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$(PhTe)_2$-Mediated Intramolecular Radical Cyclization of *o*-Ethynylaryl Isocyanides Leading to Bistellurated Quinolines upon Visible-Light Irradiation

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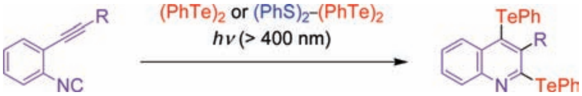
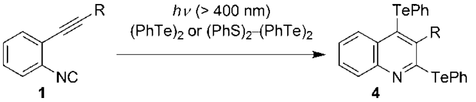
ABSTRACT



Upon treatment with $(PhTe)_2$ under visible-light irradiation, *o*-ethynylaryl isocyanides underwent intramolecular radical cyclization with introduction of telluro groups, affording the corresponding bistellurated quinolines.

Controlled radical reactions are of great importance in organic synthesis in terms of excellent chemoselectivity, use of wide-range of solvents, and simple initiation, especially visible-light irradiation. Therefore, the development of synthetically useful radical reactions is one of the notable topics. Recently, we and other groups developed a series of radical addition reactions of organic dichalcogenides into unsaturated bonds by using disulfides,[1] diselenides,[2] and ditellurides,[3] or mixed systems of these dichalcogenides.[4−6] In the 1990s, the reactivities of isocyanides in radical reactions were revealed, and they could be employed as precursors of *N*-heterocycles.[7] However, there are few reports concerning the radical cyclization reactions of isocyanides to elaborate *N*-heterocycles with the introduction of chalcogeno groups.[5b,7a−c,f] Herein, we wish to describe a novel intramolecular radical cyclization of *o*-ethynylaryl isocyanides mediated by ditelluride, affording the corresponding bistellurated quinolines (eq 1).



(1)

First, we screened the reaction of *o*-ethynylaryl isocyanide **1a** with organic dichalcogenides (Table 1).[8] Upon treatment

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(1) For the radical addition of organic disulfides, see: (a) Heiba, E. I.; Dessau, R. M. *J. Org. Chem.* **1967**, *32*, 3837. (b) Takaguchi, Y.; Katayose, Y.; Yanagimoto, Y.; Motoyoshiya, J.; Aoyama, H.; Wakahara, T.; Maeda, Y.; Akasaka, T. *Chem. Lett.* **2003**, *32*, 1124.

(2) For the radical addition of organic diselenides to acetylenes, see: (a) Back, T. G.; Krishna, M. V. *J. Org. Chem.* **1988**, *53*, 2533. (b) Ogawa, A.; Yokoyama, H.; Yokoyama, K.; Masawaki, T.; Kambe, N.; Sonoda, N. *J. Org. Chem.* **1991**, *56*, 5721. (c) Tsuchii, K.; Doi, M.; Ogawa, I.; Einaga, Y.; Ogawa, A. *Bull. Chem. Soc. Jpn.* **2005**, *78*, 1534.

(3) Ogawa, A.; Yokoyama, K.; Obayashi, R.; Han, L.-B.; Kambe, N.; Sonoda, N. *Tetrahedron* **1993**, *49*, 1177.

(4) For the radical addition reaction to unsaturated bonds mediated by a mixed system of $(PhS)_2$ and $(PhSe)_2$, see: (a) Ogawa, A.; Obayashi, R.; Ine, H.; Tsuboi, Y.; Sonoda, N.; Hirao, T. *J. Org. Chem.* **1998**, *63*, 881. (b) Tsuchii, K.; Tsuboi, Y.; Kawaguchi, S.; Takahashi, J.; Sonoda, N.; Nomoto, A.; Ogawa, A. *J. Org. Chem.* **2007**, *72*, 415.

