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Direct Synthesis of *N*-Acyl-*N*,*O*-hemiacetals *via* Nucleophilic Addition of Unactivated Amides and Their *O*-Acetylation: Access to α,α-Difunctionalized *N*-Acylimines

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Abstract: A mild, metal-free synthesis of polyfunctionalized *N*-acyl-*N*,*O*-hemiacetals was developed *via* the nucleophilic addition of unactivated amides to ketones. The protocol demonstrated a wide substrate scope, with good isolated yields. Additionally, their *O*-acetylated products serve as a precursor of α,α-difunctionalized *N*-acylimines. An addition reaction of broad scope of nucleophiles to generate *N*-acylimines is also reported.

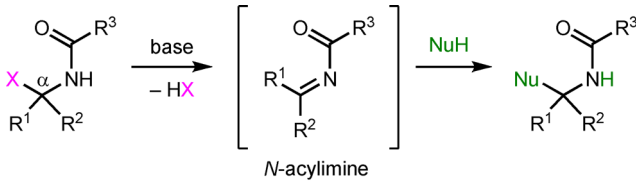
Keywords: *N*-acylimines; amidoalkylation; *N*,*O*-hemiacetals; unactivated amides; vicinal tricarbonyl compounds

Introduction

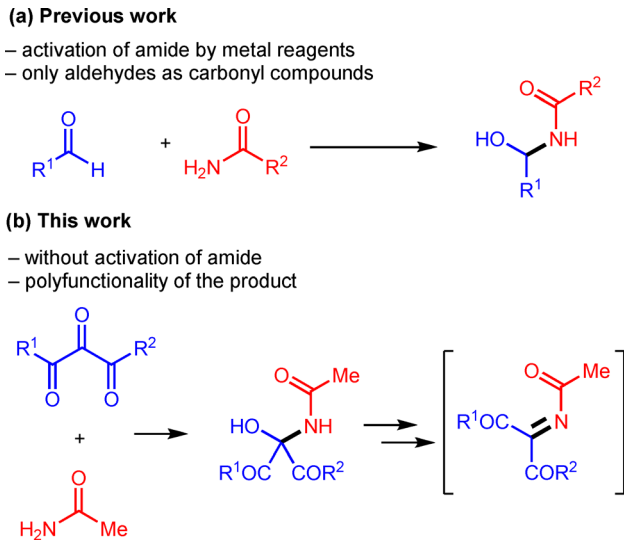
Highly electrophilic *N*-acylimines are multifunctional precursors that facilitate the synthesis of functionalized amines, amino acid derivatives, and oxaziridines.[1,2] *N*-Acylimines are widely used as reactive building blocks, as heterodienes[3] or as dienophiles[4] in Diels–Alder reactions and as enophiles in ene-reactions.[5] Most importantly, *N*-acylimines serve as active amidoalkylating reagents in the reactions with various nucleophiles.[6] Because of their overall high reactivity, *N*-acylimines are generally generated *in situ* from *N*-acylamines having a leaving group at the α-position of the nitrogen atom (Scheme 1).

Although numerous precursors for *N*-acylimines have been developed, the methods leading to the α,α-difunctionalized *N*-acylimines (R^1, R^2 = functional group) are rather limited. This maybe due to the difficulty in the synthesis of corresponding precursors. Highly and densely functionalized *N*-acylimines have broad potential in organic synthesis because they serve as a building block for polyfunctionalized compounds, such as quaternary amines and amino acids. Therefore, an efficient method for the generation of α,α-difunctionalized *N*-acylimines is still desired.

On the other hand, given the importance of *N*-acyl-*N*,*O*-hemiacetals and acetals, which are one of the precursors of *N*-acylimines as well as a structural motif found in bioactive natural products, a number of efforts have been made toward their synthesis.[7,8] Within their synthetic methods, the addition of an amide to a carbonyl function is a simpler, direct, and efficient route [Scheme 2, (a)]. This route, however, requires activation of the amide by costly metals and shows limited functional group tolerance because of the harsh reaction conditions (e.g., strongly basic conditions). In addition, the carbonyls usable for this approach are limited to aldehydes. With regard to ketones, only highly electrophilic 3,3,3-trihalo-2-oxopropanoates,[9] hexafluoroacetone,[10] and vicinal tricarbonyl compounds (VTC)[11] are used as electrophiles for the direct construction of *N*-acyl-*N*,*O*-hemiacetals, among which the former two substrates are most



Scheme 1. Generation and reaction of *N*-acylimines.



Scheme 2. Direct construction of *N*-acyl-*N*,*O*-hemiacetals and generation of *N*-acylimines.

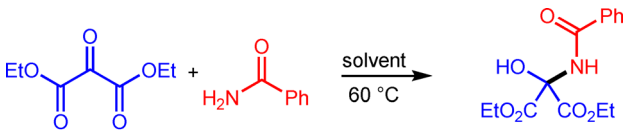
often found in the literature. In contrast, there are limited examples of the use of VTCs and amides for this reaction, with no systematic study into their reactivity. This observation prompted us to study the reaction of VTCs and amides to form α,α-difunctionalized *N*-acyl-*N*,*O*-hemiacetals [Scheme 2, (b)], which are useful building blocks for the construction of α,α-difunctionalized *N*-acylimines. In fact, we successfully generated highly reactive α,α-difunctionalized *N*-acylimines *in situ* and trapped them with versatile nucleophiles.

Results and Discussion

Initially, diethyl mesoxalate **1** and benzamide **2a** were chosen as model substrates for the synthesis of *N*-acyl-*N*,*O*-hemiacetals *via* direct nucleophilic addition of unactivated amides. The desired product **3a** was obtained in 60% NMR yield when a mixture of **1** and **2a** in hexane was heated at 60 °C in a sealed tube for 20 h, without any additive (Table 1, entry 1). We then optimized the reaction conditions by changing the solvents and found that polar aprotic solvents, such as chloroform and acetonitrile, were suitable for this reaction, affording **3a** in almost quantitative yields (entries 4 and 5). Unless otherwise specified, acetonitrile was primarily used in the following reactions. To evaluate the practicality of this method, the reaction of **1** on a 10 mmol (1.8 g) scale was conducted under the optimized conditions, which afforded 2.9 g of the product, in 97% isolated yield (entry 6).

Next, the scope and limitations of this reaction were studied using various amides **2b–o** (Table 2). Aromatic amides **2b–d** and aliphatic amides **2e–g** underwent nucleophilic addition to **1** under the optimized

Table 1. Optimization of the reaction conditions.[a]



1 **2a** (1.2 equiv.) **3a**

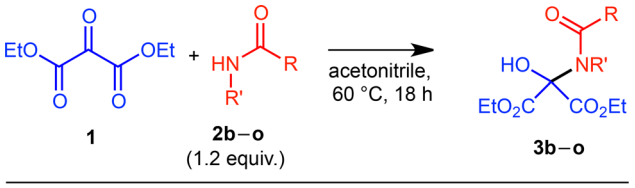
Entry	Solvent	Yield of **3a**[b] [%]
1	hexane	60
2	toluene	88
3	THF	ND[c]
4	chloroform	99
5	acetonitrile	99 (98)
6[d]	acetonitrile	(97)

[a] *Reaction conditions:* unless otherwise noted, all reactions were performed with **1** (0.5 mmol), **2a** (0.6 mmol) in solvent (2.5 mL) at 60 °C under air for 18 h.
[b] Determined by ^{1}H NMR using 1,1,2,2-tetrachloroethane as the internal standard. Numbers in parentheses are yields of isolated product.
[c] Not detected.
[d] 10 mmol (1.8 g) of **1** were used.

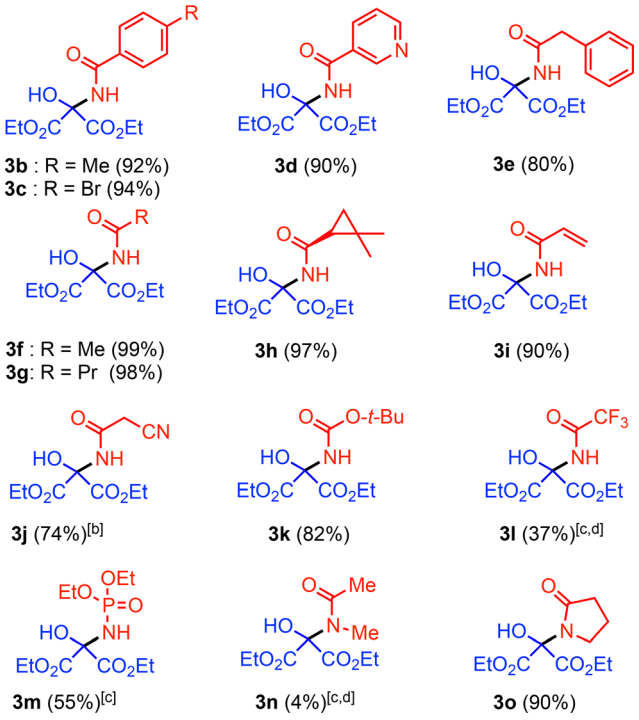
conditions to afford the corresponding *N*-acyl-*N*,*O*-hemiacetals **3b–g** in excellent yields. Importantly, this reaction could be applied to amides having versatile functional groups such as cyclopropyl, vinyl, cyano, and carbamate. In addition, the highly electron-deficient trifluoroacetamide **2l** and diethyl phosphoramidate **2m** were converted into *N*,*O*-hemiacetals in moderate yields, although a higher reaction temperature was required. Disappointingly, only a trace amount of the product was obtained when an acyclic secondary amide, *N*-methylacetamide **2n**, was used as a substrate. Contrary to this, a less sterically hindered cyclic secondary amide, 2-pyrrolidone **2o**, afforded the corresponding *N*,*O*-hemiacetal in 90% yield.

