N-Acylbenzotriazoles: Neutral Acylating Reagents for the Preparation of Primary, Secondary, and Tertiary Amides

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Readily available *N*-acylbenzotriazoles **2a**−**q** efficiently acylate aqueous ammonia and primary and secondary amines to give primary, secondary, and tertiary amides in good to excellent yields. The wide applicability of the procedure is illustrated by the preparation of (i) α-hydroxyamides from α-hydroxy acids and of (ii) perfluoroalkylated amides.

Introduction

Common routes to primary, secondary, and tertiary amides mostly involve the treatment of activated derivatives of acids, especially acyl halides, acid anhydrides, or esters, with ammonia or primary and secondary amines.[1] However, limitations are associated with these methods. Reactions of ammonia or amines with acyl halides are highly exothermic. Acid anhydrides, especially cyclic anhydrides, easily form imides with ammonia and primary amines. Acylations of ammonia, primary and secondary amines by esters frequently require strongly basic catalysts and/or high pressure. Reactions of carboxylic acids themselves with ammonia or amines are seldom of preparative value.[2] Other preparations of primary amides include the activation of carboxylic acids using 1-hydroxybenzotriazole (HOBt) and *N,N*-dicyclohexylcarbodiimide (DCC)[3] or the treatment of carboxylic acids with ammonium chloride, tertiary amine and coupling agents typically used in peptide synthesis.[4] For these last two methods, difficulties can arise from the insolubility of starting materials and products or by competitive hydrolysis of the activated carboxyl group.

As recently documented by Staab, Bauer, and Schneider,[5] acyl azolides in general, and *N*-acylimidazoles in particular, are efficient acylating reagents. They have been widely reacted with ammonia or primary amines to give the corresponding primary amides[6] or secondary amides.[7] The classical azolide method normally involves two steps (which can, however, be combined in one pot): (i) reaction of the free carboxylic acid at 20 °C with (usually) 1,1′-carbonyldiimidazole (CDI) in a 1:1 molar ratio forms the carboxylic acid imidazole via elimination of CO_2 and imidazole; (ii) after CO_2 evolution has ceased, an equimolar amount of amine is added. Thus, two molar equivalents of the imidazole moieties are used. Furthermore, relatively few reports were located for reactions of *N*-acylimidazoles with secondary amines.

N-Acylbenzotriazoles have been previously used as acylating agents: in our group specifically for formylation[8a] and trifluoroacylation[8b] and to provide oxamides[8c] and by others in isolated applications.[9] We now report a simple, mild, and general procedure for the preparation of primary, secondary, and tertiary amides. Carboxylic acids are converted in a one-pot reaction into *N*-acylbenzotriazoles and subsequently treated with ammonia or primary or secondary amines. This methodology should be particularly applicable to solid-phase syntheses.

Results and Discussion

Preparation of *N*-Acylbenzotriazoles 2a−q. 1-(Trimethylsilyl)benzotriazole, readily available from benzotriazole and *N,N*-bis(trimethylsilyl)amine,[10] was previously reacted with methanesulfonyl chloride to generate *N*-(1-methanesulfonyl)benzotriazole (**1**) in 60% yield.[11] We now find that compound **1** is produced in 89% yield by direct treatment of benzotriazole with methanesulfonyl chloride in the presence of pyridine.

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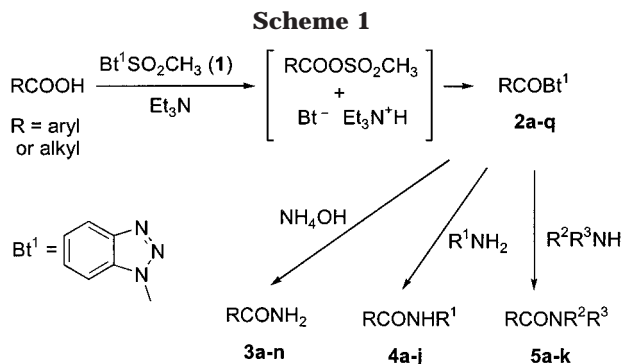
Scheme 1

