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N-[1-(Benzotriazol-1-yl)alkyl]amides from *N*-acyl-α-amino acids or *N*-alkylamides

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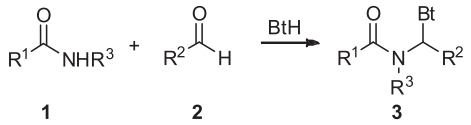
ABSTRACT

A variety of *N*-(1-methoxyalkyl)amides react with benzotriazole in the presence of $PPh_3 \cdot HBF_4$ and organic bases (Hünig's base, DBU or DABCO) or solid-state-supported bases (SiO_2-Pip or IRA-67) in $CHCl_3$ to give *N*-[1-(benzotriazol-1-yl)alkyl]amides in good yields. The most convenient and efficient procedure for obtaining *N*-[1-(benzotriazol-1-yl)alkyl]amides consists, however, of the addition of benzotriazole sodium salt to a solution of crude 1-(*N*-acylamino)alkyltriphenylphosphonium salt, obtained in situ from *N*-(1-methoxyalkyl)amides and $PPh_3 \cdot HBF_4$. A combination of these reactions with the recently described electrochemical decarboxylative α-methoxylation of *N*-acyl-α-amino acids in the presence of SiO_2-Pip enables an effective two-pot transformation of *N*-acyl-α-amino acids to *N*-[1-(benzotriazol-1-yl)alkyl] amides.

1. Introduction

α-Amidoalkylation of carbon and heteroatom nucleophiles is a well-established method for introducing the 1-(*N*-acylamino)alkyl group into a nucleophilic center, which is considered a valuable alternative to and extension of the Mannich reaction.[1] α-Amidoalkylation is employed, *inter alia*, for the formation of α-aminocarbonyl substructures and for the construction of new carbocyclic or heterocyclic rings by intramolecular α-amidoalkylations (e.g., by Pictet–Spengler-type cyclizations), especially in the syntheses of natural products and in pharmaceutical chemistry.[1–6] Benzotriazole-mediated α-amidoalkylations using *N*-[1-(benzotriazol-1-yl)alkyl]amides **3** were introduced by Katritzky and coworkers in 1988.[7] Over the past 25 years, Katritzky's research group has been extensively exploring the synthetic utility of *N*-[1-(benzotriazol-1-yl)alkyl]amides and carbamates as α-amidoalkylating reagents. *N*-[1-(Benzotriazol-1-yl)alkyl]amides have been used in a wide variety of inter- or intramolecular α-amidoalkylation reactions of *O*-, *N*-, *S*-, *P*-, and *C*-nucleophiles. The growing number of applications of this methodology has been comprehensively reviewed.[1,2,5,7–24]

N-[1-(Benzotriazol-1-yl)alkyl]amides **3** are easily synthesized, usually in good or very good yields, by condensation of a primary or secondary amide or carbamate **1**, an aldehyde **2**, and benzotriazole (Scheme 1). Primary amides and carbamates react with aldehydes on refluxing in toluene or benzene with azeotropic removal of water, whereas secondary amides require the use of catalytic amounts of *p*-toluenesulfonic acid or carrying out the reaction in acetic acid.[2,25,26] The structural diversity of *N*-[1-(benzotriazol-1-yl)alkyl]amides synthesized using these methods is, however, confined by the limited availability of structurally diverse amides **1** and aldehydes **2**.



Scheme 1. Synthesis of *N*-[1-(benzotriazol-1-yl)alkyl]amides **3**.

In this contribution we report a new, effective, one-pot condensation of *N*-(1-methoxyalkyl)amides or carbamates (**6**, R^1=R or OR, respectively) with benzotriazole in the presence of

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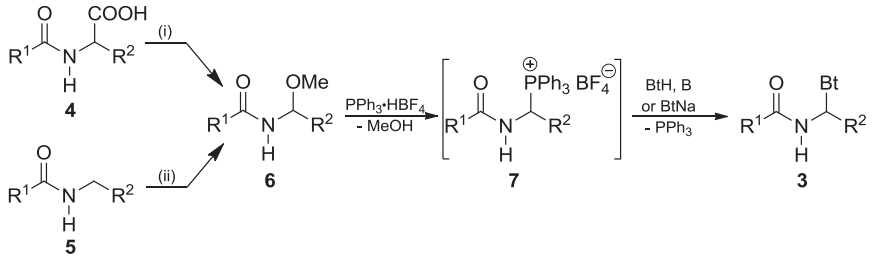
triphenylphosphonium tetrafluoroborate to the corresponding *N*-[1-(benzotriazol-1-yl)alkyl]amides **3** (Scheme 2). Recently, we described an efficient method for electrochemical decarboxylative α-methoxylation of *N*-acyl-α-amino acids **4** in the presence of 3-(1-piperidino)propyl functionalized silica gel (SiO_2-Pip) to give *N*-(1-methoxyalkyl)amides **6**.[27] A combination of these two reactions enables a convenient two-pot transformation of *N*-acyl-α-amino acids **4** to *N*-[1-(benzotriazol-1-yl)alkyl]amides **3** (Scheme 2).

