Selective Reactivity of sp^3 and sp^2 Carbanions of 1-Substituted 1,2,4-Triazoles. A Comparative Approach

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The regioselectivity of lithiation reactions of 1-*n*-alkyl-, 1-allyl-, and 1-propargyl-1*H*-1,2,4-triazoles was studied in terms of the products formed by sequential treatment with BuLi and a range of electrophiles.

Introduction

Many heteroaromatic ring systems which contain electronegative heteroatoms (N, S, O) are long known to undergo facile C-metalations of two distinct types: (i) at a sp^2-hybridized carbon atom adjacent to a heteroatom[1−4] and (ii) at an α-sp^3-hybridized carbon atom of C-alkyl substituents. In recent years, considerable attention has been paid to a third type of C-metalation, that is, that at the α-position of *N*-alkyl groups.[5]

The aforementioned considerations apply to substituted 1*H*-1,2,4-triazoles. The similar properties of C-alkyl substituents on triazoles to those on benzene are widely recognized.[6] By contrast, the reactivity of N-substituents on triazoles, as with N-substituents on heterocycles in general, has until recently been much less investigated.[6] Most studies of the lithiation of *N*-substituted triazoles have been in connection with the protection of the 1-NH during C-lithiation at C-5 and subsequent reaction with electrophiles.[3] 5-Metalated 1*N*-protected 1*H*-1,2,4-triazoles were used as nucleophiles in reactions with various electrophiles to give the corresponding 1,5-disubstituted triazoles, which were further deprotected to 3(≡5)-substituted derivatives.[7,8] In the course of such work, rearrangements between 5-C and 3-C isomers have appeared to occur readily: thus, lithiated 1-(pyrrolidinomethyl)-1*H*-1,2,4-triazole reacted with electrophiles to afford the 1,5-disubstituted product, which underwent isomerization to produce an equilibrium mixture in which the less sterically hindered 1,3-disubstituted derivative prevailed.[8] However, in fact such rearrangements involve movement of the N-substituent from 1-*N* to 2-*N*, while the C-substituent remains attached to the same ring carbon;[8] for similar behavior see ref 9. To our knowledge, substitution at the exocyclic *N*-methylene group of a 1*H*-1,2,4-triazole was previously reported only for 1-benzyl-1*H*-1,2,4-triazole, and only when benzyl halides were used as an electrophile.[10] Substitution at an exocyclic *N*-methine group in 1-(α-ethoxyallyl)-[11a] and 1-(α-ethoxypropynyl)-1*H*-1,2,4-triazole[11b] has been developed as an important synthetic procedure in our group.

There is much practical interest in triazole derivatives,[12−14] but mechanistic aspects have been relatively neglected. We now present a comparative study of the C-metalation and subsequent treatment with electrophiles of 1-alkyl-, 1-allyl-, and 1-propargyl-1*H*-1,2,4-triazoles to evaluate their substitution patterns and to help to expand the functionalization routes in this class.

The 1*H*-1,2,4-triazole derivatives **1**−**5** used as substrates for the present study are known compounds and were prepared by previously described methods. 1-*n*-Butyl- (**1**) and 1-*n*-octyl-1,2,4-triazole (**2**) were made by direct alkylation of 1*H*-1,2,4-triazole with haloalkanes.[15] 1-(1-Pyrrolidinomethyl)-1*H*-1,2,4-triazole (**3**) was obtained by a Mannich-type reaction of 1,2,4-triazole with formaldehyde and pyrrolidine.[8] 1-Allyl-1,2,4-triazole (**4**) was prepared by reacting 1*H*-1,2,4-triazole with allyl bromide,[16] while 1-propargyl-1*H*-1,2,4-triazole (**5**)[17] was obtained by adapting the method described for the preparation of 1-propargylbenzotriazole.[18]

These substrates were lithiated and subsequently reacted with D_2O (or H_2O), iodomethane, benzophenone, and phenyl isocyanate, by some or all of five standardized procedures of lithiation/treatment with electrophile which are classified below as A−E. These procedures were

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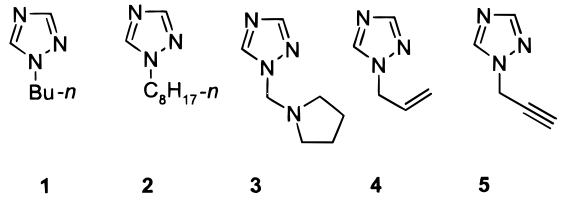


1 **2** **3** **4** **5**

aimed at the elucidation of the regioselectivity of the first and subsequent lithiations, along with the determination of the regioselectivity of the ambident carbanions in their reactions with electrophiles.

(A) For compounds **1**−**5**: reaction with 1 equiv of BuLi and subsequently with 1 equiv of electrophile. These experiments established that, for 1-alkyl- and 1-allyl-1*H*-1,2,4-triazoles, the carbanion was formed at 5-C, the position already reported as the most reactive lithiation site,[14] while for 1-propargyl-1*H*-1,2,4-triazole the first lithiation occurred at the alkyne hydrogen.

(B) For compounds **2**, **4**, and **5**: two consecutive sequences of reactions, each consisting of treatment with 1 equiv of BuLi, and subsequently 1 equiv of electrophile. These experiments showed the orientation of the second lithiation and provided information on the relative reactivities of the centers.

(C) For compounds **4** and **5**: reaction with 2 equiv of BuLi, and subsequent treatment with 2 equiv of electrophile.

(D) For compounds **4** and **5**: reaction with 2 equiv of BuLi and then with 1 equiv of an electrophile, followed by quenching with water.

(E) For compound **5**: reaction with 3 equiv of BuLi, and then 1 equiv of an electrophile (i.e., benzophenone), followed by quenching with water.

The results depicted in Schemes 1−7 and Tables 1−4 are based on preparative yields and on ^{1}H and ^{13}C NMR evaluation of the crude reaction mixtures. In all cases, GC/MS data were supported by NMR measurements.

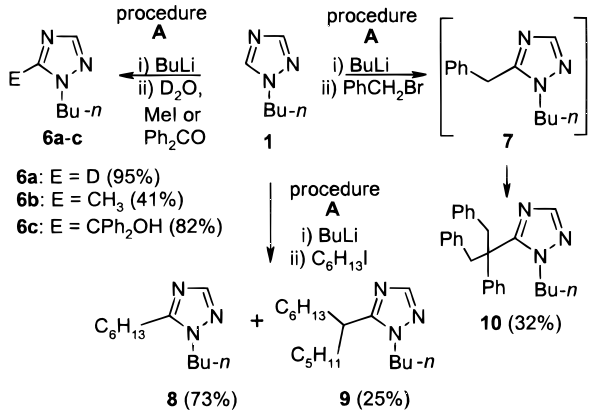
Results

1-Alkyl-1*H*-1,2,4-triazoles 1 and 2. Previous studies of the lithiation of 1-alkyl-substituted 1*H*-1,2,4-triazoles are related to the functionalization of the triazole ring.[14] Various alkyl substituents were used as protective groups for the 1-N*H* of 1*H*-1,2,4-triazole to induce lithiation at C-5. Previous examples of substitution at the exocyclic carbon of the N-substituent are uncommon.[3]

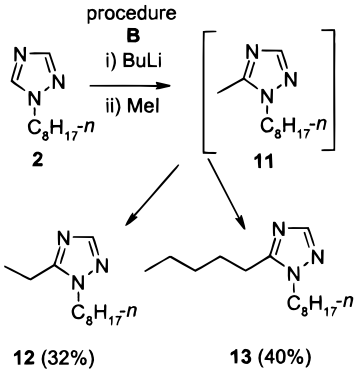
Treatment of 1-*n*-butyl-1,2,4-triazole (**1**) with BuLi and subsequently with D_2O, iodomethane, or benzophenone gave exclusively the corresponding 5-substituted derivatives **6a**−**c**, as expected. The reaction of lithiated **1** with 1 equiv of benzyl bromide followed an unexpected route, giving compound **10** with a conversion of 32% (conversion of benzyl bromide 100%), while 68% of the starting material was recovered (Scheme 1). The monoalkylated derivative **7** initially formed was not detected in the crude reaction mixture. The product **10** evidently originated from the double deprotonation of lithiated **7**. The reaction of lithiated **1** with 1 equiv of 1-iodohexane gave a mixture of the 5-monoalkylated derivative **8** and the dialkylated product **9**, in a ratio of 3:1.

