HOKKAIDO UNIVERSITY

Title	Conversion of MT-sulfone to a trifluoromethyl group by IF_5^1 : the application of an MT-sulfone anion as a trifluoromethyl anion equivalent
Author(s)	Imagawa, Yosuke; Yoshikawa, Syuhei; Fukuhara, Tadahito et al.
Citation	Chemical Communications, 47(32), 9191-9193 https://doi.org/10.1039/c1cc13232f
Issue Date	2011-08-28
Doc URL	https://hdl.handle.net/2115/49456
Rights	Chem. Commun., 2011, 47, 9191-9193 - Reproduced by permission of The Royal Society of Chemistry (RSC)
Type	journal article
File Information	CC47-32_9191-9193.pdf

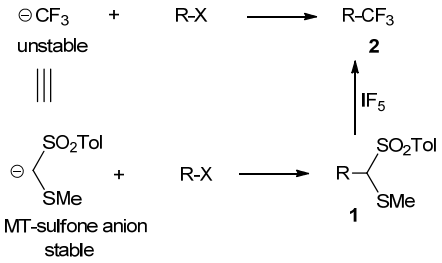
Hokkaido University Collection of Scholarly and Academic Papers : HUSCAP

Conversion of MT-Sulfone to a Trifluoromethyl group by IF_5[1]: the Application of an MT-Sulfone Anion as a Trifluoromethyl Anion Equivalent

Yosuke Imagawa, Syuhei Yoshikawa, Tadahito Fukuhara, and Shoji Hara*

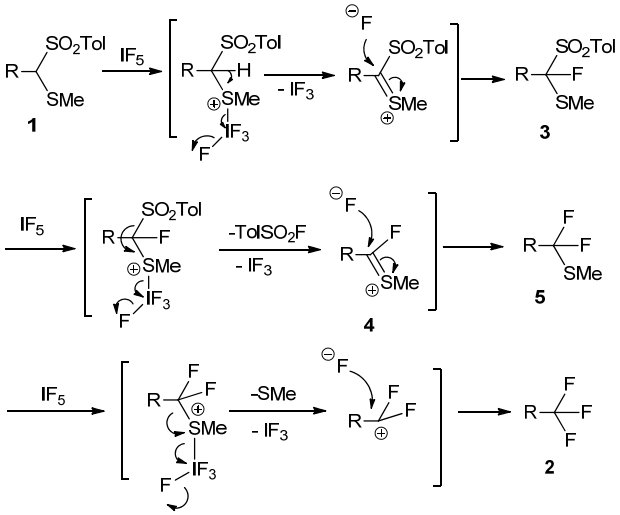
An MT-sulfone group was converted to a trifluoromethyl group by treatment with IF_5 after an alkylation reaction. Therefore, an MT-sulfone anion can be used as a trifluoromethyl anion equivalent. The formal asymmetric Michael-addition of a trifluoromethyl anion to crotonaldehyde was also performed.

The introduction of a trifluoromethyl group into a molecule is a challenging area of organic chemistry because both a trifluoromethyl anion and its cation are difficult to generate and use[2]. A carbon-carbon bond forming reaction between a trifluoromethyl anion and alkyl halides is the most fundamental method for introducing a trifluoromethyl group in the molecules, and a trifluoromethyl copper species was most successfully used, especially, for the introduction of a trifluoromethyl group into the aromatic ring or vinylic carbon[3,4]. However, a good yield cannot be expected from a reaction of the trifluoromethyl copper species with aliphatic alkyl halides[5]. Although trifluoromethyltrimethylsilane has been used as a trifluoromethyl anion equivalent[6], it is rarely used in the S_N2 reaction with alkyl halides owing to the low yield of the expected products and the formation of inseparable by-products[5c,7]. On the other hand, MT-sulfone {(methylsulfanyl)methyl tolyl sulfone} is known to afford a stable anion species by treatment with a base under mild conditions, and its subsequent reaction with alkyl halides gives alkylated derivatives **1**[8]. We found that the MT-sulfone group in **1** can be converted to a trifluormethyl group by the reaction with IF_5[9]. Therefore, the MT-sulfone can be used to introduce the trifluoromethyl group to the substrate (**Scheme 1**).



