# Synthesis of β-Alkoxy Ketones and α′-Functionalized β-Alkoxy Ketones Utilizing Benzotriazole-Stabilized Acyl Anion Synthons

Alan R. Katritzky,* Daming Feng, and Ming Qi

*Center for Heterocyclic Compounds, Department of Chemistry, University of Florida, Gainesville, Florida 32611-7200*

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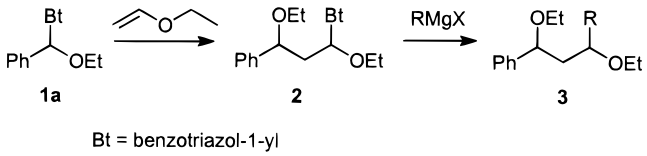
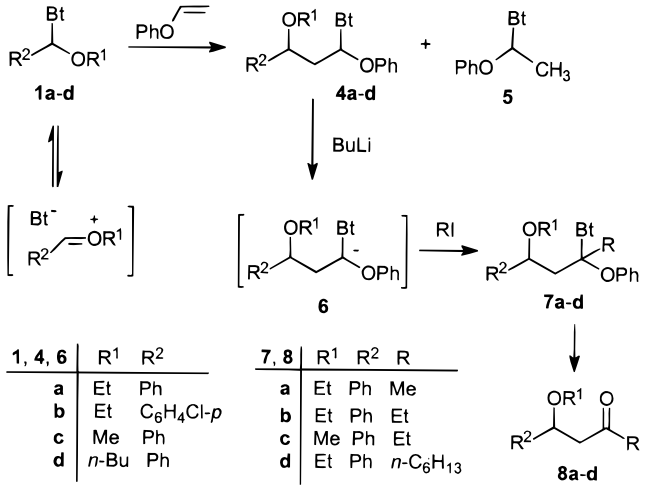
1-(α-Alkoxyalkyl)benzotriazoles **1a**−**d** add to phenyl vinyl ether to form key intermediates **4a**−**d**, which readily undergo lithiation and subsequent trapping by a variety of electrophiles to give the expected substituted derivatives **7a**−**d**, **9a**−**c**, **11**, **13**, **15**, and **18** in high yields. Subsequent hydrolysis of these compounds provides a novel high-yield acyl anion synthon approach for the synthesis of β-alkoxy ketones **8** or α′-functionalized β-alkoxy ketones **10**, **12**, **14**, **16**, and **19** by short procedures from readily available starting materials.

Previous work in our group has demonstrated that benzotriazole is a versatile and reliable synthetic auxiliary for the synthesis of complex organic compounds, including classes difficult to prepare via other methods.[1] For example, *N*-(ethoxybenzyl)benzotriazole (**1a**) adds to ethyl vinyl ether to form intermediate **2,** which undergoes subsequent reactions to give 1,3-diethers **3** (Scheme 1).[2] However, while *N*-(ethoxymethyl)benzotriazoles[3a−c] and *N*-(phenoxymethyl)-benzotriazoles[3d] are convenient, functionalized acyl anion synthon equivalents, as expected,[3d] **2** cannot be further lithiated at the methine group. We now find that **1a**−**d** add to phenyl vinyl ether to form intermediates **4a**−**d** (Scheme 2), which can now be readily lithiated and reacted with a wide range of electrophiles. Subsequent hydrolysis gives β-ethoxy ketones and α′-functionalized β-alkoxy ketones.

**Scheme 1**




**Scheme 2**




| 1, 4, 6 | $R^1$ | $R^2$ |
|---|---|---|
| a | Et | Ph |
| b | Et | $C_6H_4Cl$-*p* |
| c | Me | Ph |
| d | *n*-Bu | Ph |

| 7, 8 | $R^1$ | $R^2$ | R |
|---|---|---|---|
| a | Et | Ph | Me |
| b | Et | Ph | Et |
| c | Me | Ph | Et |
| d | Et | Ph | $n$-$C_6H_{13}$ |

## Results

**Addition of 1-(1-Alkoxy-1-arylmethyl)benzotriazoles (1) to Phenyl Vinyl Ether.** 1-(1-Alkoxy-1-arylmethyl)benzotriazoles **1a**−**d** were prepared in good to excellent yields from the reaction of aromatic aldehydes and benzotriazole with the corresponding alcohol or (in three cases) an ortho-ester (triethyl orthoformate for **1a**,**b**; trimethyl orthoformate for **1c**) in THF with a few drops of concentrated sulfuric acid as catalyst, according to our previous report.[4]

Treatment of compound **1a** with 1.2 equiv of phenyl vinyl ether at 50−60 °C for 12 h, without either solvent or catalyst, gave [1-(benzotriazol-1-yl)-3-ethoxy-3-phenyl]-propyl phenyl ether (**4a**), as a mixture of two diastereomers (ratio 1:1), in 74% yield (Scheme 2) and 10% of byproduct [1-(benzotriazol-1-yl)]ethyl phenyl ether (**5**). When the reaction was carried out with a catalytic amount of *p*-toluenesulfonic acid hydrate (PTS), only 43% yield of product **4a** was obtained, together with 40% of byproduct **5**. [1-(Benzotriazol-1-yl)-3-ethoxy-3-(*p*-chlorophenyl)]propyl phenyl ether (**4b**) was prepared in a similar manner in the absence of PTS from **1b** in 71% yield, with a very small amount of byproduct **5**. No reaction was observed between compounds **1c**,**d** and phenyl vinyl ether in the absence of PTS, even at 80−90 °C for an extended time (48 h). However, with small amounts of PTS (∼5%), compounds **1c**,**d** added to phenyl vinyl ether at 60−70 °C to afford **4c**,**d** in 60% and 67% yields, respectively; byproduct **5** was also formed in about 10% yield in both cases. The more severe reaction conditions needed for the addition of compounds **1c**,**d** to vinyl ether correspond to their higher stabilities and longer shelf life compared to **1a**,**b**, which need refrigeration for long-term storage.

