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TRIFLUOROPROPENE OXIDE AS A TRIFLUOROMETHYL SOURCE. PREPARATION OF OPTICALLY ACTIVE ALCOHOLS

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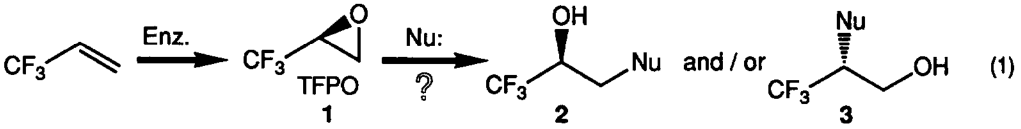
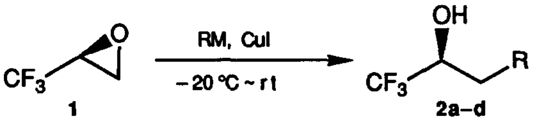
Summary: Optically active 3,3,3-trifluoropropene oxide (TFPO) was converted to 1,1,1-trifluoro-2-ols via Grignard type or Friedel-Crafts type reaction. The regio-selectivity of the latter reaction was discussed through an MO calculation.

Trifluoromethyl containing compounds have received much interest because of their physical and biological properties, and many synthetic approaches toward introduction of CF_3-groups into organic molecules have been reported.[1] TFPO (**1**), which has oxirane functionality, can be regarded as a potentially versatile building block, but few reactions of **1** have been reported[2] probably because of its limited availability.[3] Recently, optically active (–)-**1**[4] has got readily available via direct oxidation of the corresponding olefin (3,3,3-trifluoropropene) using our microbial method.[5] Now we wish to report facile conversions of **1** to trifluoromethyl containing alcohols in optically active forms (Eq. 1).

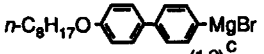


First, we examined Grignard type ring opening reaction (Eq. 2, Table 1). Epoxide **1** was added to a cooled solution (– 20 °C) of organocopper reagent which was prepared from Grignard reagent or organolithium by mixing with a catalytic or a stoichiometric amount of CuI, and the whole reaction mixture was allowed to warm to room temperature. Usual work-up gave the adduct **2** without detectable amount of the regio-isomer **3**. The present selectivity was parallel to that of the analogous reactions well-known for fluorine-free epoxides.[6] Because the bond-formation did not occur on the asymmetric carbon atom, the configulation of (–)-**1**[4] was assigned to be *S* (75 % ee) via this reaction which gave reported compounds.[1a-b]



(2)

Table 1 Grignard type ring opening reaction of **1**

RM (eq)	CuI (eq)	Solvent	Product	% Yield[a]	% ee[b]
n-$C_7H_{15}MgBr$ (1.5)[c]	0.02	THF - Et_2O (2 : 1)	**2a**[d]	77	74
$(n$-$C_4H_9)_2CuLi$ (1.2)	—	Et_2O - Hexane (1 : 1)	**2b**	77	75
 (1.2)[c]	0.02	THF	**2c**	66	nd[e]
PhMgBr (1.5)[c]	0.02	THF	**2d**[f]	89	75

a: Isolated yield. b: Determined by GLC analysis (PEG 20M, 25 m) of the corresponding MTPA-ester. c: Refers to RBr used for the metallation. d: $[\alpha]_D = -16.6°$ (MeOH). Different value was reported in ref. 1a. e: Not determined. f: $[\alpha]_D = -36.8°$ (MeOH). Literature value was −47.7° for S (98 % ee) in ref. 1a.

Second, Friedel-Crafts type reaction was examined (Scheme 1, Table 2). Epoxide **1** was added with cooling into a mixture of $AlCl_3$ (1.15 eq) and excess ArH.[7] After stirring at room temperature for 3 h, the adduct **2** was obtained as a sole product. Acidic ring-opening of epoxides generally occurs on the more substituted carbon, and in fact, fluorine-free epoxide **4** has been reported to give **3'** along with stereochemical inversion under similar conditions.[8] So it should be noted that the present products were not **3** but **2**.

