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The first Et_3N-mediated transesterification of β-keto esters using Baylis–Hillman alcohols

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Dedicated to Professors A. Baklouti and M. M. El Gaied on the occasion of their 70th birthdays

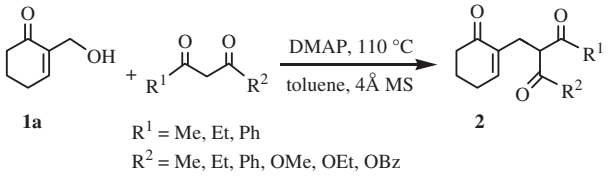
ABSTRACT

A simple and efficient Et_3N-mediated transesterification between β-keto esters and Baylis–Hillman alcohols in toluene solution at reflux using a Dean–Stark apparatus, is described. Allylic esters are exclusively obtained in moderate to good yields, with no trace amounts of γ,δ-unsaturated ketones usually expected from the Carroll decarboxylative rearrangement.

1. Introduction

β-Keto esters have been found to be useful intermediates in organic chemistry[1] and for the synthesis of natural and bioactive compounds.[2] Therefore, several synthetic methods have been reported on the preparation of these compounds. In this regard, the transesterification, known as an ester-to-ester transformation, is one of the most common procedures for the preparation of β-keto esters, which has attracted much interest during the last decades. In the 1980s, two common methods were mainly employed for the transesterification of enolisable β-keto esters, i.e., the reaction of diketene with primary or secondary alcohols[3] and DMAP-catalyzed ester exchange reactions in the presence of molecular sieves in toluene solution at reflux.[4] As diketene is corrosive and DMAP is both toxic and expensive, the two previous methods became less attractive since a large number of acid or basic catalysts have been reported for this purpose, including mainly the recently described catalysis by Zinc(II) oxide,[5] boric acid,[6] niobium(V) oxide,[7] borate zirconia,[8] I_2[9] and Zn/I_2.[10] Alternatively, a lot of effort has been put into better developing Green Chemistry for the transesterification of β-keto esters, using non-corrosive and environmentally benign catalysts. In this context, recent reports have demonstrated that boric acid,[6] montmorillonite K-10[11] and natural clays[12] can be used as efficient and reusable catalysts.

Although DMAP is well known as the common catalyst for the transesterification of β-keto esters,[4] we have recently reported that, under the above reaction conditions, there has been surprisingly a direct allylic substitution of alcohol **1a**[13] with β-keto esters and β-diketones, affording compounds **2** (Scheme 1).[14]



1a **2**

R^1 = Me, Et, Ph
R^2 = Me, Et, Ph, OMe, OEt, OBz

Scheme 1. DMAP-mediated allylation of β-dicarbonyl compounds with alcohol **1a**.

With the exception of the DMAP-catalysed ester exchange reactions,[4] it is notable that none of the above methods reported that tertiary bases, such as Et_3N could catalyse transesterification of β-keto esters. In continuation of our previous study on the chemistry of BH adducts towards β-dicarbonyl compounds,[14–16] we report herein a simple and efficient procedure for the transesterification of β-keto esters with various alcohols **1a–c** and **4a–c**,[13,17] using commercially available and inexpensive triethylamine, for the first time, as a Brønsted base catalyst.

2. Results and discussion

In order to disclose the role of triethylamine in the present protocol, our preliminary attempt between ethyl acetoacetate (2 equiv) and allylic alcohol **1a** (1 equiv) was carried out without any additive, using a Dean–Stark apparatus. We have observed that the starting materials were recovered, even after stirring the reaction mixture during 72 h in toluene at reflux.

Therefore, we investigated, in toluene at reflux, the transesterification reaction of ethyl acetoacetate with allylic alcohol **1a**, in the presence of triethylamine[18] with azeotropic removal of EtOH. Under these conditions, a mixture of transesterification and C-

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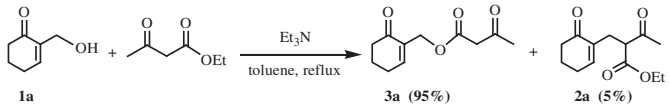
allylation products, respectively, **3a** and **2a** (**3a**/**2a**=95/5), was obtained in 98% overall yield (Scheme 2, Table 1, entry 1).

Next, in order to improve the selectivity of this procedure in favour of the transesterification product **3a**, we selected DMAP, as a highly nucleophilic amine, and 2,6-lutidine, as a weakly nucleophilic one, owing to the steric effects of the two methyl groups on the pyridine nucleus. The results of this study are summarised in Table 1.



Scheme 2. Et_3N-mediated transesterification of ethyl acetoacetate with alcohol **1a**.