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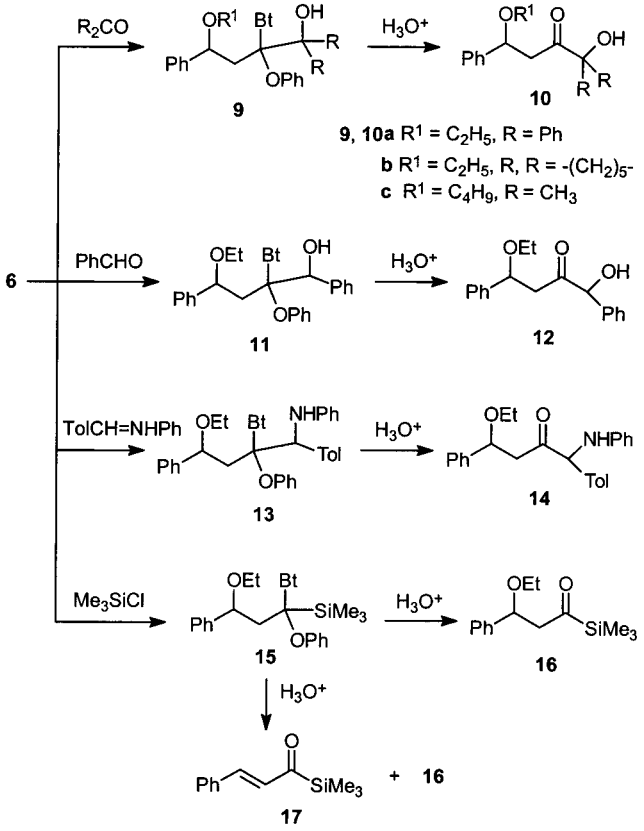
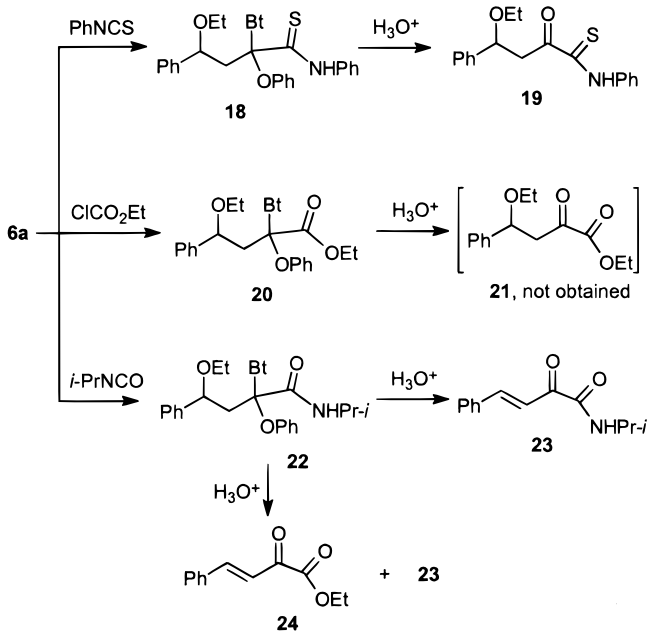
**Scheme 3**




**Scheme 4**




**Preparation of *β*-Alkoxy Ketones.** As expected,[3d] 1-(benzotriazol-1-yl)-3-alkoxy-3-arylpropyl phenyl ethers **4a**,**c** can easily be lithiated site-specifically at the position α to both the benzotriazolyl and phenoxy groups to form intermediates **6** (Scheme 2). Intermediates **6** can be trapped with 1.0 equiv of methyl or ethyl iodide at −78 °C for 10 min to give products **7a**−**c** in 82−96% yields. Subsequent hydrolysis of **7a**−**c** in dilute HCl in EtOH−$H_2O$ (1:1) at room temperature for 5−7 h produced *β*-alkoxy-substituted ketones **8a**−**c** in 76−96% yields. Treatment of **4a** with 1.0 equiv of *n*-BuLi at −78 °C and then reaction with 1.0 equiv of 1-iodohexane at −78 °C for 5 h, followed by warming to room temperature for 1 h, gave product **7d** in 66% yields. If 1-iodohexane was replaced by 1-bromohexane, only 15% of **7d** was obtained, regardless of whether 1-bromohexane was added before *n*-BuLi or after. Further hydrolysis of **7d** under the same conditions for 12 h produced *β*-ethoxy-substituted ketones **8d** in 93% yield.

**Preparation of α′-Functionalized *β*-Alkoxy Ketones.** Intermediates **6a**,**d** can also react with ketones, an aldehyde, *N*-[(4-methyl)benzylidene]aniline, and chlorotrimethylsilane to give compounds **9a**−**c**, **11**, **13,** and **15,** respectively (Scheme 3), all of which were isolated by column chromatography. In the carbonyl compound reactions, the aromatic ketone or aldehyde gave excellent yields of product **9a** or **11**; however, when aliphatic ketones were used as electrophiles, 50% of starting materials **4a** or **4d** was recovered. The yields reported of **9b**,**c** are based on the consumed starting materials.

As mentioned above, compounds **7a**−**d** can be hydrolyzed at room temperature, and compounds **9c** and **15** under similar conditions gave **10c** and *β*-alkoxyacylsilane **16**. However, some substituted analogues need elevated temperatures. Thus, compounds **9a**,**b**, **11**, and **13** were hydrolyzed at 50−60 °C to provide the corresponding α′-hydroxy-*β*-alkoxy or α′-amino-*β*-alkoxy ketones **10a**,**b**, **12**, and **14**. When **15** was hydrolyzed at 50−60 °C, cinnamoyltrimethylsilane (**17**) was obtained in 44% yield, together with 11% of **16**.

