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A Convenient Trifluoroacetylation of Arenes with 2-(Trifluoroacetoxy)pyridine

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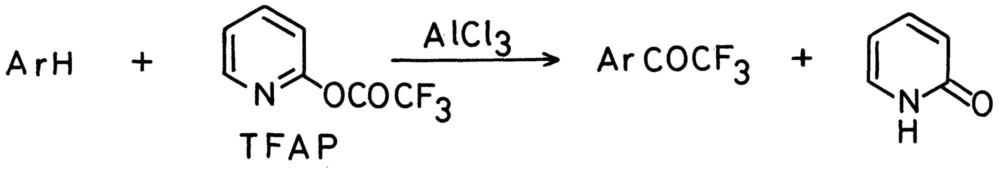
2-(Trifluoroacetoxy)pyridine (TFAP) is useful for trifluoroacetylating arenes under the Friedel-Crafts conditions. Benzene, alkylbenzenes, naphthalene, and dibenzofuran have reacted with TFAP in the presence of aluminum chloride in dichloromethane to give the corresponding trifluoromethyl aryl ketones in good isolated yields.

Trifluoromethyl aryl ketones, $ArCOCF_3$ have attracted much attention and been extensively studied.$^{1)}$ However, only a few reagents for trifluoroacetylating arenes have been known, i.e., trifluoroacetyl chloride/aluminum chloride system,$^{2)}$ trifluoroacetic anhydride,$^{3)}$ and trifluoroacetyl triflate.$^{4)}$ Trifluoroacetic anhydride and the latter mixed anhydride are only applicable to the trifluoroacetylation of activated arenes such as azulene and anthracene. Trifluoroacetyl chloride is hard to handle because of its low boiling point of -27 °C.$^{5)}$ Due to this inconvenience, $ArCOCF_3$ have been prepared so far by the reaction of appropriate Grignard reagent with trifluoroacetic acid,$^{6-7)}$ or lithium or ethyl trifluoroacetate.$^{8)}$

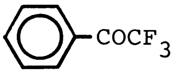
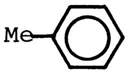
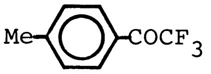
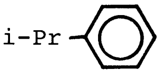
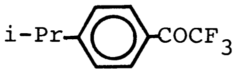
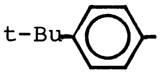
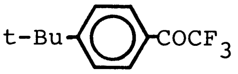
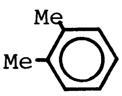
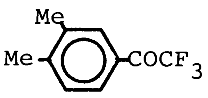
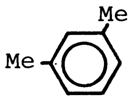
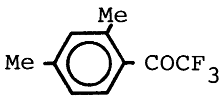
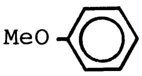
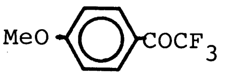
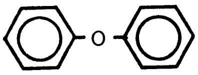
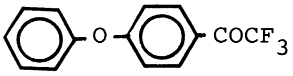
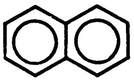
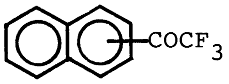
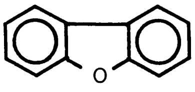
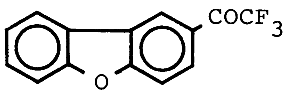
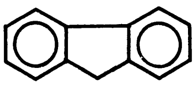
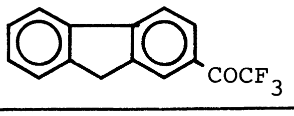
We previously reported that 2-(trifluoroacetoxy)pyridine (TFAP) is an effective reagent for the trifluoroacetylation of amines and alcohols.$^{9)}$ We now report our investigation on the reaction of arenes with TFAP in the presence of aluminum chloride, providing a convenient synthesis of $ArCOCF_3$.



A typical procedure for the trifluoroacetylation of arenes with TFAP is as follows. To a solution of isopropylbenzene (2.0 g, 16.6 mmol) and TFAP (3.81 g, 19.9 mmol) in dry dichloromethane (30 ml), well pulverized anhydrous aluminum chloride (5.32 g, 39.9 mmol) was added through a closed vessel over a period of 15 min at -10 °C. After stirring at 0 °C for 4 h, the reaction mixture was poured into ice water, and extracted with ether. The organic layer was washed with water and dried over anhydrous sodium sulfate. After evaporation of the solvent, the crude product was obtained as an oil (3.24 g, 90% yield). The distillation of the oil under the reduced pressure gave trifluoromethyl p-isopropylphenyl ketone of bp 97-98 °C/13 mmHg (2.67 g, 75% yield). Analogously, a variety of arenes were subjected to the reaction. The results are summarized in Table 1. All the products are ascertained by the IR and ^1H NMR spectra.

Benzene and alkylbenzenes involving isomeric xylenes were trifluoroacetylated by TFAP and aluminum chloride in a dichloromethane solution to give the corresponding trifluoromethyl phenyl ketones in good isolated yields. Anisole and diphenyl ether also reacted with the TFAP/aluminum chloride system to afford the corresponding ketones. Furthermore, this system trifluoroacetylated condensed aromatic compounds such as naphthalene, fluorene, and dibenzofuran in good yields. The reaction of naphthalene gave a mixture of α- and β-isomers in a ratio of 56 : 44.[10] The selectivity was poorer than that for the acetylation of naphthalene with acetyl chloride/aluminum chloride in dichloroethane,[11] even though the reactions were carried out at low temperature. The bulky complex of TFAP and aluminum chloride might be concerned with the reaction as the reacting entity.

Table 1. Results of trifluoroacetylation of arenes with the TFAP/$AlCl_3$

Arene	Product	Yield/%[a]	Mp or Bp/ °C/mmHg Found	Literature	IR/cm^{-1} νCO
		53	66-67/33	152/730[5)]	1720
		61	76-77/18	79-80/22[6)]	1717
		78	97-98/13		1720
		73	108/13	47.5-48[7)]	1714
		72	95/15	oil[7)]	1712
		74	90/19		1719
		54	122/47	70-71.2[6)]	1710
		63	128-129/1		1712
		93	oil[b)]		1710
		75	91-92 (from n-hexane)		1708
		86	83 (from EtOH)		1710

a) Isolated yield. b) A 56:44 mixture of α- and β-isomers.[10)]

All of the procedures hitherto used for the preparation of $ArCOCF_3$ have the disadvantages that they involve either limited applicability or multistage syntheses. Now, we can produce $ArCOCF_3$ by the reaction of arenes with the TFAP/$AlCl_3$ system under mild conditions. Reagent TFAP is readily prepared 9) and it is easy to handle.

References

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