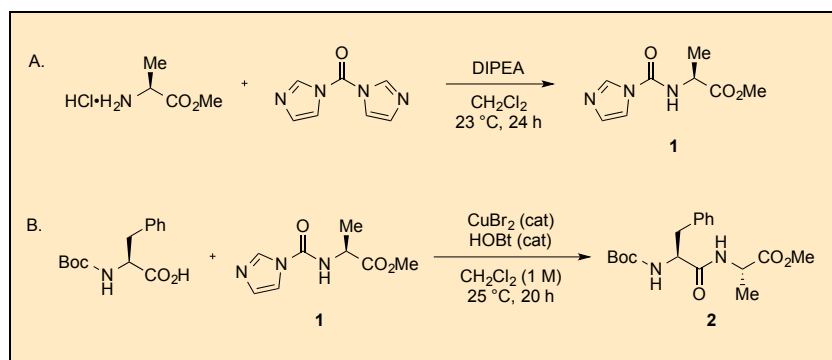


Dipeptide Syntheses via Activated α -Aminoesters

Jean-Simon Suppo, Renata Marcia de Figueiredo,* and Jean-Marc Campagne*¹

ICGM-UMR 5253 CNRS-UM-ENSCM, Ecole Nationale Supérieure de Chimie, 8 Rue de l'École Normale, 34296 Montpellier Cedex 5, France

Checked by John T. Colyer, Christopher J. Borths and Margaret Faul



Procedure

A. *Methyl (1H-imidazole-1-carbonyl)-L-alaninate (1)*. A 500-mL round-bottomed, single-necked flask, equipped with a 50 x 20 mm, Teflon-coated, oval magnetic stir bar, is charged with *N,N'*-carbonyldiimidazole (CDI) (11.6 g, 71.6 mmol) (Note 1), which is weighed into the flask under air, followed by dichloromethane (40 mL) (Note 2). Gentle stirring produces a slightly turbid suspension. The flask is sealed with a rubber septum, into which is inserted a digital thermometer probe. The flask is placed in an ice water bath to bring the temperature of the solution to 0 °C (Note 3) (Note 4). A second 250-mL round-bottomed, single-necked flask equipped with a 50 x 20 mm, Teflon-coated, oval magnetic stir bar, is then charged with L-alanine methyl ester hydrochloride ($\text{HCl}\cdot\text{H}_2\text{N-Ala-OMe}$) (10.0 g, 71.6 mmol) (Note 5), which is weighed into the flask under air, followed by

dichloromethane (80 mL) (Note 2). To the resulting white suspension is added diisopropylethylamine (DIPEA) (9.25 g, 12.5 mL, 71.6 mmol) (Note 6). At this stage, the suspension turns to a clear solution (Note 7), which is then transferred to a 250-mL dropping funnel (20 x 5 cm) (Note 8). The dropping funnel is attached to the 500-mL round-bottomed flask containing the chilled CDI suspension and fitted with a calcium chloride filled drying tube (15 g) (Notes 9 and 10). The amino acid/DIPEA solution is then added dropwise over 40 min (Note 11) to the CDI-suspension at 0 °C (Notes 4 and 12). As the reaction progresses, the suspension transforms into a clear, colorless solution. After the complete addition of the L-alanine methyl ester solution, the final mixture is stirred at room temperature (23 °C) for 20 h (Note 13). Upon completion of the reaction (Note 14), the mixture is concentrated using a rotary evaporator (30 °C water bath, 40 mmHg). Ethyl acetate (EtOAc) (200 mL) is added and the solution is transferred to a 1.0 L separatory funnel (Note 15). Additional EtOAc (50 mL) is used to assist transfer. The mixture is washed once with deionized water (150 mL). The aqueous layer is separated and further extracted with EtOAc (2 x 60 mL). The combined organic layers are dried over anhydrous magnesium sulfate (50 g) (Note 16), filtered through a glass filter funnel filled with cotton (Note 17), and concentrated using a rotary evaporator (30 °C water bath, 10 mmHg) to provide a viscous oil. The crude product is purified by flash chromatography on silica gel to afford **1** (10.21 g, 70.3%) (Notes 18, 19, and 20) as a white solid (Note 21 and 22).