Scheme 1

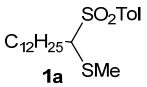
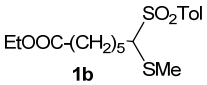
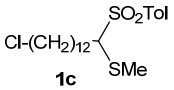
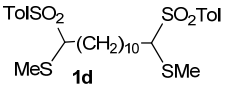
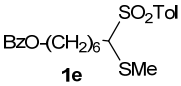
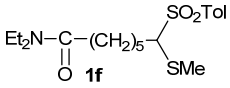
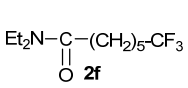
The reaction of **1** with IF_5 was performed under various conditions, and the best result was obtained by carrying out the reaction in Et_3N-5HF using 6 eq of IF_5 at 60 °C for 48 h. In this reaction, the presence of a methylsulfanyl group in **1** is critical, and the phenyl alkyl sulfone is inert to IF_5. During the reaction, the formation of tosyl fluoride was observed. From these observations, it can be assumed that the reaction proceeds as follows: the oxidative fluorination of **1** by IF_5 initially occurred to afford **3**[10]. In the second step, the tosyl group was eliminated as tosyl fluoride to afford a sulfonium salt **4**, which was converted to difluorosulfide **5** by the attack of a fluoride ion. Finally, the methylsulfanyl group in **5** was substituted by a fluoride ion to afford the trifluoromethylated product **2** (Scheme 2).



Scheme 2

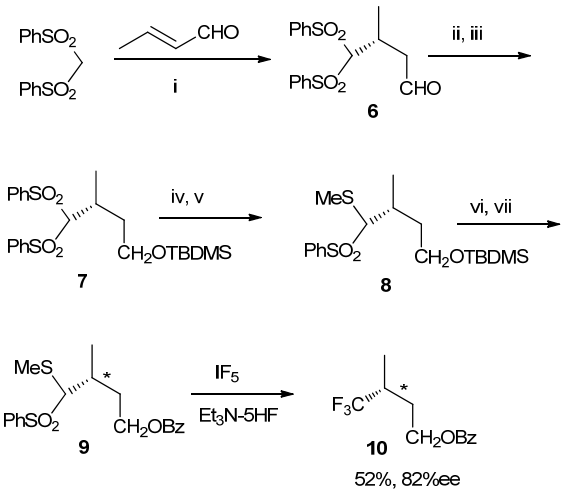
Under these conditions, an alkylated MT-sulfone **1a** was converted to 1,1,1-trifluoroalkane **2a** in good yield. Furthermore, a functional group such as an ester, an amide, and a chloride in **1** is tolerable under these conditions, and the functionalized trifluoromethyl compounds could be obtained as shown in Table 1.

Table 1. The reaction of MT-sulfone derivative with IF_5[a]

Substrate	Product	Yield (%)[b]
 **1a**	$C_{12}H_{25}$-CF_3 **2a**	87
 **1b**	EtOOC-$(CH_2)_5$-CF_3 **2b**	75
 **1c**	Cl-$(CH_2)_{12}$-CF_3 **2c**	81
 **1d**	CF_3-$(CH_2)_{10}$-CF_3 **2d**	71
 **1e**	BzO-$(CH_2)_6$-CF_3 **2e**	73
 **1f**	 **2f**	78[c]

[a] If otherwise not mentioned, the reaction was carried out using 6 eq of IF_5/Et_3N-5HF at 60 °C for 48h. [b] Isolation yield based on substrate used. [c] 8 eq of IF_5/Et_3N-5HF was used.

