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# Alkyl, Unsaturated, (Hetero)aryl, and N-Protected α-Amino Ketones by Acylation of Organometallic Reagents

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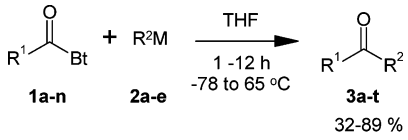


$R^1$ = alkyl, unsaturated, (hetero)aryl, α-amino

$R^2$ = alkyl, (hetero)aryl

Bt = benzotriazol-1-yl

M = MgBr or Li

Stable and easily accessible *N*-acylbenzotriazoles, derived from a variety of aliphatic, unsaturated, (hetero)aromatic, and N-protected α-amino carboxylic acids, were reacted with Grignard and heteroaryllithium reagents to afford corresponding ketones in good to excellent yields.

Great advances have been made in the application of *N*-acylbenzotriazoles in organic synthesis as activated derivatives of carboxylic acids.[1] Efficient *N*-acylbenzotriazole reagents have been easily prepared from carboxylic acids by (i) thionyl chloride and 1*H*-benzotriazole[2] (BtH) or (ii) $BtSO_2Me$ in the presence of $Et_3N$ for the N-acylation of amines[3] and amides,[3,4] the O-acylation of aldehydes,[5] and the C-acylation of ketones and heteroaromatics,[6] alkylsulfones,[7] alkylcyanides,[8] alkylazines,[9] and α-nitro alkanes.[10] Acylations with stable, crystalline *N*-acylbenzotriazoles have attracted interest since they offer an effective replacement for the corresponding acid chlorides, which are usually unstable and sometimes difficult to prepare;[11] thus *N*-acylbenzotriazoles provide a simple and efficient method to prepare peptides.[12]

Ketones have been prepared by a wide variety of methods. Among them, the reaction of Grignard or organometallic reagents with a carboxylic acid is not a practical approach because of the low yield of ketones and the formation of tertiary alcohols.[13] Previous solutions to this problem have involved the addition of Grignard or organozinc reagents to acid fluorides, chlorides, anhydrides, esters, thioesters, and acyl pyrrazolides,[14] Weinreb amides,[15] or acyl hemiacetals.[16] Rapoport and coworkers also used lithium carboxylate together with Grignard reagents to form ketones directly from specific N-protected substituted amino acids in yields which varied from 25 to 87%.[17] Acyl isoxazolidides, prepared through three steps from serine,[18] have been also used to prepare ketones.[19] Limitations associated with these literature methods have included low yields of ketones, many side reactions,[20] and additional requirements of either organic ligands or transition metal catalysts.[21] The undesired side reactions were due to reduction of acid chloride by the Grignard reagent followed by several other reactions.[20] Moreover, acylations with acid chlorides suffered from their sensitivity to moisture and handling difficulties.[22] Reactions with α,β-unsaturated acid chlorides, such as acryloyl chloride, do not work well because of the accompanying polymerization.[23] Furthermore, N-protected α-amino acid chlorides are often unstable and prone to racemization.[24] *N*-Methoxy-*N*-methyl amides (Weinreb amides) cleanly react with Grignard and organometallic reagents to produce ketones with high selectivity