2. Results and discussion

The transformation of *N*-acyl-α-amino acids to *N*-(1-methoxyalkyl)amides by electrochemical decarboxylative α-methoxylation of *N*-acyl-α-amino acids was performed in MeOH at 10 °C in the presence of a substoichiometric amount of SiO_2Pip in very good to excellent yields, as we recently described (Scheme 2, Table 1, procedure A).[27] Alternatively, a few *N*-(1-methoxyalkyl)amides were synthesized by electrochemical α-methoxylation of *N*-alkylamides or lactams in MeOH at 10 °C in the presence of tetraethylammonium *p*-toluenesulfonate (Et_4N^+ OTs^-) in good to very good yields (Scheme 2, Table 1, procedure B).



Reagents and conditions: (i) MeOH, SiO_2-Pip, -2e, 10 °C;[27] (ii) MeOH, $Et_4N^+TsO^-$, -2e, 10 °C.

Scheme 2. Transformation of *N*-acyl-α-amino acids **4** or *N*-alkylamides **5** into *N*-[1-(benzotriazol-1-yl)alkyl]amides **3**.

Alternatively, *N*-(1-methoxyalkyl)amides **6** can also be obtained by electrochemical α-methoxylation of *N*-alkylamides or lactams or *N*-alkylcarbamates (**5**, R^1=R, OR),[28–31] which additionally extends the structural diversity of *N*-[1-(benzotriazol-1-yl)alkyl]amides **3** that may to be obtained in this way (Scheme 2).

Table 1
Synthesis of *N*-[1-(benzotriazol-1-yl)alkyl]amides **3**: reaction conditions and yields

Entry	*N*-(1-Methoxyalkyl)amide				Reaction conditions		Reaction product yield (%)			
	6	Proc	R^1	R^2	Base	Molar ratio of **6**:PPh_3·HBF_4:BtM:[a]Base	**3**	Proc	Based on **6**	Based on **4** or **5**
1	**6a**	A	*t*-Bu	Me	—	1:0:1:[b]0	—	—	0	0
2	**6a**	A	*t*-Bu	Me	—	1:0:1:[c]0	—	—	0	0
3	**6a**	A	*t*-Bu	Me	$(i\text{-Pr})_2$EtN	1:0:1:[b]1	—	—	0	0
4	**6a**	A	*t*-Bu	Me	—	1:1:1:[b]0	—	—	0	0
5	**6a**	A	*t*-Bu	Me	$(i\text{-Pr})_2$EtN	1:1:1:1	**3a**	C	78	75
6	**6a**	A	*t*-Bu	Me	DBU	1:1:1:1	**3a**	C	89[d]	86[d]
7	**6a**	A	*t*-Bu	Me	DABCO	1:1:1:1	**3a**	C	64[d]	62[d]
8	**6a**	A	*t*-Bu	Me	IRA-67	1:1:1:2	**3a**	D	87	84
9	**6a**	A	*t*-Bu	Me	SiO_2-Pip	1:1:1:1	**3a**	D	65	63
10	**6a**	A	*t*-Bu	Me	—	1:1:1:0	**3a**	E	90	87
11	**6b**	A	Me	Me	$(i\text{-Pr})_2$EtN	1:1:1:1	**3b**	C	85	79
12	**6b**	B	Me	Me	$(i\text{-Pr})_2$EtN	1:1:1:1	**3b**	C	85	47
13	**6b**	A	Me	Me	—	1:1:1:0	**3b**	E	86	80
14	**6b**	B	Me	Me	—	1:1:1:0	**3b**	E	86	47
15	**6c**	A	Ph	Me	—	1:1:1:0	**3c**	E	70	69
16	**6d**	A	BnO	Ph	$(i\text{-Pr})_2$EtN	1:1:1:1	**3d**	C	86	84
17	**6e**	A	BnO	*i*-Pr	$(i\text{-Pr})_2$EtN	1:1:1:1	**3e**	C	81	79
18	**6e**	A	BnO	*i*-Pr	—	1:1:1:0	**3e**	E	83	81
19	**6f**	A	BnO	*i*-Bu	$(i\text{-Pr})_2$EtN	1:1:1:1	**3f**	C	78	73
20	**6f**	A	BnO	*i*-Bu	—	1:1:1:0	**3f**	E	75	70
21	**6g**	A	BnO	Bn	$(i\text{-Pr})_2$EtN	1:1:1:1	**3g**	C	75	70
22	**6g**	A	BnO	Bn	—	1:1:1:0	**3g**	E	74	68
23	**6h**	A	$(CH_2)_2$		—	1:1:1:0	**3h**	E	72[e]	70[e]
24	**6h**	B	$(CH_2)_2$		—	1:1:1:0	**3h**	E	72[e]	58[e]
25	**6i**	B	$(CH_2)_4$		—	1:1:1:0	**3i**	E	81	65
26	**6j**	A	BnO	CH_2O-*t*-Bu	$(i\text{-Pr})_2$EtN	1:1:1:1	**3j**	C	76	71
27	**6j**	A	BnO	CH_2O-*t*-Bu	—	1:1:1:0	**3j**	E	92	86
28	**6k**	A	BnO	CH_2CO_2-*t*-Bu	$(i\text{-Pr})_2$EtN	1:1:1:1	**3k**	C	32[f]	31[f]
29	**6k**	A	BnO	CH_2CO_2-*t*-Bu	—	1:1:1:0	**3k**	E	80	77
30	**6l**	A	BnO	$(CH_2)_2CO_2$-*t*-Bu	$(i\text{-Pr})_2$EtN	1:1:1:1	**3l**	C	74	72
31	**6m**	A	BnO	*p*-$CH_2C_6H_4OBn$	—	1:1:1:0	**3m**	E	78	62