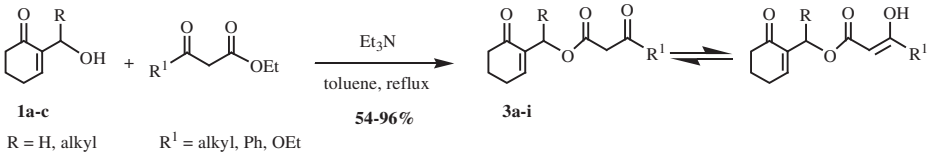
Table 1
Amine-mediated reaction of alcohol **1a** with ethyl acetoacetate

Entry	Amine	**2a** (yield %)	**3a** (yield %)	Ratio of **2a**:**3a**
1	Et_3N	6	92	5/95
2	DMAP	58	0	100/0
3	2,6-Lutidine	0	90	0/100

In contrast to Et_3N (Table 1, entry 1) that mainly mediated the transesterification of ethyl acetoacetate with alcohol **1a** (**3a**/**2a**=95/5), DMAP (Table 1, entry 2) afforded exclusively the C-allylation product **2a** in 58% yield.[14] More interestingly, the 2,6-lutidine (Table 1, entry 3), is found to be the suitable amine for the transesterification of ethyl acetoacetate with alcohol **1a**, affording exclusively the desired allylic ester **3a**, in a good yield (90%), with no trace amounts of the Carroll decarboxylative rearrangement ketone.[19]

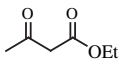
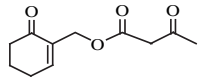
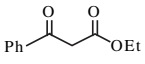
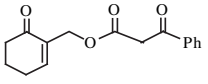
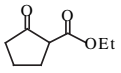
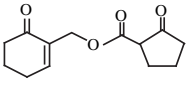
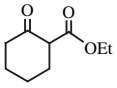
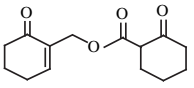
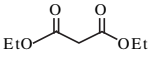
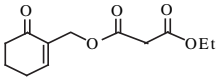
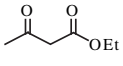
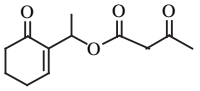
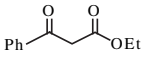
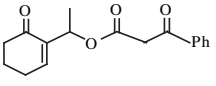
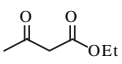
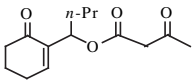
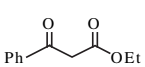
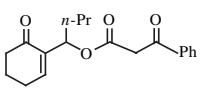
It is notable that when we have used less than 2 equiv of amines (Et_3N or 2,6-lutidine), the title reaction did not go to completion even after a prolonged reaction time of 72 h. For this reason, in all our experiments, 2 equiv of amine were required.

In order to demonstrate the scope of this synthetic methodology, we investigated a variety of commercially available β-keto esters and diethyl malonate with alcohol **1a** (Scheme 3, Table 2, entries 1–5) as well as differentially α-substituted BH alcohols **1b**,**c** (Scheme 3, Table 2, entries 6–9), using amines as Brønsted bases



Scheme 3. Et_3N-mediated transesterification of β-keto esters with alcohols **1a**–**c**.

Table 2
Amine-mediated transesterification of β-keto esters with alcohols **1a**–**c**

Entry	R (alcohol)	β-Keto ester	Amine	t/h	Product **3**	Yield %	Ratio of keto:enol
1	H (**1a**)		2,6-Lutidine	25	**3a :** 	90	92/8
2	H (**1a**)		Et_3N	24	**3b :** 	85	81/19
3	H (**1a**)		Et_3N	24	**3c :** 	54	100/0
4	H (**1a**)		Et_3N	24	**3d :** 	90	34/66
5	H (**1a**)		Et_3N	48	**3e :** 	72	100/0
6	Me (**1b**)		Et_3N	48	**3f :** 	76	92/8
7	Me (**1b**)		Et_3N	24	**3g :** 	96	80/20
8	*n*-Pr (**1c**)		Et_3N	29	**3h :** 	89	91/9
9	*n*-Pr (**1c**)		Et_3N	24	**3i :** 	90	78/22

with azeotropic removal of EtOH. As is shown in Table 2, entries 2–9, the corresponding allylic esters **3b–i** were exclusively obtained in 54–90% yields.