B. *Methyl (tert-butoxycarbonyl)-L-phenylalanyl-L-alaninate* (**2**). A 100-mL round-bottomed, single-necked flask equipped with a 30 x 16 mm, Teflon-coated, oval magnetic stir bar, is charged with methyl (1*H*-imidazole-1-carbonyl)-L-alaninate (8.0 g, 40.6 mmol) (Note 23), which is weighed into the flask under air, followed by CH₂Cl₂ (41 mL, 1.0 M) (Note 2). Gentle stirring at 20–22 °C (Note 24) gives a clear colorless solution, to which is successively added Boc-L-phenylalanine (Boc-Phe-OH) (16.16 g, 60.9 mmol), 1-hydroxybenzotriazole hydrate (HOBt hydrate) (549 mg, 10 mol%, 4.06 mmol) and copper(II) bromide (CuBr₂) (907 mg, 10 mol%, 4.06 mmol) (Note 25). The flask is closed with a rubber septum equipped with a needle (Note 26). As the reaction progresses, CuBr₂ becomes more



Figure 1. Reaction appearance

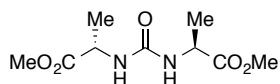
and more soluble and the solution evolves from pale blue into a deep turquoise/blue slurry (Figure 1). The reaction is stirred (Note 27) at 20-22 °C for 20 h. Upon completion of the reaction (TLC monitoring) (Note 28), the mixture is transferred into a 1.0 L Erlenmeyer flask, diluted with dichloromethane (CH_2Cl_2) (250 mL) and quenched with an aqueous solution of 0.5 N HCl (100 mL) (Note 29). Afterwards, the mixture is transferred to a 1.0 L separatory funnel. Additional CH_2Cl_2 (50 mL) is used to assist transfer. The aqueous layer is separated and further extracted with CH_2Cl_2 (1 x 50 mL). The combined organic layers are washed with a saturated solution of sodium bicarbonate (NaHCO_3) (100 mL) (Note 30), and the aqueous layer is further extracted with CH_2Cl_2 (1 x 50 mL). The combined organic layers are then washed with brine (100 mL), dried over MgSO_4 (50 g) (Note 16), filtered through a glass filter funnel filled with cotton (Note 31), and concentrated using a rotary evaporator (30 °C water bath, 10 mmHg) to give a white solid. The crude product is purified by flash chromatography on silica gel to afford **2** (11.73 g, 82.4%) (Note 32) as a white foam (Note 33 and 34) (Figure 2).

Notes

1. *N,N'*-Carbonyldiimidazole (CDI) was purchased from Sigma-Aldrich (reagent grade) and used as received.
2. Dichloromethane was purchased from Sigma-Aldrich (certified 99.8%, containing 50-150 ppm amylene as stabilizer) and used as supplied. Caution should be taken with the CH₂Cl₂ quality in order to prevent the formation of undesired side compounds. CH₂Cl₂ stabilized with EtOH should be avoided, otherwise the formation of ethyl 1*H*-imidazole-1-carboxylate could also be detected on the first step.
3. Cooling is necessary in order to avoid the formation of symmetrical urea (Note 22).
4. The mixture is stirred at 500 rpm throughout the reaction.
5. L-Alanine methyl ester hydrochloride, 99% from Sigma-Aldrich, was used as received. This compound is very hygroscopic.
6. Diisopropylethylamine (DIPEA) (99.5%) was purchased from Sigma-Aldrich and used without further purification.
7. For small scale synthesis (<15 mmol) triethylamine (Et₃N) was used as base. For operational facility on large scale DIPEA was used, which, in contrast to Et₃N, generates a soluble salt in the presence of HCl•H₂N-Ala-OMe in CH₂Cl₂. This soluble salt is easier to add dropwise into the CDI pre-cooled suspension.
8. The flask containing the mixture of L-alanine methyl ester hydrochloride and DIPEA was rinsed twice with CH₂Cl₂ (2 x 5 mL). Then, the combined 10 mL were added to the dropping funnel.
9. A dropping funnel with a Teflon tap was used for the addition of the amino acid to the CDI suspension.
10. Calcium chloride (anhydrous, granular, ≤ 7.0 mm, ≥93.0%) from Sigma-Aldrich was used as received. The drying tube containing a sintered glass filter was used.
11. The dropping funnel containing the mixture of L-alanine methyl ester hydrochloride and DIPEA was rinsed twice with CH₂Cl₂ (2 x 5 mL).
12. The slow addition of L-alanine methyl ester solution is necessary in order to avoid the symmetric urea formation (Note 22).
13. A second reaction was allowed to proceed for 22 hours.
14. The formation of the desired product was observed by TLC (on Merck silica gel 60 F₂₅₄ TLC aluminum plates) and visualized with UV light and ninhydrin staining solution (Note 35). R_f product: 0.20, eluent:

