Novel Syntheses of α,β-Unsaturated Esters, α,β-Unsaturated γ-Lactones, and 2-Alkoxypyrroles *via* 1,2,4-Triazole-Stabilized Allenic Anions

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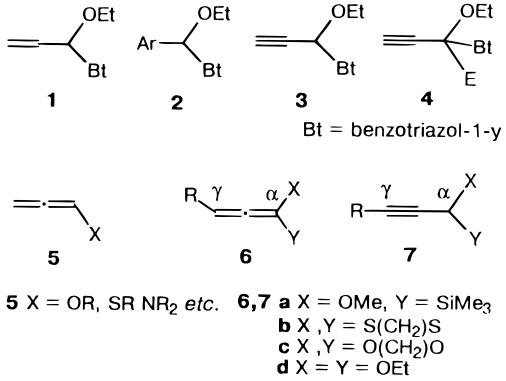
The dianion **12** (⇌ **13**) of 1-(1,2,4-triazol-1-yl)phenylpropargyl ethyl ether **11** (readily prepared from phenylpropargylaldehyde diethyl acetal **8** and 1,2,4-triazole) reacts with alkyl halides, aldehydes, ketones, and α,β-unsaturated ketones to give exclusively γ-substituted allenic products of type **10**. These adducts underwent mild *in situ* hydrolysis enabling convenient syntheses of α,β-unsaturated esters **9a**−**c** and α,β-unsaturated γ-lactones **16**, **18**, **20**, and **22**. Reactions of dianion **13** with imines generated the 1,3,4-trisubstituted 2-alkoxypyrroles **27**, **30**, and **31** in high yields. The alkyl-substituted analog **34** underwent similar reactions to give predominantly the γ-products **39**, **40**, and **42** along with a small proportion of α-analogs.

We have recently reported convenient benzotriazole acyl anion methodologies for the synthesis of a wide variety of simple and functionalized alkenyl,[1−4] aryl/heteroaryl,[5] and alkynyl[6] ketones and of alkenoyl-, alkynoyl-, aroyl-, and heteroaroylsilanes.[7] We utilized benzotriazole-stabilized carbanions derived from **1**−**3** which share the following features: (i) convenient availability of starting materials; (ii) adequate reactivity toward various electrophiles including alkyl halides, aldehydes, ketones, and imines; and (iii) the intermediates can be hydrolyzed under mild conditions. Reactions with electrophiles are also regiospecific. Thus, 1-(benzotriazol-1-yl)propargyl ethyl ethers **3**, readily accessible from propargyl diethyl acetals and benzotriazole, undergo smooth lithiation at the methine proton and subsequent reactions with a wide range of electrophiles to give regioselective α-substituted derivatives **4**.[6] We now find that use of the 1,2,4-triazole group instead of benzotriazole in **3** changes the regiochemistry of electrophilic attack and directs the alkylation to occur exlusively at the γ-position in the case of the phenyl-substituted 1-(triazol-1-yl)propargyl ethyl ether **11** and mainly at the γ-position in the case of the alkyl-substituted 1-(triazol-1-yl)propargyl ethyl ether **33**, forming synthetically useful allene derivatives of types **10** and **37**.

Allenes are very useful intermediates in organic synthesis due to their diverse transformations *via* metalations and facile additions and cyclizations.[8,9] The regioselectivity of mono- and dilithiation in allenes of type **5** with one hetero substituent has been extensively investigated and been found to depend both on the substrate and on the electrophile introduced.[10−12] However, much less work has been done on the generation, reactivity, and synthetic utility of substituted allenes of type **6** with two hetero substituents. Clinet and Linstrumelle[13] deprotonated methoxyallene (**5**, X = MeO, R = H) and subsequently reacted it with trimethylsilyl chloride to produce 1-methoxy-1-(trimethylsilyl)allene (**6a**) which, upon treatment with an alkyllithium reagent, undergoes regioselective γ-alkylation. Treatment with LDA of species **6a** (R = H) gives the lithium acetylide of 1-(trimethylsilyl)propargyl ether.[14] An alternative route for the synthesis of allenes **6** is from acetylene derivatives **7**. However, such transformations are quite limited; while for R = Me_3Si, the species **7b**,**c** in most cases undergo mainly regioselective α-lithiation and alkylations, variable amount of γ-alkylated **6b**,**c** can be generated depending on the electrophiles used,[15,16] which limits their generality and wide application. Deprotonated acetylene **7d** (R = SMe) was reported to react with alkyl halides, aldehydes, and ketones to furnish selectively allene derivatives, which were then hydrolyzed to yield β-keto esters and β-(methylthio)-α,β-unsaturated γ-lactones.[17]



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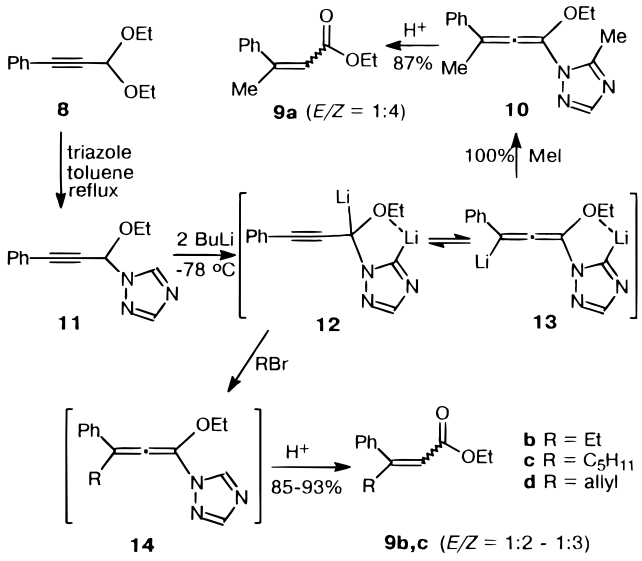
Scheme 1



Results and Discussion

Heating phenylpropargyl aldehyde diethyl acetal (**8**) with triazole in toluene for 2 days gave 1-(triazol-1-yl)-3-phenylproparyl ethyl ether (**11**) stable on storage at 20 °C for at least 3 months in 76% yield (Scheme 1). The structure of **11** was confirmed spectrally and by elemental analysis.

