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Organic Reactions Catalyzed by Solid Superacids. 5.[1] Perfluorinated Sulfonic Acid Resin (Nafion-H) Catalyzed Intramolecular Friedel-Crafts Acylation

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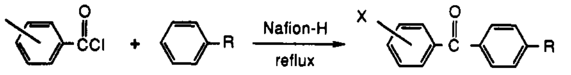
Nafion-H, a perfluorinated sulfonic acid resin, catalyzed the intramolecular Friedel-Crafts acylation of diarylalkane-2-carboxylic acids and arylalkanoic acids in refluxing *p*-xylene to provide cyclic ketones. The reactions were clean, and the water that was formed as a byproduct did not deactivate the catalyst. It was also found that the intramolecular acylation of the corresponding acid chlorides occurred under much milder reaction conditions. The mechanism of the reaction is discussed.

Introduction

The synthesis of polycyclic aromatic hydrocarbons often involves the intramolecular Friedel-Crafts acylation of such compounds as aldehydes, ketones, carboxylic acids, and acid halides. Intramolecular cyclization is generally effected by employing, as a catalyst, a strong acid like hydrogen fluoride, methanesulfonic acid, or polyphosphoric acid or, when an acid chloride is the starting material, a Lewis acid like $AlCl_3$ or $ZnBr_2$.[2-4]

Friedel-Crafts acylations generally require the use of stoichiometric amounts of catalyst. The catalyst forms strong complexes with both the acylating agent and the product carbonyl compound. Thus, aqueous acidic workup is required to decompose the complexes, and, as a result, the catalyst is usually not recovered. There is, therefore, substantial value in catalyzing these reactions with immobilized acids that do not form stable complexes with the carbonyl compounds.

Recently, one of us[5] reported a convenient and efficient acylation of aromatic hydrocarbons with aroyl chlorides and anhydrides catalyzed under heterogeneous reaction conditions by Nafion-H (a solid perfluorinated sulfonic acid resin).



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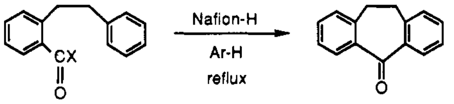
We now report an efficient and mild one-pot procedure for the intramolecular cyclization of diarylalkane-2-carboxylic acids and arylalkanoic acids catalyzed by Nafion-H.

Results and Discussion

The attempted cyclization of diphenylethane-2-carboxylic acid (**1a**), performed in refluxing benzene for 36 h in the presence of Nafion-H, failed. Only starting material was recovered. However, when the reaction was performed in refluxing *p*-xylene, the desired product, 10,11-dihydro-5*H*-dibenzo[*a*,*d*]cyclohepten-5-one (**2**), was obtained (Table I).

Product **2** was isolated simply by filtering the hot reaction mixture and distilling the solvent. The reaction was very clean. Water was the only byproduct formed. The amount of catalyst required, as a function of the amount of carboxylic acid **1a**, was between 10 and 30 wt %. Optimum yields of ketone **2** were obtained with 30 wt % of catalyst. The use of 10 wt % of catalyst gave lower yields. Cyclization of the acid chloride **1b** occurred within 30 min, even in refluxing benzene. A modification of experimental procedure permitted a one-pot conversion of the carboxylic acid **1a** directly to cyclic ketone **2**. Thus, treatment of the acid **1a** in benzene with, successively, thionyl chloride and Nafion-H gave, under subsequent reflux, cyclic ketone **2** in high yield.

Table I. Nafion-H-Catalyzed Cyclization of Diphenylethane-2-carboxylic Acid (1a) or Acid Chloride (1b)



1

2

a ; X = OH
b ; X = Cl

run	X	solvent	amt of Nafion-H (wt %)	reaction time (h)	product yield[a] (%) 2	1
1	OH	benzene	100	36	0	100
2		*p*-xylene	30	6	66	34
3		*p*-xylene	30	12	100 (90)[b]	0
4		*p*-xylene	10	12	32	68
5	Cl	benzene	30	0.5	100 (90)[b]	0

[a] The product yields were determined by GLC analysis. [b] Isolated yields are shown in parentheses.