Recently, the asymmetric trifluoromethylation reaction has received much attention and many elegant methods for producing a compound having a trifluoromethyl group at its asymmetric center have been reported[11]. However, the asymmetric Michael-addition of the trifluoromethyl anion to α,β-unsaturated carbonyl compounds has not yet been reproted. Therefore, we applied our method to introduce a trifluoromethyl group at the β-position of the carbonyl group enantioselectively. The asymmetric Michael-addition of MT-sulfone catalyzed by an organocatalyst was unsuccessful owing to the low acidity of MT-sulfone (*p*Ka = 23.4[12]). On the other hand, the organocatalyst-catalyzed asymmetric Michael-addition of bis(phenylsulfonyl)methane (*p*Ka = 12.5[13]) to α,β-unsaturated aldehydes is known[14]. Therefore, the Michael-addition of bis(phenylsulfonyl)methane to crotonaldehyde was performed in the presence of (*S*)-2-(diphenyltrimethylsiloxy)methylpyrrolidine, and the resulting adduct **6** was reduced to an alcohol[15]. After the protection of alcohol with TBDMS, one sulfonyl group was removed by SmI_2[16] and a methylsulfanyl group was introduced to afford the (methylsulfanyl)methyl phenyl sulfoxide derivative **8**. Then, the protecting group of **8** was converted to a benzoyl group, and the resulting benzoate **9** was subjected to a reaction with IF_5 / Et_3N-5HF. Under the conditions described above, the (methylsulfanyl)methyl phenyl sulfoxide group was converted to the trifluoromethyl group and 3-trifluoromethyl-1-butyl benzoate **10** was obtained in 52% yield with 85%ee. During the reactions, no racemization occurred, and the trifluoromethyl group could be introduced at the β-position of the carbonyl group enantioselectively (**Scheme 3**).



i, 20 mol% of (*S*)-2-(diphenyltrimethylsiloxy)methylpyrrole, toluene
ii, $NaBH_4$, 78% from bis(phenylsulfonyl)methane, iii TBDMSCl,
imidazole, 97%, iv SmI_2, 93% v BuLi, $MeSSO_2Me$, 79%
vi TBAF, vii BzCl, Et_3N, 72% from **5**

Scheme 3

Conclusions

We found that the MT-sulfone group can be converted to a trifluoromethyl group by the reaction with IF_5. As the MT-sulfone affords a stable anion species by treatment with a base, and its subsequent reaction with alkyl halides gives alkylated derivatives, an MT-sulfone anion can be used as a trifluoromethyl anion equivalent. We also performed the formal asymmetric Michael-addition of a trifluoromethyl anion to crotonaldehyde, where the trifluoromethyl group was introduced to β-position of crotonaldehyde enantioselectively.

Notes and references

Division of Chemical Process Engineering, Graduate School of Engineering, Hokkaido University, Sapporo 060-8628, Japan

E-mail: shara@eng.hokudai.ac.jp; Fax: +81 11 706 6556; Tel: +81 11 706 6556

1 IF_5 decomposes in air emitting hazardous HF fume, and, therefore, it should be carefully handled in a bench hood with rubber-gloved hands, and the reaction was carried out in a Teflon™ bottle (a glassware cannot be used).

2 (a) M. A. McClinton and D. A. McClinton, *Tetrahedron*, 1992, **48**, 6555; (b) K. Uneyama, Organofluorine Chemistry, Blackwell Publishing, Oxford, 2006, pp. 292; (c) J.-A. Ma and D. Cahard, *J. Fluorine Chem.*, 2007, **128,** 975.

3 (a) V.C.R. McLoughlin and J. Thrower, *Tetrahedron*, 1969, **25**, 5921; (b) K. Matsui, E. Tobita, M. Ando, and K. Kondo, *Chem. Lett.*, 1981, 1719; (c) H. Suzuki, Y. Yoshida, and A. Osuka, *Chem. Lett.*, 1982, 135; (d) G. E. Carr, R. D. Chambers, and T. F. Holmes, *J. Chem. Soc. Perkin Trans. 1*, 1988, 921; (e) H. Urata and T. Fuchikami, *Tetrahedron Lett.*, 1991, **32**, 91; (f) L. Tan, C. Chen, R. D. Larsen, T. R. Verhoeven, P. J. Reider, *Tetrahedron Lett.*, 1998, **39**, 3961; (g) F. Cottet and M. Schlosser, *Eur. J. Org. Chem.*, 2002, **67**, 327; (h) I. Nowak and M. J. Robins, *J. Org. Chem.*, 2007, **72,** 2678; (i) B. R. Langlois and N. Roques, *J. Fluorine Chem.*, 2007, **128**, 1318; (j) G. G. Dubinina, H. Furutachi, and D. A. Vicic, *J. Am. Chem. Soc.*, 2008, **130**, 8600; (k) M. Oishi, H. Kondo, and H. Amii, *Chem. Commun.*, 2009, 1909 .

