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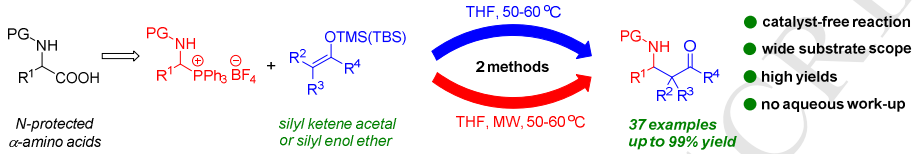

R^1 = alkyl, aryl; R^2,R^3 = alkyl; R^4 = OMe, alkyl, aryl; PG = Boc, Cbz, Bz

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ABSTRACT

A catalyst-free reaction of 1-(N-acylamino)alkyltriphenylphosphonium tetrafluoroborates with silyl enolates was developed to prepare β-amino carbonyl compounds. The reported method is a useful approach for the preparation of N-protected β-amino esters as well as N-protected β-amino ketones. The starting 1-(N-acylamino)alkyltriphenylphosphonium tetrafluoroborates are readily available from N-protected α-amino acids. Therefore, the presented approach can be considered a new method for the α-homologation of N-protected α-amino acids to prepare β-amino acid derivatives.

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1. Introduction

β-Amino carbonyl compounds, including β-amino acids, are a key structural elements of natural products and display various biological activities (Figure 1).[1,2] Moreover, these compounds are versatile synthons which are often used in the synthesis of alkaloids and nitrogen-containing pharmaceuticals and agrochemicals.[1-3] In addition, β-amino acids are used as precursors in the development of new, potent bioactive peptidomimetics.[4]

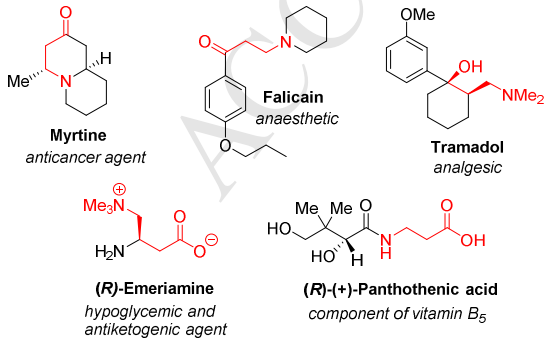

Figure 1. Selected examples of bioactive β-amino carbonyl derivatives.

Modern Mannich-type reactions are used as a standard method for the synthesis of β-amino carbonyl derivatives.[1-9] Among them, Mannich-type reactions of stable imines[5-7] or more reactive *N*-acyliminium cations[8,9] with silyl enolates have been investigated in detail (Scheme 1a, b). However, in order to efficiently perform the above-mentioned transformations, an appropriate reactant activator is required. Many promoters of electrophilic species have been reported in the literature such as Lewis acids,[5,8] e.g., metal halides or triflates, $BF_3 \cdot Et_2O$, and Brønsted acids.[6,9] Alternatively, the nucleophilic partner can be activated by a catalytic amount of Lewis base.[7] In addition, the search for new chiral catalysts that are useful in the stereoselective synthesis of β-amino carbonyl compounds has been reported extensively in the literature.[10] It needs to be stressed that in some cases, stoichiometric quantities of the various catalysts are necessary to achieve high yields.[5a,8a,8c-f,8k] Additionally, the presence of even small quantity of catalyst waste in a post-reaction mixture requires its neutralization and removal by aqueous work-up, what, in result, complicates and extend whole procees as well as puts additional material expenditure to the overall process.

In 2012, we have reported a convenient and efficient two-step protocol for the synthesis of 1-(*N*-acylamino)alkyltriphenylphosphonium tetrafluoroborates.[11] We have demonstrated that this type of phosphonium salts are

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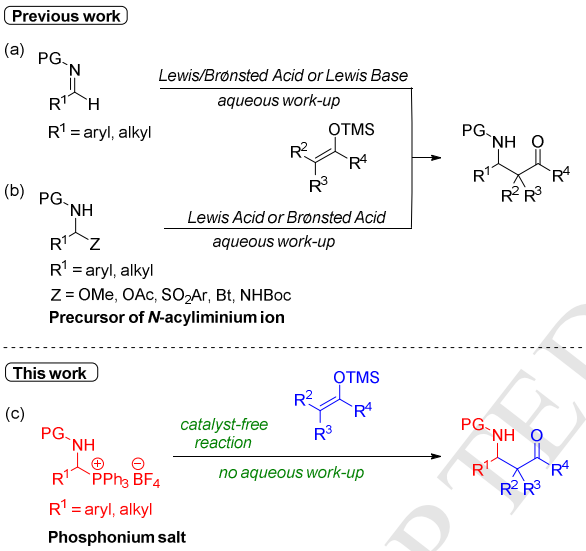
reactive α-amidoalkylating agents which can react with various nucleophiles in base-catalyzed reactions (e.g. *i*-Pr_2EtN, DBU, DABCO).[12] Very recently, Adamek *et al.* presented that 1-(*N*-acylamino)alkyltriarylphosphonium salts may also be used as precursors of *N*-acyliminium cations in the catalyst-free reactions with nucleophiles, e.g. arenes or heteroarenes.[13] However, in these reactions, the expected products were obtained efficiently when phosphonium salts derived from the more expensive triarylphosphines with electron-withdrawing substituents were used.

Although most of the modern Mannich-type reactions are highly efficient, they still require catalysts to be effective. From a synthetic standpoint, a more preferable approach would be a catalyst-free method.

In this context, we report a new catalyst-free variant of Mannich-type reaction of 1-(*N*-acylamino)alkyltriphenylphosphonium tetrafluoroborates with silyl enolates as an alternative approach for the synthesis of β-amino carbonyl compounds (Scheme 1c).

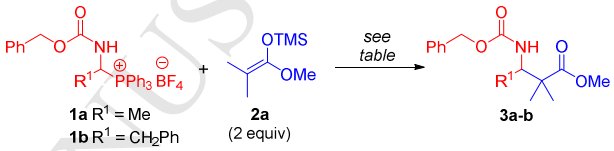


Scheme 1. Mannich-type reaction of imines or precursors of *N*-acyliminium ions with silyl enolates.

2. Result and discussion

In a preliminary study, we screened various reaction conditions for the reactions of 1-(*N*-acylamino)alkyltriphenylphosphonium tetrafluoroborates **1a-b** with silyl ketene acetal **2a** (Table 1). The process was performed in the presence of diverse catalysts. The reaction of salt **1a** with compound **2a** in CH_2Cl_2 at room temperature in the presence of Hünig's base (*i*-Pr_2EtN) gave *N*-Cbz-β-amino ester **3a** in 44% yield, nevertheless, the conversion of phosphonium salt **1a** was pretty high. Replacing CH_2Cl_2 with THF improved the selectivity and the yield of this reaction. That allowed to obtain the expected product **3a** in high yield of 82% (Table 1, entries 1 and 2). Good yields were also achieved when Lewis acids were applied (Table 1, entries 3–5). Interestingly, when the reaction was performed in THF at room temperature without any catalyst and using two equivalents of nucleophile **2a**, the yield of product **3a** increased to 98% (Table 1, entry 8). However, the reactions carried out at room temperature were sluggish. Therefore, in the next experiment, the temperature was increased to 50 °C, which allowed us to shorten the reaction time from 24 h to 1 h. The expected product **3a** was obtained in very good, 96% yield (Table 1, entry 9). Similar results were also obtained in the case of reactions using salt **1b** as the reagent (Table 1, entries 10–14). Phosphonium salt **1b** with a larger substituent at the 1-position was less reactive and its complete conversion in the reaction required approximately 2.5 h at 50 °C. The desired product **3b** was obtained in good, 74% yield (Table 1, entry 14). It was concluded, that the reactions of phosphonium salts **1** with silyl ketene acetal **2** should be carried out using a two-fold excess of the nucleophile, heating the reaction mixture at 50 °C under an argon atmosphere. However, the appropriate reaction time should be determined by 1H NMR spectroscopy.

Table 1. Screening of reaction conditions.[a]



Entry	Salt	Catalyst (x equiv)	Solvent	Temp (°C)	Time (h)	% Yield **3**[b] (% Conv. **1**)[b]
1	1a	*i*-Pr_2NEt (0.1)	CH_2Cl_2	r.t.	24	44 (80)
2	1a	*i*-Pr_2NEt (0.1)	THF	r.t.	24	82 (95)
3	1a	$Bi(OTf)_3$ (0.1)	THF	r.t.	24	90 (>99)
4	1a	$Yb(OTf)_3$(0.1)	THF	r.t.	24	81 (>99)
5	1a	$BF_3{\cdot}Et_2O$ (0.1)	THF	r.t.	24	68 (>99)
6	1a	–	CH_2Cl_2	r.t.	24	16 (82)
7[c]	1a	–	THF	r.t.	24	76 (77)
8	1a	–	THF	r.t.	24	98 (>99)
9	**1a**	**–**	**THF**	**50**	**1**	**96 (>99)**
10	1b	*i*-Pr_2NEt (0.1)	THF	r.t.	24	33 (45)
11	1b	$Bi(OTf)_3$ (0.1)	THF	r.t.	24	45 (62)
12[c]	1b	–	THF	r.t.	24	15 (17)
13	1b	–	THF	r.t.	24	32 (35)
14	**1b**	**–**	**THF**	**50**	**2.5**	**74 (>99)**

[a]Reaction conditions: phosphonium salt **1** (0.20 mmol, 1.0 equiv), silyl ketene acetal **2a** (0.40 mmol, 2.0 equiv), catalyst (0.02 mmol, 0.1 equiv), solvent (3 mL) under an argon atmosphere. Entries 6–9 and 12–14 were catalyst-free. [b]Yield of **3** and conversion of **1** were determined by the 1H NMR. [c]Silyl ketene acetal **2a** (0.24 mmol, 1.2 equiv).