[a] M=H or Na.
[b] Reaction carried out with benzotriazole.
[c] Reaction carried out with benzotriazole sodium salt.
[d] The yield estimated from ^{1}H NMR spectroscopy.
[e] A 5:4 mixture of benzotriazol-1-yl and -2-yl isomers.
[f] The yield estimated from ^{1}H NMR spectroscopy. The crude product contained also the corresponding (*E*)-enamide (53%). Attempts to isolate pure product **3k** failed.

N-(1-Methoxyethyl)pivaloylamide **6a**, when treated with benzotriazole, benzotriazole sodium salt or benzotriazole in the presence of Hünig's base in $CHCl_3$ at room temperature, gave no reaction after 4 h (Table 1, entries 1–3, respectively).

On the other hand, dissolution of *N*-(1-methoxyalkyl)amides **6** in $CHCl_3$ and the addition of triphenyphosphonium tetrafluoroborate at 20 °C caused complete disappearance of *N*-(1-methoxyalkyl)amides **6** with formation of methanol and the corresponding 1-(*N*-acylamino)alkyltriphenylphosphonium salt **7** in a few minutes and in very good yield.[27] The addition of benzotriazole to phosphonium salt **7a**, obtained in this way in situ, again gave no reaction after 4 h (entry 4). However, the addition of benzotriazole and Hünig's base $(i\text{-Pr})_2EtN$ to a reaction mixture obtained by dissolution of *N*-(1-methoxyalkyl)amide and triphenyphosphonium tetrafluoroborate in $CHCl_3$ gave, after 2 h at 20 °C, the expected *N*-[1-(benzotriazol-1-yl)alkyl]amide **3a** in a good yield (entry 5, procedure C). Similar results were obtained using DBU or DABCO instead of Hünig's base (entries 6 and 7). Thus obtained *N*-[1-(benzotriazol-1-yl)alkyl]amides **3** were easily isolated and purified by evaporation of the solvent, extraction of the product from the residue with toluene at 50 °C, evaporation of toluene and recrystallization of the crude product from toluene or ethyl acetate. Similar results were obtained using 3-(1-piperidino)propyl functionalized silica gel (SiO_2-Pip) or anionite IRA-67 as a base (entries 8 and 9, procedure D). The application of solid-state-supported bases reduces the work-up procedure to the removal of SiO_2-Pip or IRA-67 by filtration, evaporation of the solvent, and recrystallization of the product from toluene. It seems, however that the most convenient and efficient procedure for the transformation of *N*-(1-methoxyalkyl)amides to *N*-[1-(benzotriazol-1-yl)alkyl]amides consists of the addition of benzotriazole sodium salt to a solution of crude 1-(*N*-acylamino)alkyltriphenylphosphonium salt in $CHCl_3$ at room temperature (procedure E). Crude phosphonium salts were obtained by dissolution of *N*-(1-methoxyalkyl)amide and triphenyphosphonium tetrafluoroborate in $CHCl_3$ and by evaporating the solvent. After removal of sodium tetrafluoroborate by filtration and evaporation of the solvent, the crude product was purified by recrystallization. A variety of *N*-[1-(benzotriazol-1-yl)alkyl]amides **3** were obtained using these methods, usually in good to very good yields based on *N*-(1-methoxyalkyl)amides **6**, or in satisfying yields based on *N*-acyl-α-amino acids **4** or *N*-alkylamides **5**. It is noteworthy that the crude products contained both *N*-[1-(benzotriazol-1-yl)alkyl]amide and *N*-[1-(benzotriazol-2-yl)alkyl]amide in a molar ratio of 1.8:1 up to 14.7:1, depending on their structure and the reaction conditions, however, after recrystallization from toluene the pure products contained only trace amounts of the benzotriazol-2-yl derivative. A similar isomerization of benzotriazol-2-yl isomers to the more stable -1-yl isomers has been described by Katritzky and coworkers.[8] Only in the case of 5-(benzotriazolyl)pyrrolidin-2-one **3h** was a molar ratio of benzotriazol-1-yl to -2-yl isomer found to be 5:4 (after recrystallization).