To introduce further unsaturation into the α′-position of the ketone, an isothiocyanate, an isocyanate, or ethyl chloroformate was reacted with carbanion **6a** to give products **18**, **20**, and **22**, respectively, in 90−95% yields (Scheme 4). Compounds **18**, **20**, and **22** have low solubility in EtOH−$H_2O$ (1:1) at reflux; they are difficult to hydrolyze with dilute HCl in EtOH−$H_2O$ (1:1). However, the use of HCl in $CH_3CN$−$H_2O$ (1:1) solution hydrolyzed compound **18** smoothly to give *N*-phenyl 4-phenyl-4-ethoxy-2-oxobutyrothioamide (**19**) in 95% yield. In contrast, no desired α-keto ester **21** was obtained from compound **20**. *β*,*γ*-Unsaturated α-keto amide **23** was the only product from the hydrolysis (in $CH_3CN$−$H_2O$) of intermediate **22**, whereas both **23** and *β*,*γ*-unsaturated α-keto ester **24** were formed when hydrolysis of **22** was carried out in EtOH−$H_2O$. Compound **24** was formed from the esterification of the amide **23** in ethanol.

## Discussion

*β*-Alkoxy ketone units frequently occur in antibiotics, such as lasalocid A.[5] They are usually prepared by one of two methods: (i) ether exchange of *β*-alkoxy ketones[6] or (ii) the reaction of silyl enol ethers with acetals[7] or

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α-chloro ethers.[8] These two and other methods[9] all involved the formation for two components, i.e., O + C−C−C(:O)−C or O−C + C−C(:O)−C. In our new approach, the three components O−C + C−C(:O) + C are combined using umpolung and a masked acyl anion equivalent.

There are few previous reports of α′-functionalized β-alkoxy ketones of the type presently prepared. Isolated examples of the synthesis of α′-hydroxy-β-alkoxy ketones from the double hydroxylation of β-alkoxy vinyl bromide,[10] the oxidation of β-alkoxy trimethylsilyl enol ether,[11] and other routes[12] have been reported. α′-Amino-β-alkoxy ketones were prepared from α′-bromo-β-alkoxy ketones[13] and α′,β′-epoxy-β-alkoxy ketones,[14] but no general method has been published. The silyl enol ethers of acylsilanes [RCH═C(SiMe$_3$)OSiMe$_3$] were reacted effectively with acetals in the presence of BF$_3$·Et$_2$O to give β-alkoxyacylsilanes;[15] however, the starting material is difficult to prepare. β,γ-Unsaturated α-keto amides have been synthesized from palladium-catalyzed double-carbonylations of alkenyl halides,[16] but only secondary amides were reported.

In comparison to these aforementioned routes, our new approach provides a general and versatile method to synthesize β-alkoxy ketones with or without an α′-functional group.

## Experimental Section

**General Comments.** Melting points were determined on a hot stage apparatus without correction. $^1$H (300 MHz) and $^{13}$C NMR (75 MHz) spectra were recorded in CDCl$_3$ with TMS or CDCl$_3$, respectively, as the internal reference. Column chromatography was carried out on MCB silica gel (230−400 mesh). Tetrahydrofuran (THF) was freshly distilled from sodium−benzophenone. Lithiation reactions were carried out under the protection of dry nitrogen.

The preparation and characterization of 1-(1-alkoxybenzyl)-benzotriazoles **1a**−**c** have been reported by this laboratory.[4a−c]

**1-[(1-Butoxy-1-phenyl)methyl]benzotriazole (1d)** was prepared from benzotriazole, benzaldehyde, and *n*-butanol by the method previously reported,[4d] in 54% yield: colorless oil; $^1$H NMR δ 0.84 (t, 3 H, *J* = 7.3 Hz), 1.25−1.47 (m, 2 H), 1.50−1.68 (m, 2 H), 3.31−3.44 (m, 1 H), 3.65−3.77 (m, 1 H), 7.28 (s, 1 H), 7.24−7.50 (m, 8 H), 8.01−8.12 (m, 1 H); $^{13}$C NMR δ 13.6, 19.1, 31.1, 69.0, 89.6, 111.5, 119.7, 124.0, 125.8, 127.2, 128.4, 128.8, 130.9, 136.3, 146.9. Anal. Calcd for C$_{17}$H$_{19}$N$_3$O: C, 72.57; H, 6.81; N, 14.93. Found: C, 72.73; H, 6.95; N, 15.15.

**[1-(Benzotriazol-1-yl)-3-ethoxy-3-phenyl]propyl Phenyl Ether (4a)**. 1-(1-Ethoxybenzyl)benzotriazole (**1a**, 2.53 g, 10 mmol) was mixed with phenyl vinyl ether (1.2 equiv) and the mixture was stirred at 60−70 °C for 12 h. The reaction mixture was cooled, extracted with ether, and washed with water. The organic extracts were dried (MgSO$_4$) and concentrated to give a residue which was purified by column chromatography on silica gel (hexane/ethyl acetate, 13:1) to give **4a**, as two separable diastereomers. Isomer **I**: 33% yield; colorless oil; $^1$H NMR δ 1.15 (t, 3 H, *J* = 7.0 Hz), 2.71−2.82 (m, 1 H), 2.88−3.02 (m, 1 H), 3.10−3.87 (m, 2 H), 3.89 (dd, 1 H, *J* = 9.6 and 4.3 Hz), 6.83−7.00 (m, 3 H), 7.02−7.50 (m, 10 H), 7.76 (d, 1 H, *J* = 8.2 Hz), 8.04 (d, 1H *J* = 8.3 Hz); $^{13}$C NMR δ 15.2, 43.0, 64.4, 77.4, 85.6, 110.9, 116.5, 120.3, 122.9, 124.3, 126.4, 127.8, 128.0, 128.6, 129.6, 131.5, 140.9, 146.6, 156.0. Anal. Calcd for C$_{23}$H$_{23}$N$_3$O$_2$: C, 73.97; H, 6.21; N,11.25. Found: C, 73.62; H, 6.43; N, 11.10.