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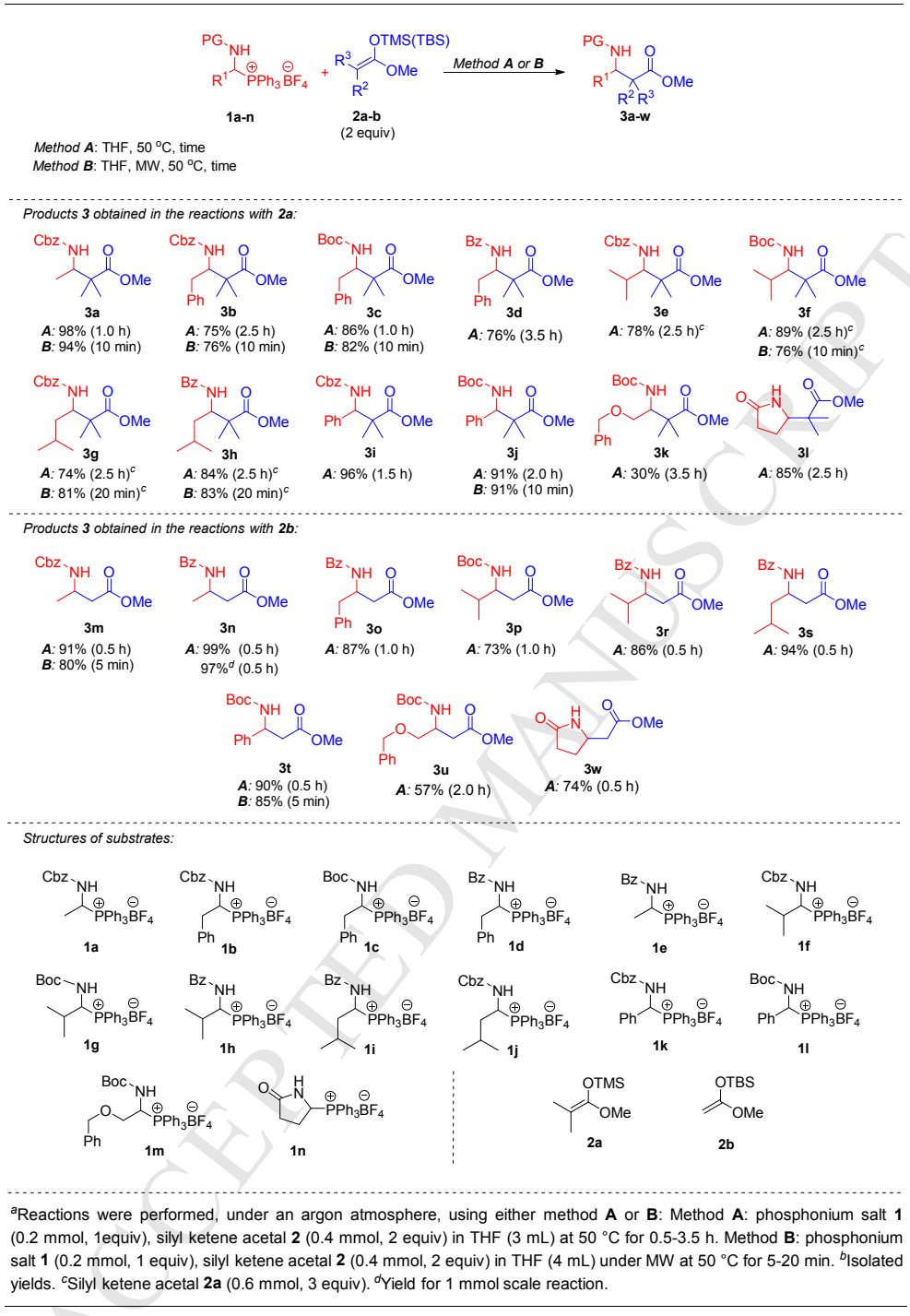

[a]Reactions were performed, under an argon atmosphere, using either method **A** or **B**: Method **A**: phosphonium salt **1** (0.2 mmol, 1equiv), silyl ketene acetal **2** (0.4 mmol, 2 equiv) in THF (3 mL) at 50 °C for 0.5-3.5 h. Method **B**: phosphonium salt **1** (0.2 mmol, 1 equiv), silyl ketene acetal **2** (0.4 mmol, 2 equiv) in THF (4 mL) under MW at 50 °C for 5-20 min. [b]Isolated yields. [c]Silyl ketene acetal **2a** (0.6 mmol, 3 equiv). [d]Yield for 1 mmol scale reaction.

Scheme 2. Scope of catalyst-free Mannich-type reaction of phosphonium salts **1** with silyl ketene acetals **2**.[a,b]

Next, the scope and applicability of the described procedure using 1-(*N*-acylamino)alkyltriphenylphosphonium tetrafluoroborates **1a-n** and two silyl ketene acetals **2a-b** were investigated. The results are summarized in Scheme 2 (Method A). Structurally diverse alkyl and aryl β-substituted β-amino esters **3a-j,l** were obtained with good to excellent yields (74–98%) by heating the mixture of phosphonium salts **1** with silyl ketene acetal **2a** for 1.0–3.5 h. The reaction conditions were compatible with Cbz, Boc, and Bz *N*-protecting groups. Among the examined examples, only the *N*-Boc protected β-amino ester **3k** was obtained with a poor, 30% yield. A deeper analysis of ^{1}H NMR spectrum revealed that the poor yield of product **3k** was probably caused by the partial deprotection of the amine group in the expected product. In the synthesis of *N*-protected β-amino esters **3e-h** with branched aliphatic substituents at the β-position, complete conversion of substrates and good yields of products were obtained only when three equivalents of nucleophile **2a** were used. However, in comparison, the reactions of salts **1** with silyl ketene acetal **2b** proceeded faster and resulted in less sterically hindered *N*-protected β-amino esters **3m-w** with very

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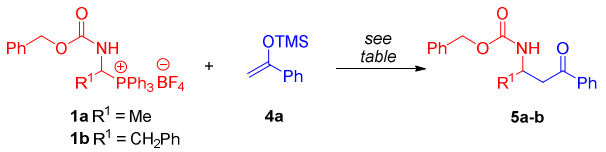
good yields (57–99%) after only 0.5–2.0 h. For compound **3n**, this reaction was scaled-up to 1 mmol of phosphonium salt, retaining high, 97% yield.

As an extension of the current studies, the influence of microwave irradiation on the investigated process was evaluated. As shown in Scheme 2 (Method B), replacing conventional heating with microwave irradiation enhanced the addition; thus, the reaction time could be significantly shortened to 5–20 min without affecting the yield.

These results encouraged us to extend the set of nucleophiles to less reactive[14] silyl enol ethers such as **4a-d** and subject them to reactions with phosphonium salts **1**. Therefore, we performed a series of reactions of phosphonium salts **1a-b** with silyl enol ether **4a** in order to determine the reaction conditions. (Table 2). The best results were obtained when the reactions were carried out at 60 °C, using a three-fold excess of the nucleophile. Furthermore, the reactions needed to be performed for no longer than 2.5 h. Otherwise, a significant decrease in yields of products **5a-b** was observed.

Table 2. Screening of reaction conditions for catalyst-free Mannich-type reaction of phosphonium salts **1a-b** with silyl enol ether **4a**.[a]



Entry	Salt	Molar ratio of Salt **1**: Nu **2a**	Temp. (°C)	% Yield **5**[b] (% Conversion **1**)[b]			
				Reaction time (h)			
				2.5	4.5	12	24
1	**1a**	1:2	r.t.	12 (13)	18 (19)	-	32 (36)
2	**1a**	1:2	60	87 (88)	89 (91)	82 (94)	-
3	**1a**	**1:3**	**60**	**92 (93)**	86 (95)	77 (96)	-
4	**1b**	1:3	r.t.	9 (9)	10 (10)	-	22 (23)
5	**1b**	**1:3**	**60**	**79 (92)**	73 (93)	60 (95)	-

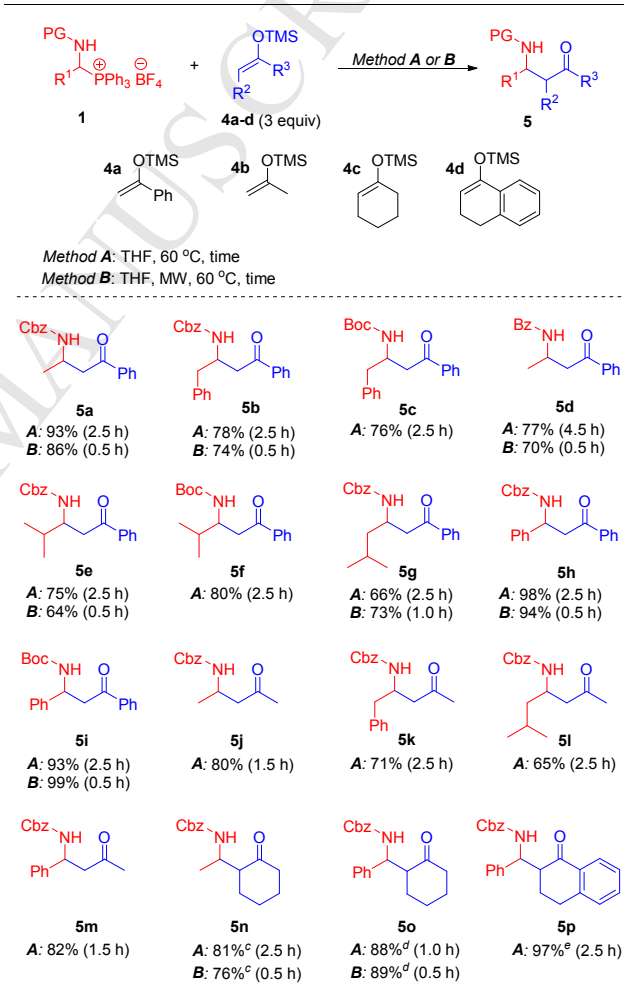
[a]Reaction conditions: phosphonium salt 1 (0.2 mmol, 1 equiv), silyl enol ether **4a** (0.4 mmol, 2 equiv or 0.6 mmol, 3 equiv) in THF (3 mL) under an argon atmosphere. [b]Yield of **5** and conversion of **1** were determined by 1H NMR spectrum.

Next, we examined the scope of catalyst-free reaction of phosphonium salts **1** with various silyl enol ethers **4a-d** (Scheme 3). As previously stated, the reactions were conducted using conventional heating and microwave irradiation techniques (Scheme 3, Methods A and B).

Under the thermal reaction conditions (Scheme 3, Method A), 16 structurally diverse aliphatic and aryl β-substituted *N*-protected β-amino ketones **5a-p** were prepared in good to excellent yields (65–98%). Again, the reaction conditions were compatible with various *N*-protecting groups. While in most of the cases, the corresponding products were obtained in 2.5 h, β-amino carbonyl products **5j**, **5m**, and **5o** were produced at a faster rate with high yields of 80%, 82% and 88%, respectively, in 1.0–1.5 h. In the case of **5d**, the reaction time was extended to 4.5 h, due to the poor solubility of the phosphonium salt. The reaction of phosphonium salts **1** with cyclic silyl enol ethers **4c-d** resulted in a mixture of diastereomeric products **5n-p** with high yields. However, diastereoselectivity was poor (50:50 for **5n** and 65:35 for **5o** and 55:45 for **5p**). Unfortunately, these products could not be separated and isolated as single isomers.