4 Recently, palladium-catalyzed cross-coupling reaction of trifluoromethyltrimethylsilane with aromatic halides was reproted; B. S. Samant and G. W. Kabalka, *Chem. Commun.*, 2011, **47**, 7236.

5 (a) Y. Kobayashi, K. Yamamoto, and I. Kumadaki, *Tetrahedron Lett.*, 1979, **42**, 4071; (b) Q.-Y. Chen and J.-X. Duan, *Tetrahedron Lett.*, 1993, **34**, 4241; (c) J. Kim and J. M. Shreeve, *Org. Biomol. Chem.*, 2004, **2**, 2728.

6 (a) G. K. S. Prakash and A. K. Yudin, *Chem. Rev.*, 1997, **97**, 757; (b) R. P. Singh and J. M. Shreeve, *Tetrahedron*, 2000, **56**, 7613; (c) G. K. S. Prakash and M. Mandal, *J. Fluorine Chem.*, 2001, **112**, 123; (d) A. D. Dilman and V. V. Levin, *Eur. J. Org. Chem.*, 2011, 831.

7 (a) D. V. Sevenard, P. Kirsh, G.-V. Röschenthaler, V. N. Movchun, A. A. Kolomeitsev, *Synlett*, 2001, 379; (b) W. Tyrra, D. Naumann, S. Quadt, S. Buslei, Y.L.Yagupolskii, and M. M. Kremlev, *J. Fluorine Chem.*, 2007, **128**, 813.

8 (a) K. Ogura, N. Yahata, K. Hashizume, K. Tsuyama, K. Takahashi, and H. Iida, *Chem. Lett.*, 1983, 767; (b) K. Ogura, K. Ohtsuki, M. Nakamura, N. Yahata, K. Takahashi, and H. Iida, *Tetrahedron Lett.*, 1985, **26**, 2455.

9 Rozen et al. reported that a tris(methylthio)methyl group in $RCH_2C(SMe)_3$ can be converted to trifluoromethyl group by the reaction with BrF_3. However, bromination at α-carbon also took place to give $RCHBrCF_3$, see: A. Hagooly, I. Ben-David and S. Rozen, *J. Org. Chem.*, 2002, **67**, 8430.

10 S. Ayuba, N. Yoneda, T. Fukuhara, and S. Hara, *Bull. Chem. Soc. Jpn.*, 2002, **75**, 1597.

11 (a) J.-A. Ma and D. Cahard, *Chem. Rev.*, 2004, **104**, 6119; (b) B. R. Langlois, T. Billard, S. Roussel, *J. Fluorine Chem.*, 2005, **126**, 173; (c) T. Billard and B. R. Langlois, *Eur. J. Org. Chem.*, 2007, 891; (d) N. Shibata, S. Mizuta, and H. Kawai, *Tetrahedron: Asymmetry*, 2008, **19**, 2633; (e) J. Nie, H.-C. Guo, D. Cahard, and J.-A. Ma, *Chem. Rev.*, 2011, **111**, 455; (f) G. Valero, X. Companyó, and R. Rios, *Chem. Eur. J.*, 2011, **17**, 2018..

12 S. Itô and T. Tsunoda, *Pure Appl. Chem.*, 1999, **71**, 1053.
13 J. Hine, J. C. Philips, and J. I. Maxwell, *J. Org. Chem*., 1970, **35**, 3943.
14 A.-N. Alba, X. Companyó, A. Moyano, and R. Rios, *Chem. Eur. J.*, 2009, **15**, 11095.
15 The enantiomeric excess of **4** was determined to be 85%ee as reported[14].
16 S. S.-Mossé, A. Alexakis, J. Mareda, G. Bollot, G. Bernardinelli, and Y. Filinchuk, *Chem. Eur. J.*, 2009, **15**, 3204.