Regiocontrol in the α,α-dialkylation of ketones

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Dedicated to Douglas Lloyd on the occasion of his 80th anniversary

Abstract
Refluxing α-halo ketones **1**, **5**, **8**, **11** with benzotriazole gave the corresponding α-benzotriazolyl ketones **2**, **6**, **9**, **12** in high yields. Regioselective introduction of an alkyl group into the α-position of these α-benzotriazolyl ketones using an appropriate halide under basic conditions gave α-alkyl-α-benzotriazolyl ketones **4a-e**, **7a-c**, **10a-c** and **13a-c**. Removal of the benzotriazole group by lithium naphthalenide and the introduction of another alkyl group were illustrated for **4c** and **13c**, which gave compounds **14** and **15**.

Keywords: Benzotriazole, α,α-dialkylation, ketones, regiocontrol, α-haloketones

Introduction

The regioselective introduction of one or two alkyl groups at the carbon α to a ketone carbonyl is important synthetically. Published general procedures for achieving this include controlling the site of alkylation by diverse activating substituents at the α-position, including: (i) another carbonyl group;[1a-d] (ii) an α-alkylthio group, which could be further reductively substituted;[2a-d] (iii) an α-benzenesulfonyl group;[3a-c] (iv) an α-cyano group.[4] There are several published procedures for introduction of two identical alkyl groups at the α-carbon of a ketone;[5a-c] however, few procedures for the introduction of two different alkyl groups at the α-carbon of a ketone have been published.[6a-c]

We now disclose a method for the regioselective α-alkylation of ketones via benzotriazole intermediates, which allows the introduction of two different α-substituents. The sequence involved three steps (Schemes 1 and 2): (i) preparation of an α-benzotriazolyl ketone; (ii) introduction of an alkyl group into the α-position using 2N or 5N NaOH aqueous solution; (iii) removal of benzotriazole by lithium naphthalenide and simultaneous introduction of another

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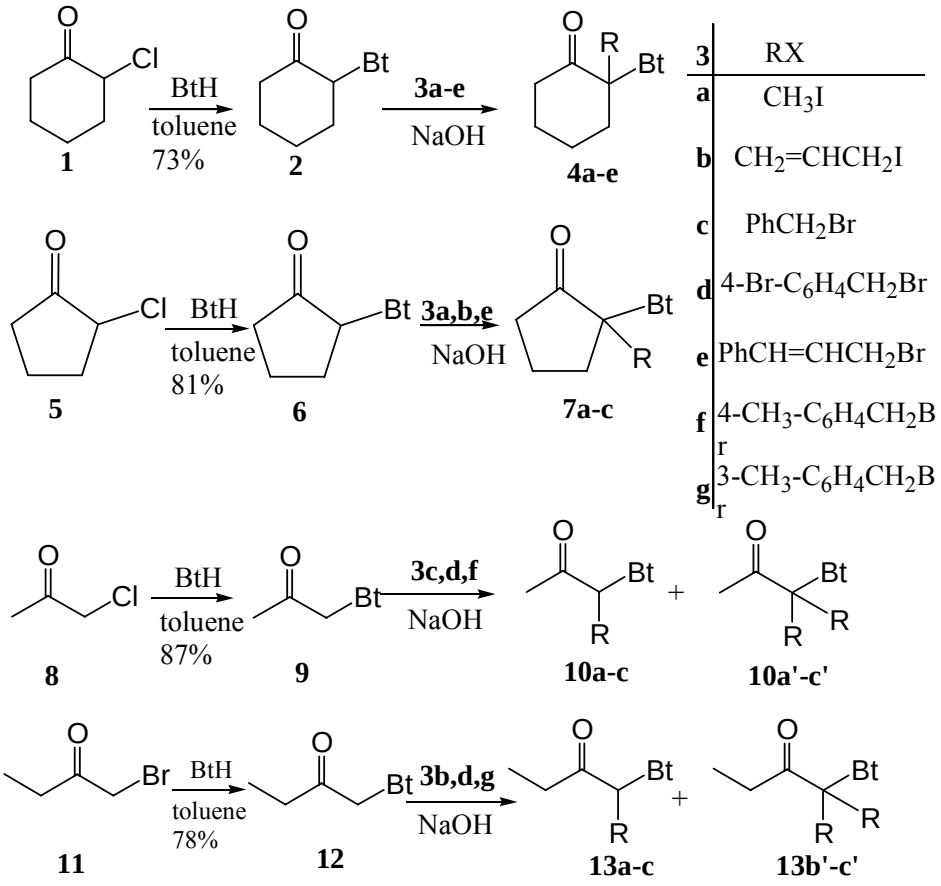
alkyl group. This new approach is convenient, with mild reaction conditions, applies commercial or readily available reagents. It complements previous routes for the α-alkylation of ketones.