β-keto esters **3** exist as a mixture of two tautomeric forms in $CDCl_3$ solution, whose relative ratios were determined by means of ^1H NMR spectroscopy (Table 2). For example, the singlet at δ_H 3.50 of **3a** was assigned to the methylene proton (−CO−CH_2−CO−) of the corresponding keto tautomer whereas the two singlets at δ_H 5.02 and δ_H 12.03 were, respectively, assigned to the vinyl proton (−C(−OH)=C*H*−) and the hydroxyl one (OH) of the corresponding enol tautomer.

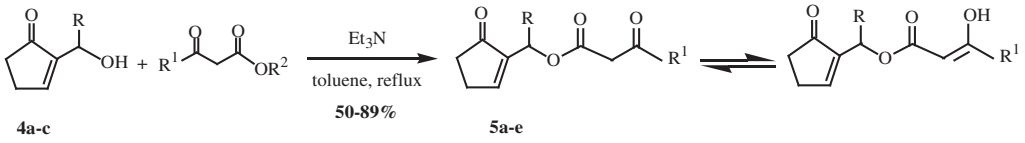
Encouraged by these successful results on the transesterification of β-dicarbonyl compounds with alcohols **1a–c** in the presence of Et_3N or 2,6-lutidine, we attempted to extend this methodology to five-membered allylic alcohols **4a–c** (Scheme 4, Table 3). Our results show that the present transesterification procedure, using Et_3N (Table 3, entries 1, 3 and 4) or 2,6-lutidine (Table 3, entries 2 and 5), still works well, yielding the corresponding transesterification products **5a–e** in moderate to good yields (Table 3, entries 1–5).

β-Keto esters **5** have also two tautomeric forms in $CDCl_3$ solution (Table 3). For instance, the singlet at δ_H 4.06 of **5b** was assigned to the methylene protons (−CO−CH_2−CO−) of the corresponding keto tautomer. The two singlets at δ_H 5.72 and δ_H 12.44 were, respectively, assigned to the vinyl proton (−C(−OH)=C*H*−) and the hydroxyl one (OH) of the corresponding enol tautomer.

latter reaction, based on the strong nucleophilic character of DMAP, was previously proposed.[14]

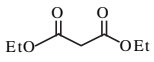
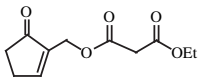
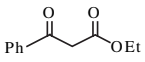
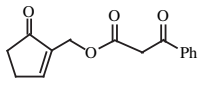
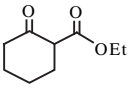
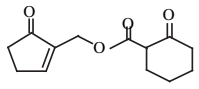
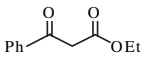
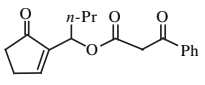
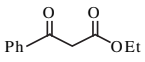
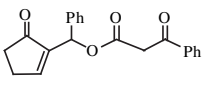
In contrast, Et_3N is usually used as a nitrogen Brønsted base, stronger than both DMAP and 2,6-lutidine.[24] The latter is weakly nucleophilic and is usually used in organic synthesis as a hindered mild base, weaker than Et_3N.[25] The high selectivity of the reaction of **1a** with ethyl acetoacetate in favour of **3a**, suggested that both Et_3N and 2,6-lutidine remarkably acted in this protocol as Brønsted bases. Moreover, a difference in the nucleophilicity of Et_3N and 2,6-lutidine has been previously reported.[26] Accordingly, we believe that the formation of small amounts of the C-allylation product **2a** (**2a**/**3a**=5/95) when Et_3N was used, reveals that this amine is slightly more nucleophilic than 2,6-lutidine, which has a large steric effect.

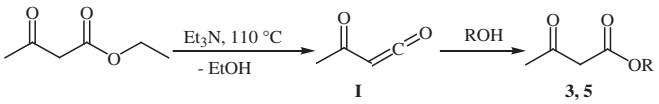
Therefore, ethyl acetoacetate, for instance, can undergo, in the presence of Et_3N or 2,6-lutidine, a β-elimination of EtOH to form an α-keto ketene intermediate **I**, highly reactive, on which further addition of allylic alcohols ROH, generates esters **3** and **5** (Scheme 5). It is notable that such reaction mechanism, involving α-keto ketene, was previously proposed by other authors[27] and supported by Witzeman studies.[28]



Scheme 4. Et_3N-mediated transesterification of β-keto esters with alcohols **4a–c**.

Table 3
Amine-mediated transesterification of β-keto esters with alcohols **4a–c**

Entry	R (alcohol)	β-Keto ester	Amine	t/h	Product **5**	Yield %	Ratio of keto:enol
1	H (**4a**)		Et_3N	24	**5a :** 	53	100/0
2	H (**4a**)		2,6-Lutidine	5	**5b :** 	50	83/17
3	H (**4a**)		Et_3N	9	**5c :** 	56	44/56
4	*n*-Pr (**4b**)		Et_3N	5	**5d :** 	89	82/18
5	Ph (**4c**)		2,6-Lutidine	6	**5e :** 	63	82/18



Scheme 5. Proposed mechanism of the Et_3N-mediated transesterification of ethyl acetoacetate.

