CHAPTER-5

Synthesis of 1,3-dicarbonyl compounds using *N*-Cbz amides as an acyl source under transition metal-free conditions at room temperature

5.1 Introduction

1,3-Dicarbonyl compounds such as *β*-ketoesters, *β*-keto amides and 1,3-diketones are important precursors in organic synthesis [1]. Both electrophilic and nucleophilic sites make 1,3-dicarbonyl compounds unique and attractive in organic chemistry. For instance, 1,3-dicarbonyl compounds have been widely used in the preparation of various natural products (e.g. prunustatin, nonactin and mokupalide), heterocyclic compounds (e.g. pyrazolones and pyrimidines), pharmaceutics (e.g. paclitaxel), materials, etc., (**Figure 5.1**) [2]. Among the different methods of preparation, 1,3-dicarbonyl compounds are typically obtained *via* Claisen condensation-type reactions [3]. In this approach, enolizable (i.e. α-hydrogen containing) ketones, esters or amides reacted with different acyl donors, including 1-acylbenzotriazoles [4a,4b], acid chlorides [4c,4d], esters [4e], acyl cyanides [4f], etc., in the presence of strong bases [4]. However, the use of harsh reaction conditions, formation of undesired side products and low yields are the common problems associated with traditional methods.

Amide is a key functional group found in natural products, drugs, proteins, enzymes, materials, etc. [5]. Recently, the transformation of amides into different functional groups *via* C(O)-N bond cleavage received considerable attention in organic synthesis [6]. In particular, the transformation of amides into amides (via transamidation) [7], esters [8], thio- and seleno esters [9], ketones [10], boronates [11], arylsulfides [12], biaryls [13], phosphonates [14], cyanates [15], sulfoxonium ylides [16] etc. [6], have been

demonstrated. In this context, the Lee group recently reported the synthesis of 1,3-dicarbonyl compounds using activated and un-activated amides as acylating reagents under mild conditions [17].

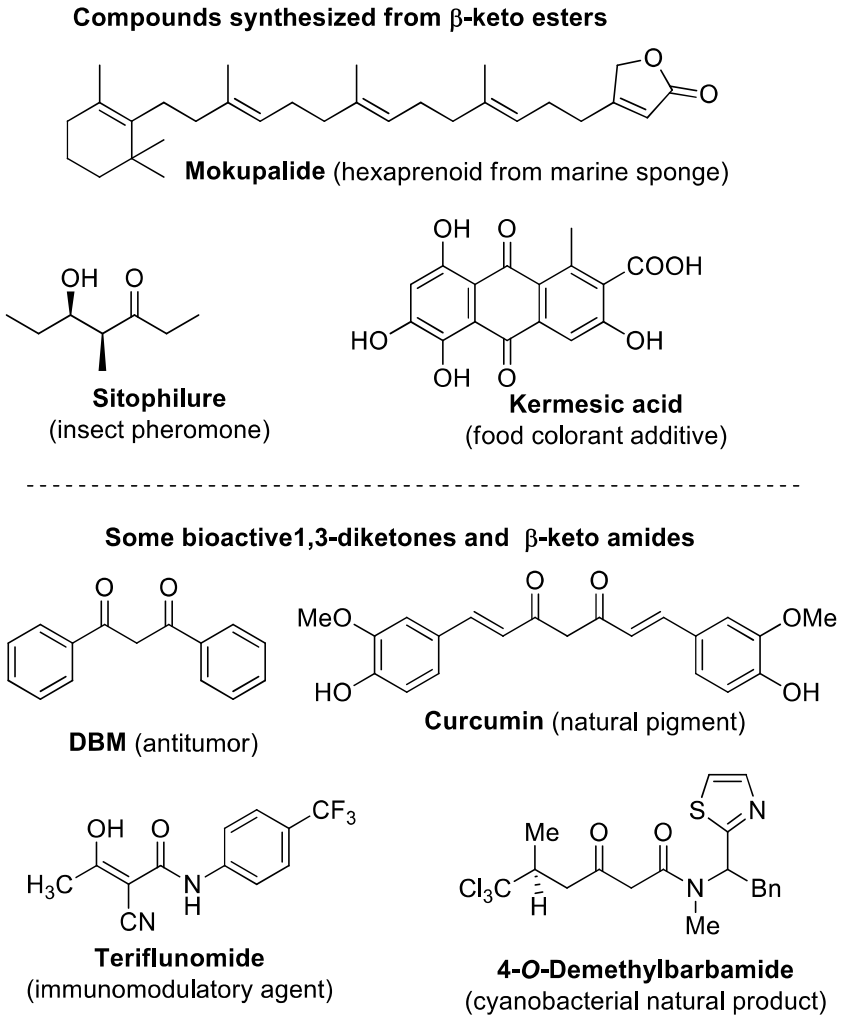
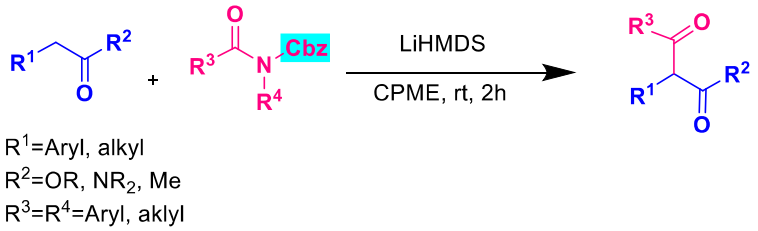


Figure 5.1 Examples of 1,3-dicarbonyl compounds as bioactive compounds and synthetic precursors.

Over the last few years, our research group has been focused on amide activation and transamidation reactions [18]. We have demonstrated a metal-free transamidation of secondary amides and *α*-ketoamides,the transformation of *N*-Boc-amides into aryl ketones with Grignard reagents, and conversion of activated amides into aldehydes. Recently, we have also demonstared the synthesis of *N*-Cbz amides and their applications in transamidation and esterification reactions [18d]. The *N*-Cbz amides are stable and easy to prepare in good yields compared with *N*-Boc and *N*-Ts amides. In view of this, here we explored the use of *N*-Cbz amides as acylating agents in the preparation of 1,3-dicarbonyl compounds such as *β*-ketoesters, and *β*-keto amides and 1,3-diketones under mild reaction conditions (**Scheme 5.1**).



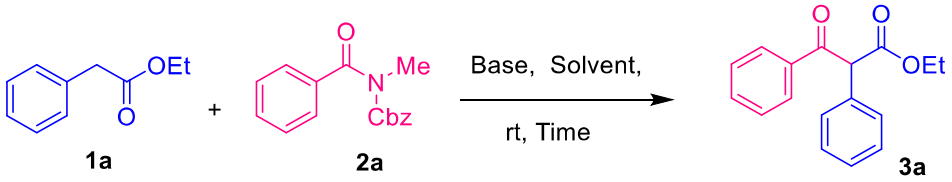
Scheme 5.1 Preparation of 1,3-dicarbonyl compoundsusing *N*-Cbz amides.

5.2 Results and discussion

In the beginning, an optimization study was performed using ethyl 2-phenylacetate (**1a**) and *N*-methyl *N*-Cbz benzamide (**2a**) as model substrates. Initially, the reaction was performed in THF in the presence of different bases, including DBU, Cs_2CO_3, NaOtBu, KOtBu, NaH and LiHMDS (**Table 5.1, entries 1-6**). Among these bases, LiHMDS gave

the desired *β*-Ketoesters **3a** in 78% yields in 8 h at room temperature (**Table 5.1, entry 6**). Later, the optimization study was performed in different solvents, including 1,4-dioxane, DCM, toluene, diethyl ether and cyclopentyl methyl ether (CPME) in the presence of base LiHMDS (**Table 5.1, entries 7-11**). Among these solvents, CPME was the best to provide the desired product **3a** in 90% yield (**Table 5.1, entry 11**).

Table 5.1 Optimization of reaction conditions.[a]

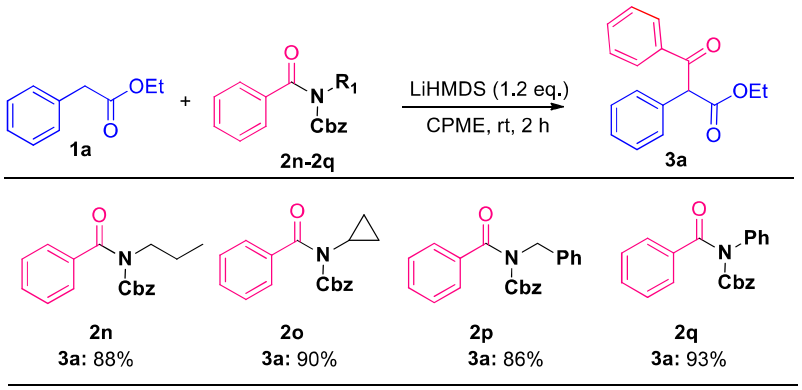


1a 2a 3a

S.No.	Base	Solvent	Time(h)	Yield (%)[b]
1.	DBU	THF	8	trace
2.	Cs_2CO_3	THF	8	trace
3.	NaO*t*Bu	THF	8	12
4.	KO*t*Bu	THF	8	15
5.	NaH	THF	8	20
6.	LiHMDS	THF	6	78
7.	LiHMDS	Dioxane	6	30
8.	LiHMDS	DCM	6	60
9.	LiHMDS	Toluene	6	75
10.	LiHMDS	Et_2O	4	80
11.	**LiHMDS**	**CPME**	**2**	**90**

[a]Reaction conditions: Substrate **1a** (0.5 mmol, 82 mg) and Base (1.2 eq.) were stirred in appropriate solvents (3 mL) for 15 min, to which *N*-Cbz amide (161 mg, 1.2 eq.) was added. [b]Isolated yield.

Further, as a part of the optimization study, we evaluated the reactivity of different *N*-functionalized *N*-Cbz benzamides (i.e. *N*-propyl, *N*-cyclopropyl and *N*-benzyl benzamides and *N*-phenyl benzamides) **2n-2q** with ethyl 2-phenylacetate in the presence of LiHMDS in CPME (**Scheme 5.2**). All these activated amides participated in the coupling reaction and gave the *β*-ketoester **3a** in 86-93% yields.

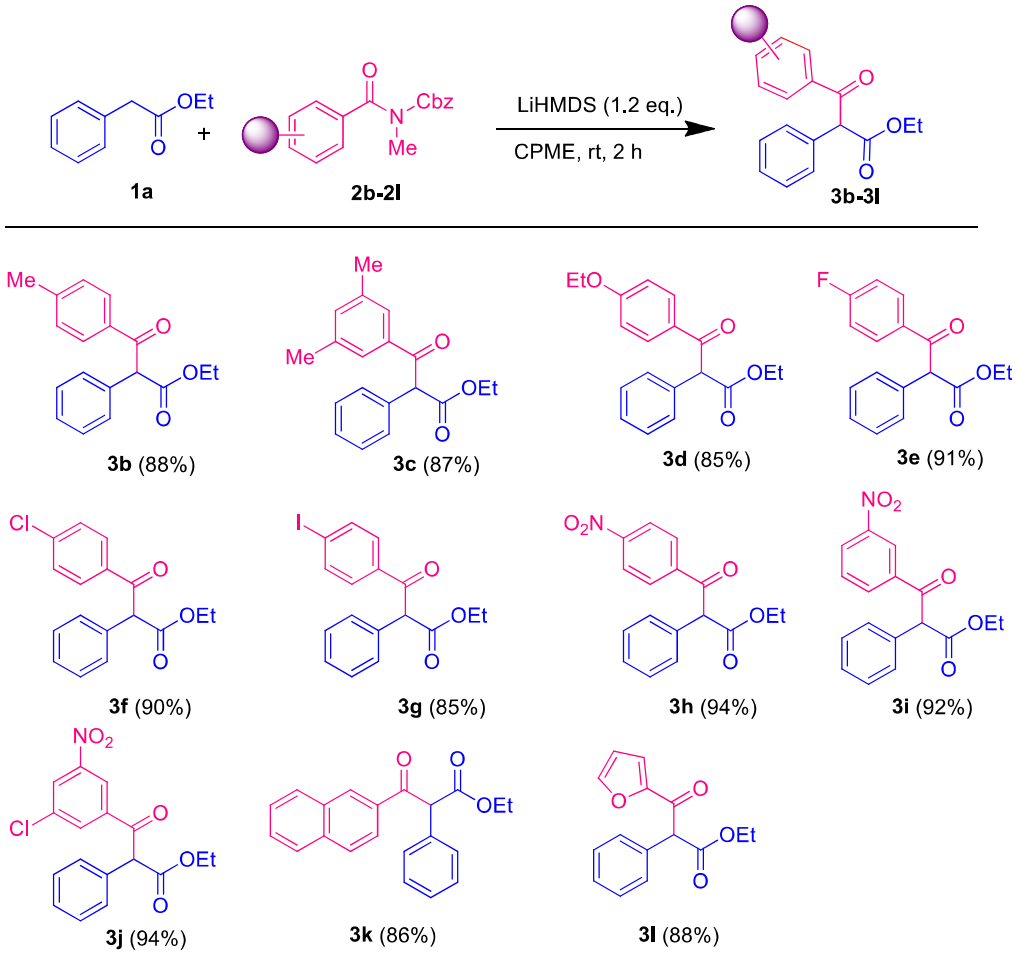


Scheme 5.2 Reaction scope of different *N*-Cbz benzamides with ethyl 2-phenylacetate (**1a**). Reaction conditions: Substrate **1a** (0.5 mmol, 82 mg) and LiHMDS (1 M solution in THF, 0.6 mL, 1.2 eq.) stirred in CPME (3 mL) for 15 min, after which *N*-Cbz amide (1.2 eq.) was added and stirred at room temperature for 2h. Isolated yields presented.