Synthesis of α,β-Unsaturated Esters. Unlike the benzotriazole analog **3**, triazole derivative **11** bears two acidic protons on the molecule, one on the methine group and the another at the 5-position of the triazole ring: 1-substituted 1,2,4-triazoles are known to undergo easy lithiation at the 5-position of the triazole ring.[18,19] Treatment of compound **11** with 1 equiv of butyllithium followed by reaction with methyl iodide or benzaldehyde led to a complex mixture including the α-, γ-, and triazole-alkylated products, as we observed from TLC and crude ^{1}H and ^{13}C NMR spectra.

Treatment of **11** with 2 equiv of butyllithium at −78 °C for a few minutes formed a dilithio derivative, which may have structure **12** or **13** or exists as a mixture of both. Subsequent reaction with 2 equiv of methyl iodide at the same temperature for a few minutes gave only **10** (>95% from NMR) in quantitative yield. The structure of **10** was determined by NMR spectra and the further analysis of the hydrolyzed product **9a**. ^{13}C NMR clearly showed the characteristic allene carbon (185 ppm) and the absence of signals for the triple bond and the quarternary carbon which would have been in the range 80−110 ppm. Attempted preparation of the analytically pure sample by column chromatography on silica gel resulted in partial hydrolysis to give rise to the expected α,β-unsaturated ester **9a**. Therefore, in a further experiment, intermediate **10** generated after lithiation of **11** and reaction with methyl iodide was directly hydrolyzed in a 50% aqueous ethanol containing a small amount of hydrochloric acid at 20 °C for 4 h without isolation. Two stereoisomers (*E*, and *Z*) of **9a** were isolated in yields of 17% and 70%, respectively. These *E* and- *Z* isomers were characterized by comparing their NMR spectra with those reported in the literature.[20]

The less reactive electrophiles ethyl bromide, pentyl bromide, and allyl bromide generated only the monoalkylated allenes **14b**−**d**. Analysis of the reaction products by ^{1}H NMR spectra showed the presence of two characteristic triazole protons and of one alkyl group (ethyl or pentyl). Accordingly, for the preparation of **9b**−**d**, only 1 equiv of the electrophile was used. Compounds **9b**−**d** were obtained in 79−93% yields when the intermediates **14b**−**d** were subjected to direct hydrolysis without isolation under similar conditions to those developed for **9a**. The ratios of the *E* and *Z* stereoisomers for **9b**,**c** are *ca.* 1:3 as determined by comparing their NMR spectra with literature.[20] For **9d** the assignment of *E* and *Z* isomers (ratio, 1:2) was accomplished by NMR (NOE technique).

The present results on the selective alkylation of the triazole ring with different electrophiles are consistent with those reported in the literature,[18,19] which indicated that the deprotonated 1-[(dialkyamino)methyl]-1,2,4-triazole reacts only with those reactive electrophiles (such as MeI, RCHO, or RCOR) to give the triazole-alkylated products. Independent of whether the triazole is alkylated or not, the triazole moiety, as a leaving group in the present work, will finally be hydrolyzed off and can be easily removed from the reaction mixture by washing with water during workup.

Synthesis of α,β-unsaturated esters is generally achieved by C=C bond formation from carbonyl compounds by Wittig−Horner,[21−23] Wadsworth−Emmons,[24] or Peterson reactions[25,26] or by reaction of mercaptoacetate derivatives including dianions[20,27,28] or of alkoxyacetylide anions.[29] Other available methods for their synthesis include oxidation of the corresponding α,β-unsaturated aldehydes[30] and addition of an organocopper reagent (nucleophile) to acetylenic esters.[31] The present approach, utilizing various electrophiles, readily affords β,β-disubstituted α,β-unsaturated esters of type **9**.

Synthesis of α,β-Unsaturated γ-Lactones. When anions **13** (⇌ **12**) were reacted with an aldehyde or a ketone followed by hydrolysis, the expected lactones of type **16a**−**c**, **18**, and **20** were easily prepared in 51−78% yields (Scheme 2). Under the acidic conditions, the hydroxyalkyl-substituted allenes **15a**−**c**, **17**, and **19** formed after lithiation and reactions with the carbonyl compounds underwent ready cyclization to give the five-membered cyclic products **16a**−**c**, **18**, and **20**. Thus, treatment of **11** with 2 equiv of butyllithium at −78 °C for 2 min, followed by reactions with the 2 equiv of cyclohexanone at this temperature for another 5 min,

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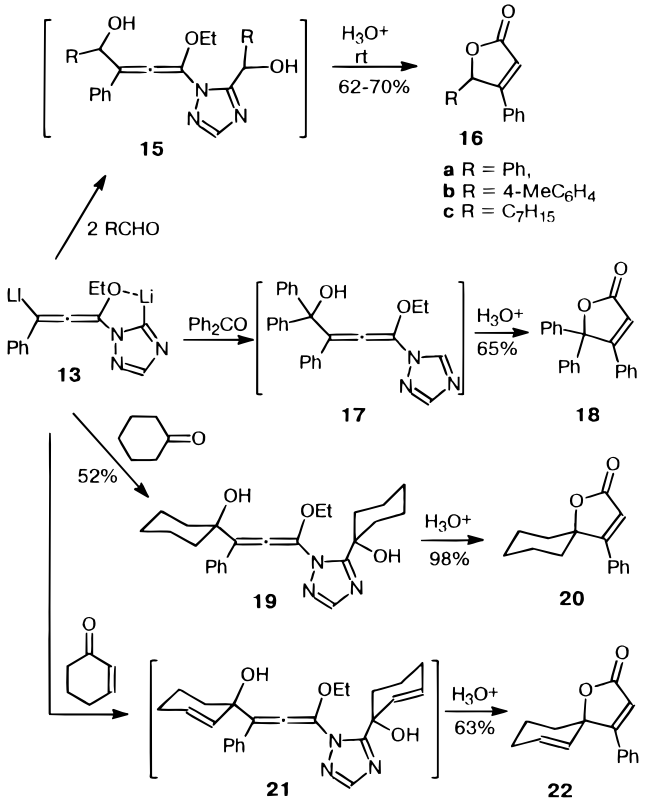
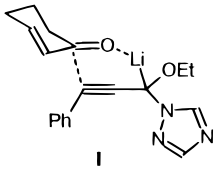
Scheme 2



gave the intermediate **19** in 62% yield. Subsequent treatment of **19** with 2 M hydrochloric acid in ethanol under reflux for 4 h gave the expected spirolactone **20** in 98% yield. Compounds **16a**−**c** and **18** were similarly prepared in 61−78% overall yields without isolation of the intermediates **15a**−**c** and **17**.