2.1. On the contrast between the behaviours of DMAP, Et_3N and 2,6-lutidine

It is well known that DMAP is a powerful nucleophilic catalyst, usually used in the esterification of alcohols[20,21] as well as related reactions.[22,23] In addition, we have previously shown that DMAP efficiently catalysed BH reactions on cyclic enones[13] as well as allylation of β-dicarbonyl compounds. A reaction mechanism of the

3. Conclusion

In conclusion, Et_3N-mediated transesterification of β-keto esters and diethyl malonate proceeds with five- and six-membered ring alcohols **1a–c** and **4a–c** in toluene at reflux. Work is in progress in our laboratory to investigate the generality of this simple

transesterification method of β-keto esters with a wide range of allylic, propargylic as well as aliphatic alcohols.

4. Experimental

4.1. General

IR spectra were recorded on a Bruker (IFS 66v/S) spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded either on a Bruker AC-300 spectrometer (300 MHz for ^{1}H and 75 MHz for ^{13}C) in $CDCl_3$, using TMS as an internal standard (chemical shifts in δ values, J in Hz). High resolution mass spectra (HRMS) were recorded as EI-HRMS on an Autospec Ultima/micromass mass spectrometer.

Analytical thin layer chromatography (TLC) was performed using Fluka Kieselgel 60 F_{254} precoated silica gel plates. Visualization was achieved by UV light (254 nm). Flash chromatography was performed using Merck silica gel 60 and a gradient solvent system (pet-ether/ether as eluant).

4.2. Typical procedure for transesterification reactions of cyclic B–H adducts with β-keto esters

A mixture of allyl alcohol **1a** (0.63 g, 5 mmol), ethyl acetoacetate (1.30 g, 10 mmol) and 2,6-lutidine (1.07 g, 10 mmol) in toluene (50 mL) was heated to 110 °C in a two-necked round bottomed flask provided with a distillation condenser to remove ethanol. After completion (TLC), the reaction mixture was cooled, washed with brine and dried. The toluene was removed and the residue was purified by column chromatography on silica gel (40% ether/petroleum ether) to give the pure allylic ester **3a** (0.945 g, 90%).

4.2.1. 6-Oxocyclohex-1-enylmethyl 3-oxobutanoate ***3a***. Yellow oil (0.945 g, 90% yield); R_f (90% Et_2O/petroleum ether) 0.55; ν ($CHCl_3$) 3530, 1743, 1716, 1672 cm^{-1}; keto (92%)-enol (8%); δ_H (keto, $CDCl_3$) 7.08 (t, J=4.0 Hz, 1H), 4.79 (s, 2H), 3.50 (s, 2H), 2.48–2.43 (m, 4H), 2.26 (s, 3H), 2.07–2.01 (m, 2H); δ_H (enol, $CDCl_3$) 12.03 (s, 1H), 7.08 (t, J=4.0 Hz, 1H), 5.02 (s, 1H), 4.79 (s, 2H), 2.48–2.43 (m, 4H), 2.26 (s, 3H), 2.07–2.01 (m, 2H); δ_C (keto, $CDCl_3$) 200.7, 197.8, 166.8, 149.2, 133.7, 62.0, 49.8, 38.0, 30.1, 25.7, 22.6; δ_C (enol, $CDCl_3$) 197.8, 175.8, 172.1, 148.6, 134.1, 89.5, 60.6, 38.0, 25.7, 22.6, 21.1; HRMS (EI): M^+, found 210.0895. $C_{11}H_{14}O_4$ requires 210.0892.

4.2.2. 6-Oxocyclohex-1-enylmethyl 3-oxo-3-phenylpropanoate ***3b***. Viscous yellow liquid (1.156 g, 85% yield); R_f (60% Et_2O/petroleum ether) 0.40; ν ($CHCl_3$) 3550, 1742, 1675, 1629, 1451 cm^{-1}; keto (81%)-enol (19%); δ_H (keto, $CDCl_3$) 7.94–7.90 (m, 2H), 7.61–7.33 (m, 3H), 6.99 (t, J=4.0 Hz, 1H), 4.82 (s, 2H), 4.03 (s, 2H), 2.43–2.33 (m, 4H), 2.15–1.92 (m, 2H); δ_H (enol, $CDCl_3$) 12.50 (s, 1H), 7.77–7.74 (m, 2H), 7.61–7.33 (m, 3H), 7.07 (t, J=4.0 Hz, 1H), 5.70 (s, 1H), 4.88 (s, 2H), 2.43–2.33 (m, 4H), 2.15–1.92 (m, 2H); δ_C (keto, $CDCl_3$)197.8, 192.4, 167.1, 148.8, 135.8, 133.7–126.0 (aromatics), 62.0, 45.8, 38.0, 25.7, 22.6; δ_C (enol, $CDCl_3$) 197.9, 172.7, 171.6, 148.7, 135.8, 133.1–128.5 (aromatics), 87.1, 61.0, 38.0, 25.7, 22.6; HRMS (EI): M^+, found 272.1046. $C_{16}H_{16}O_4$ requires 272.1049.

