m, 3H), 7.48 – 7.42 (m, 2H), 7.32 – 7.26 (m, 1H), 7.24 (d, *J* = 7.2 Hz, 0.18H), 7.13 (d, *J* = 7.2 Hz, 1.82H), 6.26 (s, 0.09H), 4.52 (s, 1.82H); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6, major isomer seen) δ 193.6, 166.9, 150.4, 135.7, 134.1, 129.7, 129.0, 128.6, 126.2, 121.7, 45.7; HRMS (EI) *m/z* calcd for $C_{15}H_{12}O_3$ $[M]^+$: 240.0786; Found:240.0777.

*Phenyl 3-oxo-4-phenylbutanoate (**3h'**)*. Colourless oil, (26 mg, 41% yield). ^1H NMR (600 MHz, DMSO-d_6) δ 7.45 – 7.41 (m, 2H), 7.36 – 7.32 (m, 2H), 7.29 – 7.26 (m, 2H), 7.25 – 7.22 (m, 2H), 7.13 – 7.08 (m, 2H), 3.97 (s, 4H); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ 201.4, 166.2, 150.3, 134.1, 129.9, 129.7, 128.5, 126.9, 126.1, 121.7, 48.9, 48.5; HRMS (EI) *m/z* calcd for $C_{16}H_{14}O_3$ $[M]^+$: 254.0943; Found:254.0961.

*Benzyl (2S)-2-(3-ethoxy-3-oxo-2-phenylpropanoyl)pyrrolidine-1-carboxylate (**3i'**)*. Colourless oil, (87 mg, 88% yield). ^1H NMR (600 MHz, DMSO-d_6, 2 diastereoisomers and their rotamers seen, ratio = 32/23: 26/19) δ 7.60 – 7.01 (m, 11H), 5.31 (s, 0.32H), 5.30 (s, 0.26H), 5.25 (s, 0.19H), 5.22 (s, 0.23H), 5.10 – 4.44 (m, 3H), 4.17 – 3.94 (m, 2H), 3.50 – 3.40 (m, 1H), 3.36 – 3.18 (m, 2H), 2.33 – 1.50 (m, 4H), 1.21 – 1.03 (m, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6, 2 diastereoisomers and their rotamers seen) δ 202.8, 202.6, 202.5, 202.4, 168.1, 168.0, 167.74, 167.71, 154.3, 154.0, 153.5, 153.4, 136.83, 136.77, 136.7, 136.6, 132.5, 132.3, 132.1, 129.7, 129.61, 129.58, 129.5, 128.40, 128.35, 128.28, 128.2, 128.1, 128.0, 127.90, 127.86, 127.72, 127.66, 127.5, 127.4, 127.3, 66.3, 66.1, 66.0, 65.7, 65.4, 65.1, 64.9, 64.2, 61.21, 61.18, 61.11, 61.07, 60.6, 60.4, 60.0, 59.9, 47.1, 47.0, 46.5, 46.4, 29.6, 29.0, 28.6, 28.3, 23.9, 23.5, 23.0, 22.5, 14.0, 13.9, 13.8; HRMS (EI) *m/z* calcd for $C_{23}H_{25}NO_5$ $[M]^+$: 395.1733; Found: 395.1716.

General procedure for synthesis of 4. To a round bottom flask was added **3a** (40 mg, 0.15 mmol) and $PhNHNH_2$ (25 mg, 0.23 mmol), then ethanol (0.5 mL) was added as solvent. The mixture was stirred at 80 °C in an oil bath and reflux for 12h. Solvent was removed under vacuum and extracted with EtOAc (3×5 mL), the combined organic layer was washed by brine, dried over anhydrous Na_2SO_4, filtered and evaporated to obtain the residue which was purified by silica gel column chromatography using DCM/MeOH (v/v, 20:1) as eluent to give 1,3,4-triphenyl-1H-pyrazol-5-ol **4** (43 mg, 92% yield) as a white solid.

*1,3,4-Triphenyl-1H-pyrazol-5-ol (**4**)*. White solid, (43 mg, 92% yield), m. p. 192.8-194.1 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 10.92 (s, 1H), 7.85 (d, *J* = 7.2 Hz, 2H), 7.63 – 7.13 (m, 13H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 149.6, 148.0, 138.4, 132.1, 129.7, 129.0, 128.3, 127.7, 126.4, 126.1, 122.0; HRMS (EI) *m/z* calcd for $C_{21}H_{16}N_2O$ $[M]^+$: 312.1263; Found:312.1255.

