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T3P® (propylphosphonic anhydride) mediated conversion of carboxylic acids into acid azides and one-pot synthesis of ureidopeptides

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ABSTRACT

A general, mild, efficient, and environmentally benign protocol, which makes use of T3P® as an acid activating agent for the direct synthesis of acid azides from carboxylic acids is described. Further, the protocol is employed for the one-pot synthesis of α-ureidopeptides starting from N-protected α-amino acids.

Acid azides are synthetically extremely valuable compounds. They form the starting materials for a vast range of reactions in organic synthesis as well as in peptides and peptidomimetic synthesis. Acid azides are extensively used for the preparation of amides, nitriles, and a variety of heterocycles through cycloaddition reactions.[1] Curtius rearrangement of acid azides into isocyanates is of profound importance in organic synthesis as this can be used for the preparation of amines, ureas, carbamates, amides, and many other class of compounds.[2] In peptide chemistry, acid azides occupy an important place wherein they form the building blocks for peptide as well as peptidomimetic synthesis. They have been employed as coupling agents for the racemization-free formation of peptide bond. These are also employed for the synthesis of peptide mimics such as partially modified retro-inverso peptides, α/β-ureidopeptides, and amino acid derivatives like formamides and alkyl-*gem*-diamines.[3] The reactions of acid azides have been used to advantage for the construction of a number of biologically valuable compounds. In this regard, development of a new and improved protocol for acid azide synthesis is significant.

Acid azides are synthesized mainly through two routes (i) a two-step protocol in which carboxylic acids are converted into stable reactive intermediates such as acid chlorides,[4] acid hydrazides,[5] and acyl benzotriazoles[6] followed by their treatment with azide ion. (ii) One-pot protocols with in situ activation of carboxylic acids in the presence of azide ion. The former approach lacks universal applications, for instance acid chloride and acid hydrazide methods are not compatible with substrates having acid and base sensitive groups, respectively. Further, the acid chloride method is constrained with respect to storage and stability aspects due to the moisture sensitivity of certain acid chlorides. Also, the poor solubility of NaN_3 in organic medium requires phase transfer catalysts, ZnI_2/Zn triflate[7] to obtain acceptable yields. Acid hydrazides have to be synthesized through a multistep process starting from acids. In case of acyl benzotriazoles, the reaction duration is prolonged. For the direct synthesis of acid azides from acids, several types of activating agents have been employed, but many of them possess certain intrinsic limitations. Some of these reagents are toxic (triphosgene),[8] irritating ($SOCl_2$/DMF),[9] expensive [diphenylphosphoryl azide (DPPA), deoxoflour],[10] while a few other reagents produce undesirable by-products which are difficult to separate and toxic which in turn requires additional handling costs and safety measures (i.e., cyanuric chloride, tetramethylflouroformamidinium hexaflourophosphate, and phenyl dichlorophosphate).[11] Reagents like NCS–Ph_3P and the recently reported Cl_3CCN–Ph_3P[12] have been employed, but the presence of triphenyl phosphine unit in them disfavors the use of acid sensitive reactants. The extensively employed mixed anhydride method[13] suffers from the problem of isomerization in case of α,β-unsaturated acids. Also, the mixed anhydride intermediates should be generated by using chloroformates, which are corrosive and irritants and harmful if inhaled, so pose handling problems.

Our group has described the first synthesis of stable N^{α}-Fmoc-amino acid azides and demonstrated their application as peptide-coupling agents. These acid azides were prepared via acid chloride and mixed anhydride methods. Recently we also reported the synthesis of acid azides using peptide-coupling agents EDC and

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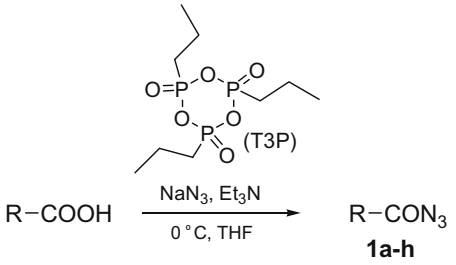


Scheme 1. Synthesis of acid azides **1a–h**.

HBTU.[14] Due to the immense utility and wide applicability of acid azides, we sought to develop a simple, alternative, and efficient protocol for the synthesis of these useful class of compounds.