- EtOAc 100%. Visualization was difficult with UV light when dilute samples were used.
- Ethyl acetate ($\geq 99.8\%$ from Sigma-Aldrich) was used as received.
 - Magnesium sulfate ($\geq 99.5\%$ from Sigma-Aldrich) was used as received.
 - Additional EtOAc (2 x 20 mL) is used during filtration to assist transfer. An M grade glass filter was used for the filtration.
 - The crude reaction product (14.5 g) was adsorbed on silica (40 g of silica with 150 mL of CH_2Cl_2 followed by evaporation) and then loaded onto a column (diameter: 7 cm, height: 70 cm) packed with silica gel (300 g of silica, pore size 60Å, 230-400 mesh, 40-63 μm particle size, Fluka Analytical) slurry in EtOAc 100%. After 500 mL of initial elution, fraction collection (250 mL fractions) is begun, and elution is continued with 4.5 L of pure EtOAc. The desired α -activated amino ester is obtained in fractions 4-18, which are concentrated by rotary evaporation (30 °C, 10 mmHg) and then dried at 0.05 mmHg. Residual ethyl acetate was difficult to remove and could be observed by ^1H NMR after 1 week under house vacuum ($<1\%$). Ethyl acetate did not hinder the formation and isolation of product during the next step.
 - Yields were adjusted for wt% of product as determined by QNMR (97.2% wt% and 98.2% wt% for Run 1 and 2, respectively).
 - The chemical yield of this step can be improved to 86% by using 1.5 equiv of CDI.
 - A second reaction at the same scale provided 10.52 g (73.2%, 98.2% wt%) of a white solid. Yields were adjusted for potency of product. Weight percent was determined by QNMR with benzyl benzoate as an internal standard. Characterization as follows: $[\alpha]_{\text{D}}^{26} +31.3$ (c 0.7, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ : 1.54 (d, $J = 7.2$ Hz, 3 H), 3.81 (s, 3 H), 4.66 (quint, $J = 7.2$ Hz, 1 H), 7.01 (br d, $J = 6.9$ Hz, 1 H), 7.08 (s, 1 H), 7.41 (t, $J = 1.4$ Hz, 1 H), 8.18 (s, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ : 17.3, 49.5, 52.5, 116.4, 129.5, 136.1, 148.7, 172.8; IR (neat): 3138.9, 2969.5, 2878.8, 2809.5, 1740.3, 1711.7, 1553.7, 1484.4, 1454.5, 1376.9, 1288.4, 1256.4, 1213.2, 1150.6, 1104.2, 1072.7, 754.8 cm^{-1} ; HRMS (ESI) $^+$ $[\text{M}+\text{H}]^+$ calcd for $\text{C}_8\text{H}_{12}\text{N}_3\text{O}_3$: 198.0879. Found: 198.0873. mp 90.0–92.5 °C; the melting point was lower than that reported by the submitters (mp 95.6–97.9 °C) due to residual solvent and impurities.
 - The symmetrical urea depicted below is generated from auto-condensation of the free α -aminoester and its activated form. Its formation is observed either when the reaction is run at higher temperatures (> 0 °C) or when the reagents are added at once. It might

be noted that on small-scale reactions, only small amounts (<7%) of this compound were observed in the crude material.⁶ A peak in ¹H NMR was observed after column chromatography that is consistent with the 6H singlet expected at ~3.7 ppm. If this resonance is assigned correctly, then 1.7% and 1% of the symmetrical urea impurity was observed, respectively, in Runs 1 and 2 after column chromatography. The impurity was removed during the subsequent isolation in Step 2.