General procedure for synthesis of 5. To a round bottom flask was added **3a** (40 mg, 0.15 mmol) and hydroxylamine hydrochloride (32 mg, 0.45 mmol), then ethanol (1 mL) was added as solvent. The mixture was stirred at 80 °C in an oil bath and reflux for 12h. Solvent was removed under vacuum and extracted with EtOAc (3×5 mL), the combined organic layer was washed by brine, dried over anhydrous Na_2SO_4, filtered and evaporated to obtain the crude product which was purified by recrystallization to give **5** (mixture of 3,4-diphenylisoxazol-5(2H)-one and 3,4-diphenylisoxazol-5(4H)-one**)** (26 mg, 73% yield) as a white solid.

*3,4-Diphenylisoxazol-5(2H)-one (**5**)*. White solid, (26 mg, 73% yield), m. p. 159.8-161.2 °C. ^1H NMR (400 MHz, $CDCl_3$, isomers seen, ratio = 77/23) δ 7.89 – 6.89 (m, 10H), 4.91 (s, 0.23H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, isomers seen) δ 176.1, 172.3, 161.30, 161.27, 132.0, 131.6, 129.9, 129.3, 129.2, 129.1, 128.8, 128.7, 128.3, 128.1, 127.7, 127.4, 127.2, 102.4, 51.4; HRMS (EI) *m/z* calcd for $C_{15}H_{11}NO_2$ $[M]^+$: 237.0790; Found:237.0784.

General procedure for synthesis of 6. To a round bottom flask was added **3i'** (50 mg, 0.13 mmol) and 10% $Pd(OH)_2/C$ (5 mg), then methanol (2 mL) was added as solvent. The mixture was stirred under H_2 atmosphere (balloon) at rt for 2h. The Pd/C was filtered and washed with little methanol, the filtrate was concentrated under vacuum to afford the residue which was then purified by silica gel column chromatography using DCM/MeOH (v/v, 20:1) as eluent to give (S)-1-hydroxy-2-phenyl-5,6,7,7a-tetrahydro-3H-pyrrolizin-3-one **6** (26 mg, 94% yield) as a light-yellow solid.

*(S)-1-Hydroxy-2-phenyl-5,6,7,7a-tetrahydro-3H-pyrrolizin-3-one (**6**)*. Light yellow solid, (25 mg, 94% yield), m. p. 191.8-193.4 °C. ^1H NMR (600 MHz, DMSO-d_6) δ 7.93 (d, *J* = 7.8 Hz, 2H), 7.31 (t, *J* = 7.8 Hz, 2H), 7.15 (t, *J* = 7.2 Hz, 1H), 4.14 (dd, J_1 = 9.0 Hz, J_2 = 6.8 Hz, 1H), 3.42 – 3.37 (m, 1H), 3.09 – 2.99 (m, 1H), 2.23 – 2.15 (m, 1H), 2.12 – 1.98

(m, 2H), 1.40 – 1.29 (m, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ 176.8, 172.9, 132.2, 127.7, 126.7, 125.7, 103.0, 62.8, 43.1, 28.5, 27.7; HRMS (EI) *m/z* calcd for $C_{13}H_{13}NO_2$ $[M]^+$: 215.0946; Found:215.0949.

Gram-scale experiment. To an oven-dried schlenk tube was added benzoic acid **1a** (671 mg, 5.5 mmol) and Ag_2O (58 mg, 0.25 mmol), then evacuated and purged with Argon three times. (Ethoxyethynyl)benzene **2a** (730 mg, 5 mmol) was dissolved in anhydrous dioxane (40 mL) and added by a syringe. The mixture was stirred at 100 °C in an oil bath for 8h, DMAP (122 mg, 1 mmol) was added and the reaction was stirred for another 5h. Solvent was removed under vacuum and the residue was purified by silica gel column chromatography using ethyl acetate/petroleum ether (v/v, 1:20) as eluent to give ethyl 3-oxo-2,3-diphenylpropanoate **3a** (1.11 g, 83% yield) as a white solid.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Crystallographic data for **3a**. (CIF).