3. Conclusion

A new, effective, one-pot condensation of *N*-(1-methoxyalkyl) amides or carbamates (**6**, R^1=R or OR, respectively) with benzotriazole in the presence of organic bases or with benzotriazole sodium salt catalyzed by triphenylphosphonium tetrafluoroborate to give *N*-[1-(benzotriazol-1-yl)alkyl]amides **3** has been developed. A combination of this reaction with the recently described efficient electrochemical decarboxylative α-methoxylation of *N*-acyl-α-amino acids **4** to *N*-(1-methoxyalkyl)amides **6**[27] enables a convenient two-pot transformation of *N*-acyl-α-amino acids **4** to *N*-[1-(benzotriazol-1-yl)alkyl]amides **3**. It has also been demonstrated that, alternatively, *N*-(1-methoxyalkyl)amides **6** can be obtained by electrochemical α-methoxylation of *N*-alkylamides or lactams **5**. The possibility of employing a large range of *N*-acyl derivatives of natural α-amino acids (both proteinogenic and nonproteinogenic acids) as well as an infinite array of unnatural α-amino acids or, alternatively, secondary amides or lactams **5** in this synthesis potentially provides easy access to a wide variety of structurally diverse *N*-[1-(benzotriazol-1-yl)alkyl]amides **3**, which significantly widens the scope of possible synthetic applications of these important α-amidoalkylating agents. The developed transformation of *N*-(1-methoxyalkyl)amides or carbamates provides easy access to a variety of *N*-[1-(benzotriazol-1-yl)alkyl]amides that otherwise would be difficult to obtain by the classical Katritzky method.

4. Experimental section

4.1. General

Melting points were determined in capillaries and are uncorrected. IR-spectra were measured on a FT-IR spectrophotometer (ATR method). ^1H and ^{13}C NMR spectra were recorded at operating frequencies of 600 or 400 and 150 or 100 MHz, respectively, using TMS as the resonance shift standard. All chemical shifts (δ) are reported in parts per million, and coupling constants (J) are reported in Hertz.

4.2. Preparation of *N*-(1-methoxyalkyl)amides 6

*4.2.1. Decarboxylative α-methoxylation of N-acyl-α-amino acids to N-(1-methoxyalkyl)amides **6** (Procedure A).*[27] To an undivided cylindrical glass electrolyzer (85 cm^3) with a thermostatic jacket, equipped with a magnetic stirrer along with a cylindrical Pt mesh anode (47 cm^2) and a similar cathode (44 cm^2), arranged concentrically to one another at a distance of 2.5±0.5 mm, were added methanol (30 cm^3), *N*-acyl-α-amino acid **4** (3.0 mmol), and SiO_2-Pip (200 mg, 0.22 mmol). The electrolysis was carried out with stirring at a current density of 0.3 A/dm^2 at 10 °C until a charge of 2.4–3.75 F/mol had passed. SiO_2-Pip was filtered off, and methanol was evaporated under reduced pressure to obtain *N*-(1-methoxyalkyl)amide **6**.

*4.2.2. Electrochemical α-methoxylation of N-alkylamides and lactams **5** (Procedure B).*[32] To an undivided cylindrical glass electrolyzer (85 cm^3) with a thermostatic jacket, equipped with a magnetic stirrer along with a cylindrical Pt mesh anode (47 cm^2) and a similar cathode (44 cm^2), arranged concentrically to one another at a distance of 2.5±0.5 mm were added methanol (40 cm^3), *N*-alkylamide or lactam **5** (8.0 mmol), and Et_4N^+ OTs^- (40.7 mg, 0.135 mmol). The electrolysis was carried out with stirring at a current density of 1.0 A/dm^2 at 10 °C until a charge of 9.0, 5.0, and 5.5 F/mol had passed for compounds **5b**, **5h**, or **5i**, respectively. The solvent was evaporated under reduced pressure, and the product was isolated by column chromatography (CH_2Cl_2/MeOH, 9:1 with 2% Et_3N). The crystalline crude compounds **6h** and **6i** were recrystallized from toluene.

*4.2.2.1. N-(1-Methoxyethyl)benzamide (**6c**).*[33] Pale yellow crystals (procedure A; 526.8 mg, 98% yield), mp 86.0–88.0 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.83–7.77 (m, 2H), 7.56–7.50 (m, 1H), 7.48–7.43 (m, 2H), 6.30 (d, J=8.4 Hz, 1H), 5.51 (dq, J=9.6, 5.9 Hz, 1H), 3.41 (s, 3H), 1.45 (d, J=6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 134.0, 131.8, 128.6, 127.0, 78.3, 55.8, 21.7; IR (ATR) 3310 (ν_{NH}), 1647 ($\nu_{C=O}$), 1530, 1337, 1284, 1134, 1082 cm^{-1}.