When 1-*n*-octyl-1*H*-1,2,4-triazole (**2**) was reacted with iodomethane under conditions B, products **12** and **13** were obtained in a ratio of 3:2 (Scheme 2 reports the experimental yields, as separated by column chromatography). A second lithiation obviously occurred at the 5-CH_3 of the intermediate **11**. Compound **13** was probably formed via 1-iodobutane, which results from exchange between BuLi and iodomethane.

Scheme 1



Scheme 2



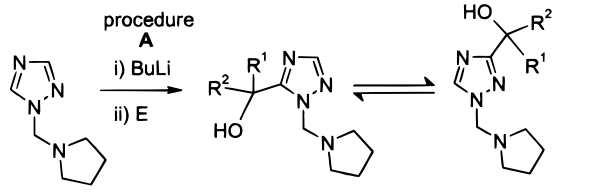
The structures of products **6a**−**c**, **8**−**10**, **12**, and **13** were confirmed by ^{1}H and ^{13}C NMR assignments: the ^{1}H NMR spectra provided evidence for the presence of a hydrogen atom at 3-C of the triazole ring (at ca. 8 ppm), while the ^{13}C NMR spectra revealed the signals for the corresponding carbon atoms (3-C=N at ca. 125 ppm). The substitution at 5-C was confirmed by the disappearance of the signal characteristic for the 5-C*H* proton. Moreover, the attached proton test (APT) showed the corresponding carbon atoms to be quaternary.

1-(1-Pyrrolidinomethyl)-1*H*-1,2,4-triazole (3). The pyrrolidinomethyl synthon is utilized as a protective group for the 1-N*H* of 1*H*-1,2,4-triazoles when synthetic purposes require functionalization of a 1*H*-1,2,4-triazole via ring lithiation.[8] In compounds of type **3** lithiation proceeds at 5-C, but the 5-substituted products are in mobile equilibrium with their 3-substituted regioisomers, because of easy rearrangement of the pyrrolidinomethyl substituent to the adjacent N-atom via cationotropy.[8,9]

Compound **3** was reacted using conditions A with benzaldehyde to give the expected product as a mixture of its 3- and 5-regioisomers **14a** and **14b**, respectively, in a ratio of 1:1 (yield 76%) (Scheme 3). When reacted with benzophenone using the same conditions (A) a mixture of regioisomers **15a** and **15b** in a ratio of 1:2 was obtained (yield 80%). The ratio of the two regioisomers in each pair was determined by NMR by using the two distinct singlets at ca. 8 ppm, characteristic for the two ring hydrogen atoms.

1-Allyl-1*H*-1,2,4-triazole (4). The stereochemical and regiochemical characteristics of many reactions of reso-

Scheme 3

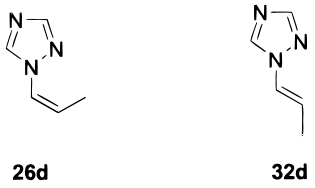


14: E = PhCHO, R^1 = Ph, R^2 = H (76%)
15: E = Ph_2CO, R^1 = Ph, R^2 = Ph (80%)

nance-stabilized allyl organometallics have raised questions on their kinetic versus thermodynamic control. Many experimental results,[19] supported by theoretical calculations[20,21] and ^{7}Li NMR measurements,[22] suggest a delocalized structure for allyllithiums and indicate that the regiochemistry of their reactions with electrophiles is strongly influenced by both electronic and solvation effects. Most previous studies of the metalation of allyl heterocycles have been associated with specific synthetic applications (e.g., 1-allyl-1*H*-benzotriazole[18]).

Scheme 4 summarizes the results of the present investigation: we interpret our results in terms of initial formation of monolithiated intermediate **16** in all four procedures (A−D). Procedure B proceeds via further monolithiated intermediates **20**−**23**. Procedures C and D give products expected to arise from dilithiated intermediates of type **17**−**19**.

(a) Reaction with Water. 1-Allyl-1*H*-1,2,4-triazole (**4**) was treated with 2 equiv of BuLi using conditions C, and after 15 min the reaction mixture was quenched with water. The starting material and its isomer **26d** (Scheme 4) were obtained in equimolar amounts. If the reaction mixture was left at room temperature for 12 h and then quenched with water, compound **26d** was formed as the major product, while the minor product was its corresponding trans diastereomer **32d** in about 10% (by ^{1}H NMR). The reaction was performed with and without TMEDA, and in concentrations between 10^{-2} and 10^{-3} M, and gave identical results.



26d **32d**

(b) Reactions with Iodomethane (Table 1). Lithiated 1-allyl-1,2,4-triazole (**4**) reacted with iodomethane using conditions A to give 1-allyl-5-methyl-1,2,4-triazole (**24a**) as the major product (conversion 81%, yield 60%), together with 8% of compound **27a** which resulted from the lithiation of compound **4** in the α-position of the exocyclic chain. Additionally, products of disubstitution at both ring and exocycle (**25a** and **26a**) were also isolated (7 and 4%, respectively).

With conditions B the second reaction with iodomethane occurred exclusively at the 5-methyl group; compound **33**, resulting from the rearrangement of the double bond, was obtained with a conversion of 80% and an isolated yield of 53%. By contrast, under conditions C the reaction with two molecules of iodomethane gave the disubstituted regioisomers **25a** and **26a**, in a **25a**:**26a** ratio of 1:3. Compound **26a** was isolated in 55% yield. With conditions D, compounds **25a**−**27a** were formed in a **25a**:**26a**:**27a** ratio of 1:1.5:3. Compound **27a** was isolated in 35% yield.

(c) Reaction with Benzophenone (Table 2). Under conditions A lithiated **4** reacted with benzophenone to give exclusively the product **24b** of substitution at 5-C (40%, Table 2). Under conditions B the second substitution with benzophenone was directed to the allyl chain, and compounds **25b** (28.5%) and **26b** (35.5%) were obtained in a ratio of 1:1.25. Under conditions C the isomeric ratio **25b**:**26b** was 2:1, and the isolated yields were 43% and 23%, respectively. Under conditions D the major fraction separated was compound **28b** (39%), and much of the starting material was recovered.

(d) Reaction with Phenyl Isocyanate (Table 3). Under conditions A the reaction of lithiated **4** and phenyl isocyanate afforded the ring-substituted compound **24c** in 61% yield (Table 4). Under conditions B after the second lithiation the anion did not react with a second mole of phenyl isocyanate, but isomerized to yield products **29c** and **30c**, isolated and characterized as a mixture in a **29c**:**30c** ratio of 1:4 (by ^{1}H NMR). However, the overall conversion of compound **4** was only 15%, and the major products **35** and **36** resulted from side reactions involving phenyl isocyanate. Under conditions C the major product in the reaction with phenyl isocyanate was disubstituted **32c** (20.2%); monosubstituted **29c** was also isolated, in a **29c**:**32c** ratio of 1:2.

