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Rare earth(III) perfluorooctanesulfonates catalyzed Friedel–Crafts alkylation in fluorous biphase system

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Abstract

The catalyst of rare earth(III) perfluorooctanesulfonates ($RE(OSO_2C_8F_{17})_3$, RE = Sc, Y, La–Lu) were prepared from either rare earth chlorides(III) or oxides and perfluorooctanesulfonic acid. The perflates thus obtained act as novel catalysts for Friedel–Crafts alkylation in fluorous biphasic system. Perfluorohexane (C_6F_{14}), perfluoromethylcyclohexane (C_7F_{14}), perfluorotoluene (C_7F_8), perfluorooctane (C_8F_{18}), perfluorooctyl bromide ($C_8F_{17}Br$) and perfluorodecalin ($C_{10}F_{18}$, *cis*- and *trans*-mixture) can be used as fluorous solvents for this reaction. By simple separation of the fluorous phase containing only catalyst, alkylation can be repeated many times.

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Keywords: Friedel–Crafts alkylation; Fluorous biphasic catalysis; Rare earth(III) perfluorooctanesulfonates; Perfluorocarbons

1. Introduction

Friedel–Crafts alkylation is a key process in the catalytic manufacturing of semiproducts for the synthesis of drugs, pesticides and dyes. However, the large-scale synthesis, involving more than stoichiometrical amount of Lewis acids such as aluminum trichloride ($AlCl_3$), makes alkylation one of the most environmentally harmful processes. Recently, many papers related with the Lewis acids of rare earth(III) perfluorooctane sulfonates ($RE(OSO_2C_8F_{17})_3$) have been published [1–4]. The characteristic features of the catalyst include low hygroscopicity, ease of handling, robustness for the recycling using and high solubility in fluorous solvent [2–4]. Shi and Cui reported in 2002 that $RE(OSO_2C_8F_{17})_3$ could catalyze Friedel–Crafts acylation effectively [4]. As the same time, researchers have found many reactions can be carried out in fluorous biphasic system (FBS) proposed by Horvath and Rabai [5]. FBS is a new separation and immobilization technique. By choosing a perfluorocarbon(PFC)/organic solvent couple that shows a thermally controlled miscibility, it is possible to carry out the reaction under homogeneous conditions. When the reaction is finished the fluorous phase containing only catalyst is easily recovered through simple phase-separation, and can be reused without further treatment in a new reaction cycle [5]. Therefore, we believe that Lewis acids $RE(OSO_2C_8F_{17})_3$ can catalyze Friedel–Crafts alkylation in FBS. In this paper, a green process of Friedel–Crafts alkylation in FBS was studied.

2. Results and discussion

The reaction of anisole with benzyl alcohol was adopted for the investigate of catalysts and solvents (Scheme 1). Table 1 shows the catalytic activity of sixteen $RE(OSO_2C_8F_{17})_3$ (RE = Sc, Y, La–Lu) complexes in perfluorodecalin ($C_{10}F_{18}$, *cis*- and *trans*-mixture) fluorous solvent. Among these catalysts, $Sc(OSO_2C_8F_{17})_3$ and $Yb(OSO_2C_8F_{17})_3$ are the most active catalysts in this reaction. The control experiment elucidates that only 6% product of alkylation could be obtained in the absence of catalyst and fluorous solvent. In addition, we found that, only 0.2 mol% catalyst loading was required in the alkylation. We even tried heptadecafluorooctanesulfonic acid ($C_8F_{17}SO_3H$) itself

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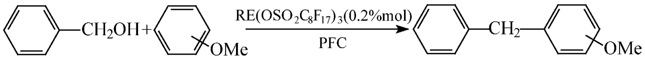
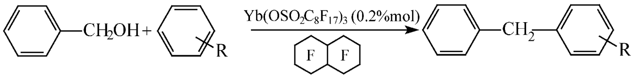


Scheme 1.



Scheme 2.