Bt = benzotriazol-1-yl or benzotriazol-2-yl

Scheme 1

Results and Discussion

Halo ketones **1**, **5**, **8**, **11** were treated with benzotriazole in toluene with (for **1**, **8**) or without triethylamine (for **5**, **11**) as a base to afford α-benzotriazolyl ketones **2**, **6**, **9**, **12** in 73%, 81%, 87% and 78% total yields respectively (Scheme 1).[7] These easy to handle reactions often give isomeric mixtures of the 1- and 2-*N*-alkylated benzotriazole (RBt^1 and RBt^2; **2**, **6**, **9**) with **12** as an exception, where only RBt^1 was obtained. The RBt^1 and RBt^2 isomers were separated for characterisation and for use in further reactions. Structures **2**, **6**, **9**, **12** are supported by ^{1}H NMR spectra which show a new set of signals at 7.0–8.2 ppm assigned to the *N*-substituted benzotriazole group. The ^{13}C NMR spectra of **2**, **6**, **9**, **12** show signals between 110 ppm and 146 ppm corresponding to the *N*-substituted benzotriazole.

Intermediates **2**, **6**, **9**, **12**, on treatment with 2 equivalents of NaOH and an alkyl halide **3a-g** in acetonitrile at 20 ^{o}C, give the corresponding α-alkyl-α-benzotriazolyl ketones **4a-e**, **7a-c**, **10a-c** and **13a-c** in average 65% yields (Scheme 1) (Table 1). Monoalkylation compounds are the major products, but dialkylation products **10a′-c′** and **13b′**,**c′** are also formed from the acyclic starting materials **9** and **12** in 5–16% yields. Dialkylation product **13a′** was not detected. The structures of α-alkyl-α-benzotriazolyl ketones **4a-e**, **7a-c**, **10a-c** and **13a-c** are supported by their ^{1}H NMR spectra which for products **4a-e** and **7a-c** show the appearance of a new set of signals corresponding to the introduced alkyl groups in place of the doublet of doublets at 5.5–6.5 ppm characteristic for the α-H to the benzotriazole group in the starting materials. The ^{13}C NMR spectra of **4a-e** and **7a-c** also show new signals corresponding to the introduced alkyl groups. The ^{1}H NMR spectra of products **10a-c** and **13a-c** show the appearance of a new doublet of doublets characteristic for the single α-H to the benzotriazole group and a new set of signals characteristic for the alkyl group introduced. The singlets at 5.0–6.0 ppm in the starting materials **9**, **12** for the two α-H to the benzotriazole group are gone. The ^{13}C NMR spectra of **10a-c** and **13a-c** also show new signals corresponding to the alkyl groups introduced.

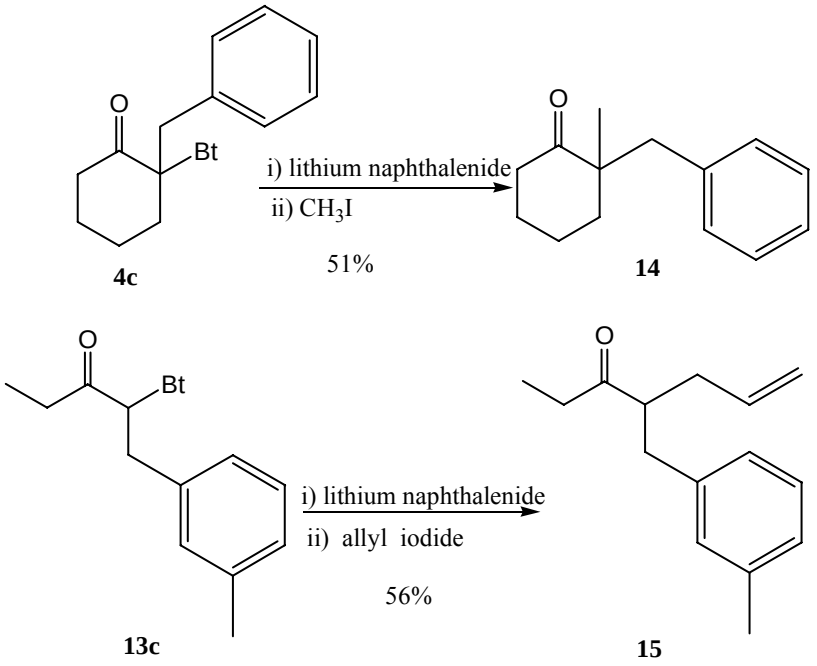
Table 1. Preparation of α-alkylated α-benzotriazolyl ketones**4a-e**, **7a-c**, **10a-c** (**a′-c′**) and **13a-c** (**b′-c′**)

Product	R	Reaction Time, h	Yield (%)*
4a	CH_3	48	54
4b	CH_2=$CHCH_2$	30	68
4c	$PhCH_2$	48	67
4d	4-Br-$C_6H_4CH_2$	8	84
4e	$PhCH$=$CHCH_2$	35	77
7a	CH_3	39	70
7b	CH_2=$CHCH_2$	39	73
7c	$PhCH$=$CHCH_2$	39	100
10a (**a′**)	$PhCH_2$	48	45 (11)
10b (**b′**)	4-Br-$C_6H_4CH_2$	42	44 (16)

* The isolated yields.