The Nafion-H-catalyzed cyclization of benzylbenzoic acid (**3a**) and its acid chloride **3b** afforded anthrone (**4**). The reaction was again performed in refluxing *p*-xylene in the case of the carboxylic acid and in refluxing benzene in the case of the acid chloride (Table II).

An attempt to apply the method to the cyclization of 2-(2-phenylethyl)phenylacetic acid (**5a**) failed. The desired ketone **6** was obtained in only low yield (7%). Ketone **7b**, which was formed by the intermolecular acylation of *p*-

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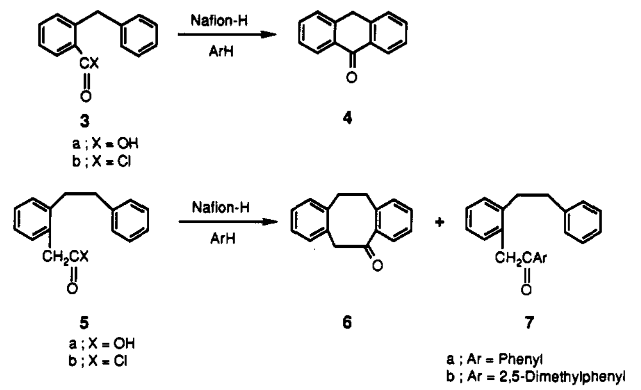
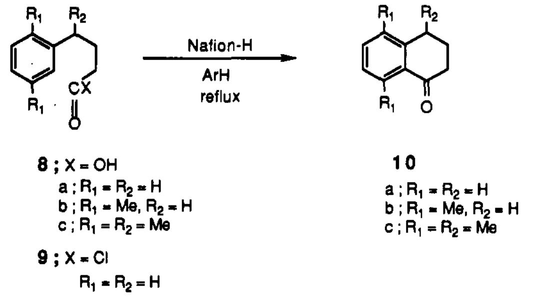
Table II. Nafion-H-Catalyzed Cyclization of 3 and 5[a]



run	substrate	solvent	reaction time (h)	product yield[b] (%)
1	**3a**	*p*-xylene	12	**4** (81)
2	**3b**	benzene	0.25	**4** (71), **3b** (7)
3	**5a**	*p*-xylene	12	**6** (7), **7b** (59), **5a** (25)
4	**5a**	chlorobenzene	12	**5a** (100)
5[c]	**5a**	nitrobenzene	12	**5a** (100)
6	**5b**	benzene	12	**6** (26), **7a** (20), **5b** (51)

[a] Reaction temperature, reflux; [Catalyst]/[Substrate] = 30 wt %. [b] The product yields were determined by GLC analysis. [c] Reaction temperature, 145–150 °C.

Table III. Nafion-H-Catalyzed Cyclization of 4-Arylbutanoic Acids 8 and Acid Chloride (9)[a]



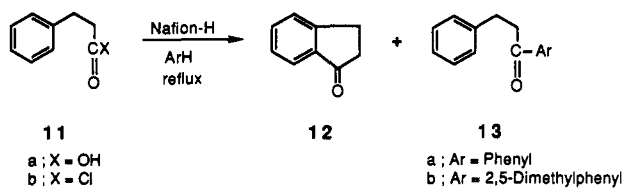
run	substrate			solvent	reaction time (h)	product yield[b] (%)
		R_1	R_2			
1	**8a**	H	H	*p*-xylene	12	**10a** (88)
2	**8b**	Me	H	*p*-xylene	12	**10b** (96)
3	**8c**	Me	Me	*p*-xylene	12	**10c** (95)
4	**9**	H	H	benzene	0.5	**10a** (95)

[a] [Catalyst]/[Substrate] = 30 wt %. [b] Isolated yields are shown in parentheses.

xylene, was obtained in 59% yield. When the reaction was performed in refluxing chlorobenzene or in nitrobenzene at 145–150 °C, the starting material, compound **5a**, was recovered in quantitative yield (Table II, runs 4,5). These results suggested that both solvents dramatically reduce the catalytic activity of Nafion-H. However, the acid chloride **5b** in refluxing benzene in the presence of Nafion-H gave cyclic ketone **6** in 26% yield, along with the phenyl ketone **7a** in 20% yield (Table II, run 6).