Crystallographic analysis of **3a**, Copies of NMR spectra of compounds **3a – 3i'**, **4 – 6** (PDF).

AUTHOR INFORMATION

Corresponding Author

slcui@zju.edu.cn

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

We are grateful for the financial support from National Natural Science Foundation of China (21472163).

REFERENCES

(1) For reviews, see: (a) Langer, P., Regio- and diastereoselective cyclization reactions of free and masked 1,3-dicarbonyl dianions with 1,2-dielectrophiles. *Chem. - Eur. J.* **2001,** *7*, 3858-3866; (b) Simon, C.; Constantieux, T.; Rodriguez, J., Utilisation of 1,3-dicarbonyl derivatives in multicomponent reactions. *Eur. J. Org. Chem.* **2004,** 4957-4980.

(2) For selected examples, see: (a) Zhu, F. L.; Wang, Y. H.; Zhang, D. Y.; Xu, J.; Hu, X. P., Enantioselective Synthesis of Highly Functionalized Dihydrofurans through Copper-Catalyzed Asymmetric Formal [3+2] Cycloaddition of beta-Ketoesters with Propargylic Esters. *Angew. Chem., Int. Edit.* **2014,** *53*, 10223-10227; (b) Wang, F.; Liu, H. X.; Fu, H.; Jiang, Y. Y.; Zhao, Y. F., An Efficient One-Pot Copper-Catalyzed Approach to Isoquinolin-1(2H)-one Derivatives. *Org. Lett.* **2009,** *11*, 2469-2472; (c) Salprima, Y. S.; Kuninobu, Y.; Takai, K., Rhenium-Catalyzed Synthesis of Stereodefined Cyclopentenes from beta-Ketoesters and Aliphatic Allenes. *Angew. Chem., Int. Edit.* **2008,** *47*, 9318-9321; (d) Michaelides, I. N.; Darses, B.; Dixon, D. J., Acid-Catalyzed Synthesis of Bicyclo[3.n.1]alkenediones. *Org. Lett.* **2011,** *13*, 664-667; (e) Liu, J. Q.; Liu, Z. H.; Liao, P. Q.; Zhang, L.; Tu, T.; Bi, X. H., Silver-Catalyzed Cross-Coupling of Isocyanides and Active Methylene Compounds by a Radical Process. *Angew. Chem., Int. Edit.* **2015,** *54*, 10618-10622; (f) Kuninobu, Y.; Kawata, A.; Nishi, M.; Takata, H.; Takai, K., Rhenium- and manganese-catalyzed insertion of acetylenes into beta-keto esters: synthesis of 2-pyranones. *Chem. Commun.* **2008,** 6360-6362.

(3) For reviews, see: (a) Hauser, C. R.; Hudson, B. E. *Org. React.* **1942**, *1*, 266-302. (b) Pollet, P. L., 3-Ketoesters by Malonic Synthesis. *J. Chem. Educ.* **1983,** *60*, 244-246; (c) Benetti, S.; Romagnoli, R.; Derisi, C.; Spalluto, G.; Zanirato, V., Mastering Beta-Keto-Esters. *Chem. Rev.* **1995,** *95*, 1065-1114.

(4) For examples, see: (a) Smith, M. B.; March, J. *AdVanced Organic Chemistry*, 5th ed.; John Wiley: New York, 2001; p 569. (b) Kürti, L.; Czakó, B. *Strategic Applications of Named Reactions in Organic Synthesis*; Elsevier: Burlington, 2005; p 86 and p 138.

(5) Honda, Y.; Katayama, S.; Kojima, M.; Suzuki, T.; Izawa, K., An efficient synthesis of gamma-amino beta-ketoester by cross-Claisen condensation with alpha-amino acid derivatives. *Tetrahedron Lett.* **2003,** 3163-3166.