N-Acylbenzotriazoles **2a**−**m** with R as aryl groups were readily prepared in 72−92% yields by the previously reported reaction of *N*-(1-methanesulfonyl)benzotriazole (**1**) with arene carboxylic acids (Scheme 1).[11] We previously synthesized *N*-(alkanecarbonyl)- or *N*-(arylacetyl)-benzotriazoles **2** (R = alkyl, arylmethyl) by the reaction of benzotriazole with alkanecarbonyl chlorides[11] or aryl-acetyl chlorides[12] in the presence of triethylamine. The reported yields of **2o**, **2p**, and **2q** are 80%, 80%, and 79%, respectively.[11,12] We now find that *N*-(alkanecarbonyl)-benzotriazoles **2o**, **2p**, and **2q** can be obtained in 84%, 89%, and 83% yield, respectively, from the corresponding aliphatic carboxylic acids and $BtSO_2CH_3$ in the presence of triethylamine (Scheme 1). The mechanism for the formation of *N*-acylbenzotriazoles **2** involves attack of the carboxylate (formed in the presence of triethylamine) on the sulfur atom of **1** followed by the departure of benzotriazole anion to give the intermediate $RCOOSO_2$-CH_3. Then the addition of benzotriazole anion to the carbonyl carbon and elimination of alkanesulfonate affords the final products **2**. *N*-Acylbenzotriazoles **2a**−**q** are listed in Table 1. The diverse carboxylic acids used include aromatic, heteroaromatic and aliphatic. Novel structures **2b**−**f** and **2l**−**n** were supported by ^{1}H, ^{13}C NMR spectra and microanalysis.

Preparation of Primary Amides 3a−n from *N*-Acylbenzotriazoles 2 with Ammonia. Direct treatment of *N*-acylbenzotriazoles **2a**−**e** and **2h**−**q** with excess ammonium hydroxide (30% aqueous solution) in EtOH/THF (1:1) at room temperature for 2−4 h gave crude products, which were recrystallized from benzene to afford pure primary amides **3a**−**n** (Scheme 1). The yields and melting points, as well as the literature melting points, for the primary amides **3a**−**n** are summarized in Table 2; melting points and spectra of the products are in accord with literature data. The benzotriazole byproduct (BtH, pK_a = 8.2[13]) formed in these reactions dissolved in the excess aqueous ammonia solution.

Preparation of Secondary Amides 4a−j from *N*-Acylbenzotriazoles 2 with Primary Amines. Treatment of *N*-acylbenzotriazoles **2** with 1 equiv of primary amines in THF at room temperature for 4 h furnished the corresponding secondary amides **4a**−**j** in 70−100% yields (Scheme 1 and Table 3). After dilution of the concentrated residue in ethyl acetate, byproduct benzotriazole was easily washed away by a 2 M NaOH aqueous solution, and simple removal of EtOAc in vacuo gave secondary amides **4a**−**j**, which were recrystallized from

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Table 1. Preparation of *N*-Acylbenzotriazoles 2a−q

2	R	yield (%)	mp (°C)	lit. mp (°C)
a	C_6H_5	89	112−113	112−113[11]
b	$2\text{-}CH_3OC_6H_4$	72	96−97	a
c	$3\text{-}ClC_6H_4$	74	120−121	a
d	$4\text{-}Et_2NC_6H_4$	85	86−87	a
e	$4\text{-}O_2N\,C_6H_4$	83	193−194	a
f	$4\text{-}ClC_6H_4$	74	138−139	a
g	$4\text{-}CH_3C_6H_4$	91	123−124	123−124[11]
h	2-furanyl	92	171−173	172−174[11]
i	2-pyridyl	91	98−100	97−100[11]
j	3-pyridyl	88	87−89	86−89[11]
k	4-pyridyl	84	149−151	148−150[11]
l	1-naphthyl	88	136−137	a
m	2-pyrazinyl	76	146−147	a
n	$PhCH_2CH_2$	84	63−64	a
o	$PhCH_2$	84	65−66	66−67[12]
p	Ph_2CH	89	88−89	106−107[12]
q	$n\text{-}C_4H_9$	83	42−44	42−44[11]

a Novel compound.