Isomer **II**: 41% yield; white solid; mp 76−78 °C; $^1$H NMR δ 1.10 (t, 3 H, *J* = 7.0 Hz), 2.46−2.61 (m, 1 H), 2.80−2.95 (m, 1 H), 3.15−3.46 (m, 2 H), 4.68 (dd, 1 H, *J* = 10.3, 3.2 Hz), 6.86−7.06 (m, 3 H), 7.10−7.51 (m, 10 H), 7.72 (d, 1 H, *J* = 8.2 Hz), 8.01 (d, 1 H, *J* = 8.2 Hz); $^{13}$C NMR δ 15.1, 43.5, 64.2, 77.4, 85.7, 110.9, 116.8, 120.0, 123.1, 124.1, 126.4, 127.5, 127.9, 128.6, 129.6, 131.5, 141.3, 146.6, 156.4. Anal. Calcd for C$_{23}$H$_{23}$N$_3$O$_2$: C, 73.97; H, 6.21; N, 11.25. Found: C, 73.72; H, 6.60; N, 10.77.

**1-(Benzotriazol-1-yl)ethyl phenyl ether (5)** was obtained as a byproduct from the reaction of compound **1a** and phenyl vinyl ether, in 10% yield: white solid; mp 60−62 °C; $^1$H NMR δ 2.00 (d, 3 H, *J* = 6.3 Hz), 6.88 (t, 1 H, *J* = 7.4 Hz), 6.95 (d, 2 H, *J* = 8.2 Hz), 7.02 (q, 1 H, *J* = 6.3 Hz), 7.13 (t, 2 H, *J* = 7.5 Hz), 7.27 (t, 1 H, *J* = 7.4 Hz), 7.40 (t, 1 H, *J* = 7.2 Hz), 7.78 (d, 1 H, *J* = 8.4 Hz), 7.99 (d, 1 H, *J* = 8.2 Hz); $^{13}$C NMR δ 20.9, 84.4, 110.8, 116.1, 119.8, 122.7, 124.0, 127.4, 129.4, 130.8, 146.4, 155.6. Anal. Calcd for C$_{14}$H$_{13}$N$_3$O: C, 70.28; H, 5.48; N,17.56. Found: C, 70.32; H, 5.49; N, 17.78.

**[2-(Benzotriazol-1-yl)-4-phenyl-4-ethoxy]-2-butyl Phenyl Ether (7a)**. To a solution of [1-(benzotriazol-1-yl)-3-ethoxy-3-phenyl]propyl phenyl ether (**4a**, 1.12 g, 3 mmol) in dry THF (50 mL) at −78 °C was added *n*-BuLi (1.6 M, 2.3 mL), then the solution was stirred at this temperature for 5−10 min, and methyl iodide (0.42 g, 3 mmol) was added. After stirring at −78 °C for 10−30 min, the solution was quenched by water (50 mL), extracted with ether, and washed with water. The organic extracts were dried (MgSO$_4$) and concentrated to give a residue which was purified by column chromatography on silica gel (hexane/ethyl acetate, 15:1) to give the pure product (referred to as procedure A later in this paper), as two separable diastereomers (ratio 1:1), in a total yield of 96%. Isomer **I**: colorless oil; $^1$H NMR δ 0.84 (t, 3 H, *J* = 7.0 Hz), 2.28 (s, 3 H), 2.66 (dd, 1 H, *J* = 14.8, 1.9 Hz), 2.90 (dd, 1 H, *J* = 14.8, 9.1 Hz), 2.97−3.23 (m, 2 H), 4.58 (dd, 1 H, *J* = 9.1, 1.9 Hz), 6.97 (d, 2 H, *J* = 7.1 Hz), 6.92−7.13 (m, 3 H), 7.14−7.53 (m, 7 H), 7.97 (d, 1 H, *J* = 8.3 Hz), 8.09 (d, 1 H, *J* = 8.1 Hz); $^{13}$C NMR δ 14.9, 23.5, 49.3, 63.9, 77.9, 95.1, 113.1, 119.8, 120.8, 124.0, 126.2, 127.4, 127.6, 128.5, 129.3, 129.4, 132.6, 142.3, 146.9, 153.6. Anal. Calcd for C$_{24}$H$_{25}$N$_3$O$_2$: C, 74.39; H, 6.50; N,10.84. Found: C, 74.07; H, 6.81; N, 10.66.

Isomer **II**: white solid; mp 79−81 °C; $^1$H NMR δ 1.08 (t, 3 H, *J* = 7.1 Hz), 2.30 (s, 3 H), 2.75−2.95 (m, 2 H), 2.97−3.30 (m, 2 H), 3.72 (dd, 1 H, *J* = 8.3, 3.6 Hz), 6.41 (d, 2 H, *J* = 7.8 Hz), 6.85−7.29 (m, 8 H), 7.37−7.53 (m, 2 H), 7.94 (d, 1 H, *J* = 7.8 Hz), 8.12 (d, 1 H, *J* = 7.7 Hz); $^{13}$C NMR δ 15.1, 23.6, 49.9, 64.2, 77.6, 95.5, 113.0, 115.5, 120.0, 121.3, 124.2, 126.0, 127.5, 127.7, 128.4, 129.4, 132.4, 141.9, 146.9, 153.4. Anal. Calcd for C$_{24}$H$_{25}$N$_3$O$_2$: C, 74.39; H, 6.50; N, 10.84. Found: C, 74.51; H, 6.68; N, 10.82.