Scheme 1

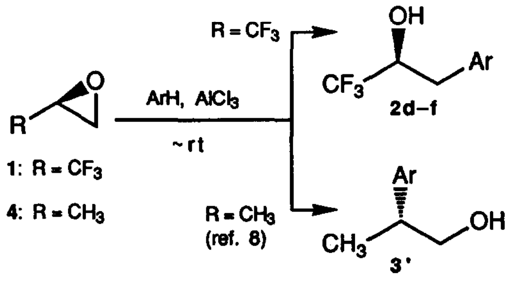
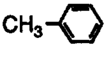
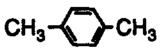


Table 2 Friedel-Crafts Type Reaction of **1**

ArH (eq)		Product	% Yield[a]
	(26)	**2d**[b] (75 % ee)[c]	75
	(22)	**2e** (2 : 2 : 1)[d]	81
	(19)	**2f**	72

a: Isolated yield. b: ^1H NMR and $[\alpha]_D$ were identical with the product shown in Table 1. c: Determined by GLC analysis of its MTPA-ester. d: Isomeric ratio which refers to the aromatic substitution patern (^{19}F NMR).

The unusual regio-selectivity could be rationalized by the strong electron-withdrowing property of CF_3 which destabilizes an α-cationic species.[9] For further rationalization, an MO calculation by PM3 method was performed with MOPAC Ver. 5.01.[10]

At first, $AlCl_3$ was attached to the oxygen atom of epoxide **1** or **4**, and the most stable structure was calculated for the each complex (T_0, Table 3). For the fluorinated T_0, C1 which was more positive than C2 would be more electrophilic, and the C1–O bond which was longer than C2–O would be more easily cleaved. On the other hand, C2 was more positive and C2–O was longer for fluorine-free T_0. These results agree with the observed regio-selectivities shown in Scheme 1.

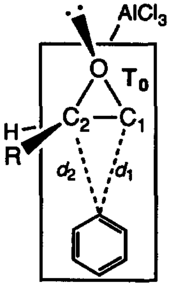
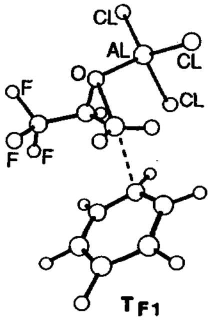


Table 3 The most stable structure of T_0

R	Atomic Charge		Bond Length (Å)	
	C1	C2	C1–O	C2–O
CF_3	+ 0.034	– 0.058	1.468	1.453
CH_3	+ 0.003	+ 0.033	1.462	1.479

Then a benzene molecule was placed on the oxirane plane as shown above with 20 Å of distance[11] between the reaction centers. The reactions at C1 and C2 were simulated by stepwise shortening of d_1 and d_2 respectively. In each step, the relative positions of all atoms were optimized. The calculation gave transition states T_{F1} and T_{F2} along with the corresponding energy barrier ΔE based on T_0 for the reaction of **1**, and also gave T_{H1} and T_{H2} for **4** (vide infra). The C–C bond formation of **1** would much more favorably occur at C1 than C2 ($\Delta\Delta E$ = 12.4 kcal/mol), by contrast, **4** would react at C2 ($\Delta\Delta E$ = 3.6 kcal/mol). These results also agree with the observed and reported[8] regio-selectivities.



