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Facile Deallylation Protocols for the Preparation of *N*-Unsubstituted Triazoles and Tetrazoles

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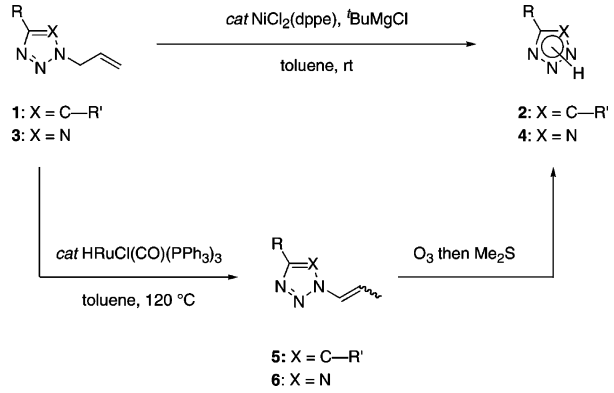

Two facile deallylation protocols have been developed for the preparation of *N*-unsubstituted triazoles and tetrazoles. The first protocol is a direct deallylation using a combination of a catalytic amount of nickel complex, $NiCl_2$(dppe), and a stoichiometric amount of Grignard reagent, ^{t}BuMgCl. The second protocol is a stepwise deallylation through consecutive reactions of isomerization and ozonolysis. The isomerization from *N*-allylazoles to *N*-vinylazoles is catalyzed by a ruthenium complex, $HRuCl(CO)(PPh_3)_3$, and the following ozonolysis of the derived *N*-vinyl intermediates affords *N*-unsubstituted azoles. These protocols can be used complementarily depending on the type of functional groups in the parent allylated azoles.

Introduction

Nitrogen-containing heteroaromatic compounds such as triazoles[1] and tetrazoles[2] are highly versatile chemicals which exhibit a wide spectrum of utilities in pharmaceutical and industrial areas.

We recently developed catalytic three-component coupling (TCC) reactions for the synthesis of allyltriazoles using a variety of alkynes, allyl carbonate, and $TMSN_3$ as starting materials. Activated alkynes with conjugation of an electron-withdrawing group afforded 2-allyltriazoles in the presence of a catalytic amount of $Pd_2(dba)_3{\cdot}CHCl_3$–dppp (eq 1, Scheme 1).[3] In the case of unactivated terminal alkynes, the formation of allyltriazoles was attained by employment of the palladium and copper bimetallic catalyst. The corresponding 2-allyltriazoles were obtained regioselectively in the presence of $Pd_2(dba)_3{\cdot}CHCl_3$–$P(OPh)_3$ and $CuCl(PPh_3)_3$ bimetallic catalyst (eq 2),[4] whereas the formation of 1-allyltriazoles took place under a combination of $Pd(OAc)_2$–PPh_3 and $CuBr_2$ catalysts (eq 3).[5] Furthermore, fully substituted diallyltriazoles were produced under $Pd_2(dba)_3{\cdot}CHCl_3$–$P(OEt)_3$ and CuCl bimetallic catalyst using silylacetylenes as a

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(1) For, reviews on 1,2,3-triazoles, see: (a) Dehne, H. In *Methoden der Organischen Chemie (Houben-Weyl)*; Schumann, E., Ed.; Thieme: Stuttgart, 1994; Vol. E8d, pp 305–405. (b) Wamhoff, H. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, 1984; Vol. 5, pp 669–732. (c) Sheradsky, T. In *The chemistry of the azido group*; Patai, S., Ed.; Interscience: London, 1971; pp 377–382. (d) Abu-Orabi, S. T.; Atfah, M. A.; Jibril, I.; Mari'i, F. M.; Ali, A. A.-S. *J. Heterocycl. Chem.* **1989**, *26*, 1461–1468.

(2) For reviews on tetrazoles, see: (a) Meier, H. R.; Heimgartner, H. In *Methoden der Organischen Chemie (Houben-Weyl)*; Schumann, E., Ed.; Georg Thieme Verlag: Stuttgart, 1994; Vol. E8d, pp 664–795. (b) Butler, R. N. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, 1984; Vol. 5, pp 791–838.

(3) Kamijo, S.; Jin, T.; Huo, Z.; Yamamoto, Y. *Tetrahedron Lett.* **2002**, *43*, 9707–9710.

(4) Kamijo, S.; Jin, T.; Huo, Z.; Yamamoto, Y. *J. Am. Chem. Soc.* **2003**, *125*, 7786–7787.

(5) Kamijo, S.; Jin, T.; Huo, Z.; Yamamoto, Y. *J. Org. Chem.* **2004**, *69*, 2386-2393.

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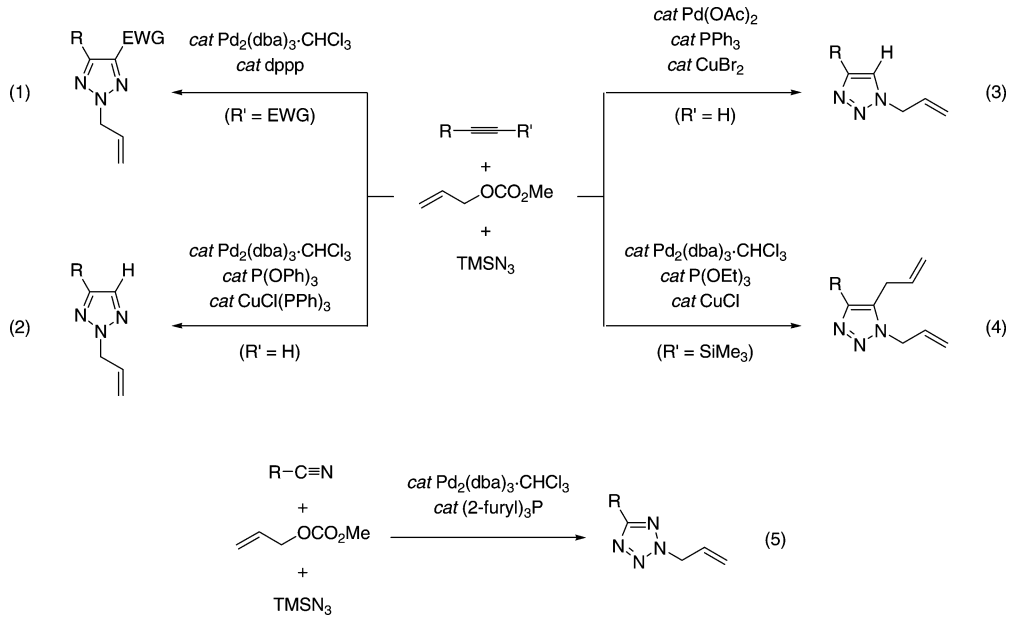
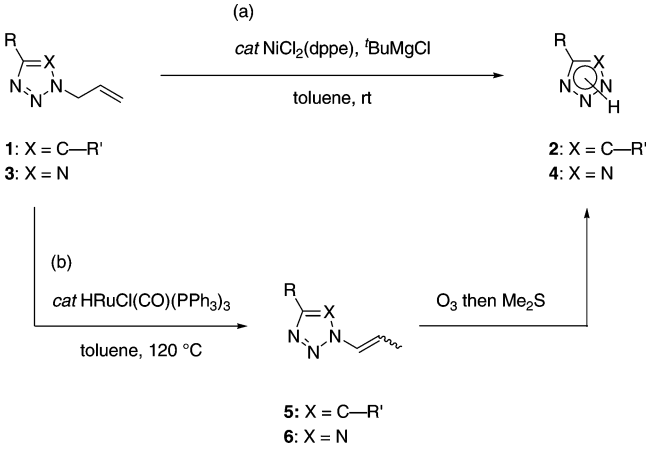
SCHEME 1