23. Charges were not adjusted for wt% of methyl (1*H*-imidazole-1-carbonyl)-L-alaninate.
24. The checkers performed this chemistry at ambient temperature (20–22 °C) in an unjacketed flask without temperature control. The submitters report that control of temperature is very important to ensure good reaction yields. Temperatures lower than 25 °C lead to the formation of dipeptides, with erosion of isolated yields.
25. The following reagents were purchased from commercial sources and used without further purification: Boc-Phe-OH, ≥99% from Aldrich; HOBt hydrate, wetted with not less than 14 wt.% water, 97% from Aldrich; CuBr₂, 99% from Aldrich.
26. The rubber septum is equipped with a needle (22G x 1½" 0.7 x 40 mm) in order to allow the removal of CO₂ that is formed during the reaction.
27. The mixture is stirred at 400 rpm throughout the reaction.
28. The formation of the dipeptide was monitored by TLC analysis on Merck silica gel 60 F₂₅₄ TLC aluminum plates and visualized with UV light and ninhydrin staining solution (Note 35). R_f dipeptide: 0.3, eluent: pentane/EtOAc 7:3. Pentane (≥99% from Sigma-Aldrich) was used as received.
29. The mixture is swirled vigorously for 10 min while deep blue color faded to very pale light blue.
30. The addition of a saturated solution of NaHCO₃ to the organic layer was followed by the formation of an emulsion, which disappears after standing in the separatory funnel for approximately 15 minutes.
31. Additional CH₂Cl₂ (2 x 20 mL) is used during filtration to assist transfer.

32. Yields are based on two full scale runs and are adjusted for wt% of product as determined by QNMR (99.6% wt% and 100% wt% for Run 1 and 2, respectively).
33. The crude product (14.0 g) was adsorbed on silica (40 g of silica with 120 mL of CH₂Cl₂ followed by evaporation) and then was loaded onto a column (diameter: 7 cm, height: 70 cm) packed with a short pad of silica gel (200 g of silica pore size 60Å, 230-400 mesh, 40-63 μm particle size, Fluka Analytical) slurry in pentane:EtOAc 7:3. After 500 mL of initial elution, fraction collection (250 mL fractions) is begun, and elution is continued with 3.25 L of additional solvent. The desired dipeptide is obtained in fractions 3-13, which are concentrated by rotary evaporation (30 °C, 10 mm Hg) and then dried at 0.05 mmHg.
34. A second reaction at the same scale provided 11.86 g (83%, 99.6% wt%) of a white foam. Yields were adjusted for potency of product. Weight percent was determined by QNMR with benzyl benzoate as an internal standard. Characterization as follows: mp 108.0–110.5 °C; [α]_D²⁶ +0.40 (c 0.99, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ: 1.34 (d, J = 7.0 Hz, 3 H), 1.40 (s, 9 H), 3.02–3.12 (m, 2 H), 3.71 (s, 3 H), 4.26–4.44 (m, 1 H), 4.52 (quint, J = 7.1 Hz, 1 H), 5.08 (br. S, 1 H), 6.46–6.66 (m, 1 H), 7.18–7.32 (m, 5 H); ¹³C NMR (100 MHz, CDCl₃) δ: 18.0, 28.1, 38.3, 47.9, 52.2, 55.4, 79.9, 126.7, 128.4, 129.3, 136.6, 155.3, 170.9, 172.8. IR (neat): 3323.4, 2984.1, 2946.6, 1751.7, 1692.8, 1655.5, 1522.4, 1445.9, 1385.8, 1366.2, 1250.5, 1159.4, 1049.5, 988.9, 859.6, 664.4 cm⁻¹; HRMS (ESI)⁺ [M+H]⁺ calcd for C₁₈H₂₇N₂O₅: 351.1920. Found: 351.1915.
35. The ninhydrin stain was prepared using 1.5 g of ninhydrin dissolved in 100 mL of *n*-butanol and 3.0 mL of AcOH.