*4.2.2.2. 5-Methoxypyrrolidin-2-one (**6h**).*[31] Colorless crystals (procedure A: 334.9 mg, 97% yield; procedure B: 745.8 mg, 81% yield), mp 59.0–60.0 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (br s, 1H),

4.89 (ddd, J=6.4, 1.4, 1.4 Hz, 1H), 3.32 (s, 3H), 2.57–2.46 (m, 1H), 2.35–2.19 (m, 2H), 2.12–2.02 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.5, 87.1, 54.4, 28.3, 27.9; IR (ATR) 3178 (ν_{NH}), 1671 ($\nu_{C=O}$), 1283, 1251, 1098, 1056, 1043 cm^{-1}.

*4.2.2.3. 7-Methoxyazepan-2-one (**6i**).*[31] Colorless crystals (procedure B; 916.5 mg, 80% yield), mp 62.0–63.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.52 (br s, 1H), 4.31 (ddd, J=5.6, 5.6, 2.0 Hz, 1H), 3.36 (s, 3H), 2.67–2.59 (m, 1H), 2.46–2.39 (m, 1H), 2.15–2.05 (m, 1H), 2.03–1.89 (m, 1H), 1.86–1.65 (m, 3H), 1.62–1.49 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.5, 83.6, 55.3, 37.3, 34.2, 23.7, 23.2; IR (ATR) 3197 (ν_{NH}), 2934, 2918, 1663 ($\nu_{C=O}$), 1625, 1433, 1356, 1079, 1068 cm^{-1}.

The analytical and spectral data for the other *N*-(1-methoxyalkyl)amides **6** were reported in our previous paper.[27]

4.3. Transformation of *N*-(1-methoxyalkyl)amides 6 to *N*-[1-(benzotriazol-1-yl)alkyl]amides 3; general procedures

4.3.1. Reactions with benzotriazole and organic bases (Procedure C). To a solution of *N*-(1-methoxyalkyl)amide **6** (1 mmol) in chloroform (2 cm^3) were added triphenylphosphonium tetrafluoroborate (350.1 mg, 1 mmol), benzotriazole (119.1 mg, 1 mmol), and Hünig's base (0.174 ml, 129.2 mg, 1 mmol). After the mixture was stirred for 2 h at 20 °C, the solvent was evaporated under reduced pressure and the residue was extracted with toluene (3×1 cm^3) at 50 °C. The solvent was evaporated under reduced pressure and the crude product was recrystallized from toluene to yield *N*-[1-(benzotriazol-1-yl)alkyl]amides **3** as colorless crystals.

4.3.2. Reactions with benzotriazole and solid-state-supported bases (Procedure D). To a solution of *N*-(1-methoxyalkyl)amide **6** (1 mmol) in chloroform (2 cm^3) was added triphenylphosphonium tetrafluoroborate (350.1 mg, 1 mmol). After a homogeneous solution was obtained, the solvent was evaporated to dryness. The residue was again dissolved in chloroform (2 cm^3) and benzotriazole (119.1 mg, 1 mmol) and solid-state-supported base SiO_2-Pip (920 mg) or weak base anion exchanger Amberlite IRA-67 (720 mg) were added. After the mixture was stirred for 2 h (Amberlite IRA-67) or 4 h (SiO_2-Pip) at 20 °C, the base was filtered off and the solvent was evaporated under reduced pressure. The crude product was recrystallized from toluene to give *N*-[1-(benzotriazol-1-yl) alkyl]amides **3** as colorless crystals.

4.3.3. Reactions with benzotriazole sodium salt (Procedure E). To a solution of *N*-(1-methoxyalkyl)amide **6** (1 mmol) in chloroform (2 cm^3) was added triphenylphosphonium tetrafluoroborate (350.1 mg, 1 mmol). After a homogeneous solution was obtained, the solvent was evaporated to dryness. The residue was again dissolved in chloroform and benzotriazole sodium salt (141.1 mg, 1 mmol) was added. After the mixture was stirred for 2 h at 20 °C, sodium tetrafluoroborate was filtered off and the solvent was evaporated under reduced pressure. The crude product was recrystallized from toluene to yield *N*-[1-(benzotriazol-1-yl)alkyl] amides **3** as colorless crystals.

*4.3.3.1. N-[1-(Benzotriazol-1-yl)ethyl]pivaloylamide (**3a**).*[34] Colorless crystals (192.1 mg, 78% yield or 214.3 mg, 87% yield or 160.1 mg, 65% yield or 221.7 mg, 90% yield, see Table 1), mp 139.5–140.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06–8.00 (m, 1H), 7.85–7.79 (m, 1H), 7.53–7.47 (m, 1H), 7.41–7.33 (m, 1H), 6.88 (dq, J=9.0, 6.7 Hz, 1H), 6.79 (d, J=8.8 Hz, 1H), 2.03 (d, J=6.4 Hz, 3H), 1.16 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.1, 145.7, 132.4, 127.7, 124.2, 119.6, 110.3, 58.5, 38.7, 27.2, 20.9; IR (ATR) 3346 (ν_{NH}), 2969, 1668 ($\nu_{C=O}$), 1511, 1193, 1153, 1067 cm^{-1}.