Next, several microwave-assisted reactions were carried out between phosphonium salts **1** and silyl enol ethers **4a** and **4c** (Scheme 3, Method B). As expected, microwave irradiation accelerated the reactions, similar to the previously mentioned reactions with silyl ketene acetals (Scheme 2, Method B). The appropriate products **5** were obtained in good to excellent yields (64–99%) in a shorter time (0.5–1.0 h).

It was observed that in the reaction of phosphonium salts **1** with silyl enolates **2** or **4**, irrespective of reaction conditions, the corresponding β-amino carbonyl compounds **3** or **5**, with both aliphatic and aromatic substituents at the β-position, were obtained with very good yields. Moreover, *N*-Cbz, *N*-Boc, and *N*-Bz protecting groups were well tolerated.



[a]Reactions were carried out, under an argon atmosphere, using either method **A** or **B**: Method **A**: phosphonium salt **1** (0.2 mmol, 1 equiv), silyl enol ether **4** (0.6 mmol, 3 equiv) in THF (3 mL) at 60 °C for 1.0-4.5 h. Method **B**: phosphonium salt **1** (0.2 mmol, 1 equiv), silyl enol ether **4** (0.6 mmol, 3 equiv) in THF (4 mL) under MW at 60 °C for 0.5-1.0 h. [b]Isolated yields. [c]dr = 50:50. [d]dr = 65:35. [e]dr = 55:45. Diastereomeric ratio (dr) was determined by 1H NMR spectroscopy.

Scheme 3. Scope of catalyst-free Mannich-type reaction of phosphonium salts **1** with silyl enol ethers **4**.[a,b]

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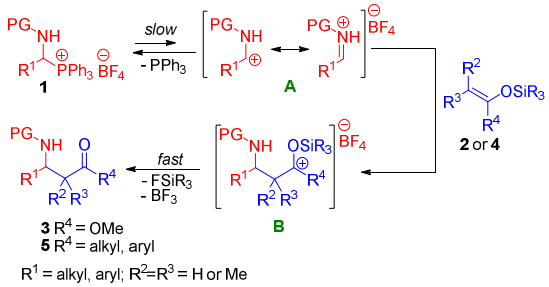
Finally, a plausible mechanism for the developed catalyst-free Mannich-type reaction was provided (Scheme 4). In the first step, reactive *N*-acyliminium cation **A**, spontaneously generated from 1-(*N*-acylamino)alkyltriphenylphosphonium tetrafluoroborate **1**, reacts slowly with silyl ketene acetal **2** or silyl enol ether **4** to produce silyloxy-substituted carbenium ion **B**. This unstable intermediate undergoes a desilylation reaction to give β-amino carbonyl compounds **3** or **5**. A similar desilylation reaction of siloxycarbenium ions has been described by Mayr *et al.*[14] The proposed mechanism confirms the observation that the entire process can be enhanced by increasing the reaction temperature. Heating or, even more markedly, microwave irradiation favor the cleavage of the polar C-P^+ bond in phosphonium salts **1**, resulting in the faster generation of the highly reactive iminium species **A**.



Scheme 4. Plausible mechanism for catalyst-free Mannich-type reaction of phosphonium salts **1** with silyl enolates.

3. Conclusion

In conclusion, an efficient catalyst-free reaction of 1-(*N*-acylamino)alkyltriphenylphosphonium tetrafluoroborates with silyl enolates was developed to prepare β-amino ketone derivatives. To the best of our knowledge, this is the first example of Mannich-type reaction of silyl enolates with a precursor of *N*-acyliminium ion in which the addition of an appropriate activator is not required. The reported method represents a useful approach in the preparation of *N*-protected β-amino esters and *N*-protected β-amino ketones. As it was demonstrated, the process can be enhanced by increasing the reaction temperature through either conventional heating or microwave irradiation. In the latter case, a significant reduction in reaction time can be achieved. It must be emphasized that these two procedures are manually simple. The additional advantage of the presented approach is that the starting 1-(*N*-acylamino)alkyltriphenylphosphonium tetrafluoroborates are readily available from *N*-protected α-amino acids. From this point of view, the reported approach can be considered a new method for the α-homologation of *N*-protected α-amino acids to prepare β-amino acid derivatives (with silyl ketene acetals as nucleophiles). Further investigations on the developed strategy, including the modification of phosphonium salt structure and improvement of the stereoselectivity of the process, are in progress.

4. Experimental section

4.1. General

Infrared spectra (IR) were recorded on a Nicolet 6700 FT-IR spectrophotometer (ATR method). ^{1}H NMR spectra were acquired on either a Varian 600 or 400 MHz at 600 or 400 MHz, respectively. Data were given as follows: chemical shift in ppm with tetramethylsilane (TMS) as the internal standard, multiplicity (s = singlet; d = doublet; t = triplet; q = quartet; br = broad; m = multiplet), coupling constant (Hz) and integration. . ^{13}C NMR spectra were measured on either a Varian 600 or 400 MHz at, as appropriate, 150 or 100 MHz. Chemical shifts were reported in ppm from the solvent resonance employed as the internal standard ($CDCl_3$ at 77.0 ppm). ^{31}P NMR spectra were measured on a Varian 400 spectrometer at 162 MHz without the resonance shift standard, with respect to H_3PO_4 as zero ppm. Melting points were determined in capillaries, in a Stuart Scientific SMP3 melting point apparatus and were uncorrected. The high-resolution mass spectra (HRMS) were obtained by electrospray ionization (ESI), using a Waters Corporation Xevo G2 QTOF instrument.

Catalyst-free Mannich type reactions with silyl enolates were performed under argon atmosphere in Schlenk flasks with magnetic stirring. Temperatures were reported as bath temperatures. The microwave reactions were carried out in a glass vial sealed with a screw cap, using a CEM Microwave (Matthews, NC, USA), model: Discover-S with *Synergy* control program. Temperature measurements were conducted using an IR sensor located below the microwave cavity floor. Reaction times refer to the total hold time at the indicated temperature. To avoid overheating the reaction mixture, the maximum wattage was set to 30 W. For TLC analysis, Merck TLC silica gel 60 F_{254} plates were used. The plates were visualized by UV light (254 nm) and/or dipped in a solution of cerium sulfate and tetrahydrate of ammonium heptamolybdate in H_2SO_{4aq} and heated. Kieselgel 60 (Merck, 0.040-0.063 mm) was used for column chromatography.

Materials. All solvents and common reagents were obtained from commercial suppliers. Only solvents used in the reactions under inert atmosphere were additionally purified. Dry THF was prepared by distillation over Na/benzophenone, and dry CH_2Cl_2 by distillation over CaH_2. Silyl ketene acetals **2a-b** and silyl enol ethers **4a-d** were purchased from Sigma-Aldrich or Alfa Aesar. 3-(1-Piperidino)propyl functionalized silica gel (SiO_2-Pip) was purchased from Sigma-Aldrich.

4.2. Substrate synthesis

The starting phosphonium salts **1a-n** were synthesized by previously described two-step protocol, which consist of electrochemical decarboxylative α-methoxylation of *N*-acyl-α-amino acids (Step 1) and transformation of the resulting *N*-protected 1-methoxyalkylamines to title 1-(*N*-acylamino)alkyltriphenylphosphonium tetrafluoroborates **1** (Step 2).[11] The analytical data and spectra of compounds **1a-b**, **1f-g**, **1j-k** were identical to those previously described.[11] For unknown phosphonium salts **1c-e**, **1h-i**, and **1l-n**, analytical and spectroscopic data are reported below.

*General procedure for the synthesis of 1-(N-acylamino)alkyltriphenylphosphonium tetrafluoroborates **1***

Step 1: The methanol (30 cm^3), *N*-acyl-α-amino acid (3.0 mmol), and SiO_2−Pip (200 mg, 0.22 mmol) were added to an undivided cylindrical glass electrolyzer (85 cm^3) with a thermostatic jacket, equipped with a magnetic stirrer, a cylindrical Pt mesh anode (47 cm^2), and a similar cathode (44 cm^2), all arranged concentrically to one another at a distance of 2.5 ± 0.5 mm. The electrolysis was conducted while stirring at a current density of 0.3 A/dm^2 at 10 °C until 3.5-3.75 F/mol charge had passed [3.5 F/mol for *N*-Cbz-valine and 3.75 F/mol for other *N*-protected α-amino acids]. When the electrolysis was finished, the SiO_2−Pip was filtered out, and methanol was evaporated under reduced pressure to afford corresponding *N*-protected 1-methoxyalkylamine. Crude *N*-protected 1-methoxyalkylamines were used in the next step without purification.

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Step 2: A mixture of the corresponding *N*-protected 1-methoxyalkylamine (1 mmol) and $Ph_3P{\cdot}HBF_4$ (343 mg, 0.98 mmol) in CH_2Cl_2 (1 cm^3) was stirred at 25 °C for 30 min, and the solvent was removed under reduced pressure. The crude product was dissolved in CH_2Cl_2 and precipitated by addition of Et_2O to afford the 1-(*N*-acylamino)alkyltriphenylphosphonium salt **1**.

4.2.1. 1-(N-tert-Butoxycarbonylamino)-2-phenylethyltriphenyl-phosphonium tetrafluoroborate **(1c)**. This product was obtained in 78% yield (446 mg). White solid; mp 142.0-143.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84-7.67 (m, 15H), 7.28-7.17 (m, 5H), 6.58 (br d, J = 9.2 Hz, 1H), 5.72-5.64 (m, 1H), 3.36 (dt, J_1 = 13.2 Hz, J_2 = 10.4 Hz), 3.15 (dt, J_1 = 18.8 Hz, J_2 = 4.4 Hz, 1H), 1.15 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.5 (d, J = 3.5 Hz), 135.1 (d, J = 2.8 Hz), 135.0, 134.3 (d, J = 9.2 Hz), 130.4 (d, J = 12.2 Hz), 129.2, 128.8, 127.5, 117.2 (d, J = 80.5 Hz), 81.0, 52.2 (d, J = 51.2 Hz), 37.1 (d, J = 8.0 Hz), 27.8. ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.0. IR (ATR): 3322, 2979, 1709, 1439, 1250, 1156, 1069 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{31}H_{33}NO_2P$ [M^+] 482.2249, found 482.2255.