**General Procedure for the Preparation of 8a−d**. Compounds **7** (1−2 mmol) were dissolved in a mixture of ethanol (25 mL), water (25 mL), and concentrated HCl (1 mL) and stirred at rt for 12 h. The resulting solution was extracted with ether and washed with saturated aqueous Na$_2$CO$_3$ solution. The organic extracts were dried (MgSO$_4$) and concentrated to give a residue which was separated by column chromatography (hexane/ethyl acetate 15:1) (referred to as procedure B later in this paper).

**1-Phenyl-1-ethoxy-3-butanone (8a)**: 76% yield; colorless oil; $^1$H NMR δ 1.14 (t, 3 H, *J* = 7.1 Hz), 2.16 (s, 3 H), 2.60 (dd, 1 H, *J* = 15.7, 4.2 Hz), 2.97 (dd, 1 H, *J* = 15.7, 9.0 Hz), 3.25−3.44 (m, 2 H), 4.75 (dd, 1 H, *J* = 9.1, 4.4 Hz), 7.22−7.45 (m, 5 H); $^{13}$C NMR δ 15.1, 31.0, 52.1, 64.3, 77.8, 126.4, 127.7, 128.5,

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141.8, 206.6. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.91; H, 8.54.

**1,1,4-Triphenyl-2-(benzotriazol-1-yl)-2-phenoxy-4-ethoxybutanol (9a)** was obtained from the reaction of **4a** and benzophenone (procedure A) in 90% yield: white microcrystals; mp 173−176 °C; $^1$H NMR (two diastereomers, 1:1) $\delta$ 1.01 (t, $J$ = 6.9 Hz) and 1.15 (t, $J$ = 7.2 Hz) (total 3 H), 2.26−2.37 (m) and 2.89−3.51 (m) (total 4 H), 4.05 (dd, $J$ = 17.1, 9.9 Hz) and 4.56 (d, $J$ = 9.6 Hz) (total 1 H), 5.91 (br s) and 6.18 (d, $J$ = 7.8 Hz) (total 1 H), 6.45−7.44 (m, 21 H), 7.84 (d, $J$ = 7.8 Hz) and 7.93 (d, $J$ = 7.8 Hz) (total 1 H), 8.10 (d, 2 H, $J$ = 7.2 Hz); $^{13}$C NMR $\delta$ 14.7 and 14.9, 43.2 and 44.0, 63.4 and 64.2, 76.3 and 79.3, 81.9 and 82.5, 100.5 and 102.4, 113.8, 118.5, 118.6, 118.9, 119.4, 123.0, 123.1, 123.5, 125.6, 126.4, 126.6, 126.9, 127.0, 127.1, 127.2, 127.3, 127.7, 127.9, 128.0, 128.4, 128.5, 128.7, 129.1, 129.6, 129.8, 134.3, 141.3, 141.5, 141.7, 142.6, 144.1, 145.1, 153.2, 153.9. Anal. Calcd for $C_{36}H_{33}N_3O_3$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.54; H, 6.37; N, 7.41.

**1,1,4-Triphenyl-1-hydroxy-4-ethoxy-2-butanone (10a)** was obtained from the hydrolysis of **9a** (procedure B) in 89% yield: colorless oil; $^1$H NMR $\delta$ 1.07 (t, 3 H, $J$ = 7.2 Hz), 2.52 (dd, 1 H, $J$ = 15.6, 4.2 Hz), 3.17−3.46 (m, 3 H), 4.77 (dd, 1 H, $J$ = 9.3, 4.2 Hz), 5.29 (s, 1 H), 7.07−7.38 (m, 13 H), 7.40−7.52 (m, 2 H); $^{13}$C NMR $\delta$ 14.9, 47.1, 64.3, 78.2, 85.0, 126.3, 127.5, 127.6, 127.7, 127.9, 128.1, 128.3, 128.7, 128.8, 140.7, 141.3, 142.1, 208.7. Anal. Calcd for $C_{24}H_{24}O_3$: C, 79.97; H, 6.71. Found: C, 79.91; H, 7.08.

**1,4-Diphenyl-2-(benzotriazol-1-yl)-2-phenoxyl-4-ethoxybutanol (11)** was obtained from the reaction of **4a** and benzaldehyde (procedure A). A single diastereomer was isolated by recrystallization from diethyl ether/hexanes in 83% yield: white microcrystals; mp 204−206 °C; $^1$H NMR $\delta$ 1.28 (t, 3 H, $J$ = 7.2 Hz), 3.20 (d, 1 H, $J$ = 16.5 Hz), 3.41 (q, 2 H, $J$ = 7.2 Hz), 3.59 (dd, 1 H, $J$ = 16.5, 9.9 Hz), 4.65 (d, 1 H, $J$ = 9.9 Hz), 5.59 (s, 1 H, OH), 5.64 (s, 1 H), 6.66 (d, 2 H, $J$ = 8.1 Hz), 6.70−6.80 (m, 2 H), 6.86−7.08 (m, 8 H), 7.09−7.24 (m, 7 H), 7.90 (d, 1 H, $J$ = 8.4 Hz); $^{13}$C NMR $\delta$ 14.9, 44.1, 64.5, 76.5, 80.4, 97.5, 113.5, 118.6, 118.9, 123.3, 123.5, 125.6, 127.2, 127.4, 127.8, 128.0, 128.1, 128.5, 129.9, 134.1, 137.1, 141.3, 145.4, 154.3; HRMS (CI) $m/z$ calcd for $C_{30}H_{29}N_3O_3$ + H 480.2287, found 480.2283.