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(2) (a) Katritzky, A. R.; Zhang, Y.; Singh, S. K. *Synthesis* **2003**, 2795. (b) Katritzky, A. R.; Meher, N. K.; Cai, C.; Singh, S. K. *Rev. Soc. Quim. Mex.* **2004**, *48*, 275.
(3) Katritzky, A. R.; He, H.-Y.; Suzuki, K. *J. Org. Chem.* **2000**, *65*, 8210.
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(6) (a) Katritzky, A. R.; Pastor, A. *J. Org. Chem.* **2000**, *65*, 3679. (b) Katritzky, A. R.; Jiang, R.; Suzuki, K. *J. Org. Chem.* **2005**, *70*, 4993. (c) Katritzky, A. R.; Meher, N. K.; Singh, S. K. *J. Org. Chem.* **2005**, *70*, 7792.
(7) Katritzky, A. R.; Abdel-Fattah, A. A. A.; Wang, M. *J. Org. Chem.* **2003**, *68*, 1443.
(8) Katritzky, A. R.; Abdel-Fattah, A. A. A.; Wang, M. *J. Org. Chem.* **2003**, *68*, 4932.
(9) Katritzky, A. R.; Abdel-Fattah, A. A. A.; Akhmedova, R. G. *ARKIVOC* **2005**, 329.
(10) Katritzky, A. R.; Abdel-Fattah, A. A. A.; Gromova, A. V.; Witek, R.; Steel, P. J. *J. Org. Chem.* **2005**, *70*, 9211.
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(12) (a) Katritzky, A. R.; Suzuki, K.; Singh, S. K. *Synthesis* **2004**, 2645. (b) Katritzky, A. R.; Angrish, P.; Hür, D.; Suzuki, K. *Synthesis* **2005**, 398. (c) Katritzky, A. R.; Angrish, P.; Suzuki, K. *Synthesis* **2006**, 411.
(13) (a) Jorgenson, M. J. *Org. React.* **1970**, *18*, 1. (b) Suga, K.; Watanabe, S.; Yamaguchi, Y.; Tohyama, M. *Synthesis* **1970**, 189. (c) Watanabe, S.; Suga, K.; Fujita, T.; Saito, N. *Aust. J. Chem.* **1977**, *30*, 427.
(14) (a) Zhang, Y.; Rovis, T. *J. Am. Chem. Soc.* **2004**, *126*, 15964. (b) Hansford, K. A.; Dettwiler, J. E.; Lubell, W. D. *Org. Lett.* **2003**, *5*, 4887. (c) Dieter, R. K. *Tetrahedron* **1999**, *55*, 4177. (d) Shirley, D. A. In *Organic Reactions*; Wiley: New York, 1954; Vol. 8, p 28. (e) Lauer, D.; Staab, H. A. *Chem. Ber.* **1969**, *102*, 1631. (f) Staab, H.; Jost, E. *Ann.* **1962**, *655*, 90. (g) Kuhn, R.; Staab, H. A. *Chem. Ber.* **1954**, *87*, 262.
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(16) Mattson, M. N.; Rapoport, H. *J. Org. Chem.* **1996**, *61*, 6071.
(17) (a) Knudsen, C. G.; Rapoport, H. *J. Org. Chem.* **1983**, *48*, 2260. (b) Maurer, P. J.; Takahata, H; Rapoport, H. *J. Am. Chem. Soc.* **1984**, *106*, 1095.
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(19) Lubell, W. D.; Jamison, T. F.; Rapoport, H. *J. Org. Chem.* **1990**, *55*, 3511.
(20) Wang, X.-J.; Zhang, L.; Sun, X.; Xu, Y.; Krishnamurthy, D.; Senanayake, C. H. *Org. Lett.* **2005**, *7*, 5593.
(21) (a) Cardelicchio, C.; Flandanese, V.; Marchese, G.; Ronzini, L. *Tetrahedron Lett.* **1987**, *28*, 2053. (b) Malanga, C.; Aronica, L. A.; Lardicci, L. *Tetrahedron Lett.* **1995**, *36*, 9185.
(22) Aldabbagh, F. *Comprehensive Organic Functional Group Transformations II*; Katritzky, A. R., Taylor, R. J. K., Eds.; Elsevier: New York, 2005; Vol. 5, p 1.
(23) (a) Fristad, W. E.; Dime, D. S.; Bailey, T. R.; Paquette, L. A. *Tetrahedron Lett.* **1979**, *20*, 1999. (b) Paquette, L. A.; Fristad, W. E.; Dime, D. S.; Bailey, T. R. *J. Org. Chem.* **1980**, *45*, 3017.
(24) Gross, M.; Meienhofer, J. *The Peptides*; Academic Press: New York, 1979.