4.2.3. 6-Oxocyclohex-1-enylmethyl 2-oxocyclopentanecarboxylate ***3c***. Yellow oil (0.637 g, 54% yield); R_f (80% Et_2O/petroleum ether) 0.43; ν ($CHCl_3$) 1750, 1726, 1670 cm^{-1}; keto (100%)-enol (0%); δ_H (300 MHz, $CDCl_3$) 7.06 (t, J=4.0 Hz, 1H), 4.88–4.76 (m, 2H), 3.19 (t, J=8.8 Hz, 1H), 2.48–2.41 (m, 4H), 2.34–2.22 (m, 4H), 2.21–1.81 (m, 4H); δ_C (75 MHz, $CDCl_3$) 212.3, 197.9, 169.0, 148.2, 133.9, 62.0, 54.7, 38.0 (2C), 27.3, 25.7, 22.6, 20.9; HRMS (EI): M^+, found 236.1053. $C_{13}H_{16}O_4$ requires 236.1049.

4.2.4. 6-Oxocyclohex-1-enylmethyl 2-oxocyclohexanecarboxylate ***3d***. Yellow oil (1.125 g, 90% yield); R_f (60% Et_2O/petroleum ether) 0.57; ν ($CHCl_3$) 1717, 1671, 1647 cm^{-1}; keto (34%)-enol (66%); δ_H (keto, $CDCl_3$) 7.09 (t, J=4.0 Hz, 1H), 4.84–4.81 (m, 4H), 3.41 (t, J=8.4 Hz, 1H), 2.49–2.43 (m, 4H), 2.15–2.10 (m, 2H), 2.05–2.00 (m, 4H), 1.69–1.59 (m, 4H); δ_H (enol, $CDCl_3$) 12.09 (s, 1H), 6.98 (t, J=4.0 Hz, 1H), 4.84–4.81 (m, 2H), 2.49–2.43 (m, 4H), 2.28–2.24 (m, 4H), 2.05–2.00 (m, 2H), 1.69–1.59 (m, 4H); δ_C (keto, $CDCl_3$) 206.2, 197.9, 169.6, 148.5, 134.0, 61.8, 57.1, 38.1, 30.0, 27.1, 25.7, 23.3 (2C), 22.6; δ_C (enol, $CDCl_3$) 197.9, 172.4, 172.1, 147.5, 134.4, 97.5, 60.8, 41.6, 38.1, 29.1, 25.7, 22.6, 22.4, 22.3; HRMS (EI): M^+, found 250.1201. $C_{14}H_{18}O_4$ requires 250.1205.

4.2.5. Ethyl 6-oxocyclohex-1-enylmethyl malonate ***3e***. Yellow oil (0.864 g, 72% yield); R_f (80% Et_2O/petroleum ether) 0.51; ν ($CHCl_3$) 1750, 1732, 1674 cm^{-1}; keto (100%)-enol (0%); δ_H (300 MHz, $CDCl_3$) 7.06 (t, J=4.0 Hz, 1H), 4.81 (s, 2H), 4.20 (q, J=6.9 Hz, 2H), 3.40 (s, 2H), 2.48–2.42 (m, 4H), 2.07–2.01 (m, 2H), 1.28 (t, J=6.9 Hz, 3H); δ_C (75 MHz, $CDCl_3$) 197.7, 166.4, 166.2, 148.6, 133.8, 62.2, 61.2, 41.4, 38.1, 25.7, 22.6, 14.0; HRMS (EI): M^+, found 240.0995. $C_{12}H_{16}O_5$ requires 240.0998.

