Novel and Convenient Routes to Functionalized Alkynyl Ketones from 1-(Benzotriazol-1-yl)propargyl Ethyl Ethers

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1-(Benzotriazol-1-yl)propargyl ethyl ethers, readily accessible from propargyl aldehyde diethyl acetals and benzotriazole, undergo smooth lithiation at the methine carbon and subsequent reactions with alkyl halides, aldehydes, ketones, imines, esters, trialkylsilyl chlorides, dialkyl carbonates, and isocyanates to yield the corresponding substituted ethers. Hydrolysis of these intermediates under acidic conditions affords a wide variety of alkynyl ketones bearing hydroxy, amino, acyl, trimethylsilyl, alkoxycarbonyl, and (alkylamino)carbonyl substituents at the α-position in good to excellent overall yields.

The facile additions and cyclizations of α,β-acetylenic carbonyl compounds make them very useful substrates in synthetic organic chemistry for the elaboration of heterocyclic systems, and considerable attention has been devoted to the preparation of these compounds. A common synthetic route to alkynyl ketones is (i) the acylation of metal (Li,[1-3] Sn,[4-6] Mn,[7,8] Zn,[9,10] Mg,[10,11] Cd,[10] Cu,[12,13] Ag[14-16]) acetylides with an activated carboxylic acid derivative, such as an acid chloride, anhydride, ester or amide. Usually a catalyst is required; thus reactive lithium acetylides need an equimolar quantity of BF_3·OEt_2.[1-3] Other methods include (ii) reactions of 1-alkynyltrimethylsilane with an acid chloride in the presence of a Lewis acid[17,18] or with a thiol ester;[19] (iii) α-oxidation of an alkyne with chromium trioxide–pyridine complex, sodium chromate,[20-22] or *tert*-butyl hydroperoxide catalyzed by chromium(VI) oxide,[23] and (iv) reaction of a metal acetylide with an aldehyde followed by oxidation or direct oxidative nucleophilic addition of an aldehyde to a vanadium acetylide.[24] Methods ii–iv are generally restricted to the generation of alkynyl ketones without sensitive functionality, such as hydroxy or amino groups, and require expensive (Pd, V) or toxic (Cr) catalysts.

Benzotriazole-assisted synthesis of a variety of organic compounds, such as amines, ethers, amides, and ketones, has blossomed in our group.[25] Recent work[26] in this laboratory has demonstrated that 1-(benzotriazol-1-yl)-allyl ethyl ether, readily available from the direct reaction of acrolein diethyl acetal with benzotriazole, can undergo facile lithiation and subsequent reaction with diverse electrophiles to give cyclopropanes, epoxides, etc. We now report an analogous methodology which successfully utilizes propargyl aldehyde diethyl acetals to prepare intermediates **4a–e, 6a,b, 8a,b, 10, 12, 14, 16, 18, 25, 28a,b, 30,** and **31** which in turn readily undergo hydrolysis to afford alkynyl ketones **5a–e, 7a,b, 9a,b, 11, 13, 15, 17, 19, 26, 29a,b, 32,** and **33**. Included are examples where the intermediates and products bear hydroxy, amino, acyl, trimethylsilyl, alkoxycarbonyl, and (alkylamino)carbonyl substituents at the α-position which are formed when aldehydes, ketones, imines, esters, trimethylsilyl chloride, diethyl carbonate or alkyl isocyanates, respectively, are used as the electrophiles. Treatment of the lithio intermediate **3** with carbon disulfide or an isothiocyanate gave the cyclized products **21** and **23.**

Significantly, the methine proton in propargyl aldehyde diethyl acetals **1** and **24** cannot be lithiated, while the replacement of an ethoxy group in the molecule by benzotriazole allows this process to proceed smoothly, once again demonstrating the advantages of this versatile synthetic auxiliary.

Results and Discussion

Heating phenylpropargyl aldehyde diethyl acetal (**1a**) with benzotriazole in toluene for 4 h gave 1-(benzotriazol-1-yl)-3-phenylpropargyl ethyl ether (**2a**) in 84% yield (Scheme 1). Most of the solid product was isolated pure

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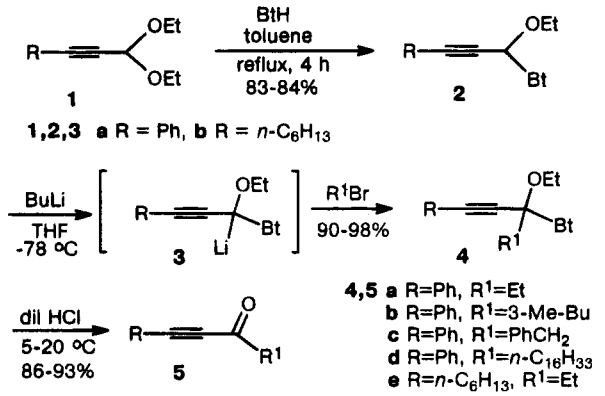
Scheme 1

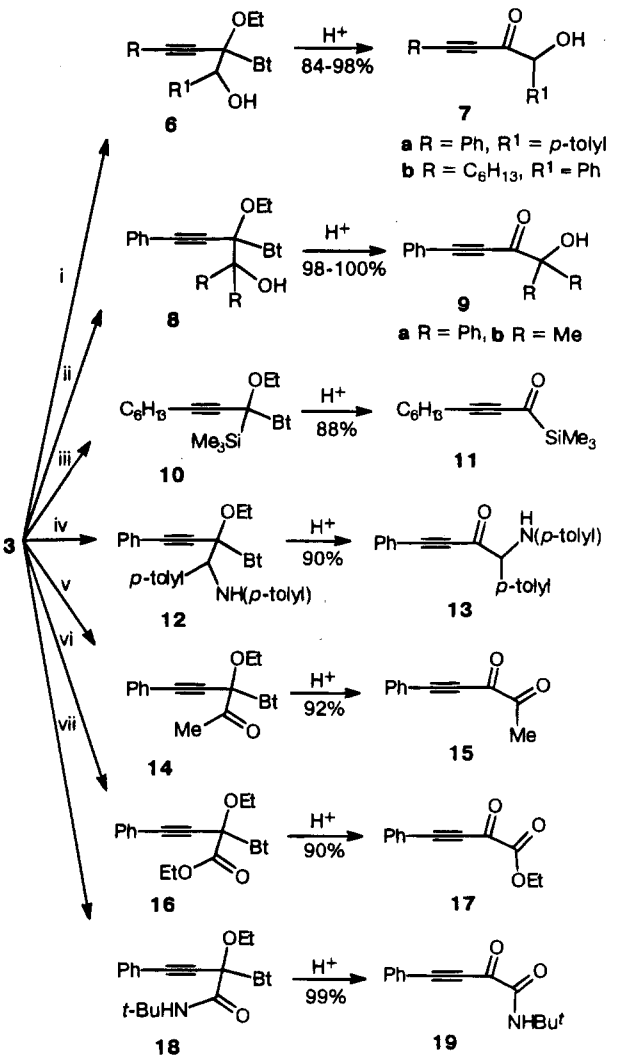


by adding hexane to the crude oil and maintaining the temperature at 0–5 °C for some time; concentration of the filtrate and separation by column chromatography afforded further material. Compound **2b** (oil) was obtained similarly in 83% yield after separation by column chromatography. The benzotriazol-2-yl isomers (ca. 5–10%) simultaneously produced in these reactions were removed during these procedures. However, as the benzotriazol-2-yl isomers undergo similar transformations, the mixtures of the 1- and 2-isomers could be used in the subsequent reactions.

Treatment of **2a** with 1 equiv of butyllithium at −78 °C for 2 min resulted in formation of the dark-blue intermediate **3**. Subsequent reaction with ethyl bromide for 2–5 min at the same temperature afforded **4a** in 98% yield. Compounds **4b–e** were similarly prepared in 90–96% yields. These substituted derivatives **4a–e** readily undergo acid hydrolysis under mild conditions. Thus, stirring 1-(benzotriazolyl)-3-phenylpropargyl ethyl ether (**4a**) in acetone (or MeOH, EtOH) containing dilute HCl at 5–20 °C for 10–20 min gave the expected 1-phenyl-1-pentyn-3-one (**5a**) in 90% yield. Analogs **5b–e** were similarly produced in excellent yields (Scheme 1). A convenient approach to ketones **5a–e** is the direct hydrolysis of intermediates **4a–e** during acidic workup without isolation.