4.2.2. 1-(N-Benzoylamino)-2-phenylethyltriphenylphosphonium tetrafluoroborate **(1d)**. This product was obtained in 86% yield (494 mg). White solid; mp 169.5-170.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.48 (d, J = 8.0 Hz, 1H), 7.83-7.55 (m, 17H), 7.42-7.28 (m, 3H), 7.24-7.15 (m, 5H), 6.17-6.09 (m, 1H), 3.62 (dt, J_1 = 14.4 Hz, J_2 = 10.8 Hz, 1H), 3.29 (dt, J_1 = 14.4 Hz, J_2 = 5.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.3, 135.1, 135.0 (d, J = 2.4 Hz), 134.6 (d, J = 9.4 Hz), 132.2, 131.6, 130.2 (d, J = 12.3 Hz), 129.2, 128.9, 128.5, 127.6, 127.3, 117.6 (d, J = 80.9 Hz), 51.7 (d, J = 49.0 Hz), 37.1 (d, J = 6.3 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 27.6. IR (ATR): 3391, 1669, 1520, 1440, 1108 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{33}H_{29}NOP$ [M^+] 486.1987, found 486.1985.

4.2.3. 1-(N-Benzoylamino)ethyltriphenylphosphonium tetrafluoroborate **(1e)**. This product was obtained in 85% yield (425 mg). White solid; mp 176.0-178.0 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.52 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.83-7.63 (m, 17H), 7.47-7.43 (m, 1H), 7.38-7.35 (m, 1H), 6.06-6.00 (m, 1H), 1.85 (dd, J_1 = 17.4 Hz, J_2 = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 168.1, 135.0 (d, J = 2.3 Hz), 134.6 (d, J = 9.1 Hz), 132.4, 131.6, 130.2 (d, J = 12.3 Hz), 128.6, 127.7, 117.8 (d, J = 81.2 Hz), 46.0 (d, J = 53.1 Hz), 18.0. ^{31}P NMR (162 MHz, $CDCl_3$): δ 28.0. IR (ATR): 3302, 2931, 1649, 1517, 1437, 1050 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{27}H_{25}NOP$[M^+] 410.1674, found 410.1675.

4.2.4. 1-(N-Benzoylamino)-2-methylpropyltriphenyl-phosphonium tetrafluoroborate **(1h)**. This product was obtained in 89% yield (468 mg). White solid; mp 183.5-185.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.61 (dd, J_1 = 7.6 Hz, J_2 = 4.0 Hz, 1H), 7.90-7.83 (m, 6H), 7.73-7.56 (m, 11H), 7.46-7.30 (m, 3H), 5.62-5.56 (m, 1H), 2.95-2.83 (m, 1H), 1.11 (d, J = 6.4 Hz, 3H), 0.90 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.1 (d, J = 2.1 Hz), 134.8 (d, J = 9.3 Hz), 134.4 (d, J = 3.1 Hz), 132.2, 131.5 (d, J = 0.7 Hz), 129.8 (d, J = 12.3 Hz), 128.5, 127.2, 119.2 (d, J = 80.3 Hz), 55.3 (d, J = 46.5 Hz) 29.1 (d, J = 5.1 Hz), 21.2 (d, J = 1.9 Hz), 20.2 (d, J = 9.7 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 28.9. IR (ATR): 3377, 2962, 1656, 1533, 1438, 1307, 1294, 1016 cm^{-1}. HRMS (ESI): *m/z*: calcd for $C_{29}H_{29}NOP$ [M^+] 438.1987, found 438.1992.

4.2.5. 1-(N-Benzoylamino)-3-methylbutyltriphenyl-phosphonium tetrafluoroborate **(1i)**. This product was obtained in 81% yield (433 mg). White solid; mp 151.0-152.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40 (d, J = 8.4 Hz, 1H), 7.79-7.63 (m, 17H), 7.46-7.32 (m, 3H) 6.08-5.99 (m, 1H), 2.62-2.51 (m, 1H), 1.97-1.85 (m, 1H), 1.47-1.37 (m, 1H), 1.01 (d, J = 6.8 Hz, 3H), 0.95 (d, J = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4 (d, J = 2.4 Hz), 135.0 (d, J = 3.1 Hz), 134.3 (d, J = 9.2 Hz), 132.3, 131.7, 130.2 (d, J = 12.2 Hz), 128.5, 127.5, 117.7 (d, J = 80.9 Hz), 48.6 (d, J = 51.8 Hz), 39.7 (d, J = 4.0 Hz), 25.8 (d, J = 12.5 Hz), 23.1, 21.0. ^{31}P NMR (162 MHz, $CDCl_3$): δ 27.0; IR (ATR): 3354, 2971, 1669, 1513, 1438, 1064 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{30}H_{31}NOP$[M^+] 452.2143, found 452.2147.

4.2.6. 1-(N-tert-Butoxycarbonylamino)phenylmethyltriphenyl-phosphonium tetrafluoroborate **(1l)**. This product was obtained in 85% yield (473 mg). White solid; mp 145.5-146.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85-7.78 (m, 3H), 7.68-7.63 (m, 12H), 7.38-7.32 (m, 1H), 7.27-7.23 (m, 2H), 7.10-7.07 (m, 3H), 6.62 (t, J = 9.8 Hz, 1H), 1.29 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.3, 135.2 (d, J = 3.1 Hz), 134.8 (d, J = 8.9 Hz), 130.7 (d, J = 3.1 Hz), 130.2 (d, J = 12.1 Hz), 130.1, 129.4 (d, J = 2.1 Hz), 129.2 (d, J = 8.4 Hz), 116.2 (d, J = 79.9 Hz), 81.8, 56.5 (d, J = 51.9 Hz), 27.9. ^{31}P NMR (162 MHz, $CDCl_3$): δ 28.5. IR (ATR): 3328, 2981, 2910, 1703, 1438, 1286, 1157, 1050 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{30}H_{31}NO_2P$ [M^+] 468.2092, found 468.2094.

4.2.7. 1-(N-tert-Butoxycarbonylamino)-2-benzyloxyethyl-triphenylphosphonium tetrafluoroborate **(1m)**. This product was obtained in 89% yield (533 mg). White solid; decomposition at 141 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78-7.75 (m, 15H), 7.25-7.19 (m, 3H), 6.97-6.91 (m, 2H), 6.70 (br d, J = 7.6 Hz, 1H), 5.74 (br s, 1H), 4.13-3.96 (m, 3H), 3.79 (br d, J = 11.2 Hz, 1H), 1.16 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.2, 136.0, 134.8 (d, J = 9.6 Hz), 134.4 (d, J = 2.9 Hz), 129.8 (d, J = 12.4 Hz), 128.3, 128.0, 127.9, 118.3 (d, J = 81.5 Hz), 81.1, 73.3, 67.0, 51.8 (J = 51.1 Hz), 27.8. ^{31}P NMR (162 MHz, $CDCl_3$): δ 30.4. IR (ATR): 3352, 2985, 1694, 1441, 1283, 1160, 1085 cm^{-1}. HMRS (ESI) *m/z*: calcd for $C_{32}H_{35}NO_3P$ [M^+] 512.2355, found 512.2357.

4.2.8. (5-Oxopyrrolidin-2-yl)triphenylphosphonium tetrafluoroborate **(1n)**. This product was obtained in 92% yield (399 mg). White solid; decomposition at 139 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87-7.69 (m, 15H), 6.85 (br s, 1H), 6.26-6.18 (m, 1H), 3.24-3.07 (m, 1H), 2.29-2.11 (m, 2H), 1.29-1.20 (m, 1H).^{13}C NMR (100 MHz, $CDCl_3$): δ 178.1, 135.7 (d, J = 3.0 Hz), 133.9 (d, J = 9.2 Hz), 130.9 (d, J = 12.1 Hz), 115.8 (d, J = 81.9 Hz), 49.1 (d, J = 56.6 Hz), 28.2, 22.5. ^{31}P NMR (162 MHz, $CDCl_3$): δ 21.8. IR (ATR): 3065, 1695, 1439, 1112, 1051 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{22}H_{21}NOP$ [M^+] 346.1361, found 346.1365.

4.3. General procedure for the synthesis of methyl esters of N-protected-β-amino acids 3

Method A: To a stirred suspension (or solution) of corresponding 1-(*N*-acylamino)alkyltriphenylphosphonium tetrafluoroborate **1** (0.2 mmol, 1 equiv) in dry THF (3 mL), the silyl ketene acetal **2a** or **2b** (0.4 mmol, 2 equiv or 0.6 mmol, 3 equiv) was added. The reaction mixture was stirred, under argon atmosphere, at 50 °C for the time given in Scheme 2. Then, the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (hexanes/AcOEt) to afford the desired methyl esters of *N*-protected-β-amino acid **3**.

Method B: 1-(*N*-Acylamino)alkyltriphenylphosphonium tetrafluoroborate **1** (0.2 mmol, 1 equiv), dry THF (4mL) and the silyl ketene acetal **2a** or **2b** (0.4 mmol, 2 equiv or 0.6 mmol, 3 equiv) were placed in a glass vial. The vial was flushed with argon and closed with a screw-cap. Then, the reaction mixture was stirred and irradiated at 50 °C and 30 W in a microwave reactor for the time given in Scheme 2. Afterwards, the solvent

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was evaporated under reduced pressure, and the product **3** was isolated by column chromatography on silica gel (hexanes/AcOEt).

4.3.1. Methyl 3-(N-benzyloxycarbonylamino)-2,2-dimethylbutanoate **(3a)**.[15] This product was obtained in 98% yield (54.7 mg) by Method A or 94% yield (52.4 mg) by Method B. Colorless oil; R_f = 0.24 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.30 (m, 5H), 5.33 (br d, J = 9.6 Hz, 1H), 5.11 (d, J = 13.2 Hz, 1H), 5.08 (d, J = 12.8 Hz, 1H), 3.84 (dq, J_1 = 9.6 Hz, J_2 = 6.8 Hz, 1H), 3.67 (s, 3H), 1.21 (s, 6H), 1.12 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 156.0, 136.6, 128.5, 128.1, 66.6, 53.4, 51.9, 46.3, 23.2, 22.9, 17.2. IR (ATR): 3346, 2978, 1704, 1507, 1455, 1234, 1141, 1051 cm^{-1}.