It was reported[5] that the attempted acylation of aromatics with acetyl chloride in the presence of Nafion-H led to thermal elimination of hydrogen chloride from acetyl chloride to form ketene and ketene-derived products. However, in the cycloacylation reaction, the analogous side reaction was not observed. This finding suggested that Nafion-H would be an effective catalyst in the intramolecular Friedel–Crafts reaction of arylalkanoic acids and their acid chloride.

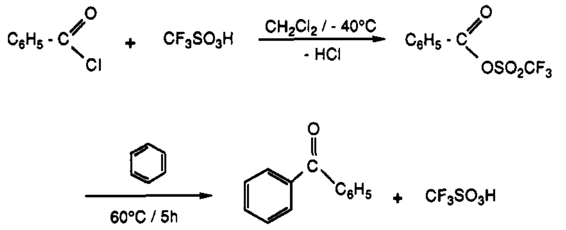
Table IV. Nafion-H-Catalyzed Cyclization of 3-Phenylpropionic Acid (11a) and Acid Chloride (11b)[a]



run	substrate	solvent	reaction time (h)	product yield[b] (%)
1	**11a**	benzene	24	no reaction[c]
2	**11a**	*p*-xylene	12	**12** (0), **13b** (12), **11a** (85)
3	**11a**	chlorobenzene	12	no reaction[c]
4[d]	**11a**	nitrobenzene	12	no reaction[c]
5	**11b**	benzene	0.5	**12** (90), **13a** (0)

[a] [Catalyst]/[substrate] = 30 wt %. [b] The product yields were determined by GLC analysis. [c] **11a** was recovered in quantitative yield. [d] Reaction temperature, 145–150 °C.

Scheme I



In fact, the 4-arylbutanoic acids **8a**–**8c** cyclized in refluxing *p*-xylene in the presence of Nafion-H to give the desired 1-tetralone analogues **10a**–**10c**, respectively, in quantitative yield. As expected, 4-arylbutanoyl acid chloride **9** reacted in refluxing benzene much faster than did the acid **8a** to give 1-tetralone (**10a**) (Table III).

When 3-phenylpropanoic acid (**11a**) was treated with Nafion-H in refluxing *p*-xylene for 12 h, the desired product, **12**, was not obtained. Only compound **13b**, the product of acylation of the solvent, was formed in 12% yield. The attempted cyclization of **11a** in either benzene, chlorobenzene, or nitrobenzene also failed, and only starting material was recovered. However, when 3-phenylpropanoic acid chloride (**11b**) and Nafion-H were refluxed together in benzene for 30 min, 1-indanone (**12**) was obtained in 90% yield (Table IV).

The reactivity of certain electrophiles can be increased by converting them to their trifluoromethanesulfonate (triflate) derivatives.[6] Mixed carboxylic sulfonic anhydrides, $RCOOSO_2CF_3$, have been found to be extremely reactive acylating agents in both the intermolecular[7] and intramolecular[8] Friedel–Crafts acylation of aromatic compounds (Scheme I).

In the reactions described here, acid chlorides react with the free sulfonic acid groups of Nafion-H to generate the mixed anhydrides in situ. Subsequently, these highly reactive species react smoothly to produce cyclic ketones. Nafion-H is regenerated in the acylation step, thus completing the catalytic cycle (Scheme II).