(6) For examples, see: (a) Wu, D.; Fu, X.; Xiao, F.; Li, J.; Zhao, N.; Wei, W.; Sun, Y., Methoxycarbonylation of ketones with dimethyl carbonate over solid base. *Catal. Commun.* **2008,** *9*, 680-684; (b) Rao, H. S. P.; Rafi, S.; Padmavathy, K., The Blaise reaction. *Tetrahedron* **2008,** *64*, 8037-8043; (c) Blaise, E. E., New reactions of orhano-metallic derivatives (II) - alpha-alcoyl-beta-ketonic ethers. *C. R. Hebd. Séances Acad. Sci.* **1901,** *132*, 478-480; (d) Blaise, E. E., New reactions of organic metallic derivatives (III) - Non-substituted beta-cetonic ethers. *C. R. Hebd. Séances Acad. Sci.* **1901,** *132*, 978-980.

(7) Breslow, D. S.; Baumgarten, E.; Hauser, C. R., A new synthesis of beta-keto esters of the type RCOCH2COOC2H5. *J. Am. Chem. Soc.* **1944,** *66*, 1286-1288.

(8) Clay, R. J.; Collom, T. A.; Karrick, G. L.; Wemple, J., A Safe, Economical Method for the Preparation of Beta-Oxo Esters. *Synthesis* **1993,** 290-292.

(9) Iida, A.; Nakazawa, S.; Okabayashi, T.; Horii, A.; Misaki, T.; Tanabe, Y., Powerful Ti-crossed Claisen condensation between ketene silyl acetals or thioacetals and acid chlorides or acids. *Org. Lett.* **2006,** *8*, 5215-5218.

(10) Korsager, S.; Nielsen, D. U.; Taaning, R. H.; Skrydstrup, T., Access to beta-Keto Esters by Palladium-Catalyzed Carbonylative Coupling of Aryl Halides with Monoester Potassium Malonates. *Angew. Chem., Int. Edit.* **2013,** *52*, 9763-9766.

(11) (a) Hashimoto, T.; Miyamoto, H.; Naganawa, Y.; Maruoka, K., Stereoselective Synthesis of alpha-Alkyl-beta-keto Imides via Asymmetric Redox C-C Bond Formation between alpha-Alkyl-alpha-diazocarbonyl Compounds and Aldehydes. *J. Am. Chem. Soc.* **2009,** *131*, 11280-11281; (b) Li, W.; Wang, J.; Hu, X. L.; Shen, K.; Wang, W. T.; Chu, Y. Y.; Lin, L. L.; Liu, X. H.; Feng, X. M., Catalytic Asymmetric Roskamp Reaction of alpha-Alkyl-alpha-diazoesters with Aromatic Aldehydes: Highly Enantioselective Synthesis of alpha-Alkyl-beta-keto Esters. *J. Am. Chem. Soc.* **2010,** *132*, 8532-8533.

(12) For selected reviews and examples about ynol ethers, see: (a) Zhang, L. M.; Kozmin, S. A., Bronsted acid-promoted cyclizations of slioxyalkynes with arenes and alkenes. *J. Am. Chem. Soc.* **2004,** *126*, 10204-10205; (b) Wang, S. H.; Li, P. H.; Yu, L.; Wang, L., Sequential and One-Pot Reactions of Phenols with Bromoalkynes for the Synthesis of (Z)-2-Bromovinyl Phenyl Ethers and Benzo[b]furans. *Org. Lett.* **2011,** *13*, 5968-5971; (c) Sun, J. W.; Kozmin, S. A., Silver-catalyzed hydroamination of siloxy alkynes. *Angew. Chem., Int. Edit.* **2006,** *45*, 4991-4993; (d) Mejuch, T.; Botoshansky, M.; Marek, I., Combined Carbometalation-Zinc Homologation-Allylation Reactions as a New Approach for Alkoxyallylation of Aldehydes. *Org. Lett.* **2011,** *13*, 3604-3607; (e) Barluenga, J.; Riesgo, L.; Vicente, R.; López, L. A.; Tomás, M., Cu(I)-catalyzed regioselective synthesis of polysubstituted furans from propargylic esters via postulated (2-furyl)carbene complexes. *J. Am. Chem. Soc.* **2008,** *130*, 13528-13529.