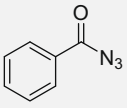
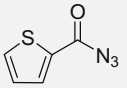
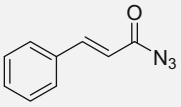
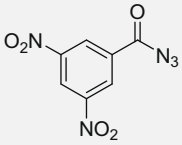
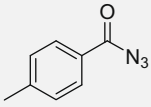
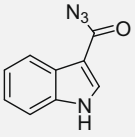
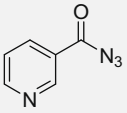
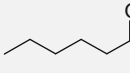
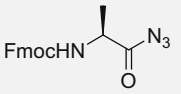
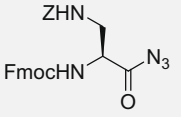
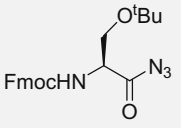
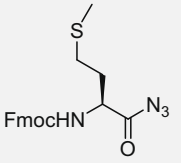
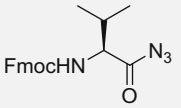
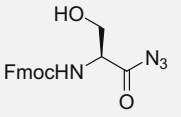
T3P® (propylphosphonic anhydride) is a highly reactive cyclic anhydride, which has been employed for the conversion of carboxylic acids, aldehydes, and amides to nitriles and formamides to isonitriles. It has also been used in the preparation of heterocycles, Weinreb amides, β-lactams, hydroxamic acids, thiohydroxamic acid anhydrides, and in acylation reactions.[15] It has been used as a peptide-coupling agent, in the segment coupling and head to tail cyclization of sterically hindered peptides.[16] T3P® offers several advantages over other reagents in terms of higher yields, shorter reaction duration, ease of isolation of the products, minimal side reactions including epimerization during peptide couplings, inexpensive, and non-toxic nature. Based on these qualities, we sought to develop a simple and efficient method for the direct synthesis of acid azides from carboxylic acids employing T3P®.

A typical reaction was carried using benzoic acid as acid component. A solution of benzoic acid and T3P® in dry CH_2Cl_2 at 0 °C was treated with NaN_3 in DMSO in the presence of Et_3N. Carboxyl group underwent activation by the T3P® and readily reacted with the azide ion to give corresponding benzoyl azide in 20 min in 92% yield. The formation of acid azide was confirmed by the presence of a strong IR peak around ν_{max} 2140–2144 cm^{-1} and finally through mass and NMR analyses. To explore the scope of this protocol, a series of aromatic acids substituted with electron-donating as well as electron-withdrawing groups and long chain aliphatic acids (hexanoic acid) were converted into corresponding acid azides, **1a–h** in good yield (Scheme 1).[17] Table 1 summarizes the results. In all these preparations, no column purification was needed, as the protocol did not result in the formation of contaminants and hence the acid azides could be isolated in pure form through simple work-up.

The protocol was extended to prepare N^{α}-Fmoc and Z-protected amino acid azides from the corresponding N^{α}-protected amino acids.[17] Several Fmoc-amino acid azides **2a–f** including the side chain protected amino acids (**2b** and **2c**) were prepared and isolated as solids (Scheme 2). In all the cases, the reaction proceeded smoothly and rapidly with quantitative yield (Table 1). *Z*-Phe-N_3 **2g** as well as the acid azide of N^{α}-*Z*-Asp-oxazolidin-5-one **2h** was prepared similarly. Interestingly, when the unprotected N^{α}-Fmoc-serine was subjected to the above-mentioned reaction conditions, the corresponding acid azide **2f** was obtained in good yield without affecting the free hydroxyl group, despite the oxidation of alcohol to aldehyde by T3P® is known.[15c] The acid azide formation requires about 20 min for completion while oxidation requires the treatment of alcohol with T3P® for overnight. Consequently, the synthesis of Fmoc-Ser-N_3 was possible.