Cyclic compound **4c** and acyclic compound **13c** were chosen as starting materials to test the benzotriazolyl group elimination and the introduction of another alkyl group. Intermediates **4c** or **13c** were treated with 5 equivalents of lithium naphthalenide in THF at –40 ^{o}C for 4 h, then the corresponding alkyl iodide was added and the mixture was stirred for 6 h at the same temperature. After general work-up, compound **14** and **15** were obtained in 51% and 56% yields, respectively. Structures **14** and **15** are supported by their ^{1}H NMR spectra which show the appearance of a new set of signals corresponding to the introduced alkyl group in place of the signals at 7.0–8.2 ppm assigned to the benzotriazolyl group. The ^{13}C NMR spectra of **14** and **15** also show new signals corresponding to the alkyl groups introduced.

In summary, a novel, simple route for the regioselective α,α-dialkylation of ketones was developed.



Scheme 2

Experimental Section

General Procedures. Melting points were determined on a hot-stage apparatus and were uncorrected. NMR spectra were recorded in $CDCl_3$ with TMS as the internal standard for ^1H (300 MHz) or a solvent as the internal standard for ^{13}C (75 MHz). Microanalyses were performed on a Carlo Erba -1106 elemental analyzer. Benzene and toluene were dried over molecular sieves. Column chromatography was conducted with silica gel 200–425 mesh.

General procedure for the preparation of α-benzotriazolyl ketones 2, **6**, **9**, **12**
The α-halo ketone **1**, **5**, **8**, or **11** (10 mmol) and benzotriazole (1.79 g, 15 mmol) in toluene (50 mL) and triethylamine (for **1**: 50 mmol; for **8**: 15 mmol) were heated under reflux for 24 h. Toluene was removed in *vacuo*. The residue was purified by column chromatography to afford an analytically pure sample.
2-(Benzotriazol-2-yl)cyclohexanone and 2-(benzotriazol-1-yl)cyclohexanone (2). the ratio of the two isomers is 1.2 : 1.
2-(Benzotriazol-2-yl)cyclohexanone. colorless flakes (ethanol), mp 131–133 °C,[8] (40%); ^1H NMR ($CDCl_3$) δ 1.70–2.00 (m, 2H), 2.04–2.24 (m, 2H), 2.44–2.72 (m, 3H), 2.78–2.90 (m, 1H), 5.59 (dd, J = 12.6, 5.7 Hz, 1H), 7.37–7.40 (m, 2H), 7.87–7.90 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 24.1, 26.7, 33.0, 41.0, 73.1, 118.2, 126.4, 144.2, 202.7.

2-(Benzotriazol-1-yl)cyclohexanone. colorless prisms (ethanol), mp 128–129 °C (33%); ^{1}H NMR ($CDCl_3$) δ 1.82–2.04 (m, 2H), 2.18–2.31 (m, 2H), 2.54–2.80 (m, 4H), 5.59 (dd, 12.6, 6.3 Hz, 1H), 7.33–7.48 (m, 3H), 8.08 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 24.6, 26.9, 33.0, 41.2, 66.6, 110.3, 120.1, 123.8, 127.2, 132.9, 146.2, 202.7. Anal. Calcd for $C_{12}H_{13}N_3O$: C, 66.96; H, 6.09; N, 19.52. Found: C, 66.97; H, 6.30; N, 19.60.

2-(Benzotriazol-2-yl)cyclopentanone and 2-(benzotriazol-1-yl)cyclopentanone (6). the ratio of the two isomers is 2 : 1.

2-(Benzotriazol-2-yl)cyclopentanone. colorless prisms (ethanol), mp 72–74 °C (54%); ^{1}H NMR ($CDCl_3$) δ 1.98–2.15 (m, 1H), 2.33–2.43 (m, 1H), 2.50–2.62 (m, 2H), 2.70–2.90 (m, 2H), 5.38 (t, *J* = 9.8 Hz, 1H), 7.30–7.42 (m, 2H), 7.78–7.90 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 18.8, 30.2, 36.2, 70.7, 118.0, 126.6, 144.5, 209.5. Anal. Calcd for $C_{11}H_{11}N_3O$: C, 65.66; H, 5.51; N, 20.88. Found: C, 65.78; H, 5.64; N, 21.04.

