Conversion of MT-sulfone to a trifluoromethyl group by IF_5: the application of an MT-sulfone anion as a trifluoromethyl anion equivalent

Imagawa, Yosuke; Yoshikawa, Syuhei; Fukuhara, Tadahito; Hara, Shoji

Chemical Communications, 47(32): 9191-9193

2011-08-28

http://hdl.handle.net/2115/49456

Chem. Commun., 2011, 47, 9191-9193 - Reproduced by permission of The Royal Society of Chemistry (RSC)

article (author version)

CC47-32_9191-9193.pdf
Conversion of MT-Sulfone to a Trifluoromethyl group by IF$_5$\textsuperscript{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\textsuperscript{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\textsuperscript{3,4}. However, a good yield cannot be expected from a reaction of the trifluoromethyl copper species with aliphatic alkyl halides\textsuperscript{5}. Although trifluoromethyltrimethylsilane has been used as a trifluoromethyl anion equivalent\textsuperscript{6}, it is rarely used in the S$_2$2 reaction with alkyl halides owing to the low yield of the expected products and the formation of inseparable by-products\textsuperscript{5c,7}. On the other hand, MT-sulfone [(methylsulfanyl)methyl tolyl sulfone] is known to afford a stable anion species by treatment with a base under mild conditions, and its subsequent reaction with alkyl halides gives alkylated derivatives\textsuperscript{8}. We found that the MT-sulfone group in 1 can be converted to a trifluoromethyl group by the reaction with IF$_5$\textsuperscript{9}. Therefore, the MT-sulfone can be used to introduce the trifluoromethyl group to the substrate (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$_3$N-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\textsuperscript{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).
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.

| Substrate | Product | Yield (%)$^b$
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>C$<em>6$H$</em>{5}$SO$_2$Tol</td>
<td>C$<em>6$H$</em>{5}$CF$_3$</td>
<td>87</td>
</tr>
<tr>
<td>$1b$</td>
<td>$2b$</td>
<td>75</td>
</tr>
<tr>
<td>$1c$</td>
<td>$2c$</td>
<td>81</td>
</tr>
<tr>
<td>$1d$</td>
<td>CF$_2$(CH$_3$)$_2$CF$_3$</td>
<td>71</td>
</tr>
<tr>
<td>$1e$</td>
<td>$2e$</td>
<td>73</td>
</tr>
<tr>
<td>$1f$</td>
<td>$2f$</td>
<td>78$^c$</td>
</tr>
</tbody>
</table>

$^a$ If otherwise not mentioned, the reaction was carried out using 6 eq of IF$_5$/Et$_3$N-5HF at 60 °C for 4 h. $^b$ Isolation yield based on substrate used. $^c$ 8 eq of IF$_5$/Et$_3$N-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 $\alpha,\beta$-unsaturated carbonyl compounds has not yet been reported. Therefore, we applied our method to introduce a trifluoromethyl group at the $\beta$-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 $\alpha,\beta$-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$_2$ 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 benzyol group, and the resulting benzoate $9$ was subjected to a reaction with IF$_5$/Et$_3$N-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 $\beta$-position of the carbonyl group enantioselectively (Scheme 3).
Conclusions

We found that the MT-sulfone group can be converted to a trifluoromethyl group by the reaction with IF₅. 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

1 IF₅ 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).

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.


9 Rozen et al. reported that a trif(methylthio)methyl group in RCH₂(C(S)Me₂) can be converted to trifluoromethyl group by the reaction with Br₃.

10 However, bromination at α-carbon also took place to give RCHBrCF₃; see: A. Hagooly, I. Ben-David and S. Rozen, J. Org. Chem., 2002, 67, 8430.


15  The enantiomeric excess of 4 was determined to be 85% ee as reported14.