As mentioned previously, the triazole anion formed can also react with the relatively reactive electrophiles. Therefore in the cases of **16a**−**c** and **20**, 2 equiv of aldehydes was used in the reactions. Otherwise, low yields were achieved. However, in the case of **18** with benzophenone as electrophile, we found that only 1 equiv of benzophenone was consumed in the reaction. This can be rationalized by the the steric effect of benzophenone which prevents its reaction with triazole anion.

We have also used the reaction of **13** (⇌ **12**) with cyclohexenone to prepare lactone **22**. Interestingly, no 1,4-addition product was observed from the crude NMR spectra, which would give a ketone carbonyl signal in the range of 190−220 ppm. Normally, reactions of lithium agents with an α,*β*-unsaturated ketones produce mixture of 1,2- and 1,4-addition products. Exclusive formation of the 1,2-addition product probably involved the six-membered ring species **I**.



I

In the present reactions, formation of cyclic products **16**, **18**, **20**, and **22** relied on the *cis* hydrolyses of **15**, **17**, **19**, and **21**. The *trans* hydrolysis would not result in the cyclic products due to the difficult geometrical constraints. The reason for the *cis* hydrolysis in the present cases is still not clear.

α,*β*-Unsaturated butenolide moieties exists in many biologically important natural products, and a number of methods are available for its construction.[32] Transition-metal-catalyzed cyclizations (Pd,[33] Mn,[34] Zr,[35] Rh[36]) of various acetylene or olefin derivatives have been frequently employed. However, such reactions often require expensive catalysts. Methods closely related to the present approach for the synthesis of α,*β*-unsaturated butenolides comprise the lithiation of 3-sulfur-functionalized (PhSO or $PhSO_2$) acid derivatives[37,38] or equivalents[39] and subsequent reactions with carbonyl compounds followed by elimination of the sulfur functional group. However, only the butenolides without α- or *β*-substituents were prepared by these methods. Iwai *et al.*[40] reported a similar procedure utilizing the reactions of the dianions of 2-phenylthiocarboxy acids with epoxides to prepare α- or *β*-substituted α,*β*-unsaturated butenolides. Further methods used include treatment of 3-chloroacrylate successively with (i) a Grignard reagent, (ii) metal lithium, and (iii) carbon dioxide;[41] oxidation of cyclobutenones;[42] cyclocondensation of 4-oxo carboxylic acids[43] and cross-aldol condensation of an α-keto dimethyl acetal and a ketone enolate, followed by acid-promoted cyclization.[44] However, all these methods are limited by the availability of the starting materials or require multisteps operations. Our method commences with readily available starting materials and is a simple and high yielding procedure.

Synthesis of 1,3,5-Trisubstituted 2-Ethoxypyrroles. When *N*-benzylidineaniline was used as an electrophile to react with anion **13** (⇌ **12**) under similar conditions as in the cases **16a**−**c**, only *γ*-phenylamino-substituted (*Z*)-α,*β*-unsaturated ester **24** was generated in 70% yield (the *Z* configuation of **24** was assigned by NOE technique) (Scheme 3). No cyclized lactam was detected from the reaction. Further treatment of **24** in refluxing ethanol containing 20% 2 M sulfuric acid still does not produce any α,*β*-unsaturated *γ*-lactam. The reason for the *trans* hydrolysis of **23** is still unclear. However, carrying out the reaction at −78 °C for 15 h and then quenching with water resulted in the formation of 5-ethoxy-1,2,3-triphenylpyrrole **27a** presumably *via* the intermediate **26a** and subsequent intramolecular displacement of the triazole moiety. When we used *N*-(4-

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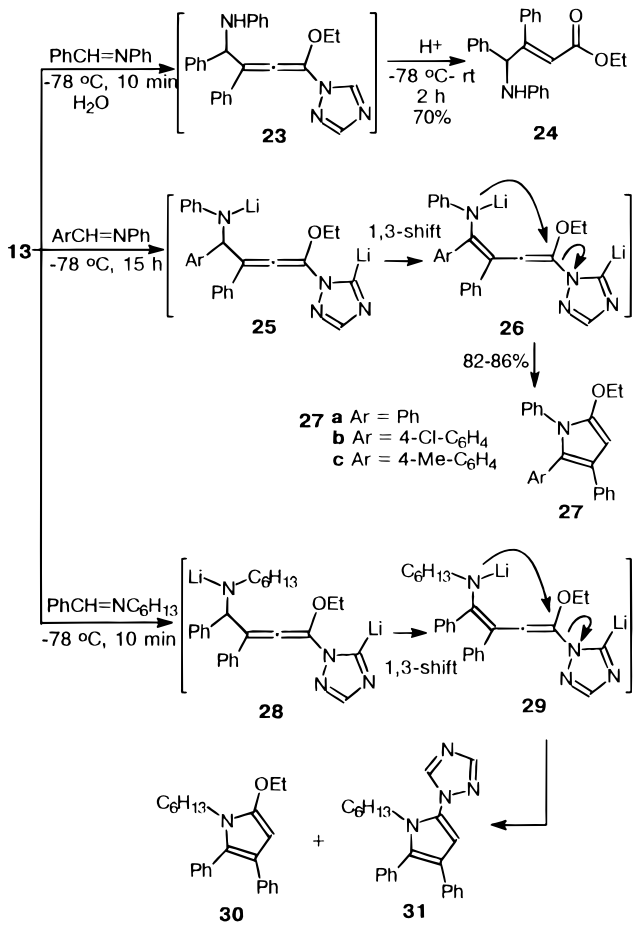
Scheme 3