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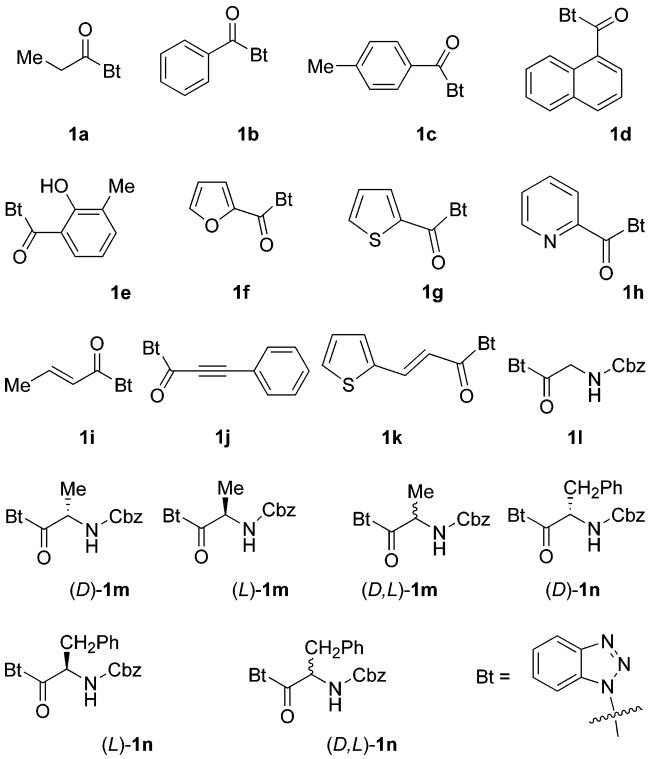



**FIGURE 1.** *N*-Acylbenzotriazoles ($R^1COBt$) **1a**−**n**.

without side reactions.[15] However, in certain cases, with hindered or highly basic reagents, the Weinreb amides show unusual reactivity.[25] Direct acylations using amino acid derivatives required specific protecting groups which were sometimes difficult to remove.[26] Acyl isoxazolidides have concurrent reductive cleavage of the N−O bond, and ring opening of these compounds was observed.[19]

Our approach to develop a general method for the synthesis of a variety of ketones involved the use of *N*-acylbenzotriazoles as the stable alternatives of corresponding acid chlorides or Weinreb amides. We now report the synthesis of alkyl, unsaturated, (hetero)aryl, and α-amino ketones in good to excellent yields from easily accessible *N*-acylbenzotriazoles with Grignard reagents or heteroaryllithiums without side reactions.

*N*-Acylbenzotriazoles **1a**−**n** were readily prepared from benzotriazole (Bt) and the corresponding carboxylic acid in excellent yields according to reported procedure (Figure 1).[2a,3,6c,12a,27] Grignard and heteroaryllithium reagents **2a**−**e** were freshly prepared in THF immediately before use (Figure 2).

We found that 1 mmol of 1-benzotriazol-1-ylpropan-1-one **1a** on reaction with 1.2 mmol of freshly prepared *p*-tolylmagnesium bromide **2a** at 0 °C for 1.5 h gave the corresponding *p*-tolylpropanone **3a** in 89% yield (Table 1). The $^1$H NMR spectra of **3a** showed the disappearance of the Bt signals in the aromatic region, indicating the loss of the benzotriazolyl group during the reaction. The $^{13}$C NMR spectra of **3a** showed a signal at 200.5 ppm corresponding to the carbonyl group of the product and the disappearance of the signal at 168.8 ppm belonging to the carbonyl group at the α position of the benzotriazolyl group