The structures of products **24**−**36** were confirmed by ^{1}H and ^{13}C NMR spectroscopy. The positions of the protons assigned to the allyl group are relatively constant: CH_2═ at about 5.5 ppm, C*H*═ at 6.4 ppm, and the allyl protons at 4.2 ppm, with coupling constants in agreement with the literature data. The cis or trans stereochemistry of the products was unequivocally confirmed by NOE experiments, as in all cases the signals were well separated and easy to irradiate.

1-Propargyl-1,2,4-triazole (5). The metalation and functionalization of *N*-propargyl- and *N*-allenyl-pyrrole[23,24] and -benzotriazole[25] have been studied.[26] The equilibrium between the allenyl and propargyl structures of such lithiated compounds is strongly influenced by the solvent, temperature, and substituents.[26] We have shown that 1-(α-ethoxypropynyl)-1*H*-1,2,4-triazole[11b] and -benzotriazole[27] are valuable and complementary reagents, their lithiated derivatives reacting at the δ and α positions, respectively. However, functionalization via metalation of 1-propargyl-1*H*-1,2,4-triazole (**5**) or its allenyl isomer

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Scheme 4

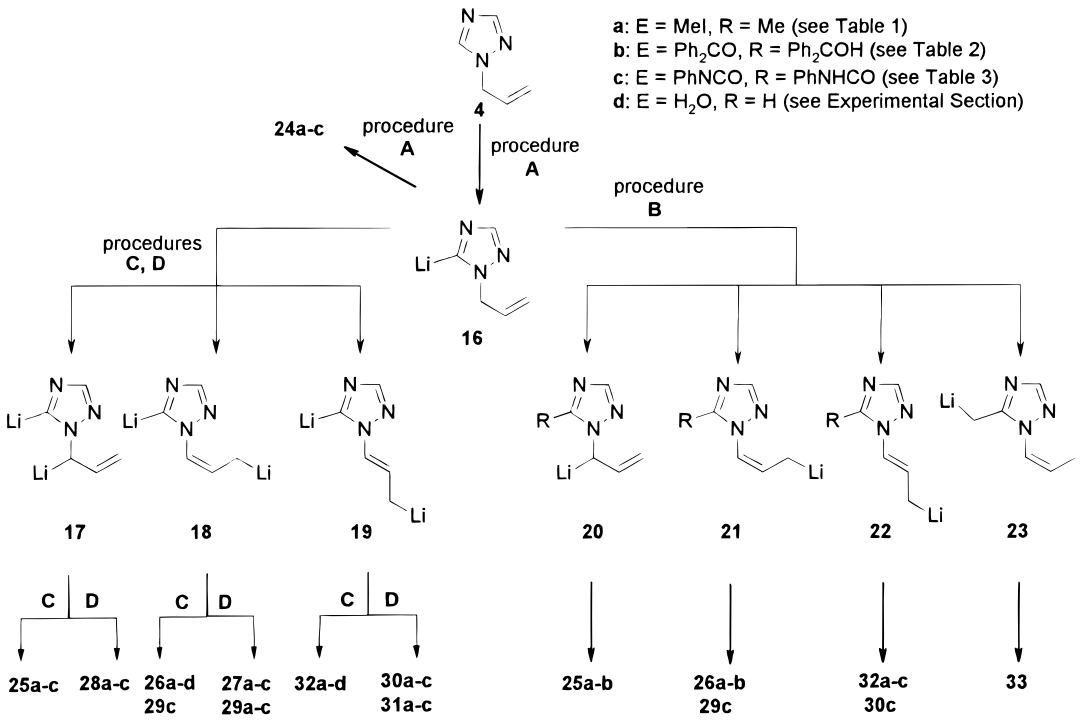


Table 1. Composition of the Reaction Mixtures in the Reaction of Lithiated 4 with Iodomethane[a]

Conditions[b]	24a	25a	26a	27a	33	unreacted 4
A	81 (60)	7	4	8		0
B					80 (53)	0[c]
C[d]		26	64 (55)			10
D[d]		28	19	53 (35)		0

[a] The reported yields are based on GC-MS values obtained from the analysis of the crude reaction mixtures and confirmed by ^{1}H NMR results. Isolated yields are indicated in parentheses. Compound **25a** was not fully characterized. [b] Reaction conditions A−D are described in detail in the Experimental Section. [c] Approximately 20% of an unidentified tris(methylated) product was also found. [d] Values calculated from the ^{1}H NMR of the crude reaction mixtures.

Table 2. Composition of the Reaction Mixtures in the Reaction of Lithiated 4 with Benzophenone (R = Ph_2COH)[a]

	24b	25b	26b	27b*	28b	29b*	Unreacted 4
A[b]	40						60
B[b]		28.5	35.5				36
C[b]		54	34				12
D[b]		4		4[c]	39	2[c]	51

[a] The compositions are calculated on the basis of the ^{1}H NMR of the crude reaction mixtures and on isolated amounts after column chromatography. Compounds whose numbers have an asterisk were not fully characterized. [b] Reaction conditions A−D are described in detail in the Experimental Section. [c] Calculated from the ^{1}H NMR spectrum of the mixture of products **27b** and **29b**.

has not previously been reported and could provide useful new insights for the functionalization of 1*H*-1,2,4-triazoles.

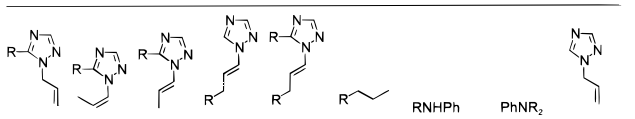
Experiments under conditions A, B, D, and E were performed on compound **5** using three of the same electrophiles as for the allyl analogue **4**: water, iodomethane, and benzophenone. Lithiated **5** reacted sluggishly with electrophiles below 0 °C; the reaction mixtures were therefore brought to 20 °C immediately after the addition of the electrophile.

(a) Reaction with Water. Under conditions A quenching of the monolithiated 1-propargyl-1,2,4-triazole (**5**) with D_2O gave quantitative incorporation of deuterium at the triple bond. When the reaction mixture was quenched with water after 15 min at −78 °C or after 12 h at 20 °C, only compound **5** was recovered; the allenyl isomer was not detected in the NMR spectra of the crude reaction mixture in any of these experiments.

(b) Reaction with Iodomethane (Scheme 5). Under conditions A the reaction with iodomethane gave products **37**, **38**, and **39**, with very similar R_f values, in a ratio of 7:1:2, as determined by the ^{1}H and ^{13}C NMR on the mixture. Well-defined signals and easily determined hyperfine coupling constants, together with heteronuclear correlation, allowed individual assignments. For example, the α-methyl groups in compound **37** and γ-proton in compound **38** are located at 1.90 ppm, while the methinic protons were revealed as a triplet of doublets in compound **38** and a triplet of quartets in compound **39**, at 5.1−5.3 ppm.