2-(Benzotriazol-1-yl)cyclopentanone. colorless prisms (ethanol) mp 62–64 °C (27%); ^{1}H NMR ($CDCl_3$) δ 2.00–2.22 (m, 1H), 2.28–2.44 (m, 1H), 2.45–2.63 (m, 2H), 2.66–2.84 (m, 2H), 5.28 (t, *J* = 9.9 Hz, 1H), 7.32–7.52 (m, 3H), 8.06 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 18.6, 28.9, 35.9, 63.8, 109.4, 119.9, 123.9, 127.4, 132.8, 145.7, 210.2. Anal. Calcd for $C_{11}H_{11}N_3O$: C, 65.66; H, 5.51; N, 20.88. Found: C, 65.68; H, 5.72; N, 20.85.

1-(Benzotriazol-1-yl)propan-2-one and 1-(benzotriazol-2-yl)propan-2-one (9). the ratio of the two isomers is 4 : 1.

1-(Benzotriazol-1-yl)propan-2-one. colorless flakes (ethanol), mp 120–122 °C, [mp 126–127 °C[9]] (65%); ^{1}H NMR ($CDCl_3$) δ 2.21 (s, 3H), 5.45 (s, 2H), 7.32–7.41 (m, 2H), 7.48 (t, *J* = 7.5 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 27.0, 56.6, 109.1, 119.9, 124.0, 127.8, 133.3, 145.8, 199.8.

1-(Benzotriazol-2-yl)propan-2-one. colorless prisms (ethanol), mp 143–144 °C,[10] (16%); ^{1}H NMR ($CDCl_3$) δ 2.15 (s, 3H), 5.52 (s, 2H), 7.41–7.44 (m, 2H), 7.88–7.91 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 27.0, 64.7, 118.2, 126.9, 144.9, 199.7.

1-(Benzotriazol-1-yl)-2-butanone (12). obtained as just one isomer, colorless needles (ethanol), mp 101–103 °C (78%); ^{1}H NMR ($CDCl_3$) δ 1.10 (t, *J* = 7.2 Hz, 3H), 2.49 (q, *J* = 7.2 Hz, 2H), 5.44 (s, 2H), 7.37–7.43 (m, 2H), 7.51 (t, *J* = 7.7 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 7.1, 33.2, 56.0, 109.1, 120.2, 124.1, 128.0, 133.4, 146.0, 202.8. Anal. Calcd for $C_{10}H_{11}N_3O$: C, 63.48; H, 5.86; N, 22.21. Found: C, 63.62; H, 6.03; N, 22.39.

General procedure for the preparation of α-alkyl α-benzotriazolyl ketones 4a-e, 7a-c, 10a-c and 13a-c

To a solution of α-benzotriazolyl ketones **2**, **6**, **9**, or **12** (3 mmol) and the corresponding alkyl halide **3a-g** (3.3 mmol) in CH_3CN (15 mL), 2 N aqueous NaOH solution (3 mL, 6 mmol) was added. The reaction mixture was stirred at room temperature for about 48 h. The reaction was monitored by TLC. The solvent was removed in *vacuo* and water was added to the residue. The mixture was extracted with ether. The combined ether extracts were dried over anhydrous $MgSO_4$. Ether was removed in *vacuo*. The residue was purified by column chromatography to afford an analytically pure sample.

2-(Benzotriazol-1-yl)-2-methylcyclohexanone (4a). yellow oil (54%); ^{1}H NMR ($CDCl_3$) δ 1.73 (s, 3H), 1.79–2.18 (m, 5H), 2.22–2.38 (m, 1H), 2.42–2.58 (m, 1H), 3.35–3.50 (m, 1H), 7.30–7.47 (m, 3H), 8.10 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 21.2, 23.0, 27.9, 39.0, 39.5, 70.0, 110.6, 120.2, 123.9, 127.5, 131.8, 146.6, 207.1. Anal. Calcd for $C_{13}H_{15}N_3O$: C, 68.10; H, 6.59; N, 18.33. Found: C, 67.82; H, 6.83; N, 18.43.

2-Allyl-2-(benzotriazol-2-yl)cyclohexanone (4b). colorless prisms (ethanol), mp 47–49 °C (68%); ^{1}H NMR ($CDCl_3$) δ 1.65–2.06 (m, 5H), 2.30–2.60 (m, 2H), 2.76 (dd, *J* = 14.1, 7.8 Hz, 1H), 2.98 (dd, *J* = 14.1, 6.6 Hz, 1H), 3.36 (dd, *J* = 14.7, 2.7 Hz, 1H), 4.84–4.95 (m, 2H), 5.48–5.64 (m, 1H), 7.38–7.48 (m, 2H), 7.84–8.00 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 21.0, 27.5, 36.7, 39.6, 42.0, 76.2, 118.2, 119.2, 126.5, 131.5, 144.0, 204.2. Anal. Calcd for $C_{15}H_{17}N_3O$: C, 70.56; H, 6.71; N, 16.46. Found: C, 70.34; H, 6.60; N, 16.48.