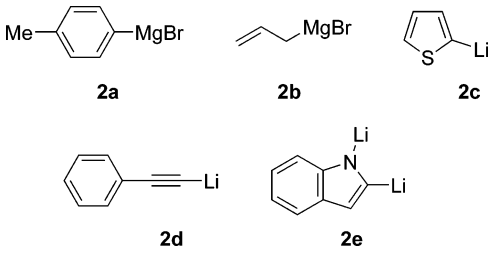
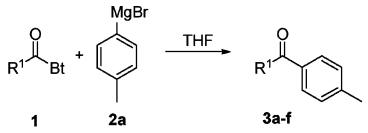
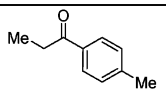
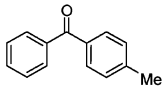
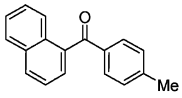
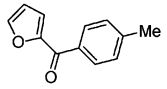
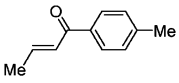
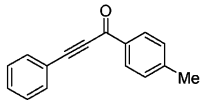



**FIGURE 2.** Grignard reagents and heteroaryllithium reagents ($R^2M$) **2a**−**e**.

**TABLE 1. Addition of Grignard Reagent 2a to *N*-Acylbenzotriazoles 1**




| $R^1COBt$ | $R^2MgBr$ | *T* (°C) | *t* (h) | product structure | | yield (%)[a,b] |
|---|---|---|---|---|---|---|
| **1a** | **2a** | 0 | 1.5 |  | **3a** | 89 |
| **1b** | **2a** | 0 | 2.0 |  | **3b** | 72 |
| **1d** | **2a** | 65 | 6.0 |  | **3c** | 65 |
| **1f** | **2a** | 65 | 3.0 |  | **3d** | 63 |
| **1i** | **2a** | 65 | 6.0 |  | **3e** | 66 |
| **1j** | **2a** | 0 | 4.0 |  | **3f** | 50 |

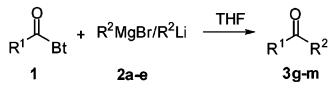
[a] Isolated yields after column purification and determined from a single experiment. [b] Reaction temperature was varied between 0 and 65 °C and reaction time between 1.5 and 6.0 h based on TLC profile (diethylether/hexanes = 10:1 to 1:1).

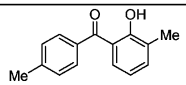
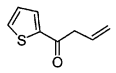
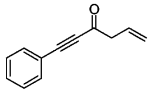
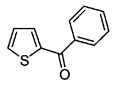
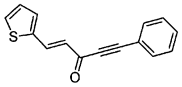
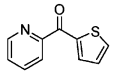
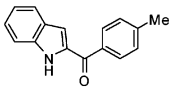
in the starting material. We then explored a wide range of *N*-acylbenzotriazoles (Figure 1) with Grignard reagents and organolithium reagents (Figure 2) in the coupling reaction to test the generality of this method. The results of our efforts are displayed in Tables 1−3.

A variety of alkyl, aryl, heteroaryl, and unsaturated *N*-acylbenzotriazoles, such as 1-benzotriazol-1-ylpropan-1-one[2a] **1a**, benzotriazol-1-ylphenylmethanone[3] **1b**, benzotriazol-1-yl-naphthalen-1-ylmethanone[3] **1d**, benzotriazol-1-ylfuran-2-yl-methanone[3] **1f**, 1-benzotriazol-1-ylbut-2-en-1-one[2a] **1i**, and 1-benzotriazol-1-yl-3-phenylpropynone[2a] **1j**, were reacted with 1.2 equiv of *p*-tolylmagnesium bromide **2a**. At the appropriate temperature and the corresponding reaction time, the desired alkyl, aryl, heteroaryl, and unsaturated ketones **3a**−**f** were obtained in 50−89% yields (Table 1). The products were

(25) (a) Graham, S. L.; Scholz, T. H. *Tetrahedron Lett.* **1990**, *31*, 6269. (b) Graham, S. L.; Scholz, T. H. *J. Org. Chem.* **1991**, *56*, 4260.
(26) Roemmele, R. C.; Rapoport, H. *J. Org. Chem.* **1988**, *53*, 2367.
(27) Katritzky, A. R.; Singh, S. K.; Cai, C.; Bobrov, S. *J. Org. Chem.* **2006**, *71*, 3364.