After establishing the optimized conditions, the scope of different *N*-Cbz amides in *β*-ketoesters synthesis was investigated (**Table 5.2**). To our delight, ethyl 2-phenylacetate (**1a**) underwent *C*-acylation smoothly with *N*-Cbz *N*-methyl benzamides bearing electron-donating groups (e.g. methyl and ethoxy) and provided the desired *β*-ketoesters **3b-3d** in 85–88% yields within 2 hours. On the other hand, the electron-withdrawing groups, including halogens and nitro groups substituted *N*-Cbz *N*-methyl benzamides, also

participated in the coupling reactions smoothly and provided the *β*-ketoesters **3e-3j** in 85-94% yields. Similarly, naphthyl and furfural *N*-Cbz amides gave the *β*-ketoesters **3k** and **3l** in good yields.

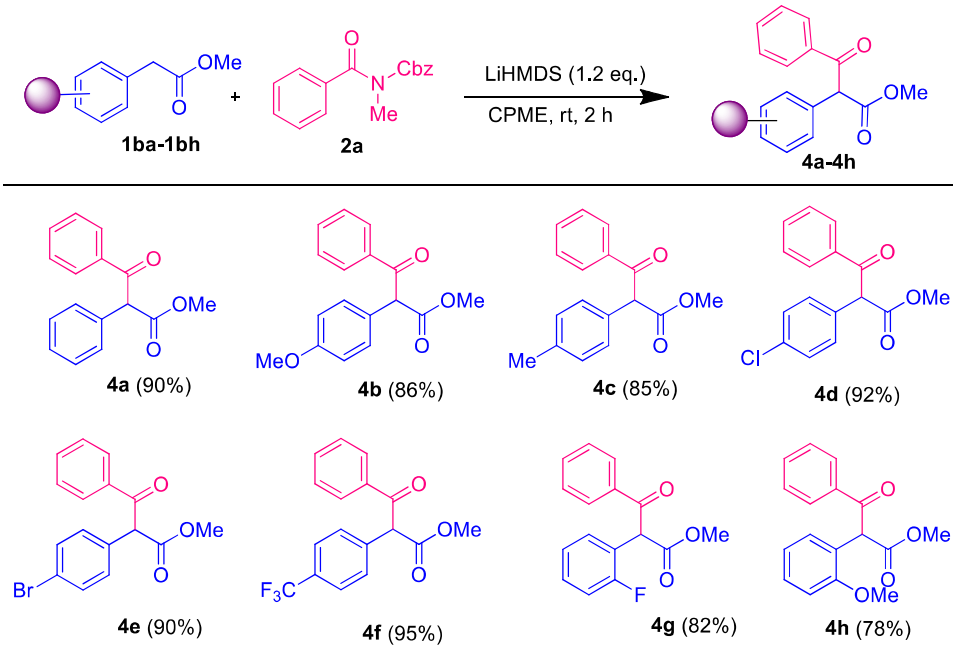
Table 5.2 Scope of *N*-Cbz amides with ethyl 2-phenylacetate (**1a**).



Reaction conditions: Substrate **1a** (0.5 mmol, 82 mg) and LiHMDS (1 M solution in THF, 0.6 mL, 1.2 eq.) were stirred in CPME (3 mL) for 15 min after which *N*-Cbz amide **2b-2l** (1.2 eq.) was added. [b]Isolated yields presented.

Further, the reactivity of various functionalized phenylacetic acid esters in the *C*-acylation reaction was investigated. The *C*-acylation reaction was performed with *N*-Cbz *N*-methyl benzamide (**2a**) in the presence of LiHMDS in CPME (**Table 5.3**).

Table 5.3 Scope of esters.

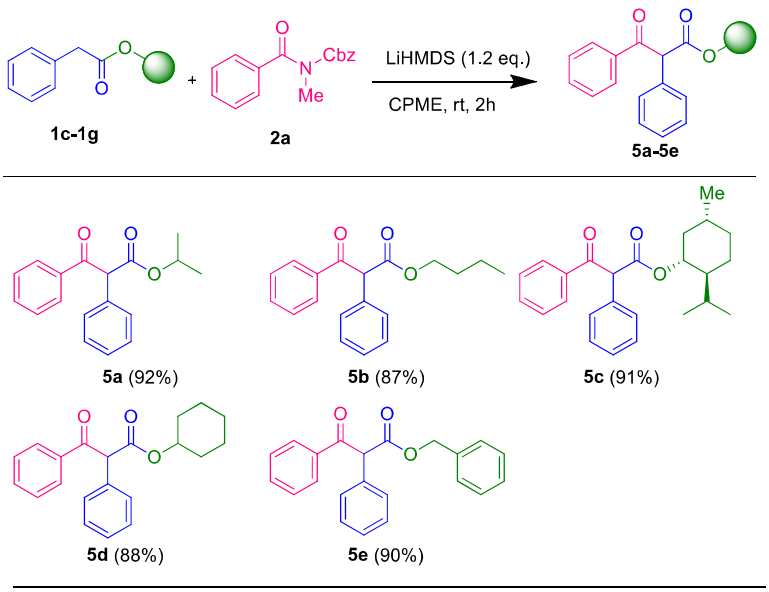


Reaction conditions: Substrate **1ba-1bh** (0.5 mmol) and LiHMDS (1 M solution in THF, 0.6 mL, 1.2 eq.) stirred in CPME (3 mL) for 15 min after which *N*-Cbz amide **2a** (161 mg, 1.2 eq.) was added. Isolated yields presented.

The reactions of methyl 2-phenylacetates bearing electron-donating groups such as methoxy and methyl on the aryl ring underwent *C*-acylation with **2a** and provided the desired *β*-ketoesters **4a-4c** in 85-90% yields. Similarly, the electron-withdrawing groups such as chloro, bromo and trifluoromethyl groups functionalized phenylacetic acid esters

underwent *C*-acylation with **2a** and gave the desired *β*-ketoesters **4d-4f** in 90-95% yields. Moreover, sterically hindered *ortho*-substituted phenylacetic acid esters also participated in the reaction efficiently and furnished the *β*-ketoesters **4g** and **4h** in 82% and 78% yields, respectively.

Table 5.4 Scope of different *O*-protected phenylacetic acid esters.

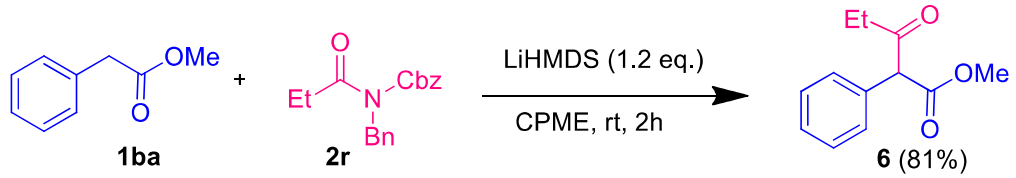


Reaction conditions: Substrate **1c-1g** (0.5 mmol) and LiHMDS (1 M solution in THF, 0.6 mL, 1.2 eq.) were stirred in CPME (3 mL) for 15 min after which *N*-Cbz amide **2a** (161 mg, 1.2 eq.) was added. Isolated yields presented.

Furthermore, the reactivity of various *O*-protected phenylacetic acid esters was investigated in *the C*-acylation reactions with *N*-Cbz *N*-methyl benzamide (**2a**) under established reaction conditions (**Table 5.4**). To our delight, isopropyl-, *n*-butyl-, l-menthyl-, cyclohexyl- and benzyl 2-phenylacetates underwent coupling with **2a** and gave the desired

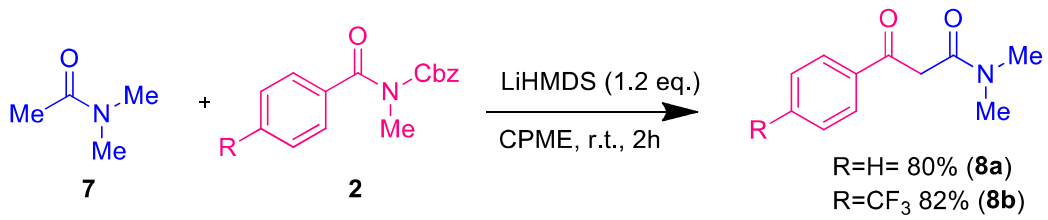
β-ketoesters **5a-5e** in 87-92% yields at room temperature. The diastereomeric compound **5c** was obtained in 1:1 ratio with 81% yield.

Further to our delight, *N*-Cbz protected alkyl amide **2r** also participated in the *C*-acylation reactions with methyl 2-phenylacetates (**1ba)** and gave the corresponding *β*-ketoester **6** in 81% yield, which increases the reliability of *N*-Cbz amides (**Scheme 5.3**).

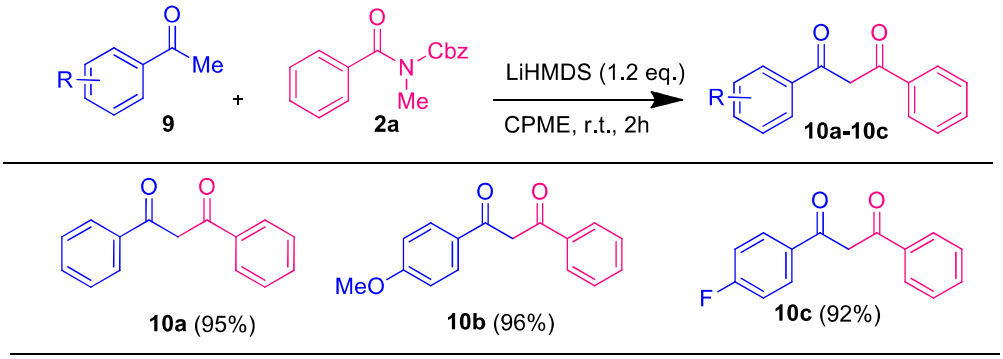


Scheme 5.3 Reaction of *N*-Cbz protected alkyl amide with methyl 2-phenylacetate.

After exploring the *β*-ketoesters preparation, we investigated the synthesis of *β*-keto amides using *N*-Cbz amides as acylating reagents under optimized conditions. The reaction of *N,N*-dimethyl acetamide (**7**) with *N*-Cbz amides **2a** and **2m** in the presence of LiHMDS in CPME gave the desired *β*-keto amides **8a** and **8b** in 80% and 82% yields, respectively (**Scheme 5.4**).



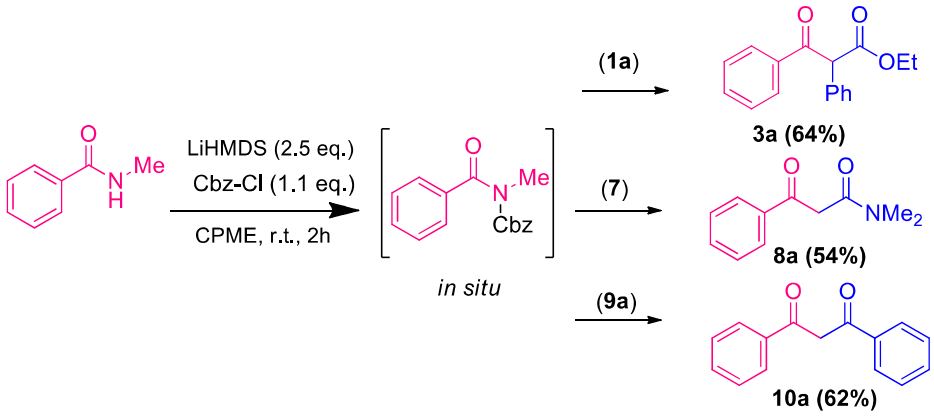
Scheme 5.4 Reaction of *N*-Cbz protected alkyl amide with *N,N*-dimethyl acetamide.



Scheme 5.5 Synthesis of 1,3-diketones from ketone and *N*-Cbz amides.

After exploring the synthesis of β-ketoesters and β-keto amides, we investigated the preparation of 1,3-diketones from *N*-Cbz amides and enolizable ketones (**Scheme 5.5**). To our delight, *N*-Cbz-*N*-methyl benzamide underwent C-C coupling with acetophenone, 4-methoxyacetophenone and 4-fluoroacetophenone smoothly and gave desired 1,3-diketones **10a-10c** in 92–96% yields.

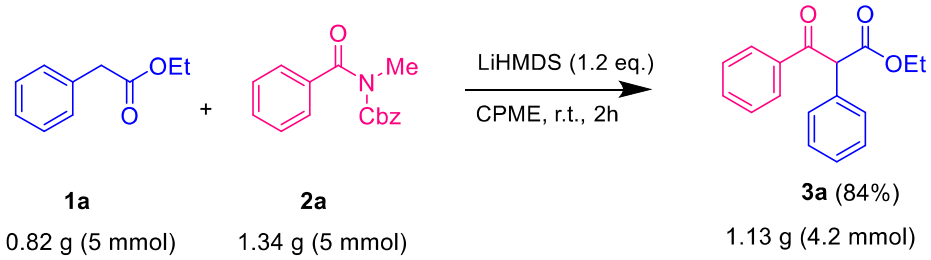
Further, a one-pot synthesis of 1,3-dicarbonyl compounds was investigated (**Scheme 5.6**).



Scheme 5.6 One-pot synthesis of 1,3-dicarbonyl compounds.

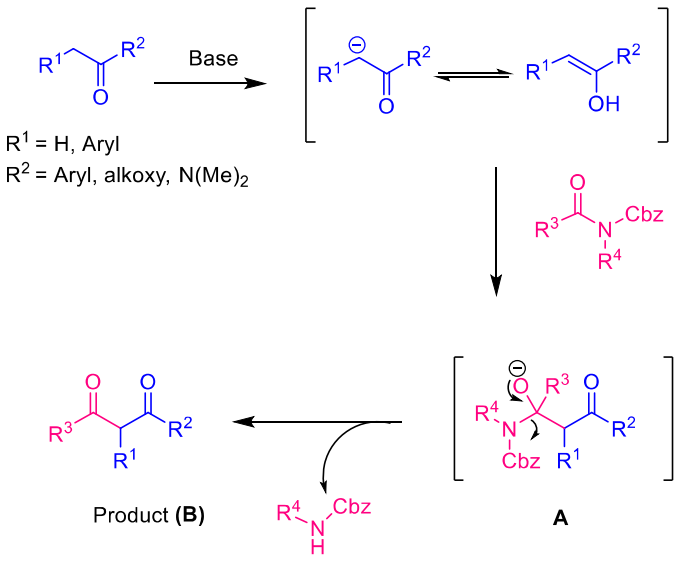
Initially, the *N*-Cbz amide was generated *in situ* from the secondary amide and subjected to the *C*-*C* coupling with ethyl 2-phenyl acetate (**1a**), *N*,*N*-dimethyl acetamide (**7**) and acetophenone (**9a**). These reactions proceeded smoothly and gave the desired products in good yields.

