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Alkynylbenzotriazoles by Direct Alkynylation of Benzotriazole Using Alkynyliodonium Salts

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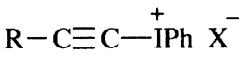
Abstract: Alkynyl(phenyl)iodonium salts react with benzotriazole ion prepared from benzotriazole and potassium *t*-butoxide to give 1-alkynylbenzotriazoles in good yields, indicating that the alkynyliodonium salts can be used for direct alkynylation of benzotriazole.

Much attention has been paid to synthetic applications of benzotriazoles as a new synthetic methodology in recent years.[1] Very recently benzotriazoles have been shown to behave as light-activatable DNA cleaving agents.[2] The synthesis of furthermore functionalized benzotriazoles is considered to become important subjects of synthetic and biological researches since they are expected to exhibit novel properties applicable to such fields. In the light of recent development of acetylene chemistry[3] ranging over material science and biochemistry as well as organic chemistry, where the acetylenic bond plays a significant role in the reactions and applications, the combination of the acetylenic bond and the benzotriazole functionality is thought to create a new chemistry. To the best of our knowledge, however, there are no reports on alkynyl-substituted benzotriazoles. Introduction of a carbon-carbon triple bond on the nitrogen atom of benzotriazole seems to be difficult because alkynyl cations are unstable and impossible to be generated except for nuclear decay of a tritiated alkyne.[4]

Hypervalent iodine chemistry has been much studied lately and increased the utility in organic synthesis.[5] Above all, alkynyl(phenyl)iodonium salts (**1**) have been recognized to be useful as synthon of alkynyl cations.[6] On the basis of such studies, we selected alkynyl(phenyl)iodonium salts **1** as the substrate for the alkynylation reaction of benzotriazole. In this paper, we report the first example of alkynylbenzotriazoles (**2**) and describe that alkynyl(phenyl)iodonium salts **1** act as an alkynylating agent for benzotriazole.



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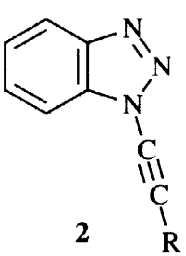

2

Alkynyl(phenyl)iodonium tosylates (**1:** X = OTs) were prepared according to the method described in the literatures.[7,8] A solution of potassium salt of benzotriazole was prepared from *t*-BuOK and benzotriazole in

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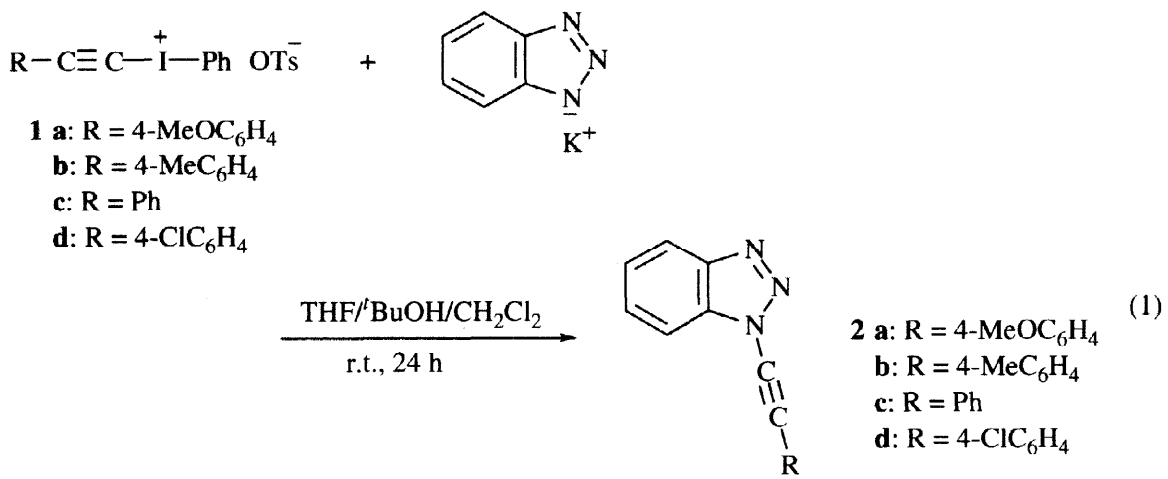
a mixed solvent of *t*-BuOH and THF. Then, solid [(4-methoxyphenyl)ethynyl]-(phenyl)iodonium tosylate (**1a**) was added into the solution. After stirring the reaction mixture for 12 h, the product mixture was extracted and submitted to column chromatography on silica gel. Elution with hexane-CH_2Cl_2 gave 1-[(4-methoxyphenyl)ethynyl]benzotriazole (**2a**) as crystals but the yield was 29%.

