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Preparation of Phosphonium Salt from (*S*)-Trifluoropropene Oxide and Wittig Type Reactions

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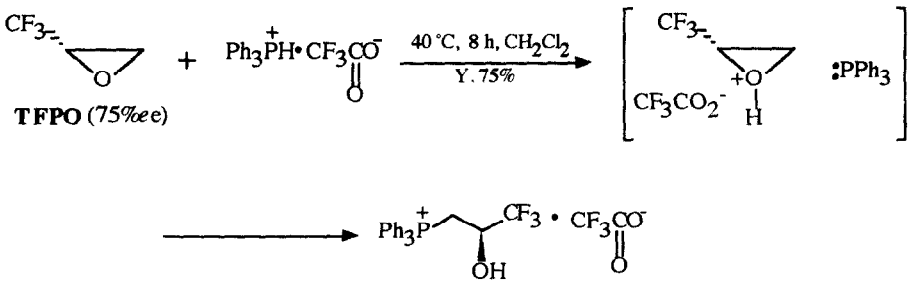
Key Words: (*S*)-trifluoropropene oxide; 1-trifluoromethylated allylic alcohols; phosphonium salt; Wittig reaction; stereoselectivity

Abstract: (*S*)-3,3,3-Trifluoropropene oxide was reacted with triphenylphosphine in the presence of trifluoroacetic acid to afford the corresponding β-hydroxyalkyl phosphonium salt. Wittig type reaction of aldehydes with the salt under basic condition readily occurred to form optically active α-trifluoromethylated allylic alcohols. The *trans*-selectivity of these reactions were discussed.

The chiral fluorine-containing organic compounds have been focused for these several years owing to their specific characters in the fields of bioactive materials[1] and opto-electronic device such as liquid crystal. Especially, 1-trifluoromethylated alcohols are important compounds for the partial structure of ferroelectronic liquid crystals.[2]

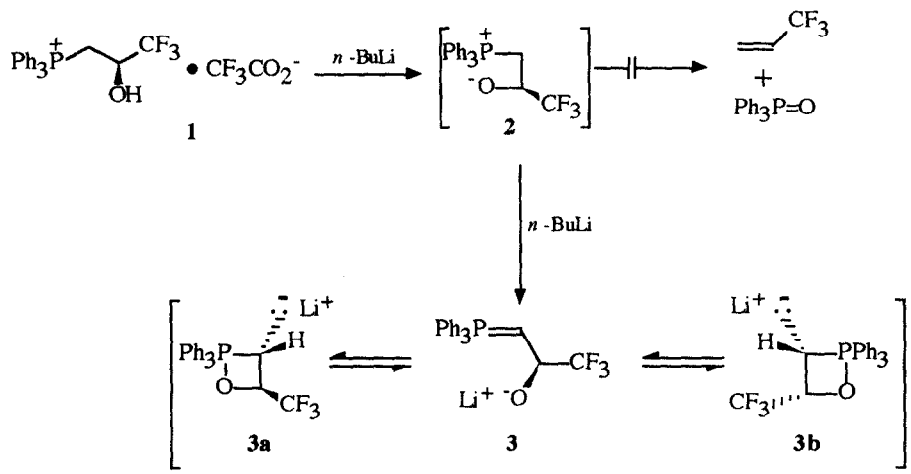
Recently, Grignard type and Friedel-Crafts type reactions of (*S*)-3,3,3-trifluoropropene oxide (TFPO) yielding 1-alkyl-2,2,2-trifluoroethanols and 1-arylmethyl-2,2,2-trifluoroethanols were reported. Because C-1 of TFPO was positively charged than C-2, 1-position always attacked by nucleophiles in these reactions.[3] On the other hand, it was also reported that the ring opening reactions of epoxides by triphenylphosphine in the presence of trifluoroacetic acid or tetrafluoroboric acid readily occurred to form β-hydroxyalkyltriphenylphosphonium salts.[4] In this paper, we wish to report the ring opening reaction of TFPO by triphenylphosphine-trifluoroacetic acid, and the preparation of 1-trifluoromethylallylic alcohols via Wittig type reactions using the obtained phosphonium salt containing a chiral β-hydroxyalkyl group with aldehydes.