When synthons **3a,b** were separately reacted with 4-tolualdehyde, benzaldehyde, benzophenone, acetone, trimethylsilyl chloride, *N*-(4-methylbenzylidene)-4′-methylaniline, ethyl acetate, diethyl carbonate, and *tert*-butyl isocyanate (Scheme 2), the expected functional groups were introduced to give the corresponding substituted intermediates **6a,b, 8a,b, 10, 12, 14, 16**, and **18** in isolated yields of 54–88% with the exception of **16** (35% yield). The reactions were accomplished in 2–5 min, and immediate decoloration was observed when the electrophile was added. After reaction with electrophiles, quenching with water was effected at −78 °C to avoid the decomposition possible at higher temperatures. This temperature control was especially critical in the cases of **6a,b, 8a,b, 12, 14, 16,** and **18**, where the new basic lithium salt produced was still present in the system. In the cases of **4a,b,d,e**, pure compounds were obtained after standard workup without further purification. Compounds **8a,b** and **12** were purified by recrystallization. The remaining compounds **4c, 6a,b, 10, 14, 16,** and **18** required purification on short silica gel columns; these chromatographic separations must be performed very quickly to avoid hydrolysis (decomposition). Thus, retaining **4d** on such a column for 12 h resulted in approximately 50% hydrolysis to produce the alkynyl

Scheme 2



(i) 4-MeC$_6$H$_4$CHO, yield 75% (**6a**); PhCHO, yield 73% (**6b**); (ii) PhCOPh, yield 77% (**8a**); MeCOMe, yield 66% (**8b**); (iii) Me$_3$SiCl, yield 78% (**10**); (iv) *p*-tolylCH=N(*p*-tolyl) yield 85% (**12**); (v) EtOAc, yield 65% (**14**); (vi) EtOCO$_2$Et, yield 35% (**16**); (vii) *t*-BuNCO, yield 54% (**18**).

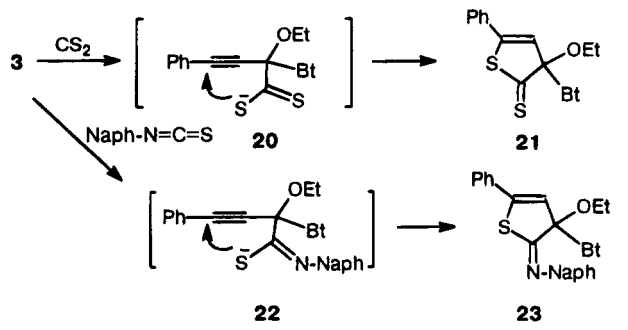
ketone **5d**; it is believed that the weakly acidic silica gel catalyzed the hydrolysis.

Similar to the cases of **4a–e** mentioned above, intermediates **6a,b, 8a,b, 10, 12, 14, 16,** and **18** were all readily hydrolyzed in dilute HCl to give the expected ketones **7a,b, 9a,b, 11, 13, 15, 17,** and **19** in 80–100% yields. The NMR spectra indicated that final products **5a–e, 7a,b, 9a,b, 11, 13, 15, 17, 19, 26, 29a,b, 32,** and **33** were all pure after hydrolysis.

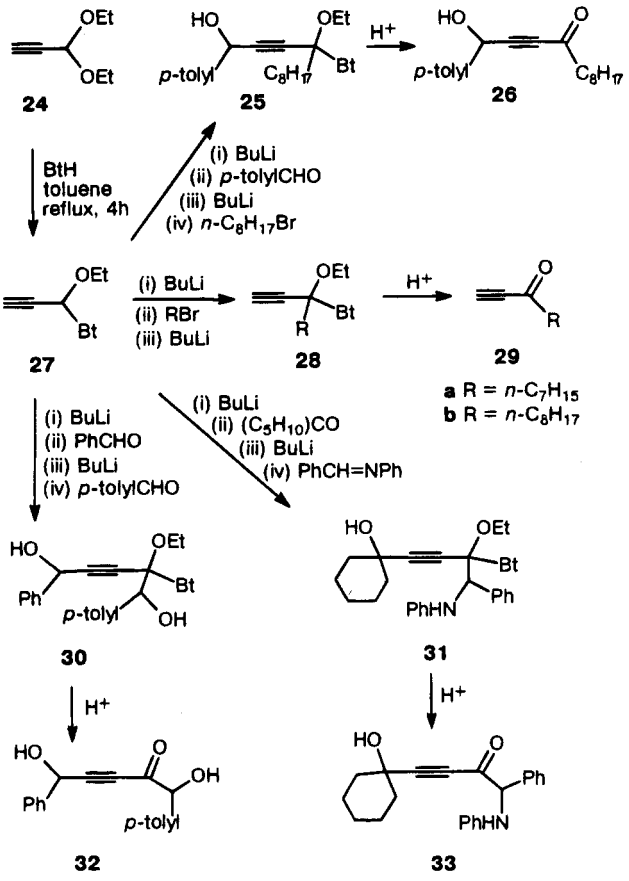
When carbon disulfide was used as the electrophile, the cyclized product **21** was obtained in 57% yield after normal workup. It is believed that lithio intermediate **3a** reacted with CS_2 to form strongly nucleophilic dithiocarboxylate anion **20** which immediately attacked the triple bond to generate **21**. In the case of compound **23**, it is formed from reaction of metalated **3** with 1-naphthyl isothiocyanate *via* intermediate **22** as shown in Scheme 3. Compounds **21** and **23** were not hydrolyzed in dilute HCl at room temperature, and use of higher temperatures led to decomposition.

Acetal **24**, containing an active hydrogen on the acetylenic group, was reacted with benzotriazole under the

Scheme 3



Scheme 4



same conditions described for compounds **1a,b** to give 1-(benzotriazolyl)propargyl ethyl ether (**27**) in 65% yield (Scheme 4). Successive treatment of compound **27** with 1 equiv of BuLi in THF, followed by quenching with *p*-tolualdehyde, then with another equivalent of butyllithium, and lastly with octyl bromide gave the doubly regiospecifically reacted intermediate **25**, which was similarly hydrolyzed under mild conditions to yield the expected product **26** in 73% overall yield. Similarly, if different aldehydes, ketones and amines were used as electrophiles, the doubly functionalized ketones **32** and **33** were prepared in 85% and 63% overall yields, respectively. The deprotonation occurred first on the more acidic acetylenic proton. Thus, the first electrophile was introduced at the acetylenic carbon, and the second electrophile was attached to the methine carbon. This was confirmed by the structural characterization of the final products. In the case of **26**, ^{13}C NMR shows a chemical shift of 64.0 ppm for the hydroxy carbon, while structures of type **7b** show a chemical shift of 76.6 ppm. Interestingly, when an alkyl bromide was used as the first electrophile in the reaction with the lithium acetylide of **27**, no reaction was observed, even at room temperature. Thus, successive treatment of 1-(benzotriazolyl)propargyl ethyl ether (**27**) with 1 equiv of BuLi in THF, followed by addition of an alkyl bromide, followed by a second equivalent of BuLi and a different alkyl bromide gave only monoalkylated (methine alkylated) derivatives. Thus, stepwise treatment of **27** with 1 equiv of BuLi at −78 °C, heptyl bromide, and a second equivalent of BuLi gave the expected product **29a** in 92% yield. Compound **29b** was similarly prepared 94% yield. Intermediates **25, 28a,b, 30,** and **31** were easily hydrolyzed under the conditions described above to afford the corresponding alkynyl ketones **26, 29a,b, 32,** and **33** in excellent yields.

The structures of all final products obtained and their associated intermediates have been confirmed by ^1H NMR and ^{13}C NMR data and elemental analyses. For known compounds, physical properties have been compared with those available in the literature.

We have reported the preparation of several classes of functionalized alkynyl ketones and we now compare the present methods with previous ones for each class.

Comparison of Present Synthetic Routes with Those Previously Available

(i) Few alkynyl α-hydroxyalkyl ketones of type **7** are recorded in the literature. 3-Hydroxy-5-tridecyn-4-one was prepared in 39% overall yield in a four-step procedure by reaction of 2-lithiobenzothiazole with propionaldehyde and subsequent quaternization with methyl iodide, alkylation with organolithium reagents, and hydrolysis in aqueous acetonitrile buffered to pH 7 containing $AgNO_3$.[27] 2-Hydroxy-4-nonan-3-one was prepared in an unspecified overall yield *via* a three-step procedure by protection of the hydroxy group of *N,N*-dimethylacetamide, subsequent treatment with lithium acetylide, and finally hydrolysis.[28] Our two-step sequence of **3** → **6** → **7** now renders a wide variety of alkynyl α-hydroxyalkyl ketones readily and conveniently available.