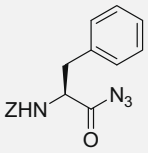
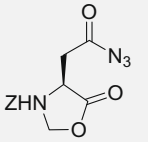
Finally, the utility of T3P® was applied for a three-step, one-pot synthesis of ureidopeptides from N^{α}-urethane protected amino acids. The one-pot protocols are of paramount importance for rapid synthesis of biologically active compounds and a large number of

Table 1
List of acid azides prepared via Schemes 1 and 2

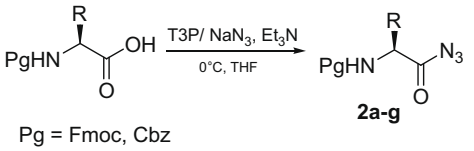
Compd No.	Acid azide	Yield[a] (%)	Mp (°C) obsd (lit.)
1a		92	26–28 (27)[14]
1b		82	34–37 (35)[14]
1c		81	81–84 (83)[14]
1d		72	104–106 (104–105)[9]
1e		84	33–35 (35)[12]
1f		85	Gum[14]
1g		86	Gum[14]
1h		76	Oil[8]
2a		94	162 (162)[1c]
2b		84	162–164 (162)[1c]
2c		86	177–178 (178)[1c]
2d		84	173–175 (172)[1c]
2e		89	166–168 (168)[1c]
2f		70	Gum

(*continued on next page*)

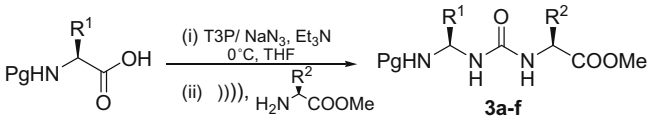
Table 1 (*continued*)

Compd No.	Acid azide	Yield[a] (%)	Mp (°C) obsd (lit.)
2g		91	148 (146)[14]
2h		76	Gum[14]

[a] Yields correspond to the isolated pure acid azides.



Scheme 2. Synthesis of N$^{\alpha}$-protected amino acid azides **2a**–**g**.



Comp. No.	Pg	R^1	R^2	Yield (%)
3a	Fmoc	CH_3	$CH(CH_3)_2$	92
3b	Fmoc	H	$(CH_2)_3$	88
3c	Z	$(CH_2)_3$	$CH_2S(Bzl)$	82
3d	Z	$CH_2C_6H_5$	$CH(CH_3)CH_2CH_3$	87
3e	Boc	$CH_2CH(CH_3)_2$	$CH(CH_3)_2$	80
3f	Boc	C_6H_5	$CH_2C_6H_5$	85

Scheme 3. Synthesis of N^{α}-urethane protected ureidopeptides **3a**–**f**.

their analogues. In case of the synthesis of N-protected-α-ureidopeptides using Boc and *Z*-amino acids as reactants, the one-pot protocols tend to furnish higher yields as the isolation of corresponding unstable acid azides can be circumvented.

The N$^{\alpha}$-protected amino acid was converted to corresponding acid azide in the presence of T3P®/NaN_3 in dry THF followed by in situ Curtius rearrangement in toluene under ultrasonic conditions into isocyanates. The transformation of acid azide into isocyanate in toluene under ultrasonic conditions was previously reported by our group.[2f] The formation of isocyanate was confirmed through the appearance of IR peak at around ν_{max} 2252–2256 cm^{-1}. Further, to the solution of isocyanate, amino acid methyl ester in dry CH_2Cl_2 was added and sonication was continued for an hour to obtain the corresponding ureidopeptide in good yield. A series of ureidopeptides **3a–f** were synthesized from N^{α}-Fmoc/*Z*/Boc amino acids.[18] In case of Boc-protected amino acids, an additional equivalent of base was used to avoid decrease in the yield, possibly due to the acidic by-product liberated.

The possibility of racemization during the synthesis of acid azides and α-ureidopeptides via the present protocol was assessed following the reported method, and it was found that the protocol was racemization-free and yielded optically pure products.[19,20]

In conclusion, we have described an alternative protocol for direct conversion of acids to acid azides by employing T3P®. A series of carboxylic acids including N^{α}-Fmoc/Z/Boc amino acids have been converted to their acid azides. The utility of the reagent has been extended for the one-pot synthesis of ureidopeptides. This protocol is mild, high yielding, economical and eco-friendly. The synthesis of acid azides as well as α-ureidopeptides via the present protocol was proved racemization free.