Table 1
Effect of catalysts for alkylation of anisole with benzalcohol

Entry	Catalyst	Yield (%)[a]	Ratio of *o*:*m*:*p*[b]
1	$Sc(OSO_2C_8F_{17})_3$	98	34:trace:66
2	$Y(OSO_2C_8F_{17})_3$	72	32:trace:68
3	$La(OSO_2C_8F_{17})_3$	53	31:trace:69
4	$Ce(OSO_2C_8F_{17})_3$	52	30:trace:70
5	$Pr(OSO_2C_8F_{17})_3$	91	39:trace:61
6	$Nd(OSO_2C_8F_{17})_3$	40	36:trace:64
7	$Sm(OSO_2C_8F_{17})_3$	60	34:trace:66
8	$Eu(OSO_2C_8F_{17})_3$	91	32:trace:68
9	$Gd(OSO_2C_8F_{17})_3$	86	34:trace:66
10	$Tb(OSO_2C_8F_{17})_3$	31	30:trace:70
11	$Dy(OSO_2C_8F_{17})_3$	56	35:trace:65
12	$Ho(OSO_2C_8F_{17})_3$	90	39:trace:61
13	$Er(OSO_2C_8F_{17})_3$	67	36:trace:64
14	$Tm(OSO_2C_8F_{17})_3$	59	31:trace:69
15	$Yb(OSO_2C_8F_{17})_3$	96	33:trace:67
16	$Lu(OSO_2C_8F_{17})_3$	94	32:trace:68
17	$C_8F_{17}SO_3H$	92	39:trace:61

All reactions were carried out in perfluorodecalin($C_{10}F_{18}$, *cis* and *trans*-mixture); temperature of reaction was 100 °C; time of reaction was 12 h.

[a] Isolated yields based on the alkylating agent.

[b] All ratios of *o*:*m*:*p* were determined by GC.

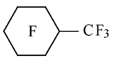
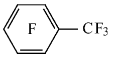
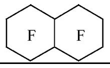
(Table 1, entry 17), finding that the catalyst also can promote reaction greatly, but it can dissolved in water, which results in the great loss of catalyst when reusing fluorous phase.

Next perfluorohexane (C_6F_{14}), perfluoromethylcyclohexane (C_7F_{14}), perfluorotoluene (C_7F_8), perfluorooctane (C_8F_{18}) and perfluorooctyl bromide ($C_8F_{17}Br$) were also selected as fluorous solvents and the effect of such solvents was examined for the Friedel–Crafts alkylation (Table 2). The results showed that the yields of alkylation in perfluorooctane (C_8F_{18}) and perfluorooctyl bromide ($C_8F_{17}Br$) are lower than other solvents. It was observed that perfluorohexane (C_6F_{14}) and perfluorotoluene (C_7F_8) are in fact miscible with aromatic substrates at room temperature, so it is impossible to recover fluorous phase by phase-separation. At the same time, we found that during repeated alkylation reactions the loss of fluorous solvent is very serious when using perfluoromethyl-cyclohexane (C_7F_{14}) as a fluorous solvent because it is very volatile (bp 76 °C). Therefore, perfluorodecalin ($C_{10}F_{18}$, *cis*- and *trans*-mixture) is the best fluorous solvent for alkylation.

Thus, in order to seek out a pratical, useful Friedel–Crafts alkylation, we decided to use the relatively cheap and similarly active $Yb(OSO_2C_8F_{17})_3$ as a catalyst and perfluorodecalin ($C_{10}F_{18}$, *cis* and *trans*-mixture) as a fluorous solvent for alkylation in FBS (Scheme 2). The alkylations of various aromatics with alkylating agents have been tested. As shown in Table 3, Friedel–Crafts alkylation can be carried out effectively in FBS. When the reaction was finished, the reaction mixture was cooled to room temperature. The fluorous phase is not miscible with aromatic substrates and dissolves only the catalysts. The fluorous phase can be easily separated from the reaction mixture and reused for the next alkylation. The fluorous phase containing only catalyst could be simply reused many times with a little decrease in activity. For example, in the $Yb(OSO_2C_8F_{17})_3$ catalyzed reaction of anisole with benzyl alcohol in perfluorodecalin ($C_{10}F_{18}$, *cis* and *trans*-mixture), the yields of alkylation from the first run to the fifth run are 96, 94, 95, 94 and 92%, respectively. This may partly be attributed to the water-repellent nature of the perfluoroalkane chain "$(-CF_2-CF_2-)_n$" of $RE(OSO_2C_8F_{17})_3$ which refuses the approach of water molecules to the central metal cation, thus maintaining its high Lewis acidity [2].