(c) Reaction with Benzophenone (Table 4, Scheme 6). Under conditions A, the reaction of γ-lithiated 1-propargyl-1*H*-1,2,4-triazole (**5**) with benzophenone afforded compound **45** in 70% yield, along with unreacted

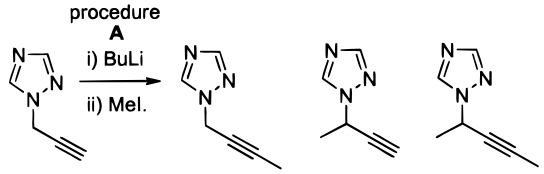
Table 3. Composition of the Reaction Mixtures in the Reaction of Lithiated 4 with Phenyl Isocyanate (R = PhNHCO)[a]



	24c	29c*	30c*	31c	32c	34	35	36	unreacted 4
A[b]	61								39
B[b]		3.0[c]	12.0[c]				24.8	44.8	85
C[b]		11.5[c]			20.2	1.0[c]	8.0	30.0	68.3
D[b]		3.0[c]	0.5[c]	6.0		0.5[c]	5.0	3.7	90.5

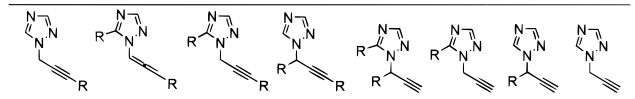
[a] Reaction conditions A−D are described in detail in the Experimental Section. Compounds whose numbers have an asterisk were not fully characterized. [b] The compositions are calculated on the basis of isolated amounts after column chromatography. [c] Percentages calculated on the basis of ^{1}H NMR spectra of the mixtures of compounds **29c**, **30c**, and **34**, as isolated by column chromatography.

Scheme 5



5 **37** (70%) **38** (10%) **39** (20%)

Table 4. Composition of the Reaction Mixtures in the Reaction of Lithiated 5 with Benzophenone (R = Ph_2COH)[a]

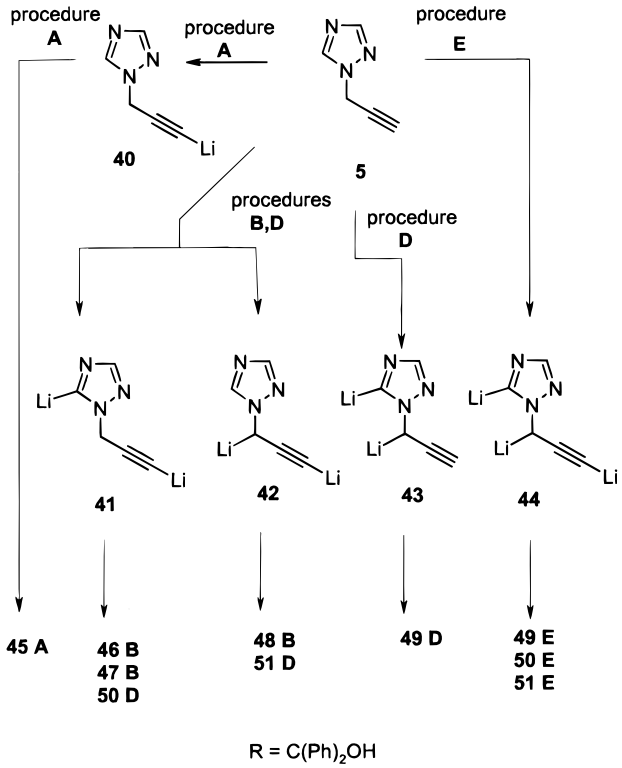


	45	46	47*[b]	48*[b]	49	50	51	recovered 5[c]
A	70.0							30.0
B	16.7	12.5	32.7	9.8				28.3
D					7.4	9.0	6.6	77
E					17	26	15	42

[a] Based on amounts isolated after column chromatography (% mol/mol). Compounds whose numbers have an asterisk were not fully characterized. [b] Ratio ((% mol/mol) determined from the ^{1}H NMR spectrum of the mixture of products **47** and **48**. [c] Recovered after column chromatography as unreacted starting material.

starting material (Scheme 6). Conditions B gave three disubstituted compounds **46**, **47**, and **48**, in a total yield of 55% and a **46**:**47**:**48** ratio of 1:3:1, along with monosubstituted **45** (16%) and 28% of unreacted compound **5**. In a separate experiment, compound **45** was lithiated under conditions A and reacted with benzophenone to afford a mixture of regioisomers **46**, **47**, and **48** in the same ratio as above. We hence assume that compound **45** was lithiated mostly in the ring at 5-C, while the allenyl compound **46** resulted from the isomerization of compound **47** during workup.[29] The reaction of 1-propargyl-1*H*-1,2,4-triazole (**5**) with benzophenone at −78 °C under conditions D afforded compounds **49**, **50**, and **51** in a **49**:**50**:**51** ratio of 1:1.3:1. No allenyl derivative was identified.

Scheme 6



Under conditions E, compound **5** was treated with 3 equiv of BuLi and then 1 equiv of benzophenone. The composition of the reaction mixture remained much the same as that under conditions D, but the conversion of 1-propargyl-1*H*-1,2,4-triazole (**5**) significantly increased from 23% (D) to 58% (E).

The identification of products **45**−**51** was based on ^{1}H and ^{13}C NMR assignments. The positions of the protons characteristic for the propargyl and allenyl groups are in the same range as indicated in the literature: allenyl CH_2= at ca. 5.5 ppm, C*H*≡ at 6.4 ppm, and the α-CH_2 at ca. 5 ppm. The signals characteristic for the 1,2,4-triazole moiety are present at values similar to those of the other derivatives described in this paper. Long-range HETCOR experiments proved the structure of compounds **47** and **49** and eliminate the possibility of a 3- to 5-isomerization.

Discussion

As expected, monolithiation of 1-alkyl-1*H*-1,2,4-triazoles **1**−**3** occurred at 5-C in the ring, and 5-substituted derivatives were generally formed in the reaction with alkyl halides, deuterium oxide, and benzophenone (Schemes 1 and 3). Rearrangement of the 5-C to the 3-C isomer occurred only in the case of the pyrrolidinomethyl derivative **3**, where cationotropy is expected.[8,9] Similar isomerizations were neither expected nor found for 1-butyl- (**1**), 1-octyl- (**2**), 1-allyl- (**4**), and 1-propargyl-1*H*-1,2,4-triazole (**5**). Subsequent lithiation in the 5-alkyl-1-*n*-octyl-1*H*-1,2,4-triazoles derived from compound **2** was directed to the α-exocyclic C*H* of the 5-substituent (Scheme 2). During the monolithiation/reaction of compounds **1** and **2** with electrophile, the product was sometimes more reactive than the starting material and underwent a second or even a third lithiation at the 5-methylene group, as shown for benzyl bromide and

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1-iodooctane (Schemes 1 and 2). No C-metalation at the exocyclic *N*-methylene group was found for any of the 1-alkyl-substituted 1*H*-1,2,4-triazoles **1**−**3**.

1-Allyl-1*H*-1,2,4-triazole (**4**) under conditions A follows the general rule of initial lithiation at the 5-position and thus of substitution at 5-C in the monolithiation/reaction with electrophile. Under conditions B, the second lithiation occurs either in the methyl group introduced into the 5-position (for iodomethane giving compound **33**) or at the exocyclic N−CH_2 (yielding compounds **25b** and **26b**). However, under conditions C and D the second lithiation now occurs readily at the exocyclic N−CH_2 leading to the formation of an ambident dianion which can react with an electrophile at one or two of the three alternative positions: the α-exocyclic C*H* in position 5 and the α- and γ-exocyclic C*H* at the 1-*N* substituent. The reaction course was dependent on the type of electrophile. With iodomethane, the first electrophile mainly attacks at the γ-position to give product **27a** and the second mainly at the 5-ring position to give compound **26a**. By contrast benzophenone attacks first mainly the a-position to give compound **28b** and then the 5-C of the ring to afford product **25b**. Phenyl isocyanate yields a greater variety of products, but **31c** and **32c** conform to the product orientation of iodomethane.