Acknowledgments

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References and notes

1. (a) Brase, S.; Gil, C.; Knepper, K.; Zimmermann, V. *Angew. Chem., Int. Ed.* **2005**, *44*, 5188–5240. and references cited therein; (b) Scriven, E. F. V.; Turnbull, K. *Chem. Rev.* **1988**, *88*, 297–368. and references cited therein; (c) Lutz, J.; Musiol, H.-J.; Moroder, L.. In *Houben-Weyl: Synthesis of Peptides and Peptidomimetics*; Goodman, M., Felix, A., Moroder, L., Toniolo, C., Eds.; Georg Thieme: Stuttgart, New York, 2004; Vol. E22a, p 427; (d) Fujii, N.; Yajima, H. J. *J. Chem. Soc., Perkin Trans. 1* **1981**, 831–841. and references cited therein; (e) Suresh Babu, V. V.; Ananda, K.; Vasanthakumar, G. R. *J. Chem. Soc., Perkin Trans. 1* **2000**, 4328–4331; (f) Chorev, M. *Biopolym. Pept. Sci.* **2005**, *80*, 67–84; (g) Fletcher, M. D.; Campbell, M. M. *Chem. Rev.* **1998**, *98*, 763–795; (h) Kangani, C. O.; Day, B. W.; Kelley, D. E. *Tetrahedron Lett.* **2008**, *49*, 914–918.
2. (a) Bermann, J. M.; Goodman, M. *Int. J. Pept. Prot. Res.* **1984**, *23*, 610–620; (b) Chorev, M.; Goodman, M. *Int. J. Pept. Prot. Res.* **1983**, *21*, 265–268; (c) Sudarshan, N. S.; Narendra, N.; Hemantha, H. P.; Sureshbabu, V. V. *J. Org. Chem.* **2007**, *72*, 9804–9807; (d) Sureshbabu, V. V.; Narendra, N.; Nagendra, G. *J. Org. Chem.* **2009**, *74*, 153–157; (e) Englund, E. A.; Gopi, H. N.; Appella, D. H. *Org. Lett.* **2004**, *6*, 213–215; (f) Sureshbabu, V. V.; Patil, B. S.; Venkataramanarao, R. *J. Org. Chem.* **2006**, *71*, 7697–7705.
3. (a) Moutevelis-Minakakis, P.; Photaki, I. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2277–2282; (b) Kokotos, G.; Markidis, T.; Constantinou-Kokotu, V. *Synthesis* **1996**, 1223–1226; (c) Sibi, M. P.; Deshpande, P. K. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1461–1466; (d) Guichard, G.; Semetey, V.; Didierjean, C.; Aubry, A.; Briand, J.-P.; Rodriguez, M. *J. Org. Chem.* **1999**, *64*, 8702–8705.
4. (a) Erhardt, P. W. *J. Org. Chem.* **1979**, *44*, 883–884; (b) Rewcastle, G. W.; Denny, W. A. *Synthesis* **1985**, 220–222; (c) Luedtke, A. E.; Timberlake, J. W. *J. Org. Chem.* **1985**, *50*, 268–270; (d) Padwa, A.; Brodney, M. A.; Liu, B.; Satake, K.; Wu, T. *J. Org. Chem.* **1999**, *64*, 3595–3607; (e) Govindan, C. K. *Org. Process Res. Dev.* **2002**, *6*, 74–77; (f) Lemmens, J. M.; Blommerde, W. W. J. M.; Thijs, L.; Zwanenburg, B. *J. Org. Chem.* **1984**, *49*, 2231–2235.
