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POLYMER-SUPPORTED AMINOPYRIDINIUM SALTS AS VERSATILE CATALYSTS FOR THE SYNTHESIS OF ARYL FLUORIDES

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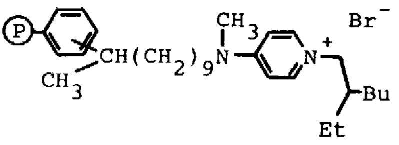
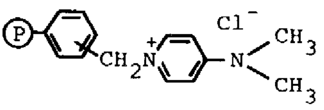
Summary: Immobilized N-alkylaminopyridinium salts on divinylbenzene cross-linked polystyrene gel was reusable at least 8 times on the reaction of 4-chloronitrobenzene with anhydrous potassium fluoride in tetrahydrothiophene 1,1-dioxide to give 4-fluoronitrobenzene in high yield. The immobilized catalyst was also successfully used for a synthesis of several aryl fluorides in good yields.

Halogen-exchange fluorination method is now established as a versatile and important synthetic technique on the preparation of aryl fluoride.1) Among various synthetic methods for aryl fluoride, it has been found to have advantages in terms of ready availability of starting materials and its experimental simplicity (the use of dangerous hydrogen fluoride is avoided). The reactions usually require, however, elevated reaction temperature owing to poor solubility of potassium fluoride in organic solvents.

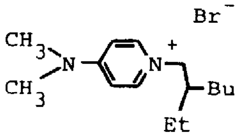
Numerous efforts have been made for acceleration of halogen-exchange fluorination reaction, including use of quaternary onium salts as catalysts.2) In general, however, ammonium and phosphonium salts show no significant catalytic activity because of their thermal instability under the basic conditions.3) Although N-alkyl-4-(N',N'-dialkyl)aminopyridinium salts such as **3** have been reported as thermally stable catalysts on the fluorination of 4-chloronitrobenzene(PCNB) with potassium fluoride, they are not only expensive but have rather moderate catalytic activity.4)



1 (1.03 mmol/g)



2 (1.17 mmol/g)



3

Ⓟ : 2% divinylbenzene cross-linked polystyrene gel

We have now found that immobilized aminopyridinium salts on divinylbenzene cross-linked polystyrene gel (**1**,**2**), compared with free N-2-ethylhexyl-4-(N',N'-dimethyl)aminopyridinium bromide (**3**), have advantages in terms of the separation of products from the catalyst and the reuse of the catalyst.

Thus, a mixture of PCNB (3.94 g, 25 mmol), spray dried potassium fluoride[5)] (2.18 g, 37.5 mmol), and **1**[6)] (2.45 g, 2.5 mmol) in anhydrous tetrahydrothiophene 1,1-dioxide (Sulfolane, $TMSO_2$) (15 g) was stirred for 4 h at 180 °C in nitrogen atmosphere. The mixture was then cooled to room temperature and filtered, and the resin was washed with 30 ml of dichloromethane twice. The combined filtrate was concentrated and distilled to give 2.5 g (71%) of 4-fluoronitrobenzene (PFNB), bp 77-82 °C/6 Torr (lit.,[7)] 109-109.5 °C/36 Torr). PFNB was obtained in only 10% yield without catalyst.

Resin 1 was washed successively with water and acetone, then stirred in tetrahydrofuran (40 ml) and 1 M HCl (10 ml) for 1 h. Filtration, washing with water and tetrahydrofuran, and being dried (50 °C, 1 day) afforded 2.33 g of the dry recovered polymer.

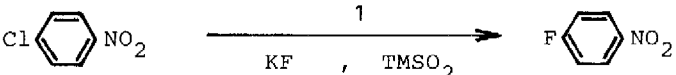
In order to examine the catalytic activity of the recovered polymer, the same fluorination reaction of PCNB was repeated in the presence of the recovered **1**. Under the same reaction conditions, PFNB was isolated in 72% yield. Though polymer 1 was recognized to be reused without significant loss in activity by the above mentioned manner, further repeated experiment of **1** was performed on the same reaction scheme. Table 1 exemplifies the fluorination of PCNB through the reuse of the present polymer **1**. After reuse of 8 times, polymer **1** holds the activity similar to that of the virgin catalyst.

This is the first example of halogen-exchange fluorination of aryl chlorides catalyzed by reusable polymer without significant loss in activity at elevated reaction temperatures (180 °C). Polymer **1** exhibited much higher activity for the fluorination of PCNB than that of free aminopyridinium salt **3**: nucleophilic decomposition at 4-position in the pyridine ring[4)] may be retarded for the polymer catalyst with more sterically crowded structure. (Table 2, No. 3)

In order to examine generality of the explored catalyzed reaction, the fluorination reactions of some aryl chlorides were next attempted. The results are summarized in Table 2. In general, the yields of aryl fluorides were good. Polymer 1 seems to be somewhat decomposed under reaction conditions at 220 °C. (Table 2, No. 7) Another type of immobilized aminopyridinium salt, **2**, was found to be used as catalyst for fluorination of 2,4-dinitrochlorobenzene in acetonitrile at 80 °C. Excellent yield of 2,4-dinitrofluorobenzene was recorded. However, 2 was unstable at higher reaction temperatures. (Table 2, No.11)

The ready availability, low cost, and high activity of grafted

Table 1. **Repeated Use of 1 in the Reaction of 4-Chloronitrobenzene with Potassium Fluoride**