2-(Benzotriazol-2-yl)-2-benzylcyclohexanone (4c). white prisms (ethanol), mp 91–93 °C (67%); ^{1}H NMR ($CDCl_3$) δ 1.64–1.84 (m, 3H), 1.84–2.04 (m, 2H), 2.19–2.28 (m, 1H), 2.52 (d, *J* = 13.7 Hz, 1H), 3.17 (d, *J* = 13.7 Hz, 1H), 3.28 (d, *J* = 14.0 Hz, 1H), 3.61 (d, *J* = 14.0 Hz, 1H), 6.52 (d, *J* = 7.8 Hz, 2H), 7.00–7.14 (m, 3H), 7.36–7.41 (m, 2H), 7.84–7.87 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 20.9, 27.5, 36.4, 39.4, 43.5, 76.4, 118.2, 126.5, 126.7, 127.7, 129.9, 134.7, 143.9, 204.3. Anal. Calcd for $C_{19}H_{19}N_3O$: C, 74.73; H, 6.27; N, 13.76. Found: C, 74.40; H, 6.35; N, 13.97.

2-(Benzotriazol-2-yl)-2-(4-bromobenzyl)cyclohexanone (4d). white prisms (ethanol) mp 139–141 °C (84%); ^{1}H NMR ($CDCl_3$) δ 1.60–1.83 (m, 3H), 1.83–2.05 (m, 2H), 2.15–2.35 (m, 1H), 2.52 (d, *J* = 12.6 Hz, 1H), 3.10–3.30 (m, 2H), 3.56 (d, *J* = 14.4 Hz, 1H), 6.39 (d, *J* = 8.3 Hz, 2H), 7.14 (d, *J* = 8.3 Hz, 2H), 7.35–7.50 (m, 2H), 7.78–7.98 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 20.9, 27.6, 36.6, 39.4, 43.0, 76.2, 118.2, 121.0, 126.7, 130.9, 131.6, 133.8, 144.0, 204.2. Anal. Calcd for $C_{19}H_{18}BrN_3O$: C, 59.39; H, 4.72; N, 10.93. Found: C, 59.33; H, 4.72; N, 10.90.

2-(Benzotriazol-2-yl)-2[(*E*)-3-phenyl-2-propenyl]cyclohexanone (4e). white needles (ethanol), mp 138–140 °C (77%); ^{1}H NMR ($CDCl_3$) δ 1.68–1.88 (m, 3H), 1.91–2.13 (m, 2H), 2.39–2.62 (m, 2H), 2.89–2.97 (m, 1H), 3.04–3.12 (m 1H), 3.34–3.44 (m, 1H), 5.89–5.99 (m, 1H), 6.21 (d, *J* = 15.9 Hz, 1H), 7.15–7.26 (m, 5H), 7.36–7.43 (m, 2H), 7.86–7.93 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 21.0, 27.5, 36.8, 39.6, 41.3, 76.6, 118.2, 123.3, 126.1, 126.6, 127.2, 128.3, 134.0, 136.9, 144.1, 204.3. Anal. Calcd for $C_{21}H_{21}N_3O$: C, 76.11; H, 6.39; N, 12.68. Found: C, 75.94; H, 6.52; N, 12.65.

2-(Benzotriazol-2-yl)-2-methylcyclopentanone (7a). colorless prisms (ethanol), mp 81–82 °C (70%); ^{1}H NMR ($CDCl_3$) δ 1.95 (s, 3H), 2.00–2.22 (m, 2H), 2.30–2.39 (m, 1H), 2.48–2.59 (m, 1H), 2.67–2.79 (m, 1H), 2.98–3.08 (m, 1H), 7.36–7.39 (m, 2H), 7.85–7.88 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 18.3, 21.0, 36.3, 38.2, 72.9, 118.1, 126.4, 144.0, 211.7. Anal. Calcd for $C_{12}H_{13}N_3O$: C, 66.96; H, 6.09; N, 19.52. Found: C, 66.67; H, 6.18; N, 19.61.

2-Allyl-2-(benzotriazol-2-yl)cyclopentanone (7b). colorless oil (73%); ^{1}H NMR ($CDCl_3$) δ 2.00–2.21 (m, 2H), 2.43–2.55 (m, 2H), 2.64–2.75 (m, 1H), 2.93 (dd, *J* = 14.3, 7.5 Hz, 1H), 3.07–3.16 (m, 1H), 3.37 (dd, *J* = 14.3, 6.9 Hz, 1H), 5.17–5.27 (m, 2H), 5.73–5.87 (m, 1H), 7.40–7.44 (m, 2H), 7.90–7.93 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 18.2, 34.2, 36.6, 38.8, 75.3, 118.2, 120.3, 126.4, 131.3, 144.0, 210.5. Anal. Calcd for $C_{14}H_{15}N_3O$: C, 69.69; H, 6.27; N, 17.41. Found: C, 69.33; H, 6.38; N, 17.76.