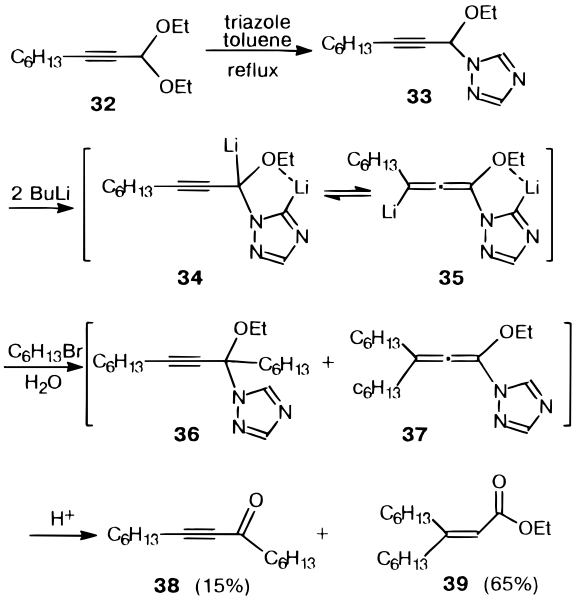
chlorobenzylidine)aniline and *N*-(4-methylbenzylidine)-aniline as electrophiles, the corresponding pyrroles **27b**,**c** were similarly prepared in 83% and 86% yields, respectively.

When an alkyl imine (obtained from benzaldehyde and primary alkylamine) was used as an electrophile to react with dianion **13** at −78 °C for a few minutes, two pyrrole derivatives **30** and **31** were obtained from the reaction. This is because the amido anion **29** formed is strongly nucleophilic and immediately attacks these α-carbon adjacent to triazolyl and ethoxy groups to generate the cyclized products **30** and **31**. In this reaction, both triazole and ethoxy have been used as leaving groups, which is different from previous cases. To the best of our knowledge, compounds of type **27**, **30**, and **31** were previously unknown.

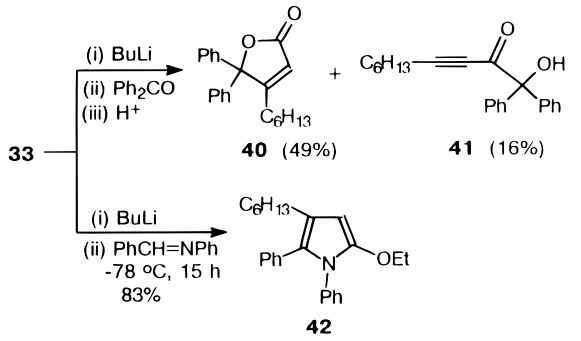
3-Alkyl-1-(triazol-1-yl)propargyl Ethyl Ether 33 as Starting Material Leading to Mainly γ-Products. Reaction of acetal **32** with triazole in refluxing toluene for 20 h produced 1-(triazol-1-yl)-3-hexylpropargyl ethyl ether (**33**) in 70% yield (Scheme 4). When compound **33** was treated with 2 equiv of butyllithium at −78 °C for a few minutes, dianion **34** (⇌ **35**) was formed similarly to the previous case. Subsequent reaction with hexyl bromide for *ca.* 10 min at the same temperature followed by hydrolysis with 2 M sulfuric acid gave α,*β*-unsaturated ester **39** and alkynyl ketone **38** in 65% and 15% yields, respectively, which is different from the phenyl-substituted case (**11**) where the *γ*-products are exclusive. The reason for this is not clear.

Use of benzophenone as an electrophile in the reaction with anion **34** (⇌ **35**) produced similar results with

Scheme 4



Scheme 5



formation of major *γ*-alkylated product **40** (49%) along with α-alkylated product **41** (16%) (Scheme 5). When we used *N*-benzylidineaniline as the electrophile, the expected pyrrole derivative **42** was obtained exclusively.

The structures for the final products and the isolated intermediates were confirmed by ^{1}H and ^{13}C NMR spectra and elemental analyses. The data for known compounds are consistent with those reported in literature.

Conclusions

Novel 1,2,4-triazole-stabilized allenic anions have been developed for the generation of α,*β*-unsaturated esters, *γ*-lactones, and 1,2,3,5-tetrasubstituted pyrroles. The simplicity and convenient availibility of the starting materials give these methods considerable potential importance in organic synthesis.

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.

Preparation of 1-(1,2,4-Triazol-1-yl)propargyl Ethyl Ethers 11 and 33. General Procedure. Propargyl aldehyde acetals **7** or **32** (30 mmol) and 1,2,4-triazole (36 mmol)

were heated under reflux in toluene (30 mL) for 30 h. The solvent was evaporated under reduced pressure, and the residues were chromatographed on silica gel (hexane/ethyl acetate 5 :1).

1-(1,2,4-Triazol-1-yl)-3-phenylpropargyl ethyl ether (11): obtained as a brown oil; yield 82%; ^{1}H NMR δ 1.25 (t, 3 H, J = 7.0 Hz), 3.63−3.80 (m, 2 H), 6.47 (s, 1 H), 7.34−7.41 (m, 3 H), 7.51−7.54 (m, 2 H), 8.02 (s, 1 H), 8.59 (s, 1 H); ^{13}C NMR δ 14.6, 63.9, 78.4, 80.9, 88.3, 120.5, 128.4, 129.6, 131.9, 142.6, 152.0. Anal. Calcd for $C_{13}H_{13}N_3O$: C, 68.71; H, 5.77; N, 18.49. Found: C, 68.50; H, 5.69; N, 18.50.

1-(1,2,4-Triazol-1-yl)-2-nonynyl ethyl ether (33): obtained as a colorless oil; yield 86%; ^{1}H NMR δ 0.91 (t, 3 H, J = 7.2 Hz), 1.21 (t, 3 H, J = 7.1 Hz), 1.28−1.44 (m, 6 H), 1.53−1.63 (m, 2 H), 2.31−2.36 (m, 2 H), 3.52−3.60 (m, 1 H), 3.62−3.72 (m, 1 H), 6.24 (t, 1 H, J = 1.9 Hz), 7.98 (s, 1 H), 8.51 (s, 1 H); ^{13}C NMR δ 13.8, 14.6, 18.5, 22.3, 27.8, 28.4, 31.1, 63.4, 72.7, 78.1, 90.1, 142.4, 151.8. Anal. Calcd for $C_{13}H_{21}N_3O$: C, 66.35; H, 8.99; N, 17.86. Found: C, 66.60; H, 9.20; N, 18.00.