4.3.2. Methyl 3-(N-benzyloxycarbonylamino)-2,2-dimethyl-4-phenylbutanoate **(3b)**.[8h] This product was obtained in 75% yield (53.3 mg) by Method A or 76% yield (54.0 mg) by Method B. White solid; mp 62.5-64.0 °C (toluene/n-pentane); R_f = 0.22 (hexanes/AcOEt = 4:1). Compound **3b** exists as a 8:2 mixture of rotamers at 25 °C in $CDCl_3$. The spectra for the major rotamer are as follows: ^{1}H NMR (400 Hz, $CDCl_3$): δ 7.37-7.15 (m, 10H), 5.16 (br d, J = 10.4 Hz, 1H), 4.97 (d, J = 12.4 Hz, 1H), 4.87 (d, J = 12.4 Hz, 1H), 4.06 (td, J_1 = 10.8 Hz, J_2 = 3.3 Hz, 1H), 3.68 (s, 3H), 2.95 (dd, J_1 = 14.0 Hz, J_2 = 3.2 Hz, 1H), 2.48 (dd, J_1 = 14.0 Hz, J_2 = 10.8 Hz, 1H), 1.32 (s, 3H), 1.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 156.2, 138.2, 136.7, 129.1, 128.4, 128.3, 127.9, 127.7, 126.3, 66.4, 58.9, 51.9, 46.6, 37.7, 23.5, 22.9. IR (ATR): 3326, 2947, 1732, 1690, 1537, 1254, 1130 cm^{-1}.

4.3.3. Methyl 3-(N-tert-butoxycarbonylamino)-2,2-dimethyl-4-phenylbutanoate **(3c)**. This product was obtained in 86% yield (55.3 mg) by Method A or 82% yield (52.7 mg) by Method B. White solid; mp 92.0-93.0 °C (toluene); R_f = 0.34 (hexanes/AcOEt = 4:1). Compound **3c** exists as a 8:2 mixture of rotamers at 25 °C in $CDCl_3$. The spectra for the major rotamer are as follows: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28-7.15 (m, 5H), 4.81 (d, J = 10.4 Hz, 1H), 4.01 (td, J_1 = 10.8 Hz, J_2 = 3.6 Hz, 1H), 3.69 (s, 3H), 2.92 (dd, J_1= 13.8 Hz, J_2 = 3.4 Hz, 1H), 2.45 (dd, J_1 = 14.0 Hz, J_2 = 11.2 Hz, 1H), 1.30 (s, 3H), 1.25 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.1, 155.6, 138.4, 129.2, 128.2, 126.2, 78.9, 58.0, 51.8, 46.7, 37.8, 28.2, 23.4, 22.7. IR (ATR): 3344, 2976, 1732, 1683, 1523, 1251, 1163 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{18}H_{27}NO_4Na$ $[M+Na]^+$ 344.1838, found 344.1833.

4.3.4. Methyl 3-(N-benzoylamino)-2,2-dimethyl-4-phenylbutanoate **(3d)**.[16] This product was obtained in 76% yield (49.6 mg) by Method A. White solid; mp 134.0-135.0 °C (Tolune/n-pentane); R_f = 0.13 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61-7.57 (m, 2H), 7.46-7.33 (m, 3H), 7.24-7.12 (m, 5H), 6.90 (br d, J = 10.0 Hz, 1H), 4.54 (td, J_1 = 10.3 Hz, J_2 = 3.9 Hz, 1H), 3.70 (s, 3H), 3.12 (dd, J_1= 14.4 Hz, J_2 = 4.0 Hz, 1H), 2.67 (dd, J_1 = 14.0 Hz, J_2 = 10.4 Hz, 1H), 1.40 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.5, 166.9, 138.0, 134.8, 131.2, 129.1, 128.4, 128.3, 126.7, 126.4, 56.8, 52.0, 46.4, 37.4, 24.5, 23.4. IR (ATR): 3311, 2981, 1731, 1639, 1541, 1324, 1133 cm^{-1}.

4.3.5. Methyl 3-(N-benzyloxycarbonylamino)-2,2,4-trimethylpentanoate **(3e)**. This product was obtained in 78% yield (41.2 mg) by Method A. Colorless oil; R_f = 0.39 (hexanes/AcOEt = 4:1). Compound **3e** exists as a 9:1 mixture of rotamers at 25 °C in $CDCl_3$. The spectra for the major rotamer are as follows: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39- 7.31 (m, 5H), 5.50 (br d, J = 10.8 Hz, 1H), 5.13 (s, 2H), 3.68 (dd, J_1 = 10.8 Hz, J_2 = 3.6 Hz, 1H), 3.66 (s, 3H), 2.00-1.92 (m, 1H), 1.24 (s, 3H), 1.20 (s, 3H), 0.94 (d, J = 6.8 Hz, 3H), 0.72 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.6, 157.1, 136.8, 128.5, 128.0, 128.0, 66.7, 62.3, 51.9, 45.4, 29.1, 24.4, 23.7, 22.1, 16.7. IR (ATR): 3348, 2961, 1712, 1507, 1229, 1191,1153, 1026 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{17}H_{26}NO_4$ $[M+H]^+$ 308.1862, found 308.1862.

4.3.6. Methyl 3-(N-tert-butoxycarbonylamino)-2,2,4-trimethylpentanoate **(3f)**.[17] This product was obtained in 89% yield (48.8 mg) by Method A or 76% yield (41.7 mg) by Method B. White solid; mp 61.5-62.5 °C (toluene); R_f = 0.44 (hexanes/AcOEt = 4:1). Compound **3f** exists as a 85:15 mixture of rotamers at 25 °C in $CDCl_3$. The spectra for the major rotamer are as follows: ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.17 (br d, J = 10.6 Hz, 1H), 3.67 (s, 3H), 3.61 (dd, J_1 = 10.8 Hz, J_2 = 3.6 Hz, 1H), 1.95-1.88 (m, 1H), 1.45 (s, 9H), 1.22 (s, 3H), 1.20 (s, 3H), 0.91 (d, J = 6.6 Hz, 3H), 0.74 (d, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 177.8, 156.5, 78.8, 61.4, 51.8, 45.5, 29.1, 28.4, 24.0, 23.8, 22.1, 16.9. IR (ATR): 3387, 2979, 1725, 1689, 1513, 1246, 1153 cm^{-1}.

4.3.7. Methyl 3-(N-benzyloxycarbonylamino)-2,2,5-trimethylhexanoate **(3g)**. This product was obtained in 74% yield (47.7 mg) by Method A or 81% yield (52.3 mg) by Method B. Colorless oil; R_f = 0.37 (hexanes/AcOEt = 4:1). Compound **3g** exists as a 9:1 mixture of rotamers at 25 °C in $CDCl_3$. The spectra for the major rotamer are as follows: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.29 (m, 5H), 5.12 (d, J = 12.4 Hz, 1H), 5.08 (d, J = 12.4 Hz, 1H), 5.03 (br d, J = 10.4 Hz, 1H), 3.84-3.78 (m, 1H), 3.66 (s, 3H), 1.68-1.59 (m, 1H), 1.21-1.13 (m, 2H), 1.20 (s, 3H), 1.18 (s, 3H), 0.92 (d, J = 6.4 Hz, 3H), 0.89 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.1 156.6, 136.7, 128.5, 128.0, 128.0, 66.7, 55.8, 51.8, 46.7, 40.8, 25.1, 23.9, 23.2, 22.5, 21.4. IR (ATR): 3339, 2953, 1698, 1533, 1256, 1139, 1051 cm^{-1} HRMS (ESI) *m/z:* calcd for $C_{18}H_{28}NO_4$ $[M+H]^+$, 322.2018, found 322.2019.

4.3.8. Methyl 3-(N-Benzoylamino)-2,2,5-trimethylhexanoate **(3h)**.[16] This product was obtained in 84% yield (49.1 mg) by Method A or 83% yield (48.6 mg) by Method B. White solid; mp 73-75 °C (toluene); R_f = 0.43 (toluene/AcOEt = 8:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.82 -7.80 (m, 2H), 7.52-7.43 (m, 3H), 6.79 (br d, J = 10.2 Hz, 1H), 4.27 (td, J_1 = 10.4 Hz, J_2 = 3.4 Hz, 1H), 3.73 (m, 3H), 1.68-1.62 (m, 1H), 1.39-1.30 (m, 2H), 1.29 (s, 3H), 1.27 (s, 3H), 0.97 (d, J = 6.0 Hz, 3H), 0.89 (d, J = 6.6 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 177.7, 167.0, 134.7, 131.3, 128.6, 126.8, 54.2, 51.9, 46.6, 40.7, 25.2, 24.0, 23.9, 23.2, 21.6. IR (ATR): 3313, 2952, 1725, 1634, 1540, 1325, 1149 cm^{-1}.

4.3.9. Methyl 3-(N-benzyloxycarbonylamino)-2,2-dimethyl-3-phenylpropanoate **(3i)**.[18] This product was obtained in 96% yield (65.9 mg) by (Method A). Colorless oil; R_f = 0.24 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.17 (m, 10H), 6.31 (br d, J = 9.2 Hz, 1H), 5.10 (d, J = 12.0 Hz, 1H), 5.01 (d, J = 12.0 Hz, 1H), 4.73 (d, J = 9.6 Hz, 1H), 3.63 (s, 3H), 1.32 (s, 3H), 1.11 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.7, 155.8, 139.2, 136.5, 128.5, 128.1, 128.1, 128.1, 127.7, 127.6, 66.8, 62.3, 52.0, 46.6, 24.7, 22.6. IR (ATR): 3358, 2951, 1701, 1497, 1230, 1133, 1041 cm^{-1}.

4.3.10. Methyl 3-(N-tert-butoxycarbonylamino)-2,2-dimethyl-3-phenylpropanoate **(3j)**.[18] This product was obtained in 91% yield (56.0 mg) by Method A or 91% yield (56.2 mg) by Method B. White crystals; mp 86.0-87.0 °C (toluene/n-pentane); R_f = 0.39 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.17 (m, 5H), 5.95 (br d, J = 8.4 Hz, 1H), 4.71 (d, J = 9.2 Hz, 1H), 3.65 (s, 3H), 1.40 (s, 9H), 1.30 (s, 3H), 1.11 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.8, 155.3 139.5, 128.0, 127.8, 127.4,

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79.4, 61.5, 51.9, 46.8, 28.4, 24.4, 22.4. IR (ATR): 3417, 2973, 1728, 1697, 1507, 1238,1139 cm^{-1}.