Subsequently, we studied the reaction of amides with various VTCs such as α,β-dioxo esters,[12] 1,2,3-triketones,[13] *tert*-butyl ethyl mesoxalate, and α,β-dioxo amide[12] (Table 3). In the case of the reaction of aryl-substituted dioxo ester **4** with butyramide **2g**, the corresponding product **10g** was isolated in 63% yield. However, the reaction of bulkier *tert*-butyl-substituted dioxo ester **5** with **2g**, resulted in a lower yield. In addition, from the reaction of the bulkier and less nucleophilic benzamide **2a**, only trace amounts of hemiacetal **11a** were obtained, with almost complete recovery of **5** and **2a**. 1,2,3-Triketones show a similar tendency, which is to say that sterically hindered 1,3-diphenyl-substituted substrate **6** gives the corresponding hemiacetals **12a**, **g** in low yield, whereas somewhat less hindered methyl phenyl-substituted triketone **7** gives hemiacetals **13a**, **g** in better isolated yield. These results indicate that

Table 2. Substrate scope for the synthesis of *N*-acyl-*N*,*O*-hemiacetals.[a]

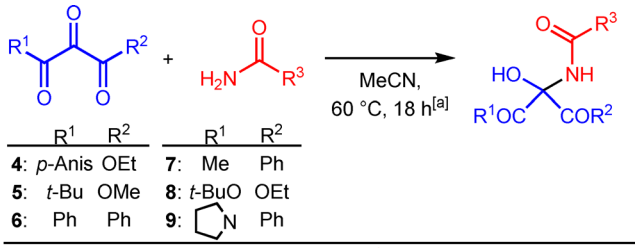


1 | 2b–o (1.2 equiv.) | 3b–o

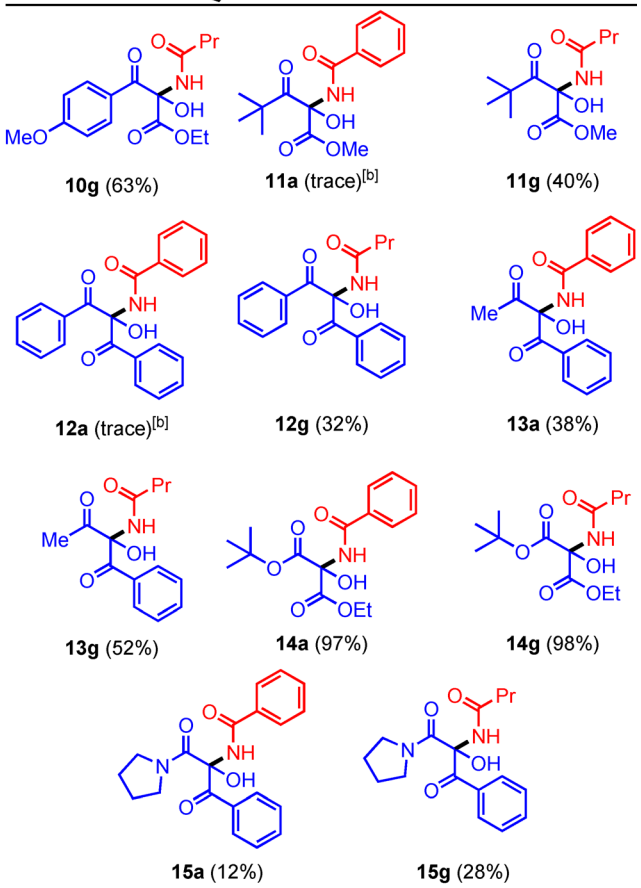


[a] *Reaction conditions:* **1** (0.5 mmol), **2** (0.6 mmol) in acetonitrile (2.5 mL) at 60 °C under air for 18 h. Yields refer to the isolated yield unless otherwise noted.
[b] In chloroform.
[c] At 120 °C in a sealed tube.
[d] Determined by ^{1}H NMR using 1,1,2,2-tetrachloroethane as the internal standard.

Table 3. Synthesis of *N*-acyl-*N*,*O*-hemiacetals using various VTCs.[a]



	R^1	R^2		R^1	R^2
4:	*p*-Anis	OEt	**7**:	Me	Ph
5:	*t*-Bu	OMe	**8**:	*t*-BuO	OEt
6:	Ph	Ph	**9**:	N	Ph

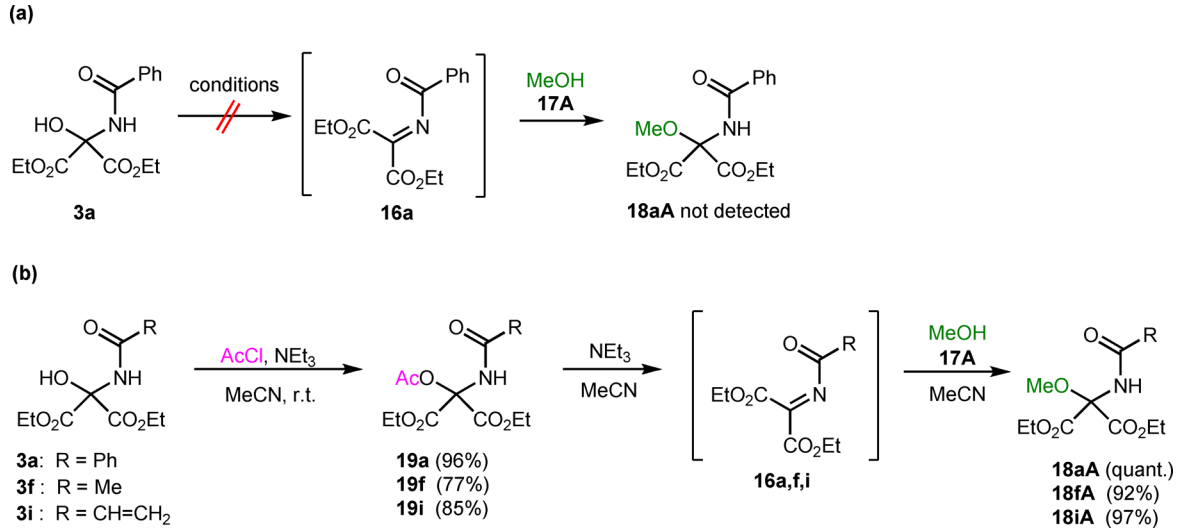


[a] *Reaction conditions:* VTCs (0.5 mmol), **2** (0.6 mmol) in acetonitrile (2.5 mL) at 60 °C under air for 18 h. Yields refer to the isolated yield unless otherwise noted.
[b] Determined by ^{1}H NMR and mass spectra of the reaction mixture.

the reactivity is strongly affected by the steric hindrance of the center carbonyl carbon of the substrate. Indeed, from the reaction of *tert*-butyl-substituted mesoxalate **8**, which is much less hindered than dioxo esters and triketones, both **14a** and **14g** were obtained in 97% and 98% yield, respectively. In the case of keto amide-derived tricarbonyl **9**, although only low yields of hemiacetals **15a**, **g** were obtained under these reaction conditions, a more thorough investigation could increase the yield.

After successful establishment of the synthetic method for α,α-difunctionalized *N*-acyl-*N*,*O*-hemiacetals **3**, we studied the generation of α,α-difunctionalized *N*-acylimines **16** *in situ via* dehydration of the obtained hemiacetals and trapping of **16** with methanol **17A** to give acetal **18aA** [Scheme 3 (a)]. Unfortunately, all of our attempts at this reaction, including heating and addition of acids, bases, and molecular sieves, failed.[14] It is noted that the whole amount of hemiacetal **3a** was decomposed to **1** and amide **2a** when potassium *tert*-butoxide was used as a base. This is presumably due to the relatively high acidity of the hydroxy group of **3a**. We then postulated that *O*-acetylation could protect the hydroxy group and increase the leaving ability.

As presented in Scheme 3 (b), the *O*-acetylation of several hemiacetals **3a**, **f**, **i** proceeded smoothly to afford the desired products **19a**,[15] **19f**, and **19i** in 96%, 77%, and 85% isolated yields, respectively.



Scheme 3. Generation and reaction of *N*-acylimines with alcohols.

Upon treatment with an excess amount of triethylamine, the desired α,α-difunctionalized *N*-acylimine **16** was generated *in situ*. The generation of *N*-acylimine **16** was confirmed by ^{13}C NMR spectroscopy in the case of **16f**: the signal corresponding to the sp^3 quaternary carbon at 81.7 ppm (C-2) disappeared, and a new signal from the imine sp^2 carbon appeared at 146.9 ppm (C-2′, Figure 1). *N*-Acylimine **16** was then trapped by methanol **17A** to obtain α,α-difunctionalized *N*-acyl-*N*,*O*-acetals **18** in excellent yield.

We then applied this method to other nucleophiles in order to examine the substrate scope (Table 4). Both *N*,*O*-acetals **18aB** and **18fB** were obtained in high yields. When the less nucleophilic *p*-methoxyphenol was used as the substrate, the corresponding adduct **18aC** can also be obtained in good yield. Furthermore, anilines **17D** and **17E** were also compatible in this reaction, providing **18aD** and **18aE** in good yields.

In order to further extend the substrate scope, we also investigated the reaction of generated imines with C-nucleophiles (Table 5). Electron-rich heteroaromatics reacted well and produced the desired adducts in good yields (**18aF**, **18fF**, **18iF**, **18aG**). Moreover, both a silyl enol ether and an enamine also reacted smoothly to give the products in moderate yields (**18aH** and **18aI**). These results suggest the broad applicability of our technique.