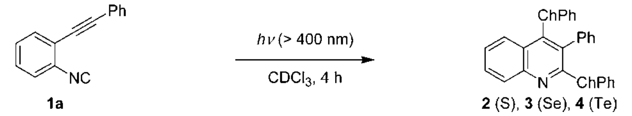
(5) For the radical reactions by using a mixed system of $(PhS)_2$ and $(PhTe)_2$, see: (a) Ogawa, A.; Ogawa, I.; Obayashi, R.; Umezu, K.; Doi, M.; Hirao, T. *J. Org. Chem.* **1999**, *64*, 86. (b) Mitamura, T.; Tsuboi, Y.; Iwata, K.; Tsuchii, K.; Nomoto, A.; Sonoda, M.; Ogawa, A. *Tetrahedron Lett.* **2007**, *48*, 5953.

(6) Ogawa, A. In *Main Group Metals in Organic Synthesis*; Yamamoto, H., Oshima, K., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 2, p 813.

(7) (a) Bachi, M. D.; Bar-Ner, N.; Melman, A. *J. Org. Chem.* **1996**, *61*, 7116. (b) Rainier, J. D.; Kennedy, A. R. *J. Org. Chem.* **2000**, *65*, 6213. (c) Tokuyama, H.; Watanabe, M.; Hayashi, Y.; Kurokawa, T.; Peng, G.; Fukuyama, T. *Synlett* **2001**, 1403. (d) Sumi, S.; Matsumoto, K.; Tokuyama, H.; Fukuyama, T. *Org. Lett.* **2003**, *5*, 1891. (e) Kotani, M.; Yamago, S.; Satoh, A.; Tokuyama, H.; Fukuyama, T. *Synlett* **2005**, 1893. (f) Minozzi, M.; Nanni, D.; Zanardi, G.; Calestani, G. *Arkivoc* **2006**, *VI*, 6.

10.1021/ol901267h CCC: $40.75

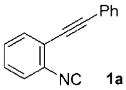
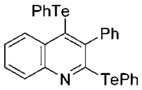
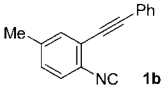
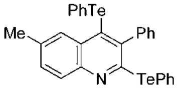
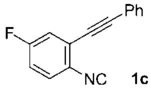
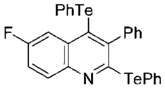
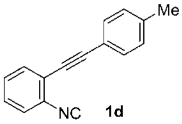
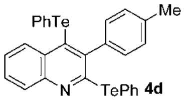
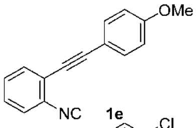
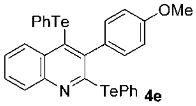
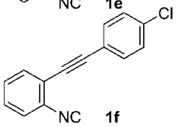
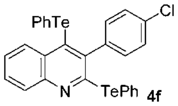
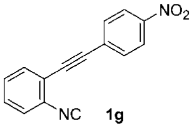
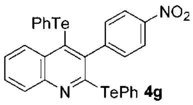
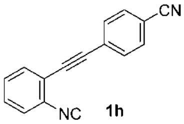
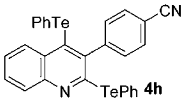
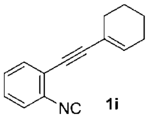
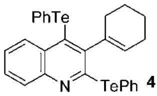
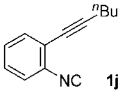
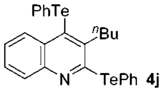
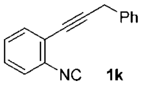
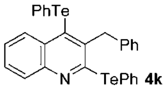
Table 1. Photoinduced Radical Cyclization Reaction of Isocyanide **1a** with Dichalcogenides[a]



entry	conditions	products (Ch)	yields (%)[b]
1	$(PhS)_2$ (2.0 equiv)	**2a** (S)	ND
2	$(PhSe)_2$ (2.0 equiv)	**3a** (Se)	mixture[c]
3	$(PhS)_2$ (1.5 equiv)/$(PhSe)_2$ (1.5 equiv)	**2a** and **3a**	mixture[c]
4	$(PhS)_2$ (1.5 equiv)/$(PhTe)_2$ (1.5 equiv)	**4a** (Te)	56
5	$(PhTe)_2$ (1.0 equiv)	**4a**	34
6	$(PhTe)_2$ (1.5 equiv)	**4a**	30
7	$(PhTe)_2$ (2.0 equiv)	**4a**	50
8	$(PhTe)_2$ (5.0 equiv)	**4a**	68