1-Propargyl-1*H*-1,2,4-triazole (**5**), unlike the other *N*-substituted 1*H*-1,2,4-triazoles studied, initially undergoes lithiation at the γ-exocyclic position, evidently as a result of the high acidity of this proton. The γ-exocyclic position is in turn attacked by each of the electrophiles (water, iodomethane, or benzophenone), although iodomethane also gives small quantities of other products (Scheme 5). The second lithiation occurs at the 5-C of the ring. The reaction of bis-lithiated 1-propargyl-1*H*-1,2,4-triazole (**5**) with 1 equiv of benzophenone formed mixtures of mono- and disubstitution products. A similar product distribution, but with higher yields, was obtained when 1-propargyl-1*H*-1,2,4-triazole (**5**) was reacted with 3 equiv of BuLi (Table 4).

Experimental Section

General. Melting points were determined with a hot-stage apparatus and are uncorrected. NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as the internal standard for ^{1}H (300 MHz) or solvent as the internal standard for ^{13}C (75 MHz), unless otherwise stated. The abbreviations for the multiplicity of the proton signals are as follows: q for quartet, qv for quintet, sx for sextet, and h for heptet. GC-MS spectra were performed on a HP5890 series II GC HP 5972 MSD instrument, equipped with a HP5 30 m column. Retention times (t_r) are given in minutes. THF was distilled under nitrogen immediately prior to use from sodium/benzophenone. All reactions with air-sensitive compounds were carried out under an argon atmosphere. Column chromatography was conducted with silica gel 230−400 mesh. 1-*n*-Butyl-1*H*-1,2,4-triazole (**1**) was prepared by a procedure previously described.[14] Benzophenone, iodomethane, 1-iodohexane, 1-iodooctane, benzyl bromide, and phenyl isocyanate were purchased from Fisher.

Note. In some cases, compounds were isolated as mixtures and, if they were not considered to present synthetical interest, further purification was not performed. Assignments were made on the basis of ^{1}H and ^{13}C NMR spectra and GC-MS results, which are presented in the Supporting Information.

Characterization data and details regarding reactions and separation of products are also presented in the Supporting Information.

1-Octyl-1*H*-1,2,4-triazole (2). Finely ground 1*H*-1,2,4-triazole (10 mmol), NaOH (40 mmol), and DMF (10 mL) were stirred for 5 min; then iodooctane (2.4 g, 10 mmol) was added. After 15 min, the reaction mixture was poured in water (50 mL), extracted with chloroform (3 × 50 mL), and dried ($MgSO_4$) and the solvent was evaporated under vacuum. The product was purified by flash vacuum chromatography on silica gel, using successively hexane and diethyl ether as eluent: yellow oil,[15] 1.3 g (70%); ^{1}H NMR δ 8.06 (s, 1H), 7.93 (s, 1H), 4.16 (t, J = 6.9 Hz, 2H), 1.89 (qv, J = 6.9 Hz, 2H), 1.32−1.20 (m, 10H), 0.87 (t, J = 6.6 Hz, 3H); ^{13}C NMR δ 13.7, 22.2, 26.1, 28.6, 28.7, 29.4, 31.3, 49.3, 142.4, 151.4.

1-(1-Pyrrolidinomethyl)-1*H*-1,2,4-triazole (3). 1*H*-1,2,4-Triazole (7.81 g, 0.11 mol), pyrrolidine (8.5 g, 0.12 mol), and a solution of formaldehyde in water (37% w/w, 10 mL, 0.12 mol) were dissolved in ethanol (50 mL). The mixture was refluxed for 4 h; then the solvent was removed under vacuum. The resulting residue was diluted with water (50 mL), extracted with chloroform (3 × 25 mL), and dried (Na_2SO_4). The extract was concentrated, and the residue was subjected to distillation (bp 100 °C/1.2 mmHg) to give a colorless oil,[7] 14.4 g (86%): ^{1}H NMR δ 8.15 (s, 1H), 7.95 (s, 1H), 5.14 (s, 2H), 2.74−2.69 (m, 4H), 1.79−1.74 (m, 4H); ^{13}C NMR δ 23.6 (2C), 49.5 (2C), 66.3, 143.3, 151.3.

1-Allyl-1*H*-1,2,4-triazole (4). 1*H*-1,2,4-Triazole (17.25 g, 0.25 mol) was added to a solution prepared from sodium metal (5.75 g, 0.25 mol) in absolute EtOH (90 mL). After complete dissolution, the reaction mixture was heated at 40 °C for 0.5 h; allyl bromide (22.7 mL, 0.26 mol) was then added in one portion. The reaction mixture was stirred at 75 °C for 12 h, then cooled to rt, filtered, and concentrated under vacuum to a semicrystalline residue which was taken up in chloroform (100 mL). The organic extract was filtered and concentrated under vacuum, and the residue was distilled (bp 94−95 °C/12 mmHg) to yield a colorless liquid,[16] 16.35 g (60%): ^{1}H NMR δ 8.12 (s, 1H), 7.96 (s, 1H), 6.01 (ddt, J = 6.0 Hz, J = 10.2 Hz, J = 17.1 Hz, 1H), 5.35 (d, J_{cis} = 10.2 Hz, 1H), 5.28 (d, J_{trans} = 17.1 Hz, 1H), 4.81 (d, J = 6.0 Hz, 2H); ^{13}C NMR δ 51.8, 119.6, 131.0, 142.5, 151.8.

1-Propargyl-1*H*-1,2,4-triazole (5). 1*H*-1,2,4-Triazole (15 g, 0.217 mol) in absolute EtOH (150 mL) was cooled to 0 °C in an ice bath, and a solution of NaOH (8.70 g, 0.217 mol, in 15 mL water) was added. When the sodium triazolate precipitated, propargyl bromide (25 mL, as 80% w/w in toluene, 0.224 mol) was added dropwise at 0 °C (about 1 h). The reaction mixture was allowed to gradually reach rt and was kept under stirring for an additional 48 h, when the final pH was below 8.5. Water (100 mL) was added until the solution was clear, and the reaction mixture was extracted with CH_2Cl_2 (3 × 150 mL). The organic solution was washed with water (50 mL, to neutrality), dried ($MgSO_4$), and concentrated under vacuum to give crude product as an orange liquid (19 g), which was purified by distillation (bp 53−55 °C/0.8−1 mmHg). The compound solidified upon standing to give yellow crystals, mp 44−6 °C (lit.[17] mp 45−6 °C); 13.86 g (58%): ^{1}H NMR δ 8.31 (s, 1H), 7.97 (s, 1H), 5.00 (d, J = 2.5 Hz, 2H), 2.64 (t, J = 2.5 Hz, 1H), ^{13}C NMR δ 39.2, 74.9, 75.7, 142.6, 152.1.

Functionalized 1-Alkyl-1*H*-1,2,4-triazoles. Conditions A: Synthesis of Compounds 6a−c, 7, 8, 10, 14a,b, and 15a,b. The appropriate 1-alkyl-1*H*-1,2,4-triazole (0.34 M in THF) was treated at −78 °C with an equimolar amount of BuLi (1.6 M solution in hexane) to give a yellow suspension. After 15 min, the theoretical amount of electrophile (20% in THF) was added and the reaction was allowed to warm to rt. The reaction was quenched with a saturated solution of NH_4Cl (50 mL) and extracted with CH_2Cl_2 (50 mL). The organic layer was dried ($MgSO_4$), the solvent was evaporated in vacuo, and the residue was subjected to column chromatography.

1-Butyl-5-*D*-1*H*-1,2,4-triazole (6a) was obtained as an oil by lithiation of 1-butyl-1*H*-1,2,4-triazole (**1**) and quenching the reaction mixture with D_2O at rt (95%).