4.3.11. Methyl 4-(benzyloxy)-3-(N-tert-butoxycarbonylamino)-2,2-dimethylbutanoate **(3k)**.[16] This product was obtained in 30% yield (21.4 mg) by Method A. Colorless oil; R_f = 0.28 (hexanes/AcOEt = 4:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.34-7.25 (m, 5H), 5.42 (br d, J = 10.2 Hz, 1H), 4.48 (d, J = 12.0 Hz, 1H), 4.42 (d, J = 11.4 Hz, 1H), 3.92-3.88 (m, 1H), 3.57 (dd, J_1= 10.2 Hz, J_2 = 4.8 Hz, 1H), 3.55 (s, 3H), 3.52 (dd, J_1 = 10.2, J_2 = 4.2 Hz, 1H), 1.45 (s, 9H) 1.23 (s, 3H), 1.22 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 177.0, 155.9, 138.0, 128.2, 127.7, 127.6, 79.2, 73.2, 70.0, 56.6, 51.7, 44.4, 28.4, 23.4, 23.3. IR (ATR): 3369, 2979, 1713, 1497, 1365, 1246, 1164 cm^{-1}.

4.3.12. Methyl 2-methyl-2-(5-oxopyrrolidin-2-yl)propanoate **(3l)**. This product was obtained in 85% yield (31.6 mg) by Method A. White solid; mp 103.0-105.0 °C (toluene). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.43 (br s, 1H), 3.90 (dd, J_1 = 8.0 Hz, J_2 = 6.0 Hz, 1H), 3.71 (s, 3H), 2.32 (t, J = 8.2 Hz, 2H), 2.19-2.10 (m, 1H), 1.89-1.80 (m, 1H), 1.17 (s, 3H), 1.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.1, 176.9, 59.5, 52.2, 45.8, 30.0, 22.0, 20.8, 19.7. IR (ATR): 3195, 2981, 1726, 1690, 1270, 1190, 1142 cm^{-1}. HRMS (ESI) *m/z:* calcd for $C_9H_{16}NO_3$ $[M+H]^+$ 186.1130, found 186.1128.

4.3.13. Methyl 3-(N-benzyloxycarbonylamino)butanoate **(3m)**. This product was obtained in 91% yield (45.9 mg) by Method A or 80% yield (40.1 mg) by Method B. White solid; mp 37.0-38.0 °C (toluene/hexanes); R_f = 0.14 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.29 (m, 5H), 5.19 (br s, 1H), 5.09 (s, 2H), 4.16-4.06 (m, 1H), 3.67 (s, 3H), 2.54 (d, J = 5.2 Hz, 2H), 1.24 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.5, 136.5, 128.5 128.1, 66.6, 51.6, 44.0, 40.3, 20.4. IR (ATR): 3319, 2988, 1728, 1682, 1534, 1255, 1066 cm^{-1}. HRMS (ESI) *m/z:* calcd for $C_{13}H_{17}NO_4Na$ $[M+Na]^+$ 274.1055, found 274.1055.

4.3.14. Methyl 3-(N-benzoylamino)butanoate **(3n)**.[16] This product was obtained in 99% yield (43.9 mg) by Method A. Furthermore, this product was obtained in 97% yield (215.1 mg) for 1 mmol reaction scale (Method A). White solid; mp 85.0-86.0 °C (toluene); R_f = 0.26 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72-7.71 (m, 2H), 7.51-7.40 (m, 3H), 6.96 (br d, J = 6.4 Hz, 1H), 4.62-4.52 (m, 1H), 3.72 (s, 3H), 2.68 (dd, J_1 = 16.0 Hz, J_2 = 5.2 Hz, 1H), 2.62 (dd, J_1 = 15.6 Hz, J_2 = 4.8 Hz, 1H), 1.34 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.5, 166.5, 134.5, 131.4, 128.5, 126.9, 51.7, 42.3, 39.5, 20.0. IR (ATR): 3299, 2981, 1735, 1633, 1530, 1295, 1195, 1158 cm^{-1}.

4.3.15. Methyl 3-(N-Benzoylamino)-4-phenylbutanoate **(3o)**.[16] This product was obtained in 87% yield (51.9 mg) by Method A. White solid; mp 111.5-112.5 °C (toluene); R_f = 0.08 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78-7.71 (m, 2H), 7.52-7.39 (m, 3H), 7.35-7.19 (m, 5H), 7.01 (br d, J = 8.4 Hz, 1H), 4.72-4.64 (m, 1H), 3.71 (s, 3H), 3.09 (dd, J_1 = 13.6 Hz, J_2 = 6.0 Hz, 1H), 2.92 (dd, J_1 = 13.6 Hz, J_2 = 8.4 Hz, 1H), 2.64 (dd, J_1= 16.4 Hz, J_2 = 5.2 Hz, 1H), 2.58 (dd, J_1 = 16.0 Hz, J_2 = 5.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6, 166.6, 137.5, 134.4, 131.4, 129.3, 128.6, 128.5, 126.8, 126.7, 51.8, 47.7, 39.9, 36.5. IR (ATR): 3302, 2951, 1733, 1636, 1537, 1208, 1153 cm^{-1}.

4.3.16. Methyl 3-(N-tert-butoxycarbonylamino)-4-methylpentanoate **(3p)**.[19] This product was obtained in 73% yield (36.0 mg) by Method A. White solid; mp 60.0-61.5 °C (toluene/n-pentane); R_f = 0.26 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.86 (br d, J = 8.0 Hz, 1H), 3.79-3.72 (m, 1H), 3.68 (s, 3H), 2.53 (dd, J_1 = 15.2 Hz, J_2 = 5.4 Hz, 1H), 2.47 (dd, J_1 = 16.0 Hz, J_2 = 7.4 Hz, 1H), 1.86-1.75 (m, 1H), 1.44 (s, 9H), 0.92 (d, J = 6.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3, 155.5, 79.1, 53.0, 51.6, 37.1, 31.8, 28.4, 19.3, 18.4. IR (ATR): 3338, 2967, 1706, 1519, 1291, 1166, 1008 cm^{-1}.

4.3.17. Methyl 3-(N-benzoylamino)-4-methylpentanoate **(3r)**.[16] This product was obtained in 86% yield (42.8 mg) by Method A. White solid; mp 90.5-92.0 °C (toluene); R_f = 0.09 (hexanes/AcOEt = 4:1). ^{1}H NMR(400 MHz, $CDCl_3$): δ 7.81-7.78 (m, 2H), 7.52-7.41 (m, 3H), 6.90 (br d, J = 9.2 Hz, 1H), 4.29-4.22 (m, 1H), 3.70 (s, 3H), 2.69 (dd, J_1 = 16.0 Hz, J_2 = 5.6 Hz, 1H), 2.63 (dd, J_1 = 16.2 Hz, J_2 = 5.0 Hz, 1H), 2.02-1.90 (m, 1H), 0.99 (d, J = 6.8 Hz, 3H), 0.98 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.8, 166.8, 134.7, 131.4, 128.5, 126.9, 51.9, 51.8, 36.1, 31.7, 19.4, 19.2. IR (ATR): 3314, 2956, 1729, 1636, 1541, 1328, 1277, 1251, 1192, 1172, 1111, 997 cm^{-1}.

4.3.18. Methyl 3-(N-Benzoylamino)-5-methylhexanoate **(3s)**.[16] This product was obtained in 94% yield (49.6 mg) by Method A. White solid; mp 70.0-71.0 °C (toluene/n-pentane); R_f = 0.11 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80-7.76 (m, 2H), 7.51-7.41 (m, 3H), 6.85 (br d, J = 8.8 Hz, 1H), 4.60-4.51 (m, 1H), 3.70 (s, 3H), 2.70 (dd, J_1 = 16.2 Hz, J_2 = 5.0 Hz, 1H), 2.60 (dd, J_1 = 16.0 Hz, J_2 = 4.8 Hz, 1H), 1.73-1.60 (m, 2H), 1.43-1.35 (m, 1H), 0.97 (d, J = 6.4 Hz, 3H), 0.94 (d, J = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.7, 166.6, 134.6, 131.4, 128.5, 126.9, 51.7, 44.5, 43.2, 38.5, 25.2 22.9, 22.2. IR (ATR): 3258, 2954, 1732, 1635, 1545, 1297, 1178 cm^{-1}.

4.3.19. Methyl 3-(N-tert-butoxycarbonylamino)-3-phenylpropanoate **(3t)**.[20] This product was obtained in 90% yield (50.2 mg) by Method A or 85% yield (47.6 mg) by Method B. White solid; mp 77.5-79.0 °C (toluene/n-pentane); R_f = 0.29 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.23 (m, 5H), 5.45 (br s, 1H), 5.10 (br s, 1H), 3.61 (s, 3H), 2.88 (dd, J_1 = 14.6 Hz, J_2 = 6.6 Hz, 1H), 2.81 (dd, J_1 = 15.2 Hz, J_2 = 5.8 Hz, 1H), 1.42 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 155.0, 141.1, 128.6, 127.5, 126.1, 79.7, 51.8, 51.2, 40.8, 28.3. IR (ATR): 3384, 2974, 1739, 1687, 1515, 1237, 1166 cm^{-1}.

4.3.20. Methyl 4-(benzyloxy)-3-(N-tert-butoxycarbonylamino)butanoate **(3u)**.[16] This product was obtained in 56% yield (36.5 mg) for Method A. Colorless oil; R_f = 0.17 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.27 (m, 5H), 5.15 (br d, J = 7.6 Hz, 1H), 4.52 (d, J = 12.4 Hz, 1H), 4.49 (d, J = 12.4 Hz, 1H), 4.16 (br s, 1H), 3.64 (s, 3H), 3.54 (dd, J_1 = 9.2 Hz, J_2 = 4.0 Hz, 1H), 3.52 (dd, J_1 = 9.4 Hz, J_2 = 5.4 Hz, 1H) 2.68-2.58 (m, 2H), 1.43 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 158.2, 137.9, 128.4, 127.7, 127.6, 79.5, 73.2, 71.0, 51.6, 47.3, 36.1, 28.3. IR (ATR): 3369, 2977, 1710, 1497, 1365, 1165 cm^{-1}.

4.3.21. Methyl 2-(5-oxopyrrolidin-2-yl)acetate **(3w)**.[21] This product was obtained in 74% yield (23.3 mg) by Method A. White wax. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.06 (br s, 1H), 4.04-3.97 (m, 1H), 3.71 (s, 3H), 2.60 (dd, J_1 = 16.4 Hz, J_2 = 4.0 Hz, 1H), 2.48 (dd, J_1 = 16.8 Hz, J_2 = 9.6 Hz, 1H), 2.40-2.29 (m, 3H), 1.81-1.71 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.4, 171.8, 52.0, 50.4, 40.8, 29.5, 26.8. IR (ATR): 3208, 2957, 1728, 1674, 1414, 1186 cm^{-1}.