4.2.6. 1-(6-Oxocyclohex-1-enyl)ethyl 3-oxobutanoate ***3f***. Yellow liquid (0.851 g, 76% yield); R_f (80% Et_2O/petroleum ether) 0.49; ν ($CHCl_3$): 3534, 1741, 1716, 1673 cm^{-1}; keto (92%)-enol (8%); δ_H (keto, $CDCl_3$) 7.01 (t, J=4.0 Hz, 1H), 5.76 (q, J=6.2 Hz, 1H), 3.48 (s, 2H), 2.45–2.41 (m, 4H), 2.27 (s, 3H), 2.02–1.95 (m, 2H), 1.35 (d, J=6.2 Hz, 3H); δ_H (enol, $CDCl_3$) 12.03 (s, 1H), 7.01 (t, J=4.0 Hz, 1H), 5.76 (q, J=6.2 Hz, 1H), 5.03 (s, 1H), 2.45–2.41 (m, 4H), 2.27 (s, 3H), 2.02–1.95 (m, 2H), 1.35 (d, J=6.2 Hz, 3H); δ_C (keto, $CDCl_3$) 200.8, 197.4, 166.0, 145.4, 139.1, 68.1, 50.1, 38.3, 30.1, 25.6, 22.5, 20.0; δ_C (enol, $CDCl_3$) 197.5, 175.7, 171.4, 144.8, 139.7, 89.8, 66.5, 38.3, 25.6, 22.5, 21.1, 20.4; HRMS (EI): M^+, found 224.1047. $C_{12}H_{16}O_4$ requires 224.1049.

4.2.7. 1-(6-Oxocyclohex-1-enyl)ethyl 3-oxo-3-phenylpropanoate ***3g***. Yellow liquid (1.372 g, 96% yield); R_f (60% Et_2O/petroleum ether) 0.51; ν ($CHCl_3$) 3550, 1739, 1678, 1603, 1451 cm^{-1}; keto (80%)-enol (20%); δ_H (keto, $CDCl_3$) 7.95–7.91 (m, 2H), 7.60–7.45 (m, 3H), 6.86 (t, J=4.4 Hz, 1H), 5.79 (q, J=6.6 Hz, 1H), 4.00 (s, 2H), 2.41–2.31 (m, 4H), 2.00–1.91 (m, 2H), 1.31 (d, J=6.6 Hz, 3H); δ_H (enol, $CDCl_3$) 12.54 (s, 1H); 7.78–7.75 (m, 2H), 7.60–7.45 (m, 3H), 7.00 (t, J=4.4 Hz, 1H), 5.89 (q, J=6.2 Hz, 1H), 5.70 (s, 1H), 2.41–2.31 (m, 4H), 2.00–1.91 (m, 2H), 1.40 (d, J=6.2 Hz, 3H); δ_C (keto, $CDCl_3$) 197.3, 192.5, 166.2, 145.1, 139.1, 136.0–126.0 (aromatics), 68.3, 46.2, 38.3, 25.6, 22.5, 15.2; δ_C (enol, $CDCl_3$) 197.4, 172.0, 171.6, 144.8, 139.7, 133.3–128.5 (aromatics), 87.4, 67.0, 38.3, 25.6, 22.5, 15.3; HRMS (EI): M^+, found 286.1208. $C_{17}H_{18}O_4$ requires 286.1205.

4.2.8. 1-(6-Oxocyclohex-1-enyl)butyl 3-oxobutanoate ***3h***. Yellow liquid (1.413 g, 89% yield); R_f (60% Et_2O/petroleum ether) 0.46; ν ($CHCl_3$) 3535, 1742, 1717, 1672 cm^{-1}; keto (91%)-enol (9%); δ_H (keto, $CDCl_3$) 6.94 (t, J=4.0 Hz, 1H), 5.68 (t, J=6.6 Hz, 1H), 3.49 (s, 2H), 2.45–2.40 (m, 4H), 2.26 (s, 3H), 2.00–1.95 (m, 2H), 1.65–1.60 (m, 2H), 1.34–1.26 (m, 2H), 0.90 (t, J=7.3 Hz, 3H); δ_H (enol, $CDCl_3$) 12.03 (s, 1H), 6.94 (t, J=4.0 Hz, 1H), 5.68 (t, J=6.6 Hz, 1H), 5.03 (s, 1H), 2.45–2.40 (m, 4H), 2.26 (s, 3H), 2.00–1.95 (m, 2H), 1.65–1.60 (m, 2H), 1.34–1.26 (m, 2H), 0.90 (t, J=7.3 Hz, 3H); δ_C (keto, $CDCl_3$) 200.7, 197.4, 166.1, 145.6, 138.4, 71.6, 50.1, 38.3, 36.4, 30.2, 25.6, 22.5, 18.6, 13.7; δ_C (enol, $CDCl_3$) 198.1, 175.7, 171.6, 145.0, 139.0, 89.7, 69.8, 38.3, 36.7, 25.6, 22.5, 21.1, 18.7, 13.8; HRMS (EI): M^+, found 252.1362. $C_{14}H_{20}O_4$ requires 252.1362.

