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The Nafion-H-catalyzed Acylation of Thiophene with Acid Anhydrides

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Synopsis. The reaction of thiophene with acyclic acid anhydrides in the presence of Nafion-H (fluorocarbon resin sulfonic acid) afforded the corresponding 2-acylthiophenes in moderate yields. Acylation with cyclic acid anhydrides gave only low yields, however. The Nafion-H catalyst could be reused for the acylation with a little loss of activity.

Ion-exchange resins have widely been used as renewable catalysts for organic synthesis. The resin catalysts are insoluble in organic solvents and can be recovered by filtration, with a retention of the catalytic activity. Considerable attention has been focused on the use of fluorocarbon resin (Nafion-H) containing strongly acidic groups, $-CF_2CF_2SO_3H$, in recent years. The catalytic activity and the stability of Nafion-H are superior to those of Amberlyst 15 (polystyrenesulfonic acid).[1] It has previously been shown that Nafion-H is a good catalyst for a variety of reactions, *e.g.*, alkylation,[2] hydration,[3] acylation,[4] and aldol condensation.[5] We have now examined the applicability of the Nafion-H-catalyzed reaction to thiophene chemistry. This paper is concerned with the Nafion-H-catalyzed acylation of thiophene with acid anhydrides and with a comparative study of the catalytic activity of Nafion-H and Amberlyst 15.

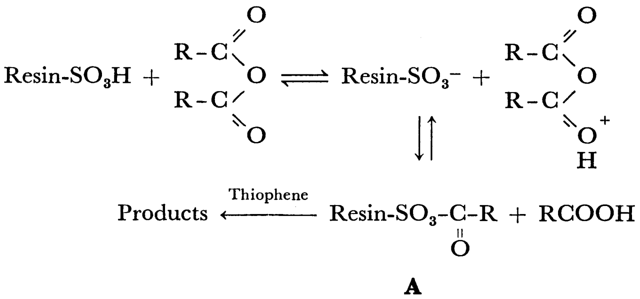
Results and Discussion

The results are summarized in Table 1. The reaction of thiophene with aliphatic acid anhydrides (**1a**—**c**) in dichloromethane under refluxing gave the corresponding ketones in sufficient yields. An increase in the chain-length of the acyl group results in a gradual increase in the yield of the ketones. This finding is consistent with the competitive acylation. The acylation rates of propionic anhydride, **1b**, and butyric anhydride, **1c**, relative to acetic anhydride, **1a**, at 38 °C in dichloromethane are as follows: **1a**, 1.00; **1b**, 1.56; **1c**, 1.88. The reactivity of the acid anhydrides increased with an increase in the +I effect of the alkyl group. The electron-releasing groups diminish the reactivity of electrophiles. In these acylations, therefore, the relative reactivity of the acid anhydrides appears to be anomalous. The acylations probably involve the mixed anhydrides intermediate, **A**, as is shown in Scheme 1. The mixed anhydride has been proposed as an intermediate in the acylation.[4]

Table 1. Nafion-H-catalyzed acylation of thiophene with acid anhydrides[a)]

Run	Acid anhydride	Reaction conditions	Product	Yield[b)] %
1	**1a**	25 °C, CH_2Cl_2	**3a**	70
2	**1a**	Reflux, CH_2Cl_2	**3a**	76
3	**1a**	25 °C, CH_2Cl_2 CH_3COOH[c)]	**3a**	31
4	**1b**	Reflux, CH_2Cl_2	**3b**	81
5	**1c**	Reflux, CH_2Cl_2	**3c**	94
6	**1d**	Reflux, CH_2Cl_2	**3d**	20
7	**1d**	Reflux, $(CH_2Cl)_2$	**3d**	89
8	**2e**	Reflux, $(CH_2Cl)_2$	—	0
9	**2f**	Reflux, $(CH_2Cl)_2$	—	0
10	**2g**	Reflux, $(CH_2Cl)_2$	—	0
11	**2h**	Reflux, $(CH_2Cl)_2$	**3h**	6

a) Thiophene (20 mmol), acid anhydride (20 mmol), Nafion-H (0.2 g), and solvent (10 ml), 16 h. b) Determined by GLC analysis. c) Acetic acid (20 mmol) was added to the reaction mixture.



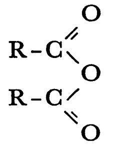
A

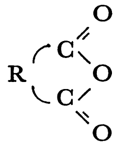
Scheme 1.

