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Facile generation of α,α-dibromodimethyl ketals from alkynes using $TsNBr_2$

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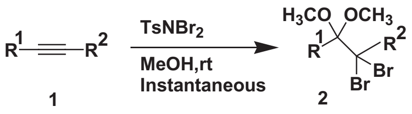
ABSTRACT

$TsNBr_2$ reacts with alkyne in the presence of methanol to form α,α-dibromodimethyl ketals instantaneously. The reaction proceeds smoothly at room temperature without using any other catalyst. The one step reaction can be carried out with both aromatic and aliphatic alkynes in excellent yield.

Activation and functionalization of carbon–carbon triple bond is an important strategy for many important organic transformations in synthetic chemistry.[1] One of the common strategies used for functionalization of carbon–carbon multiple bond is the cohalogenation reaction. This reaction is an attractive tool to produce vicinal halo-functionalized compounds regioselectively, which are useful intermediates for diverse organic transformations.[2] Although cohalogenation reaction for C–C double bond is extensively studied, this protocol is less common for C–C triple bond.

Recently, we have established that *N*,*N*-dibromo-*p*-toluenesulfonamide ($TsNBr_2$) is a very efficient and powerful reagent for various organic transformations.[3] We found that $TsNBr_2$ can be used as an electrophilic bromine source for vicinal bromo functionalization of olefin and we have successfully employed this reagent for various cohalogenation reactions.[3a,b,f] Based on this concept, we intended to investigate the reaction of alkyne with $TsNBr_2$ in the presence of nucleophilic solvent such as methanol. Interestingly, to our expectation, α,α-dibromodimethyl ketal was formed in excellent yield. However, the synthesis of α,α-dibromodimethyl ketal has received scant attention in the literature, with only a few methods outlined. Uemura found that the treatment of acetylenes with bromine in methanol at 20–25 °C leads to the formation of α,α-dibromodimethyl ketals in moderate yield.[4] The reaction also produces an isomeric mixture of α,β-dibromoalkenes along with the desired product. Similar attempt was also made by Berthelot et al. with tetrabutylammonium tribromide in methanol.[5] They carried out the reaction at 20 °C under the influence of ultrasonic irradiation as well as at room temperature with continuous stirring. Similar to Uemura's report, this procedure also leads to the formation of *E*-α,β-dibromoalkene as the side product in significant amount. Bovonsombat and McNelis reported the synthesis of some ketals of α,α-dihaloacetophenone using *N*-halosuccinimide and catalytic quantity of *p*-toluenesulfonic acid.[6] Heasley and coworkers reported a procedure for the synthesis of dihalo acetals from alkyne using NBS or NIS as the halogen source.[7] In this case, H_2SO_4 was used as a catalyst to achieve the transformation. Samuel reported another method for the synthesis of α,α-dichlorodimethyl ketals from acetylene using NCS in methanol.[8] However, most of the reported methods have some limitations such as the use of catalyst, low yield, and formation of byproducts which make the procedures inconvenient for preparations. We wish to report herein a very simple and efficient method for direct synthesis of α,α-dibromodimethyl ketals from alkyne using *N*,*N*-dibromo-*p*-toluenesulfonamide ($TsNBr_2$) as a bromine source under mild conditions (Scheme 1).

To begin with, a study was carried out with phenyl acetylene as a model substrate. A reaction was carried out by adding $TsNBr_2$ (1 mmol) to a solution of phenyl acetylene (1 mmol) in the



Scheme 1. Synthesis of α,α-dibromodimethyl ketal.

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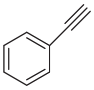
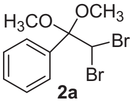
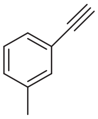
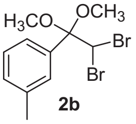
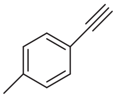
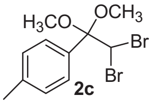
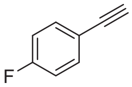
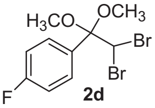
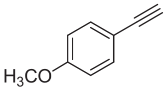
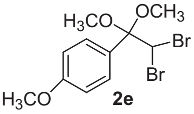
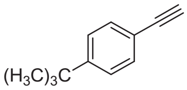
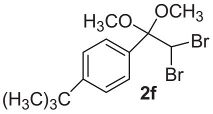
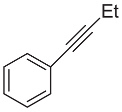
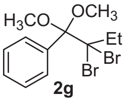
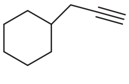
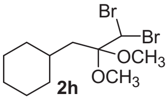
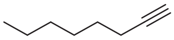
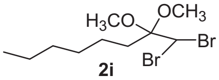
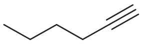
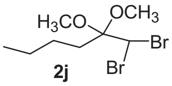
0040-4039/

presence of MeOH (2 mL). The whole process was carried out at room temperature under nitrogen atmosphere. While monitoring the reaction using TLC, we observed that the alkyne disappears immediately after the addition of the $TsNBr_2$. A sudden rise of reaction temperature was observed which indicates the exothermic nature of the reaction. The reaction mixture was stirred for another 10 min. After usual work-up, corresponding α,α-dibromodimethyl ketal was obtained in 91% yield. The structure of the compound was ascertained by comparing the spectral and melting point data with those reported in the literature.[6,9] Spectral analysis revealed that the resulting product is 1-(2,2-dibromo-1,1-dimethoxyethyl)benzene. The reaction was then studied under different reaction conditions. The change in the amount of $TsNBr_2$ from 1 mmol to 1.1 or 1.2 did not make any difference in yields. The reaction was also examined in a mixture of solvents such as CH_3CN/MeOH (4:1) and THF/MeOH (4:1). However, in both the cases, the reaction produced inferior results.