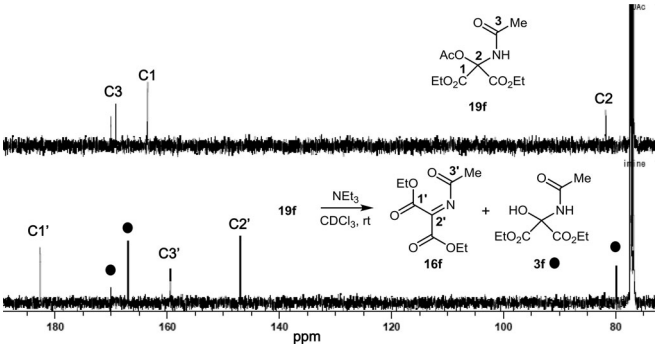
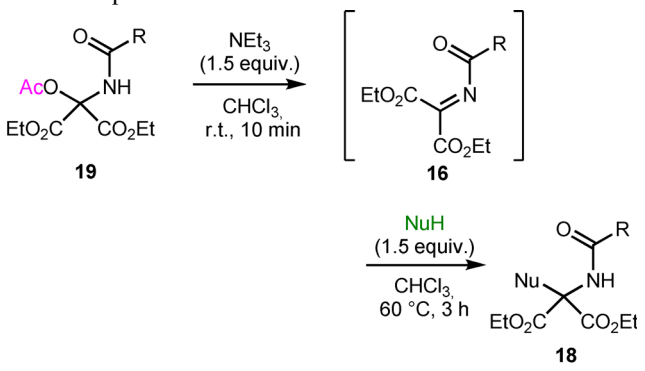
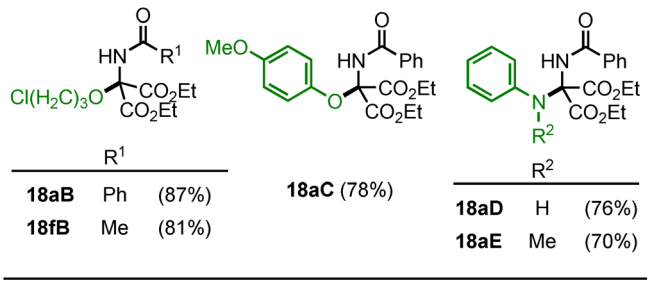


Figure 1. ^{13}C NMR monitoring of the generation of *N*-acylimine **16f**.

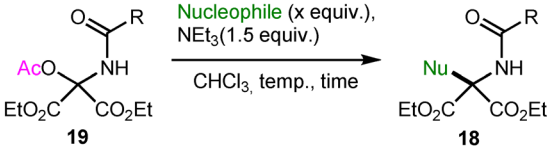
Table 4. The reaction of *N*-acylimine intermediate with various nucleophiles.[a]





[a] *Reaction conditions:* step 1, **19** (0.5 mmol), NEt_3 (0.75 mmol), chloroform (5 mL), room temperature under argon for 10 min; step 2, nucleophile (0.75 mmol) at 60 °C under argon for 3 h. Yields refer to the isolated yield.

Table 5. The reaction of *N*-acylimine intermediate with various C-nucleophiles.[a]

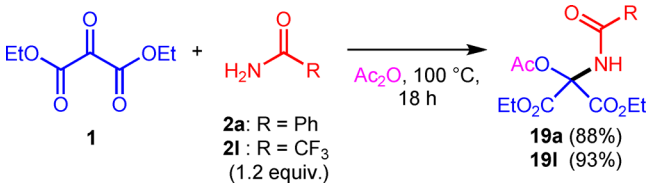


Nucleophile (equiv.) Conditions	Product			Nucleophile (equiv.) Conditions	Product
(1.2 equiv.) 60 °C, 3 h	**18aF**	Ph	(86%)	(5 equiv.) 60 °C, 16 h	**18aH** (60%)
	18fF	Me	(91%)		
	18iF	$CH=CH_2$	(72%)		
(1.2 equiv.) 60 °C, 3 h	**18aG** (61%)			(2 equiv.) rt, 10 min.	**18aI** (48%)

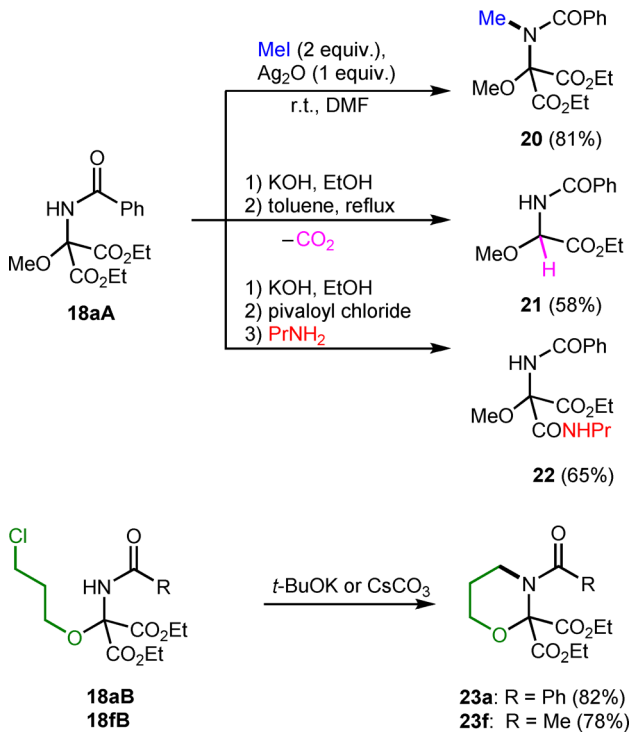
[a] The reactions were performed on a 0.5 mmol scale in 5 mL of chloroform under argon. The amount of nucleophile, reaction temperature, and reaction time required for each substrate are given. Yields refer to the isolated yield.

As a preliminary result, we performed the one-pot synthesis of *O*-acetylated *N*,*O*-acetal **19** from diethyl mesoxalate **1** with amide **2** to improve the practical utility. Based on the electrophilicities of VTC and acetic anhydride, we assumed that the amide will selectively react with VTC even in the presence of acetic anhydride. As expected, the desired product **19a** was obtained in 88% yield by the reaction of **1** with benzamide **2a** in acetic anhydride at 100 °C (Scheme 4). Most importantly, the low nucleophilic trifluoroacetamide **2l**, which afford the poor yield in the reaction with **1**, gave the *O*-acetylated product **19l** in 93% isolated yield.

Finally, the synthetic application of the obtained *N*,*O*-acetal **18aA** is shown in Scheme 5. The reaction of **18aA** with methyl iodide in the presence of silver(I) oxide afforded *N*-methylated product **20** in 81% isolated yield. It is noteworthy that this transformation is the formal introduction of an acyclic secondary amide into the VTC skeleton. The decarboxylated product **21**, which is regarded as an amino acid derivative, was obtained in moderate yield by the selective monohydrolysis and heating under toluene reflux conditions. The transformation of ester **18aA** into amide **22** was successfully achieved with 65% yield by selective saponification followed by condensation with propylamine *via* the acid anhydride. The intramolecular cyclization of 3-chloropropoxy-substituted *N*,*O*-acetals **18aB** and **18fB** with a base in acetonitrile led to *N*-acyl-1,3-oxazinanes **23a**[15] and **23f** in good yields. 1,3-Oxazinane skeletons are present in a number of biologically active compounds.[16] The present method enabled us to access the polyfunctionalized 1,3-oxazinane structure; thereby, it should find broad applications in organic synthesis.



Scheme 4. One-pot synthesis of *O*-acetyl-*N*,*O*-acetals **19**.



Scheme 5. Synthetic transformations of *N*-acyl-*N*,*O*-acetals **18**.

Conclusions

In conclusion, we have developed an efficient one-pot, metal-free method for the construction of α,α-difunctionalized *N*-acyl-*N*,*O*-hemiacetals **3** based on the nucleophilic addition of unactivated amides **2** to ketones. The hemiacetals could be easily synthesized by a simple procedure and were shelf-stable for extended periods under anhydrous conditions. The obtained *N*-

acyl-*N*,*O*-hemiacetals could be converted into α,α-difunctionalized *N*-acylimines **16** under mild reaction conditions by acetylation of the hydroxy group. In addition, a one-pot synthesis of *O*-acetyl-*N*-acyl-*N*,*O*-acetals **19** was also acheived. *O*-Acetylated compounds **19** showed quite good stability and were storable even under air. These results represent the high value of *O*-acetylated acetals **19** as precursors for synthetically useful and highly functionalized *N*-acylimines. The utility of the generated α,α-difunctionalized *N*-acylimine was successfully demonstrated by examples of the addition of various nucleophiles.

Experimental Section

General Information

^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-400 spectrometer (400 MHz and 100 MHz, respectively) in $CDCl_3$ using TMS as an internal standard. ^{1}H NMR data are reported as follows: chemical shift (δ, ppm), (chemical shift mutiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br s = broad singlet), coupling constant (Hz), integration. ^{13}C NMR data were reported in terms of chemical shift (δ, ppm). NMR signal assignments were based on additional 2D-NMR spectroscopy (e.g., COSY, NOESY, HSQC, and HMBC). A Shimadtu IR Spectrometer was used to record infrared spectra which are reported in frequency of absorption. Mass spectra were recorded on a JEOL JMS-Q1050GC. High-resolution mass spectra were obtained on an AB SCEIX Triplet TOF 4600 mass spectrometer. Melting points were recorded with a Yanaco micro-melting-points apparatus and were uncorrected. Products were purified by chromatography on silica gel.

Materials

Unless otherwise noted, all reagents were purchased from commercial sources and used without further purification. VTCs **4**–**9** were prepared according to the reported procedure.[12,13] The hydrate forms of VTCs were transformed to keto forms by azeotropic distillation with toluene just before use.

Typical Experimental Procedure for the Reaction of VTCs with Amides (Table 1. Entry 5, Table 2 and Table 3)

To an acetonitrile solution (3.0 mL) of VTC (0.5 mmol) in a round-bottom flask (10 mL), amide **2** (1.2 equiv., 0.6 mmol) was added, and the resultant mixture was heated at 60 °C for 18 h. Upon completion, the reaction mixture was concentrated under vacuum to give a residue, which was subjected to silica gel column chromatography using hexane/ethyl acetate = 1/1 as eluent affording the *N*,*O*-hemiacetals.

General Experimental Procedure for the *O*-Acetylation of 3: Method A [Scheme 3 (b)]

N,*O*-Hemiacetal **3** (1.0 mmol) was dissolved in 5 mL of dry acetonitrile, and the solution was cooled to 0 °C. Triethylamine (1.2 mmol) and acetyl chloride (1.2 mmol) were added, and the reaction mixture was stirred at ambient temperature for 1 h. Then 50 mL of water were added to the mixture, which was extracted with chloroform (3 × 20 mL). The extract was dried over magnesium sulfate and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (eluent: dichloromethane/ethyl acetate = 9/1) to afford the *O*-acetylated product **19**.