1-Butyl-5-methyl-1*H*-1,2,4-triazole (6b) was obtained as an oil by lithiation of 1-butyl-1*H*-1,2,4-triazole (**1**) and electrophilic substitution with iodomethane (41%).

(1-Butyl-1*H*-1,2,4-triazol-5-yl)(diphenyl)methanol (6c) was obtained exclusively as the 5-isomer by lithiation of

1-butyl-1*H*-1,2,4-triazole (**1**) and electrophilic substitution with benzophenone; mp 120−2 °C (82%).

1-Butyl-5-hexyl-1*H*-1,2,4-triazole (7) was obtained as an oil by lithiation of 1-butyl-1*H*-1,2,4-triazole (**1**) and electrophilic substitution with iodohexane (73%).

1-Butyl-5-(6-dodecyl)-1*H*-1,2,4-triazole (9) was obtained as an oil by lithiation of 1-butyl-1*H*-1,2,4-triazole (**1**) and electrophilic substitution with iodohexane (10%).

5-(1-Benzyl-1,2-diphenylethyl)-1-butyl-1*H*-1,2,4-triazole (10) was obtained by lithiation of 1-butyl-1*H*-1,2,4-triazole (**1**) and electrophilic substitution with benzyl bromide; white solid, mp 89−90 °C (32%).

Phenyl[(1-pyrrolidinomethyl)-*1H*-1,2,4-triazol-3(5)-yl]-methanol (14a,b) was obtained as a mixture of 3- and 5-isomers in a 1:2 ratio by lithiation of 1-(1-pyrrolidinomethyl)-1*H*-1,2,4-triazole (**3**) and electrophilic substitution with benzaldehyde; white solid, mp 86−87 °C (lit.[8] mp 87 °C) (76%).

Diphenyl[(1-pyrrolidinomethyl)-*1H*-1,2,4-triazol-3(5)-yl]methanol (15a,b) was obtained as a mixture of 3- and 5-isomers in a ratio of 2:1 by lithiation of 1-(1-pyrrolidinomethyl)-1*H*-1,2,4-triazole (**3**) and electrophilic substitution with benzophenone; white solid, mp 121−122 °C (lit.[9] mp 121−2 °C) (80%).

Conditions B: Synthesis of Compounds 12 and 13. The appropriate 1-alkyl-1*H*-1,2,4-triazole (0.34 M in THF) was lithiated at −78 °C with the equimolar amount of BuLi (1.6 M solution in hexane) to give a yellow suspension. After 15 min, the theoretical amount of electrophile (20% in THF) was added dropwise and the reaction was kept at −78 °C for 2 h. The reaction mixture was again lithiated with the equimolar amount of BuLi (1.6 M solution in hexane), and after 15 min the theoretical amount of electrophile (20% in THF) was added. The reaction was allowed to warm to rt, quenched with a saturated solution of NH_4Cl (50 mL), and extracted with CH_2Cl_2 (50 mL). The organic solution was dried ($MgSO_4$), and the solvent was evaporated in vacuo. The residue was subjected to column chromatography.

5-Ethyl-1-octyl-1,2,4-triazole (12) was obtained by lithiation of 1-octyl-1*H*-1,2,4-triazole (**2**) and electrophilic substitution with iodomethane; oil (32%).

1-Octyl-5-pentyl-1,2,4-triazole (13) was obtained by lithiation of 1-octyl-1*H*-1,2,4-triazole (**2**) and electrophilic substitution with iodomethane; oil (40%).

Functionalized 1-Allyl-1*H*-1,2,4-triazoles. Conditions A: Synthesis of Compounds 24a−c. 1-Allyl-1*H*-1,2,4-triazole (0.34 M in THF) was lithiated at −78 °C with an equimolar amount of BuLi (1.6 M solution in hexane) to give a yellow suspension. After 15 min, the theoretical amount of electrophile was added dropwise (benzophenone and phenyl isocyanate as 20% THF solution) and the reaction was allowed to reach rt. The reaction mixture was quenched with a saturated solution of NH_4Cl and extracted with CH_2Cl_2 (**24a**,**b**) or EtOAc (**24c**) (4 × 50 mL). The organic layer was dried ($MgSO_4$), the solvent was evaporated in vacuo, and the residue was subjected to column chromatography.

Conditions B: Synthesis of Compounds 24c, 25b, 26b, 29c, 30c, and 33. 1-Allyl-1*H*-1,2,4-triazole (0.34 M in THF) was lithiated at −78 °C with the equimolar amount of BuLi (1.6 M solution in hexane) to give a yellow suspension. After 15 min, the theoretical amount of electrophile was added dropwise (benzophenone and phenyl isocyanate as a solution 20% in THF) and the reaction was kept at −78 °C for 2 h (**33**), 5 h (**25b**, **26b**), or 6 h (**24c**, **29c**, and **30c**). The reaction mixture was lithiated with an equimolar amount of BuLi (1.6 M solution in hexane), and after 15 min the theoretical amount of electrophile was added (as above). The reaction was allowed to reach rt, quenched with saturated NH_4Cl (50 mL), extracted with CH_2Cl_2 (**33, 25b, 26c**) or EtOAc (**24c**, **29c**, **30c**) (4 × 50 mL), and dried (Na_2SO_4). The organic layer was worked up as described before for the reactions performed using conditions A.

Conditions C: Synthesis of Compounds 24c, 25a, 25b, 26a, 26b, 29c, 30c, and 32c. 1-Allyl-1*H*-1,2,4-triazole (0.34 M in THF) was lithiated at −78 °C with BuLi (2 equiv, 1.6 M solution in hexane, BuLi:substrate molar ratio of 2:1) to give a yellow suspension. After 15 min the electrophile (2 equiv) was added dropwise (benzophenone and phenyl isocyanate as a solution 20% in THF) and the reaction was kept at −78 °C for 2 h (**25a**, **26a**), 5 h (**25b**, **26b**), and 6 h (**24c**, **29c**, **30c**, **32c**). The reaction mixture was allowed to reach rt, quenched with saturated NH_4Cl (50 mL), extracted with CH_2Cl_2 (**25a**, **26a**, **25b**, **26b**) or EtOAc (**24c**, **29c**, **30c**, **32c**) (4 × 50 mL), and dried (Na_2SO_4). The organic layer was worked up as described above for the reactions performed using conditions A.

Conditions D: Synthesis of Compounds 24c, 25a, 26a, 27a, 25b, 27b, 28b, 29b, 29c, 30c, and 31c. 1-Allyl-1*H*-1,2,4-triazole (0.34 M in THF) was lithiated at −78 °C with 2 equiv of BuLi (1.6 M solution in hexane) to give a yellow suspension. After 15 min the electrophile (1 equiv) was added dropwise (benzophenone and phenyl isocyanate as a solution 20% in THF) and the reaction was kept at −78 °C for 2 h (**25a**, **26a**, **27a**), 5 h (**25b**, **27b**, **28b**, **29b**), and 6 h (**24c**, **29c**, **30c**, **31c**). The reaction was allowed to reach rt, quenched with saturated NH_4Cl (50 mL), extracted with CH_2Cl_2 (**25a**, **26a**, **27a**, **25b**, **27b**, **28b**, **29b**) or EtOAc (**24c**, **29c**, **30c**, **31c**) (4 × 50 mL), and dried (Na_2SO_4). The organic layer was worked up as described above for the reactions performed using conditions A.

