

SYNLETT Spotlight 326

Bromotrichloromethane

Compiled by Fanny Cros



This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

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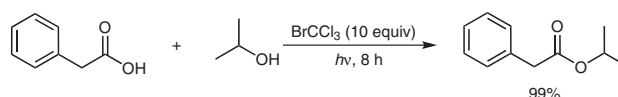
Introduction

Readily synthesized by Meunier et al.¹ in 1938, bromotrichloromethane (BrCCl_3) is a reagent of choice in organic synthesis. In recent years, many applications of this reagent have been reported. It can be used to synthesize esters, oxidize heterocycles, allow alkoxy ring-closure

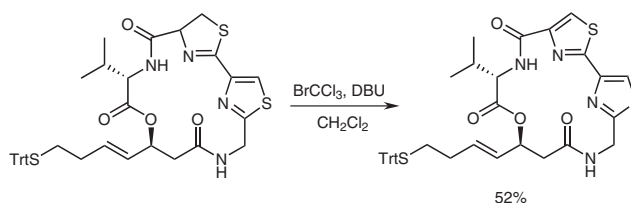
reactions, perform α -bromination of sulfones, achieve radical addition on alkenes and radical cyclization of 1,6-dienes or synthesize dichloroalkenes. Some of these reactions were used at a final stage of complex total syntheses. Moreover, bromotrichloromethane is cheap, commercially available and stable at room temperature without any observed decomposition.

Abstracts

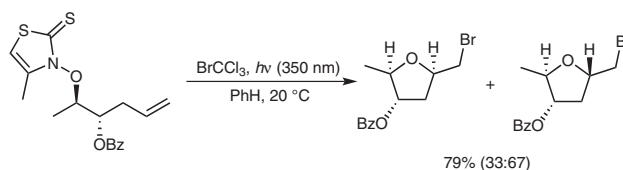
(A) Esterification is one of the most important reaction in organic synthesis.² Numerous methods have been reported, but few of them proceed under photolytic conditions.³ Hwu et al.⁴ developed a new atom-economy condensation between carboxylic acids and alcohols using BrCCl_3 to furnish esters in high yields.



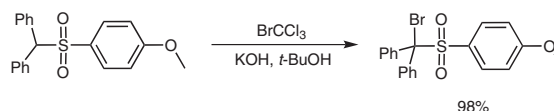
(B) The most common oxidizing method of thiazolines implies MnO_2 under classical conditions^{5a} or microwaves activation.^{5b} The use of BrCCl_3 /DBU combination constitutes an efficient alternative way for this purpose.^{6a} Recently, these conditions were applied in the final step of the total synthesis of largazole analogues.^{6b} In some cases, due to lower yields with DBU, another base was required (NaOMe , $t\text{-BuOK}$, NaH or LDA).⁷



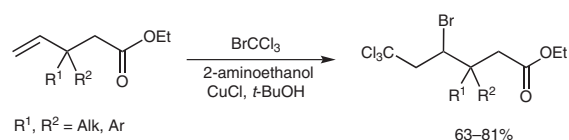
(C) The homolysis of the N–O bond of *N*-alkoxy thiazolethiones delivered an alkoxy radical. This intermediate cyclized stereoselectively to give a carbon-centred tetrahydrofurylmethyl radical which was further trapped by BrCCl_3 as a source of bromine atom.^{8a,b}



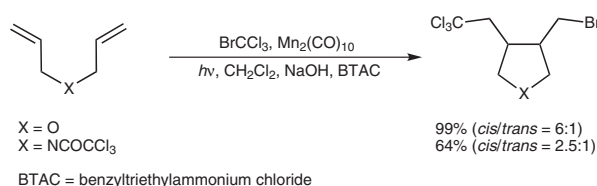
(D) Radical-anion radical pair reactions (RARP) allowed α -bromination of alkylphenyl sulfones in the presence of a $\text{KOH}/t\text{-BuOH}$ mixture.⁹ The products are formed in high yields and are stable under these reaction conditions.