4.2.9. 1-(6-Oxocyclohex-1-enyl)butyl 3-oxo-3-phenylpropanoate ***3i***. Viscous yellow liquid (1.121 g, 90% yield); R_f (60% Et_2O/petroleum ether) 0.60; ν ($CHCl_3$) 3540, 1740, 1674, 1632, 1452 cm^{-1}; keto (78%)-enol (22%); δ_H (keto, $CDCl_3$) 7.95–7.92 (m, 2H); 7.60–7.48 (m, 3H); 6.78 (t, J=4.0 Hz, 1H); 5.71–5.69 (m, 1H); 4.04 (s, 2H); 2.41–2.29 (m, 4H); 2.00–1.93 (m, 2H); 1.65–1.57 (m, 2H); 1.34–1.20 (m, 2H);

0.84 (t, J=6.9 Hz, 3H); δ_H (enol, $CDCl_3$) 12.52 (s, 1H); 7.79–7.76 (m, 2H); 7.60–7.48 (m, 3H); 6.93 (t, J=4.0 Hz, 1H); 5.80 (t, J=6.2 Hz, 1H); 5.71–5.69 (m, 1H); 2.41–2.29 (m, 4H); 2.00–1.93 (m, 2H); 1.65–1.57 (m, 2H); 1.34–1.20 (m, 2H); 0.92 (t, J=6.9 Hz, 3H); δ_C (keto, $CDCl_3$) 197.4, 192.4, 166.4, 145.4, 138.4, 136.0–126.0 (aromatics), 71.9, 46.2, 38.3, 36.4, 25.6, 22.5, 18.6, 13.7; δ_C (enol, $CDCl_3$) 197.5, 172.2, 171.7, 145.1, 139.1, 133.3–128.5 (aromatics), 87.3, 70.4, 38.3, 36.7, 25.6, 22.5, 18.7, 13.8; HRMS (EI): M^+, found 314.1520. $C_{19}H_{22}O_4$ requires 314.1518.

4.2.10. Ethyl 5-oxocyclopent-1-enylmethyl malonate ***5a***. Yellow oil (0.598 g, 53% yield); R_f (90% Et_2O/petroleum ether) 0.57; ν ($CHCl_3$) 1740, 1702, 1643 cm^{-1}; keto (100%)-enol (0%); δ_H (300 MHz, $CDCl_3$) 7.66 (t, J=4.0 Hz, 1H), 4.84 (s, 2H), 4.21 (q, J=6.9 Hz, 2H), 3.43 (s, 2H), 2.70–2.67 (m, 2H), 2.46–2.43 (m, 2H), 1.28 (t, J=6.9 Hz, 3H); δ_C (75 MHz, $CDCl_3$) 207.5, 166.4, 166.2, 161.2, 140.6, 61.6, 58.9, 41.3, 34.6, 26.9, 14.0; HRMS (EI): M^+, found 226.0839. $C_{11}H_{14}O_5$ requires 226.0841.

4.2.11. 5-Oxocyclopent-1-enylmethyl 3-oxo-3-phenylpropanoate ***5b***. Viscous yellow liquid (0.645 g, 50% yield); R_f (80% Et_2O/petroleum ether) 0.44; ν ($CHCl_3$) 1745, 1701, 1635 cm^{-1}; keto (83%)-enol (17%); δ_H (keto, $CDCl_3$) 7.94–7.90 (m, 2H), 7.65–7.39 (m, 4H), 4.84 (s, 2H), 4.06 (s, 2H), 2.60–2.56 (m, 2H), 2.45–2.36 (m, 2H); δ_H (enol, $CDCl_3$) 12.44 (s, 1H), 7.80–7.70 (m, 2H), 7.65–7.39 (m, 4H), 5.72 (s, 1H), 4.88 (s, 2H), 2.60–2.56 (m, 2H), 2.45–2.36 (m, 2H); δ_C (keto, $CDCl_3$) 207.5, 192.4, 167.1, 161.1, 140.5, 135.8–126.0 (aromatics), 58.9, 45.6, 34.6, 26.6; δ_C (enol, $CDCl_3$) 207.6, 172.6, 171.8, 161.3, 140.9, 133.0–128.6 (aromatics), 86.8, 57.7, 34.6, 26.6; HRMS (EI): M^+, found 258.0896. $C_{15}H_{14}O_4$ requires 258.0892.