Table 2. Preparation of Primary Amides 3a−n

3	R	yield (%)	mp (°C)	mp[a] (°C)
a	C_6H_5	100	128−130	130
b	$2\text{-}CH_3OC_6H_4$	100	128−129	129
c	$3\text{-}ClC_6H_4$	87	134−135	134
d	$4\text{-}NO_2C_6H_4$	100	199−200	201
e	2-furanyl	100	142−143	142−143
f	1-naphthyl	100	201−202	202
g	2-pyridyl	100	107−108	107−109
h	3-pyridyl	100	128−130	129−130
i	4-pyridyl	100	155−156	155−156
j	2-pyrazinyl	100	188−189	189−191
k	$PhCH_2$	100	158−159	157−158
l	$PhCH_2CH_2$	85	104−105	105
m	Ph_2CH	90	168−169	167−168
n	$n\text{-}C_4H_9$	72	104−105	106

a Cadogan J. I. G. et al. *Dictionary of Organic Compounds*, 6th ed.; Chapman & Hall: London, U.K. **3a**, B-0-00069; **3b**, M-0-00635; **3c**, C-0-00557; **3d**, N-0-00821; **3e**, F-0-01325; **3f**, N-0-00046; **3g**, P-0-03885; **3h**, P-0-03881; **3i**, P-0-03887; **3j**, P-0-03652; **3k**, P-0-01232; **3l**, P-0-02416; **3m**, D-0-11687; **3n**, P-0-00666.

Table 3. Preparation of Secondary Amides 4a−j

4	R	R[1]	yield (%)	mp (°C)	lit. mp (°C)
a	$4\text{-}ClC_6H_4$	$EtCH(CH_3)$	95	82−83	a
b	$4\text{-}ClC_6H_4$	C_6H_5	75	195−197	195−196[15]
c	$4\text{-}Et_2NC_6H_4$	$n\text{-}C_4H_9$	92	73−74	b
d	C_6H_5	$t\text{-}C_4H_9$	75	133−134	134−135[16]
e	2-furanyl	$n\text{-}C_4H_9$	94	40−41	40−41[17]
f	1-naphthyl	$n\text{-}C_4H_9$	92	92−93	b
g	2-pyridyl	$4\text{-}CH_3OC_6H_4$	83	86−87	b
h	4-pyridyl	$EtCH(CH_3)$	100	50−52	b
i	2-pyrazinyl	$(CH_3)_3C$	100	87−88	b
j	Ph_2CH	C_6H_5	70	117−118	117−118[18]

a IR spectrum data of **4a** were given in ref 14. *b* Novel compound.

appropriate solvents to afford pure products. The primary amines used include arylamines (phenyl, 4-nitrophenyl) and alkylamines (*n*-butyl, cyclohexyl, *sec*-butyl, and *tert*-butyl).

Preparation of Tertiary Amides 5a−k from *N*-Acylbenzotriazoles 2 with Secondary Amines. When 1*H*-1,2,3-benzotriazol-1-yl(4-chlorophenyl)methanone was reacted with tetrahydro-1*H*-pyrrole at room temperature in EtOH, the crude ^{1}H NMR spectrum showed that the isolated product was a mixture of (4-chlorophenyl)-(tetrahydro-1*H*-pyrrol-1-yl)methanone and ethyl 4-chlorobenzoate with a ratio of 9:1. The use of THF avoided the formation of esters byproducts.

Treatment of *N*-acylbenzotriazoles **2** with 1 equiv of secondary amines in THF at room temperature produced the corresponding tertiary amides **5a** and **5d**−**k** in good to excellent yields (Scheme 1 and Table 4). However,

Table 4. Preparation of Tertiary Amides 5a−k

5	R	R^2	R^3	yield (%)	mp (°C)	lit. mp (°C)
a	4-$CH_3C_6H_4$	C_2H_5	C_2H_5	44	oil	oil[a]
b	4-$CH_3C_6H_4$	i-Pr	C_2H_5	0		
c	4-$CH_3C_6H_4$	i-Pr	i-Pr	0		
d	4-$O_2NC_6H_4$	−$(CH_2)_4$−		96	73−74	b
e	C_6H_5	−$CH_2)_4$−		100	oil	oil[19]
f	2-$CH_3OC_6H_4$	−$CH_2)_4$−		98	oil	b
g	2-furanyl	C_2H_5	C_2H_5	51	oil	oil[20]
h	1-naphthyl	−$(CH_2)_4$−		94	51−52	b
i	4-pyridinyl	−$(CH_2)_4$−		100	oil	b
j	$PhCH_2$	−$(CH_2)_4$−		99	oil	oil[21]
k	Ph_2CH	−$(CH_2)_5$−		68	114−116	b