General Experimental Procedure for the Generation and Reaction of *N*-Acylimine 16 [Scheme 3 (b) and Table 4]

A flame-dried test tube was charged with the corresponding *N*,*O*-acetal **19** (0.5 mmol), molecular sieve 3 Å and anhydrous acetonitrile or chloroform (5 mL). Triethylamine (1.5 equiv., 0.75 mmol) was added and the solution was stirred at room temperature for 10 min. After the nucleophile (1.5 equiv., 0.75 mmol) was added, the reaction mixture was stirred at 60 °C for 3 h. Upon completion, the reaction mixture was evaporated and the residue was purified by silica gel column chromatography (eluent: hexane/ethyl acetate) to afford the corresponding pure compound **12**.

General Experimental Procedure for the Reaction of *N*-acylimine 16 with C-Nucleophiles (Table 5)

To a flame-dried test tube, the corresponding acetal **19** (0.5 mmol), molecular sieve 3 Å, nucleophile, and 2 mL of chloroform were added under argon. Then triethylamine (1.5 equiv., 0.75 mmol) was successively added and the mixture was stirred and heated. After completion of the reaction, water was added to the reaction mixture. The mixture was extracted with dichloromethane (2 × 5 mL), the combined organic phases were dried over anhydrous $MgSO_4$. Then, the solvent was removed under vacuum, and the residue was purified by silica gel column chromatography (eluent: hexane/ethyl acetate) to afford the product **18**.

Typical Experimental Procedure for the Synthesis of *N*,*O*-Acetals 19: Method B (Scheme 4)

To a solution of diethyl mesoxalate (**1**, 174 mg, 1 mmol) in acetic anhydride (2 mL), amide (1.2 mmol) was added under air. The resulting mixture was stirred at 100 °C for 18 h. After completion of the reaction, acetic anhydride was azeotropically removed with toluene. The residue was purified by recrystallization (hexane/chloroform) to afford the product **19**.

Experimental Procedure for the *N*-Methylation of Amide 18aA (Scheme 5)

N-Methylation of amide **18aA** (0.2 mmol scale) was performed according to the procedure described by Nair et al.[17] The crude product was purified by silica gel column

chromatography (hexane/ethyl acetate = 7/3) to afford **20** as yellow viscous liquid; yield: 52.3 mg (81%).

Experimental Procedure for the Decarboxylation of 18 (Scheme 5)

After selective monosaponification of compound **18aA** (0.2 mmol scale) according to the reported procedure by Koch et al.,[18] the decarboxylation proceeded under reflux in toluene for 1 h and gave the desired product **21** without any further purification as a yellow oil; yield: 27.5 mg (58%).

Experimental Procedure for the Transformation of Esters into Amide 22 (Scheme 5)

The compound **22** (0.2 mmol scale) was synthesized according to the reported procedure by Koch et al.[18] The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 1/1) to furnish a yellow viscous liquid; yield: 41.8 mg (65%).

Experimental Procedure for the Construction of Oxazinane 23 (Scheme 5)

A magnetic stirring bar, and anhydrous acetonitrile (2 mL) were placed in the test tube under argon. Then, 1 equivalent of base (potassium *tert*-butoxide for **18aB**, $CsCO_3$ for **18fB**: each reaction was performed on a 0.2 mmol scale) was added. The mixture was stirred at 60 °C for 6 h. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 9/1).

Diethyl 2-benzamido-2-hydroxymalonate (3a): yield: 144.5 mg (98%); white solid; mp 50.5–51.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (t, J = 7.2 Hz, 3H), 1.30 (t, J = 7.2 Hz, 3H), 4.34 (q, J = 7.2 Hz, 2H), 4.34 (q, J = 7.2 Hz, 2H), 5.22 (s, 1H), 7.45–7.49 (m, 2H), 7.54–5.58 (m, 1H), 7.83–7.85 (m, 2H), 7.99 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9 (CH_3), 63.7 (CH_2), 80.2 (C), 127.3 (CH), 128.7 (CH), 132.5 (C), 132.5 (CH), 166.8 (C), 167.1 (C); IR (ATR): ν = 1651, 1744, 3327 cm^{-1}; HR-MS (ESI-TOF): m/z = 318.0962, calcd. for $C_{14}H_{17}NNaO_6$ $[M+Na]^+$: 318.0948.

Diethyl 2-hydroxy-2-(4-methylbenzamido)malonate (3b): yield: 142.1 mg (92%); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.23 (t, J = 7.2 Hz, 6H), 2.41 (s, 3H), 4.35 (q, J = 7.2 Hz, 4H), 5.21 (s, 1H), 7.26 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 8.0 Hz, 2H) 7.94 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9 (CH_3), 21.5 (CH_3), 63.6 (CH_2), 80.3 (C), 127.4 (CH), 129.4 (CH), 129.7 (C), 143.2 (C), 166.8 (C), 167.2 (C); IR (ATR): ν = 1640, 1740, 3341 cm^{-1}; HR-MS (ESI-TOF): m/z = 337.1560, calcd. for $C_{15}H_{23}N_2O_6$ $[M+NH_4]^+$; 327.1556.

Diethyl 2-hydroxy-2-(4-bromobenzamido)malonate (3c): yield: 175.3 mg (94%); white solid; mp 36.5–37.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (t, J = 7.2 Hz, 3H), 1.30 (t, J = 7.2 Hz, 3H), 4.33 (q, J = 7.2 Hz, 2H), 4.34 (q, J = 7.2 Hz, 2H), 5.21 (s, 1H), 7.60 (d, J = 8.4 Hz, 2H), 7.70 (d, J = 8.4 Hz, 2H), 7.95 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9 (CH_3), 63.8 (CH_2), 80.2 (C),127.4 (C), 129.0 (CH), 131.4 (C), 132.1 (CH), 165.9 (C), 167.0 (C); IR (ATR): ν = 1639, 1732, 1755, 3350 cm^{-1}; HR-MS (ESI-TOF): m/z = 324.0240, calcd. for $C_{14}H_{17}BrNO_6$ $[M+H]^+$; 374.0239.

Diethyl 2-hydroxy-2-(nicotinamido)malonate (3d): yield: 133.1 mg (90%); white solid; mp 129.0–129.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (t, J = 7.2 Hz, 6H), 4.37 (q, J = 7.2 Hz, 4H), 5.21 (s, 1H), 7.42 (dd, J = 4.8, 8.0 Hz, 1H), 8.01 (br s, 1H), 8.14 (dd, J = 1.6, 8.0 Hz, 1H), 8.79 (dd, J = 1.6, 4.8 Hz, 1H), 9.07 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9 (CH_3), 63.9 (CH_2), 80.1 (C), 123.6 (CH), 128.4 (C), 135.2 (CH), 148.5 (CH), 153.2 (CH), 165.0 (C), 166.9 (C); IR (ATR): ν = 1672, 1742, 3310 cm^{-1}; HR-MS (ESI-TOF): m/z = 297.1082, calcd. for $C_{13}H_{17}N_2O_6$ $[M+H]^+$; 297.1081.

Diethyl 2-hydroxy-2-(2-phenylacetamido)malonate (3e): yield: 123.5 mg (80%); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, J = 7.2 Hz, 3H), 1.24 (t, J = 7.2 Hz, 3H), 3.61 (s, 2H), 4.25 (q, J = 7.2 Hz, 2H), 4.28 (q, J = 7.2 Hz, 2H), 5.06 (s, 1H), 7.38–7.26 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8 (CH_3), 43.2 (CH_2), 63.6 (CH_2), 79.9 (C), 127.5 (CH), 129.0 (CH), 129.3 (CH), 133.8 (C), 166.8 (C), 171.0 (C); IR (NaCl): ν = 1656, 1747, 3303 cm^{-1}; HR-MS (ESI-TOF): m/z = 310.1298, calcd. for $C_{15}H_{20}NO_6$ $[M+H]^+$; 310.1291.

Diethyl 2-acetamido-2-hydroxymalonate (3f): yield: 115.4 mg (>99%); white solid; mp 61.3–62.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (t, J = 7.1 Hz, 6H), 2.06 (s, 3H), 4.32 (q, J = 7.1 Hz, 4H), 5.07 (s, 1H), 7.31 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9 (CH_3), 22.8 (CH_3), 63.6 (CH_2), 79.9 (C), 166.9 (C), 170.1 (C); IR (NaCl): ν = 1673, 1748, 3369 cm^{-1}; HR-MS (ESI-TOF): m/z = 256.0799, calcd. for $C_9H_{15}NNaO_6$ $[M+Na]^+$; 256.0792.

Diethyl 2-butyramido-2-hydroxymalonate (3g): yield: 127.8 mg (98%); white solid; mp 81.0–81.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (t, J = 7.2 Hz, 3H), 1.29 (t, J = 7.2 Hz, 3H), 1.29 (t, J = 7.2 Hz, 3H), 1.67 (tq, J = 7.2, 7.2 Hz, 2H), 2.23 (t, J = 7.2 Hz, 2H), 4.31 (q, J = 7.2 Hz, 2H), 4.32 (q, J = 7.2 Hz, 2H), 5.06 (s, 1H), 7.27 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.5 (CH_3), 13.9 (CH_3), 18.6 (CH_2), 37.9 (CH_2), 63.6 (CH_2), 79.9 (C), 167.1 (C), 173.1 (C); IR (NaCl): ν = 1670, 1748, 3372 cm^{-1}; HR-MS (EI): m/z = 284.1111, calcd. for $C_{11}H_{19}NNaO_6$ $[M+Na]^+$: 284.1105.