2-(Benzotriazol-2-yl)-2-[(*E*)-3-phenyl-2-propenyl]cyclopentanone (7c). colorless prisms (ethanol), mp 106–107 °C (100%); ^{1}H NMR ($CDCl_3$) δ 1.97–2.15 (m, 2H), 2.39–2.56 (m, 2H), 2.60–2.72 (m, 1H), 3.01–3.08 (m, 2H), 3.49 (dd, *J* = 14.3, 6.8 Hz, 1H), 6.09–6.19 (m, 1H), 6.54 (d, *J* = 15.6 Hz, 1H), 7.17–7.32 (m, 5H), 7.33–7.43 (m, 2H), 7.82–7.93 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 18.3, 34.3, 36.6, 38.0, 75.6, 118.2, 122.7, 126.2, 126.5, 127.6, 128.5, 135.2, 136.7, 144.0, 210.7. Anal. Calcd for $C_{20}H_{19}N_3O$: C, 75.69; H, 6.03; N, 13.24. Found: C, 75.31; H, 6.17; N, 13.23.

3-(Benzotriazol-1-yl)-4-phenyl-2-butanone (10a). colorless oil (45%); ^{1}H NMR ($CDCl_3$) δ 2.03 (s, 3H), 3.55 (dd, *J* = 14.3, 10.2 Hz, 1H), 3.76 (dd, *J* = 14.3, 5.3 Hz, 1H), 5.60 (dd, *J* = 10.2, 5.3 Hz, 1H), 6.94–6.98 (m, 2H), 7.10–7.13 (m, 3H), 7.27–7.44 (m, 3H), 8.04–8.08 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 27.0, 35.8, 69.4, 109.2, 120.2, 124.2, 127.0, 127.9, 128.6, 128.7, 132.9, 135.9, 146.0, 202.1. Anal. Calcd for $C_{16}H_{15}N_3O$: C, 72.43; H, 5.70; N, 15.84. Found: C, 72.52; H, 5.86; N, 15.91.

3-(Benzotriazol-1-yl)-3-benzyl-4-phenyl-2-butanone (10a′). colorless needles (ethanol), mp 109–111 °C (11%); ^{1}H NMR ($CDCl_3$) δ 1.76 (s, 3H), 3.71–3.86 (m, 4H), 6.83 (d, *J* = 6.1 Hz, 4H), 7.10–7.18 (m, 7H), 7.38–7.41 (m, 2H), 8.12–8.15 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 26.9, 40.1, 76.9, 110.6, 120.6, 124.1, 127.3, 127.8, 128.3, 130.3, 132.9, 134.2, 146.6, 205.3. Anal. Calcd for $C_{23}H_{21}N_3O$: C, 77.72; H, 5.96; N, 11.82. Found: C, 77.77; H, 6.22; N, 11.81.

3-(Benzotriazol-1-yl)-4-(4-bromophenyl)-2-butanone (10b). colorless oil (44%); ^{1}H NMR ($CDCl_3$) δ 2.02 (s, 3H), 3.53 (dd, *J* = 14.3, 10.2 Hz, 1H), 3.70 (dd, *J* = 14.3, 5.0 Hz, 1H), 5.56 (dd, *J* = 10.2, 5.0 Hz, 1H), 6.84 (d, *J* = 7.3 Hz, 2H), 7.23 (d, *J* = 7.3 Hz, 2H), 7.28–7.49 (m, 3H), 8.07 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 26.9, 35.1, 69.0, 109.0, 120.4, 121.0, 124.4, 128.1, 130.4, 131.7, 132.8, 134.9, 146.0, 201.8. HRMS (FAB) Calcd for $C_{16}H_{15}BrN_3O$: 344.0399. Found: 344.0399.

3-(Benzotriazol-1-yl)-3-(4-bromobenzyl)-4-(4-bromophenyl)-2-butanone (10b′). white plates (ethanol), mp 141–143 °C (16%); ^{1}H NMR ($CDCl_3$) δ 1.74 (s, 3H), 3.65 (d, *J* = 14.7 Hz, 2H), 3.76 (d, *J* = 14.7 Hz, 2H), 6.68 (d, *J* = 8.4 Hz, 4H), 7.09 (d, *J* = 7.8 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 4H), 7.39–7.47 (m, 2H), 8.16 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 27.1, 39.7, 76.5, 110.3, 120.8, 121.7, 124.5, 128.1, 131.6, 131.9, 132.7, 133.0, 146.6, 205.2. Anal. Calcd for $C_{23}H_{19}Br_2N_3O$: C, 53.83; H, 3.73; N, 8.19. Found: C, 53.91; H, 3.47; N, 8.12.