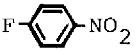
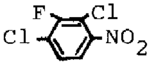
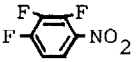
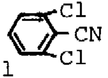
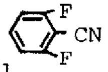
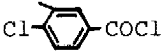
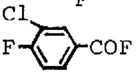
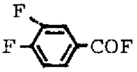
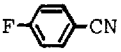
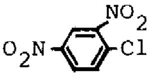
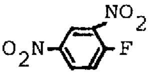


PCNB **PFNB**

Reuse number	GLC yield of **PFNB** (%)	Isolated yield(%)	Reuse number	GLC yield of **PFNB** (%)	Isolated yield(%)
1	87		5	88	
2	91		6	89	82
3	91		7	85	
4	91	84	8	89	

All experiments were carried out with PCNB(25 mmol),spray dried KF(37.5 mmol), **1**(2.5 mmol), and $TMSO_2$(15 g) at 180 °C for 5 h. Virgin **1** of an amount of lost polymer in the reaction(ca. 5%) was added each time.

Table 2. **Synthesis of Aryl Fluorides Catalyzed by Immobilized Aminopyridinium Salts on Polystyrene Support**

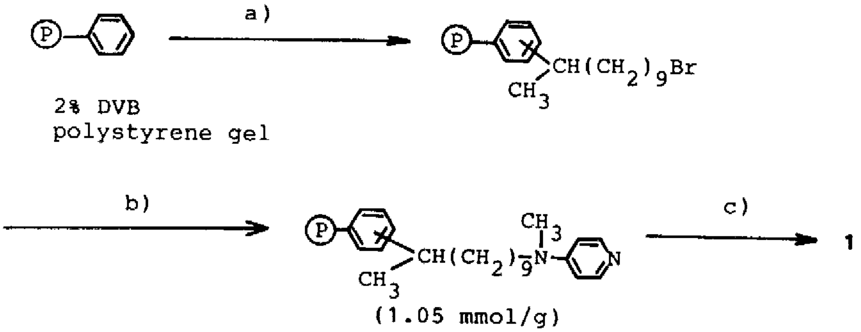
No.	Substrate	Catalyst a)	Solvent	Temp °C	Time h	KF equiv.	Product	Yield(%) b)	
								1st run	2nd run c)
1		**1**	$TMSO_2$	180	4	1.5		71	72
2	"	none	"	"	4	"	"	(10)	
3	"	**3**	"	"	5	"	"	(65)	
4		**1**	$TMSO_2$	180	2	3.0		68	72
5		**1**	$TMSO_2$	180	4	3.0		82	
6		**1**	$TMSO_2$	190	5	3.0		(79) 52	
								(9)	
7		**1**	$TMSO_2$	220	9	1.5		(61)	(61) d)
8	"	none	"	"	3	"	"	(2)	
9		**2**	CH_3CN	80	10	1.5		98 e)	99 e)
10	"	none	"	"	9	"	"	(11)	
11	"	**2**	C_6H_5Cl	135	20	"	"	86 e)	32 e)

a) The catalyst(0.1 equiv.) was used. b) Isolated yield; numbers in parentheses refer to GLC yields. c) Recovered catalyst was used. d) In third run, 4-fluorobenzonitrile was produced in 45% GLC yield. e) GLC yield using an internal standard technique.

copolymers such as **1** and **2** for fluorination should make them very attractive candidates for laboratory and industry use.

References and Notes

1) G.C. Finger and C.W. Kruse, J. Am. Chem. Soc., **78**, 6034 (1956); N. Ishikawa, Yuki Gosei Kagaku Kyokai Shi, **25**, 808 (1967); N. Ishikawa and T. Kitazume, ibid, **34**, 173 (1976); M.R.C. Gerstenberger and A. Haas, Angew. Chem. Int. Ed. Engl.,**20**, 647 (1981).
2) Y. Kimura, Yuki Gosei Kagaku Kyokai Shi, **47**, 258 (1989).
3) For example, in the reaction of PCNB and potassium fluoride in dimethylsulfoxide, Aliquat 336 catalyst was added in each half hour for a total of seven additions for completion of the reaction: C.R. White, USP 4418229; Chem. Abstr., **100**, 67983 (1984).
4) G.L. Cantrell, WO (World Patent) 87-4148, 4149, 4150 (1987). Aromatic nucleophilic displacement reaction with the aid of N-alkyl-4-(N',N'-dialkylamino)pyridinium salts catalyst was also reported: D.J. Brunelle and D.A. Singleton, Tetrahedron Lett., **25**, 3383 (1984).
5) It was purchased from Reidel de Haen Co., which was dried at 150 °C (1 Torr) for 4 h before use.
6) Polymer **1** was prepared in the following reaction scheme: M. Tomoi. M. Goto, H. Kakiuchi, and Y. Noguchi, Makromol. Chem. Rapid Commun., **6**, 397 (1985).



a)CH_2=$CH(CH_2)_9Br$, CF_3SO_3H in 1,2-dichloropropane, 45-50 °C, 41 h b)4-methylaminopyridine, NaH in DMF, Bu_4NBr, RT, 16 h then 60 °C, 72 h c)2-ethylhexylbromide in C_6H_5Cl, 120 °C, 17 h.

Pyridinium content in polymer was determined by using the method previously reported: M. Tomoi and W.T. Ford, J. Am. Chem. Soc., **103**, 3821 (1981).

7) H.L. Bradlow and C.A. VanderWerf, J. Am. Chem. Soc., **70**, 654 (1948).

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