(ii) Compound **9b** was prepared in 12% overall yield in a five-step procedure starting from acetone and lithium phenylacetylide.[29,30] The present procedure is obviously much higher yielding, more simple, and convenient.

(iii) Acetylenic acylsilanes of type **11** were previously prepared from expensive (trimethylsilyl)methanol in 24–60% overall yields by oxidation of intermediate (α-hydroxyalkyl)silanes.[31] Alternatively, compounds **11** were also prepared in 38–47% overall yields by a four-step manipulation of propargyl ethers including triple lithiations *via* selenium intermediates.[32-34] Our method commences with readily available starting materials and is a simple and high-yielding procedure.

(iv) Recently, Khim and Mariano[35] reported the preparation of α-alkylamino-substituted alkynyl ketones from

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alanine in unspecified overall yield by alkylation of the amino group of alaninol, oxidation of the CH_2OH group to the aldehyde, and reaction with lithium acetylides followed by Swern oxidation. Our method provides the first synthetically practical preparation of compounds of type **13**.

(v) Acetylenic α-diketones of type **15** and acetylenic α-keto esters of type **17** have been prepared by reaction of metal acetylides with acid chlorides[36] (8–70% yields) and diethyl oxalate (25–78% yields),[37-40] respectively, with formation of the C–C bond between the alkynyl and the carbonyl groups. The present method offers a novel preparation by creation of a new bond between the two carbonyl groups.

(vi) Only one example was found in the literature for the preparation of an alkynyl α-keto amide of type **19**: 2-oxo-4-phenyl-3-butynanilide was obtained as a byproduct when ethyl 2-oxo-4-phenyl-3-butynoate was treated with aniline.[41] No yield was reported. The present method enables compounds of type **19** to be conveniently and practically prepared from isocyanates.

(vii) α-Hydroxy (to the acetylenic group) substituted alkynyl ketones of type **26** were previously prepared by oxidation of the corresponding dihydroxy-substituted derivatives with CrO_3, MnO_2, or H_2O_2.[42-44] In these reactions symmetrical dihydroxy compounds and special controls were required to prevent the generation of two different oxidative products[43] or overoxidation. Another method available for the preparation of compounds of type **26** involves treatment of a protected (hydroxymethyl)acetylene with a strong base ($NaNH_2$), subsequent reaction with an anhydride followed by deprotection (32–45% overall yields),[45] or reaction of the lithium salt of 1-phenylpropyn-1-one with aldehydes (poor yield).[46] The present approach, utilizing different electrophiles, can readily afford compounds of type **26** in high yield.

(viii) Compounds of types **32** and **33** are, we believe, completely novel. In our approach, if different electrophiles are used, a variety of doubly functionalized acetylenic ketones can easily be synthesized.

In conclusion, novel and convenient routes have been developed for the preparation of various functionalized alkynyl ketones. Most such functionalized α,β-acetylenic carbonyl compounds were not easily accessible by previous methods. The present methodology, employing commercially available starting materials and inexpensive benzotriazole, offers many advantages in the synthesis of these classes of compounds.

Experimental Section

Melting points were recorded on a hot stage apparatus without correction. ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded in $CDCl_3$. Elemental analyses were performed within the department. Propargyl aldehyde acetals **1a,b** and **24** were purchased from Aldrich and Lancaster.

Preparation of 1-(Benzotriazol-1-yl)propargyl Ethyl Ethers 2a,b and 27. General Procedure. Propargyl aldehyde acetals **1a,b** or **24** (50 mmol) and benzotriazole (75 mmol) were heated under reflux in toluene (40 mL) for 4 h. Diethyl ether (200 mL) was added, and the solution was washed with saturated Na_2CO_3 solution (2 × 100 mL) and water (1 × 100 mL). Evaporation of the solvent gave a residual oil. In the case of **2a**, hexane (10 mL) was added and the solution placed in a refrigerator for 2 h, during which time a white solid crystallized from the solution. The filtrate was concentrated and chromatographed on silica gel (hexane/ethyl acetate = 100:1). In the cases of **2b** and **27**, the products were obtained after chromatographic separation (hexane/ethyl acetate = 100:1).

1-(Benzotriazol-1-yl)-3-phenylpropargyl ethyl ether (2a): yield 84%; mp 69–70 °C; ^1H NMR δ 1.19 (t, 3 H, J = 7.0 Hz), 3.40–3.50 (m, 1 H), 3.65–3.75 (m, 1 H), 7.04 (s, 1 H), 7.30–7.50 (m, 6 H), 7.54 (t, 1 H, J = 7.1 Hz), 8.04 (d, 1 H, J = 8.3 Hz), 8.09 (d, 1 H, J = 8.3 Hz); ^{13}C NMR δ 14.6, 64.5, 79.0, 81.4, 88.1, 111.5, 120.0, 120.8, 124.4, 127.8, 128.3, 129.4, 131.2, 131.9, 146.8. Anal. Calcd for $C_{17}H_{15}N_3O$: C, 73.61; H, 5.46; N, 15.16. Found: C, 73.93; H, 5.46; N, 15.10.

1-(Benzotriazol-1-yl)-3-hexylpropargyl ethyl ether (2b): obtained as an oil; yield 83%; ^1H NMR δ 0.85 (t, 3 H, J = 6.9 Hz), 1.15 (t, 3 H, J = 7.0 Hz), 1.20–1.40 (m, 6 H), 1.48–1.54 (m, 2 H), 2.30 (dt, 2 H, J = 7.1, 1.9 Hz), 3.32–3.42 (m, 1 H), 3.58–3.68 (m, 1 H), 6.81 (t, 1 H, J = 1.9 Hz), 7.41 (t, 1 H, J = 7.0 Hz), 7.53 (t, 1 H, J = 7.0 Hz), 8.00 (d, 1 H, J = 8.3 Hz), 8.10 (d, 1 H, J = 8.3 Hz); ^{13}C NMR δ 13.8, 14.5, 18.5, 22.3, 27.8, 28.4, 31.1, 64.1, 73.1, 78.7, 89.8, 111.6, 119.8, 124.2, 127.5, 131.1, 146.7. Anal. Calcd for $C_{17}H_{23}N_3O$: C, 71.53; H, 8.13; N, 14.73. Found: C, 71.75; H, 8.13; N, 14.82.

1-(Benzotriazol-1-yl)-3-propargyl ethyl ether (27): yield 65%; mp 48–49 °C; ^1H NMR δ 1.15 (t, 3 H, J = 7.0 Hz), 2.89 (d, 1 H, J = 2.2 Hz), 3.35–3.45 (m, 1 H), 3.55–3.65 (m, 1 H), 6.82 (d, 1 H, J = 2.2 Hz), 7.41 (t, 1 H, J = 7.1 Hz), 7.54 (t, 1 H, J = 7.1 Hz), 7.97 (d, 1 H, J = 8.3 Hz), 8.10 (d, 1 H, J = 8.3 Hz); ^{13}C NMR δ 14.4, 64.3, 76.7, 77.4, 77.8, 111.3, 119.8, 124.4, 127.8, 130.9, 146.5. Anal. Calcd for $C_{11}H_{11}N_3O$: C, 65.64; H, 5.71; N, 20.89. Found: C, 65.55; H, 5.50; N, 21.15.

General Procedure for the Lithiation of Compounds 2a,b. Preparation of 4a-e, 6a,b, 8a,b, 10, 12, 14, 16, 18, 21, and 23. To a solution of 1-(benzotriazol-1-yl)-3-propargyl ethyl ether (**2a** or **2b**, 5 mmol) in THF (70 mL) at −78 °C was added *n*-butyllithium (2 M in cyclohexane, 2.5 mL, 5 mmol). The solution was stirred at this temperature for 2 min, during which time the solution became dark blue. The appropriate electrophile (EtBr, 3-Me-BuBr, $PhCH_2Br$, n-$C_{16}H_{33}Br$, *p*-tolualdehyde, benzaldehyde, benzophenone, acetone, trimethylsilyl chloride, *N*-tolyltolylmethanimine, ethyl acetate, diethyl carbonate, *tert*-butyl isocyanate, carbon disulfide, or 1-naphthyl isothiocyanate) was then added, and the solution was kept at −78 °C for an additional 2–5 min. The reaction was quenched at this temperature with water (30 mL), and the mixture was extracted with diethyl ether (2 × 60 mL) and dried with $MgSO_4$. Evaporation of the solvent gave a residue. In the cases of **4a,b,d,e**, pure compounds were afforded. The solid products **8a,b, 12, 21,** and **23** were recrystallized from ether and hexane. In the remaining cases **4c, 6a,b, 10, 14, 16,** and **18**, pure compounds were obtained after column chromatography (hexane/ethyl acetate = 30:1).