[a] Reaction conditions: isocyanide (**1a**, 0.15 mmol), diphenyl dichalcogenides (amounts shown in the table), $CDCl_3$ (0.5 mL), irradiated by a super-high-pressure Hg lamp through a glass filter (>400 nm). [b] Isolated yield. [c] Mixture including no small amounts of **3a**.

Table 2. Photoinduced Radical Cyclization of Isocyanides with $(PhTe)_2$[a]

entry	substrate	product	yield (%)[a]	
			condition = A[b]	B[c]
1	 **1a**	 **4a**	50	
2				56
3	 **1b**	 **4b**	65	
4				51
5	 **1c**	 **4c**	46	
6				49
7	 **1d**	 **4d**	42	
8				67
9	 **1e**	 **4e**	51	
10				68
11	 **1f**	 **4f**	50	
12				55
13	 **1g**	 **4g**	34	
14				32
15	 **1h**	 **4h**	28	
16				30
17	 **1i**	 **4i**	71	
18				64
19	 **1j**	 **4j**	82	
20				88
21	 **1k**	 **4k**	46	
22				63

[a] Isolated yield. [b] Reaction conditions (A): isocyanide (**1**, 0.15 mmol), $(PhTe)_2$ (0.30 mmol), $CDCl_3$ (0.5 mL), irradiated by a super-high-pressure Hg lamp through a glass filter (>400 nm). [c] Reaction conditions (B): $(PhS)_2$ (0.22 mmol) and $(PhTe)_2$ (0.22 mmol) employed in place of $(PhTe)_2$ for reaction conditions (A).

of **1a** with $(PhS)_2$ under photoirradiation, unfortunately, the desired cyclization reaction did not proceed, and instead, oligomerization of **1a** took place mainly (entry 1).[9] In the case of $(PhSe)_2$ or a mixed system of $(PhS)_2$ and $(PhSe)_2$, the reaction gave a complex mixture involving the corresponding cyclic product **3a** (entries 2 and 3).[10] In contrast, the reaction using a mixed system of $(PhS)_2$ and $(PhTe)_2$ upon visible-light irradiation afforded a bistellurated quinoline **4a** in moderate yield (entry 4). More interestingly, when **1a** was treated with $(PhTe)_2$ alone, the desired cyclization reaction also took place to give **4a** in good yields (entries 5—8).[11]

The bistellurated radical cyclization reactions of several isocyanides were conducted using 2 equiv of $(PhTe)_2$ (condition A) or a mixed system of 1.5 equiv of $(PhS)_2$ and 1.5 equiv of $(PhTe)_2$ (condition B), and these results are summarized in Table 2. These reaction conditions could be employed with aryl-substituted isocyanides **1b** and **1c**, affording the corresponding bistellurated quinolines **4b** and **4c** in each condition, respectively (entries 3—6). Upon treatment of the aryl isocyanides bearing *o*-(2-aryl-ethynyl) groups with $(PhTe)_2$ (or $(PhS)_2$ and $(PhTe)_2$) under visible-light irradiation, the desired reactions also took place to give the corresponding cyclic products successfully (entries 7—16). In the cases of isocyanides **1d** and **1e** bearing electron-donating groups such as methyl and methoxy groups, the corresponding quinolines **4d** and **4e** were obtained (entries 7—10). In particular, when **1d** and **1e** were treated with a mixed system of $(PhS)_2$ and $(PhTe)_2$ (condition B), the reactions provided the corresponding cyclic products **4d** and **4e** in good yields, respectively (entries 8 and 10). When the reaction was applied to isocyanides **1f**, **1g**, and **1h** bearing electron-withdrawing substituents such as chloro,

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(8) Unfortunately, *o*-ethynylaryl isocyanides are unstable to isolate. Thus, isocyanides were employed for the radical cyclization reaction without purification prior to use.