After exploring the versatility of the developed method in *β*-ketoesters, *β*-keto amides and 1,3-diketones, a gram scale reaction was performed with model substrates i.e. *N*-methyl *N*-Cbz benzamide (**2a,** 1.34 g) and ethyl 2-phenylacetate (**1a,** 0.82 g) (**Scheme 5.7**). The reaction provided the desired ester **3a** in 84% yields which describes the practical applicability of the developed methodology.



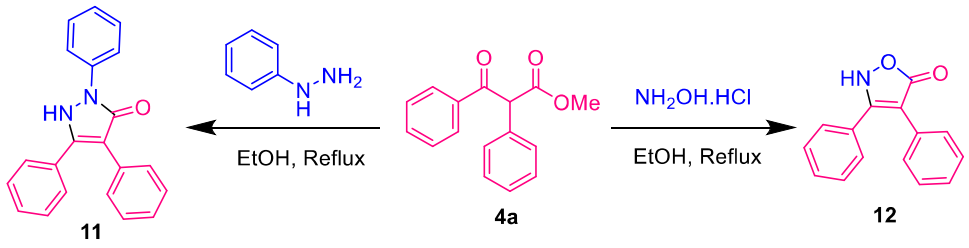
Scheme 5.7 Coupling reaction in a gram scale.

A plausible mechanism for the *C*-acylation reaction is shown in **Scheme 5.8**. Initially, the carbonyl compound (e.g. arylacetic acid ester, acetophenone, *N,N* Dimethylacetamide) undergoes enolization in the presence of a base. Further, the *C*-nucleophile undergoes addition reaction with activated *N*-Cbz amide and generates the tetrahedral intermediate **A**. This unstable intermediate undergoes C-N bond cleavage to provide the desired C-C coupled product **B**.



Scheme 5.8. Proposed mechanism for the reaction of *N*-Cbz amides with esters.

Further, some applications of *β*-ketoester in heterocyclic compounds preparation were investigated. The reaction of *β*-ketoester **4a** with phenylhydrazine and hydroxylamine in ethanol under reflux conditions afforded biologically relevant 1,2-dihydro-3*H*-pyrazol-3-one (**11**) and isoxazol-5(2*H*)-one (**12**) in good yields (**Scheme 5.9**)[19].



Scheme 5.9 Applications of *β*-ketoester in heterocyclic compounds synthesis.

In conclusion, the synthesis of 1,3-dicarbonyl compounds such as *β*-ketoesters, *β*-keto amides and 1,3-diketones from enolizable esters, amides or ketones was demonstrated

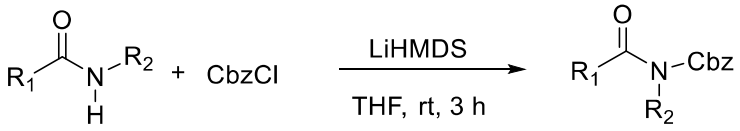
under mild reaction conditions. Various functionalized *N*-Cbz amides were used as acyl donors in the presence of LiHMDS in cyclopentyl methyl ether (CPME). The desired 1,3-dicarbonyl compounds were obtained in good to excellent yields at room temperature. Broad substrate scope, wide functional groups tolerance and metal-free conditions are the important features of the developed methodology.

5.3 Experimental Section

5.3.1. Procedure for *C*-acylation reactions

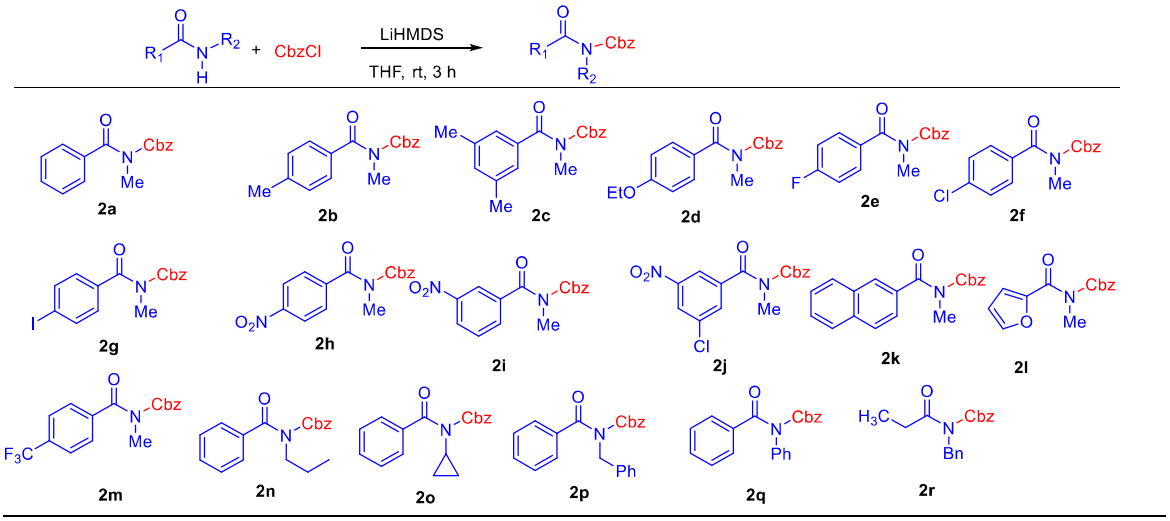
An oven-dried round bottom flask (25 mL) with a stir bar was charged with *N*-Cbz amide (0.5 mmol) and LiHMDS (1 M solution in THF, 0.6 mmol, 0.6 mL) in CPME (3 mL) to which the ester/amide/ketone (1.2 eq.) was added. The resulting mixture was stirred for 2h under N_2 atmosphere and was diluted with ethyl acetate, and washed with 1M HCl solution and brine. The organic layer was then dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The resulting crude product was purified by column chromatography (EtOAc/hexanes) to obtain the pure products.

5.3.2. General Procedure for synthesis of *N*-Cbz amides from Secondary Amides [18d]:

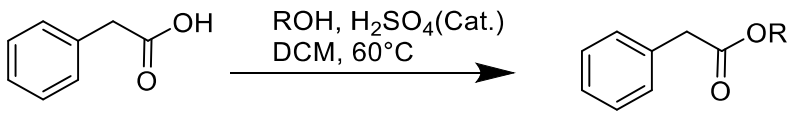


An oven-dried round-bottomed flask (100 mL) was charged with amide (1.0 mmol) in THF (5 mL) to which lithium bis(trimethylsilyl) amide (LiHMDS, 1 M solution in THF,

1.2 mmol, 1.2 mL) was added at 0 °C. The resulting mixture was allowed to stir for 15 min after which benzyl chloroformate (Cbz-Cl, 1.2 mmol, 170 µL) was added slowly. The reaction mixture was allowed to stir at room temperature for 3h. After completion, the reaction mixture was quenched with 1 M HCl solution, extracted with ethyl acetate and washed with brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated. The crude product was purified by silica gel (100-200 mesh) column chromatography (SiO_2: ethyl acetate/hexane: 10/90) to obtain the pure *N*-Cbz amides (**2a-2r**). The analytical data of **2a-r** was already reported by our groups [18d].



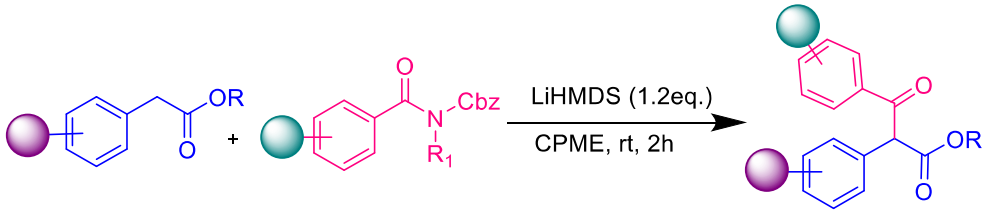
5.3.3 General procedure for synthesis of alkyl arylacetate [20].



A 50 mL round bottom flask was charged with alcohol (in the case of methanol and ethanol, 6 mL was used; in other cases, 2 equiv. of alcohol was dissolved in 6 mL DCM and used), phenyl acetic acid (500 mg) and H_2SO_4 (0.2 mL). The reaction mixture was stirred at 50 °C and monitored by TLC. After completion of the reaction, the product was extracted with ethyl acetate, washed with aqueous $NaHCO_3$, water and brine, dried over anhydrous Na_2SO_4, the resulting crude product was purified by column chromatography (EtOAc/hexane) to obtain the corresponding phenyl acetic acid esters.

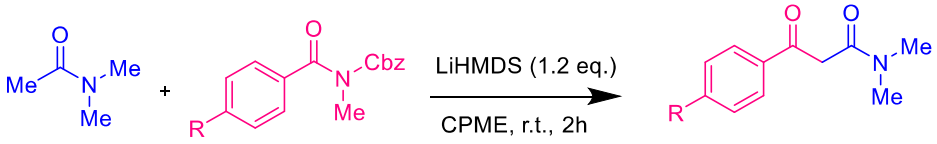
5.3.4. General Procedures for the synthesis of 1,3-dicarbonyl compounds

5.3.5. Procedure for the synthesis of *β*-keto esters



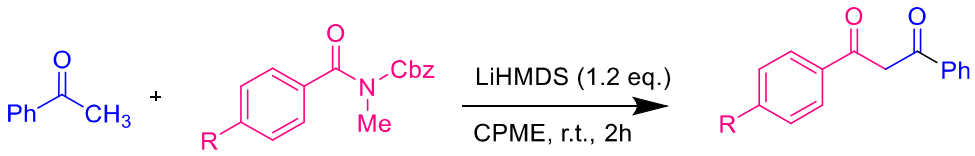
An oven-dried round bottom flask (25 mL) with a stir bar was charged with corresponding ester (0.5 mmol) and LiHMDS (1 M solution in THF, 0.6 mmol, 0.6 mL) in CPME (3 mL) to which the *N*-Cbz amide (1.2 equiv.) was added. The resulting mixture was stirred under N_2 atmosphere for 2 h and was diluted with ethyl acetate and washed with 1M HCl solution and brine. The organic layer was then dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The resulting crude product was purified by column chromatography (EtOAc/hexane) to obtain the *β*-keto esters.

5.3.6. Procedure for the synthesis of *β*-keto amides



An oven-dried round bottom flask (25 mL) with a stir bar was charged with *N,N*-dimethyl acetamide (0.5 mmol) and LiHMDS, 1 M solution in THF, 0.6 mmol, 0.6 mL) in CPME (3 mL) to which *N*-Cbz amide (1.2 equiv.) was added. The resulting mixture was stirred for 2h and was diluted with ethyl acetate and washed with 1 M HCl solution and brine. The organic layer was then dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The resulting crude product was purified by column chromatography (EtOAc/hexane) to obtain *β*-keto amides.

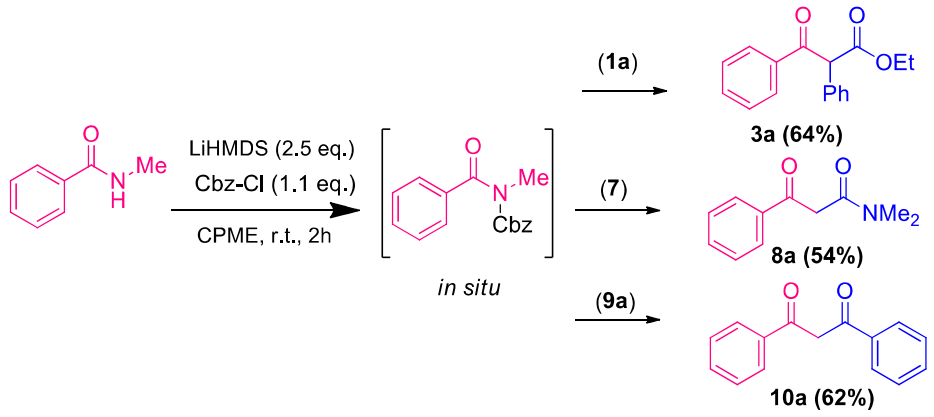
5.3.7. Procedure for the synthesis of 1,3-diketones



An oven-dried round bottom flask (25 mL) with a stir bar was charged with acetophenone (0.5 mmol) and LiHMDS, 1 M solution in THF, 0.6 mmol, 0.6 mL) in CPME (3 mL) to which corresponding *N*-Cbz amide (1.2 equiv.) was added. The resulting mixture was stirred for 2 h and was diluted with ethyl acetate and washed with 1 M HCl solution and brine. The organic layer was then dried over anhydrous Na_2SO_4, filtered and evaporated

under reduced pressure. The resulting crude product was purified by column chromatography (EtOAc/hexane) to obtain *β*-keto amides.