*4.3.3.2. N-[1-(Benzotriazol-1-yl)ethyl]acetamide (**3b**).* Colorless crystals (173.6 mg, 85% yield or 175.6 mg, 86% yield, see Table 1), mp 122.0–124.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04–7.98 (m, 1H), 7.89–7.81 (m, 1H), 7.54–7.47 (m, 1H), 7.40–7.34 (m, 1H), 7.15 (d, J=10.0 Hz, 1H), 6.89 (dq, J=9.2, 6.8 Hz, 1H), 2.03 (d, J=6.8 Hz, 3H), 2.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 145.7, 132.5, 127.7, 124.3, 119.5, 110.4, 58.3, 23.0, 20.6; IR (ATR) 3202 (ν_{NH}), 3045, 1676 ($\nu_{C=O}$), 1549, 1373, 1272, 1157, 1077 cm^{-1}. HRMS (TOF-ESI) calcd for $C_{10}H_{12}N_4ONa$ $[M+Na]^+$ 227.0909, found 227.0908.

*4.3.3.3. N-[1-(Benzotriazol-1-yl)ethyl]benzamide (**3c**).*[34] Colorless crystals (186.4 mg, 70% yield), mp 151.5–152.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03–7.97 (m, 1H), 7.95–7.90 (m, 1H), 7.82–7.78 (m, 2H), 7.62 (d, J=9.2 Hz, 1H), 7.54–7.45 (m, 2H), 7.42–7.31 (m, 3H), 7.13 (dq, J=9.2, 6.8 Hz, 1H), 2.14 (d, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 145.7, 132.8, 132.6, 132.2, 128.6, 127.8, 127.3, 124.3, 119.5, 110.5, 58.9, 20.7; IR (ATR) 3259 (ν_{NH}), 1659 ($\nu_{C=O}$), 1530, 1329, 1274, 1151, 1070 cm^{-1}.

*4.3.3.4. Benzyl N-[1-(benzotriazol-1-yl)phenylmethyl]carbamate (**3d**).*[26,35] Colorless crystals (308.2 mg, 86% yield), mp 131.5–132.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12–8.06 (m, 1H), 7.66 (d, J=9.6 Hz, 1H), 7.60–7.52 (m, 1H), 7.51–7.42 (m, 1H), 7.41–7.23 (m, 10H), 7.20–7.12 (m, 1H), 6.36 (d, J=8.0 Hz, 1H), 5.17 (d, J=12.0 Hz, 1H), 5.07 (d, J=12.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 146.0, 136.0, 135.5, 132.6, 129.4, 129.1, 128.6, 128.4, 128.2, 127.9, 126.3, 124.3, 120.1, 109.7, 67.8, 67.3; IR (ATR) 3276 (ν_{NH}), 1717 ($\nu_{C=O}$), 1527, 1451, 1241, 1226, 1211, 1140, 1042 cm^{-1}.

*4.3.3.5. Benzyl N-[1-(benzotriazol-1-yl)-2-methylpropyl]carbamate (**3e**).*[8,26] Colorless crystals (262.8 mg, 81% yield or 269.3 mg, 83% yield, see Table 1), mp 165.0–167.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09–8.03 (m, 1H), 7.74 (d, J=8.4 Hz, 1H), 7.55–7.47 (m, 1H), 7.42–7.34 (m, 1H), 7.34–7.27 (m, 4H), 7.20–7.14 (m, 1H), 6.10 (dd, J=9.6, 9.6 Hz, 1H), 5.94 (d, J=9.2 Hz, 1H), 5.12 (d, J=12.4 Hz, 1H), 4.98 (d, J=12.0 Hz, 1H), 2.82–2.69 (m, 1H), 1.20 (d, J=6.8 Hz, 3H), 0.79 (d, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 145.5, 135.6, 133.3, 128.5, 128.3, 128.1, 127.7, 124.1, 119.8, 109.8, 70.3, 67.5, 33.3, 19.0, 18.7; IR (ATR) 3196 (ν_{NH}), 3027, 1719 ($\nu_{C=O}$), 1545, 1287, 1239, 1154, 1042, 1027 cm^{-1}.