In conclusion, $RE(OSO_2C_8F_{17})_3$ are demonstrated to be new and highly effective catalysts for Friedel–Crafts alkylation in FBS. By simple separation of the fluorous phase containing only catalyst, alkylation can be repeated many times. Further study on the application of FBS to other

Table 2
Effect of solvents for alkylation of anisole with benzalcohol

Entry	PFC	Yield (%)[a]	Ratio of *o*:*m*:*p*[b]
1	$CF_3(CF_2)_4CF_3$	88	40:trace:60
2		99	46:trace:54
3		99	42:trace:58
4	$CF_3(CF_2)_6CF_3$	82	34:trace:66
5	$CF_3(CF_2)_6CF_2Br$	74	28:trace:72
6		96	33:trace:67

All reactions were carried out in the presence of $Yb(OSO_2C_8F_{17})_3$ catalyst; temperature of reaction was 100 °C; time of reaction was 12 h.

[a] Isolated yields based on the alkylating agent.

[b] All ratios of *o*:*m*:*p* were determined by GC.

Table 3
Friedel–Crafts alkylations in FBS

Entry	Aromatics	Alkyltion agents	Yield (%)[a]	Ratio of *o*:*m*:*p*[b]
1	C_6H_6	$PhCH_2OH$	48	–
2	PhMe	$PhCH_2OH$	95	26:6:68
3	PhEt	$PhCH_2OH$	87	20:2:78
4	*i*-Pr-Ph	$PhCH_2OH$	82	11:trace:89
5	PhCl	$PhCH_2OH$	18	6:trace:94
6	PhF	$PhCH_2OH$	84	4:trace:96
7	PhOMe	Cyclohexanol	62	44:trace:56
8	PhOMe	$(CH_3)_2CHOH$	41	41:4:55
9	C_6H_6	$PhCH_2Cl$	14	–
10	PhMe	$PhCH_2Cl$	58	4:trace:96
11	PhOMe	$PhCH_2Cl$	46	1:trace:99

Temperature of all reactions was 100 °C; time of all reaction was 12 h.

[a] Isolated yields based on the alkylating agent.

[b] All ratios of *o*:*m*:*p* were determined by GC.

reactions, which can promote by such Lewis acids is under way in this laboratory.

3. Experimental

3.1. General

MPs were obtained with Shimadzu DSC-50 thermal analyzer. IR spectra were recorded on a Bumem MB154S infrared analyzer. ^{1}H NMR spectra were measured on Bruke Advance DMX500. Mass spectra were recorded with a Saturn 2000GC/MS instrument. Inductively coupled plasma (ICP) spectra were measured on Ultima2C apparatus. Elemental analyses were performed on a Yanagimoto MT3CHN corder. The orientation of alkylation was determined by HP4890 GC analyzer with HP-5 silica chromatography column. Commercially available reagents were used without further purification.

3.2. Typical procedure for preparation of $RE(OSO_2C_8F_{17})_3$

$RE(OSO_2C_8F_{17})_3$ was prepared according to the literatures [2] (Method A). The mixture of $C_8F_{17}SO_3H$ solution (aq) and $YbCl_3{\cdot}6H_2O$ solution (aq) was stirred at room temperature (Method B). The mixture of $C_8F_{17}SO_3H$ solution (aq) and Yb_2O_3 powder was stirred at boiling. In both methods, the resulting gelatin-like solid was collected, washed and dried at 150 °C in vacuo to give a white solid, which does not have a clear melting point up to 500 °C, but shrinks around 380 and 450 °C. IR (KBr) υ1 237 (CF_3), 1 152 (CF_2), 1 081 (SO_2), 1 059 (SO_2), 747 (S–O) and 652 (C–S) cm^{-1}. ICP: Calcd for $C_{24}O_9F_{51}SYb$: Yb, 10.30%. Found: Yb, 9.88%. Anal. Calcd for $C_{24}O_9F_{51}SYb{\cdot}H_2O$: C, 17.21%; H, 0.10%. Found: C, 17.03%; H, 0.40%.

