2-Acyloxypyridine/Trifluoroacetic Acid System as an Acylating Agent for Arenes

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Acylation is one of the most important reactions in organic chemistry. Contrary to the synthesis of aliphatic ketones, only a few routes for the synthesis of aromatic ketones are known[1]. The Friedel-Crafts reaction using aluminum chloride as catalyst is the most useful means[2]. However, in the reaction we sometimes encounter inconveniences of more than the stoichiometric requirement of the catalyst, impossibility of the recovery, inducement of side reactions, evolution of hydrochloric acid and so on, particularly in the large scale reactions.

Recently, some procedures for the synthesis of aromatic ketones without the use of classical catalysts have been developed[3,4,5,6,7]. Above all, it is interesting that acyl trifluoroacetates in acid are useful for ketone synthesis[4,7]. However, this kind of mixed anhydride, prepared from carboxylic acid and excess trifluoroacetic anhydride, is generally sen-

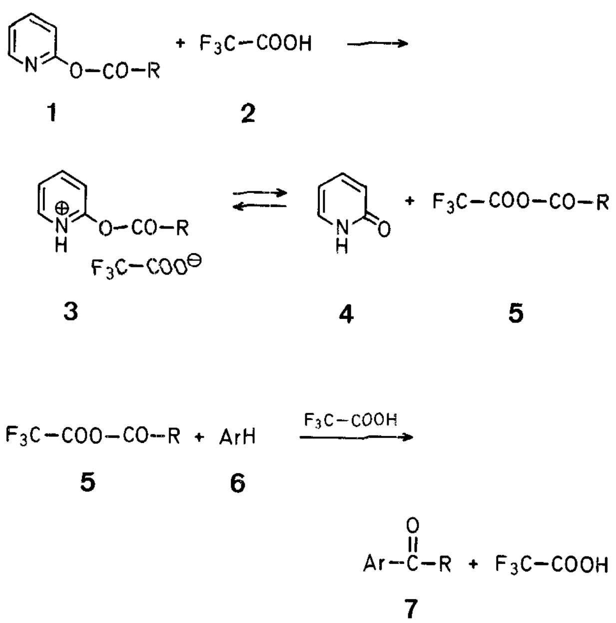
0039-7881/80/0232-0139 $ 03.00

sitive to moisture and tends to disproportionate[7]. We have now found a procedure using neither the mixed anhydride nor trifluoroacetic anhydride to obtain aromatic ketones. We report here that 2-acyloxypyridines **1a-l** are useful as acylating agents for arenes in conjunction with trifluoroacetic acid.

First, the benzoylation of some arenes with **1i** (R = C_6H_5) in trifluoroacetic acid was investigated. For instance, 2-benzoylthiophene was isolated in 98% yield by heating a mixture of thiophene, **1i**, and trifluoroacetic acid in a molar ratio of 1:1.2:10 under reflux for 5 h. In contrast, we could not obtain the ketone by the classical Friedel-Crafts reaction using aluminum chloride because of the formation of tarry materials[8]. Other activated arenes were also benzoylated with **1i** in trifluoroacetic acid to give the corresponding ketones in satisfactory yields. The results are summarized in Table 1.

Then, the utility of compounds **1** as acylating agents for arenes was investigated by an examination of the reaction of fluorene with a wide variety of **1**. The results are summarized in Table 2. All the reactions shown in Table 2 were carried out under the same conditions as described for acetylfluorene. Compounds **1**, except for **1l**, gave rise to the corresponding acylfluorenes in good yields. Especially, compounds **1** bearing aliphatic acyl groups or aroyl groups having an electron-donating substituent gave the ketones **7** in high yields.

The reaction seems to proceed via the pyridinium salt **3** followed by the acyl trifluoroacetate **5**, in the course of the reaction as shown below.



Trifluoroacetic acid has a moderately low boiling point and can be recovered from the reaction mixture by distillation. Compounds **1** are easy to prepare and are relatively sta-

Table 1. Benzoylation of Arenes **6** with 2-Benzoyloxypyridine (**1i**) in Trifluoroacetic Acid

Arene **6**	Position of Benzoyl Group in **7**	Time [h]	Yield[a] [%]	m.p. [°C] or b.p. [°C]/torr[b] found	reported	I.R. (KBr) $\nu_{C=O}$ [cm^{-1}]
durene	3	10	87	119–120	119[11]	1670
1,4-dimethoxybenzene	2	10	77	50–52	51[13]	1665
mesitylene	2	10	89	156–157/6	189/17[14]	1670[c]
anisole	4	5	92	61–63	61–63[15]	1650
thiophene	2	5	98	55–57	56–57[16]	1625
fluorene	2	10	82	122–123	122[17]	1645
dibenzofuran	2	5	21	136–137	136–137[18]	1655

[a] Yield of isolated product.