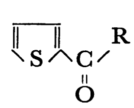
It has been reported that an equimolar mixture of acetic anhydride and acetic acid was efficient in the Nafion-H-catalyzed acylation of reactive alkylbenzenes, and that acetic anhydride alone was not an effective acylating agent under the reaction conditions.[4] In our reaction conditions, however, the addition of acetic acid decreased the yield of 2-acetylthiophene.

Thiophene reacted with benzoic anhydride in the 1,2-dichloroethane solvent to give 2-benzoylthiophene in a good yield. Acylation with cyclic anhydrides (**2e**—**h**) gave only low yields under similar conditions.

The catalytic activity of Nafion-H was compared with that of Amberlyst 15. Under the same reac-







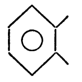
1	**2**	**3**
R	-R-	R
a: Me	**e**: 	**a**: Me
b: Et	**f**: -CH=CH-	**b**: Et
c: *n*-Pr	**g**: $-(CH_2)_2-$	**c**: *n*-Pr
d: Ph	**h**: $-(CH_2)_3-$	**d**: Ph
		h: $-(CH_2)_3COOH$

TABLE 2. REPEATED USE OF NAFION-H: ACYLATION OF THIOPHENE WITH ACID ANHYDRIDES[a)]

Run	Nafion-H (mg)		Acid anhydride	Product	Yield[b)] %
4	Virgin	200	**1b**	**3b**	81
12	Recovered from Run 4	209	**1b**	**3b**	74
13	Recovered from Run 12	225	**1b**	**3b**	52
5	Virgin	200	**1c**	**3c**	94
14	Recovered from Run 5	—[c)]	**1c**	**3c**	78
15	Recovered from Run 14	—[c)]	**1c**	**3c**	70

a) Thiophene (20 mmol), acid anhydride (20 mmol), Nafion-H, and CH_2Cl_2 (10 ml). Reactions were carried out under refluxing for 16 h. b) Determined by GLC analysis. c) Not determined.

tion conditions (Runs 5 and 7), the acylation with **1c** and **1d** catalyzed by Amberlyst 15 gave **3c** and **3d** in 75 and 74% yields respectively. Judging from the yield, the Nafion-H catalyst is superior to the Amberlyst 15 catalyst. We also investigated the stability of Nafion-H under the present reaction conditions. Repeating the reaction of thiophene with propionic anhydride with the recovered catalyst gave the ketone in a somewhat lower yield than that using the original one. (Table 2). The recovered catalyst was black, and its weight increased. The loss of the catalytic activity seems to be ascribable to the adsorption of polymeric materials on the catalyst.

The present procedure offers a convenient method for the preparation of 2-acylthiophenes with an easy work-up. After the removal of the catalyst, the products were obtained by the fractional distillation of the reaction mixture. The yield of **1a** was comparable to that with the standard method.[6)]

Experimental

Catalysts. Nafion-511 resin, as the potassium salt of the fluorocarbon resin sulfonic acid, was obtained from the Mitsui Fluorochemicals Co., Ltd. Nafion-H, the acid form of the resin sulfonic acid, was generated by the treatment of the resin with 15% hydrochloric acid at room temperature for 12 h, followed by washing with deionized water. After the acid-treatment had been repeated four times, the resin was dried under evacuation at 80 °C for 4 h. The dried resin contained 0.80 mequiv. of SO_3H groups per gram of resin. Amberlyst 15 (Rohm & Haas Co.) was dried under a vacuum at 80 °C for 6 h. The ion-exchange capacity of the resin was 2.88 mequiv./g.

Acylation of Thiophene. A mixture of thiophene (20 mmol), acid anhydride (20 mmol), Nafion-H (0.2 g), or Amberlyst 15 (0.06 g), and a solvent (10 ml) was stirred under refluxing for 16 h. The catalyst was then filtered off and washed with dichloromethane. The filtrate was analyzed by gas chromatography. Naphthalene or *p*-di-*t*-butylbenzene was used as the internal standard. The products were identified by means of infrared and ^1H NMR spectroscopies. The recovered catalyst was dried in an air-oven at 105—110 °C for reuse.

Competitive Acylation. A mixture of thiophene (10 mmol), acetic anhydride (10 mmol), propionic anhydride (10 mmol), and Nafion-H (0.1 g) in dichloromethane (5 ml) was stirred at 38 °C for 4 h. The liquid phase was then analyzed by gas chromatography. The relative yield of **3b** to **3a** was 1.56:1. The conversion of propionic anhydride was less than 30% under these conditions.

Competitive acylation with propionic anhydride and butyric anhydride was carried out in a manner similar to that described above. The relative yield of **3c** to **3b** was 1.21:1.

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