3.3. Typical procedure for Friedel–Crafts alkylations

Benzyl alcohol (1.1 ml, 12 mmol) was slowly added into a mixture of $Yb(OSO_2C_8F_{17})_3$ (40 mg, 0.024 mmol), anisole (2.2 ml, 20 mmol) and perfluorodecalin ($C_{10}F_{18}$, *cis* and *trans*-mixture, 1.5 ml). The mixture was stirred at 100 °C for 12 h. Then, the fluorous layer on the bottom was separated for the next alkylation. The reaction mixture (organic phase and water phase) was washed with 10% $NaHCO_3$ solution (10 ml) and water (10 ml × 2), then extracted with hexane. The combined organic layers were dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by a silica gel column chromatongraph (eluent:petroleum ether/EtOAC = 5/1) to give a colorless liquid (2.28 g, 96%). *p*-Benzylanisole ^{1}H NMR (300 MHz, TMS, $CDCl_3$) δ 2.26 (3H, s, CH_3), 3.78 (2H, s, CH_2), 6.80–7.10 (9H, m, Ar). MS (EI) *m/z* 198 (M^+).

Diphenylmethane A colorless liquid; ^{1}H NMR (300 MHz, TMS, $CDCl_3$) δ 3.89 (2H, s, CH_2), 6.95–7.30 (10H, m, Ar). MS (EI) *m/z* 168 (M^+).

p-Benzyltoluene A colorless liquid; ^{1}H NMR (300 MHz, TMS, $CDCl_3$) δ 2.30 (3H, s, CH_3), 3.85 (2H, s, CH_2), 6.81–7.12 (9H, m, Ar). MS (EI) *m/z* 182 (M^+).

(p-Benzyl)ethylbenzene A colorless liquid; ^{1}H NMR (300 MHz, TMS, $CDCl_3$) δ 1.27–1.38 (3H, t, CH_3), 2.21–2.62 (2H, m, CH_2), 3.82 (2H, s, CH_2), 6.82–7.18 (9H, m, Ar). MS (EI) *m/z* 196 (M^+).

(p-Benzyl)i-propyllbenzene A colorless liquid; ^{1}H NMR (300 MHz, TMS, $CDCl_3$) δ 1.12$\sim$1.29 (6H, d, CH_3), 2.50–3.01 (H, m, CH), 3.80 (2H, s, CH_2), 6.79–7.19 (9H, m, Ar). MS (EI) *m/z* 196 (M^+).

(p-Benzyl)chlorobenzene A colorless liquid; ^{1}H NMR (300 MHz, TMS, $CDCl_3$) δ 3.90 (2H, s, CH_2), 6.98–7.22 (5H, m, Ar), 7.32–7.70 (4H, m, Ar). MS (EI) *m/z* 202 204 (M^+).

(p-Benzyl)fluorobenzene A colorless liquid; ^{1}H NMR (300 MHz, TMS, $CDCl_3$) δ 3.92 (2H, s, CH_2), 6.96–7.24 (5H, m, Ar), 7.36–7.62 (4H, m, Ar). MS (EI) *m/z* 186 (M^+).

p-Cyclohexylanisole A colorless solid; ^{1}H NMR (300 MHz, TMS, $CDCl_3$) δ 1.15–1.68 (10H, d, $(CH_2)_5$), 1,74 (1H, m, CH) 2.24 (3H, s, CH_3), 6.84–7.21 (4H, m, Ar). MS (EI) *m/z* 190 (M^+).

p-(i-Propyl)anisole A colorless liquid; ^{1}H NMR (300 MHz, TMS, $CDCl_3$) δ 2.20 (3H, s, CH_3), 2.48–3.10 (H, m, CH), 6.70–7.06 (4H, m, Ar). MS (EI) *m/z* 150 (M^+).

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