substrate (eq 4).[6] We also developed a regiocontrolled synthesis of 2-allyltetrazoles employing a palladium-catalyzed TCC reaction of nitriles, allyl carbonate, and $TMSN_3$ (eq 5).[7] However, one or two allyl groups are attached on one or two nitrogen atoms of all the azoles obtained through these TCC reactions.[8] These nitrogen-containing heteroaromatic compounds are often applied in the field of medicinal chemistry; *N*-unsubstituted tetrazoles are especially well-known to serve as a surrogate for carboxylic acid functionality.[9] Easy availability of *N*-allyltriazoles and -tetrazoles through our TCC reaction strategy and their potential applicabilities in medicinal chemistry motivated us to explore *N*-deallylation protocols for these compounds.

Due to the existence and importance of a wide range of naturally occurring products and biologically active compounds containing a nitrogen atom such as alkaloids and amino acids, various ways to protect a nitrogen atom have been invented, and the allyl group is one of them.[10] Compared to a number of protecting groups developed for amines and amides,[11] protecting groups for a nitrogen atom in the heteroaromatic rings are relatively unexplored. We now report two facile *N*-deallylation protocols for allylated triazoles and tetrazoles to obtain the corresponding *N*-unsubstituted azoles. The first protocol is a direct deallylation using $NiCl_2$(dppe) catalyst and a stoichiometric amount of ^{t}BuMgCl (Scheme 2a). The second protocol is a stepwise deallylation through consecutive reactions of a ruthenium-catalyzed isomerization and ozonolysis (Scheme 2b).[12]

SCHEME 2. Deallylation Protocols for a Preparation of *N*-Unsubstituted Triazoles and Tetrazoles



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(8) Recently, we have succeeded in synthesizing *N*-substituted triazoles and monosubstituted tetrazoles; see: (a) Jin, T.; Kamijo, S.; Yamamoto, Y. *Eur. J. Org. Chem.* **2004**, 3789−3791 (triazole). (b) Jin, T.; Kamijo, S.; Yamamoto, Y. *Tetrahedron Lett.* **2004**, *45*, 9435−9437 (tetrazole).

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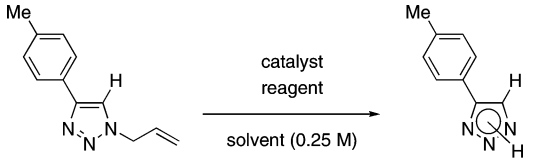
(12) For preliminary results, see: (a) Reference 4 (2-allyltriazole). (b) Reference 7b (2-allyltetrazole).

TABLE 1. Optimization of Reaction Conditions for a Direct *N*-Deallylation of the Allyltriazole 1a



1a **2a**

entry	catalyst (mol %)	reagent (equiv)	solvent	*T*, °C (time)	NMR yield,[a] %
1	$NiCl_2$(dppp) (5)	DIBALH (2)	toluene	0 (2 h) to rt (12 h)	47[b]
2	$NiCl_2$(dppp) (5)	Me_3Al (2)	toluene	0 °C (2 h) to rt (12 h)	0[c]
3	$NiCl_2$(dppp) (5)	^{t}BuMgCl (2)	toluene	0 °C (2 h)	85[b]
4	$NiCl_2$(dppe) (5)	^{t}BuMgCl (2)	toluene	0 °C (0.5 h)	85[b]
5	$NiCl_2(PPh_3)_2$ (5)	^{t}BuMgCl (2)	toluene	0 °C (1 h)	70
6	$NiCl_2$ (5)	^{t}BuMgCl (2)	toluene	0 °C (2 h) to rt (4 h)	35[c]
7	$PdCl_2$(dppp) (5)	^{t}BuMgCl (2)	toluene	0 °C (2 h) to rt (12 h)	78
8	CuCl (5)	^{t}BuMgCl (2)	toluene	0 °C (0.5 h)	68
9	$FeCl_3$ (5)	^{t}BuMgCl (2)	toluene	0 °C (2 h) to rt (1 h)	86
10	$NiCl_2$(dppe) (5)	^{t}BuMgCl (2)	CH_2Cl_2	0 °C (0.5 h)	85
11	$NiCl_2$(dppe) (5)	^{t}BuMgCl (2)	THF	0 °C (1 h)	73
12	$NiCl_2$(dppe) (5)	^{t}BuMgCl (2)	dioxane	0 °C (2 h) to rt (24 h)	38[c]
13	$NiCl_2$(dppe) (2)	^{t}BuMgCl (1.4)	toluene	rt (5 min)	86[b]
14	$NiCl_2$(dppe) (2)	^{i}PrMgCl (1.4)	toluene	rt (5 min)	27[c]
15	$NiCl_2$(dppe) (2)	PrMgCl (1.4)	toluene	rt (5 min)	35[c]
16	$NiCl_2$(dppe) (2)	MeMgCl (1.4)	toluene	rt (5 min)	0[c]
17	$NiCl_2$(dppe) (2)	PhMgCl (1.4)	toluene	rt (5 min)	58[d]

[a] NMR yield otherwise noted. [b] Isolated yield. [c] The recovery of the substrate **1a** was observed. [d] Allylbenzene was obtained as a byproduct.