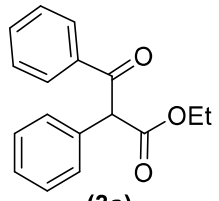
5.3.8. Procedure for the one-pot synthesis



An oven-dried round-bottomed flask was charged with *N*-methyl benzamide (0.5 mmol, 68 mg) in CPME (5 mL) to which lithium bis(trimethylsilyl) amide (LiHMDS, 1 M solution in THF, 1.25 mmol, 1.25 mL) was added at 0 °C. The resulting mixture was allowed to stir for 15 min after which benzyl chloroformate (Cbz-Cl, 0.6 mmol, 85 µL) was added slowly. The reaction mixture was allowed to stir at room temperature for 3h after which ethyl 2-phenyl acetate (**1a**) (or) *N*-*N*-dimethyl acetamide (**7**) (or) acetophenone (**9a**) was added. The resulting mixture was stirred for 2h and was diluted with ethyl acetate and washed with 1 M HCl solution and brine. The organic layer was then dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The resulting crude product was purified by column chromatography (EtOAc/hexane) to obtain **3a** (**64%**)**, 8a** (54%) and **10a** (62%)**.**

5.4 Analytical Data of the Products:

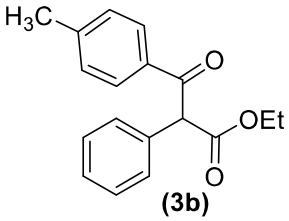
5.4.1. Ethyl 3-oxo-2,3-diphenylpropanoate(3a) [3l]



(3a)

The title compound was obtained as a white solid. M.p. 69.8−71.6 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), Rf = 0.60; Yield 90% (120 mg). 1H NMR (500 MHz, CDCl3) δ = 7.98–7.96 (m, 2H), 7.54 (dd, J = 10.6, 4.2 Hz, 1H), 7.44–7.41 (m, 4H), 7.37–7.34 (m, 2H), 7.32–7.29 (m, 1H), 5.62 (s, 1H), 4.27–4.19 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H).13C NMR (125 MHz, CDCl3) δ = 193.2, 168.8, 135.7, 133.4, 133.0, 129.5, 128.8, 128.7, 128.6, 128.0, 61.7, 60.5, 13.9.

5.4.2. Ethyl 3-oxo-2-phenyl-3-(p-tolyl)propanoate(3b) [3k]

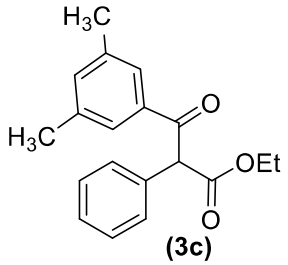


(3b)

The title compound was obtained as a colourless oil. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 88% (124 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.86 (d, J = 8.2 Hz, 2H), 7.41–7.40 (m, 2H), 7.36–7.34 (m, 2H), 7.30 (ddd, J= 8.4, 4.3, 1.3 Hz, 1H), 7.22 (d, J = 8.2 Hz, 2H), 5.59 (s, 1H), 4.26–4.19 (m, 2H), 2.37 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H).**^{13}C**

NMR (125 MHz, $CDCl_3$) δ = 192.8, 168.9, 144.4, 133.1, 133.0, 129.5, 129.3, 129.0, 128.7, 128.0, 61.6, 60.4, 21.6, 14.0.

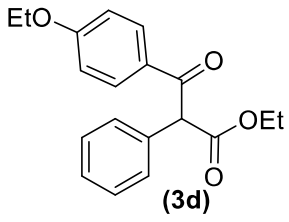
5.4.3. Ethyl 3-(3,5-dimethylphenyl)-3-oxo-2-phenylpropanoate(3c)



(3c)

The title compound was obtained as a colourless oil. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 87% (128 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.58 (s, 2H), 7.41 (d, J = 8.0 Hz, 2H), 7.36 (t, J = 7.6 Hz, 2H), 7.32–7.28 (m, 1H), 7.17 (s, 1H), 5.60 (s, 1H), 4.26–4.17 (m, 2H), 2.33 (s, 6H), 1.24 (t, J = 7.1 Hz, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 193.5, 168.9, 138.3, 135.8, 135.1, 133.1, 129.5, 128.7, 128.0, 126.6, 61.6, 60.4, 21.2, 14.1. **HRMS:** Calc. for $C_{19}H_{21}O_3$ $[M+H]^+$: 297.1491, Obser.: 297.1489.

5.4.4. Ethyl 3-(4-ethoxyphenyl)-3-oxo-2-phenylpropanoate(3d)

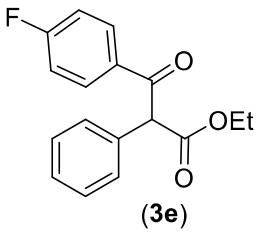


(3d)

The title compound was obtained as a colourless oil. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 85% (132 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.94–7.93 (m, 2H),

7.41 (dd, J = 8.2, 1.1 Hz, 2H), 7.35 (t, J = 7.4 Hz, 2H), 7.29 (ddd, J = 8.3, 2.5, 1.2 Hz, 1H), 6.87 (d, J = 9.0 Hz, 2H), 5.57 (s, 1H), 4.27–4.18 (m, 2H), 4.06 (q, J = 7.0 Hz, 2H), 1.41 (t, J = 7.0 Hz, 3H), 1.25 (t, J = 7.1 Hz, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 191.7, 169.0, 163.1, 133.3, 131.2, 129.4, 128.7, 128.3, 127.9, 114.2, 63.7, 61.6, 60.2, 14.5, 14.0. **HRMS:** Calc. for $C_{19}H_{21}O_4$ $[M+H]^+$: 313.1440, Obser.: 313.1431.

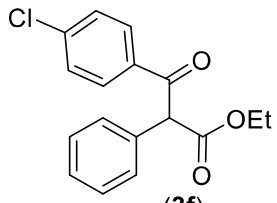
5.4.5. Ethyl 3-(4-fluorophenyl)-3-oxo-2-phenylpropanoate(3e)



(**3e**)

The title compound was obtained as a white solid. M.p. 68-70 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 91% (130 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 8.02–7.96 (m, 2H), 7.37 (dt, J = 15.0, 7.8 Hz, 4H), 7.31 (dd, J = 8.3, 5.6 Hz, 1H), 7.09 (t, J = 8.5 Hz, 2H), 5.55 (s, 1H), 4.23 (ddd, J = 9.4, 7.1, 2.7 Hz, 2H), 1.25 (t, J = 7.1 Hz, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 191.7, 168.5, 166.8, 164.8, 132.8, 132.0, 131.6(d, J = 8.75 Hz), 129.4, 128.8, 128.2, 115.8 (d, J = 22.5 Hz), 61.8, 60.5, 14.0.

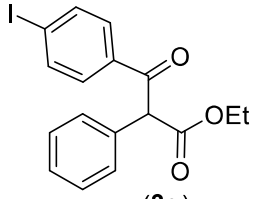
5.4.6. Ethyl 3-(4-chlorophenyl)-3-oxo-2-phenylpropanoate(3f) [3l]



(**3f**)

The title compound was obtained as a white solid. M.p. 77.8−79.5 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 90% (136 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.89 (d, J = 7.9 Hz, 2H), 7.40–7.35 (m, 6H), 7.32 (dd, J = 5.2, 2.4 Hz, 1H), 5.53 (s, 1H), 4.27–4.18 (m, 2H), 1.25 (t, J = 7.1 Hz, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 192.1, 168.5, 140.0, 133.9, 132.7, 130.2, 129.5, 129.0, 128.9, 128.2, 61.8, 60.6, 14.0.

5.4.7. Ethyl 3-(4-iodophenyl)-3-oxo-2-phenylpropanoate (3g)

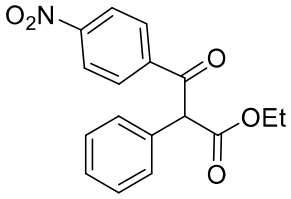


(**3g**)

The title compound was obtained as a colourless liquid. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 85% (167 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.78 (dd, J = 8.8, 2.0 Hz, 2H), 7.66–7.64 (m, 2H), 7.39–7.33 (m, 4H), 7.31 (ddd, J = 8.5, 5.1, 2.5 Hz, 1H), 5.52 (s, 1H), 4.28 – 4.18 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 192.6, 168.4, 138.0, 134.9, 132.6, 130.1, 129.4, 128.9, 128.2, 61.8, 60.5, 14.0.

HRMS: Calc. for $C_{17}H_{16}IO_3$ $[M+H]^+$: 295.0144, Obser.: 295.0137.

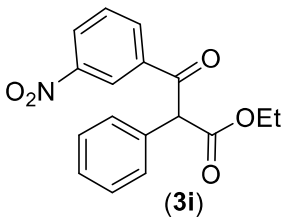
5.4.8. Ethyl 3-(4-nitrophenyl)-3-oxo-2-phenylpropanoate(3h) [3l]



(**3h**)

The title compound was obtained as a yellow oil. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 94% (147 mg). keto enol isomers ratio 1:1. **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 13.58 (s, 1H), 8.26 (d, J = 8.7 Hz, 2H), 8.09 (d, J = 8.6 Hz, 2H), 7.99 (d, J = 8.9 Hz, 2H), 7.40–7.37 (m, 6H), 7.35–7.32 (m, 1H), 7.25–7.22 (m, 3H), 7.09–7.05 (m, 2H), 5.56 (s, 1H), 4.31-4.27 (m, 2H), 4.23 (ddt, J = 10.8, 7.3, 3.7 Hz, 2H), 1.26 (t, J = 7.1 Hz, 6H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 191.9, 172.9, 168.0, 167.8, 150.3, 147.8, 141.1, 140.2, 133.8, 132.0, 131.7, 130.2, 129.8, 129.5, 129.0, 128.5, 128.2, 127.4, 123.8, 122.7, 62.0, 61.5, 61.1, 14.0, 13.9.

5.4.9. Ethyl 3-(3-nitrophenyl)-3-oxo-2-phenylpropanoate (3i)

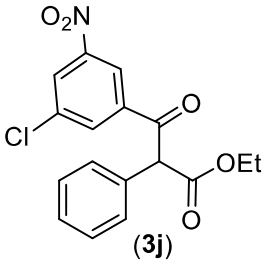


(**3i**)

The title compound was obtained as a yellow oil. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 92% (144 mg).

keto enol isomers ratio 3.3:1. **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 13.62 (s, 0.3H), 8.79 (s, 1H), 8.38 (dd, J = 8.2, 1.1 Hz, 1H), 8.26 (d, J = 7.8 Hz, 1H), 7.64 (t, J = 8.0 Hz, 1.2H), 7.49 (d, J = 7.8 Hz, 0.6H), 7.44–7.28 (m, 5.6H), 7.26–7.21 (m, 1H), 7.10 (dd, J = 6.5, 3.0 Hz, 0.6H), 5.59 (s, 14H), 4.31–4.21 (m, 2.75H), 1.26 (td, J = 7.1, 4.0 Hz, 4H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 191.2, 148.4, 136.9, 135.0, 134.3, 133.8, 132.0, 131.7, 130.0, 129.5, 129.1, 128.5, 128.5, 128.3, 127.6, 127.4, 124.4, 124.1, 123.7, 62.0, 61.5, 60.8, 14.0. **HRMS:** Calc. for $C_{17}H_{16}NO_5$ $[M+H]^+$: 314.1028, Obser.: 314.1022.

5.4.10. Ethyl 3-(3-chloro-5-nitrophenyl)-3-oxo-2-phenylpropanoate (3j)

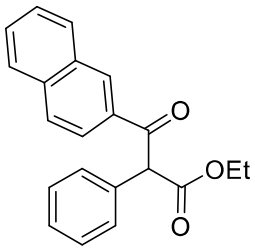


(**3j**)

The title compound was obtained as a yellow oil. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 94% (163 mg). keto enol isomers isomers ratio 2:1 ratio. **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 13.61 (s, 0.5H), 8.44 (d, J = 2.1 Hz, 1H), 8.05 (dd, J = 8.4, 2.1 Hz, 1H), 7.78 (d, J = 0.9 Hz, 0.5H), 7.62 (d, J = 8.4 Hz, 1H), 7.39–7.36 (m, 10H), 7.28 (dd, J = 5.4, 2.3 Hz, 5H), 7.11–7.09 (m, 2H), 5.52 (s, 1H), 4.30–4.21 (m, 3H), 1.28–1.23 (m, 4.5H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 190.2, 172.9, 167.8,

166.0, 147.9, 134.8, 133.5, 132.6, 132.5, 132.2, 131.7, 131.5, 131.0, 129.4, 129.1, 128.6, 128.5, 127.7, 126.4, 125.8, 62.1, 61.6, 60.6, 14.0, 13.9. **HRMS:** Calc. for $C_{17}H_{15}ClNO_5$ $[M+H]^+$: 348.0639, Obser.: 348.0635.

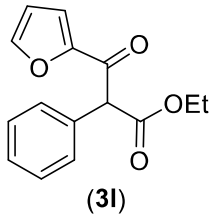
5.4.11. Ethyl 3-(naphthalen-2-yl)-3-oxo-2-phenylpropanoate(3k) [3l]



(**3k**)

The title compound was obtained as a colourless oil. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 86% (136 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 8.50 (s, 1H), 8.02 (dd, J = 8.7, 1.7 Hz, 1H), 7.93 (d, J = 8.1 Hz, 1H), 7.85 (t, J = 8.2 Hz, 2H), 7.62–7.57 (m, 1H), 7.56–7.52 (m, 1H), 7.48–7.47 (m, 2H), 7.37 (t, J = 7.5 Hz, 2H), 7.32–7.29 (m, 1H), 5.78 (s, 1H), 4.30–4.21 (m, 2H), 1.26 (t, J = 7.1 Hz, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 193.2, 168.8, 135.6, 133.0, 133.0, 132.3, 130.8, 129.6, 129.5, 128.8, 128.6, 128.1, 127.7, 126.8, 124.2, 61.7, 60.5, 14.0.

5.4.12. Ethyl 3-(furan-2-yl)-3-oxo-2-phenylpropanoate (3l) [3l]

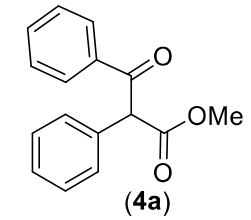


(**3l**)

The title compound was obtained as a colourless oil. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 88% (113 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.57–7.56 (m, 1H), 7.44 (dd, J =

8.2, 1.1 Hz, 2H), 7.37–7.34 (m, 2H), 7.33–7.29 (m, 1H), 7.27–7.24 (m, 1H), 6.51 (dt, J = 3.0, 1.5 Hz, 1H), 5.43 (s, 1H), 4.25–4.19 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 181.9, 168.2, 151.4, 146.8, 132.3, 129.6, 128.5, 128.1, 118.6, 112.6, 61.7, 60.1, 13.9.