**TABLE 2. Addition of Grignard and Organolithium Reagents 2a−e to *N*-Acylbenzotriazoles 1**




| $R^1COBt$ | $R^2MgBr/R^2Li$ | $T$ (°C) | $t$ (h) | product structure | | yield[a,b] |
|---|---|---|---|---|---|---|
| **1e** | **2a** | 25 | 4.0 |  | **3g**[c] | 80 |
| **1g** | **2b** | 65 | 4.0 |  | **3h** | 53 |
| **1j** | **2b** | 25 | 6.0 |  | **3i** | 69 |
| **1b** | **2c** | -78 | 1.0 |  | **3j** | 70 |
| **1k** | **2d** | -78 | 1.0 |  | **3k** | 32 |
| **1h** | **2c** | -78 | 1.0 |  | **3l** | 48 |
| **1c** | **2e** | -78 | 1.0 |  | **3m**[c] | 72 |

[a] Isolated yields after column purification and determined from a single experiment. [b] Reaction temperature was varied between −78 to 65 °C and reaction time between 1.0 and 6.0 h based on TLC profile (diethylether/hexanes = 10:1 to 1:1). [c] 2.2 equiv of Grignard reagents was used.

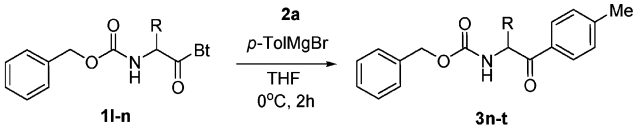
isolated by column chromatography and were fully characterized by $^1H/^{13}C$ NMR spectroscopy and elemental analysis. Compound **3e**, where there is a possibility of geometrical isomerism, is in the *E*-form as evidenced from the coupling constants ($J$ = 15.6 Hz) between protons attached to the carbon−carbon double bond.

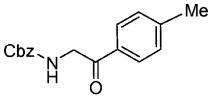
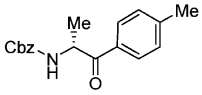
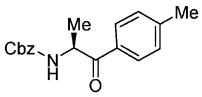
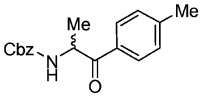
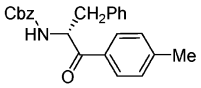
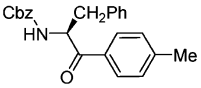
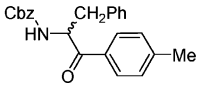
We then attempted to synthesize more complex ketones by varying both the coupling partners. Coupling reactions were carried out with one more Grignard reagent as well as some aryl and (hetero)aryllithium reagents. Thus, *p*-tolylmagnesium bromide **2a**, allylmagnesium bromide **2b**, 2-thienyllithium **2c**, phenylethynyllithium **2d**, and 1*H*-indol-2-yllithium lithium salt[28] **2e** were reacted with *N*-acylbenzotriazoles, such as benzotriazol-1-yl-2-hydroxy-3-methylphenylmethanone[27] **1e** (2.2 equiv of Grignard reagents was used in the presence of a free hydroxyl group), benzotriazol-1-ylthiophen-2-ylmethanone[2a] **1g**, benzotriazol-1-ylphenylmethanone[3] **1b**, (*E*)-1-benzotriazol-1-yl-3-thiophen-2-ylpropenone[6c] **1k**, benzotriazol-1-ylpyridin-2-ylmethanone[3] **1h**, and benzotriazol-1-yl-*p*-tolylmethanone[3] **1c**, to give the desired diheteroaryl and unsaturated heteroaryl ketones **3g−l** in 32−80% yield (Table 2).