Results and Discussion

Direct *N*-Deallylation Using a Combination of Nickel Catalyst and Grignard Reagent. We first applied some standard palladium-catalyzed deallylation protocols to cleave the allyl group in an allyltriazole.[13] The treatment of 4,5-di(methoxycarbonyl)-2-allyl-1,2,3-triazole with NDMBA (1,3-dimethylbarbituric acid) in the presence of a catalytic amount of $Pd(PPh_3)_4$ gave a complex mixture of products.[14] The reaction with $Pd(PPh_3)_4$ catalyst and Et_3N/HCO_2H resulted in recovery of the starting allyltriazole.[15] The reaction between the allyltriazole and sodium malonate in the presence of $Pd(PPh_3)_4$ catalyst did not give the desired deallylated product at all, and only the starting material was recovered. Accordingly, we concluded that the standard palladium-catalyzed allylic substitution reaction mentioned above did not work efficiently for deprotecting an allyl group of the triazole.

We then turned our attention to a deallylation protocol using a stronger base with a catalytic amount of a transition metal (Table 1). The treatment of the allyltriazole **1a** with DIBALH (diisobutylaluminum hydride) in the presence of $NiCl_2$(dppp) catalyst gave the desired *N*-unsubstituted triazole **2a** in a moderate yield (entry 1).[16] The reaction with Me_3Al did not yield the product **2a**, and a significant amount of the starting material **1a** was recovered (entry 2). The employment of ^{t}BuMgCl increased the yield of **2a** (entry 3). The reaction time was shortened when $NiCl_2$(dppe) was used instead of $NiCl_2$(dppp) (entry 4). $NiCl_2(PPh_3)_2$ and $NiCl_2$ showed catalytic activity, but the yields of **2a** were decreased (entries 5 and 6). The reaction proceeded with other transition-metal catalysts, such as $PdCl_2$(dppp), CuCl, and $FeCl_3$[17] as well, but no improvement of the catalytic activity was observed (entries 7−9). We also examined solvent effects using $NiCl_2$(dppe) and ^{t}BuMgCl. The reactions were complete in shorter times with high yields of **2a** in less polar solvents, such as toluene and CH_2Cl_2 (entries 4 and 10), compared to the reactions in ethereal solvents, such as THF and 1,4-dioxane (entries 11 and 12). Among the Grignard reagents we tested, ^{t}BuMgCl was most effective. The desired product **2a** was obtained in 86% isolated yield in the reaction of **1a** with 1.4 equiv of ^{t}BuMgCl under $NiCl_2$(dppe) catalyst (2 mol %) in toluene at rt for 5 min (entry 13). ^{i}PrMgCl and PrMgCl produced **2a** in lower yields with a recovery of **1a** (entries 14 and 15). With MeMgCl, the reaction did not proceed at all under the same conditions, and the starting allyltriazole **1a** was recovered quantitatively (entry 16). The reaction with PhMgCl resulted in formation of the desired compound **2a** in a moderate yield with formation of allylbenzene (entry 17).

With optimized conditions in hand, we examined the direct deallylation of various 1-allyltriazoles **1a**−**g** (Table 2). As mentioned above, the treatment of 1-allyl-4-(*p*-

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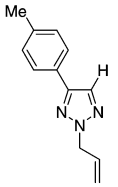
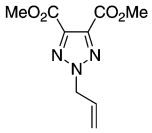
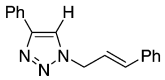
TABLE 2. Direct *N*-Deallylation of Allyltriazoles 1 with ^{t}BuMgCl under $NiCl_2$(dppe) Catalyst

entry	R	R'	1	Time, min	2	yield, %[a]
1	4-Me-C_6H_4	H	**1a**	5	**2a**	86
2	4-MeO-C_6H_4	H	**1b**	5	**2b**	91
3	Ph	H	**1c**	5	**2c**	91
4	4-MeO_2C-C_6H_4	H	**1d**	180	**2d**	16[b]
5	$CH_3(CH_2)_5$	H	**1e**	5	**2e**	96
6	4-Me-C_6H_4	$CH_2CH{=}CH_2$	**1f**	180	**2f**	91
7	4-Me-C_6H_4	$CH_2CH{=}CH_2$	**1f**	5	**2f**	92[c]
8	$CH_2CH{=}CH_2$	$CH_2CH{=}CH_2$	**1g**	5	**2g**	80[c]
9			**1h**	40	**2a**	88[c]
10			**1i**	180	**2i**	-[c,d]
11			**1j**	5	**2c**	78[e]

[a] Isolated yield. [b] The recovery of **1d** (27%) and the formation of byproducts were observed. [c] 4 mol % of $NiCl_2$(dppe) was used. [d] Complex mixture. [e] A mixture of (1-propenyl)benzene and allylbenzene was obtained in 52% yield with a ratio of 94:6.

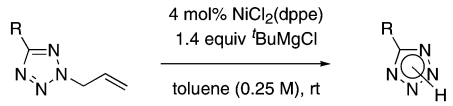
tolyl)-1,2,3-triazole **1a** with ^{t}BuMgCl (1.4 equiv) under a catalytic amount of $NiCl_2$(dppe) (2 mol %) in toluene (0.25 M) at rt for 5 min furnished 4-(*p*-tolyl)-1,2,3-triazole **2a** in 86% isolated yield (entry 1). We could not determine the position of a proton on a nitrogen atom of the products **2** except for the case of **2g**. Anisyl- and phenyl-attached allyltriazoles **1b** and **1c** produced the corresponding products **2b** and **2c** in high yields, respectively (entries 2 and 3). As expected, many side reactions occurred with the substrate **1d** bearing an ester group (entry 4). The alkyl-substituted allyltriazole **1e** afforded an excellent yield of **2e** (entry 5). It took 3 h to consume the starting material in the reaction of 1,5-diallyl-4-(*p*-tolyl)-1,2,3-triazole **1f**, although the corresponding product **2f** was formed in a high yield (entry 6). The reaction time was reduced dramatically from 180 to 5 min when 4 mol % of the Ni catalyst was used (entry 7). In the case of the reaction using 1,4,5-triallyltriazole **1g** as a starting material, 4,5-diallyl-2*H*-1,2,3-triazole **2g** was obtained as a product (entry 8).[18] The reaction of 2-allyltriazole **1h** gave the product **2a** in a high yield, which was exactly the same compound derived from the corresponding 1-allyltriazole **1a** (entry 9). Due to the presence of reactive ester group, the reaction of 2-allyl-4,5-di-(methoxycarbonyl)-1,2,3-triazole **1i** resulted in formation of many compounds (entry 10). We also carried out the reaction of the *N*-cinnamyl-substituted triazole **1j** (entry 11). The desired product **2c** was obtained in good yield along with formation of (1-propenyl)benzene and allylbenzene in 52% combined yield with a ratio of 94:6.