5. (a) Bodanszky, M.; Bodanszky, A. *The Practice of Peptide Synthesis*; Springer: Berlin, 1984. p 91; (b) Macor, J. E.; Mullen, G.; Verhoest, P.; Sampognaro, A.; Shepardson, B.; Mack, R. A. *J. Org. Chem.* **2004**, *69*, 6493–6495; (c) Nettekoven, M.; Jenny, C. *Org. Process Res. Dev.* **2003**, *7*, 38–43.
6. Katritzky, A. R.; Widyan, K.; Kirichnko, K. *J. Org. Chem.* **2007**, *72*, 5802–5804.
7. (a) Pfister, J. R.; Wymann, W. E. *Synthesis* **1983**, 38–39; (b) Suryaprakash, G. K.; Iyer, P. S.; Arvanaghi, M.; Olah, G. A. *J. Org. Chem.* **1983**, *48*, 3358–3359.
8. (a) Gumasthe, V. K.; Bhawel, B. M.; Deshmukh, A. R. A. S. *Tetrahedron Lett.* **2002**, *43*, 1345–1346; (b) Bao, W.; Wang, Q. *J. Chem. Res., Synop.* **2003**, 700–701.
9. Arrieta, A.; Aizprua, J. M.; Palomo, C. *Tetrahedron Lett.* **1984**, *25*, 3365–3368.
10. (a) Sureshbabu, V. V.; Chennakrishnareddy, G.; Narendra, N. *Tetrahedron Lett.* **2008**, *49*, 1408–1412; (b) Hemantha, H. P.; Chennakrishnareddy, G.; Vishwanatha, T. M.; Sureshbabu, V. V. *Synlett* **2009**, 407–410.
11. (a) Bandgar, B. P.; Pandith, S. S. *Tetrahedron Lett.* **2002**, *43*, 3413–3414; (b) El-Pham, A.; Abdul-Ghani, M. *Org. Prep. Proceed. Int.* **2003**, *35*, 369–374; (c) Lago, J. M.; Arrieta, A.; Palomo, C. *Synth. Commun.* **1983**, *13*, 289–296.
12. (a) Froyen, P. *Phosphorus, Sulfur and Silicon Relat. Elem.* **1994**, *89*, 57–61; (b) Kim, J.-G.; Jang, D. O. *Synlett* **2008**, 2072–2074.
13. (a) Chorev, M.; MacDonald, S. A.; Goodman, M. *J. Org. Chem.* **1984**, *49*, 821–827; (b) Bolm, C.; Dinter, C. L.; Schiffers, I.; Defrere, L. *Synlett* **2001**, 1875–1877; (c) Boekman, R. K.; Reeder, L. M. *Synlett* **2004**, 1399–1405; (d) Dussault, P. H.; Chunping, X. *Tetrahedron Lett.* **2004**, *45*, 7455–7457.
14. Sureshbabu, V. V.; Lalithamba, H. S.; Narendra, N.; Hemantha, H. P. *Org. Biomol. Chem.* **2010**, *8*, 835–840.
15. (a) Llanes, A. L. *Synlett* **2007**, 1328–1329. and references cited therein; (b) Augustine, J. K.; Atta, R. N.; Ramappa, B. K.; Boodappa, C. *Synlett* **2009**, 3378–