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general

guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

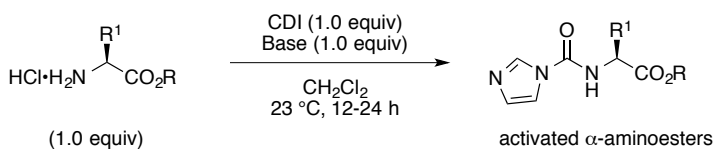
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

Discussion

The amide functionality is of paramount relevance in organic and pharmaceutical chemistry, being present in natural and unnatural bioactive compounds, polymers and materials. Nowadays, around 25% of all drugs on the market hold at least one amide bond on their structure.² Although several different methods for amidation in general are described,³ options are still more scarce in peptide chemistry.⁴ The most widespread method for peptide bond formation relies on the use of a peptide coupling reagent⁵ in order to transform a carboxylic acid function into a more reactive intermediate, being thus prone to react with a free amine. High yielding procedures are guaranteed by very effective peptide coupling reagents. However, this strategy suffers from major drawbacks, including racemization, low atom economy, high cost, and constraints with regard to the direction of the peptide synthesis (i.e., C→N direction).

Recently, we have developed a practical and efficient procedure for the formation of peptide bonds on the basis of a new mode of activation of amino acids.⁶ The method relies on the use of activated α -aminoesters,

(obtained from α -aminoesters and inexpensive N,N' -carbonyldiimidazole - CDI),⁷ instead of classical carboxylic acid activation. These activated compounds are prepared under mild conditions, they are readily purified by simple filtration over silica gel and they are stable for months when stored at 4 °C (Scheme 1).

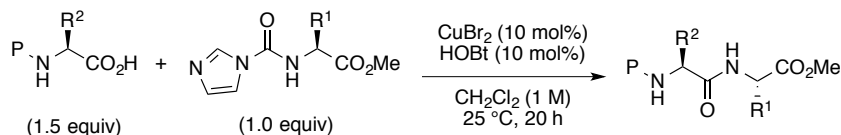


R = Me, Et, *t*-Bu, Allyl
R¹ = Proteogenic amino acid side chains

Readily available and stable substrates
Excellent amino acid residues tolerance
Easy work-up
High Yields
More than 15 examples synthesized

Scheme 1. CDI-mediated synthesis of activated α -aminoesters⁶

From the optimized procedure, it was found that the peptide-bond formation is accomplished under very mild conditions, without the need for a base. Whereas the coupling reaction can proceed in the sole presence of a free amino acid residue and an activated α -aminoester in CH_2Cl_2 as solvent, it was found that catalytic amounts (10 mol%) of CuBr_2 and HOBT has a synergic effect on the condensation reaction, yielding the required dipeptides in improved isolated yields (Scheme 2).



R = Me, Et, *t*-Bu, Allyl
 P = Fmoc, Boc, Cbz
 R¹, R² = Proteogenic amino acid side chains

Mild reaction conditions
Practical procedure
No need to add a base
Compatible with N-urethane protecting groups
High yields
More than 20 dipeptides synthesized

Scheme 2. Dipeptide syntheses via activated α -aminoesters

The above procedure is representative of the synthesis of diversely substituted dipeptides. Indeed, amino acids bearing the most common *N*-urethane protecting groups (e.g. Fmoc, Boc and Cbz) as well as amino acid residues with functionalized side-chains are compatible with the method. Moreover, the strategy features a convenient issue to the less common reverse *N*→*C* direction peptide synthesis (ribosomal peptide direction synthesis) as the preparation of an illustrative tetrapeptide model has been made.⁶ Besides, this system presents new opportunities for the preparation of a key amide functional group in pharmaceutical chemistry.⁸

