Lithium Tetrakis(pentafluorophenyl)borate-Catalyzed Friedel–Crafts Benzylation Reactions

Teruaki Mukaiyama, Masakazu Nakano, Wataru Kikuchi, and Jun-ichi Matsuo
Department of Applied Chemistry, Faculty of Science, Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo 162-8601

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Lithium tetrakis(pentafluorophenyl)borate [$LiB(C_6F_5)_4$], a neutral salt, effectively catalyzed Friedel–Crafts benzylation reactions of aromatic compounds with benzyl chloride or mesylate and their substituted derivatives. The $LiB(C_6F_5)_4$-catalyzed reactions proceeded more efficiently in the coexistence of magnesium oxide.

Tetrakis(pentafluorophenyl)borate ion[1] is one of the most weakly-coordinating anions[2] whose counter ion exists as a naked cation. Moreover, its counter metal ion is soluble even in nonpolar organic solvents because of the lipophilic character of borate ion. Besides in olefin polymerization,[3] the borates are employed in synthetic organic reactions as activators of various electrophiles.

Recently, it was reported from our laboratory that a catalytic amount of borate compounds such as $TrB(C_6F_5)_4$ was enough to work effectively as a Lewis acid in glycosylation reactions[4] and also in aldol reactions of silyl enol ethers and acetals or aldehydes.[5]

Now, Friedel–Crafts benzylation reactions of aromatic compounds with benzyl chloride or mesylate[6] were tried on the assumption that lithium tetrakis(pentafluorophenyl)borate[7] [$LiB(C_6F_5)_4$] **1**, a neutral salt, would mildly generate an active benzylating species by coordinating to the benzylating reagents. By using this active species, the reaction is then expected to proceed under milder conditions than of convensional ones catalyzed by classical Lewis acids such as aluminium trichloride ($AlCl_3$). The yield of mono-benzylated product of $AlCl_3$ was not so high sometimes, because of the formation of a mixture of two dibenzylated products. In this case, the yield of mono-benzylated product was improved to some extent in the coexistence of montmorillonite.[8]

Further, it was also reported that the benzylation reactions were promoted by using 30 mol% of lanthanoid chloride[9] and were catalyzed effectively also by $Hf(OTf)_4$ in the further addition of lithium perchlorate in nitromethane.[10] Therefore, exploration of a catalyst which efficiently promotes the above reaction under milder conditions is still required.

We would like to describe here a unique catalytic activity of **1** in Friedel–Crafts benzylations of aromatic compounds by using benzyl chloride or mesylate and their substituted derivatives together with the effect of magnesium oxide (MgO) which improved the catalyst turnover of this reaction.

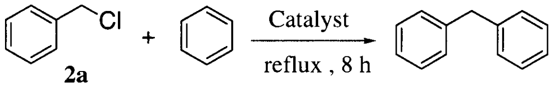


Table 1. Effects of catalyst **1** and metal oxides on Friedel-Crafts benzylation[a]

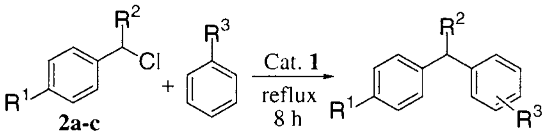
Entry	Catalyst / mol%		Metal oxide	Yield / %
1	**1**	10	-	96
2	LiOTf	10	-	N.R.
3	$LiBF_4$	10	-	N.R.
4	$AlCl_3$	10	-	75[b]
5	**1**	5	-	76
6	**1**	1	-	29
7	**1**	1	MgO	84
8	-	-	MgO	N.R.
9	**1**	1	CaO	37
10	**1**	1	BaO	25
11	**1**	1	SrO	21

[a]The reactions were carried out with 30 equiv of benzene and 1 equiv of metal oxides. [b]The reaction was carried out at room temperature and the reaction time was 1.5 h. Dibenzylbenzene was obtained as a by-product in an 8% yield.

When a catalytic amount (10 mol%) of **1** was added to a mixture of benzyl chloride (1.0 mmol) and benzene (30 mmol) at 80 ˚C, the benzylation reaction took place and gave the mono-benzylated product, diphenylmethane, in high yield (Table 1, entry 1). However, the benzylation did not proceed at all when LiOTf or $LiBF_4$ was added in place of **1** in the above reaction (entries 2 and 3). On the other hand, if $AlCl_3$ was used in the same reaction, diphenylmethane was obtained in 75% along with 8% of dibenzylbenzene (entry 4). It is noted that **1**-catalyzed benzylation reaction afforded diphenylmethane in 96% yield with trace amounts of dibenzylated products although the catalytic efficiency of **1** under this condition turned out to be rather low (entries 1, 5 and 6). Then, addition of a suitable base which would not form a complex with **1** was considered in order to accelerate regeneration of **1** more efficiently by trapping a co-product, hydrogen chloride. This should improve the turnover of the catalyst **1**. Metal oxides were thus chosen for this purpose and thus the above benzylation reactions were tried in the presence of several metal oxides (entries 7–11). It was found that MgO was the most effective of all the metal oxides examined and the catalyst turnover was considerably improved in the presence of MgO.[11] But, it is noted that MgO itself did not catalyze the benzylation reaction.