3-(Benzotriazol-1-yl)-3-ethoxy-1-phenyl-1-pentyne (4a): obtained as an oil; yield 98%; ^1H NMR δ 1.06 (t, 3 H, J = 7.4 Hz), 1.22 (t, 3 H, J = 7.0 Hz), 2.55 (q, 2 H, J = 7.4 Hz), 3.22–3.32 (m, 1 H), 3.90–4.00 (m, 1 H), 7.35–7.45 (m, 4 H), 7.49 (t, 1 H, J = 7.2 Hz), 7.60–7.65 (m, 2H), 7.99 (d, 1 H, J = 8.3 Hz), 8.13 (d, 1 H, J = 8.3 Hz); ^{13}C NMR δ 8.6, 14.8, 35.0, 61.1, 83.4, 89.4, 91.8, 112.2, 120.0, 121.4, 124.0, 127.3, 128.4, 129.3, 131.7, 132.0, 146.7. Anal. Calcd for $C_{19}H_{19}N_3O$: C, 74.73; H, 6.27; N, 13.76. Found: C, 75.02; H, 6.40; N, 13.34.

3-(Benzotriazol-1-yl)-3-ethoxy-6-methyl-1-phenyl-1-heptyne (4b): obtained as an oil; yield 96%; ^1H NMR δ 0.83 (d, 3 H, J = 6.6 Hz), 0.89 (d, 3 H, J = 6.4 Hz), 1.22 (t, 3 H, J = 7.1 Hz), 1.15–1.20 (m, 1 H), 1.53–1.70 (m, 2 H), 2.54 (d, 1 H,

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J = 9.2 Hz), 2.57 (d, 1 H, J = 9.2 Hz), 3.20–3.30 (m, 1 H), 3.90–4.00 (m, 1 H), 7.35–7.45 (m, 4 H), 7.50 (t, 1 H, J = 7.1 Hz), 7.60–7.65 (m, 2 H), 8.00 (d, 1 H, J = 8.3 Hz), 8.10 (d, 1 H, J = 8.3 Hz); ^{13}C NMR δ 14.7, 22.2, 22.4, 27.6, 32.8, 39.6, 60.9, 83.7, 89.3, 91.3, 112.1, 120.0, 121.3, 123.9, 127.3, 128.3, 129.2, 131.6, 132.0, 146.6. Anal. Calcd for $C_{22}H_{25}N_3O$: C, 76.04; H, 7.26; N, 12.10. Found: C, 76.37; H, 7.34; N, 12.05.

3-(Benzotriazol-1-yl)-3-ethoxy-1,4-diphenyl-1-butyne (4c): yield 95%; mp 102–104 °C; ^{1}H NMR δ 1.24 (t, 3 H, J = 7.1 Hz), 3.25–3.35 (m, 1 H), 3.74 (d, 1 H, J = 12.3 Hz), 3.77 (d, 1 H, J = 12.3 Hz), 3.95–4.05 (m, 1 H), 7.00–7.20 (m, 5 H), 7.30–7.50 (m, 7 H), 7.87 (d, 1 H, J = 8.2 Hz), 8.08 (d, 1 H, J = 8.2 Hz); ^{13}C NMR δ 14.7, 48.4, 61.5, 83.3, 90.9, 91.2, 112.1, 120.0, 121.2, 123.9, 127.3, 127.4, 127.8, 128.4, 129.3, 130.7, 131.9, 132.2, 133.9, 146.5. Anal. Calcd for $C_{24}H_{21}N_3O$: C, 78.44; H, 5.76; N, 11.44. Found: C, 78.33; H, 5.74; N, 11.41.

3-(Benzotriazol-1-yl)-3-ethoxy-1-phenyl-1-nonadecyne (4d): obtained as an oil; yield 94%; ^{1}H NMR δ 0.86 (t, 3 H, J = 6.9 Hz), 1.20–1.40 (m, 30 H), 1.70–1.80 (m, 1 H), 2.51 (t, 2 H, J = 7.2 Hz), 3.20–3.30 (m, 1 H), 3.90–4.00 (m, 1 H), 7.35–7.42 (m, 4 H), 7.49 (t, 1 H, J = 7.1 Hz), 7.59–7.65 (m, 2 H), 8.00 (d, 1 H, J = 8.3 Hz), 8.10 (d, 1 H, J = 8.3 Hz); ^{13}C NMR δ 14.1, 14.8, 22.6, 22.7, 24.0, 29.0, 29.2, 29.3, 29.4, 29.5, 29.6, 31.6, 31.9, 41.7, 61.0, 83.7, 89.4, 91.3, 112.2, 120.1, 121.4, 124.0, 127.4, 128.4, 129.3, 131.7, 132.1, 146.7. Anal. Calcd $C_{33}H_{47}N_3O$: C, 78.98; H, 9.45; N, 8.38. Found: C, 79.28; H, 9.56; N, 8.15.

3-(Benzotriazol-1-yl)-3-ethoxy-4-undecyne (4e): obtained as an oil; yield 90%; ^{1}H NMR δ 0.90 (t, 3 H, J = 7.1 Hz), 0.96 (t, 3 H, J = 7.4 Hz), 1.17 (t, 3 H, J = 7.0 Hz), 1.25–1.52 (m, 6 H), 1.60–1.70 (m, 2 H), 2.40–2.50 (m, 4 H), 3.10–3.20 (m, 1 H), 3.78–3.88 (m, 1 H), 7.37 (t, 1 H, J = 7.1 Hz), 7.46 (t, 1 H, J = 7.1 Hz), 7.94 (d, 1 H, J = 8.3 Hz), 8.09 (d, 1 H, J = 8.3 Hz); ^{13}C NMR δ 8.5, 13.9, 14.7, 18.7, 22.4, 28.1, 28.4, 31.2, 35.0, 60.7, 74.8, 90.9, 91.5, 112.3, 119.9, 123.8, 127.1, 131.6, 146.6. Anal. Calcd for $C_{19}H_{27}N_3O$: C, 72.79; H, 8.69; N, 13.41. Found: C, 73.15; H, 8.88; N, 13.07.

3-(Benzotriazol-1-yl)-3-ethoxy-4-hydroxy-4-(4-methylphenyl)-1-phenyl-1-butyne (6a). This compound was obtained as two diastereomers of *ca.* equal amount: total yield 75%. **Isomer 1**: mp 145–147 °C; ^{1}H NMR δ 1.34 (t, 3 H, J = 7.1 Hz), 2.22 (s, 3 H), 3.41 (d, 1 H, J = 2.7 Hz), 3.42–3.50 (m, 1 H), 4.10–4.20 (m, 1 H), 5.45 (d, 1 H, J = 2.5 Hz), 6.82–6.90 (m, 4 H), 7.35–7.42 (m, 5 H), 7.60 (d, 2 H, J = 8.0 Hz), 7.70–7.73 (m, 1 H), 8.04–8.10 (m, 1 H); ^{13}C NMR δ 14.8, 21.1, 62.3, 77.2, 79.0, 92.0, 93.6, 112.1, 120.0, 123.9, 127.3, 127.5, 128.3, 128.4, 128.5, 129.6, 132.1, 132.8, 132.9, 138.4, 146.3. Anal. Calcd for $C_{25}H_{23}N_3O_2$: C, 75.53; H, 5.84; N, 10.58. Found: C, 75.70; H, 5.87; N, 10.48. **Isomer 2**: mp 147–148 °C; ^{1}H NMR δ 1.21 (t, 3 H, J = 7.0 Hz), 2.30 (s, 3 H), 3.30 (s, 1 H), 3.31–3.40 (m, 1 H), 3.88–3.98 (m, 1 H), 5.51 (d, 1 H, J = 3.0 Hz), 7.06 (d, 2 H, J = 7.9 Hz), 7.24 (d, 2 H, J = 8.1 Hz), 7.30–7.40 (m, 5 H), 7.51 (d, 2 H, J = 8.0 Hz), 7.83 (d, 1 H, J = 8.2 Hz), 8.00 (d, 1 H, J = 8.00 Hz); ^{13}C NMR δ 14.7, 21,2, 62.1, 79.0, 80.8, 91.8, 93.3, 112.5, 120.0, 123.9, 127.4, 127.9, 128.2, 128.3, 128.4, 129.5, 132.0, 133.0, 134.2, 138.1, 146.3. Anal. Calcd for $C_{25}H_{23}N_3O_2$: C, 75.53; H, 5.84; N, 10.58. Found: C, 75.62; H, 5.86; N, 10.46.