When using allyl Grignard reagent **2b**, we noticed the formation of side products on TLC. This may be due to the formation of products arising from the conjugation of the olefin to provide the α,β-unsaturated ketones. However, we were not able to isolate any of the side products due to their small quantity. Also, we found that the pure products **3h**, **3i**, and **3k** are not stable at room temperature and decomposed considerably after 2−3 days when stored at room temperature.

(28) Herbert, J. M.; Maggiani, M. *Synth. Commun.* **2001**, *31*, 947.

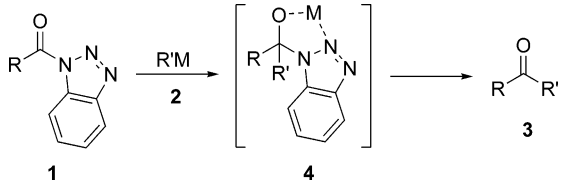
**TABLE 3. Addition of Grignard Reagent 2a to *N*-Acylbenzotriazoles 1l−n**




| $R^1COBt$ | product structure | | yield[a,b] |
|---|---|---|---|
| **1l** |  | **3n** | 64 |
| (*D*)-**1m** |  | **3o** | 50 |
| (*L*)-**1m** |  | **3p** | 55 |
| (*D,L*)-**1m** |  | **3q** | 67 |
| (*D*)-**1n** |  | **3r** | 40 |
| (*L*)-**1n** |  | **3s** | 50 |
| (*D,L*)-**1n** |  | **3t** | 56 |

[a] Isolated yields after column purification (eluent: diethylether/hexanes = 10:1 to 1:1) and determined from a single experiment. [b] 2.2 equiv of Grignard reagents was used.

**SCHEME 1**




We found that tertiary alcohols were not obtained as the side products in the reaction even after we used excess Grignard reagent. We therefore propose the tetrahedral intermediate **4** to explain the preferential formation of ketones over tertiary alcohols (Scheme 1). The effective chelation of metal ion between carbonyl oxygen and nitrogen of the benzotriazole moiety prevents the collapse of the tetrahedral intermediate **4** until the aqueous acidic work up.

Our method proved successful with a wide variety of organometallic reagents and *N*-acylbenzotriazoles. Ketone **3h**

has been prepared previously with low yields (16%) by the Friedel−Crafts reaction of thiophene with 4-chlorobutyryl chloride.[29] The present procedure is obviously higher yielding, more simple, and convenient. Few examples of unsaturated heteroaryl ketones are known in the literature. Synthesis of the unsaturated heteroaryl ketone **3k** may be helpful for the access of complex natural products. Ketone **3m** containing the indole moiety was also conveniently prepared by our method.

Because one of the most important features of biologically active amino ketones is associated with the presence of an asymmetric α-carbon in their structures, total control of chirality represents a major goal during the synthesis of these amino ketones. Literature synthesis of chiral aryl α-amino ketones via Friedel−Crafts-type reactions involves N-protected α-amino acid chlorides.[30] Direct acylation using amino acids has been described by Rapoport.[16,17] We reacted the *N*-acylbenzotriazole derivatives, such as (2-benzotriazol-1-yl-2-oxoethyl)carbamic acid benzyl ester[12a] **1l**, (2-benzotriazol-1-yl-1-methyl-2-oxoethyl)carbamic acid benzyl ester[12a] **1m**, and (2-benzotriazol-1-yl-1-benzyl-2-oxoethyl)carbamic acid benzyl ester[12a] **1n**, with 2.2 equiv of *p*-tolylmagnesium bromide **2a** to give the novel aryl α-amino ketones **3n**−**t** in 40−67% yield (Table 3). To demonstrate that racemization does not occur during the reaction, D, L, and D,L mixtures of ketones **3o**−**q** and **3r**−**t** were synthesized from D, L, and D,L mixtures of *N*-acylbenzotriazoles **1m** and **1n**, respectively. As determined by chiral HPLC analysis (using Chirobiotic T column, detection at 254 nm, flow rate 0.5 mL/min, solvent MeOH/$H_2O$ = 99:1, solution concentration 0.1 mg/mL), **3r** and **3s** showed single peaks at 6.2 and 6.5 min, respectively, where as the D,L mixture **3t** showed two peaks at 6.2 and 6.5 min. A doping experiment was carried out by mixing the solution of **3r** with 2 drops of the solution of **3t**, and the HPLC showed an enhanced peak at 6.2 min corresponding to **3r** and a small peak at 6.5 min corresponding to **3t**. The same doping experiment was also carried out with **3s** and **3t**, and the HPLC traces have been included in the Supporting Information.