*4.3.3.6. Benzyl N-[1-(benzotriazol-1-yl)-3-methylbutyl]carbamate (**3f**).*[8,35] Colorless crystals (264.0 mg, 78% yield or 253.8 mg, 75% yield, see Table 1), mp 129.5–130.5 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 (d, J=8.4 Hz, 1H), 7.82 (d, J=8.4 Hz, 1H), 7.54–7.49 (m, 1H), 7.40–7.35 (m, 1H), 7.34–7.25 (m, 5H), 6.56–6.49 (m, 1H), 5.89 (d, J=9.6 Hz, 1H), 5.12 (d, J=12.6 Hz, 1H), 4.97 (d, J=12.0 Hz, 1H), 2.44–2.35 (m, 1H), 2.26–2.17 (m, 1H), 1.54–1.44 (m, 1H), 0.96 (d, J=6.6 Hz, 3H), 0.95 (d, J=4.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.5, 145.6, 135.6, 132.8, 128.4, 128.2, 128.0, 127.6, 124.1, 119.7, 110.1, 67.3, 63.4, 42.9, 24.5, 22.1, 22.0; IR (ATR) 3199 (ν_{NH}), 2962, 1717 ($\nu_{C=O}$), 1554, 1257, 1242, 1160, 1100, 1034, 1026 cm^{-1}.

*4.3.3.7. Benzyl N-[1-(benzotriazol-1-yl)-2-phenylethyl]carbamate (**3g**).*[26,35] Colorless crystals (275.6 mg, 74% yield or 279.3 mg, 75% yield, see Table 1), mp 125.5–127.0 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00–7.97 (m, 1H), 7.55 (d, J=8.4 Hz, 1H), 7.42–7.35 (m, 1H), 7.32–7.25 (m, 4H), 7.24–7.19 (m, 2H), 7.18–7.10 (m, 3H), 7.09–7.04 (m, 2H), 6.68–6.62 (m, 1H), 6.27 (d, J=9.6 Hz, 1H), 5.09 (d, J=12.6 Hz, 1H), 4.95 (d, J=12.0 Hz, 1H), 3.73 (dd, J=13.5, 8.7 Hz, 1H), 3.64 (dd, J=9.2, 6.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.3, 145.5, 135.5, 134.7, 133.0, 129.0, 128.9, 128.5, 128.3, 128.0, 127.6, 127.3, 124.1, 119.6, 109.8, 67.4, 65.9, 40.9; IR (ATR) 3176 (ν_{NH}), 3009, 1712 ($\nu_{C=O}$), 1548, 1280, 1261, 1245, 1196, 1022 cm^{-1}.

*4.3.3.8. 5-(Benzotriazolyl)pyrrolidin-2-one (**3h**).*[17] Colorless crystals (145.6 mg, 72% yield), mp 145.5–147.0 °C, found to be a 5:4 mixture of benzotriazol-1-yl and -2-yl isomers by ^{1}H NMR. Data for benzotriazol-1-yl isomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04–8.01 (m, 1H), 8.00 (br s, 1H), 7.55–7.51 (m, 1H), 7.49–7.45 (m, 1H), 7.39–7.34 (m, 1H), 6.52–6.48 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 178.3, 146.4, 131.3, 127.9, 124.3, 120.2, 109.3, 68.6, 28.9, 27.6. Data for benzotriazol-2-yl isomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82–7.78 (m, 2H), 7.75 (br s, 1H), 7.55–7.51 (m, 2H), 6.42 (ddd, J=7.2, 1.4, 1.4, Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 178.7, 144.3, 126.9, 128.2, 74.8, 28.2, 28.0. Data for mixture of regioisomers: ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.92–2.60 (m, 3H), 2.51–2.34 (m, 1H); IR (ATR) 3169 (ν_{NH}), 3100, 1702 ($\nu_{C=O}$), 1450, 1279, 1252, 1084 cm^{-1}.

*4.3.3.9. 7-(Benzotriazol-1-yl)azepan-2-one (**3i**).* Colorless crystals (186.5 mg, 81% yield), mp 145.5–147.0 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11–8.07 (m, 1H), 7.63–7.59 (m, 1H), 7.54–7.49 (m, 1H), 7.43–7.39 (m, 1H), 6.88–6.80 (m, 1H), 6.19 (d, J=8.4 Hz, 1H), 2.79–2.72 (m, 1H), 2.66–2.59 (m, 1H), 2.59–2.52 (m, 1H), 2.38–2.32 (m, 1H), 2.23–2.15 (m, 1H), 1.95–1.86 (m, 2H), 1.84–1.76 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.4, 146.2, 131.7, 128.1, 124.5, 120.4, 109.7, 68.0, 36.9, 34.7, 26.6, 22.5; IR (ATR) 3186 (ν_{NH}), 2960, 1659 ($\nu_{C=O}$), 1391, 1281, 1199, 1164, 1058 cm^{-1}. HRMS (TOF-ESI) calcd for $C_{12}H_{14}N_4ONa$ $[M+Na]^+$ 253.1065, found 253.1062.