[a] Cadogan J. I. G. et al. *Dictionary of Organic Compounds*, 6th ed.; Chapman & Hall: London, U.K. **5a**, M-01138. [b] Novel compound.

when using *N*-ethyl-*N*-(1-methylethyl)amine or *N,N*-bis-(1-methylethyl)amine as a secondary amine, no desired *N*-ethyl-4-methyl-*N*-(1-methylethyl)- or 4-methyl-*N,N*-bis(1-methylethyl)benzamide (**5b** or **5c**) was isolated, probably due to the heavily hindered nitrogen. Reaction of less hindered *N,N*-diethylamine with 1*H*-1,2,3-benzotriazol-1-yl(4-methylphenyl)methanone (**2g**) produced *N,N*-diethyl-4-methylbenzamide (**5a**) in moderate yield (44%). A moderate yield (51%) was also obtained for *N,N*-diethylfuran-2-amine (**5g**) from *N,N*-diethylamine. These results show that the cyclic aliphatic amines, e.g., tetrahydro-1*H*-pyrrole, produce the secondary amides in much better yields than the acyclic aliphatic amines, e.g., *N,N*-diethylamine.

Preparation of α-Hydroxyamides Using BtSO$_2$CH$_3$. Development of synthetic methods for α-hydroxyamides has attracted considerable interest, since they include valuable therapeutic agents and also possess synthetic utility. General routes to α-hydroxyamides include: (i) the reduction of α-keto-amides with sodium borohydride,[22] with other metal borohydrides, such as LiBEt$_3$H, KBEt$_3$H, and Zn(BH$_4$)$_2$[23] or with magnesium- or titanium-based reagents;[24] (ii) the hydrogenation of α-keto-amides in the presence of palladium on charcoal[25] or neutral rhodium (I) complexes;[26] (iii) the oxidation of acyclic, tetra-substituted amide-enolates by oxaziridines with yields of around 50%.[27] Methods i and ii need α-keto-amides prepared, e.g., from α-ketoacids[22b] or α-keto-acyl chlorides.[22c] The only previous direct conversion of α-hy-

Scheme 2

7a, R = C_6H_5
7b, R = 4-$CH_3C_6H_4$
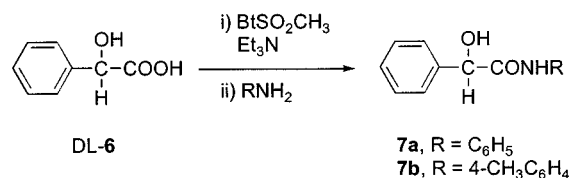
droxycarboxylic acids to α-hydroxyamides is their reaction with *N*-sulfinylamines (RNSO).[28]

After reaction of BtSO$_2$CH$_3$ with 2-hydroxy-2-phenyl-acetic acid (**6**) in the presence of triethylamine, we failed to isolate the corresponding α-hydroxy-*N*-acylbenzotria-zoles probably due to their instability. However, when 1 equiv of aniline or 4-methylaniline was added into the mixture obtained by refluxing **6**, BtSO$_2$CH$_3$, and Et$_3$N in dry THF for about 20 min, α-hydroxyamides **7a** and **7b** were obtained in 68% and 72% yields, respectively (Scheme 2). Products **7a** and **7b** were not formed in the absence of BtSO$_2$CH$_3$. When *n*-butylamine or pyrrolidine was used as the amine reactant, no desired products were obtained. The role of BtSO$_2$CH$_3$ is as with other reactions.