Diethyl (*R*)-2-(2,2-dimethylcyclopropane-1-carboxamido)-2-hydroxymalonate (3h): yield: 139.0 mg (97%); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80 (dd, J = 4.8, 8.0 Hz, 1H), 1.11 (dd, J = 4.8, 4.8 Hz, 1H), 1.15 (s, 3H), 1.17 (s, 3H), 1.29 (t, J = 7.2 Hz, 6H), 1.36 (dd, J = 4.8, 8.0 Hz, 1H), 4.30 (t, J = 7.2 Hz, 4H), 5.07 (s, 1H), 7.39 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9 (CH_3), 18.5 (CH), 20.9 (CH_2), 23.2 (C), 27.0 (CH_3), 28.4 (CH_3), 63.5 (CH_2), 79.9 (C), 167.1 (C), 167.3 (C), 171.7 (C); IR: ν = 1670, 1742, 3337; HR-MS (ESI-TOF): m/z = 288.1433, calcd. for $C_{13}H_{22}NO_6$ $[M+H]^+$; 288.1447.

Diethyl 2-acrylamido-2-hydroxymalonate (3i): yield: 110.1 mg (90%); white solid; mp 61.2–61.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (t, J = 7.1 Hz, 6H), 4.33 (q, J = 7.1 Hz, 4H), 5.12 (s, 1H), 5.77 (d, J = 10.3 Hz, 1.1 Hz, 1H), 6.16 (dd, J = 17.0 Hz, 10.3 Hz, 1H), 6.34 (d, J = 17.0 Hz, 1.1 Hz, 1H), 7.38 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9 (CH_3), 63.7 (CH_2), 80.0 (C), 128.8 (CH), 129.4 (CH_2), 165.0 (C), 166.9 (C); IR (ATR): ν = 1628, 1661, 1736, 3345 cm^{-1}; HR-MS (ESI-TOF): m/z = 268.0784, calcd. for $C_{10}H_{15}NNaO_6$ $[M+Na]^+$: 268.0791.

Diethyl 2-(2-cyanoacetamido)-2-hydroxymalonate (3j): yield: 95.5 mg (74%); white solid; mp 102.5–103.0 °C; ^{1}H NMR ($CDCl_3$): δ = 1.31 (t, J = 7.2 Hz, 6H), 3.43 (s, 2H),

4.34 (q, J=7.2 Hz, 4H), 5.05 (s, 1H), 7.82 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.9 (CH_3), 25.9 (CH_2), 64.1 (CH_2), 79.8 (C), 113.3 (C), 160.9 (C), 166.3 (C); IR (ATR): ν=1674, 1751, 3356 cm^{-1}; HR-MS (ESI-TOF): m/z=281.0742, calcd. for $C_{10}H_{14}N_2NaO_6$ $[M+Na]^+$: 281.0744.

Diethyl 2-[(*tert*-butoxycarbonyl)amino]-2-hydroxymalonate (3k): yield: 118.9 mg (82%); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.29 (t, J=7.2 Hz, 6H), 1.44 (s, 9H), 4.26–4.37 (m, 4H), 4.95 (br s, 1H), 6.42 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.9 (CH_3), 28.2 (CH_3), 63.5 (CH_2), 80.4 (C), 81.3 (C), 167.0 (C), 167.2 (C); IR (ATR); ν=1717, 1744, 3439 cm^{-1}; HR-MS (ESI-TOF): m/z=309.1676, calcd. for $C_{12}H_{25}N_2O_7$ $[M+NH_4]^+$; 309.1662.

Diethyl 2-hydroxy-2-(2,2,2-trifluoroacetamido)malonate (3l): During isolation by silica gel column chromatography, the product was easily decomposed to starting materials; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.30 (t, J=7.2 Hz, 6H), 4.34 (q, J=7.2 Hz, 4H), 5.12 (br s, 1H), 8.09 (br s, 1H); MS: m/z=287. Satisfactory analytical data were not obtained because of the instability of **3l**.

Diethyl 2-[(diethoxyphosphoryl)amino]-2-hydroxymalonate (3m): yield: 89.7 mg (55%); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.31 (t, J=7.2 Hz, 6H), 1.32 (t, J=7.2 Hz, 3H), 1.33 (t, J=7.2 Hz, 3H), 4.09 (q, J=7.2 Hz, 2H), 4.11 (q, J=7.2 Hz, 2H), 4.32 (q, J=7.2 Hz, 4H), 4.76 (J_{H-P}=9.6 Hz, 1H), 5.04 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.9 (CH_3), 16.0 (CH_3, d, $J_{C,P}$=7.0 Hz), 62.8 (CH_2 d, $J_{C,P}$=5.0 Hz), 63.5 (CH_2), 81.5 (C, d, $J_{C,P}$=3.0 Hz), 168.0 (C, d, $J_{C,P}$=9.0 Hz); IR (ATR): ν=1742, 3337 cm^{-1}; HR-MS (ESI-TOF): m/z=350.0975, calcd. for $C_{11}H_{22}NNaO_8P$ $[M+Na]^+$: 350.0975.

Diethyl 2-hydroxy-2-(*N*-methylacetamido)malonate (3n): yield: 5.0 mg (4%); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.30–1.40 (m, 6H), 2.35 (s, 1H), 3.26 (s, 1H), 4.31–4.39 (m, 4H), 4.74 (s, 1H); MS: m/z=247. Satisfactory analytical data were not obtained because of the instability of **3n**.

Diethyl 2-hydroxy-2-(2-oxopyrrolidin-1-yl)malonate (3o): yield: 116.6 mg (90%); mixture of two conformers; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.32 (t, J=7.2 Hz, 6H), 2.10 (tt, J=7.6, 7.6 Hz, 2H), 2.41 (t, J=7.6 Hz, 2H), 3.62 (t, J=7.6 Hz, 2H), 4.33 (q, J=7.2 Hz, 4H), 5.04 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): major: δ=13.9 (CH_3), 18.5 (CH_2), 30.9 (CH_2), 45.2 (CH_2), 63.4 (CH_2), 83.4 (C), 166.8 (C), 176.9 (C); minor δ=13.9 (CH_3), 20.9 (CH_2), 29.8 (CH_2), 42.1 (CH_2), 63.5 (CH_2), 90.2 (C), 168.5 (C), 179.0 (C); IR (NaCl): ν=1684, 1749, 3367 cm^{-1}; HR-MS (ESI-TOF): m/z=282.0936, calcd. for $C_{11}H_{17}NNaO_6$ $[M+Na]^+$: 282.0948.

Ethyl 2-butyramido-2-hydroxy-3-(4-methoxyphenyl)-3-oxopropanoate (10g): yield: 101.8 mg (63%); white solid; mp 65.4–66.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.91 (t, J=7.2 Hz, 3H), 1.12 (t, J=7.2 Hz, 3H), 1.60–1.68 (m, 2H), 2.23 (t, J=7.2 Hz, 2H), 3.88 (s, 3H), 4.15–4.25 (m, 2H), 5.80 (s, 1H), 6.91 (d, J=8.8 Hz, 2H), 7.77 (br s, 1H), 8.15 (d, J=8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.6 (CH_3), 13.8 (CH_3), 18.6 (CH_2), 38.0 (CH_2), 55.6 (CH_3), 63.3 (CH_2), 83.0 (C), 113.9 (CH), 124.8 (C), 132.6 (CH), 164.5 (C), 168.8 (C), 173.2 (C), 187.8 (C); IR (ATR): ν=1647, 1717, 3329 cm^{-1}; HR-MS (ESI-TOF): m/z=346.1246, calcd. for $C_{16}H_{21}NNaO_6$ $[M+Na]^+$; 346.1261.

Methyl 2-benzamido-2-hydroxy-4,4-dimethyl-3-oxopentanoate (11a): ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.25 (s, 9H), 3.84 (s, 3H), 5.11–5.27 (br, 1H), 7.20–7.42 (m, 2H), 7.42 (br s, 1H), 7.45–7.47 (m, 1H), 7.81–7.85 (m, 2H); MS: m/z=293. Satisfactory analytical data were not obtained because of the instability of **11a**.

Methyl 2-butyramido-2-hydroxy-4,4-dimethyl-3-oxopentanoate (11g): yield: 51.8 mg (40%); white solid; mp 81.0–81.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.95 (t, J=7.2 Hz, 3H), 1.24 (s, 9H), 1.61–1.70 (m, 2H), 2.22 (t, J=7.2 Hz, 2H), 3.81 (s, 3H), 5.68 (br s, 1H), 7.50 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.6 (CH_3), 18.6 (CH_2), 27.7 (CH_3), 38.1 (CH_2), 44.5 (C), 53.6 (CH_3), 83.7 (C), 168.3 (C), 173.5 (C), 205.4 (C); IR (ATR): ν=1649, 1719, 1744, 3329 cm^{-1}; HR-MS (ESI-TOF): m/z=282.1314, calcd. for $C_{12}H_{21}NNaO_5$ $[M+Na]^+$: 282.1312.

2-Butyramido-1,3-diphenyl-2-hydroxypropane-1,3-dione (12g): yield: 51.8 mg (32%); white solid; mp 121.1–121.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.76 (t, J=7.2 Hz, 3H), 1.52 (tq, J=7.2, 7.2 Hz, 2H), 2.17 (t, J=7.2 Hz, 2H), 6.23 (br s, 1H), 7.35 (dd, J=7.2, 7.2 Hz, 4H), 7.50 (t, J=7.2 Hz, 2H), 7.99 (d, J=7.2 Hz, 4H), 8.09 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.4 (CH_3), 18.5 (CH_2), 38.1 (CH_2), 86.8 (C), 128.6 (CH), 130.0 (CH), 132.9 (C), 134.2 (CH), 172.6 (C), 192.3 (C); IR (NaCl): ν=1683, 1732, 3392 cm^{-1}; HR-MS (ESI-TOF): m/z=345.1211, calcd. for $C_{19}H_{19}NNaO_4$ $[M+Na]^+$: 348.1206.