*4.3.3.10. Benzyl N-[1-(benzotriazol-1-yl)-2-tert-butoxyethyl]carbamate (**3j**).* Colorless crystals (280.0 mg, 76% yield or 338.9 mg, 92% yield, see Table 1), mp 136.5–138.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J=8.4 Hz, 1H), 7.82–7.72 (m, 1H), 7.52–7.41 (m, 1H), 7.40–7.14 (m, 6H), 6.63 (dt, J=8.8, 4.6 Hz, 1H), 6.21 (d, J=8.0 Hz, 1H), 5.14 (d, J=12.8 Hz, 1H), 5.02 (d, J=11.6 Hz, 1H), 4.05–3.95 (m, 2H), 1.07 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 145.9, 135.6, 132.8, 128.5, 128.3, 128.2, 127.3, 123.9, 119.7, 110.9, 74.4, 67.5, 65.7, 63.3, 27.2; IR (ATR) 3206 (ν_{NH}), 2969, 1722 ($\nu_{C=O}$), 1557, 1287, 1259, 1240, 1192, 1165, 1033, 1022, 1009 cm^{-1}. HRMS (TOF-ESI) calcd for $C_{20}H_{24}N_4O_3Na$ $[M+Na]^+$ 391.1746, found 391.1749.

*4.3.3.11. Benzyl N-[1-(benzotriazol-1-yl)-2-tert-butoxycarbonylethyl]carbamate (**3k**).* Colorless crystals (317.1 mg, 80% yield), mp 120.0–121.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05–7.99 (m, 1H), 7.87 (d, J=7.2 Hz, 1H), 7.55–7.45 (m, 1H), 7.41–7.34 (m, 1H), 7.34–7.22 (m, 5H), 6.88–6.78 (m, 1H), 6.54 (d, J=9.2 Hz, 1H), 5.15 (d, J=12.4 Hz, 1H), 5.03 (d, J=12.4 Hz, 1H), 3.42 (dd, J=16.4, 7.2 Hz, 1H), 3.31 (dd, J=16.0, 5.6 Hz, 1H), 1.33 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 155.3, 145.8, 135.6, 132.6, 128.5, 128.4, 128.2, 127.8, 124.3, 119.7, 110.6, 82.3, 67.5, 61.5, 40.0, 27.8; IR (ATR) 3273 (ν_{NH}), 1733 ($\nu_{C=O}$), 1694 ($\nu_{C=O}$), 1552, 1276, 1248, 1155, 1048, 1033 cm^{-1}. HRMS (TOF-ESI) calcd for $C_{21}H_{24}N_4O_4Na$ $[M+Na]^+$ 419.1695, found 419.1693.

*4.3.3.12. Benzyl N-[1-(benzotriazol-1-yl)-3-tert-butoxycarbonylpropyl]carbamate (**3l**).* Colorless oil (303.8 mg, 74% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07–7.99 (m, 1H), 7.80 (d, J=8.4 Hz, 1H), 7.55–7.44 (m, 1H), 7.42–7.20 (m, 6H), 6.66–6.55 (m, 1H), 6.27 (d, J=9.2 Hz, 1H), 5.11 (d, J=11.2 Hz, 1H), 4.97 (d, J=12.4 Hz, 1H), 2.77–2.54 (m, 2H), 2.40–2.29 (m, 1H), 2.28–2.15 (m, 1H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 155.4, 145.7, 135.6, 132.8, 128.5, 128.3, 128.1, 127.7, 124.2, 119.7, 110.1, 81.2, 67.4, 64.2, 31.0, 29.5, 28.0; IR (ATR) 3309 (ν_{NH}), 2977, 1721 ($\nu_{C=O}$), 1526, 1367, 1237, 1153, 1050 cm^{-1}. HRMS (TOF-ESI) calcd for $C_{22}H_{26}N_4O_4Na$ $[M+Na]^+$ 433.1852, found 433.1851.

*4.3.3.13. Benzyl N-[1-(benzotriazol-1-yl)-2-(4-benzyloxyphenyl)ethyl]carbamate (**3m**).* Colorless crystals (373.2 mg, 78% yield), mp 143.0–144.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03–7.97 (m, 1H), 7.55 (d, J=8.0 Hz, 1H), 7.43–7.13 (m, 12H), 7.01–6.92 (m, 2H), 6.80–6.72 (m, 2H), 6.65–6.52 (m, 1H), 6.02 (d, J=9.6 Hz, 1H), 5.10 (d, J=12.0 Hz, 1H), 4.96 (d, J=12.0 Hz, 1H), 4.94 (s, 2H), 3.67 (dd, J=14.0, 8.2 Hz, 1H), 3.55 (dd, J=14.0, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 155.3, 145.6, 136.8, 135.6, 133.0, 130.2, 128.5, 128.4, 128.1, 128.0, 127.6, 127.4, 127.0, 126.6, 124.1, 119.7, 115.1, 109.8, 70.0, 67.5, 66.0, 40.3; IR (ATR) 3256 (ν_{NH}), 1722 ($\nu_{C=O}$), 1514, 1292, 1262, 1242, 1201, 1025 cm^{-1}. HRMS (TOF-ESI) calcd for $C_{29}H_{26}N_4O_3Na$ $[M+Na]^+$ 501.1903, found 501.1899.

Supplementary data

^{1}H, ^{13}C NMR and IR spectra of all new *N*-[1-(benzotriazol-1-yl) alkyl]amides **3**. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2014.06.068.

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