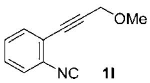
(9) Because of relatively lower carbon radical capturing ability of $(PhS)_2$, oligomerization took place exclusively. See: Curran, D. P.; Martin-Esker, A. A.; Ko, S. B.; Newcomb, M. *J. Org. Chem.* **1993**, *58*, 4691.

(10) Most probably because the rate constant for capturing carbon radical by $(PhSe)_2$ is nearly equal to that of intramolecular cyclization, a complex mixture including **3a** was obtained. The rate constant for capturing 5-hexenyl radical with $(PhSe)_2$ is 1.2×10^7 M^{-1} s^{-1} (in the case of 0.6 M, the rate constant is 7.2×10^6 s^{-1}); see: (a) Russell, G. A.; Tashtoush, H. *J. Am. Chem. Soc.* **1983**, *105*, 1398. The rate constant for the intramolecular radical cyclization (e.g., 5-*exo* ring closure is 1.4×10^6 s^{-1}); see (b) Schiesser, C. H.; Wild, L. M. *Tetrahedron* **1996**, *52*, 13265.

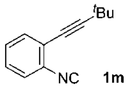
(11) The photoinduced reaction using a mixed system of $(PhSe)_2$ and $(PhTe)_2$ provided a complex mixture including **3a** and **4a**.

nitro, and cyano substituents, **1f** afforded the corresponding quinoline **4f** in moderate yields (entries 11 and 12); however, low yields of the cyclic products **4g** and **4h** were obtained (entries 13—16). Furthermore, isocyanide **1i** bearing a 1-cyclohexenyl group underwent the desired cyclization to form the corresponding quinoline **4i** in good yields (entries 17 and 18). These reaction systems can be applied to isocyanides bearing aliphatic group on the ethynyl groups. When the reactions of isocyanide **1j** were performed under both conditions, the corresponding quinoline **4j** was obtained in 82% (condition A) and 88% (condition B) yields, respectively (entries 19 and 20). Isocyanides **1k** having propargylic protons also afforded **4k** in good yields (entries 21 and 22).

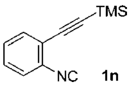
In the case of **1l**, oligomerization of **1l** took place predominantly. Unfortunately, isocyanides **1m** and **1n** did not react under these reaction conditions (most subatrates were recovered unchanged). These results suggest that the presence of bulky substituents such as *t*-Bu and TMS groups at ethynyl groups inhibited the desired reactions.



1l



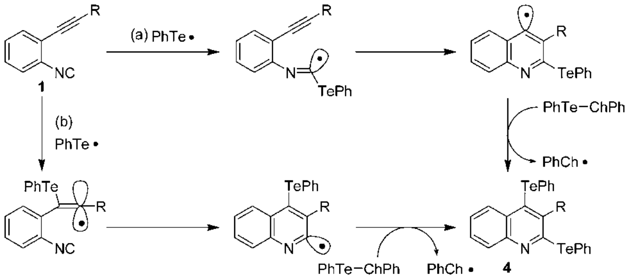
1m



1n

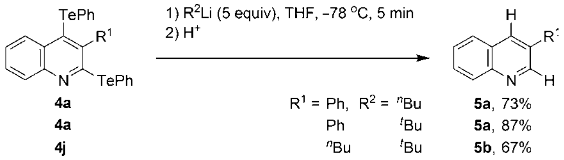
The possible reaction pathways considered for this photoinduced radical cyclization are shown in Scheme 1. Path (a): radical addition of PhTe$^•$ to the isocyano group, forming an imidoyl radical; intramolecular cyclization; abstraction of the telluro group to afford **4**. Path (b): radical addition of PhTe$^•$ to the ethynyl group, forming a vinyl radical; intramolecular cyclization; abstraction of the telluro group to give **4**.[12]