2-Benzamido-2-hydroxy-1-methyl-3-phenylpropane-1,3-dione (13a): yield: 56.4 mg (38%); white solid; mp 117.5–118.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.21 (s, 3H), 6.14 (brs, 1H), 7.40–7.47 (m, 4H), 7.52–7.60 (m, 2H), 7.80 (d, J=7.2 Hz, 2H), 8.07 (d, J=7.2 Hz, 2H), 8.44 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=23.7 (CH_3), 87.5 (C), 127.3 (CH), 128.4 (CH), 128.8 (CH), 129.7 (CH), 132.2 (C), 132.5 (CH), 132.5 (C), 166.4 (C), 191.8 (C), 200.7 (C); IR (NaCl): ν=1683, 1732, 3392 cm^{-1}; HR-MS (ESI-TOF): m/z=320.0892, calcd. for $C_{17}H_{15}NNaO_4$ $[M+Na]^+$: 320.0893.

2-Butyramido-2-hydroxy-1-methyl-3-phenylpropane-1,3-dione (13g): yield: 68.4 mg (52%); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.81 (t, J=7.4 Hz, 3H), 1.55 (tq, J=7.2, 7.4 Hz, 2H), 2.15 (s, 3H), 2.18 (t, J=7.2 Hz, 2H), 6.07 (brs, 1H), 7.41 (dd, J=7.2, 7.2 Hz, 2H), 7.58 (t, J=7.2 Hz, 1H), 8.00 (d, J=7.2 Hz, 2H), 8.09 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.4 (CH_3), 18.5 (CH_3), 23.7 (CH_2), 37.8 (CH_2), 87.2 (C), 128.7 (CH), 129.6 (CH), 132.3 (C), 134.4 (CH), 172.9 (C), 191.9 (C); IR (NaCl): ν=1652, 1680, 3292 cm^{-1}; HR-MS (ESI-TOF): m/z=286.1056, calcd. for $C_{14}H_{17}NNaO_4$ $[M+Na]^+$: 286.1050.

1-(*tert*-Butyl)-3-ethyl 2-benzamido-2-hydroxymalonate (14a): yield: 156.8 mg (97%); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.31 (t, J=7.2 Hz, 3H), 1.50 (s, 9H), 4.32–4.38 (m, 2H), 5.16 (s, 1H), 7.46 (dd, J=7.2, 7.2 Hz, 2H), 7.55 (t, J=7.2 Hz, 1H), 7.83 (d, J=7.2 Hz, 2H), 7.95 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=14.0 (CH_3), 27.7 (CH_3), 63.4 (CH_2), 80.3 (C), 84.9 (C), 127.3 (CH), 128.7 (CH), 132.3 (CH), 132.8 (C), 165.9 (C), 166.6 (C), 167.5 (C); IR (NaCl): ν=1681, 1747, 3425 cm^{-1}; HR-MS (ESI-TOF): m/z=346.1254. calcd. for $C_{16}H_{21}NNaO_6$ $[M+Na]^+$: 346.1261.

1-(*tert*-Butyl)-3-ethyl 2-butyramido-2-hydroxymalonate (14g): yield: 141.7 mg (98%); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.96 (t, J=7.2 Hz, 3H), 1.29 (t, J=7.2 Hz, 3H), 1.48 (s, 9H), 1.64–1.70 (m, 2H), 2.22 (t, J=

7.2 Hz, 2H), 4.29–4.35 (m, 2H), 5.05 (br s, 1H), 7.25 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.5 (CH_3), 13.9 (CH_3), 18.7 (CH_2), 27.6 (CH_3), 37.9 (CH_2), 63.2 (CH_2), 79.9 (C), 84.6 (C), 165.8 (C), 167.4 (C), 172.7 (C); IR (NaCl): ν= 1673, 1743, 3374 cm^{-1}; HR-MS (ESI-TOF): m/z=312.1408, calcd. for $C_{13}H_{23}NNaO_6$ $[M+Na]^+$: 312.1418.

2-Benzamide-2-hydroxy-1-pyrrolidinopropane-1,3-dione (15a): yield: 21.1 mg (12%); white solid; mp 135.9–136.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.68–1.72 (m, 1H), 1.77–1.84 (m, 3H), 3.06–3.11 (m, 1H), 3.54–3.60 (m, 2H), 3.64–3.67 (m, 1H), 3.12 (br s, 1H), 7.39–7.45 (m, 4H), 7.50 (t, J= 7.3 Hz, 1H), 7.55 (t, J=7.4 Hz, 1H), 7.79 (d, J=7.2 Hz, 2H), 8.16 (d, J=7.2 Hz, 2H), 9.00 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=23.2 (CH_2), 26.4 (CH_2), 46.8 (CH_2), 48.5 (CH_2), 83.5 (C), 127.3 (CH), 128.7 (CH), 128.8 (CH), 129.7 (CH), 132.2 (CH), 132.4 (C), 133.1 (C), 134.3 (CH), 164.3 (C), 165.9 (C), 192.1 (C); IR (NaCl): ν=1636, 3376 cm^{-1}; HR-MS (ESI-TOF): m/z=375.1320, calcd. for $C_{20}H_{20}N_2NaO_4$ $[M+Na]^+$: 375.1315.

2-Butyramide-2-hydroxy-1-pyrrolidinopropane-1,3-dione (15g): yield: 44.5 mg (28%); white solid; mp 102.0–103.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.77 (t, J=7.4 Hz, 3H), 1.51 (tq, J=7.2, 7.4 Hz, 2H), 1.61–1.90 (m, 4H), 2.08–2.19 (m, 2H), 3.01–3.09 (m, 1H), 3.50–3.54 (m, 2H), 3.55–3.68 (m, 1H), 5.96 (brs, 1H), 7.42 (dd, J=7.2, 7.3 Hz, 4H), 7.57 (t, J=7.3 Hz, 2H), 8.10 (d, J=7.2 Hz, 4H), 8.24 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.4 (CH_3), 18.5 (CH_2), 23.1 (CH_2), 26.4 (CH_2), 38.1 (CH_2), 46.7 (CH_2), 48.4 (CH_2), 83.3 (C), 128.6 (CH), 129.5 (CH), 132.5 (C), 134.1 (CH), 164.1 (C), 172.3 (C), 192.2 (C); IR (NaCl): ν=1637, 2876, 2965, 3336 cm^{-1}; HR-MS (ESI-TOF): m/z=341.1480, calcd. for $C_{17}H_{22}N_2NaO_4$ $[M+Na]^+$: 341.1472.

Diethyl 2-benzamido-2-methoxymalonate (18aA): yield: 154.7 mg (>99%); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ =.32 (t, J=7.2 Hz, 6H), 3.42 (s, 3H), 4.33–4.39 (m, 4H), 7.48 (dd, J=7.2, 7.2 Hz, 2H), 7.55 (t, J=7.2 Hz, 1H), 7.82 (br s, 1H), 7.87 (d, J=7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=14.0 (CH_3), 52.4 (CH_3), 63.2 (CH_2), 84.7 (C), 127.4 (CH), 128.8 (CH), 132.5 (CH), 132.8 (C), 165.7 (C), 166.3 (C); IR (NaCl): ν=1683, 1747, 1775, 3411 cm^{-1}; HR-MS (ESI-TOF): m/z=332.1097, calcd. for $C_{15}H_{19}NNaO_6$ $[M+Na]^+$: 332.1105.

Diethyl 2-acetamido-2-methoxymalonate (18fA): yield: 113.7 mg (92%); yellow viscous liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.30 (t, J=7.2 Hz, 6H), 2.12 (s, 3H), 3.35 (s, 3H), 4.31 (q, J=7.2 Hz, 4H), 7.24 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.8 (CH_3), 22.8 (CH_3), 52.0 (CH_3), 62.9 (CH_2), 84.3 (C), 165.5 (C), 169.6 (C); IR (NaCl): ν= 1682, 1750, 3353 cm^{-1}; HR-MS (ESI-TOF): m/z=270.0942, calcd. for $C_{10}H_{17}NNaO_6$ $[M+Na]^+$: 270.0948.

Diethyl 2-acrylamido-2-methoxymalonate (18iA): yield: 125.8 mg (98%); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.30 (t, J=7.2 Hz, 6H), 3.34 (s, 3H), 4.33 (q, J= 7.2 Hz, 4H), 5.78 (dd, J=1.2, 10.4 Hz, 1H), 6.23 (dd, J= 10.4, 17.2 Hz, 1H), 6.38 (d, J=17.2 Hz, 2H), 7.21 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.9 (CH_3), 52.3 (CH_3), 63.1 (CH_2), 84.4 (C), 128.8 (CH_2), 129.5 (C), 164.5 (C), 165.5 (C); IR (NaCl): ν=1632, 1692, 1748, 3347 cm^{-1}; HR-MS (ESI-TOF): m/z=282.0944, calcd. for $C_{11}H_{17}NNaO_6$ $[M+Na]^+$: 282.0948.

Diethyl 2-benzamido-2-(3-chloropropoxy)malonate (18aB): yield: 161.7 mg (87%); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.31 (t, J=7.2 Hz, 6H), 2.08 (tt, J= 6.0, 6.0 Hz, 2H), 3.68 (t, J=6.0 Hz, 2H), 3.75 (t, J=6.0 Hz, 2H), 4.31–4.38 (m, 4H), 7.48 (dd, J=7.2, 7.2 Hz, 2H), 7.56 (t, J=7.2 Hz, 1H), 7.85 (d, J=7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=14.0 (CH_3), 32.4 (CH_2), 41.7 (CH_2), 61.2 (CH_2), 63.2 (CH_2), 84.2 (C), 127.4 (CH), 128.8 (CH), 132.4 (CH), 132.8 (C), 165.7 (C), 166.4 (C); IR (ATR): ν= 1682, 1746 cm^{-1}; HR-MS (ESI-TOF): m/z=394.1032, calcd. for $C_{17}H_{22}ClNNaO_6$ $[M+Na]^+$: 394.1028.