We then carried out the direct deallylation of 2-allyltetrazoles **3a**−**c**, and the results are summarized in Table 3. The reaction of the phenyl-substituted allyltetrazole **3a** with ^{t}BuMgCl in the presence of $NiCl_2$(dppe) catalyst proceeded smoothly to give the corresponding *N*-unsubstituted tetrazole **4a** in an excellent yield (entry 1). The spectroscopic data of the derived product **4a** showed good agreement with those of commercially available 5-phenyl-1*H*-tetrazole. The allyltetrazoles **3b** and **3c** bearing morpholino and indolyl groups, respectively, furnished the corresponding products **4b** and **4c** in good yields (entries 2 and 3).

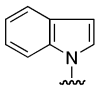
The most plausible mechanism for the present nickel-catalyzed direct *N*-deallylation of allyltriazoles and allyltetrazoles would be a pathway via hydronickelation

(18) Due to the symmetrical structure of **2g**, the position of a proton attached to nitrogen atom was easily determined; see the Supporting Information for details.

TABLE 3. Direct *N*-Deallylation of 2-Allyltetrazoles 3 with ^{t}BuMgCl under $NiCl_2$(dppe) Catalyst



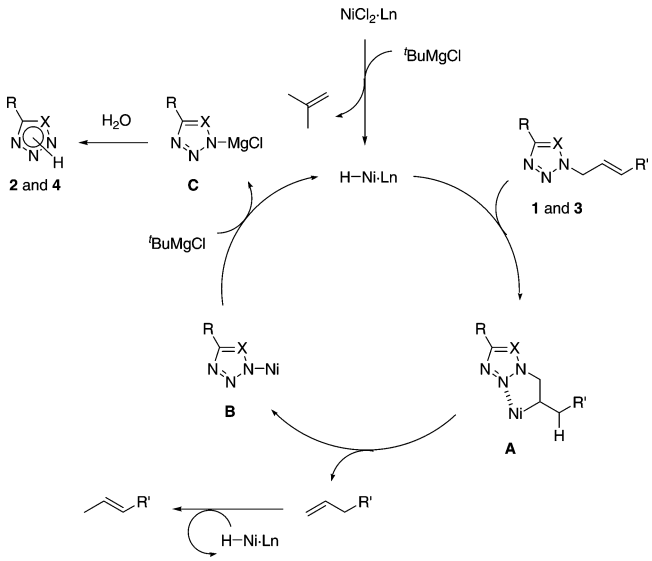
3 **4**

entry	R	3	time, min	4	yield, %[a]
1	Ph	**3a**	5	**4a**	95
2		**3b**	5	**4b**	80
3		**3c**	5	**4c**	87

[a] Isolated yield.

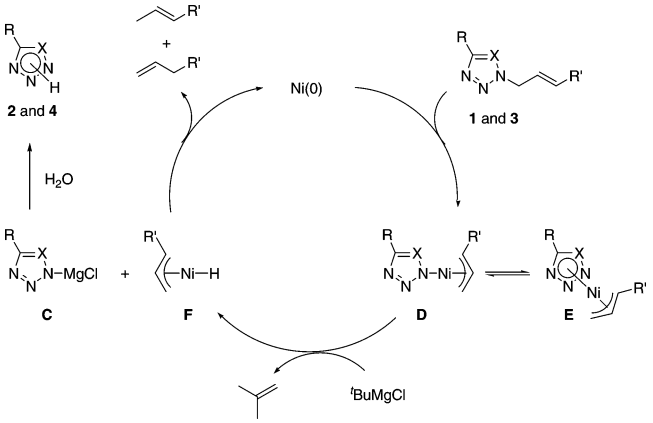
4a

SCHEME 3. Mechanism via Hydronickelation for the Direct *N*-Deallylation under ^{t}BuMgCl and Ni Catalyst



of the olefin in the allyl group as shown in Scheme 3.[19] The active catalytic hydridonickel species is generated initially via the reaction of $NiCl_2$(dppe) with ^{t}BuMgCl.[20] This explains why MeMgCl is not suitable for the deallylation but Grignard reagents having α-hydrogen,

SCHEME 4. Mechanism through π-Allylnickel Intermediates for the Direct *N*-Deallylation under ^{t}BuMgCl and Ni Catalyst



such as ^{t}BuMgCl, ^{i}PrMgCl, and PrMgCl, give the desired deallylation products (see Table 1, entries 13−16). Hydronickelation of the C−C double bond in the starting materials **1** and **3** gives the intermediate **A**. Subsequent β-elimination affords the intermediate **B** and allylbenzene when R′ = Ph. Allylbenzene is known to isomerize into (1-propenyl)benzene in the presence of a hydridonickel species, which is consistent with the result obtained in Table 2, entry 11.[16c] Transmetalation between **B** and ^{t}BuMgCl produces the intermediate **C** and regenerates the active catalytic species with extrusion of isobutylene. The *N*-unsubstituted azoles**2** and **4** are obtained upon aqueous workup.