2-(Benzotriazol-1-yl)-2-ethoxy-1-hydroxy-1-phenyl-3-decyne (6b). This compound was obtained as two diastereomers of *ca.* equal amount: total yield 73%. **Isomer 1**: an oil; ^{1}H NMR δ 0.90 (t, 3 H, J = 6.9 Hz), 1.22–1.50 (m, 9 H), 1.64 (quint, 2 H, J = 7.9 Hz), 2.43 (t, 2 H, J = 7.2 Hz), 3.28–3.38 (m, 1 H), 3.56 (d, 1 H, J = 2.7 Hz), 3.99–4.09 (m, 1 H), 5.36 (d, 1 H, J = 2.7 Hz), 6.91 (d, 2 H, J = 7.7 Hz), 7.04 (t, 2 H, J = 7.2 Hz), 7.10–7.18 (m, 1 H), 7.28–7.36 (m, 2 H), 7.60–7.65 (m, 1 H), 7.98–8.05 (m, 1 H); ^{13}C NMR δ 13.9, 14.7, 18.8, 22.4, 27.9, 28.5, 31.2, 61.8, 72.1, 79.0, 93.1, 94.0, 112.1, 119.8, 129.7, 127.2, 127.3, 127.4, 128.3, 132.7, 136.0, 146.1. Anal. Calcd for $C_{24}H_{29}N_3O_2$: C, 73.61; H, 7.47; N, 10.74. Found: C, 73.95; H, 7.64; N, 10.57. **Isomer 2**: an oil; ^{1}H NMR δ 0.88 (t, 3 H, J = 6.9 Hz), 1.17 (t, 3 H, J = 7.0 Hz), 1.21–1.40 (m, 6 H), 1.57 (quint, 2 H, J = 7.3 Hz), 2.38 (t, 2 H, J = 7.2 Hz), 3.20–3.30 (m, 1 H), 3.63 (d, 1 H, J = 4.4 Hz), 3.80–3.90 (m, 1 H), 5.43 (d, 1 H, J = 4.2 Hz), 7.18–7.38 (m, 7 H), 7.75 (d, 1 H, J = 8.2 Hz), 7.93 (d, 1 H, J = 8.2 Hz); ^{13}C NMR δ 13.9, 14.5, 18.7, 22.4, 27.8, 28.5, 31.1, 61.6, 72.8, 78.8, 92.9, 93.7, 112.5, 119.6, 123.7, 127.1, 127.2, 128.0, 128.1, 132.8, 137.3, 146.0. Anal. Calcd for $C_{24}H_{29}N_3O_2$: C, 73.61; H, 7.47; N, 10.74. Found: C, 73.91; H, 7.68; N, 10.61.

3-(Benzotriazol-1-yl)-3-ethoxy-4-hydroxy-1,4,4-triphenyl-1-butyne (8a): yield 77%; mp 110–111 °C; ^{1}H NMR δ 1.40 (t, 3 H, J = 7.1 Hz), 3.40–3.50 (m, 1 H), 3.84 (br s, 1 H), 4.25–4.35 (m, 1 H), 6.88–95 (m, 1 H), 7.02–7.40 (m, 15 H), 7.55–7.65 (m, 2 H), 7.93 (d, 1 H, J = 8.3 Hz); ^{13}C NMR δ 14.7, 62.6, 83.2, 84.1, 93.4, 95.9, 112.5, 119.3, 120.8, 123.2, 126.8, 127.2, 127.4, 127.5, 127.6, 128.0, 128.4, 129.1, 129.6, 131.9, 133.3, 145.4. Anal. Calcd for $C_{30}H_{25}N_3O_2$: C, 78.41; H, 5.48; N, 9.14. Found: C, 78.40; H, 5.65; N, 8.92.

3-(Benzotriazol-1-yl)-3-ethoxy-4-hydroxy-4-methyl-1-phenyl-1-pentyne (8b): yield 66%; mp 172–173 °C; ^{1}H NMR δ 1.29 (s, 3 H), 1.34 (t, 3 H, J = 7.1 Hz), 1.58 (s, 3 H), 2.85 (br s, 1 H), 3.37–3.47 (m, 1 H), 4.08–4.18 (m, 1 H), 7.30–7.50 (m, 5 H), 7.58–7.62 (m, 2 H), 7.95 (d, 1 H, J = 8.4 Hz), 8.04 (d, 1 H, J = 8.4 Hz); ^{13}C NMR δ 14.7, 24.7, 25.6, 62.5, 78.4, 82.9, 90.6, 96.0, 113.7, 119.6, 121.1, 123.7, 127.3, 128.4, 129.4, 132.0, 133.2, 146.1. Anal. Calcd for $C_{20}H_{21}N_3O_2$: C, 71.62; H, 6.31; N, 12.53. Found: C, 71.62; H, 6.28; N, 12.53.

1-(Benzotriazol-1-yl)-1-ethoxy-1-(trimethylsilyl)-2-nonyne (10): obtained as an oil; yield 78%; ^{1}H NMR δ 0.30 (s, 9 H), 0.88 (t, 3 H, J = 7.1 Hz), 1.13 (t, 3 H, J = 7.1 Hz), 1.25–1.70 (m, 8 H), 2.43 (t, 2 H, J = 7.1 Hz), 3.25–3.35 (m, 1 H), 3.95–4.05 (m, 1 H), 7.33 (t, 1 H, J = 7.1 Hz) 7.44 (t, 1 H, J = 7.1 Hz), 8.03 (d, 1 H, J = 8.4 Hz), 8.10 (d, 1 H, J = 8.4 Hz); ^{13}C NMR δ −2.7, 13.9, 15.0, 18.9, 22.4, 28.3, 28.5, 31.2, 61.8, 75.1, 86.0, 93.5, 112.9, 119.7, 123.6, 126.7, 133.6, 146.1. Anal. Calcd for $C_{20}H_{31}N_3OSi$: C, 67.18; H, 8.75; N, 11.76. Found: C, 67.50; H, 9.10; N, 11.72.

3-(Benzotriazol-1-yl)-3-ethoxy-4-(*p*-methylphenyl)-4-[(*p*-methylphenyl)amino]-1-phenyl-1-butyne (12): yield 85%; mp 143–145 °C; ^{1}H NMR δ 1.20 (t, 3 H, J = 7.1 Hz), 2.03 (s, 3 H), 2.23 (s, 3 H), 3.30–3.40 (m, 1 H), 3.90–4.00 (m, 1 H), 4.67 (d, 1 H, J = 7.4 Hz), 5.21 (d, 1 H, J = 7.4 Hz), 6.32 (d, 2 H, J = 8.5 Hz), 6.72 (d, 2 H, J = 8.5 Hz), 7.02 (d, 2 H, J = 8.0 Hz), 7.20–7.35 (m, 7 H), 7.49–7.55 (m, 2 H), 7.75 (d, 1 H, J = 8.2 Hz), 7.99 (d, 1 H, J = 8.2 Hz); ^{13}C NMR δ 14.4, 20.0, 20.9, 61.9, 65.9, 81.6, 91.6, 93.2, 111.8, 113.6, 119.8, 120.8, 123.7, 126.6, 127.3, 128.3, 128.7, 129.2, 129.4, 132.0, 134.1, 137.4, 143.7, 146.3. Anal. Calcd for $C_{32}H_{30}N_4O$: C, 78.97; H, 6.22; N, 11.52. Found: C, 79.16; H, 6.23; N, 11.52.

3-(Benzotriazol-1-yl)-3-ethoxy-1-phenyl-1-pentyn-4-one (14): yield 65%; mp 94–95 °C; ^{1}H NMR δ 1.26 (t, 3 H, J = 7.1 Hz), 2.51 (s, 3 H), 3.30–3.40 (m, 1 H), 4.08–4.14 (m, 1 H), 7.35–7.55 (m, 5 H), 7.64 (d, 2 H, J = 8.1 Hz), 7.71 (d, 1 H, J = 8.3 Hz), 8.12 (d, 1 H, J = 8.2 Hz); ^{13}C NMR δ 14.7, 24.1, 62.1, 79.6, 90.6, 92.8, 111.6, 120.1, 120.4, 124.3, 128.0, 128.5, 129.9, 132.0, 132.1, 146.5, 195.0. Anal. Calcd for $C_{19}H_{17}N_3O_2$: C, 71.44; H, 5.37; N, 13.16. Found: C, 71.67; H, 5.35; N, 13.18.