Isomerization of 1-Allyl-1*H*-1,2,4-triazole (4) to (*Z*)-1-(Propen-1-yl)-1*H*-1,2,4-triazole (26d). 1-Allyl-1*H*-1,2,4-triazole (2.00 g, 0.0183 mol) in THF (54 mL) was lithiated with BuLi (23 mL, 1.6 M in hexane, 0.0366 mol) at −78 °C to give a yellow fine suspension. Eleven samples were collected at −78 °C after 1, 2, 3, 4, 6, 9, 15, 25, 35, and 50 min and then after 7, 8, and 9 h. The ^{1}H NMR spectra indicated for all these samples an equimolar ratio between **4** and **43**. The reaction mixture was then allowed to reach rt and was quenched with saturated NH_4Cl (25 mL). The aqueous layer was extracted with EtOAc (3 × 25 mL), dried ($MgSO_4$), and allowed to stand at 4 °C for 24 h, when the polymeric deposits were filtered off and the solvent was evaporated in vacuo. The oily residue was subjected to column chromatography (40 g silica gel, eluent EtOAc) to yield a mixture of isomers, in a **26d**(***Z***):**32d**(***E***) of 10:1; 1.00 g (50%): ^{1}H NMR δ (*Z*) 8.26 (s, 1H), 8.02 (s, 1H), 6.82 (dq, $J_{allylic}$ = 1.8 Hz, J_{cis} = 9.1 Hz, 1H), 5.63 (dq, J = 7.3 Hz, J_{cis} = 9.1 Hz, 1H), 1.95 (dd, J = 7.3 Hz, J = 1.8 Hz, 3H), (*E*) 8.22 (s, 1H), 7.96 (s, 1H), 6.60 (dq, $J_{allylic}$ = 1.8 Hz, J_{trans} = 14.0 Hz, 1H), 6.31 (m, J = 7.0 Hz, J_{trans} = 14.0 Hz, 1H), 1.85 (dd, J = 7.0 Hz, J = 1.8 Hz, 3H); ^{13}C NMR $\delta\delta$ (*Z*) 12.5, 119.7, 123.0, 143.1 151.2; (*E*) 14.4, 117.5, 123.6, 140.9, 151.4; HRMS (EI) 109.0641, calcd for $C_5H_7N_3$ 109.0639.

Reactions with Iodomethane. Conditions A: 1-allyl-5-methyl-1,2,4-triazole (24a) was obtained starting from compound **4** (1.5 g, 0.0137 mol) and separated by column chromatography as the main fraction, using EtOAc as eluent; yellow oil, 1.00 g (60%).

Conditions B: (*Z*)-1-allyl-5-ethyl-1,2,4-triazole (33) was obtained from compound **4** (1.50 g, 0.0137 mol) and separated by column chromatography as the main fraction, using as eluent EtOAc; yellow oil, 1.00 g (53%).

Conditions C: (*Z*)-1-buten-1-yl-5-methyl-1,2,4-triazole (26a) was obtained from compound **4** (1.50 g, 0.0137 mol) and separated by column chromatography as the main fraction, using EtOAc as eluent; yellow oil, 1.04 g (55%). The second fraction in the column chromatography separation was **2-(5-methyl-1,2,4-triazol-1-yl)-3-butene (25a)**, as a mixture with **26a**; yellow oil, 0.100 g (28% **25a**).

Conditions D: (*Z*)-1-buten-1-yl-1,2,4-triazole (27a) was obtained from compound **4** (1.50 g, 0.0137 mol) and separated by column chromatography as the main fraction, using as eluent EtOAc; yellow oil, 0.57 g (35%).

Reactions with Benzophenone. Conditions A: 1-allyl-5-(hydroxydiphenylmethyl)-1,2,4-triazole (24b) was obtained from compound **4** (1.50 g, 0.0137 mol) and separated by column chromatography using as eluent hexanes−EtOAc (2:1); white crystals, mp 151−3 °C; 1.57 g (40%).

Conditions B: (*Z*)-1,1-diphenyl-4-(5-diphenylhydroxymethyl-1,2,4-triazol-1-yl)-3-buten-1-ol (26b) was obtained from compound **4** (1.50 g, 0.0137 mol) and separated by column chromatography (first fraction compound **25b**, 1.84 g, 28.5%),

using as eluent hexanes−EtOAc (2:1); white crystals, mp 166−8 °C; 2.30 g (35.5%).

Conditions C: (α-diphenylhydroxymethyl)-1-allyl-5-(diphenylhydroxymethyl)-1,2,4-triazole (25b) was obtained from compound **4** (1.50 g, 0.0137 mol) and separated by column chromatography using as eluent hexanes−EtOAc (2:1) (the second fraction compound **26b**, 1.00 g, 23%); white crystals, mp 172−4 °C, 1.86 g (43%).

Conditions D: (α-diphenylhydroxymethyl)-1-allyl-1,2,4-triazole (28b) was obtained from compound **4** (1.50 g, 0.0137 mol) and separated by column chromatography using hexanes−EtOAc (2:1) as eluent; white crystals, mp 118−20 °C; 1.54 g (39%).

1,1-Diphenyl-4-(1*H*-1,2,4-triazol-1-yl)-(*Z*)-3-buten-1-ol (27b) and (*Z*)-5-Diphenylhydroxymethyl-1-propen-1-yl-1,2,4-triazole (29b) were obtained from compound **4** (1.50 g, 0.0137 mol) and separated by column chromatography as a second fraction, using hexanes−EtOAc (2:1) as eluent; mixture in a **27b**:**29b** ratio of 2:1 (see Note); 0.25 g (6.0%). Compound **25b** was also separated using conditions D (0.25 g, 4%).

Reactions with Phenyl Isocyanate. Conditions A: 1-allyl-5-*N*-phenylcarbamoyl-1,2,4-triazole (24c) was obtained from compound **4** (0.95 g, 0.0087 mol), and separated by column chromatography as the main fraction; eluent hexanes−EtOAc (3:1); yellow oil, 1.20 g (61%).

Conditions B. Starting from compound **4** (1.50 g, 0.0137 mol) the following compounds were isolated after column chromatography, using as eluent hexanes−EtOAc (3:1): **(*Z*/*E*)-1-Propen-1-yl-5-N-phenylcarbamoyl-1,2,4-triazole (29c/30c)** as a yellow oil, in a **29c**:**30c** ratio of 3.7:1; 0.340 g (14%). ***N,N*-Diphenylurea (35)**: white crystals, mp 235−7 °C (methanol) (lit.[28] mp 238−40 °C); 0.270 g (24.8% based on phenyl isocyanate). ***N,N*-Di-*N*-phenylcarbamoyl-aniline (36)**: white crystals, mp 156−8 °C (methanol) (lit.[29] mp 148 °C); 0.490 g (44.8% based on phenyl isocyanate).

Conditions C. Starting from compound **4** (1.50 g, 0.0137 mol) the following compounds were isolated after column chromatography using as eluent hexanes−EtOAc (3:1):

(*Z*)-1-Propen-1-yl-5-*N*-phenylcarbamoyl-1,2,4-triazole (29c) (see conditions B above) in a mixture with ***N*-phenyl *n*-butylcarbamate (34)**[30] as a reddish oil; the **29c**:**34** ratio was ca. 4.5:1 (by ^{1}H NMR); 0.440 g (11.5% **29c** and 1% **34**). ***N,N*-Diphenylurea (35):** 0.180 g (8% based on phenyl isocyanate). ***N,N*-Di-*N*-phenylcarbamoylaniline (36):** 0.680 g (30.1%, based on phenyl isocyanate).

(*E*)-5-*N*-Phenylcarbamoyl-1-(3-*N*-phenylcarbamoyl-1-propen-1-yl)-1,2,4-triazole (32c) was isolated after column chromatography using as eluent hexanes−diethyl ether (1:1): yellow crystals, mp 185−7 °C; 0.96 g (20.4%).