An alternative pathway through formation of π-allylnickel intermediate might also be proposed as shown in Scheme 4.[21] The active Ni(0) catalytic species generated from $NiCl_2$(dppe) and ^{t}BuMgCl would add oxidatively to the starting materials **1** and **3** to form the π-allylnickel intermediate **D**. This complex **D** could be in equilibrium with the (η^5-azolyl)(η^3-allyl)nickel species **E**.[22] Transmetalation between the intermediate **D** and ^{t}BuMgCl gives the intermediates **F** and **C** along with extrusion of isobutylene. Aqueous workup furnishes the corresponding products **2** and **4** from the intermediate **C**, while reductive elimination of the π-allylnickel intermediate **F** yields (1-propenyl)benzene and allylbenzene. This mechanism would be operative in the case of the reaction with the Ni catalyst and PhMgCl (see Table 1, entry 17). Transmetalation between **D** and PhMgCl explains the formation of allylbenzene as a byproduct through the analogue of the π-allylnickel intermediate **F**.

Stepwise *N*-Deallylation through Ruthenium-Catalyzed Isomerization and Ozonolysis. We established the direct *N*-deallylation protocol using ^{t}BuMgCl and a nickel catalyst in the previous section; however, this method is not applicable to the substrates bearing a functional group, such as an ester, which is incompatible with the Grignard reagent. We thus decided to explore an alternative protocol for a cleavage of allyl group on a nitrogen atom of azoles. As a result, we found a stepwise deallylation protocol through consecutive reactions; ru-

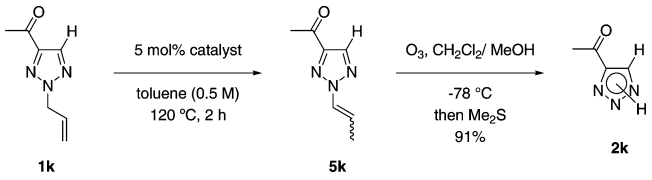
(19) Related mechanisms for nickel-catalyzed deallylation reactions; see ref 16b,c.

(20) For recent applications of a hydridonickel species in a catalytic reaction generated from a nickel complex and a Grignard reagent, see: (a) Milburn, R. R.; Snieckus, V. *Angew. Chem., Int. Ed.* **2004**, *43*, 888−891. (b) Milburn, R. R.; Snieckus, V. *Angew. Chem., Int. Ed.* **2004**, *43*, 892−894 and references therein.

(21) Pawlas, J.; Nakao, Y.; Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 3669−3679.

(22) Analogous palladium intermediates are proposed in refs 3−7.

TABLE 4. Optimization of Reaction Conditions for the Isomerization from 1k to 5k



entry	catalyst	solvent	NMR yield of **5k**,[a] %
1	$HRuCl(CO)(PPh_3)_3$	toluene	83[b]
2	$H_2Ru(CO)(PPh_3)_3$	toluene	trace[c]
3	$H_2Ru(PPh_3)_4$	toluene	trace[c]
4	$RuCl_2(PPh_3)_3$	toluene	0[c]
5	$Cl_2(Cy_3P)_2Ru(=CHPh)$	toluene	0[c]
6	$Ru_3(CO)_{12}$	toluene	0[c]
7	$RuCl_3 \cdot nH_2O$	toluene	0[c]
8	$HRh(CO)(PPh_3)_3$	CH_3CN/H_2O	8.5[c]
9[d]	$RhCl(PPh_3)_3$	toluene	0[c]
10[e]	$IrCl(CO)(PPh_3)_2$	toluene	0[c]
11	$PdCl_2(PPh_3)_2$	toluene	0[c]
12	$HRuCl(CO)(PPh_3)_3$	dioxane	59[c]
13	$HRuCl(CO)(PPh_3)_3$	CH_3CN	15[c]
14	$HRuCl(CO)(PPh_3)_3$	2-propanol	54[c]

[a] NMR yield otherwise noted. [b] Isolated yield. [c] The recovery of **1k** was observed. [d] The reaction was carried out at 100 °C for 10 h. [e] The reaction was carried out for 24 h.

thenium-catalyzed isomerization of *N*-allylazoles **1** and **3** to *N*-vinylazoles **5** and **6** and oxidative cleavage of the intermediates **5** and **6** to the corresponding *N*-unsubstituted azoles **2** and **4** by a treatment with O_3 (Scheme 2b).

We first screened various transition-metal catalysts for the isomerization of the allyltriazole **1k** to the corresponding vinyltriazole **5k**. The representative results are summarized in Table 4.[23] We found that the transformation from **1k** to **5k** was efficiently catalyzed by the $HRuCl(CO)(PPh_3)_3$ complex in toluene at 120 °C for 2 h (entry 1).[24] The hydridoruthenium catalysts such as $H_2Ru(CO)(PPh_3)_3$ and $H_2Ru(PPh_3)_4$ afforded a trace amount of the desired product **5k** (entries 2 and 3), whereas the rest of the ruthenium catalysts did not promote the isomerization at all (entries 4−7). The hydridorhodium catalyst, $HRh(CO)(PPh_3)_3$, gave a low yield of **5k** (entry 8), although no reaction took place with Wilkinson's catalyst, $RhCl(PPh_3)_3$, Vaska's catalyst, $IrCl(CO)(PPh_3)_2$, and $PdCl_2(PPh_3)_2$, and a quantitative recovery of the starting material **1k** was observed (entries 9−11). We also examined solvent effects using $HRuCl(CO)(PPh_3)_3$ as a catalyst. The reactions in polar solvents such as 1,4-dioxane, CH_3CN, and 2-propanol did not consume all of the starting material even after 24 h at 120 °C and gave the lower yields of **5k** with a recovery of **1k** (entries 12−14), whereas **1k** was consumed completely in 2 h when the reaction was carried out in toluene and the isomerized product **5k** was obtained in high yield (entry 1). With the desired vinyltriazole **5k** in hand, we examined removal of the vinyl group on a nitrogen atom in the triazole ring. The standard acidic treatments in an alcoholic solvent, used for common vinylamines and vinylamides, did not work at all, and the starting material **5k** was recovered.[25] To our surprise, oxidative cleavage of the vinyl group in **5k** using O_3 produced the *N*-unsubstituted triazole **2k** in a high yield without forming the corresponding formamide.[26]