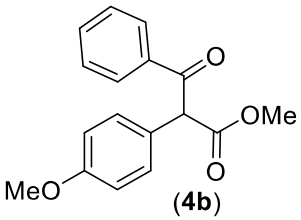
5.4.13. Methyl 3-oxo-2,3-diphenylpropanoate(4a) [21]



(4a)

The title compound was obtained as a white solid. M.p. 73-74 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 90% (114 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.97–7.95 (m, 2H), 7.55–7.52 (m, 1H), 7.42 (ddd, J = 5.9, 5.0, 1.5 Hz, 4H), 7.38–7.35 (m, 2H), 7.32– 7.29 (m, 1H), 5.65 (s, 1H), 3.76 (s, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 193.1, 169.2, 135.5, 133.5, 132.8, 129.5, 128.9, 128.8, 128.7, 128.1, 60.3, 52.7.

5.4.14. Methyl 2-(4-methoxyphenyl)-3-oxo-3-phenylpropanoate(4b) [21]

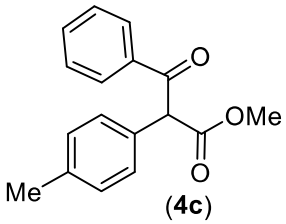


(4b)

The title compound was obtained as a white solid. M.p. 92-94 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 86% (122 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.96–7.94 (m, 2H), 7.53 (t,

J = 10.5, 1H), 7.42 (t, J = 7.7 Hz, 2H), 7.33–7.30 (m, 2H), 6.90–6.87(m, , 2H), 5.59 (s, 1H), 3.77 (s, 3H), 3.76 (s, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 193.4, 169.6, 159.4, 135.4, 133.4, 130.6, 128.9, 128.6, 128.4, 124.8, 114.3, 59.4, 55.1, 52.7.

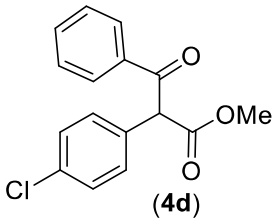
5.4.15. Methyl 3-oxo-3-phenyl-2-(*p*-tolyl)propanoate (4c) [22]



(**4c**)

The title compound was obtained as a white solid. M.p. 68-70 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 85% (113 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.97 (t, J = 9.1 Hz, 2H), 7.55 (d, J = 2.8 Hz, 1H), 7.44 (dd, J = 10.0, 7.0 Hz, 2H), 7.31 (d, J = 6.9 Hz, 2H), 7.18 (t, J = 8.9 Hz, 2H), 5.63 (s, 1H), 3.78 (s, 3H), 2.34 (s, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 193.3, 169.4, 137.9, 135.5, 133.4, 129.8, 129.6, 129.3, 128.9, 128.6, 60.0, 52.7, 21.0.

5.4.16. Methyl 2-(4-chlorophenyl)-3-oxo-3-phenylpropanoate (4d) [23]

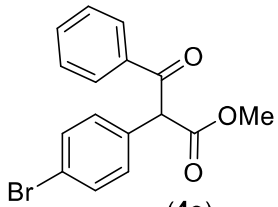


(**4d**)

The title compound was obtained as a white solid. M.p. 68-70 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 92% (132 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.94 (d, J = 8.1 Hz, 2H),

7.56 (dd, J = 10.5, 4.3 Hz, 1H), 7.44 (dd, J = 11.1, 4.2 Hz, 2H), 7.37–7.30 (m, 4H), 5.62 (s, 1H), 3.75 (d, J = 1.3 Hz, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 192.8, 168.9, 135.2, 134.2, 133.7, 131.2, 130.8, 129.0, 128.8, 128.7, 59.4, 52.8.

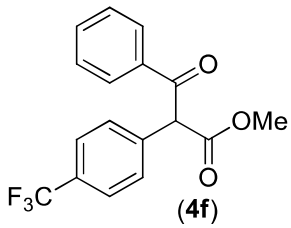
5.4.17. Methyl 2-(4-bromophenyl)-3-oxo-3-phenylpropanoate(4e) [24]



(**4e**)

The title compound was obtained as a white solid. M.p. 68-70 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 90% (149 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.94 (dd, J = 7.5, 1.0 Hz, 2H), 7.57– 7.54 (m, 1H), 7.50–7.48 (m, 2H), 7.44 (dd, J = 11.1, 4.5 Hz, 2H), 7.30–7.28 (m, 2H), 5.60 (s, 1H), 3.76 (s, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 192.7, 168.8, 135.2, 133.7, 132.0, 131.7, 131.2, 128.8, 128.8, 122.5, 59.5, 52.9.

5.4.18. Methyl 3-oxo-3-phenyl-2-(4-(trifluoromethyl)phenyl)propanoate (4f)

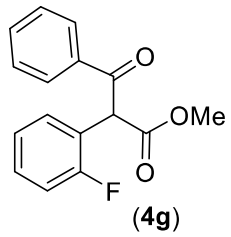


(**4f**)

The title compound was obtained as a white solid. M.p. 68-70 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 95% (152 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.96–7.95 (m, 2H), 7.63 (d, J = 8.2 Hz, 2H), 7.59–7.54 (m, 3H), 7.47–7.44 (m, 2H), 5.71

(s, 1H), 3.77 (s, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 192.41, 168.60, 136.64, 135.23, 133.94, 132.34, 130.01, 129.17, 128.90, 128.88, 127.84, 125.7(q, J = 3.75 Hz), 122.61, 59.81, 53.03. **HRMS:** Calc. for $C_{17}H_{14}F_3O_3$ $[M+H]^+$: 323.0895, Obser.: 323.0885.

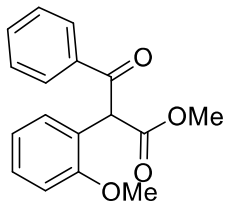
5.4.19. Methyl 2-(2-fluorophenyl)-3-oxo-3-phenylpropanoate (4g)



(**4g**)

The title compound was obtained as a white solid. M.p. 68-70 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 82% (111 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.97 (dd, J = 8.2, 0.9 Hz, 2H), 7.58–7.53 (m, 1H), 7.44 (t, J = 7.7 Hz, 3H), 7.32–7.27 (m, 1H), 7.15–7.07 (m, 2H), 6.01 (s, 1H), 3.78 (s, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 192.94, 168.74, 160.94, 158.99, 135.17, 133.80, 130.9 (d, J = 2.5 Hz), 130.0 (d, J = 8.75 Hz), 128.8 (d, J = 3.75 Hz), 128.5 (d, J = 3.75 Hz), 127.7, 124.5, 124.4, 120.2 (d, J = 13.75 Hz), 115.4 (d, J = 22.5 Hz),, 52.88, 51.8. **HRMS:** Calc. for $C_{16}H_{13}FNaO_3$ $[M+Na]^+$: 295.0746, Obser.: 295.0745.

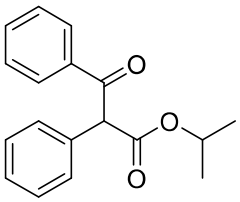
5.4.20. Methyl 2-(2-methoxyphenyl)-3-oxo-3-phenylpropanoate (4h)



(**4h**)

The title compound was obtained as a white solid. M.p. 68-70 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 78% (110 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.96–7.94 (m, 2H), 7.52 (t, J = 7.4 Hz, 1H), 7.40 (t, J = 7.8 Hz, 2H), 7.29–7.26 (m, 2H), 6.92 (t, J = 7.6 Hz, 2H), 6.14 (s, 1H), 3.90 (s, 3H), 3.77 (s, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 194.4, 169.7, 156.1, 135.5, 133.4, 130.2, 129.4, 128.7, 128.6, 121.6, 120.9, 110.7, 55.6, 52.9, 52.6.

5.4.21. Isopropyl 3-oxo-2,3-diphenylpropanoate (5a)

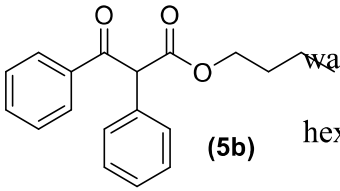


(**5a**)

The title compound was obtained as a colourless oil. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 92% (129 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 8.00–7.94 (m, 2H), 7.56–7.50 (m, 1H), 7.45–7.40 (m, 4H), 7.36 (dd, J = 10.2, 4.8 Hz, 2H), 7.30 (ddd, J = 7.0, 5.5, 1.3 Hz, 1H), 5.57 (s, 1H), 5.08 (dt, J = 12.5, 6.2 Hz, 2H), 1.24 (d, J = 6.2 Hz, 3H), 1.19 (d, J = 6.3 Hz, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 193.2, 168.2, 135.7, 133.3, 133.0, 129.5, 128.8, 128.7, 128.6, 128.0, 69.3, 60.7, 21.5, 21.4. **HRMS:**

Calc. for $C_{18}H_{19}O_3$ $[M+H]^+$: 283.1334, Obser.: 283.1327.

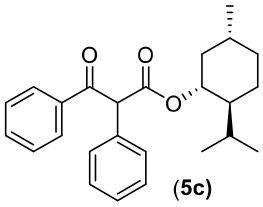
5.4.22. Butyl 3-oxo-2,3-diphenylpropanoate (5b)



(5b)

The title compound was obtained as a colourless oil. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (99:01), R_f = 0.60; Yield 87% (128 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.97 (dd, J = 8.3, 1.1 Hz, 2H), 7.57–7.49 (m, 1H), 7.46–7.39 (m, 4H), 7.39–7.33 (m, 2H), 7.33–7.28 (m, 1H), 5.61 (s, 1H), 4.23–4.11 (m, 2H), 1.62–1.55 (m, 2H), 1.30 (dq, J = 15.1, 7.5 Hz, 2H), 0.88 (t, J = 7.4 Hz, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 193.2, 168.8, 135.6, 133.4, 132.9, 129.5, 128.8, 128.7, 128.6, 128.0, 65.5, 60.5, 30.4, 18.9, 13.5. **HRMS:** Calc. for $C_{19}H_{21}O_3$ $[M+H]^+$:297.1491, Obser.: 297.1485.

5.4.23. (1R,2S,5R)-2-isopropyl-5-methylcyclohexyl-3-oxo-2,3-diphenylpropanoate (5c)

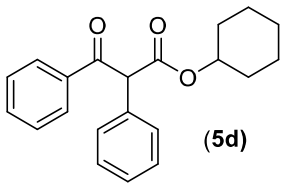


(5c)

The title compound was obtained as a colourless oil. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 91% (171 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 8.04–7.94 (m, 2H), 7.58 – 7.50 (m, 2H), 7.47–7.39 (m, 4H), 7.39–7.28 (m, 3H), 5.59 (d, J = 6.5 Hz, 1H), 4.73 (tdd, J = 10.9, 4.2, 2.4 Hz, 1H), 2.10–1.94 (m, 1H),

1.81–1.59 (m, 2H), 1.58–1.39 (m, 1H), 1.39–1.23 (m, 1H), 1.08–0.93 (m, 2H), 0.92–0.79 (m, 6H), 0.73 (dd, J = 19.7, 7.0 Hz, 3H), 0.59 (d, J = 6.9 Hz, 1.5H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 193.2, 192.9, 168.3, 135.9, 133.4, 133.3, 133.1, 133.0, 129.6, 129.5, 129.3, 129.3, 128.8, 128.7, 128.6, 128.6, 128.5, 128.3, 128.1, 128.1, 128.0, 127.9, 75.9, 75.8, 61.0, 60.8, 46.8, 46.8, 40.4, 40.2, 34.1, 31.3, 31.3, 25.8, 25.8, 23.1, 23.1, 21.9, 20.6, 20.6, 15.9, 15.8. **HRMS:** Calc. for $C_{25}H_{31}O_3$ $[M+H]^+$: 379.2273, Obser.: 379.2262.

5.4.24. Cyclohexyl 3-oxo-2,3-diphenylpropanoate (5d)

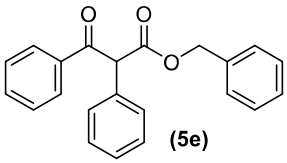


(5d)

The title compound was obtained as colourless oil. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 88% (141 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.98–7.96 (m, 2H), 7.55–7.52 (m, 1H), 7.44–7.40 (m, 4H), 7.36 (t, J = 7.4 Hz, 2H), 7.30 (t, J = 7.2 Hz, 1H), 5.57 (s, 1H), 4.87–4.82 (m, 1H), 1.83–1.73 (m, 3H), 1.63 (d, 1H), 1.49–1.42 (m,3H), 1.37–1.28 (m, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 193.2, 168.1, 135.8, 133.3, 133.1, 129.5, 128.8, 128.7, 128.6, 127.9, 74.0, 60.8, 31.2, 31.1, 25.2, 23.3.

HRMS: Calc. for $C_{21}H_{23}O_3$ $[M+H]^+$: 323.1647, Obser.: 323.1640.

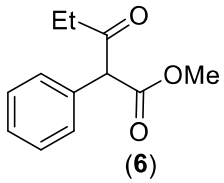
5.4.25. Benzyl 3-oxo-2,3-diphenylpropanoate(5e) [25]



(5e)

The title compound was obtained as a white solid. M.p. 68-70 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 90% (148 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.95 (dd, J = 8.3, 1.1 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.45–7.39 (m, 4H), 7.39–7.34 (m, 3H), 7.32 (m, 5H), 5.67 (s, 1H), 5.22 (s, 2H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 193.0, 168.6, 135.5, 135.3, 133.4, 132.7, 129.5, 128.9, 128.8, 128.6, 128.4, 128.2, 128.1, 67.3, 60.5.