General Procedure for the Preparation of Allenes 10 and 19, α,β-Unsaturated Ester 9a, and Butenolide 20. To a solution of 1-(1,2,4-triazol-1-yl)propargyl ethyl ether (**11**) (5 mmol) in THF (70 mL) at −78 °C was added *n*-butyllithium (2.5 M in cyclohexane, 4 mL, 10 mmol). The solution was stirred at this temperature for 5 min, and the appropriate electrophile (MeI or cyclohexanone; 10 mmol) was then added. After the solution was stirred at −78 °C for an additional 5 to 10 min, the reaction was quenched at this temperature with water (50 mL) and the solution was extracted with diethyl ether (3 × 100 mL). Evaporation of the solvent gave a residue. In the case of **10**. The pure (>95%) compound was obtained. In the case of **19**, pure compound was obtained after column chromatography (hexane/ethyl acetate 20:1). **Hydrolysis.** In the case of **9a**, the compound **10** was dissolved in a mixture of ethanol (15 mL), water (15 mL), and HCl (2 mL) and kept for 2 h. In the case of **20**, compound **19** was dissolved in a mixture of ethanol (15 mL), water (15 mL), and HCl (2 mL) and heated under reflux for 2 h. The resulting solution was extracted with diether (3 × 100 mL), washed with water (100 mL), and dried over anhydrous $MgSO_4$. Evaporation of the solvent gave a residue which was separated by column chromatography (hexane/ethyl acetate 25:1).

1-Ethoxy-1-[5-methyl-1,2,4-triazol-1-yl]-3-methyl-3-phenylallene (10): obtained as a colorless oil; yield 100%; ^{1}H NMR δ 1.40 (t, 3 H, J = 7.1 Hz), 2.39 (s, 3 H), 2.50 (s, 3 H), 3.88 (q, 2 H, J = 7.1 Hz), 7.30−7.42 (m, 3 H), 7.56−7.60 (m, 2 H), 7.89 (s, 1 H); ^{13}C NMR δ 12.8, 14.2, 19.7, 64.9, 120.4, 126.5, 128.4, 128.6, 128.7, 135.7, 151.0, 152.9, 185.0.

1-Ethoxy-1-[5-(1-hydroxycyclohexyl)-1,2,4-triazol-1-yl]-3-(1-hydroxycyclohexyl)-3-phenylallene (19): yield 52%; mp 127−129 °C; ^{1}H NMR δ 1.10−2.15 (m, 23 H), 3.55 (s, 1 H), 3.86−4.00 (m, 3 H), 7.30−7.45 (m, 5 H), 7.34 (s, 1 H); ^{13}C NMR δ 14.4, 21.4, 21.5, 21.6, 21.7, 25.0, 25.1, 36.2, 36.8, 65.2, 71.1, 74.2, 127.8, 128.1, 128.6, 130.5, 134.0, 135.6, 149.9, 160.7, 185.1. Anal. Calcd for $C_{25}H_{33}N_3O_3$: C, 70.89; H, 7.85; N, 9.92. Found: C, 71.12; H, 8.10; N, 10.13.

Ethyl 3-phenyl-2-butenoate (9a): obtained as two diastereoisomers. ***E* isomer:** a colorless oil, lit.[20] bp 115−116 °C/5 mmHg; yield 17%; ^{1}H NMR δ 1.34 (t, 3 H, J = 7.1 Hz), 2.61 (s, 3 H), 4.23 (q, 2 H, J = 7.1 Hz), 6.16−6.17 (m, 1 H), 7.37−7.40 (m, 3 H), 7.47−7.51 (m, 2 H); ^{13}C NMR δ 14.3, 17.9, 59.7, 117.1, 126.2, 128.4, 128.6, 128.9, 133.0, 142.2, 155.4, 166.8. ***Z* isomer:** a colorless oil; yield 70%; ^{1}H NMR δ 1.07 (t, 3 H, J = 7.1 Hz), 2.17 (s, 3 H), 3.99 (q, 2 H, J = 7.1 Hz), 5.90 (s, 1 H), 7.18−7.21 (m, 2 H), 7.29−7.34 (m, 3 H); ^{13}C NMR δ 13.9, 27.1, 59.7, 117.8, 126.8, 127.6, 127.8, 140.8, 155.2, 165.9.

3′-Phenylcyclohexanespiro-4′-α,β-butenolide (20): yield 98%; mp 77−79 °C; ^{1}H NMR δ 1.22−2.07 (m, 10 H), 6.17 (s, 1 H), 7.45−7.55 (m, 5 H); ^{13}C NMR δ 22.0, 24.4, 34.4, 89.3, 115.5, 127.4, 128.8, 130.2, 130.8, 171.6, 172.7. Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 78.95; H, 7.30.

General Procedure for the Preparation of 9b−d, 24, and 39. To a solution of 1-(1,2,4-triazol-1-yl)propargyl ethyl ethers **11** or **33** (5 mmol) in THF (70 mL) at −78 °C was added *n*-butyllithium (2.5 M in cyclohexane, 4 mL, 10 mmol). The solution was stirred at this temperature for 5 min, and the appropriate electrophile (EtBr, $C_5H_{11}Br$, allyl bromide or *N*-benzylidineaniline; 5 mmol; for $C_6H_{13}I$, 10 mmol) was then added. After the solution was stirred at −78 °C for an additional 5 to 10 min, the reaction was quenched at this temperature with water (50 mL). The mixture was extracted with diethyl ether (3 × 100 mL). Evaporation of the solvent gave a residue, which was hydrolyzed in a mixture of ethanol (15 mL), water (15 mL), and HCl (2 mL) at room temperature for 2 h. The resulting solution was extracted with diether (3 × 100 mL), washed with water (100 mL), and dried over anhydrous $MgSO_4$. Evaporation of the solvent gave a residue which was separated by column chromatography (hexane/ethyl acetate, 25:1).