Preparation of 1-(1*H*-1,2,3-Benzotriazol-1-yl)-2,2,3,3,-4,4,4-heptafluorobutan-1-one (8) and Its Perfluoroacylation with Primary and Secondary Amines. In 1997, we reported (trifluoroacetyl)benzotriazole as a convenient trifluoroacetylating agent for amines and alcohols.[8b] (Trifluoroacetyl)benzotriazole was prepared by the reaction of benzotriazole with trifluoroacetic anhydride [(CF$_3$CO)$_2$O]; thus, trifluoroacetic acid was formed as a byproduct. The analogous preparation of perfluoroacylbenzotriazoles, e.g., 1-(1*H*-1,2,3-benzotriazol-1-yl)-2,2,3,3,4,4,4-heptafluorobutan-1-one (**8**) from *n*-(C$_3$F$_7$-CO)$_2$O, means that half of the carbon−fluorine moiety is not utilized.

No reaction occurred between BtSO$_2$CH$_3$ and *n*-C$_3$F$_7$-COOH in the presence of Et$_3$N. However, reaction of 1-(trimethylsilyl)benzotriazole (BtTMS) with 1 equiv of 2,2,3,3,4,4,4-heptafluorobutanoyl chloride (*n*-C$_3$F$_7$COCl) gave **8** in 86% yield (NMR yield) as a sole Bt^1 isomer, together with byproduct BtH, due to the easy hydrolysis of BtTMS. The ^{1}H NMR spectrum of the mixture shows the molar ratio of **8** to BtH is about 6:1. Attempts to obtain pure **8** by washing with aqueous sodium hydroxide solution to remove BtH failed because of rapid hydrolysis of **8**. Compound **8** cannot be separated from BtH by column chromatography, as they have almost identical R_f values. Nevertheless, the presence of BtH should not affect the perfluoroacylation of amines with *n*-C$_3$F$_7$COBt (**8**), which will also generate benzotriazole as a byproduct. Therefore, the mixture of **8** and BtH was used for the subsequent reactions without separation, and indeed treatment of primary and secondary amines with **8** readily produced the perfluoroalkylated amides **9a−d** in good yields (Scheme 3).

In summary, a simple and efficient method for the preparation of primary, secondary and tertiary amides has been developed by the treatment of *N*-acylbenzo-triazoles with ammonia, primary and secondary amines, respectively. Advantages of this procedure include: (1) neutral reaction condition is useful for ammoniation and amination of compounds possessing acid- or base-sensi-

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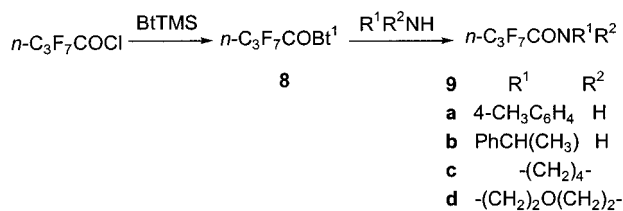
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Scheme 3

tive substituents; (2) the use of acyl chlorides is avoided; (3) most *N*-acylbenzotriazoles can be recrystallized and are stable to storage over months; (4) workup is very simple; (5) primary, secondary and tertiary amides were generally obtained in good to excellent yields; (6) the method could be extended to α-hydroxyamides and perfluoroalkylated amides.

Experimental Section

^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded on a 300 NMR spectrometer in CDCl$_3$ (with TMS for ^{1}H and CDCl$_3$ for ^{13}C as the internal reference). ^{19}F NMR spectra were recorded on a 300 NMR spectrometer at 282 MHz in CDCl$_3$ with CFCl$_3$ as an internal reference.

Modified Procedure for the Preparation of *N*-(1-Methanesulfonyl)benzotriazole (1). To an ice-cold solution of benzotriazole (11.9 g, 0.10 mol) and pyridine (12.0 g, 0.16 mol) in dry toluene (120 mL) was added dropwise methylsulfonyl chloride (9.3 mL, 0.12 mol) in toluene (30 mL). The mixture was then stirred overnight at room temperature. AcOEt (150 mL) and H$_2$O (100 mL) were added. The organic layer was separated, successively washed with water and brine, and dried over anhydrous MgSO$_4$. Removal of solvents in vacuo gave a solid, which was recrystallized from benzene to afford *N*-(1-methanesulfonyl)benzotriazole (1) (17.5 g, 89%) as colorless needles: mp 110−112 °C (mp[11,29] 110−112 °C).