The method described here provides excellent yields of the desired compounds, enables the easy isolation of the products, and permits the ready regeneration of the cat-

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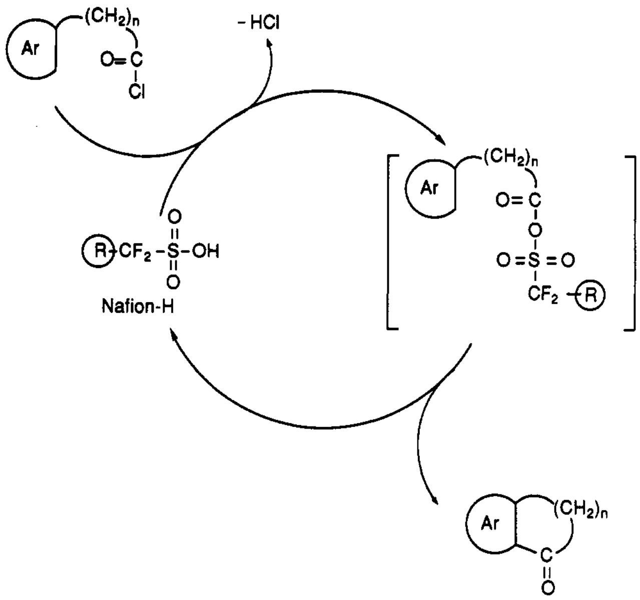
Scheme II



alyst without the loss of catalytic activity.

Experimental Section

The diarylalkane-2-carboxylic acids and the arylalkanoic acids were the purest commerically available materials. (2-(2-Phenylethyl)phenylacetic acid (**5a**)[9] and 4-arylbutanoic acids **8b** and **8c**[10] were prepared by literature methods. Nafion-H catalyst was prepared from commerically available (Du Pont) Nafion-K resin, as previously described.[11] All melting points are uncorrected.

General Procedure for the Cyclization of Diarylalkane-2-carboxylic Acids and Arylalkanoic Acids and Their Respective Acid Chlorides in the Presence of Nafion-H. A mixture of the acid (10 mmol), Nafion-H (30 wt %), and *p*-xylene (35 mL) was refluxed until the reaction was complete as monitored by GLC (2-m silicone OV-1 column). The resin was then removed by filtration, and the filtrate was analyzed by GLC. The solvent was evaporated from the filtrate in vacuo. The residue was either distilled under reduced pressure or was recrystallized.

10,11-Dihydro-5*H*-dibenzo[*a*,*d*]cyclohepten-5-one (2): colorless prisms (hexane), mp 32–35 °C (lit.[12] mp 34–35 °C).

Anthrone (4): colorless prisms (hexane), mp 155–158 °C (lit.[12] mp 155–156 °C).

11,12-Dihydrodibenzo[*a*,*e*]cycloocten-5(6*H*)-one (6): colorless prisms (hexane), mp 92–95 °C (lit.[9] mp 94–96 °C).

1-Tetralone (10a): a colorless liquid, bp 113–116 °C (6 mm) [lit.[13] bp 93 °C (1.3 mm)]. **10b**: colorless prisms (petroleum ether), mp 31.5–33.5 °C (lit.[10] mp 33 °C). **10c**: a colorless liquid, bp 138 °C (12 mm) [lit.[10] bp 90 °C (0.5 mm)].

1-Indanone (12): colorless prisms (hexane), mp 40–42 °C (lit.[14] mp 39.5–41 °C).

One-Pot Procedure for the Conversion of Diphenylethane-2-carboxylic Acid (1a) to 2. To a solution of **1a** (2.12 g, 10 mmol) in benzene (35 mL) at room temperature was added $SOCl_2$ (4 mL, 33 mmol). The mixture was refluxed for 1 h and then was cooled to room temperature. The, Nafion-H (640 mg, 30 wt %) was added, and the mixture was refluxed for 30 min. Workup as described previously gave 1.87 g (90%) of **2**.

Regeneration of Nafion-H Catalyst. The spent catalyst was washed several times with acetone and deionized water, and then it was dried at 105 °C for 10 h. The activity of the regenerated catalyst was the same as that of fresh catalyst.

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