TFPO (75% ee) was dropped into the suspension of triphenylphosphonium hydrotrifluoroacetate which was formed *in situ* in dichloromethane, and the following 8 h heating at 40 °C gave 2-hydroxy-3,3,3-trifluoropropyl triphenylphosphonium trifluoroacetate (**1**) in good yield. Mechanistically, it is thought that C-1 of the protonated TFPO intermediate was attacked by triphenylphosphine to form **1** (mp 144-146 °C, $[\alpha]_D^{25}$ -27.6° (*c* 2.0, MeOH), and therefore, the configuration of the 2-position was maintained through the salt formation. **1** was very stable crystal and non-hygroscopic.



1

Generally, the treatment of β-hydroxyalkylated phosphonium salt with an equivalent amount of base affords alkene and phosphine oxide via the betaine and oxaphosphetane intermediate.[5] However, in the case of the treatment of **1** with an equimolar of *n*-butyllithium, the signals of trifluoromethyl groups of betaine **2** and/or 3,3,3-trifruoropropene by ^{19}F-NMR spectrum were not observed, but those of which were possibly considered to be due to the 1:1 mixture of the unreacted starting material **1** and the corresponding ylide **3** or the anions of oxaphosphetane (**3a** and/or **3b**). On the other hand, when two equivalents of *n*-butyllithium were used, **1** was converted to **3**, **3a** and/or **3b** completely. As the β-trifluoromethyl group exhibits the stabilization effect for oxaphosphetane intermediate[6] and the pentavalent phosphorane structure was stabilized by a 2,2,2-trifluoroethoxy group,[7] the formation of oxaphosphetane anions (**3a** or **3b**) may be reasonable in the latter case.



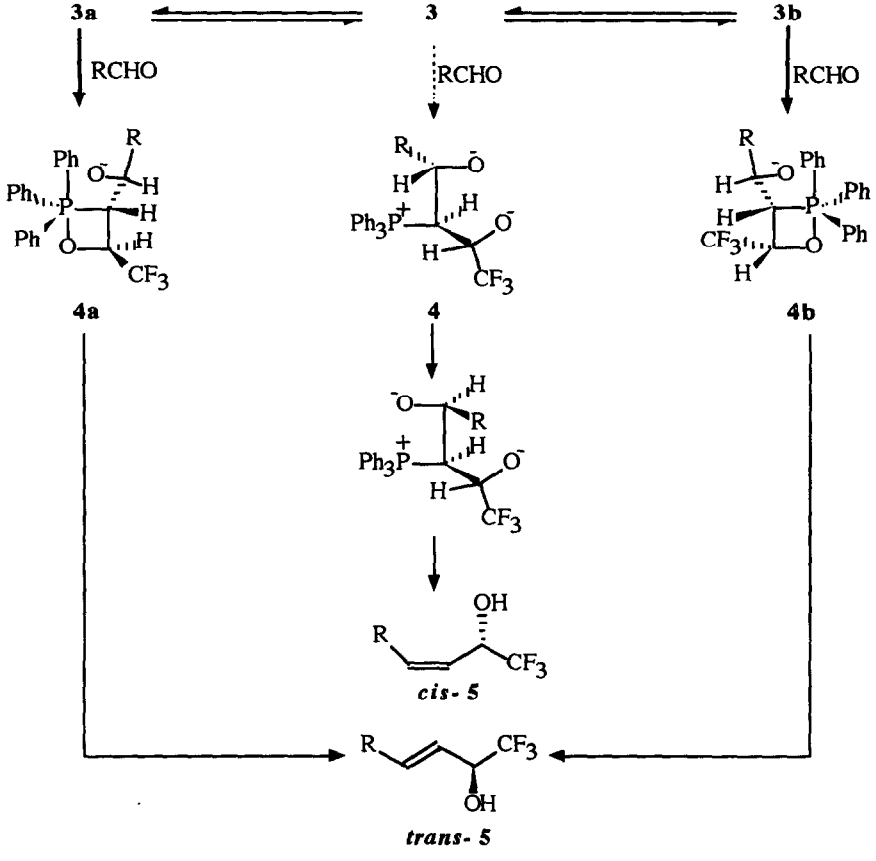
1 **2** **3a** **3** **3b**

Into the THF solution containing **3**, **3a** or **3b** generated *in situ*, an aldehyde was dropped at -78 °C. After 2 h at the same temperature, the reaction mixture was treated as usual. The corresponding 1-trifluoromethylated allylic alcohols **5** were obtained in good yields.