Ethyl 2-(benzotriazol-1-yl)-2-ethoxy-4-phenyl-3-butynoate (16): obtained as an oil; yield 35%; ^{1}H NMR δ 1.20 (t, 3 H, J = 7.1 Hz), 1.25 (t, 3 H, J = 7.1 Hz), 3.39–3.49 (m, 1 H), 4.00–4.10 (m, 1 H), 4.30 (q, 2 H, J = 7.1 Hz), 7.35–7.45 (m, 4 H), 7.51 (t, 1 H, J = 7.2 Hz), 7.61 (dd, 2 H, J = 6.6, 2.1 Hz), 7.84 (d, 1 H, J = 8.3 Hz), 8.10 (d, 1 H, J = 8.3 Hz); ^{13}C NMR δ 13.7, 14.6, 62.0, 63.5, 79.7, 86.4, 90.9, 111.5, 120.0, 120.5, 124.3, 127.9, 128.3, 129.7, 131.7, 132.1, 146.4, 164.0. Anal. Calcd for $C_{20}H_{19}N_3O_3$: C, 68.74; H, 5.48; N, 12.03. Found: C, 68.99; H, 5.72; N, 12.25.

3-(Benzotriazol-1-yl)-3-ethoxy1-phenyl-3-[(*tert*-butylamino)carbonyl]-1-butyne (18): yield 54%; mp 131–132 °C; ^{1}H NMR δ 1.22 (t, 3 H, J = 7.1 Hz), 1.45 (s, 9 H), 3.24–3.34 (m, 1 H), 4.10–4.20 (m, 1 H), 6.97 (br s, 1 H), 7.34–7.42 (m, 4 H), 7.49 (t, 1 H, J = 7.2 Hz), 7.64 (dd, 2 H, J = 6.6, 2.0 Hz), 7.80 (d, 1 H, J = 8.3 Hz), 8.10 (d, 1 H, J = 8.3 Hz); ^{13}C NMR δ 14.7, 28.4, 52.0, 62.2, 80.9, 87.2, 90.2, 111.5, 120.0, 120.7, 124.1, 127.7, 128.4, 129.7, 132.0, 132.2, 146.5, 162.7. Anal. Calcd for $C_{22}H_{24}N_4O_2$: C, 70.18; H, 6.43; N, 14.89. Found: C, 70.48; H, 6.47; N, 14.92.

3-(Benzotriazol-1-yl)-2,3-dihydro-3-ethoxy-5-phenyl-2-thiophenethione (21): yield 57%; mp 120–122 °C; ^{1}H NMR δ 1.40 (t, 3 H, J = 7.0 Hz), 3.75–3.90 (m, 2 H), 6.88 (s, 1 H),

7.37 (t, 1 H, J = 7.1 Hz), 7.47–7.52 (m, 4 H), 7.60–7.66 (m, 2 H), 8.02 (d, 1 H, J = 8.4 Hz), 8.21 (d, 1 H, J = 8.4 Hz); ^{13}C NMR δ 15.1, 61.5, 104.2, 114.7, 119.4, 119.6, 124.3, 126.8, 127.5, 129.2, 130.7, 130.8, 131.9, 144.9, 146.4, 230.8. Anal. Calcd for $C_{18}H_{15}N_3S_2O$: C, 61.18; H, 4.28; N, 11.90. Found: C, 61.46; H, 4.55; N, 11.87.

3-(Benzotriazol-1-yl)-2,3-dihydro-3-ethoxy-1-(naphthylimino)-5-phenylthiophene (23): yield 64%; mp 158–159 °C; ^{1}H NMR δ 1.44 (t, 3 H, J = 7.0 Hz), 3.75–3.85 (m, 1 H), 3.98–4.08 (m, 1 H), 6.88 (s, 1 H), 7.08 (d, 1 H, J = 7.3 Hz), 7.22–7.60 (m, 11 H), 7.65 (d, 1 H, J = 6.5 Hz), 7.77 (d, 1 H, J = 6.5 Hz), 8.12 (d, 1 H, J = 8.3 Hz), 8.40 (d, 1 H, J = 8.3 Hz); ^{13}C NMR δ 15.3, 61.2, 101.8, 113.3, 114.8, 115.0, 119.5, 123.1, 124.2, 125.4, 126.0, 126.2, 126.5, 126.6, 126.7, 127.5, 127.7, 128.8, 130.4, 132.1, 132.5, 133.9, 144.4, 146.4, 146.7, 165.2. Anal. Calcd for $C_{28}H_{22}N_4SO$: C, 72.70; H, 4.80; N, 12.12. Found: C, 72.83; H, 4.79; N, 12.04.

General Procedure for the Preparation of Alkynyl Ketones 5a–e, 7a,b, 9a,b, 11, 13, 15, 17, 19, 26, 29a,b, 32, and 33. 3-(Benzotriazol-1-yl)-3-ethoxyalkynes **4a–e, 6a,b, 8a,b, 10, 12, 14, 16, 18, 25, 28a,b, 30,** and **31** (5 mmol) were dissolved in 15 mL of acetone (or MeOH, EtOH). The solution was cooled to 5 °C, and a cold HCl (or H_2SO_4) solution (4 mL in 15–20 mL of acetone or MeOH) was added. The mixture was stirred for 10–20 min at 5–20 °C. The solution was then extracted with ether (2 × 50 mL), washed with a saturated Na_2CO_3 solution (2 × 100 mL), and dried with $MgSO_4$. Evaporation of the solvent gave pure products. In the case of **13**, a white precipitate was collected after the addition of water.

1-Phenyl-1-pentyn-3-one (5a). This compound was obtained as an oil:[47] yield 90%; ^{1}H NMR δ 1.20 (t, 3 H, J = 7.4 Hz), 2.67 (q, 2 H, J = 7.4 Hz), 7.32–7.45 (m, 3 H), 7.55 (d, 2 H, J = 6.8 Hz); ^{13}C NMR δ 8.0, 38.6, 87.5, 90.4, 119.9, 128.4, 130.5, 132.8, 188.2. Anal. Calcd for $C_{11}H_{10}O$: C, 83.51; H, 6.38. Found: C, 83.49; H, 6.59.

6-Methyl-1-phenyl-1-heptyn-3-one (5b): obtained as an oil; yield 93%; ^{1}H NMR δ 0.96 (d, 6 H, J = 5.5 Hz), 1.60–1.70 (m, 3 H), 2.68 (t, 2 H, J = 7.1 Hz), 7.45–7.50 (m, 3 H), 7.57 (d, 2 H, J = 8.2 Hz); ^{13}C NMR δ 22.3, 27.6, 32.9, 43.6, 87.9, 90.5, 120.1, 128.6, 130.6, 133.0, 188.3. Anal. Calcd for $C_{11}H_{10}O$: C, 83.95; H, 8.06. Found: C, 83.74; H, 8.17.

1,4-Diphenyl-1-butyn-3-one (5c): obtained as an oil; yield 86%; ^{1}H NMR δ 3.93 (s, 2 H), 7.30–7.50 (m, 10 H); ^{13}C NMR δ 52.1, 87.7, 92.8, 119.7, 127.3, 128.5, 128.6, 129.8, 130.7, 133.0, 133.2, 185.1. Anal. Calcd for $C_{16}H_{12}O$: C, 87.24; H, 5.50. Found: C, 86.99; H, 5.74.

1-Phenyl-1-nondecyn-3-one (5d): yield 86%; mp 45–46 °C; ^{1}H NMR δ 0.89 (t, 3 H, J = 6.5 Hz), 1.20–1.40 (m, 26 H), 1.75 (quint, 2 H, J = 7.5 Hz), 2.67 (t, 2 H, J = 7.5 Hz), 7.30–7.45 (m, 3 H), 7.56 (d, 2 H, J = 6.5 Hz); ^{13}C NMR δ 14.1, 22.6, 22.7, 24.2, 29.0, 29.3, 29.4, 29.5, 29.6, 29.7, 31.6, 31.9, 45.5, 87.8, 90.4, 120.1, 128.6, 130.6, 133.0, 188.1. Anal Calcd for $C_{25}H_{38}O$: C, 84.68; H, 10.81. Found: C, 84.54; H, 10.93.