We then examined the scope and limitation of the present stepwise protocol for deallylation of allylated azoles. The results of the reaction using 1-allyltriazoles **1c**, **1d**, and **1l** are summarized in Table 5. The reaction of 4-phenyl-1-allyl-1,2,3-triazole **1c** with a catalytic amount of $HRuCl(CO)(PPh_3)_3$ (5 mol %) in toluene at 120 °C was completed in 2 h to give 4-phenyl-1-(1-propenyl)-1,2,3-triazole **5c** in 92% yield as an 85:15 mixture of *trans* and *cis* isomers (entry 1). Subsequently ozonolysis of the vinyltriazole **5c** was carried out in CH_2Cl_2/MeOH (3/2, 0.1 M) at −78 °C, and the reaction mixture was then treated with Me_2S. The corresponding *N*-unsubstituted triazole **2c** was obtained in 93% yield. The allyltriazole **1d** afforded the corresponding vinyltriazole **5d** in 85% yield, and ozonolysis gave **2d** in an excellent yield (entry 2). The reaction of the diallyltriazole **1l** required a higher loading of the catalyst and a longer time and gave 1,5-di(1-propenyl)-4-phenyl-1,2,3-triazole **5l′** in 81% yield as a mixture of possible four stereoisomers (entry 3). The treatment of **5l′** with O_3 took place to produce 4-formyl-5-phenyl-1,2,3-triazole **2l′** as the final product in a moderate yield.

The results of the stepwise deallylation of 2-allyltriazoles **1m**, **1k**, and **1i** are summarized in Table 6. The phenyl-substituted 2-allyltriazole **1m** gave the desired 2-vinyltriazole **5m** with the Ru catalyst, and ozonolysis furnished the corresponding product **2c** in a high yield (entry 1). The product obtained in entry 1 was exactly identical with the compound derived from the corresponding 1-allyltriazole **1c**. The allyltriazoles **1k** and **1i** bearing electron-withdrawing groups afforded the isomerized vinyltriazoles **5k** and **5i**, and the following ozonolysis gave the *N*-unsubstituted triazoles **2k** and **2i** in high yields, respectively (entries 2 and 3). On the basis of the analysis of its spectroscopic data, the compound **2i** is found to be 4,5-di(methoxycarbonyl)-2*H*-1,2,3-triazole.[27]

We next investigated the deallylation of *N*-allyltetrazoles **3b**, **3d**, and **3e** by utilizing the same stepwise

(23) For representative transition metals used for isomerization of allylamines and/or allylamides, see: (a) Stille, J. K.; Becker, Y. *J. Org. Chem.* **1980**, *45*, 2139−2145 (Ru, Fe). (b) Tani, K.; Yamagata, T.; Akutagawa, S.; Kumobayashi, H.; Taketomi, T.; Yakaya, H.; Miyashita, A.; Noyori, R.; Otsuka, S. *J. Am. Chem. Soc.* **1984**, *106*, 5208−5217 (c) Tani, K. *Pure. Appl. Chem.* **1985**, *57*, 1845−1854 (Rh). (d) Sonesson, C.; Hallberg, A. *Tetrahedron Lett.* **1995**, *36*, 4505−4506 (Pd). (e) Neugnot, B.; Cintrat, J.-C.; Rousseau, B. *Tetrahedron Lett.* **2004**, *60*, 3575−3579 (Ir). (f) Alcaide, B.; Almendros, P.; Alonso, J. M.; Aly, M. F. *Org. Lett.* **2001**, *3*, 3781−3784 (Ru). (g) Sergeyev, S.; Hesse, M. *Synlett* **2002**, 1313−1317 (Fe). (h) Moreau, B.; Lavielle, S.; Marquet, A. *Tetrahedron Lett.* **1977**, *30*, 2591−2594 (Rh, Pt, Pd). (i) Alcaide, B.; Almendros, P.; Alonso, J. M. *Chem. Eur. J.* **2003**, *9*, 5793−5799 (Ru). (j) Alcaide, B.; Almendros, P.; Alonso, J. M. *Tetrahedron Lett.* **2003**, *44*, 8693−8695 (Ru).

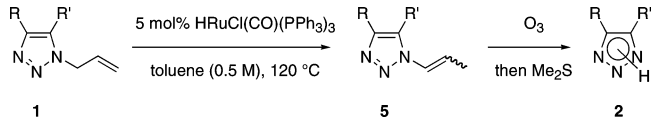
(24) (a) Wakamatsu, H.; Nishida, M.; Adachi, N.; Mori, M. *J. Org. Chem.* **2000**, *65*, 3966−3970. (b) Domíngues, G.; Casarrubios, L.; Rodríguez-Noriega, J.; Pérez-Castells, J. *Helv. Chim. Acta* **2002**, *85*, 2856−2861. (c) Krompiec, S.; Pigulla, M.; Szczepankiewicz, W.; Bieg, T.; Kuznik, N.; Leszczynska-Sejda, K.; Kubicki, M.; Borowiak, T. *Tetrahedron Lett.* **2001**, *42*, 7095−7098.

(25) In ref 10a, pp 574−576 and references therein.

(26) Protecting groups for nitrogen-containing heteroaromatics, see: (a) Theodoridis, G. *Tetrahedron Lett.* **1998**, *39*, 9365−6368 (triazolinone). (b) Hartley, D. J.; Iddon, B. *Tetrahedron Lett.* **1997**, *38*, 4647−4650 (imidazole). (c) Montgomery, J. A.; Thomas, H. J. *J. Org. Chem.* **1965**, *30*, 3235−3236 (purine). (d) Kimbonguila, A. M.; Boucida, S.; Guibé, F.; Loffet, A. *Tetrahedron* **1997**, *53*, 12525−12538 (imidazole).

(27) Due to the symmetrical structure of **2i**, the position of a proton attached to nitrogen atom was easily determined; see the Supporting Information for details.

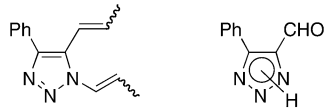
TABLE 5. Stepwise *N*-Deallylation of 1-Allyltriazoles 1 through Isomerization and Ozonolysis



1 5 2

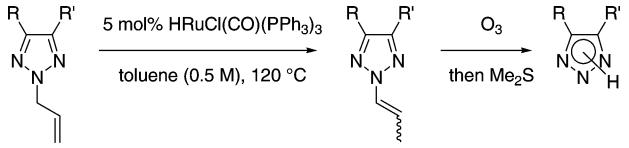
entry	R	R′	1	time, h	5	yield of **5**,[a] % (*trans*/*cis*)	2	yield of **2**,[b] %
1	Ph	H	**1c**	2	**5c**	92 (85/15)	**2c**	93
2	4-MeO_2C-C_6H_4	H	**1d**	3	**5d**	85 (83/17)	**2d**	97
3[c]	Ph	$CH_2CH{=}CH_2$	**1l**	24	**5l′**	81	**2l′**	63

[a] Isolated yield. The *trans*/*cis* ratio was determined by ^{1}H NMR. [b] Isolated yield. [c] The reaction was conducted under 10 mol % $HRuCl(CO)(PPh_3)_3$ for 24 h.