Then, the same reaction was conducted in the reverse order of the addition. The solution of potassium salt of benzotriazole in THF and *t*-BuOH was added to a solution of alkynyliodonium tosylate **1a** in a mixed solvent of *t*-BuOH and CH_2Cl_2 and the mixture was stirred at room temperature for 24 h. After workup of the reaction mixture and separation by chromatography on silica gel, crystalline 1-alkynylbenzotriazole **2a** was obtained in a 56% yield. Similar treatments of other alkynyl(phenyl)iodonium tosylates (**1b-1d**) gave the corresponding 1-alkynylbenzotriazoles (**2b-2d**) as crystals in 45-62% yields (eq. 1 and Table 1).



(1)

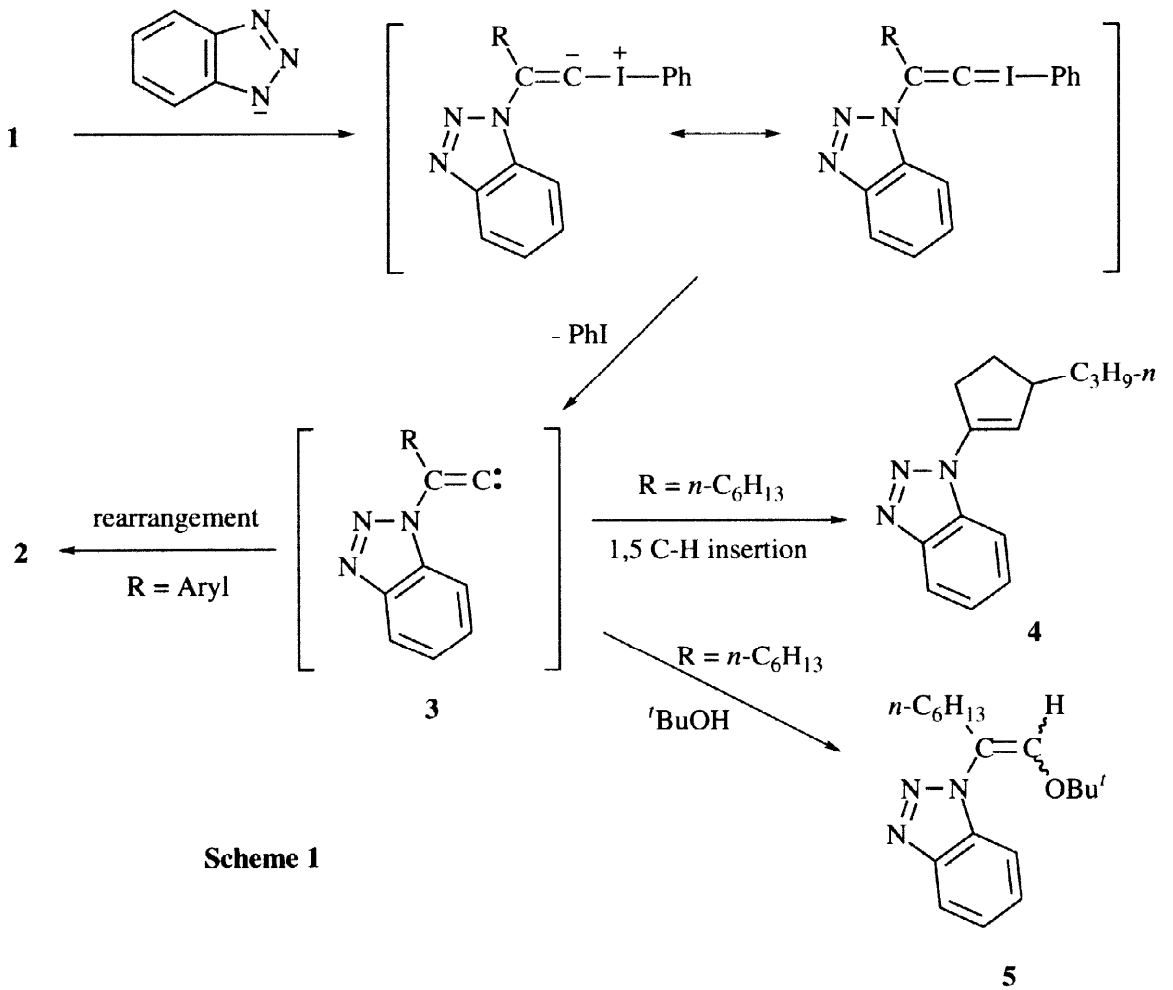
Table 1. Yields and selected spectral data of new alkynylbenzotriazoles **2**