4.4. General procedure for the synthesis of *N*-protected-β-amino ketones 5

Method A: 1-(*N*-Acylamino)alkyltriphenylphosphonium tetrafluoroborate **1** (0.2 mmol, 1 equiv) and silyl enol ether **4a-d** (0.6 mmol, 3 equiv) in dry THF (3 mL) were stirred, under argon atmosphere, at 60 °C for the time given in Scheme 3. Then, the solvent was evaporated under reduced pressure, and the remaining residue was purified by column chromatography on

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silica gel (hexanes/AcOEt) to give the corresponding *N*-protected-β-amino ketone **5**.

Method B: 1-(*N*-Acylamino)alkyltriphenylphosphonium tetrafluoroborate 1 (0.2 mmol, 1 equiv), dry THF (4 mL) and the appropriate silyl enol ether **4a** or **4c** (0.6 mmol, 3 equiv) were placed in a glass vial. The vial was flushed with argon and closed with a screw-cap. The reaction mixture was stirred and irradiated at 60 °C and 30 W in a microwave reactor for the time given in Scheme 3. Afterwards, the solvent was evaporated under reduced pressure, and the desired product **5** was isolated by column chromatography on silica gel (hexanes/AcOEt).

4.4.1. Benzyl N-(4-oxo-4-phenylbutan-2-yl)carbamate **(5a)**. This product was obtained in 93% yield (55.4 mg) by Method A or 86% yield (51.5 mg) by Method B. White solid; mp 81.0-82.0 °C (toluene); R_f = 0.2 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 7.6 Hz, 2H), 7.58-7.54 (m, 1H), 7.47-7.25 (m, 2H), 7.37-7.28 (m, 5H), 5.32 (br s, 1H), 5.10 (d, J = 12.0 Hz, 1H), 5.07 (d, J = 12.0 Hz, 1H), 4.30-4.20 (m, 1H), 3.37 (br d, J =16.0 Hz, 1H), 3.06 (dd, J_1 = 16.4 Hz, J_2 = 6.4 Hz, 1H), 1.30 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.6, 155.6, 136.9, 136.5, 133.3, 128.6, 128.5, 128.1, 128.0, 128.0, 66.5, 44.3, 44.1, 20.4. IR (ATR): 3376, 2971, 1711, 1680, 1529, 1250, 1052 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{18}H_{20}NO_3$ $[M+H]^+$ 298.1443, found 298.1445.

4.4.2. Benzyl N-(4-oxo-1,4-diphenylbutan-2-yl)carbamate **(5b)**. This product was obtained in 78% yield (58.5 mg) by Method A or 70% yield (52.6 mg) by Method B. White solid; mp 106.0-107.0 °C (toluene); R_f = 0.21 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, J = 7.2 Hz, 2H), 7.58-7.54 (m, 1H), 7.45-7.41 (m, 2H), 7.36-7.15 (m, 10H), 5.49 (br d, J = 7.2 Hz, 1H), 5.06 (br s, 2H), 4.40-4.32 (m, 1H), 3.26 (dd, J_1 = 17.0 Hz, J_2 = 3.8 Hz, 1H), 3.10 (dd, J_1 = 17.2 Hz, J_2 = 5.6 Hz, 1H), 3.06 (dd, J_1 = 14.8 Hz, J_2 = 6.0 Hz, 1H), 2.96 (dd, J_1 = 13.1 Hz, J_2 =7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.0, 155.7, 138.0, 136.8, 136.5, 133.4, 129.3, 128.6, 128.6, 128.5, 128.0, 128.0, 127.9, 126.6, 66.5, 49.7, 40.7, 39.9. IR (ATR): 3347, 1678, 1519, 1256, 1215, 1040 cm^{-1}. HRMS (ESI) *m/z:* calcd for $C_{24}H_{24}NO_3$ $[M+H]^+$ 374.1756, found 374.1754.

4.4.3. Tert-butyl N-(4-oxo-1,4-diphenylbutan-2-yl)carbamate **(5c)**. This product was obtained in 76% yield (51.7 mg) by Method A. White solid; mp 125.0-126.5 °C (toluene); R_f = 0.23 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89-7.86 (m, 2H), 7.58-7.54 (m, 1H), 7.44 (t, J = 7.6 Hz, 2H), 7.29-7.17 (m, 5H), 5.22 (br s, 1H), 4.32-4.24 (m, 1H), 3.21 (dd, J_1 = 17.0 Hz, J_2 = 4.6 Hz, 1H), 3.09 (dd, J_1 =16.8 Hz, J_2 = 5.6 Hz, 1H), 3.05 (dd, J_1 = 15.2 Hz, J_2 = 5.6 Hz, 1H), 2.93 (dd, J_1 = 13.4 Hz, J_2 = 7.8 Hz, 1H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.3, 155.3, 138.3, 136.9, 133.3, 129.3, 128.6, 128.5, 128.0, 126.5, 79.2, 49.2, 40.9, 40.1, 28.3. IR (ATR): 3349, 2977, 1687, 1678, 1529, 1451, 1324, 1161, 1022 cm^{-1}. HRMS (ESI) *m/z:* calcd for $C_{21}H_{26}NO_3$ $[M+H]^+$ 340.1913, found 340.1908.

4.4.4. N-(4-Oxo-4-phenylbutan-2-yl)benzamide **(5d)**.[22] This product was obtained in 77% yield (41.8 mg) by Method A. White solid; mp 167.5-168.0 °C (AcOEt/Hexane); R_f = 0.09 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J = 7.6 Hz, 2H), 7.78 (d, J = 7.2 Hz, 2H), 7.60-7.56 (m, 1H), 7.49-7.40 (m, 5H), 7.05 (br d, J = 6.8 Hz, 1H), 4.74-4.64 (m, 1H), 3.47 (dd, J_1 = 16.8 Hz, J_2 = 4.0 Hz, 1H), 3.20 (dd, J_1 = 16.8 Hz, J_2 = 6.0 Hz, 1H), 1.41 (d, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.6, 166.6, 136.9, 134.6, 133.5, 131.4, 128.7, 128.5, 128.1, 126.9, 43.2, 42.9, 20.1. IR (ATR): 3310, 2977, 1684, 1635, 1546, 1221 cm^{-1}.

4.4.5. Benzyl N-(4-methyl-1-oxo-1-phenylpentan-3-yl)carbamate **(5e)**.[8h] This product was obtained in 75% yield (49.0 mg) by Method A or 64% yield (41.9 mg) by Method B. White solid; mp 57.5-58.5 °C (toluene); R_f = 0.22 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, J = 7.6 Hz, 2H), 7.59-7.54 (m, 1H), 7.47-7.44 (m, 2H), 7.36-7.29 (m, 5H), 5.29 (br d, J = 8.8 Hz, 1H), 5.08 (d, J = 12.0 Hz, 1H), 5.05 (d, J = 12.0 Hz, 1H), 3.97-3.90 (m, 1H), 3.31 (dd, J_1 = 16.8 Hz, J_2 = 5.6 Hz, 1H), 3.12 (dd, J_1 = 16.8 Hz, J_2 = 5.0 Hz, 1H), 2.08-1.99 (m, 1H), 0.97 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.9, 156.1, 136.9, 136.6, 133.3, 128.7, 128.4, 128.0, 128.0, 128.0, 66.6, 53.9, 40.2, 31.2, 19.7, 18.7. IR (ATR): 3328, 2961, 1684, 1537, 1249, 1038 cm^{-1}.

4.4.6. Tert-butyl N-(4-methyl-1-oxo-1-phenylpentan-3-yl)carbamate **(5f)**.[23] This product was obtained in 80% yield (46.5 mg) by Method A. White solid; mp 103.0-104.5 °C (toluene); R_f = 0.28 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96-7.93 (m, 2H), 7.59-7.54 (m, 1H), 7.48-7.44 (m, 2H), 5.02 (br d, J = 7.6 Hz, 1H), 3.89-3.82 (m, 1H), 3.26 (dd, J_1 = 16.2 Hz, J_2 = 5.4 Hz, 1H), 3.11 (dd, J_1 = 16.2 Hz, J_2 = 5.0 Hz, 1H), 2.04-1.96 (m, 1H), 1.40 (s, 9H), 0.96 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.2, 155.6, 137.0, 133.2, 128.6, 128.1, 79.0, 53.4, 40.5, 31.3, 28.3, 19.7, 18.7. IR (ATR): 3305, 2964, 1707, 1690, 1678, 1540, 1388, 1167, 1040 cm^{-1}.

4.4.7. Benzyl N-(5-methyl-1-oxo-1-phenylhexan-3-yl)carbamate **(5g)**.[24] This product was obtained in 66% yield (44.9 mg) by Method A or 73% yield (49.7 mg) by Method B. White solid; mp 54.0-55.5 °C (toluene); R_f = 0.33 (hexanes/AcOEt = 4:1).^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, J = 7.6 Hz, 2H), 7.58-7.54 (m, 1H), 7.47-7.43 (m, 2H), 7.37-7.27 (m, 5H), 5.32 (br d, J = 8.4 Hz, 1H), 5.07 (s, 2H), 4.24-4.15 (m, 1H), 3.34 (dd, J_1 = 16.8 Hz, J_2 = 4.0 Hz, 1H), 3.12 (dd, J_1 = 16.8 Hz, J_2 = 5.6 Hz, 1H), 1.70-1.60 (m, 2H), 1.40-1.36 (m, 1H), 0.92-0.90 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.9, 155.8, 137.0, 136.6, 133.2, 128.6, 128.4, 128.0, 128.0, 127.9, 66.5, 46.6, 43.3, 42.9, 25.1, 23.1, 21.9. IR (ATR): 3340, 2954, 1686, 1526, 1467, 1448, 1260, 1215, 1026 cm^{-1}.

4.4.8. Benzyl N-(3-oxo-1,3-diphenylpropyl)carbamate **(5h)**.[24] This product was obtained in 98% yield (70.2 mg) by Method A or 94% yield (67.7 mg) by Method B. White solid; mp 114.0-115.0 °C (toluene); R_f = 0.27 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89-7.86 (m, 2H), 7.56-7.52 (m, 1H), 7.44-7.40 (m, 2H), 7.35-7.20 (m, 10H), 5.85 (br s, 1H), 5.35-5.30 (m, 1H), 5.10 (d, J = 12.4 Hz, 1H), 5.07 (d, J = 12.4 Hz, 1H), 3.69 (br d, J = 16.8 Hz, 1H), 3.44 (dd, J_1 = 16.8 Hz, J_2 = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.8, 155.7, 141.3, 136.6, 136.4, 133.4, 128.6, 128.5, 128.1, 127.5, 126.3, 66.8, 51.8, 43.9. IR (ATR): 3363, 1716, 1679, 1523, 1450, 1289, 1239, 1220, 1020 cm^{-1}.