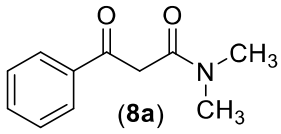
5.4.26. Methyl 3-oxo-2-phenylpentanoate (6) [22]



(**6**)

The title compound was obtained as colourless oil. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 81% (83 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.39–7.32 (m, 5H), 4.73 (s, 1H), 3.75 (s, 3H), 2.50 (qd, J = 7.2, 2.0 Hz, 2H), 1.02 (t, J = 7.2 Hz, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 204.2, 169.0, 132.6, 129.3, 128.8, 128.2, 64.6, 52.5, 34.9, 11.1, 7.7.

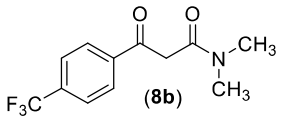
5.4.27. *N,N*-Dimethyl-3-oxo-3-phenylpropanamide (8a) [26]



(8a)

The title compound was obtained as colourless oil. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 80% (77 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 8.02 (d, J = 7.7 Hz, 2H), 7.78 (dd, J = 7.8, 1.6 Hz, 1H), 7.58 (t, J = 7.4 Hz, 1H), 7.47 (dd, J = 15.0, 7.4 Hz, 2H), 7.44–7.38 (m, 1.7H), 5.79 (s, 0.5H), 4.11 (s, 2H), 3.07 (s, 2.5H), 3.05 (s, 3H), 3.00 (s, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 193.8, 172.2, 166.9, 136.1, 135.0, 133.6, 130.5, 128.6, 128.6, 128.3, 125.8, 84.5, 46.0, 38.0, 35.5.

5.4.28. *N,N*-Dimethyl-3-oxo-3-(4-(trifluoromethyl)phenyl)propenamide (8b)

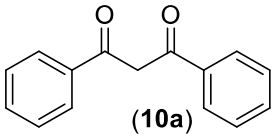


(8b)

The title compound was obtained as colourless oil. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 82% (107 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 8.14 (d, J = 8.2 Hz, 1H), 7.88 (d, J = 8.2 Hz, 2H), 7.74 (d, J = 8.2 Hz, 1H), 7.66 (d, J = 8.3 Hz, 2H), 5.84 (s, 1H), 4.11 (s, 1H), 3.09 (s, 3H), 3.08 (s, 3H), 2.99 (s, 1.5H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 193.0, 171.9, 169.5, 138.4, 132.1 (q, J = 32.5 Hz), 129.1, 126.2, 125.7 (q, J = 3.75

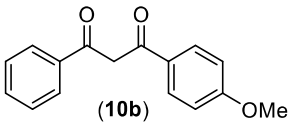
Hz), 125.5 (q, J = 3.75 Hz), 124.0 (q, J =270 Hz), 85.8, , 46.0, 38.0, 35.6.**HRMS:** Calc. for $C_{12}H_{13}F_3NO_2$ $[M+H]^+$: 260.0898, Obser.: 260.0896.

5.4.29. 1,3-Diphenylpropane-1,3-dione(10a) [17b]



The title compound was obtained as a white solid. M.p. 77-78 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 95% (106 mg). keto enol isomers ratio 1:1. **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 16.88 (s, 1H), 8.01–7.99 (m, 4H), 7.58–7.55 (m, 2H), 7.51–7.48 (m, 4H), 6.87 (s, 1H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 185.7, 135.5, 132.4, 128.6, 127.1, 93.1.

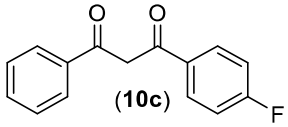
5.4.30. 1-(4-methoxyphenyl)-3-Phenylpropane-1,3-dione(10b) [17b]



The title compound was obtained as a white solid. M.p. 127-128 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 96% (121 mg). keto enol isomers ratio 1:1. **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 17.02 (s, 1H), 7.99–7.97 (m, 4H), 7.56–7.52 (m, 1H), 7.50 – 7.46 (m, 2H), 6.99–6.96 (m, 2H), 6.80 (s, 1H), 3.88 (s, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 186.1, 183.9, 163.2, 135.5,

132.1, 129.2, 128.5, 128.1, 126.9, 113.9, 92.3, 55.4.

5.4.31. 1-(4-fluorophenyl)-3-Phenylpropane-1,3-dione(10c) [17b]



The title compound was obtained as a white solid. M.p. 78-79 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 92% (111 mg); keto enol isomers ratio 1:1. **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 16.89 (s, 1H), 8.02–7.97 (m, 4H), 7.56 (dd, J = 8.3, 6.3 Hz, 1H), 7.49 (t, J = 7.5 Hz, 2H), 7.17 (dd, J = 12.0, 5.3 Hz, 2H), 6.80 (s, 1H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 185.0, 166.3, 164.3, 135.2, 132.4, 131.8 (d, J = 2.5 Hz), 129.5 (d, J = 8.75 Hz), 128.7, 128.6, 127.0, 115.7 (d, J = 25 Hz), 92.7.

5.5 General Procedure for Synthesis of (11) [3l]

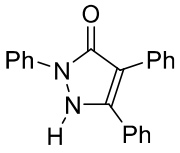
To a round-bottom flask, **4a** (76 mg, 0.30 mmol) was taken in ethanol (2 mL) to which $PhNHNH_2$ (50 mg, 0.46 mmol) was added. The resulting mixture was allowed to stir for 12 hat 80 °C. Solvent was removed under vacuum to obtain the residue, which was purified by silica gel column chromatography using DCM/ MeOH (v/v, 20:1) as the eluent to give **11**(1,3,4-triphenyl-1*H*-pyrazol-5-ol) as a white solid.

5.6 General Procedure for Synthesis of (12) [3l]

To a round-bottom flask, **4a** (76 mg, 0.30 mmol) was taken in ethanol (2 mL) to which

hydroxylamine hydrochloride (65 mg, 1 mmol) was added. The mixture was refluxed at 80 °C for 12 h. Solvent was removed under vacuum to obtain the crude product, which was purified by recrystallization to give **12** (mixture of 3,4-diphenylisoxazol-5(2*H*)-one and 3,4-diphenylisoxazol-5(4*H*)-one) as a white solid.

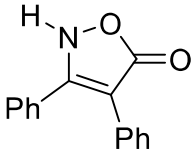
5.6.1. 2,4,5-Triphenyl-1,2-dihydro-3H-pyrazol-3-one (11) [3l]



(**11**)

The title compound was obtained as a white solid. M.p. 192.8-194.1°C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.60; Yield 72% (113 mg). **^{1}HNMR** (500 MHz, $CDCl_3$) δ = 10.41 (s, 1H), 7.39–7.27 (m, 5H), 7.25–7.18 (m, 5H), 7.07 (d, J = 7.4 Hz, 1H), 7.02–6.98 (m, 2H), 6.93–6.90 (m, 1H), 6.74 (d, J = 7.9 Hz, 1H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ = 155.2, 134.8, 134.8, 132.1, 130.6, 129.8, 129.4, 129.3, 128.7, 128.6, 128.4, 128.2, 127.9, 127.7, 121.9, 121.3, 109.9, 109.7.

5.6.2. 3,4-Diphenylisoxazol-5(2H)-one (12) [3l]



(**12**)

The title compound was obtained as a white solid. M.p. 159.8-161.2 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:20), R_f = 0.60; Yield 75% (88 mg). **^{1}H NMR** (500 MHz, DMSO) δ = 7.55–7.52 (m,

1H), 7.46 (dt, J = 8.5, 4.7 Hz, 4H), 7.31–7.27 (m, 4H), 7.24–7.20 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 170.5, 160.5, 130.9, 130.0, 129.0, 128.3, 128.1, 127.9, 127.7, 126.6, 96.1.

5.7 Spectral Data of Few Products

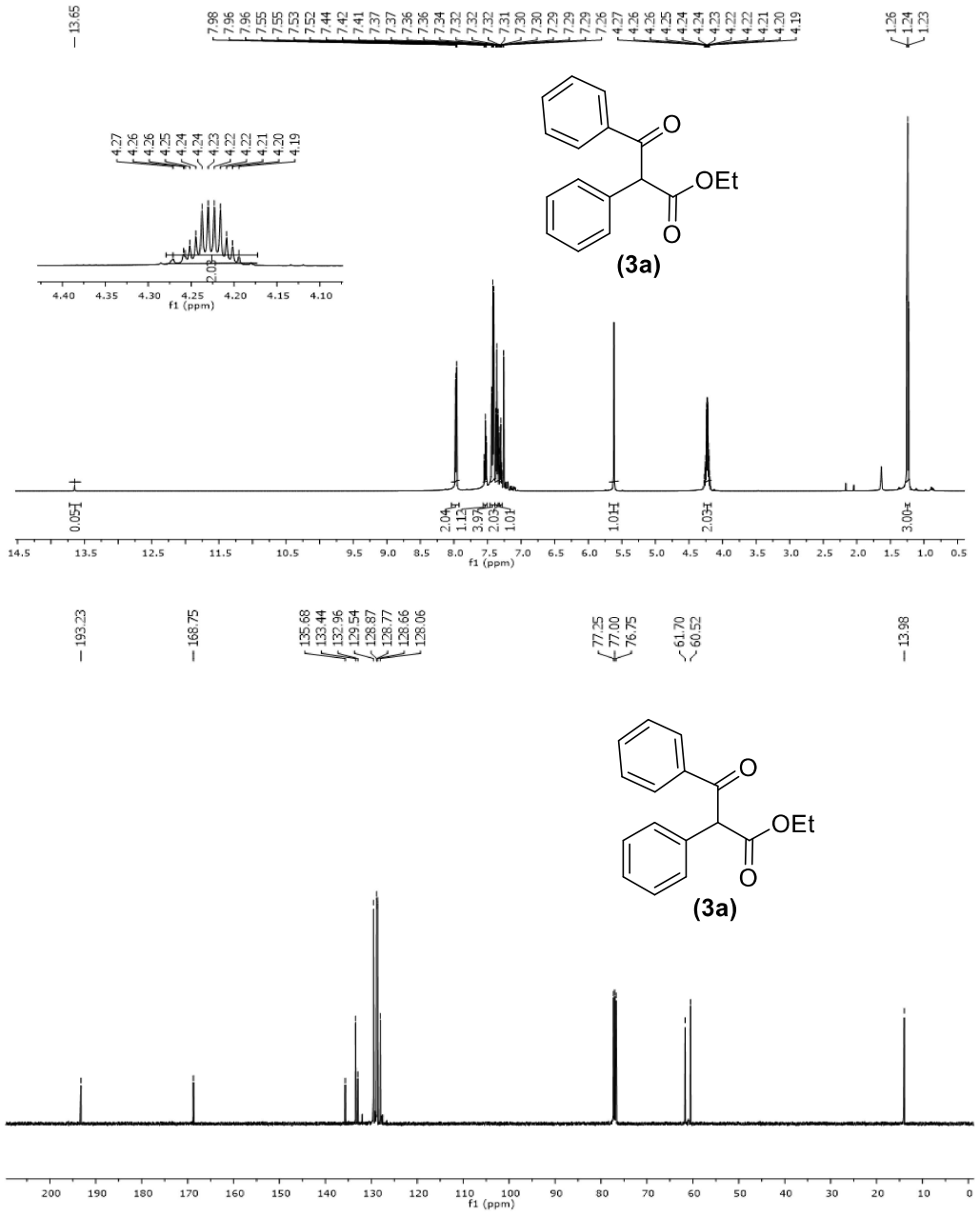


Figure 5.2 ^{1}H and ^{13}C NMR of product **3a** in$CDCl_3$.

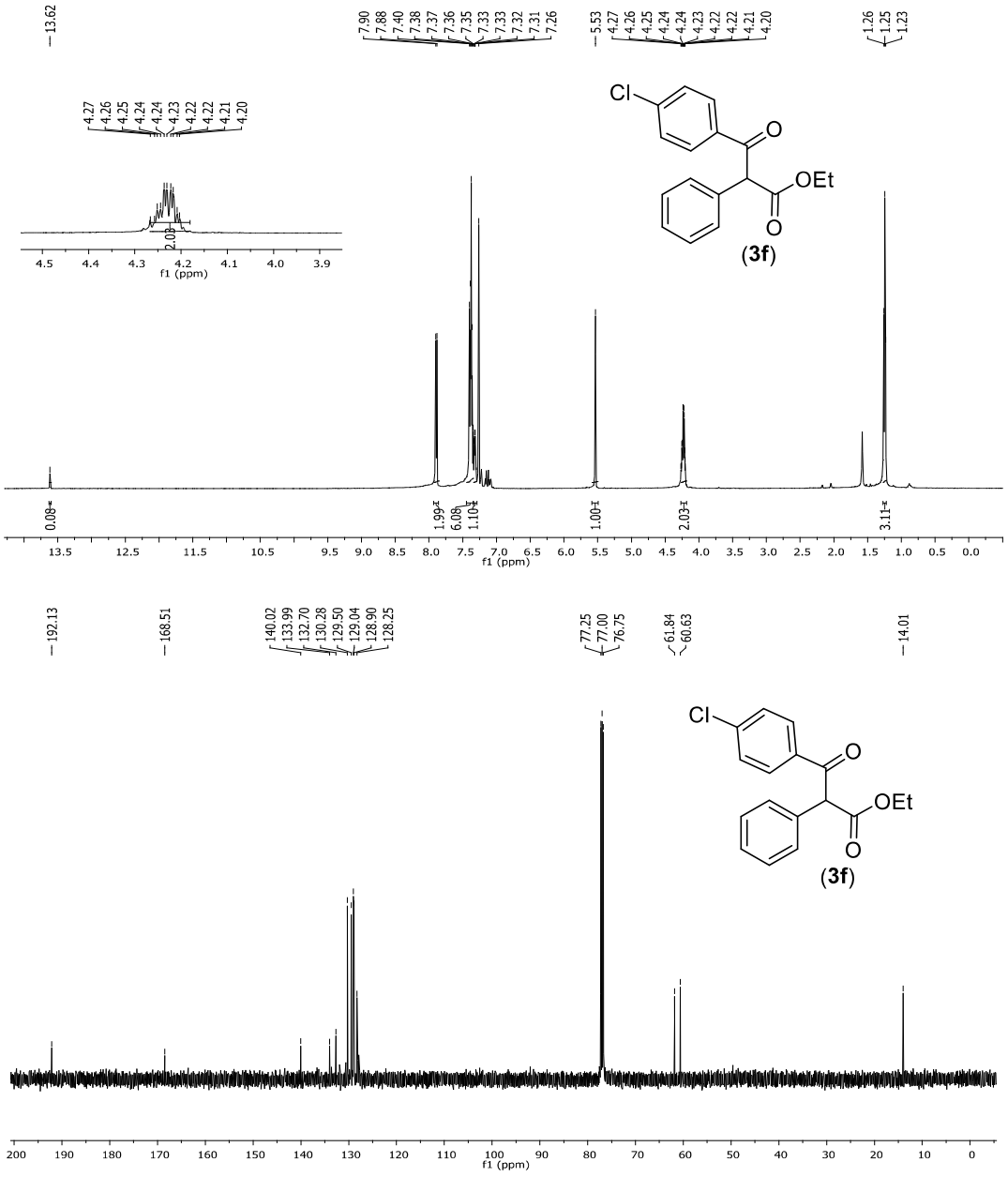


Figure 5.3 ^{1}H and ^{13}C NMR of product **3f** in $CDCl_3$.