2	yield/%	mp/°C	selected spectral data
2a	56	99-101	^{1}H NMR ($CDCl_3$) δ 3.71(s, CH_3), 6.79(d, J=7.8Hz, ArH) 7.33(d, J=7.5Hz, ArH), 7.42-7.51(m, ArH) 7.58(d, J=8.0Hz, ArH), 7.97(d, J=8.2Hz, ArH); ^{13}C NMR ($CDCl_3$) δ 54.32(Me), 74.86(C_{sp}), 79.91(C_{sp}), 134.38, 143.98; IR 2246 cm^{-1} (C≡C)
2b	45	82-85	^{1}H NMR ($CDCl_3$) δ 2.39(s, CH_3), 7.21(d, J=7.8Hz, ArH) 7.42-7.64(m, ArH), 7.73(d, J=8.2Hz, ArH) 8.11(d, J=8.3Hz, ArH); ^{13}C NMR ($CDCl_3$) δ 21.44(Me), 75.20(C_{sp}), 79.84(C_{sp}), 134.16, 143.81; IR 2244 cm^{-1} (C≡C)
2c	55	77-78	^{1}H NMR ($CDCl_3$) δ 7.36-7.44(m, ArH), 7.55-7.67(m, ArH), 8.05(d, J=8.3Hz, ArH); ^{13}C NMR ($CDCl_3$) δ 75.48, 79.46, 133.77, 143.47; IR 2259 cm^{-1} (C≡C)
2d	62	147-148	^{1}H NMR ($CDCl_3$) δ 7.44-7.67(m, ArH, 5H), 7.72(d, J=6.8Hz, ArH, 1H), 7.79(d, J=7.8Hz, ArH, 1H), 8.19(d, J=8.2Hz, ArH, 1H); ^{13}C NMR ($CDCl_3$) δ 78.71, 134.05, 143.82; IR 2261 cm^{-1} (C≡C)

The alkynylbenzotriazoles **2** show characteristic spectra of the acetylenic bond in the ^{13}C NMR (δ 74-75 and 78-80 ppm) and IR spectra (2240-2260 cm^{-1}). Also, the characteristic signal of protons adjacent to the nitrogen were observed at 8.0-8.2 ppm in the ^{1}H NMR spectrum and the signals of C-8 and C-9 of the benzotriazole ring appeared at 134-135 and 143-144 ppm in the ^{13}C NMR spectrum.

The formation of alkynylbenzotriazoles indicates that alkynyliodonium salts **1** behave as the alkynylating agent of benzotriazole and are regarded as the synthon of alkynyl cations. However, the present reaction is reasonably considered to proceed via the Michael addition of benzotriazole ion to the β carbon of the triple bond, the formation of alkylidenecarbenes (**3**), and finally the rearrangement to the alkynes **2**, as it has been well recognized in the reaction of alkynyliodonium salts.[6]

In order to understand the mechanism on the reaction of alkynyliodonium salts **1** with benzotriazole ion, we further examined the reaction of 1-octynyl(phenyl)iodonium tosylate (**1d**: R = *n*-C_6H_{13}). The treatment of **1d** with benzotriazole ion afforded 1-(3-propyl-1-cyclopentenyl)benzotriazole (**4**)[9] and 1-(2-*tert*-butoxy-1-hexylvinyl)benzotriazole (**5**)[6] in 29 and 31% yields, respectively. The formation of **4** and **5** indicates that the reaction of **1** with benzotriazole ion proceeds via alkylidenecarbene **3** which undergoes a typical intramolecular 1,5 C–H insertion and an electrophilic attack toward *tert*-BuOH, and supports the mechanism involving alkylidenecarbenes **3** shown in Scheme 1.



Scheme 1

In summary, we have for the first time synthesized novel 1-alkynylbenzotriazoles **2** by use of alkynyliodonium salts **1** and benzotriazole ion. The utility of alkynylation reaction using alkynyliodonium salts **1** has been further advanced. The useful functionality of the alkynyl and benzotriazole groups will be developed in the near future. The details on this subject are now in progress.