4.4.9. Tert-butyl N-(3-oxo-1,3-diphenylpropyl)carbamate **(5i)**. This product was obtained in 93% yield (60.8 mg) by Method A or 99% (64.3 mg) by Method B. White solid; mp 132.0-133.0 °C (toluene); R_f = 0.28 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91-7.88 (m, 2H), 7.57-7.52 (m, 1H), 7.45-7.20 (m, 7H), 5.55 (br s, 1H), 5.27-5.22 (m, 1H), 3.65 (br d, J = 16.8 Hz, 1H), 3.43 (dd, J_1 = 16.8 Hz, J_2 = 6.2 Hz, 1H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.0, 155.2, 141.7, 136.7, 133.3, 128.6, 128.6, 128.1, 127.3, 126.3, 79.6, 51.4, 44.3, 28.3. IR (ATR): 3353, 2973, 1690, 1679, 1523, 1450, 1366, 1296, 1159, 1042 cm^{-1}. HRMS (ESI) *m/z:* calcd for $C_{20}H_{24}NO_3$ $[M+H]^+$ 326.1756, found 326.1751.

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4.4.10. Benzyl N-(4-oxopentan-2-yl)carbamate **(5j)**. This product was obtained in 80% yield (37.7 mg) by Method A. White solid; mp 43.5-45.0 °C (toluene); R_f = 0.13 (hexanes/AcOEt = 4:1). ^{1}H NMR (600 MHz, CDCl3): δ 7.37-7.29 (m, 5H), 5.17 (br s, 1H), 5.09 (d, J = 12.0 Hz, 1H), 5.08 (d, J = 13.2 Hz, 1H) 4.11-4.04 (m, 1H), 2.72 (dd, J_1 = 16.8 Hz, J_2 = 4.2 Hz, 1H), 2.60 (dd, J_1 = 16.8 Hz, J_2 = 6.0 Hz, 1H), 2.14 (s, 3H), 1.23 (d, J = 6.6 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 207.4, 155.5, 136.5, 128.5, 128.1, 128.0, 66.5, 49.1, 43.8, 30.6, 20.5. IR (ATR): 3324, 2989, 1712, 1679, 1529, 1256, 1070 cm^{-1}. HRMS (ESI) *m/z:* calcd for $C_{13}H_{17}NO_3Na$ $[M+Na]^+$ 258.1106, found 258.1107.

4.4.11. Benzyl N-(4-oxo-1-phenylpentan-2-yl)carbamate **(5k)**. This product was obtained in 71% yield (44.4 mg) by Method A. White solid; mp 52.0-54.0 °C (toluene/n-pentane); R_f = 0.11 (hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.12 (m, 10H), 5.31 (br d, J = 6.8 Hz, 1H), 5.05 (s, 2H), 4.23-4.14 (m, 1H), 2.95 (dd, J_1 = 13.2 Hz, J_2 = 6.4 Hz, 1H), 2.84 (dd, J_1 = 13.4 Hz, J_2 = 7.8 Hz, 1H), 2.67-2.56 (m, 2H), 2.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.6, 155.7, 137.8, 136.5, 129.2, 128.6, 128.5, 128.0, 127.9, 126.6, 66.5, 49.1, 45.8, 40.0, 30.5. IR (ATR): 3367, 3034, 1710, 1686, 1537, 1258, 1060 cm^{-1}. HRMS (ESI) *m/z:* calcd for $C_{19}H_{21}NO_3Na$ $[M+Na]^+$ 334.1419, found 334.1422.

4.4.12. Benzyl N-(2-methyl-6-oxoheptan-4-yl)carbamate **(5l)**. This product was obtained in 65% yield (34.4 mg) by Method A. Colorless oil; R_f = 0.11(hexanes/AcOEt = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.27 (m, 5H), 5.13 (br d, J = 8.4 Hz, 1H), 5.07 (s, 2H), 4.07-3.97 (m, 1H), 2.69 (dd, J_1 = 17.0 Hz, J_2 = 5.0 Hz, 1H), 2.63 (dd, J_1 = 16.8 Hz, J_2 = 5.2 Hz, 1H), 2.13 (s, 3H), 1.64-1.46 (m, 2H), 1.30-1.23 (m, 1H), 0.92 (d, J = 8.4 Hz, 3H), 0.90 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.7 155.8, 136.6, 128.5, 128.0, 128.0, 66.5, 48.1, 46.2, 43.6, 30.6, 25.0, 23.0, 22.0.IR (ATR): 3331, 2956, 1697, 1526, 1228, 1045 cm^{-1}. HRMS (ESI) *m/z:* calcd for $C_{16}H_{23}NO_3Na[M+Na]^+$ 300.1576, found 300.1577.

4.4.13. Benzyl N-(3-oxo-1-phenylbutyl)carbamate **(5m)**.[25] This product was obtained in 82% yield (46.5 mg) by Method A. White solid; mp 65.5-67.0 °C (toluene); R_f = 0.14 (hexanes/AcOEt = 4:1).^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37-7.24 (m, 10H), 5.74 (br s, 1H), 5.19-5.13 (m, 1H), 5.11 (d, J = 12.0 Hz, 1H), 5.09 (d, J = 12.6 Hz, 1H), 3.08 (d, J = 13.8 Hz, 1H), 2.93 (dd, J_1 = 16.5 Hz, J_2 = 5.7 Hz, 1H), 2.08 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 206.7, 155.6, 141.1, 136.3, 128.7, 128.5, 128.1, 127.5, 126.2, 66.8, 51.4, 48.6, 30.6. IR (ATR): 3332, 1711, 1687, 1530, 1254, 1051 cm^{-1}.

4.4.14. Benzyl N-[1-(2-oxocyclohexyl)ethyl]carbamate **(5n)**. This product was obtained in 81% yield (44.6 mg) by Method A or 76% yield (41.9 mg) by Method B. Compound **5n**, in each method, was obtained as a mixture of diastereomers (dr = 50:50). White solid; R_f = 0.17 (hexanes/AcOEt = 4:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37-7.29 (m, 5H), 5.49 (d, J = 9.6 Hz, 0.5H), 5.45 (d, J = 9.0 Hz, 0.5H), 5.12-5.03 (m, 2H), 3.91-3.85 (m, 0.5H), 3.85-3.79 (m, 0.5H), 2.57-2.21 (m, 3H), 2.08-1.87 (m, 3H), 1.70-1.51 (m, 3H), 1.24 (d, J = 7.2 Hz, 1.5H), 1.20 (d, J = 6.6 Hz, 1.5H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 212.9, 212.3, 156.1, 155.7, 136.6, 136.6, 132.1, 132.0, 128.4, 128.0, 128.0, 66.5, 55.1, 54.6, 48.0, 47.6, 42.9, 42.5, 31.8, 31.0, 28.0, 27.2, 24.9, 24.7, 19.8, 16.8. IR (ATR): 3295, 2970, 1770, 1683, 1541, 1291, 1254, 1090, 1049 cm^{-1}. HRMS (ESI) *m/z:* calcd for $C_{16}H_{22}NO_3$ $[M+H]^+$ 276.1600, found 276.1596.

4.4.15. Benzyl N-[(2-oxocyclohexyl)(phenyl)methyl]carbamate **(5o)**.[26] This product was obtained in 88% yield (59.6 mg) by Method A or 89% yield (60.0 mg) by Method B. Compound **5o**, in each method, was obtained as a mixture of diastereomers (dr = 65:35). White solid; R_f = 0.19 (hexanes/AcOEt = 4:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.36-7.20 (m, 10H), 6.12 (br d, J = 7.8 Hz, 0.35H), 6.06 (br d, J = 7.8 Hz, 0.65H), 5.10-5.01 (m, 2H), 4.96 (dd, J_1 = 8.4 Hz, J_2 = 6.6 Hz, 0.65H), 4.90 (dd, J_1 = 8.1 Hz, J_2 = 3.3 Hz, 0.35H), 2.94-2.90 (m, 0.35H), 2.90-2.81 (m, 0.65H), 2.38-1.33 (m, 8H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 212.5, 211.4, 156.2, 155.7, 141.2, 140.1, 140.0, 136.4, 128.4, 128.3, 128.3, 128.0, 128.0, 127.9, 127.3, 127.1, 126.6, 66.7, 55.9, 55.7, 54.9, 42.5, 42.3, 32.6, 30.5, 28.1, 26.8, 24.5, 24.4. IR (ATR): 3317, 2951, 2862, 1701, 1678, 1530, 1243, 1143, 1143, 1047 cm^{-1}.

4.4.16. Benzyl N-[1-(1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)ethyl]carbamate **(5p)**.[27] This product was obtained in 97% yield (74.9 mg) by Method A. Compound **5p** was obtained as a mixture of diastereomers (dr = 55:45). White solid, R_f = 0.26 (hexanes/AcOEt = 4:1).^{1}H NMR (600 MHz, $CDCl_3$): δ 8.00 (d, J = 7.8 Hz, 0.45H), 7.95 (d, J = 7.8 Hz, 0.55H), 7.50-7.12 (m, 13H), 6.93 (br d, J = 9.6 Hz, 0.45H), 5.90 (br s, 0.55H), 5.16-5.01 (m, 3H), 3.15-2.87 (m, 3H), 2.29-1.73 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 198.9, 198.5, 156.0, 155.7, 143.7, 143.4, 141.0, 139.6, 136.5, 136.4, 133.7, 133.7, 132.7, 132.5, 132.1, 132.0, 128.7, 128.6, 128.5, 128.4, 128.3, 128.1, 128.0, 127.9, 127.5, 127.4, 127.3, 66.8, 66.7, 56.9, 55.4, 52.6, 52.1, 29.2, 27.9, 27.2, 27.0. 39.2, 29.7, 23.3. IR (ATR): 3338, 3029, 1682, 1496, 1454, 1495, 1226, 1156, 1046 cm^{-1}.

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Supplementary Material

^{1}H, ^{13}C and ^{31}P NMR spectra for unknown 1-(*N*-acylamino)alkyltriphenylphosphonium tetrafluoroborates **1**. ^{1}H NMR spectra for known or ^{1}H and ^{13}C NMR spectra for unknown β-amino carbonyl products **3** and **5**. (PDF). Supplementary data associated with this article can be found in the online version.

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