Scheme 1



The cyclization products have two kinds of telluro groups, which are formally imidoyltelluro and aryltelluro groups, and are potentially useful synthetic intermediates.[13] Thus, we next examined the reductive elimination of telluro groups via Te/Li exchange reactions.[14] Upon treatment of **4a** and **4j** with *t*-BuLi, the reductive elimination of telluro groups took place successfully, leading to the corresponding quinolines **5a** and **5b** in good yields, respectively (Scheme 2).

Scheme 2



In summary, we have developed a novel visible-light-induced intramolecular radical cyclization of *o*-ethynylaryl isocyanides, affording the corresponding bistellurated quinolines, selectively. We also showed that the generated C−Te bonds can be reduced by an organolithium reagent.

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Supporting Information Available: General experimental procedures, characterization data, and ^{1}H and ^{13}C NMR spectra for bistellurated quinolines and 3-substituted quinolines. This material is available free of charge via the Internet at http://pubs.acs.org.

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[12] Another possible reaction pathway is the Bergman-like cyclization under photoirradiation to generate a biradical species and sequential abstraction of telluro groups. However, the determination of the precise reaction pathways should wait for further detailed mechanistic study.

[13] (a) Barton, D. H. R.; Ramesh, M. *J. Am. Chem. Soc.* **1990**, *112*, 891. (b) Ueda, Y.; Watanabe, H.; Uemura, J.; Uneyama, K. *Tetrahedron Lett.* **1993**, *34*, 7933. (c) Crich, D.; Chen, C.; Hwang, J.-T.; Yuan, H.; Papadatos, A.; Walter, R. I. *J. Am. Chem. Soc.* **1994**, *116*, 8937. (d) Nishibayashi, Y.; Cho, C. S.; Uemura, S. *J. Organomet. Chem.* **1996**, *507*, 197. (e) Engman, L.; Laws, M. J.; Malmström, J.; Schiesser, C. H.; Zugaro, L. M. *J. Org. Chem.* **1999**, *64*, 6764. (f) Yamago, S.; Miyazoe, H.; Goto, R.; Hashidume, M.; Sawazaki, T.; Yoshida, J. *J. Am. Chem. Soc.* **2001**, *123*, 3697. (g) Fujiwara, S.; Shimizu, Y.; Shin-ike, T.; Kambe, N. *Org. Lett.* **2001**, *3*, 2085. (h) Zeni, G.; Lüdtke, D. S.; Panatieri, R. B.; Braga, A. L. *Chem. Rev.* **2006**, *106*, 1032. (i) Yamago, S.; Matsumoto, A. *J. Org. Chem.* **2008**, *73*, 7300. (j) Fujiwara, S.; Shimizu, Y.; Imahori, Y.; Toyofuku, M.; Shin-ike, T.; Kambe, N. *Tetrahedron Lett.* **2009**, *50*, 3628.

[14] (a) Hiiro, T.; Morita, Y.; Inoue, T.; Kambe, N.; Ogawa, A.; Ryu, I.; Sonoda, N. *J. Am. Chem. Soc.* **1990**, *112*, 455. (b) Ogawa, A.; Tsuboi, Y.; Obayashi, R.; Yokoyama, K.; Ryu, I.; Sonoda, N. *J. Org. Chem.* **1994**, *59*, 1600. (c) Tucci, F. C.; Chieffi, A.; Comasseto, J. V.; Marino, J. P. *J. Org. Chem.* **1996**, *61*, 4975. (d) Moraes, D. N.; Barrientos-Astigarraga, R. E.; Castelani, P.; Comasseto, J. V. *Tetrahedron* **2000**, *56*, 3327.