Diethyl 2-acetamido-2-(3-chloropropoxy)malonate (18fB): yield: 125.4 mg (81%); colorless viscous liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.29 (t, J=6.8 Hz, 6H), 2.03–2.09 (m, 2H), 2.10 (s, 3H), 3.65–3.68 (m, 4H), 4.26–4.33 (m, 4H), 7.14 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.9 (CH_3), 23.0 (CH_3), 32.3 (CH_2), 41.8 (CH_2), 60.8 (CH_2), 63.1 (CH_2), 83.9 (C), 165.6 (C), 169.5 (C); IR (NaCl): ν=1684, 1749, 3318 cm^{-1}; HR-MS (ESI-TOF): m/z=332.0873, calcd. for $C_{12}H_{20}ClNNaO_6$ $[M+Na]^+$: 332.0871.

Diethyl 2-benzamido-2-(4-methoxyphenoxy)malonate (18aC): yield: 156.6 mg (78%); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.32–1.36 (m, 6H), 3.72 (s, 3H), 4.31–4.48 (m, 2H), 6.74 (d, J=6.8 Hz, 2H), 6.93 (d, J= 6.8 Hz, 2H), 7.43 (dd, J=7.2, 7.2 Hz, 2H), 7.54 (t, J= 7.2 Hz, 1H), 7.74 (d, J=7.2 Hz, 2H), 7.75 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.9 (CH_3), 55.4 (CH_3), 63.3 (CH_2), 85.7 (C), 114.3 (CH), 123.9 (CH), 127.3 (CH), 128.8 (CH), 132.5 (CH), 132.7 (C), 146.2 (C), 156.9 (C), 165.3 (C), 166.1 (C); IR (NaCl): ν=1682, 1747, 3416 cm^{-1}; HR-MS (ESI-TOF): m/z=424.1375, calcd. for $C_{21}H_{23}NNaO_7$ $[M+Na]^+$: 424.1367.

Diethyl 2-benzamido-2-(phenylamino)malonate (18aD): yield: 139.6 mg (76%); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.21 (t, J=7.2 Hz, 6H), 4.25–4.36 (m, 4H), 5.91 (br s, 1H), 6.73 (d, J=7.4 Hz, 2H), 6.78 (t, J=7.4 Hz, 1H), 7.14 (dd, J=7.4, 7.4 Hz, 2H), 7.42 (dd, J=7.2, 7.2 Hz, 2H), 7.50 (t, J=7.2 Hz, 1H), 7.76 (d, J=7.2 Hz, 2H), 8.05 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.9 (CH_3), 63.7 (CH_2), 72.7 (C), 115.7 (CH), 119.9 (CH), 127.2 (CH), 128.6 (CH), 129.1 (CH), 132.1 (CH), 133.2 (C), 143.0 (C), 166.2 (C), 167.3 (C); IR (NaCl): ν=1672, 1739, 3409 cm^{-1}; HR-MS (ESI-TOF): m/z=393.1402, calcd. for $C_{20}H_{22}N_2NaO_5$ $[M+Na]^+$: 393.1421.

Diethyl 2-Benzamido-2-[methyl(phenyl)amino]malonate (18aE): yield: 130.9 mg (70%); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.19 (t, J=7.2 Hz, 6H), 3.16 (s, 3H), 4.12–4.38 (m, 4H), 7.11–7.17 (m, 1H), 7.20–7.29 (m, 4H), 7.47 (dd, J=7.2, 7.2 Hz, 2H), 7.55 (t, J=7.2 Hz, 1H), 7.74 (br s, 1H), 7.84 (d, J=7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.8 (CH_3), 40.3 (CH_3), 62.8 (CH_2), 79.1 (C), 125.9 (CH), 126.7 (CH), 127.1 (CH), 128.7 (CH), 128.9 (CH), 132.0 (CH), 133.7 (C), 148.8 (C), 166.2 (C), 166.8 (C); IR (NaCl): ν=1681, 1741, 1771, 3407 cm^{-1}; HR-MS (ESI-TOF): m/z=407.1571, calcd. for $C_{21}H_{24}N_2NaO_5$ $[M+Na]^+$: 407.1577.

Diethyl 2-benzamido-2-(1*H*-pyrrol-2-yl)malonate (18aF): yield: 148.1 mg (86%); colorless crystals; mp 104.8–105.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.29 (t, J=7.2 Hz, 6H), 4.31–4.39 (m, 4H), 6.01–6.03 (m, 1H), 6.09–6.12 (m, 1H), 6.78–6.80 (m, 1H), 7.45 (dd, J=7.2, 7.2 Hz, 2H), 7.54 (t, J= 7.2 Hz, 1H), 7.83 (d, J=7.2 Hz, 2H), 7.96 (br s, 1H), 9.75 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.9 (CH_3), 63.2 (CH_2), 64.9 (C), 107.3 (CH), 107.3 (CH), 118.9 (CH),

126.8 (C), 127.2 (CH), 128.7 (CH), 132.2 (CH), 133.0 (C), 166.9 (C), 166.9 (C); IR (ATR): ν = 1651, 1728, 3411 cm^{-1}; HR-MS (ESI-TOF): m/z = 367.1265, calcd. for $C_{18}H_{20}N_2NaO_5$ $[M+Na]^+$: 367.1264.

Diethyl 2-acetamido-2-(1*H*-pyrrol-2-yl)malonate (18fF): yield: 128.5 mg (91%); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.28 (t, J = 7.0 Hz, 6H), 2.04 (s, 3H), 4.31 (q, J = 7.0 Hz, 4H), 5.96 (dd, J = 1.2, 2.0 Hz, 1H), 6.09 (dd, J = 2.0, 2.8 Hz, 1H), 6.76 (dd, J = 1.2, 2.8 Hz, 1H), 7.29 (br s, 1H), 9.60 (br s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 13.9 (CH_3), 22.9 (CH_3), 63.1 (CH_2), 64.8 (C), 107.1 (CH), 107.2 (CH), 118.9 (CH), 127.0 (C), 166.8 (C), 170.1 (C); IR (NaCl): ν = 1668, 1740, 3398 cm^{-1}; HR-MS (ESI-TOF): m/z = 305.1110, calcd. for $C_{13}H_{18}N_2NaO_5$ $[M+Na]^+$: 305.1108.

Diethyl 2-acrylamido-2-(1*H*-pyrrol-2-yl)malonate (18iF): yield: 105.9 mg (72%); brown solid; mp 60.2–61.0 °C; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.29 (t, J = 7.2 Hz, 6H), 4.33 (q, J = 7.2 Hz, 4H), 5.73 (dd, J = 1.6, 10.0 Hz, 1H), 5.95–5.97 (m, 1H), 6.09 (dd, J = 2.8, 6.4 Hz, 1H), 6.19 (dd, J = 10.0, 17.2 Hz, 1H), 6.31 (dd, J = 1.6, 17.2 Hz, 1H), 6.76–6.78 (m, 1H), 7.36 (s, 1H), 9.65 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 13.9 (CH_3), 63.3 (CH_2), 64.8 (C), 107.3 (CH), 107.3 (CH), 119.0 (CH), 126.7 (C), 128.1 (CH_2), 129.7 (CH), 165.1 (C), 166.8 (C); IR (ATR): ν = 1627, 1662, 1734, 3392 cm^{-1}; HR-MS (ESI-TOF): m/z = 317.1096. calcd. for $C_{13}H_{18}N_2NaO_5$ $[M+Na]^+$: 305.1108.

Diethyl 2-benzamido-2-(1*H*-indol-3-yl)malonate (18aG): yield: 120.3 mg (61%); white solid: mp 174.0–174.6 °C; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.22 (dd, J = 7.1, 7.1 Hz, 6H), 4.25 (dq, J = 7.1, 10.7 Hz, 2H), 4.33 (dq, J = 7.1, 10.7 Hz, 2H), 6.99–7.05 (m, 2H), 7.16–7.18 (m, 1H), 7.42 (dd, J = 7.2, 7.2 Hz, 2H), 7.50 (t, J = 7.2 Hz, 1H), 7.63–7.67 (m, 1H),7.69 (d, J = 2.4 Hz, 1H), 7.84 (d, J = 7.2 Hz, 2H), 8.07 (br s, 1H), 8.64 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0 (CH_3), 62.8 (CH_2), 65.3 (C), 109.2 (C), 111.7, (CH), 119.7 (CH), 119.7 (CH), 121.7 (CH), 125.1 (C), 126.3 (CH), 127.2 (CH), 128.6 (CH), 131.9 (CH), 133.6 (C) 136.3 (C), 165.9 (C), 167.7 (C); IR (NaCl): ν = 1653, 1733, 3391 cm^{-1}; HR-MS (ESI-TOF): m/z = 417.1402, calcd. for $C_{22}H_{22}N_2NaO_5$ $[M+Na]^+$: 417.1421.

Diethyl 2-benzamido-2-(2-oxoethyl)malonate (18aH): yield: 96.4 mg (60%); colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.25 (dd, J = 7.2, 7.2 Hz, 6H), 3.82 (s, 2H), 4.28 (dq, J = 1.2, 7.2 Hz, 2H), 4.29 (dq, J = 1.2, 7.2 Hz, 2H), 7.45 (dd, J = 7.2, 7.2 Hz, 2H), 7.54 (t, J = 7.2 Hz, 1H), 7.70 (br s, 1H), 7.80 (d, J = 7.2 Hz, 2H), 9.70 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0 (CH_3), 47.3 (CH_2), 63.2 (C), 63.3 (CH_2), 127.3 (CH), 128.8 (CH), 132.3, (CH), 133.3 (C), 166.6 (C), 167.0 (C), 198.5 (C); IR (NaCl): ν = 1667, 1725, 1746, 3418 cm^{-1}; HR-MS (ESI-TOF): m/z = 344.1105, calcd. for $C_{16}H_{19}NNaO_6$ $[M+Na]^+$: 344.1105.

