CHEMISTRY LETTERS, pp. 1099-1102, 1977. Published by the Chemical Society of Japan

APPLICATION OF 2-TRIFLUOROMETHANESULFONYLOXYPYRIDINE IN TRIFLUOROACETIC ACID TO ACYLATION OF AROMATICS

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New method for synthesis of aromatic ketones was investigated. 2-Trifluoromethanesulfonyloxypyridine (TSP) in trifluoroacetic acid was very useful in the condensation of carboxylic acids with some aromatic compounds to give aromatic ketones. The reaction of arenes with benzoic acid in the presence of TSP in trifluoroacetic acid gave benzoylarenes. By the same method, 2-acylfluorenes were obtained from carboxylic acids and fluorene.

Acylation is one of the most important reaction in organic chemistry. Contrary to synthesis of aliphatic ketones, only a few routes for synthesis of aromatic ketones have been known.[1)] The Friedel-Crafts reaction is a most useful means of synthesis of aromatic ketones, but on a large scale, it is unconvenient.

In the present communication, we wish to report that 2-trifluoromethanesulfonyloxypyridine (TSP) in trifluoroacetic acid is a very useful reagent in the condensation of carboxylic acids with activated aromatic compounds to give aromatic ketones.

TSP, a new reagent, was synthesized as follows: To a mixture of 2-hydroxypyridine (0.18 mol) and sodium hydride (0.18 mol) in dry dioxane (130 ml), a solution of trifluoromethanesulfonylchloride[2)] (0.18 mol) in dry tetrahydrofuran (20 ml) was added slowly at room temperature. The mixture was stirred for 1 hour at room temperature, filtered, and the solvent in the filtrate was removed by distillation. The residue was distilled under reduced pressure to give TSP in yield of 45 %. bp: 109 °C/27 mmHg, IR(Neat): 1600, 1430, 1260, 1175, and 890 cm^{-1}, Found: N 6.18 %, MS (m/e): 227 (M^+), Calcd for $C_6H_4NO_3SF_3$: N 6.17 %, Mw 227.2.

The results of benzoylation of some aromatic compounds with benzoic acid by the use of TSP in trifluoroacetic acid are summarized in Table 1.

Table 1. Benzoylation of some aromatic compounds with benzoic acid and TSP in trifluoroacetic acid[a]

Aromatic compound	Crude product		Isolated product		IR $\nu_{C=O}$
	mp (°C),	Yield (%)	Compound	mp or bp (°C) (Reference)	cm^{-1}
Fluorene (F)	117-120	93	2-Benzoyl-F	122-123 (122)	1645
Dibenzofuran (DF)	107-123	75	2-Benzoyl-DF	136-137 (136-137)	1655
Dibenzothiophene (DT)	120-133	85	2-Benzoyl-DT	159-160 (159-160)	1657
Durene (D)	110-115	100	Benzoyl-D	119-120 (119)	1670
Mesithylene (M)	oil	96	Benzoyl-M	156-157/6 (189/17)	1670
p-Dimethoxybenzene (DM)	43-47	93	2-Benzoyl-DM	49-50 (51)	1665
Anisole (A)	57-58	97	4-Benzoyl-A	61-63 (61-63)	1650
Thiophene (T)	48-50	100	2-Benzoyl-T	51 (56-57)	1625
Benzene	oil	17[b]	Benzophenone	48 (49)	1655
p-Xylene (X)	oil	19[b]	2-Benzoyl-X	36 (36)	1668

a) All the reactions were carried out under reflux of a solution of 6 mmol of aromatic compound, 7 mmol of benzoic acid, and 7 mmol of TSP in trifluoroacetic acid (5 ml) for 5 hours.

b) The yields were obtained by GLC.