References

1. Institut Charles Gerhardt Montpellier (ICGM), UMR 5253 CNRS-UM-ENSCM, Ecole Nationale Supérieure de Chimie, 8 Rue de l'École Normale, 34296 Montpellier Cedex 5, France. E-mail: jean-marc.campagne@enscm.fr and renata.marcia_de_figueiredo@enscm.fr. The Agence Nationale de la Recherche (ANR) under the Programme Jeunes Chercheuses Jeunes Chercheurs (JCJC) 2012, grant agreement ANR-12-JS07-0008-01 (NIPS project) is gratefully acknowledged for financial support.

2. a) Ghose, A. K.; Viswanadhan, V. N.; Wendoloski J. J. *J. Combin. Chem.* **1999**, *1*, 55-68; b) Carey, J. S.; Laffan, D.; Thomson, C.; Williams, M. T. *Org. Biomol. Chem.* **2006**, *4*, 2337-2347.
3. Selected examples of amide formation throughout non-conventional carboxylic acid activation: a) Bode, J. W.; Fox, R. M.; Baucom, K. D. *Angew. Chem. Int. Ed.* **2006**, *45*, 1248-1252; b) Shen, B.; Makley, D. M.; Johnston, J. N. *Nature* **2010**, *465*, 1027-1032; c) Wang, T.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2012**, *134*, 13244-13247; d) Kolakowski, R. V.; Shangguan, N.; Sauers, R. R.; Williams, L. J. *J. Am. Chem. Soc.* **2006**, *128*, 5695-5702; e) Wilson, R. M.; Stockdill, J. L.; Wu, X.; Li, X.; Vadola, P. A.; Park, P. K.; Wang, P.; Danishefsky, S. J. *Angew. Chem. Int. Ed.* **2012**, *51*, 2834-2848; f) Chen, W.; Shao, J.; Hu, M.; Yu, W.; Giulianotti, M. A.; Houghten, R. A.; Yu, Y. *Chem. Sci.* **2013**, *4*, 970-976; g) Schuemacher, A. C.; Hoffmann, R. W. *Synthesis* **2001**, 243-250; h) Sasaki, K.; Crich, D. *Org. Lett.* **2011**, *13*, 2256-2259; i) Crich, D.; Sasaki, K. *Org. Lett.* **2009**, *11*, 3514-3517; j) Nordstrøm, L. U.; Vogt, H.; Madsen, R. *J. Am. Chem. Soc.* **2008**, *130*, 17672-17673.
4. a) Jones, J. *The Chemical Synthesis of Peptides*, Oxford Science Publications, Oxford, **1991**; b) *Synthesis of Peptides and Peptidomimetics*, Goodman, M.; Felix, A.; Moroder, L.; Toniolo, C. *Houben-Weyl, Methods of Organic Chemistry, Vol E22a*, Thieme, Stuttgart, **2002**; c) Sewald, N.; Jakubke, H.-D. *Peptides: Chemistry and Biology*, Wiley-VCH, Weinheim, **2002**; d) Guzmán, F.; Barberis, S.; Illanes, A. *Electron. J. Biotechnol.* **2007**, *10*, 279-314.
5. Selected reviews: a) Albericio, F.; Chinchilla, R.; Dodsworth, D. J.; Nájera, C. *Org. Prep. Proced. Int.* **2001**, *33*, 203-303; b) Han, S.-Y.; Kim, Y.-A. *Tetrahedron* **2004**, *60*, 2447-2467; c) Montalbetti, C. A. G. N.; Falque, V. *Tetrahedron* **2005**, *61*, 10827-10852; d) Valeur, E.; Bradley, M. *Chem. Soc. Rev.* **2009**, *38*, 606-631; e) El-Faham, A.; Albericio, F. *Chem. Rev.* **2011**, *111*, 6557-6602; f) Joullié, M. M.; Lassen, K. M. *ARKIVOC* **2010**, 189; g) Amblard, M.; Fehrentz, J.-A.; Martinez, J.; Subra, G. *Mol. Biotechnol.* **2006**, *33*, 239-254; h) Lanigan, R. M.; Sheppard, T. D. *Eur. J. Org. Chem.* **2013**, 7453-7465.
6. Suppo, J.-S.; Subra, G.; Bergès, M.; de Figueiredo R. M.; Campagne, J.-M. *Angew. Chem. Int. Ed.* **2014**, *53*, 5389-5393.
7. a) Paul, R.; Anderson, G. W. *J. Am. Chem. Soc.* **1960**, *82*, 4596-4600; b) Staab, H. A. *Angew. Chem. Int. Ed.* **1962**, *1*, 351-367; c) Heller, S. T.; Sarpong, R. *Org. Lett.* **2010**, *12*, 4572-4575; d) Heller, S. T.; Fu, T.; Sarpong, R. *Org. Lett.* **2012**, *14*, 1970-1973.