4-Undecyn-3-one (5e): obtained as an oil;[1] yield 92%; ^{1}H NMR δ 0.91 (t, 3 H, J = 6.6 Hz), 1.14 (t, 3 H, J = 7.4 Hz), 1.22–1.48 (m, 6 H), 1.54–1.65 (m, 2 H), 2.37 (t, 2 H, J = 7.1 Hz), 2.55 (q, 2 H, J = 7.4 Hz); ^{13}C NMR δ 8.0, 13.9, 18.8, 22.4, 27.6, 28.4, 31.1, 38.7, 80.6, 94.1, 188.6. Anal. Calcd for $C_{11}H_{18}O$: C, 79.45; H, 10.92. Found: C, 79.11; H, 11.14.

4-Hydroxy-4-(*p*-methylphenyl)-1-phenyl-1-butyn-3-one (7a): yield 84%; mp 69–71 °C; ^{1}H NMR δ 2.33 (s, 3 H), 4.15 (br s, 1 H), 5.29 (s, 1 H), 7.20 (d, 2 H, J = 7.8 Hz), 7.30–7.37 (m, 4 H), 7.40–7.46 (m, 3 H); ^{13}C NMR δ 21.1, 80.8, 85.2, 98.0, 119.3, 127.4, 128.6, 129.4, 131.2, 133.0, 134.0, 138.6, 186.5. Anal. Calcd for $C_{17}H_{14}O_2$: C, 81.57; H, 5.64. Found: C, 81.25; H, 5.61.

1-Hydroxy-1-phenyl-3-decyn-2-one (7b): obtained as an oil; yield 98%; ^{1}H NMR δ 0.87 (t, 3 H, J = 6.9 Hz), 1.15–1.30 (m, 6 H), 1.44 (quint, 2 H, J = 7.3 Hz), 2.28 (t, 2 H, J = 7.0 Hz), 4.12–4.25 (br s, 1 H), 5.18 (s, 1 H), 7.40–7.50 (m, 5 H); ^{13}C NMR δ 13.8, 19.0, 22.3, 27.2, 28.2, 31.0, 78.0, 80.9, 102.4, 127.4, 128.4, 137.0, 186.4. Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.64; H, 8.26. Found: C, 78.48; H, 8.43.

4-Hydroxy-1,4,4-triphenyl-1-butyn-3-one (9a): obtained as an oil; yield 98%; ^{1}H NMR δ 4.76 (s, 1 H), 7.30–7.45 (m, 11 H), 7.55–7.60 (m, 4 H); ^{13}C NMR δ 85.8, 86.3, 100.3, 119.4, 128.1, 128.2, 128.3, 128.6, 131.3, 133.0, 141.2, 188.0. Anal. Calcd for $C_{22}H_{16}O_2$: C, 84.59; H, 5.16. Found: C, 84.66; H, 5.33.

4-Hydroxy-4-methyl-1-phenyl-1-butyn-3-one (9b): obtained as an oil;[29,30] yield 100%; ^{1}H NMR δ 1.56 (s, 6 H), 3.70 (s, 1 H), 7.39–7.52 (m, 3 H), 7.60 (d, 2 H, J = 6.9 Hz); ^{13}C NMR δ 26.3, 77.0, 84.3, 96.3, 119.1, 128.4, 130.9, 132.8, 192.0. Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.56; H, 6.43. Found: C, 76.35; H, 6.64.

1-(Trimethylsilyl)-2-nonyn-1-one (11): obtained as an oil; yield 88%; ^{1}H NMR δ 0.26 (s, 9 H), 0.91 (t, 3 H, J = 6.9 Hz), 1.24–1.50 (m, 6 H), 1.62 (quint, 2 H, J = 6.9 Hz), 2.47 (t, 2 H, J = 7.1 Hz); ^{13}C NMR δ –3.7, 13.9, 19.4, 22.4, 27.8, 28.5, 31.2, 84.5, 103.9, 226.5. Anal. Calcd for $C_{12}H_{22}OSi$: C, 68.52; H, 10.55. Found: C, 68.28; H, 10.60.

4-(*p*-Methylphenyl)-4-[(*p*-methylphenyl)amino]-1-phenyl-1-butyn-3-one (13): yield 90%; mp 124–126 °C; ^{1}H NMR δ 2.20 (s, 3 H), 2.33 (s, 3 H), 5.22 (s, 1 H), 5.85 (br s, 1 H), 6.60 (d, 2 H, J = 8.5 Hz), 6.92 (d, 2 H, J = 8.6 Hz), 7.20 (d, 2H, J = 7.8 Hz), 7.30–7.50 (m, 7 H); ^{13}C NMR δ 20.4, 21.2, 69.6, 86.3, 95.5, 114.5, 119.6, 128.1, 128.2, 128.6, 129.7, 129.8, 131.0, 133.1, 133.2, 138.5, 142,6, 183.8. Anal. Calcd for $C_{24}H_{21}NO$: C, 84.92; H, 6.24; N, 4.13. Found: C, 84.61; H, 6.59; N, 4.12.

1-Phenyl-1-pentyne-3,4-dione (15): obtained as an oil;[48] yield 92%; ^{1}H NMR δ 2.45 (s, 3 H), 7.40–7.55 (m, 3 H), 7.66 (d, 2 H, J = 7.0 Hz); ^{13}C NMR δ 23.7, 85.8, 99.3, 119.3, 128.6, 131.5, 133.6, 175.6, 194.1. Anal. Calcd for $C_{11}H_8O_2$: C, 76.72; H, 4.69. Found: C, 76.91; H, 4.80.

Ethyl 2-oxo-4-phenyl-3-butynoate (17): obtained as an oil; yield 90%; ^{1}H NMR δ 1.41 (t, 3 H, J = 7.2 Hz), 4.39 (q, 2 H, J = 7.2 Hz), 7.41 (t, 2 H, J = 7.5 Hz), 7.51 (t, 3 H, J = 7.6 Hz), 7.67 (d, 2 H, J = 7.0 Hz); ^{13}C NMR δ 13.9, 63.2, 87.1, 97.8, 119.0, 128.7, 131.7, 133.7, 159.1, 169.5. Anal. Calcd for $C_{12}H_{10}O_3$: C, 71.26; H, 4.99. Found: C, 71.08; H, 5.37.

***N*-*tert*-Butyl-2-oxo-4-phenyl-3-butynamide (19):** obtained as an oil; yield 99%; ^{1}H NMR δ 1.44 (s, 9 H), 6.92 (br s, 1 H), 7.43 (t, 2 H, J = 7.5 Hz), 7.50 (t, 1 H, J = 7.6 Hz), 7.71 (d, 2 H, J = 7.0 Hz); ^{13}C NMR δ 29.8, 53.2, 88.2, 101.1, 121.0, 130.2, 133.1, 135.4, 159.4, 177.1. Anal. Calcd for $C_{14}H_{15}O_2N$: C, 73.33; H, 6.60; N, 6.11. Found: C, 73.39; H, 6.71; N, 6.05.

1-Hydroxy-1-(*p*-tolyl)-2-dodecyn-4-one (26): obtained as an oil; yield 99%; ^{1}H NMR δ 0.89 (t, 3 H, J = 7.0 Hz), 1.20–1.32 (m, 10 H), 1.64 (quint, 2 H, J = 7.3 Hz), 2.35 (s, 3 H), 2.56 (t, 2 H, J = 7.3 Hz), 3.45 (br s, 1 H), 5.53 (s, 1 H), 7.19 (d, 2 H, J = 7.9 Hz), 7.36 (d, 2 H, J = 8.2 Hz); ^{13}C NMR δ 14.0, 21.1, 22.5, 23.8, 28.9, 29.2, 31.7, 45.3, 64.0, 84.4, 91.1, 126.5, 129.4, 136.0, 138.5, 188.1. Anal. Calcd for $C_{19}H_{26}O_2$: C, 79.67; H, 9.16. Found: C, 79.46; H, 9.29.

1-Decyn-3-one (29a): obtained as an oil;[49] yield 92%; ^{1}H NMR δ 0.90 (t, 3 H, J = 7.0 Hz), 1.25–1.35 (m, 8 H), 1.65–1.72 (m, 2 H), 2.60 (t, 2 H, J = 7.5 Hz), 3.26 (s, 1 H); ^{13}C NMR δ 13.9, 22.5, 23.7, 28.8, 28.9, 31.5, 45.4, 78.2, 81.4, 187.4. Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.60. Found: C, 78.57; H, 10.74.