The typical reaction procedure is described for the benzoylation of durene: To a mixture of benzoic acid (7 mmol) and TSP (7 mmol) in trifluoroacetic acid (5 ml), durene (6 mmol) was added. After the mixture had been refluxed for 5 hours, it was poured into ice-water, and the precipitate was filtered and washed with water and dilute alkali solution to give the crude 1-benzoyl-2,3,5,6-tetramethylbenzene [1] (mp 110-115 °C) in quantitative yield. Recrystallization of the product from methanol gave [1] (mp 119-120 °C) in yield of 85 %.

Activated arenes such as durene and thiophene are benzoylated by benzoic acid and TSP in trifluoroacetic acid in good yields, but benzene and p-xylene were not so benzoylated.

Furthermore, the reactions of fluorene with some carboxylic acids and TSP in trifluoroacetic acid were attempted. The results are summarized in Table 2.

Table 2. Acylation of fluorene with carboxylic acids and TSP in trifluoroacetic acid[a)]

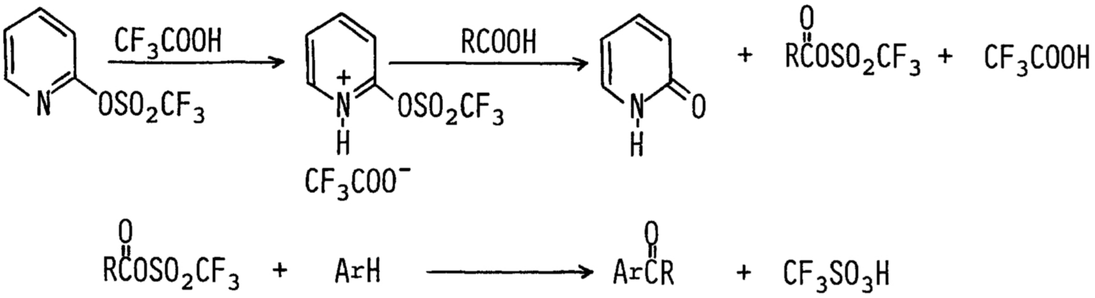
Carboxylic acid	Crude product		2-Acylfluorene		
	mp (°C),	Yield (%)	mp (°C),	IR(KBr) $\nu_{C=O}$ $^{-1}$	Solvent of rycryst.
CH_3COOH	116-117	81	130-131	1678	EtOH
CH_3CH_2COOH	112-116	82	118-119	1675	EtOH
p-$CH_3OC_6H_4COOH$	150-153	82	155-156	1640	EtOH
p-$CH_3C_6H_4COOH$	109-113	96	118-119	1645	EtOH
C_6H_5COOH	117- 120	93	122-123	1645	EtOH
p-$NO_2C_6H_4COOH$	177-183	34	184-185	1644	Benzene

a) All the reactions were carried out under reflux of a solution of 6 mmol of fluorene, 7 mmol of carboxylic acid, and 7 mmol of TSP in trifluoroacetic acid (5 ml) for 5 hours.

Except of p-nitrobenzoic acid, all carboxylic acids in Table 2 in the presence of TSP in trifluoroacetic acid gave 2-acylfluorenes in satisfactory yields. All the products in Table 1 and 2 were identified by comparing of melting points or boiling points and IR spectra of them with ones of the authentic samples synthesized by usual Friedel-Crafts reaction.

Effenberger[3)] had reported that the mixed anhydrides synthesized from the silver salt of trifluoromethanesulfonic acid and acylchlorides were able to acylate aromatic compounds without Friedel-Crafts catalyst. The mixed anhydride will probably be formed in the course of the reaction and it acylates aromatic compounds as shown in scheme 1. The procedure proposed by Effenberger has following disadvantages. 1) The silver salt of trifluoromethanesulfonic acid is very expensive.

2) Each of the mixed anhydrides has to be prepared for each acylation of the different type. 3) Some of the mixed anhydrides are too unstable to isolate. On the other hand, by means of our method, we can synthesize some aromatic ketones in good yields from carboxylic acids and aromatic compounds with TSP which is easy to handle.



Scheme 1

Consequently, TSP seems useful for the condensation of carboxylic acids with activated aromatic compounds to give aromatic ketones.

References

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(Received June 7, 1977)