3382; (c) Meudt, A.; Scherer, S.; Böhm, C. PCT Int. Appl. WO 2005102978, 2005; *Chem. Abstr.* **2005**, *143*, 440908

16. (a) Wissmann, H.; Kleiner, H.-J. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 133–134; (b) Escher, R.; Bunning, P. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 277–278; (c) Glauder, J. *Specialit. Chem. Mag.* **2004**, *24*, 30. and references cited therein; (d) Wehner, M.; Kirschbaun, B.; Deutcher, L.; Wagner, H. J.; Hoessl, H. PCT Int.Appl. WO 2005014604, 2005; *Chem. Abstr.* **2005**, *142*, 198208; (e) Klose, J.; Bienert, M.; Mollenkopf, C.; Wehle, D.; Zhang, C. W.; Carpino, L. A.; Henklein, P. *Chem. Commun.* **1999**, 1847–1848.
17. *General procedure for the synthesis of acid azides*: (**1**, **2**). To a solution of acid (1.0 mmol) and T3P® (0.36 mL, 1.2 mmol) in dry THF (8.0 mL) was added Et_3N (0.20 mL, 1.5 mmol) at 0 °C followed by NaN_3 (98 mg, 1.5 mmol) in DMSO (2–3 drops) and the reaction mixture was stirred for 15–20 min. Then the reaction mixture was concentrated and diluted with CH_2Cl_2 (20 mL). The organic layer was washed with 5% Na_2CO_3 (2 × 10 mL), water (2 × 10 mL), brine (10 mL) and dried over anhydrous Na_2SO_4. Solvent was evaporated in vacuo to obtain acid azide quantitatively.
18. *Typical procedure for the synthesis of ureidopeptide* **3d**: To a solution of *Z*-Phe-OH (0.30 g, 1.0 mmol) and T3P® (0.40 mL, 1.2 mmol) in dry THF (8.0 mL), Et_3N (0.25 mL, 1.5 mmol) was added at 0 °C followed by NaN_3 (100.0 mg, 1.5 mmol) in DMSO (2–3 drops) and the reaction mixture was stirred for 20 min. Toluene was added to the reaction mixture which was subjected to ultrasonication at 45 °C for about 20 min followed by the addition of H-Ile-OMe (175.0 mg, 1.2 mmol). The reaction mixture was then sonicated for an hour. The solvent was then evaporated and diluted with cold water. The solid was separated out and washed with 20% Na_2CO_3 (10 mL) followed by 10% HCl (10 mL) and water (20 mL). Finally, the crude product was recrystallized from DMSO:H_2O.
19. Fmoc-Phe-N_3 prepared via the present protocol was converted into two epimeric ureidopepitdes Fmoc-Phe-ψ[NHCONH]-(*R*)-1-phenylethylamine (**3g**) and Fmoc-Phe-ψ[NHCONH]-(*S*)-1-phenylethylamine (**3h**) as outlined in Scheme 3 by coupling separately with (*R*)- and (*S*)-1-phenylethylamine, respectively. Further, an equimolar mixture of these two epimers was obtained by coupling with the racemic mixture of 1-phenylethylamine. The ^{1}H NMR spectrum of the crude sample of **3g** and **3h** contained distinct methyl group doublet at δ 1.41, 1.43; and 1.38, 1.40, respectively. The epimeric mixture showed –CH_3 group signals at 1.38, 1.40, 1.42, 1.43 corresponding to two doublets. These studies showed that the sample of ureidopeptides analyzed contained a single optically pure epimer. Consequently, it was concluded that the synthesis of acid azides as well as the one-pot preparation of ureidopeptides was free from racemization. The absence of racemization was also confirmed by conducting NMR analysis of dipeptidyl ureas Fmoc-Phe-ψ[NHCONH]-L-Ala-OMe (**3i**) and Fmoc-Phe-ψ[NHCONH]-D-Ala-OMe (**3j**). The sample of **3i** showed distinct –CH_3 group doublet at δ 1.29 and 1.32 and **3j** at 1.24 and 1.28. The equimolar mixture of **3i** and **3j** showed two doublets at δ 1.24, 1.28, 1.32, 1.34, which confirmed that the samples analyzed contained a single optically pure compound.
20. *Characterization data for representative compounds*:
Thiophene-2-carboxylic acid azide (**1b**): white solid; R_f 0.54 (hexane/EtOAc, 9:1), IR (KBr) ν_{max} = 2148 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.08–7.20 (m, 1H), 7.62–7.70 (m, 1H), 7.78–7.90 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 128.2, 134.1, 134.6, 135.0, 168.4 ppm; HRMS calcd for $C_5H_3N_3OS$ *m/z*: 175.9870 [M+Na], found 175.9873.
Fmoc-Val-N_3 (**2e**): white solid; R_f 0.62 (hexane/EtOAc, 8:2), IR (KBr) ν_{max} = 2142 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.92–0.93 (br, 6H), 2.11 (m, 1H), 4.15–4.34 (m, 2H), 4.35 (d, *J* = 7.2 Hz, 1H), 4.41 (d, *J* = 6.4 Hz, 1H), 5.15 (m, 1H), 7.20–7.73 (m, 8H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.75, 31.35, 47.59, 60.85, 67.43, 124.88, 126.24, 127.62, 130.11, 140.23, 145.02, 158.32, 183.21 ppm; HRMS calcd for $C_{20}H_{20}N_4O_3$ *m/z*: 387.1433 [M+Na], found 387.1437.
Boc-Leu-ψ[NHCONH]-Val-OMe (**3e**): white solid; R_f 0.4 ($CHCl_3$/MeOH, 9:1); IR (KBr) ν_{max} = 1649 cm^{-1}; ^{1}H NMR (DMSO, 400 MHz): δ 0.86 (br, 12H), 1.37 (s, 9H), 1.55 (br, 2H) 2.06 (br, 2H), 3.64 (s, 3H), 4.20 (m, 1H), 4.32 (m, 1H), 5.05 (br, 1H), 6.40-6.58 (m, 2H) ppm; ^{13}C NMR (DMSO, 100 MHz): δ 17.12, 17.88, 18.56, 27.15, 31.08, 48.11, 52.96, 55.14, 63.18, 76.31, 155.82, 156.33, 172.68 ppm; HRMS calcd for $C_{17}H_{33}N_3O_5$ *m/z*: 382.2318 (M+Na), found 382.2316.