**1,4-Diphenyl-1-hydroxy-4-ethoxy-2-butanone (12)** was obtained from the hydrolysis of **11** (procedure B) in 54% yield: green microcrystals; mp 40−42 °C; $^1$H NMR (single isomer) $\delta$ 1.10 (t, 3 H, $J$ = 7.2 Hz), 2.61 (dd, 1 H, $J$ = 15.4, 5.8 Hz), 2.96 (dd, 1 H, $J$ = 15.4, 8.0 Hz), 3.21−3.40 (m, 2 H), 4.42 (d, 1 H, $J$ = 3.6, Hz), 4.71 (dd, 1 H, $J$ = 7.9, 6.1 Hz), 4.90 (d, 1 H, $J$ = 3.3 Hz), 7.15−7.45 (m, 10 H); $^{13}$C NMR $\delta$ 15.1, 46.6, 64.3, 77.8, 80.0, 126.4, 127.4, 128.0, 128.5, 128.6, 128.8, 137.4, 140.9, 207.3. Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.32; H, 7.35.

**1-[1-(*p*-Tolyl)-2-(benzotriazol-1-yl)-2-phenoxy-4-phenyl-4-ethoxy]butylaniline (13)** was obtained as one predominant isomer from the reaction of **4a** and *N*-[(4-methyl)-benzylidene]aniline (procedure A) in 92% yield: yellow microcrystals; mp 98−101 °C; $^1$H NMR $\delta$ 1.16 (t, 3 H, $J$ = 7.2 Hz), 2.15 (s, 3 H), 3.20 (q, 2 H, $J$ = 7.0 Hz), 3.29 (dd, 1 H, $J$ = 15.9, 9.3 Hz), 3.69 (dd, 1 H, $J$ = 15.6, 3.6 Hz), 4.77 (dd, 1 H, $J$ = 9.3, 3.6 Hz), 5.12 (d, 1 H, $J$ = 8.1 Hz), 5.32 (d, 1 H, $J$ = 8.4 Hz), 6.48 (d, 2 H, $J$ = 8.4 Hz), 6.53−6.80 (m, 7 H), 6.81−7.43 (m, 12 H), 7.76 (d, $J$ = 7.8 Hz), 7.95 (d, $J$ = 8.4 Hz) (total 2 H); $^{13}$C NMR $\delta$ 15.4, 20.9, 39.9, 62.7, 64.0, 78.2, 98.5, 113.4, 113.8, 117.7, 118.1, 119.0, 119.7, 123.0, 123.7, 126.5, 127.2, 127.7, 128.3, 128.4, 128.7, 129.1, 133.1, 137.6, 141.8, 146.0, 154.1. Anal. Calcd for $C_{37}H_{36}N_4O_2$: C, 78.14; H, 6.38; N, 9.85. Found: C, 78.42; H, 6.37; N, 9.70.

**1-(*p*-Tolyl)-1-phenylamino-4-phenyl-4-ethoxy-2-butanone (14)** was obtained from the hydrolysis of **13** (procedure B) in 64% yield: green oil; $^1$H NMR (two diastereomers, about 1:1) $\delta$ 1.11 (t, 3 H, $J$ = 7.2 Hz), 2.26 (s) and 2.30 (s) (total 3 H), 2.32−3.05 (m, 2 H), 3.28−3.44 (m, 2 H), 4.76 (dd, 1 H, $J$ = 8.7, 4.2 Hz), 5.07 (s, 1 H), 5.37 (s, 1 H), 6.45−6.66 (m, 3 H), 7.01−7.95 (m, 11 H); $^{13}$C NMR $\delta$ 15.1, 21.0 and 21.8, 47.8, 64.1 and 64.4, 67.7 and 68.4, 78.1, 113.3, 117.4, 122.5, 126.2, 126.5, 127.6, 127.8, 128.0, 128.4, 128.5, 128.8, 129.0, 129.6, 129.8, 130.2, 131.4, 134.1, 138.0, 141.2, 146.1, 148.6, 203.8 and 204.3. Anal. Calcd for $C_{25}H_{27}NO_2$: C, 80.40; H, 7.29; N, 3.75. Found: C, 80.33; H, 7.32; N, 3.13.

**[1-(Benzotriazol-1-yl)-1-trimethylsilyl-3-phenyl-3-ethoxy]propyl phenyl ether (15)** was obtained from the reaction of compound **4a** and chlorotrimethylsilane (procedure A, except the reaction mixture was warmed to rt before being quenched) in 71% yield: white microcrystals; mp 59−61 °C; $^1$H NMR (two diastereomers, about 1:1) $\delta$ 0.25 (s) and 0.29 (s) (total 9 H), 0.61 (t, $J$ = 7.1 Hz) and 0.78 (t, $J$ = 7.1 Hz) (total 3 H), 2.57−2.71 (m) and 2.98−3.11 (m) (total 1 H), 2.75−2.97 (m) and 3.30−3.53 (m) (total 3 H), 4.42 (d, $J$ = 8.8 Hz) and 4.57 (dd, $J$ = 7.6, 2.7 Hz) (total 1 H), 6.46 (d, 1 H, $J$ = 7.7 Hz), 6.52 (d, 1 H, $J$ = 7.9 Hz), 6.85−7.42 (m, 10 H), 7.58 (d, $J$ = 8.2 Hz) and 7.72−7.75 (m) (total 1 H), 7.97−8.08 (m, 1 H); $^{13}$C NMR $\delta$ −0.8 and −0.1, 14.5, 45.6 and 47.9, 63.3, 76.9, 94.9 and 95.4, 113.5, 114.0, 119.4, 119.5, 120.5 and 120.6, 123.3 and 123.4, 123.7, 126.0 and 126.2, 126.9, 127.3 and 127.4, 128.3, 129.0 and 129.2, 133.9 and 134.0, 142.5 and 142.8, 146.0, 155.5 and 155.9. Anal. Calcd for $C_{26}H_{31}N_3O_2Si$: C, 70.08; H, 7.01; N, 9.43. Found: C, 69.67; H, 6.97; N, 9.25.