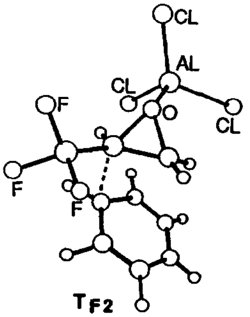
T_{F1}

ΔE_{F1} = 29.6 kcal/mol

d_1 = 2.10 Å

C1–O = 1.57 Å

C2–O = 1.43 Å



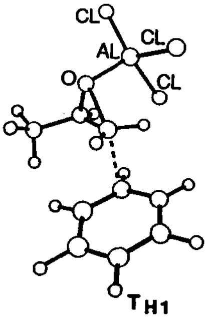
T_{F2}

ΔE_{F2} = 42.0 kcal/mol

d_2 = 2.07 Å

C1–O = 1.44 Å

C2–O = 1.56 Å



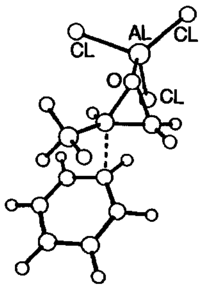
T_{H1}

ΔE_{H1} = 33.3 kcal/mol

d_1 = 2.05 Å

C1–O = 1.60 Å

C2–O = 1.44 Å



T_{H2}

ΔE_{H2} = 29.7 kcal/mol

d_2 = 2.17 Å

C1–O = 1.43 Å

C2–O = 1.64 Å

In conclusion, we showed facile conversions of TFPO to optically active 1,1,1-trifluoro-2-ols via Grignad type or Friedel-Crafts type reaction. In particular, the former reaction would be applicable for preparation of a wide variety of CF_3 compounds. In addition, a unique property of TFPO was demonstrated through an MO caluculation in relation to the latter reaction. Further investigations on TFPO as a CF_3 source are now in progress.

References and notes

1. a: J.-T. Lin, T. Yamazaki, and T. Kitazume, *J. Org. Chem.*, **52**, 3211 (1987); b: P. Bravo, M. Frigerio, and G. Resnati, *Synthsis*, **1988**, 955; c: J. T. Welch, *Tetrahedron*, **43**, 3123 (1987); d: "Synthesis of Fluoroorganic Compounds," ed by I. L. Knunyants and G. G. Yakobson, Springer-Verlag, Berlin (1985).
2. E. T. McBee, C. E. Hathaway, and C. W. Roberts, *J. Am. Chem. Soc.*, **78**, 3851 (1956) and some papers on polymerization of **1**.
3. E. T. McBee and T. M. Burton, *J. Am. Chem. Soc.*, **74**, 3022 (1952); I. L. Knunyants, E. Y. Pervova, and V. V. Tyuleneva, *Izv. Akad. Nauk SSSR, Otdel. Khim. Nauk.*, **1956**, 843; R. H. Groth, *J. Org. Chem.*, **25**, 102 (1960). Direct epoxidation of 3,3,3-trifluoropropene has not been reported.
4. $[\alpha]_D = -9.2^\circ$ ($c = 5.3$, $CHCl_3$).
5. H. Saeki and K. Furuhashi, IUMS Congress, Bactriology & Mycology, Osaka, Japan, September 1990: Trifluoropropene containing air was bubbled into an aqueous suspension of *Nocardia corallina* B-276, and **1** in the off-gas was trapped using a dry-ice ethanol condenser. *Cf.* K. Furuhashi, M. Shintani, and M. Takagi, *Appl. Microbiol. Biotechnol.*, **23**, 218 (1986); O. Takahashi, J. Umezawa, K. Furuhashi, and M. Takagi, *Tetrahedron Lett.*, **30**, 1583 (1989).
6. R_2CuLi: G. H. Posner, *Org. React.*, **22**, 253 (1975). RMgX / Cu(I): S. Takano, M. Yamase, M. Takahashi, and K. Ogasawara, *Chem. Lett.*, **1987**, 2017; C. Huynh, F. Derguini-Boumechal, and G. Linstrumelle, *Tetrahedron Lett.*, **1979**, 1503 and related papers.
7. Reactions with stoichiometric toluene in CH_2Cl_2 or CH_3NO_2 were unsuccessful.
8. T. Nakajima, S. Suga, T. Sugita, and K. Ichikawa, *Bull. Chem. Soc. Jpn.*, **40**, 2980 (1967); Idem, *Tetrahedron*, **25**, 1807 (1969); A. Guest, P. H. Hoffman, and M. J. Nugent, *J. Am. Chem. Soc.*, **94**, 4241 (1972).
9. *Cf.* Olefinic Friedel-Crafts reactions of 3,3,3-trifluoropropene: Y. Kobayashi, I. Kumadaki, T. Nagai, A. Takahashi, and Y. Yamauchi, *Chem. Pharm. Bull*, **32**, 4382 (1984).
10. MOPAC Ver. 5: J. J. P. Stewart, *QCPE Bull.*, **9**, 10 (1989); Revised as Ver. 5.01 for UNIX 4.3 BSD by T. Hirano, *JCPE Newsletter*, **1** (2), 36 (1989).
11. The initial *d* (20 Å) could be regarded as infinity.

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