4.2.12. 5-Oxocyclopent-1-enylmethyl 2-oxocyclohexanecarboxylate ***5c***. Yellow oil (0.66 g, 56% yield); R_f (60% Et_2O/petroleum ether) 0.50; ν ($CHCl_3$) 1747, 1703, 1656, 1613 cm^{-1}; keto (44%)-enol (56%); δ_H (keto, $CDCl_3$) 7.71 (t, J=4.0 Hz, 1H), 4.94–4.76 (m, 2H), 3.48–3.42 (m, 1H), 2.69–2.64 (m, 2H), 2.52–2.38 (m, 4H), 2.18–2.10 (m, 2H), 1.77–1.59 (m, 4H); δ_H (enol, $CDCl_3$) 12.05 (s, 1H), 7.60 (t, J=4.0 Hz, 1H), 4.94–4.76 (m, 2H), 2.69–2.64 (m, 2H), 2.52–2.38 (m, 2H), 2.29–2.23 (m, 4H), 1.77–1.59 (m, 4H); δ_C (keto, $CDCl_3$) 207.6, 206.2, 169.6, 161.0, 140.8, 58.7, 57.1, 34.7, 30.0, 27.1, 26.9, 23.4 (2C); δ_C (enol, $CDCl_3$) 207.7, 172.7, 172.1, 160.6, 141.3, 97.4, 57.8, 41.6, 34.7, 29.1, 26.9, 22.3, 21.8; HRMS (EI): M^+, found 236.1049. $C_{13}H_{16}O_4$ requires 236.1049.

4.2.13. 1-(5-Oxocyclopent-1-enyl)butyl 3-oxo-3-phenylpropanoate ***5d***. Viscous yellow liquid (1.335 g, 89% yield); R_f (60% Et_2O/petroleum ether) 0.48; ν ($CHCl_3$) 1741, 1697, 1637 cm^{-1}; keto (82%)-enol (18%); δ_H (keto, $CDCl_3$) 7.95–7.92 (m, 2H); 7.60–7.41 (m, 4H); 5.61–5.57 (m 1H); 4.09–4.03 (m, 2H); 2.56–2.54 (m, 2H); 2.41–2.38 (m, 2H); 1.72–1.67 (m, 2H); 1.29–1.25 (m, 2H); 0.90–0.85 (m, 3H); δ_H (enol, $CDCl_3$) 12.46 (s, 1H); 7.77–7.76 (m, 2H); 7.60–7.41 (m, 4H); 5.72–5.70 (m, 2H); 2.56–2.54 (m, 2H); 2.41–2.38 (m, 2H); 1.72–1.67 (m, 2H); 1.29–1.25 (m, 2H); 0.90–0.85 (m, 3H); δ_C (keto, $CDCl_3$) 207.2, 192.6, 166.7, 159.0, 144.8, 136.0–126.1 (aromatics), 70.8, 46.1, 35.2 (2C), 26.6, 18.3, 13.7; δ_C (enol, $CDCl_3$) 207.3, 172.4, 171.9, 158.8, 145.5, 133.4–128.6 (aromatics), 87.2, 69.3, 35.5, 35.2, 26.6, 18.6, 13.8; HRMS (EI): M^+, found 300.1369. $C_{18}H_{20}O_4$ requires 300.1362.

4.2.14. (5-Oxocyclopent-1-enyl)phenylmethyl 3-oxo-3-phenylpropanoate ***5e***. Viscous yellow liquid (1.052 g, 63% yield); R_f (80% Et_2O/petroleum ether) 0.53; ν ($CHCl_3$) 1744, 1700, 1635 cm^{-1}; keto (82%)-enol (18%); δ_H (keto, $CDCl_3$) 7.93–7.90 (m, 2H); 7.58–7.27 (m, 4H); 6.57 (s, 1H); 4.04 (AB, J=15.4 Hz, 2H); 2.59–2.56 (m, 2H); 2.41–2.38 (m, 2H); δ_H (enol, $CDCl_3$) 12.34 (s, 1H); 7.78–7.74 (m, 2H); 7.58–7.27 (m, 4H); 6.68 (s, 1H); 5.76 (s, 1H); 2.59–2.56 (m, 2H); 2.41–2.38 (m, 2H); δ_C (keto, $CDCl_3$) 206.3, 192.3, 166.1, 159.4, 144.7, 137.3–126.1 (aromatics), 71.8, 46.0, 34.9, 26.7; δ_C (enol, $CDCl_3$) 206.4, 172.1, 171.8, 159.3, 145.3, 137.9–128.4 (aromatics), 87.0, 70.2, 34.9, 26.7; HRMS (EI): M^+, found 334.1201. $C_{21}H_{18}O_4$ requires 334.1205.

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