Ethyl 3-phenyl-2-pentenoate (9b): Obtained as two diastereoisomers. ***E*-isomer:** a colorless oil, lit.[20] bp 91−94.5 °C/1 mmHg; yield 23%; ^{1}H NMR δ 1.08 (t, 3 H, J = 7.5 Hz), 1.32 (t, 3 H, J = 7.1 Hz), 3.11 (q, 2 H, J = 7.5 Hz), 4.21 (q, 2 H, J = 7.1 Hz), 6.02 (s, 1 H), 7.35−7.39 (m, 3 H), 7.42−7.46 (m, 2 H); ^{13}C NMR δ 13.5, 14.3, 24.3, 59.8, 116.8, 128.6, 128.8, 141.2, 162.0, 166.4. ***Z*-isomer:** a colorless oil; yield 70%; ^{1}H NMR δ 1.03−1.09 (m, 6 H), 2.45 (q, 2 H, J = 7.2 Hz), 3.98 (q, 2 H, J = 7.1 Hz), 5.88 (s, 1 H), 7.13−7.17 (m, 2 H), 7.29−7.36 (m, 3 H); ^{13}C NMR δ 12.0, 13.9, 33.3, 59.6, 116.3, 126.9, 127.4, 127.7, 140.4, 160.8, 166.1.

Ethyl 3-phenyl-2-octenoate (9c): obtained as two diastereoisomers. ***E* isomer:** a colorless oil; yield 15%; ^{1}H NMR δ 0.86 (t, 3 H, J = 7.1 Hz), 1.25−1.50 (m, 9 H), 3.10 (t, 2 H, J = 7.4 Hz), 4.22 (q, 2 H, J = 7.1 Hz), 6.03 (s, 1 H), 7.34−7.48 (m, 5 H); ^{13}C NMR δ 14.0, 14.3, 22.4, 28.7, 31.0, 31.9, 59.8, 117.3, 126.7, 128.5, 128.7, 141.5, 160.8, 166.5. ***Z* isomer:** a colorless oil; yield 64%; ^{1}H NMR δ 0.85 (t, 3 H, J = 7.1 Hz), 1.05 (t, 3 H, J = 7.2 Hz), 1.24−1.30 (m, 4 H), 1.31−1.41 (m, 2 H), 2.42 (t, 2 H, J = 6.9 Hz), 3.97 (q, 2 H, J = 7.2 Hz), 5.87 (s, 1 H), 7.12−7.18 (m, 2 H), 7.28−7.36 (m, 3 H); ^{13}C NMR δ 13.9, 22.3, 26.9, 31.2, 40.3, 59.6, 117.1, 127.0, 127.4, 127.7, 140.3, 159.7, 166.0. Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.89; H, 9.36.

Ethyl 3-phenyl-2,5-hexadienoate (9d): obtained as two diastereoisomers. ***E* isomer:** a colorless oil; yield 28%; ^{1}H NMR δ 1.31 (t, 3 H, J = 7.1 Hz), 3.87−3.90 (m, 2 H), 4.21 (q, 2 H, J = 7.1 Hz), 4.99−5.14 (m, 2 H), 5.83−5.92 (m, 1 H), 6.15 (s, 1 H), 7.33−7.36 (m, 3 H), 7.44−7.49 (m, 2H); ^{13}C NMR δ 14.2, 35.3, 59.8, 116.1, 117.9, 126.7, 128.4, 128.9, 135.2, 141.0, 156.7, 166.1. Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 78.13; H, 7.66. ***Z* isomer:** a colorless oil; yield 52%; ^{1}H NMR δ 1.07 (t, 3 H, J = 7.2 Hz), 3.16−3.19 (m, 2 H), 3.99 (q, 2 H, J = 7.2 Hz), 5.07−5.13 (m, 2 H), 5.76−5.85 (m, 1 H), 5.90 (s, 1 H), 7.17−7.20 (m, 2 H), 7.30−7.37 (m, 3 H); ^{13}C NMR δ 13.8, 44.1, 59.6, 117.9, 118.0, 127.0, 127.5, 127.7, 133.6, 140.0, 157.0, 165.8. Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 78.03; H, 7.64.

Ethyl (*Z*)-3,4-diphenyl-4-(phenylamino)-2-butenoate (24): yield 70%; mp 128−130 °C; ^{1}H NMR δ 1.03 (t, 3 H, J = 7.1 Hz), 3.96 (q, 2 H, J = 7.1 Hz), 4.14 (d, 1 H, J = 4.1 Hz), 5.08 (d, 1 H, J = 4.1 Hz), 6.41 (s, 1 H), 6.67 (d, 2 H, J = 8.5 Hz), 6.77 (t, 1 H, J = 7.2 Hz), 6.98−7.02 (m, 2 H), 7.18−7.30 (m, 10 H); ^{13}C NMR δ 13.8, 59.9, 65.8, 113.4, 118.2, 118.5, 127.6, 127.7, 127.9, 128.1, 128.8, 129.2, 138.1, 139.1, 146.5, 156.8, 166.1. Anal. Calcd for $C_{24}H_{23}NO_2$: C, 80.64; H, 6.49; N, 3.92. Found: C, 81.03; H, 6.62; N, 3.84.

Ethyl 3-hexyl-2-nonenoate (39): obtained as a colorless oil; yield 65%; ^{1}H NMR δ 0.88−0.97 (m, 6 H), 1.26−1.50 (m, 19 H), 2.14 (t, 2 H, J = 7.4 Hz), 2.60 (t, 2 H, J = 7.4 Hz), 4.15 (q, 2 H, J = 7.1 Hz), 5.63 (s, 1 H); ^{13}C NMR δ 14.0, 14.3, 22.5, 22.6, 27.6, 28.7, 29.0, 29.6, 31.6, 31.7, 32.2, 38.4, 59.4, 115.0, 164.8, 166.6. Anal. Calcd for $C_{17}H_{32}O_2$: C, 76.06; H, 12.02. Found: C, 75.89; H, 12.21.