3-(Benzotriazol-1-yl)-4-(4-methylphenyl)-2-butanone (10c). colorless oil (45%); ^{1}H NMR ($CDCl_3$) δ 2.03 (s, 3H), 2.20 (s, 3H), 3.52 (dd, *J* = 14.3, 9.9 Hz, 1H), 3.72 (dd, *J* = 14.3, 5.4 Hz, 1H), 5.59 (dd, *J* = 9.9, 5.4 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 2H), 6.93 (d, *J* = 8.0 Hz, 2H), 7.32–7.47 (m, 3H), 8.06 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 20.9, 27.1, 35.3, 69.6, 109.4, 120.2, 124.2, 127.9, 128.6, 129.3, 132.7, 132.9, 136.6, 146.1, 202.3. Anal. Calcd for $C_{17}H_{17}N_3O$: C, 73.10; H, 6.13; N, 15.04. Found: C, 72.74; H, 6.34; N, 15.39.

3-(Benzotriazol-1-yl)-3-(4-methylbenzyl)-4-(4-methylphenyl)-2-butanone (10c′). colorless needles (ethanol), mp 113–115 °C (11%); ^{1}H NMR ($CDCl_3$) δ 1.76 (s, 3H), 2.24 (s, 6H), 3.66–3.82 (m, 4H), 6.71 (d, *J* = 7.8 Hz, 4H), 6.94 (d, *J* = 7.8 Hz, 4H), 7.16 (d, *J* = 7.2 Hz, 1H), 7.37–7.40 (m, 2H), 8.11–8.15 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 20.9, 26.8, 39.3, 76.9, 110.6, 120.5, 124.0, 127.6, 128.9, 130.0, 131.0, 132.8, 136.8, 146.5, 205.4. HRMS (FAB) Calcd for $C_{25}H_{26}N_3O$: 384.2076. Found: 384.2074.

4-(Benzotriazol-1-yl)-6-hepten-3-one (13a). yellow oil (57%); ^{1}H NMR ($CDCl_3$) δ 0.98 (t, *J* = 7.2 Hz, 3H), 2.20–2.40 (m, 2H), 3.03–3.22 (m, 2H), 4.94–5.05 (m, 2H), 5.51 (dd, *J* = 9.6, 6.0 Hz, 1H), 5.57–5.71 (m, 1H), 7.38–7.54 (m, 3H), 8.10 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 7.2, 32.7, 33.8, 67.1, 109.5, 119.3, 120.3, 124.3, 127.9, 131.9, 132.7, 146.2, 205.1. Anal. Calcd for $C_{13}H_{15}N_3O$: C, 68.10; H, 6.59; N, 18.33. Found: C, 67.85; H, 6.80; N, 18.71.

2-(Benzotriazol-1-yl)-1-(4-bromophenyl)-3-pentanone (13b). colorless prisms (ethanol), mp 84–86 °C (42%); ^{1}H NMR ($CDCl_3$) δ 0.97 (t, *J* = 7.1 Hz, 3H), 2.13–2.38 (m, 2H), 3.53 (dd, *J* = 14.5, 10.1 Hz, 1H), 3.71 (dd, *J* = 14.5, 5.4 Hz, 1H), 5.60 (dd, *J* = 10.1, 5.4 Hz, 1H), 6.85 (d, *J* = 8.3 Hz, 2H), 7.23 (d, *J* = 8.3 Hz, 2H), 7.33–7.41 (m, 2H), 7.46 (t, *J* = 7.5 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 7.2, 32.9, 35.2, 68.4, 109.1, 120.3, 121.0, 124.3, 128.1, 130.5, 131.7, 132.8, 135.0, 146.0, 204.8. Anal. Calcd for $C_{17}H_{16}BrN_3O$: C, 57.00; H, 4.50; N, 11.73. Found: C, 57.00; H, 4.44; N, 11.55.

2-(Benzotriazol-1-yl)-2-(4-bromobenzyl)-1-(4-bromophenyl)-3-pentanone (13b′). yellow oil (7%); ^{1}H NMR ($CDCl_3$) δ 0.83 (t, *J* = 7.1 Hz, 3H), 1.96 (q, *J* = 7.1 Hz, 2H), 3.64 (d, *J* = 14.7 Hz, 2H), 3.80 (d, *J* = 14.7 Hz, 2H), 6.65 (d, *J* = 8.6 Hz, 4H), 7.11–7.15 (m, 1H), 7.27 (d, *J* = 8.6 Hz, 4H), 7.40–7.50 (m, 2H), 8.15–8.18 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 7.4, 32.4, 39.8, 76.3, 110.5, 120.9, 121.6, 124.4, 128.1, 131.5, 131.9, 132.7, 133.1, 146.7, 208.0. Anal. Calcd for $C_{24}H_{21}Br_2N_3O$: C, 54.67; H, 4.01; N, 7.97. Found: C, 55.00; H, 4.57; N, 7.57.