(13) For selected reviews and examples about ynamides, see: For selected reviews, see: (a) Zificsak, C. A.; Mulder, J. A.; Hsung, R. P.; Rameshkumar, C.; Wei, L. L., Recent advances in the chemistry of ynamines and ynamides. *Tetrahedron* **2001,** *57*, 7575-7606; (b) Wang, X. N.; Yeom, H. S.; Fang, L. C.; He, S. H.; Ma, Z. X.; Kedrowski, B. L.; Hsung, R. P., Ynamides in Ring Forming Transformations. *Acc. Chem. Res.* **2014,** *47*, 560-578; (c) Pan, F.; Shu, C.; Ye, L. W., Recent progress towards gold-catalyzed synthesis of N-containing tricyclic compounds based on ynamides. *Org. Biomol. Chem.* **2016,** *14*, 9456-9465; (d) Evano, G.; Coste, A.; Jouvin, K., Ynamides: Versatile Tools in Organic Synthesis. *Angew. Chem., Int. Edit.* **2010,** *49*,

2840-2859; (e) DeKorver, K. A.; Li, H. Y.; Lohse, A. G.; Hayashi, R.; Lu, Z. J.; Zhang, Y.; Hsung, R. P., Ynamides: A Modern Functional Group for the New Millennium. *Chem. Rev.* **2010,** *110*, 5064-5106.

(14) Lecomte, M.; Evano, G., Aryl Ynol Ethers: Stable, Readily Available and Useful Precursors of Highly Reactive Ketenium Ions. *Lett. Org. Chem.* **2017,** *14*, 539-542.

(15) Yin, J.; Bai, Y. H.; Mao, M. Y.; Zhu, G. G., Silver-Catalyzed Regio- and Stereoselective Addition of Carboxylic Acids to Ynol Ethers. *J. Org. Chem.* **2014,** *79*, 9179-9185.

(16) For other reports using different catalysts, see: (a) Vongvilai, P.; Larsson, R.; Ramström, O., Direct asymmetric dynamic kinetic resolution by combined lipase catalysis and nitroaldol (Henry) reaction. *Adv. Synth. Catal.* **2008,** *350*, 448-452; (b) Klomp, D.; Djanashvili, K.; Svennum, N. C.; Chantapariyavat, N.; Wong, C. S.; Vilela, F.; Maschmeyer, T.; Peters, J. A.; Hanefeld, U., Combined epimerisation and acylation: Meerwein-Ponndorf-Verley-Oppenauer catalysts in action. *Org. Biomol. Chem.* **2005,** *3*, 483-489.

(17) Zeng, L. W.; Huang, B.; Shen, Y. Y.; Cui, S. L., Multicomponent Synthesis of Tetrahydroisoquinolines. *Org. Lett.* **2018,** *20*, 3460-3464.

(18) (a) Huang, B.; Zeng, L. W.; Shen, Y. Y.; Cui, S. L., One-Pot Multicomponent Synthesis of beta-Amino Amides. *Angew. Chem., Int. Edit.* **2017,** *56*, 4565-4568; (b) Shen, Y. Y.; Huang, B.; Zeng, L. W.; Cui, S. L., Single Reactant Replacement Approach of Passerini Reaction: One-Pot Synthesis of beta-Acyloxyamides and Phthalides. *Org. Lett.* **2017,** *19* , 4616-4619; (c) Chen, R. J.; Zeng, L. W.; Huang, B.; Shen, Y. Y.; Cui, S. L., Decarbonylative Coupling of alpha-Keto Acids and Ynamides for Synthesis of beta-Keto Imides. *Org. Lett.* **2018,** *20*, 3377-3380; (d) Chen, R. J.; Liu, Y.; Cui, S. L., 1,4-Conjugate addition/esterification of ortho-quinone methides in a multicomponent reaction. *Chem. Commun.* **2018,** *54*, 11753-11756.

(19) Duffey, T. A.; Shaw, S. A.; Vedejs, E., AcOLeDMAP and BnOLeDMAP: Conformationally Restricted Nucleophilic Catalysts for Enantioselective Rearrangement of Indolyl Acetates and Carbonates. *J. Am. Chem. Soc.* **2009,** *131*, 14-15.

(20) CCDC 1871766.

(21) Gottlieb, H. E.; Kotlyar, V.; Nudelman, A., NMR chemical shifts of common laboratory solvents as trace impurities. *J. Org. Chem.* **1997,** *62*, 7512-7515.