Conditions D. Starting from compound **4** (2.00 g, 0.0183 mol) the following compounds were isolated by column chromatography using as eluent hexanes−EtOAc (3:1): compounds **29c**, **30c**, and **34** as a mixture in a **29c**:**30c**:**34** ratio of 6:1:1 (by ^{1}H NMR); yellow oil, 0.14 g (3% **29c**, 0.5% **30c**, 0.5% **34**). ***N,N*-Diphenylurea (35)**: 0.17 g (5% based on phenyl isocyanate) (see conditions B above). ***N,N*-Di-*N*-(phenylcarbamoyl)aniline (36)**: 0.22 g (3.7% based on phenyl isocyanate).

(*E*)-1-(3-*N*-Phenylcarbamoyl)-1-propen-1-yl-1,2,4-triazole (31c) was obtained by column chromatography using as eluent CH_2Cl_2:ether (1:1); yellow crystals, mp 202−4 °C; 0.17 g (6%).

Functionalized 1-Propargyl-1*H*-1,2,4-triazoles. Conditions A. 1-Propargyl-1*H*-1,2,4-triazole (0.28 M solution in THF) was lithiated at −78 °C with an equimolar amount of BuLi (1.6 M solution in hexane) to give an orange suspension. After 15 min the appropriate electrophile (1 equiv) was added dropwise (iodomethane or benzophenone as 20% THF solution). The reaction mixture was allowed to warm at rt overnight, then was quenched with saturated NH_4Cl, extracted with EtOAc (reported to the reaction volume, ca. 4-fold amount of EtOAc is recommended), and dried ($MgSO_4$). The organic solution was concentrated in vacuo, and the crude reaction mixture was separated by column chromatography (**37**−**39**) or recrystallized from methanol (**45**).

Reaction with Iodomethane. Starting from compound **5** (1.50 g, 0.014 mol), a mixture of isomers **37**−**39** was isolated after column chromatography (eluent EtOAc), as an oil (see Note); 1.12 g (60%). According to the ^{1}H NMR spectrum of the mixture, the assignments and percentages are as follows: **1-(1,2,4-triazol-1-yl)-2-butyne (37)**, 70%; **3-(1,2,4-triazol-1-yl)-1-butyne (38)**, 10%; **2-(1,2,4-triazol-1-yl)-3-pentyne (38)**, 20%.

Reaction with Benzophenone: 1,1-Diphenyl-4-(1,2,4-triazol-1-yl)-2-butyn-1-ol (45): white crystals, mp 149−50 °C (methanol) (70%).

Conditions B: Synthesis of Compounds 45−48. 1-Propargyl-1*H*-1,2,4-triazole (**5**) (0.28 M solution in THF) was lithiated at −78 °C with an equimolar amount of BuLi (1.6 M in hexane) to give an orange suspension. After 15 min benzophenone (1 equiv as 20% THF solution) was added dropwise. The resulted solution was further lithiated at −78 °C with BuLi (1 equiv) to give a purple solution. After 15 min benzophenone (1 equiv as 20% THF solution) was added dropwise. The reaction mixture was maintained at −78 °C for 8 h and then allowed to reach rt. The reaction mixture was quenched with saturated NH_4Cl and worked up as described in conditions A. Starting from 1.25 g (0.0117 mol) of compound **5**, the following compounds were isolated by column chromatography, using as eluent hexanes−EtOAc (1.5:1): **1,1-Diphenyl-4-(5-diphenylhydroxymethyl-1,2,4-triazol-1-yl)-2,3-butadien-1-ol (46)**: white crystals; mp 100−1 °C (ether); 0.690 g (12.3%). **1,1-Diphenyl-4-(5-diphenylhydroxymethyl-1,2,4-triazol-1-yl)-2-butyn-1-ol (47) and 1,1,4,4-tetraphenyl-1,2,4-triazol-1-yl-3-butyn-1,4-diol (48)**: isolated as a mixture in a **47**:**48** ratio of 3.3:1; white crystals, mp 120−142 °C; 2.34 g (42.5%). **1,1-Diphenyl-4-(1,2,4-triazol-1-yl)-2-butyn-1-ol (45)**: eluted from the chromatography column with dry acetone (see conditions A above); 0.57 g (17%).

Conditions D: Synthesis of Compounds 49−51. 1-Propargyl-1*H*-1,2,4-triazole (**5**) (0.014 mol, 0.28 M in THF) was lithiated at −78 °C with BuLi (2 equiv, 1.6 M in hexane) to yield an orange suspension. After 15 min, benzophenone (1 equiv as 20% in THF) was added dropwise. After 4 h the reaction mixture (as a green solution) was quenched at −78 °C and worked up as described above to give after column chromatography compounds **49**−**51**. The column was finally eluted with dry acetone to afford unreacted starting material **4**, 0.97 g (77%).

1,1-Diphenyl-2-(5-diphenylhydroxymethyl-1,2,4-triazol-1-yl)-3-butyn-1-ol (49). Hexanes−EtOAc (1.5:1) was used as eluent to obtain white crystals, mp 142−4 °C (ether); 0.35 g (7.4%).

5-Diphenylhydroxymethyl-1-propyn-1-yl-1,2,4-triazole (50). Hexanes−EtOAc (1.5:1) was used as eluent to obtain white crystals, mp 170−1 °C; 0.43 g (9.0%).

1,1-Diphenyl-2−1,2,4-triazol-1-yl-3-butyn-1-ol (51). Hexanes−EtOAc (1.5:1) was used as eluent to obtain white crystals, mp 165−7 °C (ether); 0.31 g (6.6%).

Conditions E: Alternative Synthesis of Compounds 49−51. 1-Propargyl-1*H*-1,2,4-triazole (**5**) (1.50 g, 0.014 mol, 0.28 M in THF) was lithiated at −78 °C with BuLi (3 equiv, 1.6 M in hexane) to give an orange suspension. After 15 min benzophenone (2 equiv as 20% THF solution) was added dropwise. The deep green reaction mixture was maintained at −78 °C for an additional 8 h and then was quenched and worked up as described above. Compounds **45**−**47** were separated by column chromatography, using as eluent hexanes−EtOAc (1.5:1). The unreacted starting material was finally eluted with dry acetone; 0.69 g (42%). **1,1-Diphenyl-2-(5-diphenylhydroxymethyl-1,2,4-triazol-1-yl)-3-butyn-1-ol (49)**: 0.755 g (17%). **5-Diphenylhydroxymethyl-1-propyn-1-yl-1,2,4-triazole (50)**: 1.16 g (26%). **1,1-Diphenyl-2−1,2,4-triazol-1-yl-3-butyn-1-ol (51)**: 0.69 g (15%).

(30) McGhee, W.; Riley, D.; Christ, K.; Pan, Y.; Parnas, B. *J. Org. Chem.* **1995**, *60*, 2820.

Supporting Information Available: ^{1}H NMR, ^{13}C NMR, and HRMS spectra for compounds **6a**,**b**, **9**, **13**, **24a**, **26a**, **27a**, **26d**, and **33** and ^{1}H and ^{13}C NMR for compound **8** and the mixtures of compounds referred to in Note. Characterization data and experimental details for the following compounds: **6a**−**c**, **7**, **8**−**10**, **12**−**15**, **24a**−**c**, **25a**−**b**, **26a**−**b**, **27a**−**b**, **28b**, **29b**−**c**, **30c**, **31c**, **32c**, **33**−**39**, **45**−**51**. 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.

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