General Procedure for the Preparation of 16a−c. To a solution of 1-(1,2,4-triazol-1-yl)propargyl ethyl ethers **11** (5 mmol) in THF (70 mL) at −78 °C was added *n*-butyllithium (2.5 M in cyclohexane, 2 mL, 10 mmol). The solution was stirred at this temperature for 5 min, and the appropriate electrophile (benzaldehyde, 4-tolualdehyde, or octanal; 10 mmol) was then added. After the solution was stirred at −78 °C for an additional 5 to 10 min, the reaction was quenched at this temperature with water (50 mL). HCl (2 M, 8 mL) was

added, and the mixture was kept for 4 h at room temperature. The resulting solution was extracted with diether (3 × 100 mL), washed with water (100 mL), and dried over anhydrous $MgSO_4$. Evaporation of the solvent gave a residue which was separated by column chromatography (hexane/ethyl acetate 25:1).

3,4-Diphenyl-α,β-butenolide (16a): yield 67%; mp 151−153 °C; (lit.[45] mp 149 °C); ^{1}H NMR δ 6.34 (d, 1 H, J = 1.6 Hz), 5.56 (d, 1 H, J = 1.5 Hz), 7.31−7.44 (m, 10 H); ^{13}C NMR δ 84.3, 114.6, 127.5, 127.8, 128.9, 129.1, 129.5, 129.6, 131.2, 134.9, 165.8.

4-(4-Methylphenyl)-3-phenyl-α,β-butenolide (16b): yield 61%; mp 129−131 °C; ^{1}H NMR δ 2.31 (s, 3 H), 6.32 (d, 1 H, J = 1.6 Hz), 6.56 (d, 1 H, J = 1.6 Hz), 7.13−7.23 (m, 4 H), 7.3−7.44 (m, 5 H); ^{13}C NMR δ 21.1, 84.1, 114.4, 127.4, 127.7, 128.8, 129.7, 131.1, 131.8, 139.5, 165.7, 172.6. Anal. Calcd for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.54; H, 5.69.

4-Heptyl-3-phenyl-α,β-butenolide (16c): obtained as a colorless oil: yield 70%; ^{1}H NMR 0.87 (t, 3 H, J = 6.6 Hz), 1.19−1.66 (m, 11 H), 1.97−2.07 (m, 1 H), 5.50−5.55 (m, 1 H), 6.29 (d, 1 H, J = 1.5 Hz), 7.30−7.53 (m, 5 H); ^{13}C NMR δ 13.9, 22.5, 24.4, 28.9, 29.0, 31.5, 33.4, 82.2, 114.2, 127.0, 129.1, 130.1, 131.2, 167.8, 172.8. Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 79.03; H, 9.01.

General Procedure for the Preparation of 18, 22, 24, 40, and 41. To a solution of 1-(1,2,4-triazol-1-yl)propargyl ethyl ethers **11** or **33** (5 mmol) in THF (70 mL) at −78 °C was added *n*-butyllithium (2.5 M in cyclohexane, 2 mL, 10 mmol). The solution was stirred at this temperature for 5 min, and the appropriate electrophile (benzophenone, 5 mmol; cyclohexenone, 10 mmol) was then added. After the solution was stirred at −78 °C for an additional 5 to 10 min, the reaction was quenched at this temperature with water (50 mL). The mixture was extracted with diethyl ether (3 × 100 mL). Evaporation of the solvent gave a residue, which was hydrolyzed in a mixture of ethanol (15 mL), water (15 mL), and HCl (2 mL) under reflux for 4 h. The resulting solution was extracted with diether (3 × 100 mL), washed with water (100 mL), and dried over anhydrous $MgSO_4$. Evaporation of the solvent gave a residue which was separated by column chromatography (hexane/ethyl acetate, 25:1).

3,4,4-Triphenyl-α,β-butenolide (18): yield 78%; mp 203−205 °C; ^{1}H NMR δ 6.50 (s, 1 H), 7.28−7.40 (m, 15 H); ^{13}C NMR δ 93.4, 116.6, 128.2, 128.4, 128.7, 128.8, 130.8, 138.0, 170.0, 171.4. Anal. Calcd for $C_{22}H_{16}O_2$: C, 84.59; H, 5.16. Found: C, 84.56; H, 5.07.

3′-Phenyl-2-cyclohexenespiro-4′-α,β-butenolide (22): yield 64%; mp 90−92 °C; ^{1}H NMR δ 1.81−2.36 (m, 6 H), 5.70 (dd, 1 H, J = 9.8, 1.5 Hz), 6.32−6.38 (m, 2 H), 7.42−7.49 (m, 3 H), 7.62−7.68 (m, 2 H); ^{13}C NMR δ 18.4, 24.1, 33.2, 85.0, 114.6, 125.0, 127.4, 128.7, 129.8, 130.7, 134.9, 170.0, 171.3. Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.96; H, 6.35.

4,4-Diphenyl-3-hexyl-α,β-butenolide (40): yield 49%; mp 58−60 °C; ^{1}H NMR δ 0.85 (t, 3 H, J = 7.2 Hz), 1.18−1.32 (m, 6 H), 1.45−1.55 (m, 2 H), 2.33 (t, 2 H, J = 7.1 Hz), 6.00 (s, 1 H), 7.26−7.39 (m, 10 H); ^{13}C NMR δ 13.6, 22.1, 26.9, 28.3, 28.4, 31.0, 93.8, 115.4, 127.3, 128.2, 128.4, 138.4, 171.9, 175.6. Anal. Calcd for $C_{22}H_{24}O_2$: C, 82.46; H, 7.55. Found: C, 82.10; H, 7.73.

1-Hydroxy-1,1-diphenyl-3-decyn-2-one (41): obtained as an oil; yield 16%; ^{1}H NMR δ 0.86 (t, 3 H, J = 7.0 Hz), 1.17−1.30 (m, 6 H), 1.37−1.45 (m, 2 H), 2.29 (t, 2 H, J = 7.0 Hz), 4.73 (s, 1 H), 7.32−7.39 (m, 6 H), 7.45−7.50 (m, 4 H); ^{13}C NMR δ 13.9, 19.3, 22.3, 27.1, 28.3, 31.1, 79.0, 85.6, 104.6, 127.6, 128.0, 128.1, 141.0, 187.8. Anal. Calcd for $C_{22}H_{24}O_2$: C, 82.46; H, 7.55. Found: C, 82.44; H, 7.89.