Table 1
Synthesis of α,α-dibromodimethyl ketals[a]

SI No	Substrate	Product	Yield[b]
1		 **2a**	91
2		 **2b**	86
3		 **2c**	83
4		 **2d**	79
5		 **2e**	88
6		 **2f**	84
7		 **2g**	90
8		 **2h**	83
9		 **2i**	83
10		 **2j**	87

[a] Reaction conditions: alkyne (1 mmol), $TsNBr_2$ (1 mmol), MeOH (2 mL), rt, N_2-atmosphere.
[b] Isolated yields.

After gaining success for phenyl acetylene, the process was extended for different alkynes which are summarized in the Table 1.[10] It can be seen from Table 1 that both aromatic as well as aliphatic alkynes react efficiently under reaction conditions. All reactions were completed instantaneously with excellent yield of the desired product.

It is noteworthy that this process led to the formation of only one regioisomer. During our investigations, we found that $TsNBr_2$ is a good source of Br^+ ion.[3] Obviously, there could be a strong reason to believe that the reaction proceeds through the formation of a three-membered cyclic bromonium ion intermediate. The regioselectivity can be explained by considering the fact that the β-position is more positive than the α-position. Opening of the cyclic bromonium intermediate by nucleophilic solvent is most likely from the more electrophilic β-position. This is the reason why this process produced only the 1,1-dibromo-2,2-dimethoxy ketal as the product.

In summary, we have developed a very simple, efficient, and rapid method for the synthesis of α,α-dibromodimethyl ketals by treating alkynes with $TsNBr_2$. The reaction completes instantaneously in case of both aromatic and aliphatic alkynes with excellent yield.

Acknowledgment

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2014.01.123.

References and notes

1. (a) Liu, B.; De Brabander, J. K. *Org. Lett.* **2006**, *8*, 4907–4910; (b) Yusubov, M. S.; Yusubova, R. Y.; Kirschning, A.; Park, J. Y.; Chi, K.-W. *Tetrahedron Lett.* **2008**, *49*, 1506–1509; (c) Goossen, L. J.; Rodriguez, N.; Goossen, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 9592–9594.
2. (a) Shakya, N.; Srivastav, N. C.; Desroches, N.; Agrawal, B.; Kunimoto, D. Y.; Kumar, R. *J. Med. Chem.* **2010**, *53*, 4130–4140; (b) Ros, A.; Magriz, A.; Dietrich, H.; Fernández, R.; Alvarez, E.; Lassaletta, J. M. *Org. Lett.* **2006**, *8*, 127–130; (c) Damin, B.; Garapon, J.; Sillion, B. *Tetrahedron Lett.* **1980**, *21*, 1709–1710; (d) Rolston, J. H.; Yates, K. *J. Am. Chem. Soc.* **1969**, *91*, 1469–1476; (e) Dewkar, G. K.; Narina, S. V.; Sudalai, A. *Org. Lett.* **2003**, *5*, 4501–4504.
3. (a) Phukan, P.; Chakraborty, P.; Kataki, D. *J. Org. Chem.* **2006**, *71*, 7533–7537; (b) Saikia, I.; Phukan, P. *Tetrahedron Lett.* **2009**, *50*, 5083–5087; (c) Saikia, I.; Chakraborty, P.; Phukan, P. *ARKIVOC* **2009**, *xiii*, 281–286; (d) Saikia, I.; Kashyap, B.; Phukan, P. *Synth. Commun.* **2010**, *40*, 2647–2652; (e) Saikia, I.; Kashyap, B.; Phukan, P. *Chem. Commun.* **2011**, 2967–2969; (f) Saikia, I.; Rajbongshi, K. K.; Phukan, P. *Tetrahedron Lett.* **2012**, *53*, 761–768; (g) Borah, A. J.; Phukan, P. *Tetrahedron Lett.* **2012**, *53*, 3035–3037; (h) Borah, A. J.; Phukan, P. *Chem. Commun.* **2012**, 5491–5493.
4. Uemura, S.; Okazaki, H.; Okano, M.; Sawada, S.; Okada, A.; Kuwabara, K. *Bull. Chem. Soc. Jan.* **1978**, *51*, 1911–1912.
5. Berthelot, J.; Beammar, Y.; Desmazieres, B. *Synth. commun.* **1997**, *27*, 2865–2876.
6. Bovonsombat, P.; McNelis, E. *Tetrahedron Lett.* **1992**, *33*, 4123–4126.
7. Heasley, V. L.; Shellhamer, D. F.; Chappell, A. E.; Cox, J. M.; Hill, D. J.; McGovern, S. L.; Eden, C. C.; Kissel, C. L. *J. Org. Chem.* **1998**, *63*, 4433–4437.
8. Reed, S. F. *J. Org. Chem.* **1964**, *30*, 2195–2198.
9. Tanaka, R.; Rodgers, M.; Simonaitis, R.; Miller, S. I. *Tetrahedron* **1971**, *27*, 2651–2669.
10. Experimental procedure: To a solution of alkyne (1 mmol) in methanol (2 mL), $TsNBr_2$ (1 mmol) was added under N_2 atmosphere at room temperature. After 5 min of stirring, excess solvent was removed in rotary evaporator and sodium thiosulfate (200 mg approx.) was added followed by the addition of water (5 mL). The reaction mixture was stirred for another 5 min and taken up in ethyl acetate. Organic layer was separated, and dried over anhydrous sodium sulfate, and concentrated. The crude product was purified by flash chromatography on silica gel (230–400 mesh) with petroleum ether/ethyl acetate as eluent.