When borate **1** was applied to some other Friedel–Crafts benzylations of aromatic compounds with benzylating agents (Table 2), almost all the reactions proceeded to give the desired products in good to excellent yields. The addition of MgO was notably effective in improving the yields of the desired products (entries 3, 6, 10 and 12).

The **1**-catalyzed Friedel–Crafts benzylation by using several benzyl mesylates proceeded under milder conditions than the case using benzyl chlorides (Table 3). In every case, the reactions proceeded smoothly at room temperature to give the mono-benzylated products in high yields. The result of a reaction between 4-chloromethylbenzyl mesylate **3c** and benzene shown in Table 3 (entry 7) is interesting. When the

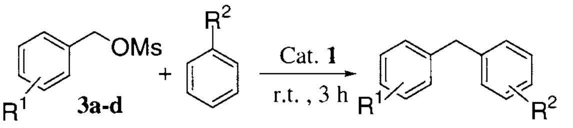


2b:R^1=H, R^2=Me; **2c**:R^1=Cl, R^2=H

Table 2. Friedel-Crafts benzylation reactions of aromatic compounds with benzyl chlorides by using a catalytic amount of **1**[a]

Entry	Substrate	R^3	**1** / mol%	Yield / % (ratio of *o*:*p*)[f]
1	**2a**	Me	10	99 (43:57)
2		Me	1	42 (44:56)
3		Me	1	72[b] (44:56)
4		OMe	1	97[c] (43:57)
5	**2b**	H	10	58[d]
6		H	10	63[b, d]
7		Me	10	89 (7:93)
8		OMe	10	80 (37:63)
9	**2c**	H	10	73
10		H	10	quant.[b]
11		Me	10	76[e](44:56)
12		Me	10	97[b](45:55)
13		OMe	1	83 (49:51)

[a]The reactions were carried out by using 30 equiv of aromatic compounds except for entries 4, 8 and 13 (10 equiv). [b]Magnesium oxide (1 equiv) was added. [c]The reaction temperature was 140 °C. [d]The reaction temperature was 50 °C. [e]The reaction time was 24 h. [f]Determined by ^{1}H NMR.



3a:R^1=H **3b**:R^1=*p*-Cl **3c**:R^1=*p*-CH_2Cl **3d**:R^1=*o*-CH_2Cl

Table 3. Friedel-Crafts benzylation reactions of aromatic compounds with benzyl mesylates by using a catalytic amount of **1**[a]

Entry	Substrate	R^2	**1** / mol%	Yield / % (ratio of *o*:*p*)[c]
1	**3a**	H	1	81
2		Me	1	87 (44:56)
3		OMe	10	99 (46:54)
4		OMe	-	N.R.
5	**3b**	H	5	89
6		Me	5	90 (45:55)
7	**3c**	H	5	97
8	**3d**	H	5	85[b]

[a]The reactions were carried out by using 30 equiv of the aromatic substrates except for entries 3 and 4 (10 equiv). [b]The reaction time was 10 h. [c]Determined by ^{1}H NMR.

Friedel–Crafts reaction was tried by using **3c** which has two reaction sites, benzylic chloride and benzylic mesylate moieties, only the mesylate site reacted to give 4-chloromethylbenzylbenzene in an excellent yield. This shows selective Friedel–Crafts benzylation reaction of aromatic compounds to be performed by the present **1**-catalyzed reactions.

A typical experimental procedure is described for the reaction of benzene with benzyl chloride (Table 1, entry 7): to a mixture of **1** (0.5×10^{-2} mmol, 1 mol%) and MgO (0.5 mmol) was added a solution of benzyl chloride (0.5 mmol) in benzene (15 mmol) at room temperature. The mixture was stirred for 8 h at 80 °C and then filtered through silica gel. The eluent was concentrated in vacuo, and the crude product was purified by preparative TLC to afford diphenylmethane.

Thus, it is noted that a new and convenient method for Friedel–Crafts benzylation reactions of aromatic compounds with benzyl chloride or mesylate and their substituted derivatives in the presence of a catalytic amount of, a neutral salt, **1** was established. Further, it was found that the turnover of the present catalyst **1** is improved by the addition of MgO.

Further investigations to develop other synthetic reactions using catalytic amounts of **1** as well as to clarify the role of the MgO in this reaction are now in progress.

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7 Lithium Tetrakis(pentafluorophenyl)borate–Ethyl Ether Complex was purchased from Tokyo Chemical Industry Co., Ltd. and was stirred under 0.5 mmHg at 60 °C for 3 h before use in the Friedel–Crafts reaction. By ^{1}H NMR measurement, it was determined that the above pretreated lithium tetrakis(pentafluorophenyl)borate contained 1.9–2.3 moles of ether and 0.9–1.1 mole of water.

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