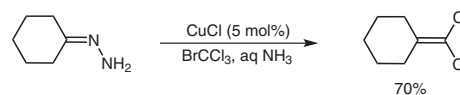
(E) Nedelec and co-workers¹⁰ reported the addition of the trichloromethyl radical to alkenes with moderate selectivities. More recently, the group of Mirzabekova developed a new method for generating this radical and the method was directly applied to the total synthesis of permethrinic acid.¹¹



(F) Homolytic cleavage of the metal–metal bond of $[\text{Mn}_2(\text{CO})_{10}]$ generates two manganese pentacarbonyl radicals which can perform hydrogen or halogen atom abstraction reactions.^{12a} In the presence of bromotrichloromethane, bromine atom transfer reactions can also be carried out on 1,6-dienes.^{12b}



(G) *gem*-Dichloroolefins are valuable products in organic synthesis. Nenajdenko et al.¹³ developed a convenient olefination method for the synthesis of dichloroalkenes from hydrazones using BrCCl_3 and in the presence of CuCl as catalyst.



References

- (1) Simons, J. H.; Sloat, T. K.; Meunier, A. C. *J. Am. Chem. Soc.* **1938**, *61*, 435.
- (2) Otera, J. *Angew. Chem. Int. Ed.* **2001**, *40*, 2044.
- (3) Lee, A. S.-Y.; Yang, H.-C.; Su, F.-Y. *Tetrahedron Lett.* **2001**, *42*, 301.
- (4) Hwu, J. R.; Hsu, C.-Y.; Jain, M. L. *Tetrahedron Lett.* **2004**, *45*, 5151.
- (5) (a) You, S.-L.; Kelly, J. W. *Tetrahedron Lett.* **2005**, *46*, 2567. (b) Bagley, M. C.; Chapanei, K.; Dale, J. W.; Xiong, X.; Bower, J. *J. Org. Chem.* **2005**, *70*, 1389.
- (6) (a) Mislin, G. L.; Burger, A.; Abdallah, M. A. *Tetrahedron* **2004**, *60*, 12139. (b) Bowers, A. A.; West, N.; Newkirk, T. L.; Troutman-Youngman, A. E.; Schreiber, S. L.; Wiest, O.; Bradner, J. E.; Williams, R. M. *Org. Lett.* **2009**, *11*, 1301.
- (7) Chorell, E.; Das, P.; Almqvist, F. *J. Org. Chem.* **2007**, *72*, 4917.
- (8) (a) Hartung, J.; Knever, R. *Eur. J. Org. Chem.* **2000**, 1677. (b) Hartung, J.; Knever, R. *Tetrahedron: Asymmetry* **2003**, *14*, 3019.
- (9) Meyers, C. Y.; Chan-Yu-King, R.; Hua, D. H.; Kolb, V. M.; Matthews, W. S.; Parady, T. E.; Horii, T.; Sandrock, P. B.; Hou, Y.; Xie, S. *J. Org. Chem.* **2003**, *68*, 500.
- (10) Heintz, M.; Le, N. y. C.; Nedelec, J. Y. *Tetrahedron Lett.* **1984**, *25*, 5767.
- (11) Mirzabekova, N. S.; Kuz'mina, N. E.; Lukashov, O. I.; Sokolova, N. A.; Golosov, S. N.; Kazakov, P. V.; Perlova, T. G.; Potapova, V. V.; Kheinman, V. A.; Ivanova, G. B. *Russ. J. Org. Chem.* **2008**, *44*, 1139.
- (12) (a) Gilbert, B. C.; Parsons, A. F. *J. Chem. Soc., Perkin Trans. 2* **2002**, 367. (b) Huther, N.; McGrail, P. T.; Parsons, A. F. *Eur. J. Org. Chem.* **2004**, 1740.
- (13) Nenajdenko, V. G.; Shastin, A. V.; Muzalevskii, V. M.; Balenkova, E. S. *Russ. Chem. Bull., Int. Ed.* **2004**, 2647.