General Procedure for the Preparation of 27a−c, 30, 31, and 42. To a solution of 1-(1,2,4-triazol-1-yl)propargyl ethyl ethers **11** or **33** (5 mmol) in THF (70 mL) at −78 °C was added *n*-butyllithium (2.5 M in cyclohexane, 2 mL, 10 mmol). The solution was stirred at this temperature for 5 min, and the appropriate electrophile (*N*-benzylidineaniline, *N*-(4-chlorobenzylidine)aniline, *N*-(4-methylbenzylidine)aniline, or *N*-benzylidinehexylamine; 5 mmol) was then added. After the solution was stirred at −78 °C for an additional 15 h, the reaction was quenched at this temperature with water (50 mL). The mixture was extracted with diethyl ether (3 × 100 mL) and dried over anhydrous $MgSO_4$. Evaporation of the solvent gave a residue, which was chromatographed on silica gel (hexane/ethyl acetate 25:1).

2-Ethoxy-*N*,4,5-triphenylpyrrole (27a): yield 82%; mp 99−101 °C; ^{1}H NMR δ 1.33 (t, 3 H, J = 7.1 Hz), 4.09 (q, 2 H, J = 7.1 Hz), 5.67 (s, 1 H), 6.98−7.28 (m, 15 H); ^{13}C NMR δ 14.7, 66.8, 86.0, 120.7, 122.5, 125.3, 126.2, 126.6, 127.8, 128.0, 128.3, 130.9, 132.4, 136.6, 136.8, 148.1. Anal. Calcd for $C_{24}H_{21}NO$: C, 84.92; H, 6.24; N, 4.13. Found: C, 84.49; H, 6.24; N, 3.94.

2-Ethoxy-*N*,4-diphenyl-5-(4-chlorophenyl)pyrrole (27b): yield 83%; mp 137−139 °C; ^{1}H NMR δ 1.32 (t, 3 H, J = 7.1 Hz), 4.08 (q, 2 H, J = 7.1 Hz), 5.64 (s, 1 H), 6.89 (d, 1 H, J = 8.2 Hz), 7.02−7.30 (m, 12 H); ^{13}C NMR δ 14.7, 66.8, 86.3, 121.1, 121.5, 125.6, 126.9, 128.1, 128.2, 128.3, 128.4, 130.9, 132.0, 136.4, 136.6, 148.3. Anal. Calcd for $C_{24}H_{20}NOCl$: C, 77.10; H, 5.39; N, 3.75. Found: C, 77.36; H, 5.35; N, 3.62.

2-Ethoxy-*N*,4-diphenyl-5-(4-methylphenyl)pyrrole (27c): yield 86%; mp 107−109 °C; ^{1}H NMR δ 1.31 (t, 3 H, J = 7.1 Hz), 2.22 (s, 1 H), 4.07 (q, 2 H, J = 7.1 Hz), 5.65 (s, 1 H), 6.88 (s, 4 H), 7.09−7.27 (m, 10 H); ^{13}C NMR δ 14.7, 21.1, 66.8, 85.9, 113.2, 120.4, 122.6, 125.2, 126.6, 128.0, 128.2, 128.4, 128.6, 130.8, 135.8, 136.8, 136.9, 147.9. Anal. Calcd for $C_{25}H_{23}NO$: C, 84.95; H, 6.56; N, 3.96. Found: C, 85.29; H, 6.73; N, 3.88.

2-Ethoxy-*N*-hexyl-4,5-diphenylpyrrole (30): obtained as a colorless oil; yield 41%; ^{1}H NMR δ 0.83 (t, 3 H, J = 7.1 Hz), 1.10−1.28 (m, 6 H), 1.42−1.60 (m, 5 H), 3.70 (t, 2 H, J = 7.5 Hz), 4.13 (q, 2 H, J = 7.1 Hz), 5.55 (s, 1 H), 7.00−7.18 (m, 5 H), 7.26−7.37 (m, 5 H); ^{13}C NMR δ 13.9, 14.9, 22.4, 26.2, 30.3, 31.2, 42.2, 66.0, 83.8, 119.2, 122.1, 124.7, 127.1, 127.6, 127.9, 128.4, 133.3, 136.9, 147.8. Anal. Calcd for $C_{24}H_{29}NO$: C, 82.95; H, 8.41; N, 4.03. Found: C, 82.68; H, 8.61; N, 4.09.

***N*-Hexyl-2,5-diphenyl-5-(1,2,4-triazol-1-yl)pyrrole (31):** yield 40%; mp 87−89 °C; ^{1}H NMR δ 0.76 (t, 3 H, J = 7.2 Hz), 0.90−1.00 (m, 4 H), 1.02−1.15 (m, 2 H), 1.25−1.35 (m, 2 H), 3.74 (t, 2 H, J = 7.7 Hz), 6.53 (s, 1 H), 7.03−7.20 (m, 5 H), 7.30−7.40 (m, 5 H), 8.16 (s, 1 H), 8.35 (s, 1 H); ^{13}C NMR δ 13.5, 21.9, 25.7, 30.2, 30.5, 43.9, 105.1, 121.3, 124.4, 125.3, 127.4, 127.9, 128.0, 128.4, 130.3, 103.8, 131.8, 134.9, 145.6, 152.5. Anal. Calcd for $C_{24}H_{26}N_4$: C, 77.80; H, 7.07; N, 15.12. Found: C, 77.82; H, 7.00; N, 15.20.

2-Ethoxy-4-hexyl-*N*,5-diphenylpyrrole (42): yield 83%; mp 57−59 °C; ^{1}H NMR δ 0.87 (t, 3 H, J = 7.0 Hz), 1.22−1.40 (m, 11 H), 1.55−1.65 (m, 2 H), 2.52 (t, 2 H, J = 7.5 Hz), 3.99 (q, 2 H, J = 7.1 Hz), 5.39 (s, 1 H), 7.00−7.22 (m, 10 H); ^{13}C NMR δ 14.1, 14.7, 22.6, 22.7, 29.3, 31.3, 31.7, 66.5, 85.8, 121.4, 122.3, 125.4, 125.9, 127.6, 127.8, 128.1, 130.0, 132.9, 137.7, 147.7. Anal. Calcd for $C_{24}H_{29}NO$: C, 82.95; H, 8.41; N, 4.03. Found: C, 82.72; H, 8.58; N, 3.97.

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