**(3-Phenyl-3-ethoxy)propanoyltrimethylsilane (16)** was obtained from the hydrolysis of **15** (procedure B, except at rt for 4 h) in 67% yield: orange oil; $^1$H NMR $\delta$ 0.17 (s, 9 H), 1.12 (t, 3 H, $J$ = 7.1 Hz), 2.65 (dd, 1 H, $J$ = 15.7, 4.4 Hz), 3.21−3.37 (m, 3 H), 4.78 (dd, 1 H, $J$ = 8.5, 4.4 Hz), 7.22−7.45 (m, 5 H); $^{13}$C NMR $\delta$ −3.5, 15.2, 55.9, 64.1, 77.1, 126.4, 127.4, 128.4, 142.4, 246.9. Anal. Calcd for $C_{14}H_{22}O_2Si$: C, 67.15; H, 8.86. Found: C, 67.35; H, 8.98.

**Cinnamoyltrimethylsilane (17)** was obtained from the hydrolysis of compound **15** using procedure B in 44% yield (together with 11% of compound **16**): orange oil; $^1$H NMR $\delta$ 0.31 (s, 9 H), 6.88 (d, 1 H, $J$ = 16.5 Hz), 7.21−7.43 (m, 4 H), 7.44−7.58 (m, 2 H); $^{13}$C NMR $\delta$ −2.1, 128.2, 128.9, 130.4, 131.2, 134.9, 142.7, 236.0. Anal. Calcd for $C_{12}H_{16}OSi$: C, 70.53; H, 7.89. Found: C, 70.14; H, 7.79.

***N*-Phenyl-[2-(benzotriazol-1-yl)-2-phenoxy-4-phenyl-4-ethoxy]butyrothioamide (18)** was obtained from the reaction of compound **4a** and phenyl isothiocyanate (procedure A) in 93% yield (two diastereomers, ratio 1.7:1): green microcrystals; mp 168−171 °C; $^1$H NMR $\delta$ 0.91 (t, $J$ = 7.1 Hz) and 1.22 (t, $J$ = 6.9 Hz) (total 3 H), 3.06−3.22 (m) and 4.03 (dd, $J$ = 15.5, 10.2 Hz) (total 3 H), 3.57 (dd, $J$ = 15.4, 2.5 Hz) and 3.69 (dd, $J$ = 15.6, 2.4 Hz) (total 1 H), 4.87 (dd, $J$ = 10.7, 2.8 Hz) and 4.69 (dd, $J$ = 10.0, 2.2 Hz) (total 1 H), 6.61 (t, 2 H, $J$ = 7.8 Hz), 6.47−6.85 (m, 14 H), 8.01−8.11 (m, 3 H), 11.14 (s) and 10.96 (s) (total 1 H); $^{13}$C NMR $\delta$ 15.5 and 15.0, 42.4 and 43.7, 64.2, 76.8 and 78.6, 97.2 and 98.8, 111.4 and 111.9, 119.2 and 120.3, 120.2 and 122.1, 122.4 and 122.6, 124.3 and 124.6, 125.5, 126.4 and 126.5, 127.1 and 127.4, 127.8, 127.9 and 128.0, 128.4 and 128.5, 129.1 and 129.3, 129.4 and 129.8, 131.9 and 132.3, 137.9 and 138.1, 141.3 and 141.5, 146.6 and 146.7, 152.2 and 152.5, 191.3 and 192.9. Anal. Calcd for $C_{30}H_{28}N_4O_2S$: C, 70.84; H, 5.55; N, 11.02. Found: C, 70.91; H 5.76; N, 10.74.

***N*-Phenyl (2-oxo-4-phenyl-4-ethoxy)butyrthioamide (19)** was obtained from the hydrolysis of **15** (procedure B, except at rt for 4 h) in 95% yield: red oil; $^1$H NMR $\delta$ 1.14 (t, 3 H, $J$ = 7.1 Hz), 3.32−3.42 (m, 2 H), 3.46 (dd, 1 H, $J$ = 16.8, 4.4 Hz), 3.82 (dd, 1 H, $J$ = 16.8, 9.0 Hz), 4.91 (dd, 1 H, $J$ = 9.0, 4.4 Hz), 7.18−7.60 (m, 8 H), 7.97 (d, 2 H, $J$ = 7.8 Hz), 10.5 (s, 1 H); $^{13}$C NMR $\delta$ 15.0, 45.3, 64.2, 77.8, 121.6, 126.5, 126.9, 127.7, 128.4, 128.8, 137.6, 141.2, 184.6, 190.8. Anal. Calcd for $C_{18}H_{19}NO_2S$: C, 68.98; H, 6.11; N, 4.47. Found: C, 69.23; H, 6.09; N, 4.68.