In the general Wittig reaction using ylide which is not stabilized by an electron-withdrawing group such as a carbonyl group, *cis*-preference has been observed at the newly formed carbon-carbon double bond.[5a,8] If the present reactions occurred via ylide **3**, it is considered that intermediate **4** was formed at the initial stage which

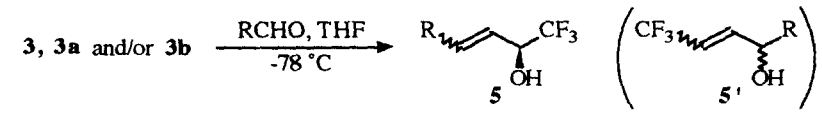
has less steric hindrance, and then, *cis*-product was obtained predominantly. However, in the Wittig type reactions using **3**, *trans*-allylic alcohols were, in fact, obtained predominantly (**5a-f**). Especially, when benzaldehyde was used as a substrate, only the *trans*-product (**5c**) was obtained. This *trans*-selectivity is rationalized as the result that the oxaphosphetane anion (**3a**, **3b**) attacked aldehydes in the most favored direction. From the result that the absolute configurations of **5a** and **5c** were *S* (about 75% ee), it is inferred that the racemization of 2-position of TFPO did not occur through the phosphonium salt formation nor Wittig type reaction (Table 1).

Furthermore, the formation of 1-alkyl-4,4,4-trifluorocrotyl alcohols **5'** from these intermediates was possible, but it was not obtained. It would be understood as follows: the C-O bond close to a trifluoromethyl group in **4**, **4a** and/or **4b** is shorter, stronger and therefore less nucleophilic than the other, because of the electron-withdrawing effect of this group.



In conclusion, we showed facile conversion of TFPO to optically active β-hydroxyalkyl phosphonium salt **1** and the preparation of α-trifluoromethylated allylic alcohols via Wittig type reaction. In addition, it was discussed that the stereoselectivity of the Wittig type reaction was opposed to that of the general version using unstabilized ylides. Further investigations of **1** as a CF_3 source are now in progress.

Table 1 The preparation of 1-trifluoromethylated allylic alcohols



Aldehyde	Product	Yield(%)[a]	*trans* : *cis*	configuration (%*ee*)
n-$C_6H_{13}CHO$	**5a**	76	71 : 29	*S* [b] (74)[e]
n-$C_5H_{11}CHO$	**5b**	71	56 : 24	nd[c] (75)[e]
PhCHO	**5c**	65	*trans*-only	*S* [d] (75)[e]
Ph, CHO	**5d**	67	65 : 35	nd[c] (74)[e]
CHO	**5e**	89	68 : 32	nd[c] (75)[f]
Ph, CHO	**5f**	46	73 : 27	nd[c]

a: Isolated yield. b: Determined by the specific rotation after conversion of **5a** to the corresponding saturated alcohol by reduction using a Pt/C-H_2 system. $[\alpha]_D^{22}$ -16.5° (*c* 0.88, MeOH). Literature value was -16.6° (MeOH) for *S* (74% ee) in ref. 3. c: Not determined. d: $[\alpha]_D^{23}$ +17.8° (*c* 1.06, MeOH). Literature value was +16.3° (*c* 1.06, MeOH) for (*S*)-*trans* (76% ee) in ref. 9. e: Determined by ^{19}F NMR signal intensities of the corresponding MTPA-esters. f: Determined by GLC analysis (CP-Cyclodextrine-β-236M-19, 25 m, Chrompack).

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