General Procedure for the Preparation of *N*-Acylbenzotriazoles 2. A mixture of aromatic or aliphatic acid (10.0 mmol) and 1-(methylsulfonyl)benzotriazole **1** (1.97 g, 10.0 mmol) and triethylamine (2.0 mL, 14.0 mmol) were refluxed in THF (50 mL) overnight. The solvent was evaporated and the residue was dissolved in chloroform (100 mL). The organic layer was washed with water, dried over anhydrous MgSO$_4$, and evaporated to give a crude product, which was recrystallized from an appropriate solvent to give pure *N*-(arylcarbonyl)- or *N*-(alkanecarbonyl)benzotriazole **2a−q**.

1*H*-1,2,3-Benzotriazol-1-yl(2-methoxyphenyl)methanone (2b): yield 72%; colorless flakes (recrystallized from ethanol); mp 96−97 °C; ^{1}H NMR δ 8.38 (d, *J* = 8.4 Hz, 1H), 8.12 (d, *J* = 8.4 Hz, 1H), 7.69 (t, *J* = 7.5 Hz, 1H), 7.63−7.50 (m, 3H), 7.14−7.05 (m, 2H), 3.77 (s, 3H); ^{13}C NMR δ 166.9 (C=O), 157.8, 146.0, 133.5, 131.4, 130.2, 130.1, 126.1, 122.6, 120.4, 120.0, 114.4, 111.7, 55.7 (CH$_3$). Anal. Calcd for C$_{14}$H$_{11}$N$_3$O$_2$: C, 66.38; H, 4.38; N, 16.60. Found: C, 66.53; H, 4.41; N, 16.66.

1*H*-1,2,3-Benzotriazol-1-yl(3-chlorophenyl)methanone (2c): yield 74%; colorless needles (recrystallized from chloroform/hexane); mp 120−121 °C; ^{1}H NMR δ 8.38 (d, *J* = 8.4 Hz, 1H), 8.20−8.11 (m, 3H), 7.75−7.65 (m, 2H), 7.60−7.53 (m, 2H); ^{13}C NMR δ 165.3 (C=O), 145.7, 134.6, 133.6, 133.1, 132.1, 131.5, 130.6, 129.8, 129.7, 126.6, 120.3, 114.7. Anal. Calcd for C$_{13}$H$_8$ClN$_3$O: C, 60.60; H, 3.13; N, 16.31. Found: C, 60.75; H, 3.01; N, 16.38.

General Procedure for the Reaction of *N*-Acylbenzotriazoles 2 with Aqueous Ammonia. The *N*-acylbenzotriazole **2** (2.5 mmol) was stirred with ammonium hydroxide (30% aqueous solution, 5 mL, 43 mmol) in EtOH (5 mL) and THF (5 mL) at room temperature for 2−4 h. After evaporation of solvents in vacuo, 2 M NaOH (20 mL) was added to the residue and the mixture then extracted with EtOAc. The combined

organic layers were dried over anhydrous MgSO$_4$. Evaporation of the solvent gave a solid, which was recrystallized from benzene to afford the pure primary amide **3a−n**. The isolated yields, melting points, and reported melting points of **3a−n** are summarized in Table 2.

General Procedure for the Reaction of *N*-Acylbenzotriazoles 2 with Primary Amines. The *N*-acylbenzotriazole **2** (1 mmol) was stirred with the appropriate primary amine (1 mmol) in THF (10 mL) at room temperature for 4 h. After evaporation of solvents in vacuo, the residue was added to 2 M NaOH (20 mL) and extracted with EtOAc. The combined organic layers were dried over anhydrous MgSO$_4$. Evaporation of the solvent gave a secondary amide **4a−j**, which was recrystallized from appropriate solvents.

General Procedure for the Reaction of *N*-Acylbenzotriazoles 2 with Secondary Amines. The same procedure as the preparation of the secondary amides **4** afforded pure tertiary amides **5a−k**.