**Ethyl [2-(benzotriazol-1-yl)-2-phenoxy-4-ethoxy-4-phenyl]butyroate (20)** was obtained from the reaction of **4a** and ethyl chloroformate (procedure A) in 89% yield: yellow microcrystals; mp 113−116 °C; $^1$H NMR (two diastereomers, 1:1) $\delta$ 1.03 (t, $J$ = 7.0 Hz) and 1.08 (t, $J$ = 7.1 Hz) (total 3 H), 1.17 (t, $J$ = 7.1 Hz) and 1.28 (t, $J$ = 7.1 Hz) (total 3 H), 2.95−3.62 (m, 4 H), 4.14−4.41 (m, 2 H), 4.72 (dd, $J$ = 10.4, 1.2 Hz) and 4.86 (dd, $J$ = 8.8, 2.3 Hz) (total 1 H), 6.37 (d, 1 H, $J$ = 7.7 Hz), 6.59 (d, 1 H, $J$ = 8.0 Hz), 6.82−7.63 (m, 10 H), 7.67 (d, $J$ = 8.2 Hz) and 7.78 (d, $J$ = 8.2 Hz) (total 1 H), 8.07 (d, $J$ = 8.2 Hz) and 8.12 (d, $J$ = 8.2 Hz) (total 1 H); $^{13}$C NMR $\delta$ 13.7 and 13.8,

14.7 and 14.8, 41.4 and 43.4, 62.2 and 62.6, 63.9 and 64.5, 76.1 and 77.0, 91.1 and 92.7, 112.4 and 114.1, 115.4, 119.8, 120.0 and 121.3, 124.1 and 124.4, 124.5 and 124.7, 125.9, 126.5, 127.6 and 127.7, 127.8 and 128.2, 128.3 and 129.2, 129.3 and 129.4, 132.1 and 132.9, 141.2 and 141.7, 146.2, 152.2 and 152.7, 166.0 and 166.2. Anal. Calcd for $C_{26}H_{27}N_3O_4$: C, 70.10; H, 6.11; N, 9.43. Found: C, 70.25; H, 6.34; N, 8.89.

***N*-Isopropyl-[2-(benzotriazol-1-yl)-2-phenoxy-4-phenyl-4-ethoxy]butyramide (22)** was obtained from the reaction of **4a** and isopropyl isocyanate (procedure A) in 95% yield: white microcrystals; mp 183−186 °C; $^1$H NMR (two diastereomers, 1:1) $\delta$ 1.03−1.22 (m, 3 H), 1.23−1.50 (m, 6 H), 3.00 (dd, $J$ = 15.1, 9.8 Hz) and 3.64 (dd, $J$ = 15.4, 10.2 Hz) (total 1 H), 3.15−3.48 (m, 3 H), 4.12−4.37 (m, 1 H), 4.60 (d, $J$ = 9.9 Hz) and 4.68 (d, $J$ = 9.6 Hz) (total 1 H), 6.43 (d, 1 H, $J$ = 7.6 Hz), 6.53 (d, 1 H, $J$ = 8.0 Hz), 6.90−7.17 (m, 4 H), 7.18−7.55 (m, 7 H), 7.67 (d, $J$ = 8.2 Hz) and 7.74 (d, $J$ = 8.2 Hz) (total 1 H), 8.05 (d, $J$ = 8.2 Hz) and 8.09 (d, $J$ = 8.4 Hz) (total 1 H); $^{13}$C NMR $\delta$ 15.0 and 15.3, 22.4 and 22.5, 22.7 and 22.8, 41.2, 42.2 and 42.4, 63.8 and 64.1, 76.1 and 77.7, 92.7 and 93.5, 111.5 and 111.6, 119.1 and 120.1, 121.9, 124.2 and 124.3, 125.0, 126.2 and 126.4, 127.7, 127.6 and 127.8, 128.4, 129.3 and 129.7, 132.2 and 132.5, 141.5 and 142.0, 146.5 and 146.6, 151.9 and 152.5, 165.1 and 165.2. Anal. Calcd for $C_{27}H_{30}N_4O_3$: C, 70.72; H, 6.59; N, 12.22. Found: C, 70.97; H, 6.93; N, 12.25.

(17) Sugimura, H.; Yoshida, K. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 3209.

***N*-Isopropyl-2-oxo-4-phenyl-but-3-enamide (23)** was obtained from the hydrolysis of compound **22** (procedure B, except in refluxing $CH_3CN-H_2O$ (1:1) for 12 h) in 75% yield: green microcrystals; mp 72−73 °C; $^1$H NMR $\delta$ 1.24 (d, 6 H, $J$ = 6.6 Hz), 4.03−4.22 (m, 1 H), 7.05 (br s, 1 H), 7.32−7.54 (m, 3 H), 7.59−7.63 (m, 2 H), 7.78 (d, 1 H, $J$ = 16.1 Hz), 7.94 (d, 1 H, $J$ = 16.1 Hz); $^{13}$C NMR $\delta$ 22.4, 41.7, 118.8, 129.0, 129.1, 131.3, 134.4, 147.7, 160.4, 185.8. Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96; N, 6.45. Found: C, 72.09; H, 7.21; N, 6.07.

**Ethyl 2-oxo-4-phenyl-but-3-enoate (24)**[17] was obtained as a byproduct from the hydrolysis of **22** (procedure B) in 46% yield (together with 35% of **23**): colorless oil; $^1$H NMR $\delta$ 1.42 (t, 3 H, $J$ = 7.1 Hz), 4.40 (q, 2 H, $J$ = 7.1 Hz), 7.24−7.53 (m, 4 H), 7.54−7.73 (m, 2 H), 7.87 (d, 1 H, $J$ = 16.2 Hz); $^{13}$C NMR $\delta$ 14.0, 62.4, 120.7, 129.0, 129.1, 131.6, 134.1, 148.4, 162.2, 182.9.

**Supporting Information Available:** Full detailed analysis data ($^1$H NMR, $^{13}$C NMR, and microanalysis) of compounds **4b**−**d**, **7b**−**d**, **8b**−**d**, **9b**,**c,** and **10b**,**c**, and $^1$H NMR, $^{13}$C NMR, and HRMS spectra for intermediate **11** (8 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information and Internet access instructions.

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