1-Undecyn-3-one (29b): obtained as an oil;[50] yield 94%; ^{1}H NMR δ 0.88 (t, 3 H, J = 6.9 Hz), 1.25–1.35 (m, 10 H), 1.65–1.72 (m, 2 H), 2.59 (t, 2 H, J = 7.5 Hz), 3.23 (s, 1 H); ^{13}C NMR δ 14.0, 22.6, 23.7, 28.8, 29.0, 29.2, 31.7, 45.4, 78.2, 81.4, 187.4. Anal. Calcd for $C_{11}H_{18}O$: C, 79.45; H, 10.92. Found: C, 79.22; H, 11.16.

1,5-Dihydroxy-5-phenyl-1-(*p*-tolyl)-3-pentyn-2-one (32): obtained as an oil (a mixture of two diasteromers): yield 98%; ^{1}H NMR δ 2.30 (s, 3 H), 3.88–3.97 (m, 1 H), 4.27–4.31 (m, 1 H), 5.05–5.10 (br s, 1 H), 5.30–5.38 (m, 1 H), 7.02–7.30 (m, 9 H); ^{13}C NMR δ 21.1, 63.8 (63.9), 80.6, 80.7 (81.8), 97.8 (98.0),

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126.4 (126.5), 127.4, 128.51 (128.55), 128.6, 129.4, 133.3, 138.1 (138.2), 138.6, 186.3 (186.4). Anal. Calcd for $C_{18}H_{16}O_3$: C, 77.11; H, 5.76. Found: C, 76.93; H, 6.03.

1-Phenyl-1-(phenylamino)-4-(1′-hydroxycyclohexyl)-3-butyn-2-one (33): yield 98%; mp 112–114 °C; ^{1}H NMR δ 1.15–1.68 (m, 8 H), 1,76–1.88 (m, 2 H), 2.59 (br s, 1 H), 5.10 (s, 1 H), 5.26 (br s, 1 H), 6.56 (d, 2 H, J = 7.6 Hz), 6.67 (t, 1 H, J = 7.4 Hz), 7.11 (t, 2 H, J = 7.4 Hz), 7.30–7.39 (m, 3 H), 7.47 (d, 2 H, J = 6.6 Hz); ^{13}C NMR δ 22.7, 22.8, 24.7, 38.8, 38.9, 68.6, 69.1, 81.2, 100.2, 113.5, 118.1, 128.1, 128.6, 129.0, 129.1, 136.6, 145.7, 190.0. Anal. Calcd for $C_{22}H_{23}O_2N$: C, 79.24; H, 6.96; N, 4.20. Found: C, 78.94; H, 7.12; N, 4.55.

General Procedure for the Lithiation of Compound 27. Preparation of 25, 28a,b, 30, and 31. To a solution of 1-(benzotriazol-1-yl)propargyl ethyl ether (**27**) (5 mmol) in THF (70 mL) at −78 °C was added n-butyllithium (2 M in cyclohexane, 2.5 mL, 5 mmol), and the solution was stirred for 2 min at this temperature. After the appropriate electrophile (p-tolualdehyde, $C_7H_{15}Br$, $C_8H_{17}Br$, benzaldehyde, or cyclohexanone; 5 mmol) was added, the mixture was stirred at this temperature for 20 min. A second equivalent of BuLi (2 M in cyclohexane, 2.5 mL, 5 mmol) was added, and the solution was kept at −78 °C for an additional 2 min. In the cases of **28a,b**, the reaction was quenched at this temperature with water (30 mL), and the mixture was extracted with diethyl ether (2 × 100 mL) and dried with $MgSO_4$. Evaporation of the solvent gave the expected product in pure form without further purification. In the cases of **25, 30,** and **31**, a second electrophile ($C_8H_{17}Br$, p-tolualdehyde, or PhCH=NPh; 5 mmol) was added, and the solution was reacted for another 2 min. The reaction was quenched at this temperature with water (30 mL), and the mixture was extracted with diethyl ether (2 × 100 mL) and dried with $MgSO_4$. Evaporation of the solvent gave a residue, which was purified by column chromatography on silica gel (hexane/ethyl acetate = 10:1). As compounds **30** and **31** are mixtures of several diastereomers due to the existence of three chiral centers, the NMR spectra were complex. Only elemental analyses are given for these two compounds.

4-(Benzotriazol-1-yl)-4-ethoxy-1-hydroxy-1-(p-tolyl)-2-dodecyne (25): obtained as an oil; yield 73%; ^{1}H NMR δ 1.09 (t, 3 H, J = 6.9 Hz), 1.30–1.55 (m, 14 H), 1.70–1.80 (m, 1 H), 2.59 (s, 3 H), 2.60–2.68 (m, 2 H), 3.30–3.40 (m, 1 H), 4.02–4.12 (m, 1 H), 5.23 (d, 1 H, J = 5.5 Hz), 6.02 (d, 1 H, J = 5.4 Hz), 7.43 (d, 2 H, J = 7.9 Hz), 7.59 (t, 1 H, J = 7.2 Hz), 7.64 (t, 1 H, J = 7.2 Hz), 7.79 (d, 2 H, J = 6.2 Hz), 8.16 (d, 1 H, J = 8.3 Hz), 8.29 (d, 1 H, J = 8.3 Hz); ^{13}C NMR δ 13.8, 14.5, 20.9, 22.4, 23.7, 28.9, 29.0, 31.6, 41.5, 61.0, 63.9, 80.0, 90.4, 90.9, 112.2, 119.7, 124.0, 126.7, 127.4, 129.0, 131.4, 137.3, 137.7, 146.3. Anal. Calcd for $C_{27}H_{35}N_3O_2$: C, 74.78; H, 8.14; N, 9.70. Found: C, 75.00; H, 8.30; N, 9.43.

3-(Benzotriazol-1-yl)-3-ethoxy-1-decyne (28a): obtained as an oil; yield 90%; ^{1}H NMR δ 0.85 (t, 3 H, J = 7.0 Hz), 1.15–1.35 (m, 12 H), 1.65–1.75 (m, 1 H), 2.44 (t, 2 H, J = 7.9 Hz), 3.11 (s, 1 H), 3.15–3.25 (m, 1 H), 3.85–3.95 (m, 1 H), 7.40 (t, 1 H, J = 7.5 Hz), 7.51 (t, 1 H, J = 7.1 Hz), 7.94 (d, 1 H, J = 8.3 Hz), 8.10 (d, 1 H, J = 8.3 Hz); ^{13}C NMR δ 13.8, 14.5, 22.3, 23.6, 28.7, 28.8, 31.4, 41.2, 60.9, 77.4, 77.9, 90.3, 111.9, 119.9, 123.9, 127.3, 131.2, 146.6. Anal. Calcd for $C_{18}H_{25}N_3O$: C, 72.19; H, 8.42; N, 14.04. Found: C, 72.48; H, 8.58; N, 13.95.

3-(Benzotriazol-1-yl)-3-ethoxy-1-undecyne (28b): obtained as an oil; yield 95%; ^{1}H NMR δ 0.86 (t, 3 H, J = 7.0 Hz), 1.10–1.35 (m, 14 H), 1.60–1.70 (m, 1 H), 2.41 (t, 2 H, J = 8.2 Hz), 3.05 (s, 1 H), 3.15–3.21 (m, 1 H), 3.86–3.91 (m, 1 H), 7.40 (t, 1 H, J = 7.1 Hz), 7.50 (t, 1 H, J = 7.0 Hz), 7.92 (d, 1 H, J = 8.3 Hz), 8.10 (d, 1 H, J = 8.3 Hz); ^{13}C NMR δ 14.0, 14.7, 22.5, 23.8, 28.9, 29.0, 29.1, 31.7, 41.4, 61.0, 77.9, 78.1, 90.6, 112.1, 120.2, 124.1, 127.5, 131.4, 146.8. Anal. Calcd for $C_{19}H_{27}N_3O$: C, 72.79; H, 8.69; N, 13.41. Found: C, 73.10; H, 8.94; N, 13.07.

2-(Benzotriazol-1-yl)-1,5-dihydroxy-2-ethoxy-5-phenyl-1-(p-tolyl)-3-pentyne (30): obtained as an oil; yield 85%. Anal. Calcd for $C_{26}H_{25}N_3O_3$: C, 73.04; H, 5.90; N, 9.83. Found: C, 72.70; H, 5.87; N, 9.90.

2-(Benzotriazol-1-yl)-2-ethoxy-4-(1′-hydroxycyclohexyl)-1-phenyl-1-(phenylamino)-3-butyne (31): obtained as an oil; yield 63%. Anal. Calcd for $C_{30}H_{32}N_4O_2$: C, 74.96; H, 6.72; N, 11.66. Found: C, 75.30; H, 6.95; N, 11.56.

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