References

1. A recent review, see: Katritzky, A. R.; Lan, X.; Fan, W.-Q. *Synthesis* **1994**, 445-456; Katritzky, A. R.; Lan, X. *Chem. Soc. Rev.* **1994**, 363-373.
2. Wender,P. A.; Touami, S. M.; Alayrac, C.; Philipp, U. C. *J. Am. Chem. Soc.* **1996**, *118*, 6522-6523.
3. Stang, P. J.; Diederich, F. *Modern Acetylene Chemistry*; VCH: Weinheim, 1995.
4. Angelini, G.; Hanack, M.; Vermehren, J.; Speranza, M. *J. Am. Chem. Soc.* **1988**, *110*, 1298-1299.
5. For recent reviews and books, see: Koser, G. F. in*The Chemistry of Functional Groups, Supplement D*; Patai, S.; Rappoport, Z. Eds.; John Wiley & Sons: New York, 1983; Chapters 18 and 25; Varvoglis, A. *Synthesis* **1984**, 709-726; Moriarty, R. M.; Prakash, O. *Acc. Chem. Res.* **1986**, *19*, 244-250; Merkushev, E. B. *Russ. Chem. Rev. (Eng. Transl.)* **1987**, *56*, 826-845; Moriarty, R. M.; Vaid, R. K. *Synthesis* **1990**, 431-447; Moriarty, R. M.; Vaid, R. K.; Koser, G. F. *Synlett* **1990**, 365-383; Varvoglis, A. *The Organic Chemistry of Polycoordinated Iodine*; VCH Publishers: New York, 1992; Kita, Y.; Tohma, H.; Yakura, T. *Trends in Organic Chemistry* **1992**, *3*, 113-128; Prakash, O.; Saini, N.; Sharma, P. K. *Synlett* **1994**, 221-227; Kitamura, T. *Yuki Gosei Kagaku Kyokai Shi* **1995**, *53*, 893-905; Stang, P. J.; Zhdankin, V. V. *Chem. Rev.* **1996**, *96*, 1123-1178; Varvoglis, A. *Hypervalent Iodine in Organic Synthesis*; Academic Press: San Diego, 1997; Kitamura, T.; Fujiwara, Y. *Org. Prep. Proced. Int.* **1997**, *29*, 409-458.
6. Ochiai, M.; Nagao, Y. *Yuki Gosei Kagaku Kyokai Shi* **1986**, *44*, 660-673; Ochiai, M. *Rev. Heteroatom Chem.* **1989**, *2*, 92-111; Stang, P. J. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 274-285; Stang, P. J. in *Supplement C: The chemistry of triple-bonded functional groups*; Patai, S. Ed.; John Wiley & Sons: Chichester, 1994, Chapter 20; Stang, P. J. ref. 3, Chapter 3.
7. Koser, G. F.; Rebrovic, L.; Wettach, R. H. *J. Org. Chem.* **1981**, *46*, 4324-4326; Rebrovic, L.; Koser, G. F. *ibid.* **1984**, *49*, 2462-2472.
8. Stang, P. J.; Surber, B. W. *J. Am. Chem. Soc.* **1985**, *107*, 1452-1453; Stang, P. J.; Surber, B. W.; Chen, Z.-C.; Roberts, K. A.; Anderson, A. G. *ibid.* **1987**, *109*, 228-235.
9. **4**: Oil; ^{1}H NMR ($CDCl_3$) δ 0.96 (t, J=7Hz, Me), 1.26-1.48 (m, CH_2), 1.7 (m, CH), 2.3 (m, CH), 2.9 (m, CH), 3.1 (m, CH_2), 6.61 (d, J=2Hz, =CH), 7.32-7.40 (m, ArH), 7.83-7.90 (m, ArH); ^{13}C NMR ($CDCl_3$) δ 14.18, 20.83, 29.08, 30.88, 38.17, 44.09, 117.53, 118.03, 118.20, 125.38, 126.91, 135.97, 138.64, 144.50.

   5: One isomer could be separated from a mixture of the (E) and (Z) isomers. ^{1}H NMR ($CDCl_3$) δ 0.84 (t, J=7Hz, Me), 1.23-1.40 (m, CH_2 and ^{t}Bu), 2.66 (t, J=7Hz, CH_2), 6.50 (s, =CH), 7.35-7.38 (m, ArH), 7.90-7.93 (m, ArH); ^{13}C NMR ($CDCl_3$) δ 13.98, 22.50, 27.42, 27.82, 28.37, 31.43, 31.75, 78.31, 117.52, 118.18, 121.32, 125.90, 125.96, 126.90, 135.94, 143.95. Another isomer was contaminated with the isomer and the ^{1}H NMR is as follows: ^{1}H NMR ($CDCl_3$) δ 0.82 (t, J=7Hz, Me), 1.19-1.26 (m, CH_2 and ^{t}Bu), 2.72 (t, J=7Hz, CH_2), 6.79 (s, =CH), 7.3-7.5 (m, ArH).