2-(Benzotriazol-1-yl)-1-(3-methylphenyl)-3-pentanone (13c). white prisms (ethanol), mp 81–83 °C (50%); ^{1}H NMR ($CDCl_3$) δ 0.97 (t, *J* = 7.2 Hz, 3H), 2.16 (s, 3H), 2.19–2.42 (m, 2H), 3.50 (dd, *J* = 14.0, 9.9 Hz, 1H), 3.72 (dd, *J* = 14.0, 5.4 Hz, 1H), 5.62 (dd, *J* = 9.9, 5.4 Hz, 1H), 6.77 (s, 2H), 6.90–6.93 (m, 1H), 7.01 (t, *J* = 7.8 Hz, 1H), 7.33–7.46 (m, 3H), 8.05 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 7.3, 21.1, 33.1, 35.9, 68.9, 109.5, 120.2, 124.2, 125.7,127.7, 127.8, 128.5, 129.5, 132.9, 135.9, 138.2, 146.1, 205.1. Anal. Calcd for $C_{18}H_{19}N_3O$: C, 73.69; H, 6.53; N, 14.32. Found: C, 73.56; H, 6.66; N, 14.39.

2-(Benzotriazol-1-yl)-2-(3-methylbenzyl)-1-(3-methylphenyl)-3-pentanone (13c′). colorless oil (5%); ^{1}H NMR ($CDCl_3$) δ 0.83 (t, *J* = 7.1 Hz, 3H), 2.03 (q, *J* = 7.1 Hz, 2H), 2.17 (s, 6H), 3.69 (d, *J* = 14.7 Hz, 2H), 3.82 (d, *J* = 14.7 Hz, 2H), 6.56 (s, 2H), 6.62 (d, *J* = 7.5 Hz, 2H), 6.96–7.06 (m, 4H), 7.13–7.16 (m, 1H), 7.38–7.42 (m, 2H), 8.13–8.16 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 7.3, 21.2, 32.3, 40.1, 76.8, 110.8, 120.5, 124.1, 127.1, 127.6, 128.0, 128.1, 131.2, 133.0, 134.2, 137.8, 146.6, 208.1. Anal. Calcd for $C_{26}H_{27}N_3O$: C, 78.56; H, 6.85; N, 10.57. Found: C, 78.25; H, 7.11; N, 10.53.

General procedure for the preparation of α,α-dialkylketones 14, 15

To a solution of naphthalene (0.6 g, 4.68 mmol) and lithium metal (26 mg, 3.65 mmol) in small pieces was added dry THF (20 mL). The reaction mixture was stirred at room temperature under argon atmosphere until lithium metal completely dissolved (~19.5 h). The resulting dark green solution of lithium naphthalenide (LN) was then cooled to –40 °C by acetonitrile–dry ice bath for 1 h, followed by addition of a solution of the appropriate α-benzotriazolyl ketone (0.73 mmol) in THF (5 mL) dropwise over 5 min. The resulting mixture was stirred at –40 °C for 4 h. An appropriate electrophile (21.9 or 7.3 mmol) was then added and the reaction mixture was further stirred at –40 °C for 6 h. Saturated aqueous ammonium chloride was added into the

reaction mixture, which was then extracted with ether. The solvent was removed in *vacuo* and the residue was purified by column chromatography to afford the pure sample.

2-Benzyl-2-methyl-cyclohexanone (14). yellow oil,[11] (51%); ^{1}H NMR ($CDCl_3$) δ 1.09 (s, 3H), 1.55–1.64 (m, 1H), 1.72–1.96 (m, 5H), 2.47–2.64 (m, 2H), 2.94 (s, 2H), 7.14–7.18 (m, 2H), 7.23–7.35 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 21.1, 22.7, 27.2, 38.0, 38.8, 43.0, 49.2, 126.2, 127.9, 130.5, 137.6, 215.4.

4-(3-Methylbenzyl)-6-hepten-3-one (15). yellow oil (56%); ^{1}H NMR ($CDCl_3$) δ 0.90 (t, J = 7.2 Hz, 3H), 2.04–2.44 (m, 7H), 2.61–2.70 (m, 1H), 2.78–2.92 (m, 2H), 5.02 (d, J = 9.3 Hz, 1H), 5.03 (d, J = 18.0 Hz, 1H), 5.64–5.78 (m, 1H), 6.92 (d, J = 8.1 Hz, 1H), 6.93 (s, 1H), 7.00 (d, J = 7.2 Hz, 1H), 7.15 (t, overlap of dd, J = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 7.2, 21.3, 36.1, 37.1, 37.8, 53.4, 117.0, 125.8, 127.0, 128.3, 129.6, 135.4, 138.0, 139.5, 214.2. HRMS (FAB) Calcd for $C_{15}H_{21}O$ (M+1): 217.1592. Found: 217.1592.

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