General Procedure for the Preparation of α-Hydroxyamides. A mixture of BtSO$_2$CH$_3$ (0.49 g, 2.5 mmol), 2-hydroxy-2-phenylacetic acid (0.38 g, 2.5 mmol), and Et$_3$N (0.35 g, 3.5 mmol) was refluxed in dry THF for about 20 min, and then an appropriate amine (2.5 mmol) was added and the mixture was refluxed for 18 h. After the mixture was concentrated, EtOAc (50 mL) was added, and the organic phase was washed with 2 M NaOH and dried over anhyd MgSO$_4$. Removal of the solvent gave a solid, which was recrystallized from CHCl$_3$ to furnish α-hydroxyamide **7a**,**b**.

2-Hydroxy-*N*,2-diphenylacetamide (7a): yield 68%; colorless flakes; mp 143−144 °C (lit.[28] mp 150−151 °C); ^{1}H NMR δ 9.08 (br s, 1H), 7.59−7.51 (m, 2H), 7.49−7.40 (m, 2H), 7.40−7.20 (m, 5H), 7.07 (t, *J* = 7.4 Hz, 1H), 6.07 (br s, 1H), 5.13 (s, 1H); ^{13}C NMR δ 170.5 (C=O), 139.7, 137.2, 128.4, 127.9, 127.6, 126.3, 123.7, 119.2, 73.8. Anal. Calcd for C$_{14}$H$_{13}$NO$_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 73.72; H, 5.91; N, 6.14.

2-Hydroxy-*N*-(4-methylphenyl)-2-phenylacetamide (7b): yield 72%; colorless flakes; mp 169−170 °C (lit.[28] mp 170−172 °C); ^{1}H NMR δ 9.02 (br s, 1H), 7.53−7.45 (m, 4H), 7.37−7.24 (m, 1H), 7.33 (d, *J* = 7.5 Hz, 2H), 7.09 (d, *J* = 8.3 Hz, 2H), 6.11 (d, *J* = 4.4 Hz, 1H), 5.14 (d, *J* = 4.2 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR δ 170.2 (C=O), 139.9, 134.7, 133.1, 128.8, 127.8, 127.5, 126.3, 119.1, 73.7, 20.3. Anal. Calcd for C$_{15}$H$_{15}$NO$_2$: C, 74.67; H, 6.27; N, 5.80. Found: C, 74.43; H, 6.63; N, 5.77.

Preparation of 1-(1*H*-1,2,3-Benzotriazol-1-yl)-2,2,3,3,4,4,4-heptafluorobutan-1-one (8). To a solution of BtTMS (1.9 g, 10 mmol) in dry THF (20 mL) under argon was added dropwise *n*-C$_3$F$_7$COCl (2.3 g, 10 mmol). The mixture was stirred at room temperature for 3 h. Then, removal of the solvent afforded C$_3$F$_7$COBt (**8**), together with byproduct BtH. The ^{1}H NMR spectrum of the mixture shows that the molar ratio of these two compounds is 6:1.

1-(1*H*-1,2,3-Benzotriazol-1-yl)-2,2,3,3,4,4,4-heptafluorobutan-1-one (8): white powder (a mixture with benzotriazole with ratio as 6:1); yield determined by ^{1}H NMR, 86%; ^{1}H NMR δ 8.28 (d, *J* = 8.1 Hz, 1H), 8.22 (d, *J* = 8.1 Hz, 1H), 7.79 (t, *J* = 7.2 Hz, 1H), 7.65 (t, *J* = 7.2 Hz, 1H); ^{19}F NMR δ −80.7 (t, *J* = 9.3 Hz, 3F, CF$_3$), −112.5 to −112.7 (m, 2F, −CF$_2$CO−), −124.8 (s, 2F, −CF$_2$−).

General Procedure for the Reaction of 8 with Primary and Secondary Amines. The mixture of **8** and BtH (212 mg, 0.63 mmol of **8**) and an appropriate amine (0.63 mmol) was stirred at room temperature for 6 h. After being concentrated, the mixture was washed with 2 M NaOH and extracted with EtOAc (20 mL × 2). The organic phase was dried over anhyd MgSO$_4$. Removal of the solvent in vacuo afforded perfluoroalkylated amide **9a−d**. The isolated yields of **9a−d** were based on *n*-C$_3$F$_7$COBt.

Supporting Information Available: ^{1}H and ^{13}C NMR spectra data and CHN analyses or HRMS for compounds **2d−f,l−n,p**, **4c,f−i**, **5d,f,h,i,k**, and **9a−d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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