Diethyl 2-benzamido-2-(2-oxocyclopentyl)malonate (18aI): yield: 86.7 mg (48%); colorless crystals; mp 98.9–99.4 °C; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.21 (t, J = 7.2 Hz, 3H), 1.30 (dd, J = 7.3, 7.3 Hz, 3H), 1.75–1.90 (m. 1H), 1.93–2.12 (m, 3H), 2.27–2.38 (m, 1H), 2.65–2.78 (m, 1H), 3.40 (dd, J = 8.9, 11.8 Hz, 1H), 4.23 (q, J = 7.2 Hz, 2H), 4.34 (dq, J = 2.4, 7.3 Hz, 2H), 4.35 (dq, J = 2.4, 7.3 Hz, 2H), 7.44 (dd, J = 7.2, 7.2 Hz, 1H), 7.53 (t, J = 7.2 Hz, 1H), 7.57 (br s, 1H), 7.81 (d, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9 (CH_3), 14.0 (CH_3), 20.5 (CH_2), 26.9 (CH_2), 38.0 (CH_2), 55.7 (CH), 62.4 (CH_2), 63.2 (CH_2), 66.0 (C), 127.2 (CH), 128.7 (CH), 132.1 (CH), 133.4 (C), 166.5 (C), 166.8 (C), 168.1 (C), 217.4 (C); IR (NaCl): ν = 1679, 1745 cm^{-1}; HR-MS (ESI-TOF): m/z = 384.1399, calcd. for $C_{19}H_{23}NNaO_6$ $[M+Na]^+$: 384.1418.

Diethyl 2-acetoxy-2-benzamidomalonate (19a): yield (Method A): 161.7 mg (96%), (Method B): 148.1 mg (88%); white solid; mp 74.0–74.9 °C; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.29 (t, J = 7.2 Hz, 6H), 2.20 (s, 3H), 4.34 (q, J = 7.2 Hz, 4H), 7.47 (dd, J = 7.2, 7.2 Hz, 2H), 7.56 (t, J = 7.2 Hz, 1H), 7.84 (d, J = 7.2 Hz, 2H), 8.11 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9 (CH_3), 20.9 (CH_3), 63.7 (CH_2), 82.1 (C), 127.5 (C), 128.8 (C), 132.3 (C), 132.6 (C), 163.6 (C), 165.9 (C), 170.2 (C); IR (ATR): ν = 1672, 1744, 3318 cm^{-1}; HR-MS (ESI-TOF): m/z = 360.1059, calcd. for $C_{16}H_{19}NNaO_7$ $[M+Na]^+$: 360.1054.

Diethyl 2-acetamido-2-acetoxymalonate (19f): yield (Method A): 211.9 mg (77%); white solid; mp 111.5–113.3 °C; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.27 (t, J = 7.2 Hz, 6H), 2.06 (s, 3H), 2.18 (s, 3H), 4.30 (q, J = 7.2H, 4H), 7.43 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8 (CH_3), 20.8 (CH_3), 22.8 (CH_3), 63.6 (CH_2), 81.7 (C), 163.5 (C), 169.1 (C), 170.1 (C); IR (KBr): ν = 1699, 1763, 3364 cm^{-1}; HR-MS (ESI-TOF): m/z = 298.0888, calcd. for $C_{11}H_{17}NNaO_7$ $[M+Na]^+$: 298.0897.

Diethyl 2-acetoxy-2-acrylamidomalonate (19i): yield (Method A): 244.2 mg (85%); white solid; mp 104.5–105.6 °C; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.27 (t, J = 7.2 Hz, 6H), 2.18 (s, 3H), 4.31 (q, J = 7.2 Hz, 4H), 5.78 (dd, J = 3.6, 10.4 Hz, 1H), 6.17 (dd, J = 17.2, 10.4 Hz, 1H), 6.36 (dd, J = 17.2, 3.6 Hz, 1H), 7.53 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8 (CH_3), 20.8 (CH_3), 63.6 (CH_2), 81.8 (C), 129.2 (CH), 129.2 (CH_2), 163.4 (C), 164.1 (C), 170.1 (C); IR (KBr): ν = 1695, 1761, 3356 cm^{-1}; HR-MS (ESI-TOF): m/z = 288.1064, calcd. for $C_{12}H_{18}NO_7$ $[M+H]^+$: 288.1078.

Diethyl 2-acetoxy-2-(trifluoroacetamido)malonate (19l): yield (Method B): 305.0 mg (93%); white solid; mp 69.3–70.1 °C; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.29 (dd, J = 7.2, 7.2 Hz, 6H), 2.22 (s, 3H), 4.27–4.34 (m, 4H), 8.26 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8 (CH_3), 20.6 (CH_3), 64.3 (CH_2), 81.1 (C), 114.0 (CF_3, q, $J_{C,F}$ = 286.0 Hz), 156.0 (C, q, $J_{C,F}$ = 156.0 Hz), 162.2 (C), 169.6 (C); ^{13}F NMR (376 MHz, $CDCl_3$): δ = −75.9; IR (NaCl): ν = 1667, 1748, 3147 cm^{-1}; MS: m/z = 329.

Diethyl 2-methoxy-2-(*N*-methylbenzamido)malonate (20): yield: 52.3 mg (81%); yellow viscous liquid; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.31 (t, J = 7.2 Hz, 6H), 2.95 (s, 3H), 3.65 (s, 3H), 4.31 (q, J = 7.2 Hz, 4H), 7.41–7.50 (m, 3H), 7.59 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9 (CH_3), 35.1 (CH_3), 53.5 (CH_3), 62.5 (CH_2), 90.0 (C), 127.7 (CH), 128.5 (CH), 130.9 (CH), 135.0 (C), 164.8 (C), 173.7 (C); IR (NaCl): ν = 1660, 1754 cm^{-1}; HR-MS (ESI-TOF): m/z = 346.1269, calcd. for $C_{16}H_{21}NNaO_6$ $[M+Na]^+$: 346.1261.

Ethyl 2-benzamido-2-methoxyacetate (21): yield: 27.5 mg (58%); white solid; mp 76.2–77.0 °C; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.33 (t, J = 7.1 Hz, 3H), 3.52 (s, 3H), 4.28 (q, J = 7.1 Hz, 2H), 5.75 (d, J = 9.1 Hz, 1H), 7.36 (d, J = 9.1 Hz, 1H) 7.45 (dd, J = 7.2, 7.2 Hz, 2H), 7.54 (t, J = 7.2 Hz, 1H), 7.86 (d, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0 (CH_3), 56.7 (CH_3), 62.2 (CH_2), 78.8 (CH), 127.3 (CH), 128.7 (CH), 132.2 (CH), 133.2 (C), 167.5 (C), 168.2 (C); IR

(NaCl): $\nu = 1660$, 1748, 2834, 2984, 3335 cm^{-1}; HR-MS (ESI-TOF): $m/z = 260.0900$, calcd. for $C_{12}H_{15}NNaO_4$ $[M+Na]^+$: 260.0893.

Ethyl 2-benzamido-2-methoxy-3-oxo-3-(propylamino)propanoate (22): yield: 41.8 mg (65%); yellow viscous liquid; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.95$ (t, $J = 7.6$ Hz, 3H), 1.28 (t, $J = 7.2$ Hz, 3H), 1.56–1.63 (m, 2H), 3.29–3.36 (m, 2H), 3.33 (s, 3H), 4.26–4.35 (m, 2H), 6.71–6.90 (m, 1H), 7.46 (dd, $J = 8.4$, 8.4 Hz, 2H), 7.55 (t, $J = 8.4$ Hz, 1H), 7.88 (d, $J = 8.4$ Hz, 2H), 8.00 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 10.2$ (CH_3), 12.9 (CH_3), 21.6 (CH_2), 40.7 (CH_2), 50.8 (CH_3), 62.1 (CH_2), 84.8 (C), 126.4 (CH), 127.7 (CH), 131.3 (CH), 132.1 (C), 164.3 (C), 165.6 (C), 166.0 (C); IR (NaCl): $\nu = 1640$, 1683, 1749, 3358 cm^{-1}; HR-MS (ESI): $m/z = 343.1417$, calcd. for $C_{16}H_{22}N_2NaO_5$ $[M+Na^+]$: 345.1421.

Diethyl 3-benzoyl-1,3-oxazinane-2,2-dicarboxylate (23a): yield: 55.0 mg (82%); yellow solid; mp 60.0–61.0 °C; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.35$ (t, $J = 7.2$ Hz, 6H), 1.82 (tt, $J = 5.6$, 6.0 Hz, 2H), 3.56 (t, $J = 6.0$ Hz, 2H), 3.96 (t, $J = 5.6$ Hz, 2H), 4.37 (q, $J = 7.2$ Hz, 6H), 7.41–7.46 (m, 3H), 7.50–7.53 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 14.0$ (CH_3), 23.9 (CH_2), 44.6 (CH_2), 62.7 (CH_2), 64.3 (CH_2), 88.8 (C), 127.3 (CH), 128.6 (CH), 130.5 (CH), 134.7 (C), 165.2 (C), 172.0 (C); IR (NaCl): $\nu = 1659$, 1747 cm^{-1}; HR-MS (ESI-TOF): $m/z = 336.1458$, calcd. for $C_{17}H_{22}NO_6$ $[M+H]^+$: 336.1442.

Diethyl 3-acetyl-1,3-oxazinane-2,2-dicarboxylate (23f): yield: 42.6 mg (78%); yellow viscous liquid; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.33$ (t, $J = 7.2$ Hz, 3H), 1.33 (t, $J = 7.2$ Hz, 3H), 1.91 (tt, $J = 5.6$, 6.0 Hz, 2H), 2.14 (s, 3H), 3.57 (t, $J = 6.0$ Hz, 2H), 3.87 (t, $J = 5.6$ Hz, 2H), 4.31 (q, $J = 7.2$ Hz, 2H), 4.32 (q, $J = 7.2$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 14.0$ (CH_3), 21.9 (CH_3), 23.4 (CH_2), 42.6 (CH_2), 62.6 (CH_2), 63.7 (CH_2), 88.6 (C), 165.3 (C), 171.5 (C); IR (NaCl): $\nu = 1647$, 1747 cm^{-1}; HR-MS (ESI-TOF): $m/z = 274.1277$, calcd. for $C_{12}H_{20}NO_6$ $[M+H]^+$: 274.1285.

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[15] CCDC 1446784 and CCDC 1446786 (**13a** and **16a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.
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