Yields for **3b**−**f**, **3h**−**m**, and **3n**−**t** were calculated for the pure isolated products after the purification by column chromatography. In all the cases, 10−20% of the corresponding starting materials was recovered. Compounds containing unsaturated bonds such as **3e**,**f**, **3h**,**i**, and **3k** were found to be unstable at room temperature. We were not able to isolate any side products in all the above reactions. Efforts were made to optimize the yields of **3c**−**e** and **3h** by refluxing the reaction mixture for several hours in THF.

In summary, a simple, efficient, and broadly applicable general method for the preparation of alkyl, unsaturated, (hetero)aryl, and N-protected α-amino ketones by acylation of the corresponding *N*-acylbenzotriazoles with Grignard and heteroaryllithium reagents has been developed. Features of this method include the following: (i) stable and easily accessible acylating agents are used; (ii) additional transition metal catalysts or organic ligands are avoided; and (iii) useful to excellent yields of ketones are obtained.

## Experimental Section

**General Procedure:** To a stirred solution of *N*-acylbenzotriazole (1 mmol) in dry THF (5 mL) under nitrogen was added dropwise a freshly prepared solution of Grignard or heteroaryllithium reagent in THF (*c* = 0.5 M, 2.4 mL, 1.2 mmol or 4.8 mL, 2.2 mmol for *N*-acylbenzotriazoles containing acidic hydrogens) at the appropriate temperature. The reaction mixture was stirred until completed (followed by TLC, solvent system: diethylether/hexanes = 10:1 to 1:1) and then quenched by saturated ammonium chloride solution. After extraction by ethyl acetate, the organic layer was washed with brine and water, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The crude product was then purified by chromatography over silica gel column (eluent: diethylether/hexanes = 10:1 to 1:1).

**(2-Hydroxy-3-methylphenyl)-*p*-tolylmethanone (3g):** Yield 0.18 g (80%); yellow crystal; mp = 62 °C; $^1$H NMR $\delta$ 7.59 (d, $J$ = 8.0 Hz, 2H), 7.45 (d, $J$ = 8.0 Hz, 1H), 7.36 (d, $J$ = 8.0 Hz, 1H), 7.30 (d, $J$ = 8.0 Hz, 2H), 6.78 (t, $J$ = 8.0 Hz, 1H), 2.45 (s, 3H), 2.32 (s, 3H); $^{13}$C NMR $\delta$ 201.5, 161.4, 142.5, 136.8, 135.3, 131.1, 129.4, 128.9, 127.2, 118.4, 117.8, 21.5, 15.5. Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 78.98; H, 6.48.