8. Roughley, S. D.; Jordan, A. M. *J. Med. Chem.* **2011**, *54*, 3451–3479.

Appendix

Chemical Abstracts Nomenclature (Registry Number)

L-Alanine methyl ester hydrochloride; (2491-20-5)
Diisopropylethylamine; (7087-68-5)
N,N'-Carbonyldiimidazole; (530-62-1)
Boc-L-phenylalanine; (13734-34-4)
Copper(II) bromide; (7789-45-9)
1-Hydroxybenzotriazole hydrate; (123333-53-9)



Jean-Simon Suppo was born in Briançon, France, in 1989. He received his Master's degree in Chemistry from Aix-Marseille University in 2012 under the direction of Prof. Laurence Feray. Then, he moved to Montpellier and began his doctoral studies under the guidance of Prof. Jean-Marc Campagne and Dr. Renata Marcia de Figueiredo. His graduate research focuses on inverse peptide synthesis through amine activation.



Renata Marcia de Figueiredo was born in Boa Esperança-MG, Brazil. She received her Ph.D. degree from the University of Paris Sud (Orsay-France) in 2005. Then, she moved to Germany as a postdoctoral research fellow in the group of Prof. M. Christmann in RWTH-Aachen. In 2008, she was appointed CNRS researcher at the Ecole Nationale Supérieure de Chimie de Montpellier (ENSCM) where she has joined the group of Prof. J.-M. Campagne. Her research interests include the development and the application of catalytic asymmetric methodologies to the total synthesis of natural products and biologically active targets.



Jean-Marc Campagne was born in Pau, France, in 1967. After studies at the Ecole Nationale Supérieure de Chimie de Montpellier (ENSCM), he received his Ph.D. at the University of Montpellier in 1994. After post-doctoral training with Prof. B. Trost (Stanford University, USA) and Prof. L. Ghosez (Université Catholique de Louvain, Belgium), he was appointed CNRS researcher at the Institut de Chimie des Substances Naturelles in Gif-sur-Yvette in 1998. Since 2005 he moved to the ENSCM where he was appointed as Professor. His current interests concern the development of catalytic asymmetric transformations and their application to the total synthesis of natural products.



John T. Colyer was born in Columbus, Indiana in 1977. In 2000 he earned his B. S. in chemistry from Indiana University-Purdue University Indianapolis working under the guidance of Professor William H. Moser. He completed his M.S. in 2004 at the University of Arizona under the guidance of Professor Michael P. Doyle, where he studied dirhodium (II) carboxamidate catalysis. In 2004 he joined Amgen in Thousand Oaks, CA and currently works in the Chemical Process Research and Development group.



Christopher J. Borths received a B.S. in Chemistry and Biology from the University of Kentucky in 1998. He began his graduate studies in Chemistry at the University of California, Berkeley, earning a M.S. in 2000, and in 2004 he obtained a Ph.D. from the California Institute of Technology for the development of novel organocatalytic methods with Prof. David MacMillan. He then joined the Chemical Process Research and Development group at Amgen where he is currently a Senior Scientist.