5.8 References

[1] a) P. Langer, "Regio-and Diastereoselective Cyclization Reactions of Free and Masked 1,3-Dicarbonyl Dianions with 1,2-Dielectrophile," *Chemistry–A European Journal*, **7**(2001) 3858-3866; b) P. Langer, "Cyclization reactions of 1, 3-bis-silyl enol ethers and related masked dianions," *Synthesis*, **2002**(2002) 0441-0459; c) C. Pettinari, F. Marchetti, A. Drozdov, "1.6-*β*-Diketones and Related Ligands," *Comprehensive Coordination Chemistry II*, J. A. McCleverty, T. J. Meyer, Eds. Pergamon: Oxford, **2003**, 97-115; d) J. Christoffers, A. Baro, T. Werner, "*α*-Hydroxylation of *β*-Dicarbonyl Compounds," *Advanced Synthesis & Catalysis*, **346**(2004) 143-151; e) C. Simon, T. Constantieux, J. Rodriguez, "Utilisation of 1, 3-dicarbonyl derivatives in multicomponent reactions," *European Journal of Organic Chemistry*, **2004**(2004) 4957-4980; f) D. Bonne, Y. Coquerel, T. Constantieux, J. Rodriguez, "1, 3-Dicarbonyl compounds in stereoselective domino and multicomponent reactions," *Tetrahedron: Asymmetry*, **21**(2010) 1085-1109; g) N. Kaur, P. Grewal, K. Poonia, "Dicarbonyl compounds in *O*-heterocycle synthesis," *Synthetic Communications*, **51**(2021) 2423-2444; h) W. Li, Y. Zheng, E. Qu, J. Bai, Q. Deng, "β-Keto Amides: A Jack-of-All-Trades Building Block in Organic Chemistry," *European Journal of Organic Chemistry*, **2021**(2021) 5151-5192; i) T. Govender, P. I. Arvidsson, G. E. Maguire, H. G. Kruger, T. Naicker, "Enantioselective organocatalyzed transformations of *β*-ketoesters," *Chemical Reviews*, **116**(2016) 9375-9437.

[2] a) D. J. Hogenkamp, T. B. Johnstone, J. C. Huang, W. Y. Li, M. Tran, E. R. Whittemore, K. W. Gee, "Enaminone amides as novel orally active GABAA receptor modulators," *Journal of medicinal chemistry*, **50**(2007) 3369-3379; b) G. P. Jadhav, S. R. Chhabra, G. Telford, D. S. Hooi, K. Righetti, P. Williams, P. M. Fischer, "Immunosuppressive but non-LasR-inducing analogues of the Pseudomonas aeruginosa quorum-sensing molecule *N*-(3-oxododecanoyl)-l-homoserine lactone," *Journal of medicinal chemistry*, **54**(2011) 3348-3359; c) D. S. Coffey, L .E. Overman, F. Stappenbeck, "Enantioselective Total Syntheses of 13, 14, 15-Isocrambescidin 800 and 13, 14, 15-Isocrambescidin 657," *Journal of the American Chemical Society*, **122**(2000) 4904-4914; d) F. A. Davis, J. Zhang, Y. Li, H. Xu, C. De Brosse, "Asymmetric synthesis of 2, 4, 5-trisubstituted piperidines from sulfinimine-derived *δ*-amino *β*-ketoesters. Formal synthesis of pseudodistomin

B triacetate," *The Journal of Organic Chemistry*, **70**(2005) 5413-5419; e) M. D. Hill, M. Movassaghi, "New strategies for the synthesis of pyrimidine derivatives," *Chemistry–A European Journal*, **14**(2008) 6836-6844; f) D. Simoni, F. P. Invidiata, R. Rondanin, S. Grimaudo, G. Cannizzo, E. Barbusca, M. Tolomeo, "Structure− activity relationship studies of novel heteroretinoids: Induction of apoptosis in the hl-60 cell line by a novel isoxazole-containing heteroretinoid," *Journal of medicinal chemistry*, **42**(1999) 4961-4969; g) Z. Khademi, M. M. Heravi, "Applications of Claisen condensations in total synthesis of natural products. An old reaction, a new perspective," *Tetrahedron*, **103**(2022) 132573.

[3] a) S. Benetti, R. Romagnoli, C. De Risi, G. Spalluto, V. Zanirato, "Mastering. beta.-keto esters," *Chemical reviews*, **95**(1995) 1065-1114; b) A.V. Kel'in, "Recent advances in the synthesis of 1, 3-diketones," *Current Organic Chemistry*, **7**(2003) 1691-1711;c) H. S. P. Rao, S. Rafi, K. Padmavathy, "The Blaise reaction," *Tetrahedron*, **64**(2008) 8037-8043; d) G. Hilt, D. F. Weske, "Aromatic compounds as synthons for 1, 3-dicarbonyl derivatives," *Chemical Society Reviews*, **38**(2009) 3082-3091; e) E. A. Shokova, J. K. Kim, V. Kovalev, "1, 3-Diketones. Synthesis and properties," *Russian journal of organic chemistry*, **51**(2015) 755-830; f) S. E. El-Meligie, N. A. Khalil, H. B. El-Nassan, A. A. Ibraheem, "A Review on the Synthetic Routes to *β*-keto amides," *Current Organic Chemistry*, **23**(2019) 2005-2015; g) G. de Gonzalo, A. R. Alcántara, "Recent Developments in the Synthesis of β-Diketones," *Pharmaceuticals*, **14**(2021) 1043; h) M. C. Hennessy, T. P. O'Sullivan, "Recent advances in the transesterification of β-keto esters," *RSC advances*, **11**(2021) 22859-22920; i) B. Wahl, H. Bonin, A. Mortreux, S. Giboulot, F. Liron, G. Poli, M. Sauthier, "A General and Efficient Method for the Alkoxycarbonylation of *α*-Chloro Ketones," *Advanced Synthesis & Catalysis*, **354**(2021) 3105-3114; j) Z. Zhang, Y. Liu, M. Gong, X. Zhao, Y. Zhang, J. Wang, "Palladium-Catalyzed Carbonylation/Acyl Migratory Insertion Sequence," *Angewandte Chemie International Edition*, **49**(2010) 1139-1142; k) M. Rahaman, M. S. Ali, K. Jahan, D. Hinz, J. B. Belayet, R. Majinski, M. M. Hossain, "Synthetic scope of Brønsted acid-catalyzed reactions of carbonyl compounds and ethyl diazoacetate," *The Journal of Organic Chemistry*, **86**(2021) 6138-6147; l) L. Zeng, Z. Lai, S. Cui, "One-pot reaction of carboxylic acids and ynol ethers for the synthesis of *β*-keto esters," *The Journal of Organic Chemistry*, **83**(2018) 14834-

14841; m) M. A. Sanchez-Carmona, D. A. Contreras-Cruz, L. D. Miranda, "Base-free two-step synthesis of 1, 3-diketones and β-ketoesters from α-diazocarbonyl compounds, trialkylboranes, and aromatic aldehydes," *Organic & Biomolecular Chemistry*, **9**(2011) 6506-6508.

[4] a) Akhmedov, A. R. Katritzky, Z. Wang, M. Wang, C. R. Wilkerson, C. D. Hall, N. G. Akhmedov, "Preparation of *β*-keto esters and *β*-diketones by *C*-acylation/deacetylation of acetoacetic esters and acetonyl ketones with 1-acylbenzotriazoles," *The Journal of Organic Chemistry*, **69**(2004) 6617-6622; b) G. Zhou, D. Lim, F. Fang, D. M. Coltart, "A Practical Synthesis of *β*-Keto Thioesters by Direct Crossed-Claisen Coupling of Thioesters and *N*-Acylbenzotriazoles," *Synthesis*, **2009**(2009) 3350-3352; c) D. S. Breslow, E. Baumgarten, C. R. Hauser, "A New Synthesis of *β*-Keto Esters of the Type RCOCH2COOC2H5," *Journal of the American Chemical Society*, **66**(1944) 1286-1288; d) R. J. Clay, T. A. Collom, G. L. Karrick, J. A. Wemple, *Synthesis*, **3**(1993) 290−292; e) R. J. Clay, T. A. Collom, G. L. Karrick, J.Wemple, "A safe, economical method for the preparation of *β*-oxo-esters," *Synthesis (Stuttgart)*, **3**(1993) 290-292; f) H. S. P. Rao, S. Rafi, K. Padmavathy, "The Blaise reaction," *Tetrahedron*, **64**(2008) 8037-8043; g) L. Kürti, B. Czako, "Strategic Applications of Named Reactions in Organic Synthesis" Elsevier: Burlington, **2005,** 86-138; h) R. J. Ouellette, J. D. Rawn, *Organic Chemistry (Second Edition)*, R. J. Ouellette, J. D. Rawn, Eds. Academic Press: **2018**, 711-762.

[5] a) A. Greenberg, C. M. Breneman, J. F. Liebman, Wiley-Interscience: New York, **2000**; b) J. S. Carey, D. Laffan, C. Thomson, M. T. Williams, "Analysis of the reactions used for the preparation of drug candidate molecules," *Organic & biomolecular chemistry*, **4**(2006) 2337-2347; c) S. D. Roughley, A. M. Jordan, "The medicinal chemist's toolbox: an analysis of reactions used in the pursuit of drug candidates," *Journal of medicinal chemistry*, **54**(2011) 3451-3479; d) J. R. Dunetz, J. Magano, G. A. Weisenburger, "Large-scale applications of amide coupling reagents for the synthesis of pharmaceuticals," *Organic Process Research & Development*, **20**(2016) 140-177.

[6] a) P. Acosta-Guzmán, A. Mateus-Gómez, D. Gamba-Sánchez, "Direct transamidation reactions: mechanism and recent advances," *Molecules*, **23**(2018) 2382; b) M. B. Chaudhari, B. Gnanaprakasam, "Recent Advances in the Metal-Catalyzed Activation of Amide Bonds," *Chemistry–An Asian*

Journal, **14**(2019) 76-93; c) G. Meng, S. Shi, M. Szostak, "Cross-coupling of amides by N–C bond activation," *Synlett*, **27**(2016) 2530-2540; d) J. E. Dander, N. K. Garg, "Breaking amides using nickel catalysis," *ACS catalysis*, **7**(2017) 1413-1423; e) S. Shi, S. P. Nolan, M. Szostak, "Well-Defined Palladium (II)-NHC (NHC= N-Heterocyclic Carbene) 265 Precatalysts for Cross-Coupling Reactions of Amides and Esters by Selective Acyl CO–X (X= N, O) 266 Cleavage," *Acc. Chem. Res*, **51**(2018) 2589-2599; f) Y Bourne-Branchu, C. Gosmini, G. Danoun, "*N*-Boc-Amides in Cross-Coupling Reactions," *Chemistry–A European Journal*, **25**(2019) 2663-2674; g) G. Li, S. Ma, M. Szostak, "Amide bond activation: the power of resonance," *Trends in Chemistry*, **2**(2020) 914-928; h) G. Li, M. Szostak, "Transition-Metal-Free Activation of Amides by N−C Bond Cleavage," *The Chemical Record*, **20**(2020) 649-659; i) G. Li, M. Szostak, "Non-classical amide bond formation: Transamidation and amidation of activated amides and esters by selective N–C/O–C cleavage," *Synthesis*, **52**(2020) 2579-2599; j) G. Meng, J. Zhang, M. Szostak, "Acyclic twisted amides," *Chemical Reviews*, **121**(2021) 12746-12783; k) R. Szostak, S. Shi, G. Meng, R. Lalancette, M. Szostak, "Ground-state distortion in *N*-acyl-*tert*-butyl-carbamates (Boc) and *N*-acyl-tosylamides (Ts): twisted amides of relevance to amide N–C cross-coupling," *The Journal of Organic Chemistry*, **81**(2016) 8091-8094; l) C. Liu, M. Szostak, "Twisted Amides: From Obscurity to Broadly Useful Transition-Metal-Catalyzed Reactions by N−C Amide Bond Activation," *Chemistry–A European Journal*, **23**(2017) 7157-7173; m) R. Takise, K. Muto, J. Yamaguchi, "Cross-coupling of aromatic esters and amides," *Chemical Society Reviews*, **46**(2017) 5864-5888; n) G. Li, T. Zhou, A. Poater, L.Cavallo, S. P. Nolan, M. Szostak, "Buchwald–Hartwig cross-coupling of amides (transamidation) by selective N–C (O) cleavage mediated by air-and moisture-stable [Pd (NHC)(allyl) Cl] precatalysts: catalyst evaluation and mechanism," *Catalysis Science & Technology*, **10**(2020) 710-716; o) C. Liu, M. Szostak, "Decarbonylative cross-coupling of amides," *Organic & Biomolecular Chemistry*, **16**(2018) 7998-8010; p) T. Zhou, C. L. Ji, X. Hong, M. Szostak, "Palladium-catalyzed decarbonylative Suzuki–Miyaura cross-coupling of amides by carbon–nitrogen bond activation," *Chemical science*, **10**(2019) 9865-9871; q) E. Massolo, M. Pirola,M. menaglia, "Amide bond formation strategies: Latest advances on a dateless transformation," *European Journal of Organic Chemistry*, **2020**(2020) 4641-4651; r) G. Meng, S. Shi, R.