5l′ 2l′

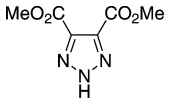
TABLE 6. Stepwise *N*-Deallylation of 2-Allyltriazoles 1 through Isomerization and Ozonlysis



1 5 2

entry	R	R′	1	time, h	5	yield of **5**,[a] % (*trans*/*cis*)	2	yield of **2**,[b] %
1	Ph	H	**1m**	2	**5m**	94 (84/16)	**2c**	88
2	COMe	H	**1k**	2	**5k**	83 (88/12)	**2k**	91
3	CO_2Me	CO_2Me	**1i**	2	**5i**	88 (87/13)	**2i**	80

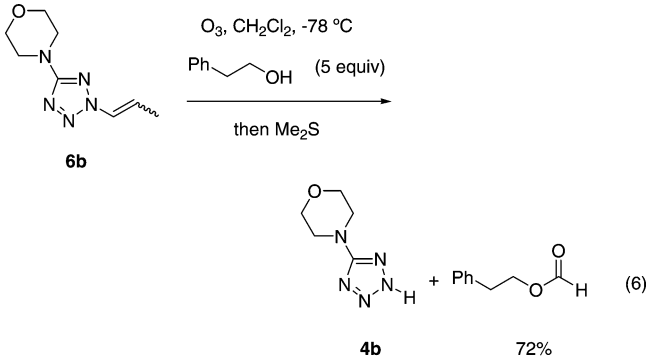
[a] Isolated yield. The *trans*/*cis* ratio was determined by ^{1}H NMR. [b] Isolated yield.



2i

protocol (Table 7). The reaction of allyltetrazole **3b** substituted with a morpholino group gave the expected vinyltetrazole **6b** in 85% yield with 87:13 ratio of *trans* and *cis* isomers (entry 1). The oxidative treatment of **6b** with O_3 gave the corresponding *N*-unsubstituted tetrazole **4b** in a good yield. The allyltetrazole **3d** bearing a cyano group also afforded the isomerized product **6d** in a good yield, although a longer reaction time was needed (entry 2). Ozonolysis of **6d** gave the product **4d** in a good yield. The allyltetrazole **3e** bearing indolyl group afforded the corresponding vinyltetrazole **6e** in a moderate yield, however following ozonolysis resulted in decomposition of the starting material **6e** (entry 3). It seemed that cleavage of a C−C double bond in the indole ring might occur. We also attempted the isomerization of 2-cinnamyl-4-morpholinotetrazole **3f**; however, no reaction took place after 24 h.

A proposed reaction pathway for the ruthenium-catalyzed isomerization of *N*-allylazoles to *N*-vinylazoles is shown in Scheme 5. First, hydroruthenation of the olefin in the allyl group of the starting materials **1** and **3** takes place, where the hydride adds to the terminal carbon atom and the ruthenium adds to the internal carbon atom of the C−C double bond to form the intermediate **G**. Then, β-elimination proceeds to give the *N*-(1-propenyl)azoles **5** and **6** with regeneration of the active catalytic hydridoruthenium species. Ozonolysis of the intermediates **5** and **6** proceeds in an unusual manner. In general, ozonolysis of C−C double bonds results in a formation of two corresponding aldehydes.[28] Accordingly, in this case, the corresponding *N*-formylazoles should be obtained in the first step. However, the reaction directly affords the *N*-unsubstituted azoles **2** and **4** without formation of the expected *N*-formyl heterocycles. It is known that *N*-vinylimidazoles also exhibit a similar type of reactivity in ozonolysis.[26b] Indeed, when ozonolysis of **6b** was carried out in the presence of an excess amount of phenethyl alcohol instead of MeOH, formylation of the alcohol took place in situ to give the expected *N*-unsubstituted tetrazole **4b** along with phenethyl formate (eq 6). It is therefore probable that the formyl group on a nitrogen atom of azoles is immediately trapped by an alcohol.



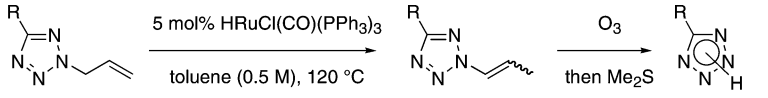
6b 4b 97% 72%

Conclusions

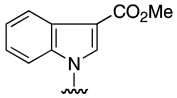
We have developed two facile deallylation protocols for a preparation of *N*-unsubstituted triazoles and tetrazoles. A treatment of *N*-allylazoles with a stoichiometric amount

(28) For stepwise cleavage of allylamines, see: (a) Lessen, T. A.; Demko, D. M.; Weinreb, S. M. *Tetrahedron Lett.* **1990**, *31*, 2105−2108. (b) Georg, G. I.; Kant, J.; He, P.; Ly, A. M.; Lampe, L. *Tetrahedron Lett.* **1988**, *29*, 2409−2412. (c) Bose, A. K.; Manhas, M. S.; Vincent, J. E.; Gala, K.; Fernandez, I. F. *J. Org. Chem.* **1982**, *47*, 4075−4081.