**D-(1-Benzyl-2-oxo-2-*p*-tolylethyl)carbamic Acid Benzyl Ester (3r):** Yield 0.21 g (56%), oil; $[\alpha]^{25}_D$ = −10 ($CHCl_3$, $c$ = 1.2); $^1$H NMR $\delta$ 7.85 (d, $J$ = 8.1 Hz, 2H), 7.34−7.30 (m, 5H), 7.26 (d, $J$ = 8.1 Hz, 2H), 7.20−7.18 (m, 3H), 6.97−6.95 (m, 2H), 5.74 (d, $J$ = 8.0 Hz, 1H), 5.58 (dd, $J$ = 11.7, 5.8 Hz, 1H), 5.10 (s, 2H), 3.26 (dd, $J$ = 13.8, 6.0 Hz, 1H), 2.99 (dd, $J$ = 13.8, 5.4 Hz, 1H), 2.41 (s, 3H); $^{13}$C NMR $\delta$ 197.3, 155.6, 144.8, 136.4, 135.5, 132.0, 129.6, 129.5, 128.7, 128.5, 128.3, 128.1, 127.9, 126.9, 66.8, 56.3, 39.1, 21.7. Anal. Calcd for $C_{24}H_{23}NO_3$: C, 77.19; H, 6.21; N, 3.75. Found: C,76.99; H, 6.33; N, 3.57.

**L-(1-Benzyl-2-oxo-2-*p*-tolylethyl)carbamic Acid Benzyl Ester (3s):** Yield 0.14 g (40%), oil; $[\alpha]^{25}_D$ = +10 ($CHCl_3$, $c$ = 1.0); $^1$H NMR $\delta$ 7.85 (d, $J$ = 8.1 Hz, 2H), 7.33−7.31 (m, 5H), 7.26 (d, $J$ = 8.1 Hz, 2H), 7.19−7.16 (m, 3H), 6.98−6.95 (m, 2H), 5.74 (d, $J$ = 8.0 Hz, 1H), 5.58 (dd, $J$ = 11.7, 5.8 Hz, 1H), 5.09 (s, 2H), 3.26 (dd, $J$ = 13.8, 6.0 Hz, 1H), 2.98 (dd, $J$ = 13.8, 5.4 Hz, 1H), 2.41 (s, 3H); $^{13}$C NMR $\delta$ 197.3, 155.6, 144.7, 136.4, 135.5, 132.0, 129.6, 129.5, 128.7, 128.5, 128.3, 128.1, 127.9, 126.9, 66.8, 56.3, 39.1, 21.6. Anal. Calcd for $C_{24}H_{23}NO_3$: C, 77.19; H, 6.21; N, 3.75. Found: C, 76.87; H, 6.42; N, 3.45.

**D,L-(1-Benzyl-2-oxo-2-*p*-tolylethyl)carbamic Acid Benzyl Ester (3t):** Yield 0.18 g (50%), oil; $^1$H NMR $\delta$ 7.85 (d, $J$ = 8.1 Hz, 2H), 7.33−7.30 (m, 5H), 7.27 (d, $J$ = 8.1 Hz, 2H), 7.09−7.17 (m, 3H), 6.98−6.94 (m, 2H), 5.72 (d, $J$ = 8.0 Hz, 1H), 5.58 (dd, $J$ = 11.7, 5.8 Hz, 1H), 5.10 (dd, $J$ = 20.6, 12.4 Hz, 2H), 3.26 (dd, $J$ = 13.8, 6.0 Hz, 1H), 2.99 (dd, $J$ = 13.8, 5.4 Hz, 1H), 2.41 (s, 3H); $^{13}$C NMR $\delta$ 197.3, 155.6, 144.8, 136.4, 135.5, 132.0, 129.5, 129.4, 128.7, 128.4, 128.2, 128.0, 127.9, 126.8, 66.7, 56.2, 39.0, 21.7. Anal. Calcd for $C_{24}H_{23}NO_3$: C, 77.19; H, 6.21; N, 3.75. Found: C, 76.96; H, 6.76; N, 3.50.

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**Supporting Information Available:** Experimental procedures, spectroscopic data, elemental analysis, and melting points for compounds **3a**−**f** and **3h**−**q**. This material is available free of charge via the Internet at http://pubs.acs.org.

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