Lalancette, R. Szostak, M. Szostak, "Reversible twisting of primary amides via ground state N–C (O) destabilization: highly twisted rotationally inverted acyclic amides," *Journal of the American Chemical Society*, **140**(2018) 727-734; s) G. Li, Y. Xing, H. Zhao, J. Zhang, X. Hong, M. Szostak, "Chemoselective Transamidation of Thioamides by Transition-Metal-Free N−C (S) Transacylation," *Angewandte Chemie International Edition*, **61**(2022) e202200144.

[7] a) E. L. Baker, M. M. Yamano, Y. Zhou, S. M. Anthony, N. K. Garg, "A two-step approach to achieve secondary amide transamidation enabled by nickel catalysis," *Nature communications*, **7**(2016) 1-5; b) C. W. Cheung, M. L. Ploeger, X. Hu, "Nickel-catalyzed reductive transamidation of secondary amides with nitroarenes," *ACS Catalysis*, **7**(2017) 7092-7096; c) J. E. Dander, E. L. Baker, N. K. Garg, "Nickel-catalyzed transamidation of aliphatic amide derivatives," *Chemical science*, **8**(2017) 6433-6438; d) Y. Liu, S. Shi, M. Achtenhagen, R. Liu, M. Szostak, "Metal-Free Transamidation of Secondary Amides via Selective N–C Cleavage under Mild Conditions," *Organic letters*, **19**(2017) 1614-1617; e) G. Li, M. Szostak, "Highly selective transition-metal-free transamidation of amides and amidation of esters at room temperature," *Nature communications*, **9**(2018) 1-8; f) G. Meng, P. Lei, M. Szostak, "A general method for two-step transamidation of secondary amides using commercially available, air-and moisture-stable palladium/NHC (N-heterocyclic carbene) complexes," *Organic letters*, **19**(2017) 2158-2161; g) S. Shi, M. Szostak, "Pd–PEPPSI: A general Pd–NHC precatalyst for Buchwald–Hartwig cross-coupling of esters and amides (transamidation) under the same reaction conditions," *Chemical communications*, **53**(2017) 10584-10587; h) D. Joseph, M. S. Park, S. Lee, "Metal-free transamidation of benzoylpyrrolidin-2-one and amines under aqueous conditions," *Organic & Biomolecular Chemistry*, **19**(2021) 6227-6232; i) W. Guo, J. Huang, H. Wu, T. Liu, Z. Luo, J. Jian, Z. Zeng, "One-pot transition-metal free transamidation to sterically hindered amides," *Organic Chemistry Frontiers*, **5**(2018) 2950-2954; j) G. Li, M. Szostak, "Highly selective transition-metal-free transamidation of amides and amidation of esters at room temperature," *Nature communications*, **9**(2018) 1-8; k) O. Verho, M. Pourghasemi Lati, M. Oschmann, "A two-step procedure for the overall transamidation of 8-aminoquinoline amides proceeding via the intermediate *N*-acyl-Boc-carbamates," *The Journal of organic chemistry*, **83**(2018) 4464-4476; l) R. Ramkumar, S. Chandrasekaran, "Catalyst-Free, Metal-Free, and Chemoselective

Transamidation of Activated Secondary Amides," *Synthesis*, **51**(2019) 921-932; m) M. M. Rahman, G. Li, M. Szostak, "Metal-Free Transamidation of Secondary Amides by N–C Cleavage," *The Journal of Organic Chemistry*, **84**(2019) 12091-12100; n) G. Li, C. L. Ji, X. Hong, M. Szostak, "Highly chemoselective, transition-metal-free transamidation of unactivated amides and direct amidation of alkyl esters by N–C/O–C cleavage," *Journal of the American Chemical Society*, **141**(2019) 11161-11172; o) J. Chen, Y. Xia, S. Lee, "Transamidation for the synthesis of primary amides at room temperature," *Organic letters*, **22**(2020) 3504-3508; (p) S. Yu, T. Shin, M. Zhang, Y. Xia, H. Kim, S. Lee, "Nickel/Briphos-Catalyzed Direct Transamidation of Unactivated Secondary Amides Using Trimethylsilyl Chloride," *Organic Letters*, **20**(2018) 7563-7566; (q) P. Lei, Y. Wang, Y. Mu, Y. Wang, Z. Ma, J. Feng, M. Szostak, "Green-Solvent Selection for Acyl Buchwald–Hartwig Cross-Coupling of Amides (Transamidation)," *ACS Sustainable Chemistry & Engineering*, **9**(2021) 14937-14945.

[8] a) G. Li, P. Lei, M. Szostak, "Transition-metal-free esterification of amides via selective N–C cleavage under mild conditions *Organic letters*, **20**(2018) 5622-5625; b) D. Ye, Z. Liu, H. Chen, J. L. Sessler, C. Lei, "Cesium carbonate catalyzed esterification of *N*-benzyl-*N*-Boc-amides under ambient conditions," *Organic letters*, **21**(2019) 6888-6892.

[9] a) M. M. Rahman, G. Li, M. Szostak, "Thioesterification and selenoesterification of amides via selective N–C cleavage at room temperature: N–C (O) to S/Se–C (O) interconversion," *Synthesis*, **52**(2020) 1060-1066; b) Y. Liu, X. Mo, I. Majeed, M. Zhang, H. Wang, Z. Zeng, "An efficient and straightforward approach for accessing thionoesters via palladium-catalyzed C–N cleavage of thioamides," *Organic & Biomolecular Chemistry*, **20**(2022) 1532-1537.

[10] a) P. Lei, G. Meng, Y. Ling, J. An, S. P. Nolan, M. Szostak, "General method for the Suzuki–Miyaura cross-coupling of primary amide-derived electrophiles enabled by [Pd (NHC)(cin) Cl] at room temperature," *Organic letters*, **19**(2017) 6510-6513; b) G. Li, M. Szostak, "Kinetically controlled, highly chemoselective acylation of functionalized grignard reagents with amides by N−C cleavage," *Chemistry–A European Journal*, **26**(2020) 611-615; c) P. Lei, Y. Mu, Y. Wang, Z. Ma, J. Feng, X. Liu, M. Szostak, "Green-Solvent Selection for Acyl Buchwald–Hartwig Cross-Coupling of Amides (Transamidation)," *ACS Sustainable Chemistry & Engineering*, **9**(2021) 14937-14945; d) P. Lei, G. Li, Y. Ling, J. An, S. P. Nolan,

M. Szostak, "Protocol for Palladium/N-Heterocyclic Carbene-Catalyzed Suzuki–Miyaura Cross-Coupling of Amides by N–C (O) Activation," *Synthesis*, **53**(2021) 682-687; e) P. Gao, M. Szostak, "Highly Selective and Divergent Acyl and Aryl Cross-Couplings of Amides via Ir-Catalyzed C–H Borylation/N–C (O) Activation," *Organic letters*, **22**(2020) 6010-6015; f) J. Buchspies, M. M. Rahman, R. Szostak, M. Szostak, "N-Acylcarbazoles and *N*-Acylindoles: Electronically Activated Amides for N–C (O) Cross-Coupling by Nlp to Ar Conjugation Switch," *Organic letters*, **22**(2020) 4703-4709; g) S. Ma, T. Zhou, G. Li, M. Szostak, "Suzuki-Miyaura Cross-Coupling of Amides using Well-Defined, Air-Stable [(PR3) 2Pd (II) X2] Precatalysts," *Advanced Synthesis & Catalysis*, **362**(2020) 1887-1892; h) S. Shi, R. Lalancette, R. Szostak, M. Szostak, "Triflamides: Highly Reactive, Electronically Activated *N*-Sulfonyl Amides in Catalytic N–C (O) Amide Cross-Coupling," *Organic letters*, **21**(2019) 1253-1257; i) C. Liu, G. Li, S. Shi, G. Meng, R. Lalancette, R. Szostak, M. Szostak, "Acyl and Decarbonylative Suzuki 646 Coupling of *N*-Acetyl Amides: Electronic Tuning of Twisted, Acyclic Amides in Catalytic Carbon− Nitrogen Bond Cleavage," *ACS Catal*, **8**(2018) 9131-9139.; j) F. Yang, D. Zou, S. Chen, H. Wang, Y. Zhao, L. Zhao, L. Li, J. Li, P. J. Walsh, "Transition Metal-Free Aroylation of Diarylmethanes with *N*-Bn-*N*-Boc Arylamides and *N*-Acylpyrroles," *Advanced Synthesis & Catalysis*, **362**(2020) 3423-3430.

[11] a) F. Bie, X. Liu, Y. Shi, H. Cao, Y. Han, M. Szostak, C. Liu, "Rh-Catalyzed Base-Free Decarbonylative Borylation of Twisted Amides," *The Journal of Organic Chemistry*, **85**(2020) 15676-15685; b) S. Shi, M. Szostak, "Decarbonylative borylation of amides by palladium catalysis," *ACS omega*, **4**(2019) 4901-4907.

[12] F. Bie, X. Liu, H. Cao, Y. Shi, T. Zhou, M. Szostak, C. Liu, "Pd-catalyzed double-decarbonylative aryl sulfide synthesis through aryl exchange between amides and thioesters," *Organic letters*, **23**(2021) 8098-8103.

[13] T. Zhou, C. L. Li, X. Hong, M. Szostak, "Palladium-catalyzed decarbonylative Suzuki–Miyaura cross-coupling of amides by carbon–nitrogen bond activation," *Chemical science*, **10**(2019) 9865-9871.

[14] C. Liu, M. Szostak, "Decarbonylative Phosphorylation of Amides by Palladium and Nickel Catalysis: The Hirao Cross-Coupling of Amide Derivatives," *Angewandte Chemie International Edition*, **56(**2017) 12718-12722.

[15] S. Shi, M. Szostak, "Decarbonylative cyanation of amides by palladium catalysis," *Organic letters*, **19**(2017) 3095-3098.

[16] M. M. Rahman, M. Szostak, "Synthesis of Sulfoxonium Ylides from Amides by Selective N–C (O) Activation," *Organic letters*, **23**(2021) 4818-4822.

[17] a) M. M. Rahman, M. Szostak, "Synthesis of Sulfoxonium Ylides from Amides by Selective N–C (O) Activation," *Organic letters*, **23**(2021) 4818-4822.; (b) J. Chen, Y. Xia, S. Lee, "Coupling of amides with ketones via C–N/C–H bond cleavage: a mild synthesis of 1, 3-diketones," *Organic Chemistry Frontiers*, **7**(2020) 2931-2937; (c) J. Chen, D. Joseph, Y. Xia, S. Lee, "Amide/Ester Cross-Coupling via C–N/C–H Bond Cleavage: Synthesis of *β*-Ketoesters," *The Journal of Organic Chemistry*, **86**(2021) 5943-5953; d) D. Joseph, M. S. Oh, A. Jayaraman, S. Lee, "Amides Activation: Transition Metal-Free Coupling Between C-N Activated Amides and Enolizable Amides," *Bulletin of the Korean Chemical Society*, **42**(2021) 1293-1295.

[18] a) P. Sureshbabu, S. Azeez, N. Muniyappan, S. Sabiah, J. Kandasamy, "Chemoselective synthesis of aryl ketones from amides and Grignard reagents via C (O)–N bond cleavage under catalyst-free conditions," *The Journal of Organic Chemistry*, **84**(2019) 11823-11838; b) P. Sureshbabu, S. Azeez, P. Chaudhary, J. Kandasamy, "*tert*-Butyl nitrite promoted transamidation of secondary amides under metal and catalyst free conditions," *Organic & Biomolecular Chemistry*, **17**(2019) 845-850; c) S. Singh, P. Sureshbabu, S. Sabiah, J. Kandasamy, "Synthesis of *N*-Aryl *α*-Ketoamides, *α*-Ketoesters, *α*-Ketothioesters and Their Applications in Quinoxalinone Preparation," *Asian Journal of Organic Chemistry*, **11**(2022) e202200122; d) P. Sureshbabu, S. Azeez, K. Pattanaik, S. Sabiah, J. Kandasamy, "Synthesis of *N*-Cbz Amides and Their Applications in the Transamidation Reactions at Room Temperature," *Asian Journal of Organic Chemistry*, (2022) e202200076; e) S. Azeez, P. Sureshbabu, S. Sabiah, J. Kandasamy, "Controlled reduction of activated primary and secondary amides into aldehydes with diisobutylaluminum hydride," *Organic & Biomolecular Chemistry*, **20**(2022) 2048-2053; f) S. Singh, S. Popuri, Q. M. Junaid, S. Sabiah, J. Kandasamy, "Diversification of *α*-ketoamides via transamidation reactions with alkyl and benzyl amines at room temperature," *Organic & Biomolecular Chemistry*, **19**(2021) 7134-7140; (g) V. K. Kanaujiya, V. Tiwari, K. Pattanaik, S. Sabiah, J. Kandasamy, "Synthesis of Glycouronamides by Transamidation

Approach at Room Temperature," *Asian Journal of Organic Chemistry*, (2022) e202200315.

[19] L. Zeng, Z. Lai, S. Cui, "One-pot reaction of carboxylic acids and ynol ethers for the synthesis of *β*-keto esters," *The Journal of Organic Chemistry*, **83**(2018) 14834-14841.