TABLE 7. Stepwise *N*-Deallylation of 2-Allyltetrazoles 3 through Isomerization and Ozonolysis

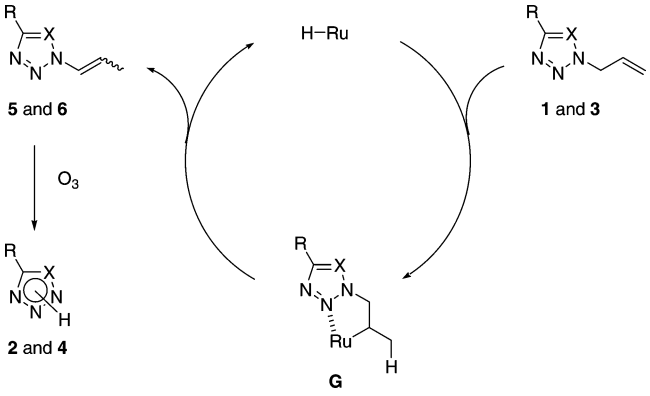


3 6 4

entry	R	3	time, h	6	yield of 6, % (*trans/cis*)[a]	4	yield of 4, %[b]
1		**3b**	3	**6b**	85 (87/13)	**4b**	79
2		**3d**	24	**6d**	77 (73/27)	**4d**	78
3		**3e**	24	**6e**	51 (59/41)	**4e**	-[c]

[a] Isolated yield. The *trans/cis* ratio was determined by ^{1}H NMR. [b] Isolated yield. [c] Decomposition of the starting material **6e**.

SCHEME 5. Mechanism for the Stepwise *N*-Deallylation through Ru-Catalyzed Isomerization and Ozonolysis



of ^{t}BuMgCl under a catalytic amount of $NiCl_2$(dppe) complex directly produced *N*-unsubstituted azoles in good to high yields. This protocol is applicable to substrates having an olefinic substituent and/or a heteroatom containing substituent, but it is not effective for the substrates bearing a functional group, like ester, that is not compatible with the Grignard reagent. A stepwise deallylation through consecutive reactions of isomerization and ozonolysis worked well for *N*-allylated azoles containing an electron-withdrawing group such as ester and cyano group. The isomerization of *N*-allylazoles to *N*-vinylazoles was promoted by $HRuCl(CO)(PPh_3)_3$ catalyst, and ozonolysis of the derived *N*-vinylazoles directly produced *N*-unsubstituted azoles. This latter protocol, however, is not very efficient for substrates having an olefinic and/or a heteroatom substituent. A heteroatom tends to retard the progress of the Ru-catalyzed isomerization, and an olefin interferes with both isomerization and ozonolysis. Accordingly, the two protocols complement each other, and we are now in a position to prepare various types of *N*-unsubstituted triazoles and tetrazoles from the corresponding allylated precursors.

Experimental Section

Typical Procedure for the Nickel-Catalyzed Deallylation of *N*-Allylazoles Leading to *N*-Unsubstituted Azoles. A toluene solution (2 mL, 0.25 M) of 4-(*p*-tolyl)-1-allyl-1,2,3-triazole **1a** (85.6 mg, 0.5 mmol) and a catalytic amount of $NiCl_2$(dppe) (5.3 mg, 0.01 mmol) was added ^{t}BuMgCl (0.7 mL, 0.7 mmol; 1.0 M solution in THF) at rt under Ar atmosphere. After the substrate was consumed, the reaction was quenched with saturated aqueous Na_2CO_3, and the reaction mixture was extracted with ether. The residue was purified by a silica gel column chromatography (*n*-hexane/AcOEt) to afford 4-(*p*-tolyl)-1,2,3-triazole **2a** in 86% yield (68.4 mg).

4-(*p*-Tolyl)-1,2,3-triazole (2a): white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (3H, s), 7.25 (2H, br d, J = 8.0 Hz), 7.68 (2H, br d, J = 8.0 Hz), 7.91 (1H, s), 11.73 (1H, br s); ^{13}C NMR (67.8 MHz, CD_3OD) δ 21.5, 127.1, 127.6, 128.3, 130.8, 139.8, 146.9; IR (KBr) 3150−2500 (br), 1664, 1479, 1130, 1076, 821 cm^{-1}; HRMS (EI) calcd for $C_9H_9N_3$ (M^+) 159.0791, found 159.0792. Anal. Calcd for $C_9H_9N_3$: C, 67.90; H, 5.69; N, 26.39. Found: C, 67.79; H, 5.90; N, 26.20.

Typical Procedure for the Ruthenium-Catalyzed Isomerization of *N*-Allylazoles to *N*-Vinylazoles. A toluene solution (1 mL, 0.5 M) of 4-acetyl-2-allyl-1,2,3-triazole **1k** (75.6 mg, 0.5 mmol) and a catalytic amount of $HRuCl(CO)(PPh_3)_3$ (23.8 mg, 0.025 mmol) was heated at 120 °C for 2 h under Ar atmosphere. Then, the solution was cooled to rt, and the reaction mixture was filtered through a short Florisil column. The eluent was concentrated, and the residue was purified by a silica gel column chromatography (*n*-hexane/AcOEt) to afford 4-acetyl-2-(1-propenyl)-1,2,3-triazole **5k** in 83% yield (62.4 mg). The ratio of *trans* and *cis* isomers was 88:12, which was determined by using ^{1}HNMR.

Typical Procedure for the Ozonolysis of *N*-Vinylazoles Leading to *N*-Unsubstituted Azoles. 4-Acetyl-2-(1-propenyl)-1,2,3-triazole **5k** (75.6 mg, 0.5 mmol) was dissolved in a combined solution of CH_2Cl_2 (3 mL) and MeOH (2 mL). The reaction mixture was cooled to −78 °C, and O_3 was passed through until the color of the solution turned slight blue. Then, Me_2S was added to the solution, and the mixture was gradually warmed to rt. After concentration under reduced pressure, the residue was purified by a silica gel column chromatography (*n*-hexane/AcOEt) to give 4-acetyl-1,2,3-triazole **2k** in 91% yield (50.3 mg).

4-Acetyl-1,2,3-triazole (2k): white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.68 (3H, s), 8.20 (1H, s); ^{13}C NMR (67.8 MHz, CD_3OD) δ 27.4, 130.7, 147.3, 193.6; IR (KBr) 3107 (NH), 1678 (C=O), 1490, 1253 cm^{-1}; HRMS (EI) calcd for $C_4H_5N_3O$ (M^+) 111.0432, found 111.0433. Anal. Calcd for $C_4H_5N_3O$: C, 43.24; H, 4.54; N, 37.82. Found: C, 43.12; H, 4.57; N, 37.68.

Acknowledgment. We thank the members in the Research and Analytical Center for Giant Molecules at the Graduate School of Science, Tohoku University, for the measurements of mass spectra and elemental analyses.

Supporting Information Available: Analytical data of the triazoles **2a**−**g**,**i**,**k**,**l′** and tetrazoles **4a**−**d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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