[b] Uncorrected.

[c] Neat.

Table 2. Acylation of Fluorene with 2-Acyloxypyridine **1** in Trifluoroacetic Acid

2-Acyloxypyridine **1** No.	R	Yield[a] [%]	m.p. [°C][b]	Molecular Formula[c] or Lit. m.p. [°C]		I.R. (KBr)[b] $\nu_{C=O}$ [cm^{-1}]
a	CH_3	91	130–131	128–129[12]		1678
b	C_2H_5	90	118–119	$C_{16}H_{14}O$	(222.3)	1675
c	n-C_3H_7	90	118–119	$C_{17}H_{16}O$	(236.3)	1670
d	3-H_3CO—C_6H_4	73	99–100	$C_{21}H_{16}O_2$	(300.4)	1645
e	4-H_3CO—C_6H_4	84	155–156	$C_{21}H_{16}O_2$	(300.4)	1640
f	2-H_3C—C_6H_4	84	138–139	$C_{21}H_{16}O$	(284.4)	1660
g	3-H_3C—C_6H_4	75	115–116	$C_{21}H_{16}O$	(284.4)	1655
h	4-H_3C—C_6H_4	83	118–119	$C_{21}H_{16}O$	(284.4)	1645
i	C_6H_5	81	122–123	122[17]		1645
j	3-Cl—C_6H_4	60	149–151	$C_{20}H_{13}ClO$	(304.8)	1650
k	4-Cl—C_6H_4	63	180–182	$C_{20}H_{13}ClO$	(304.8)	1648
l	4-O_2N—C_6H_4	9	184–186	$C_{20}H_{13}NO_3$	(315.3)	1644

[a] Yield of isolated ketone. All reactions were carried out under the same conditions. The remainder is the unreacted fluorene.

[b] m.p. and I.R. data of isolated 2-acylfluorene; m.p.'s are not corrected.

[c] The microanalyses were in satisfactory agreement with the calculated values (C ±0.15, H ±0.15).

ble[9,10]. We can acylate arenes in excellent yields with **1** in trifluoroacetic acid without the use of the classical Friedel-Crafts procedure, any unstable mixed anhydrides, or even trifluoroacetic anhydride. Consequently, the 2-acyloxypyridine/trifluoroacetic acid system seems to offer a valuable procedure for aromatic ketone synthesis.

Benzoylation of Durene with 2-Benzoyloxypyridine (1i):
To a mixture of durene (1.00 g, 7.5 mmol) and **1i** (1.79 g, 9 mmol), trifluoroacetic acid (5 ml) is added and the mixture is heated under reflux for 5 h. After cooling, water (30 ml) is added, the resultant precipitates are collected by filtration, washed with water, and aqueous sodium carbonate, and dried to give the crude benzoylated durene; yield: 1.71 g (96%); m.p. 105–121 °C. Crystallization from ethanol gives pure 3-benzoyldurene; yield: 1.55 g (87%); m.p. 119–120 °C (Ref. [11], m.p. 119 °C).

Acetylation of Fluorene with 2-Acetyloxypyridine (1a):
To a mixture of fluorene (1.00 g, 6 mmol) and **1a** (0.99 g, 7.2 mmol), trifluoroacetic acid (5 ml) is added and the mixture is heated under reflux for 5 h. After cooling, water (30 ml) is added to the mixture and then, after distillating off the unreacted fluorene with steam, the residue is collected by filtration, washed with water, and dried to give the crude acetylated fluorene; yield: 1.14 g (91%); m.p. 122–128 °C. Crystallization from ethanol gives pure 2-acetylfluorene; yield: 1.00 g (80%); m.p. 130–131 °C (Ref. [12], m.p. 128–129 °C). Unreacted fluorene (0.08 g) is recovered from the distillate.

Received: October 15, 1979

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0039-7881/80/0232-0141 $ 03.00