

A New Procedure for Formylation of Less Active Aromatics

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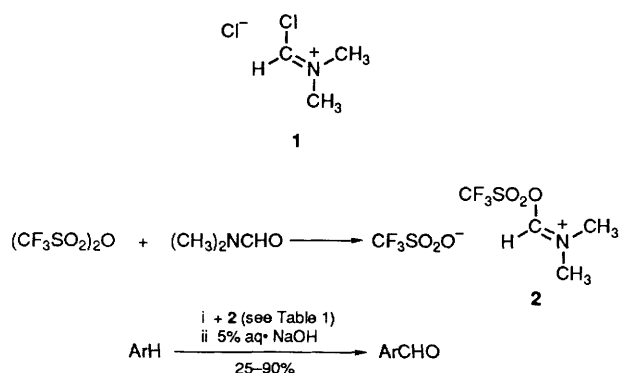
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The formylation of aromatic compounds with trifluoromethanesulphonic anhydride/dimethylformamide complex **2** takes place easily as compared to the normal Vilsmeier–Haack reaction.

The formylation of aromatic compounds is an important synthetic step in organic chemistry.¹ A simple procedure for this involves the reaction of aromatic compounds with dimethylformamide/phosphorus oxychloride complex **1** (Vilsmeier–Haack reaction²). However, this reaction is suitable only for electron-rich substrates.³

We have now found that the use of trifluoromethanesulphonic anhydride, instead of phosphorus oxychloride, leads to a very reactive iminium salt **2**[†] resulting in the functionalization of relatively less activated aromatic compounds under mild conditions. Thus, the hydrocarbons **3–7** afford the corresponding formylated products **10–14**, respectively, in a much better yield than the DMF/POCl₃ complex **1**[‡] (see Table 1).



[†] M.p. = 52–54 °C. IR (KBr): ν = 1705 (C=N), 1250, 1160, 1030 (OTf) cm^{-1} . ¹H NMR (CD₃CN): δ 3.00 (s, 3H, CH₃), 3.20 (s, 3H, CH₃), 8.0 (s, 1H, CH).

[‡] *General Procedure:* Trifluoromethanesulphonic anhydride (2.82 g, 10 mmol) was added dropwise to DMF (10 mmol) at 0 °C, whereby a white precipitate of trifluoromethanesulphonyloxy-methylen-*N,N*-dimethyliminium trifluoromethanesulphonate **2** is formed. A solution of the aromatic substrate (10 mmol) in the corresponding solvent (10 ml) (Table 1) (or without solvent) was added and the mixture heated in a sealed glass ampoule. After cooling, the mixture was hydrolysed with 5% NaOH (20 ml) and extracted with CH₂Cl₂ (3 × 20 ml). The combined CH₂Cl₂ layers were washed with water (2 × 20 ml) and dried (MgSO₄). After removal of the solvent, the crude product was purified by column chromatography on silica gel (2 × 45 cm, eluent: hexane–CH₂Cl₂) or recrystallized.

Table 1 Formylation of aromatic compounds with trifluoromethanesulphonic anhydride/DMF complex **2**[‡]

Substrate	Reagent/solvent	Reaction conditions Time/h; Temp./°C	Product(s)	Yield ^a (%)
1,3,5-Trimethylbenzene 3	1	—	No reaction	
	2 /—	96/125	2,4,6-Trimethylbenzaldehyde 10	60
Naphthalene 4	1	—	No reaction ³	
	2	48/130	1-Naphthalenecarbaldehyde 11	50
Acenaphthene 5	1 /xylene	6/95	5-Acenaphthenecarbaldehyde 12	30 ⁶
	2 /CHCl ₃	72/130		90
Anthracene 6	1 /1,2-Cl ₂ C ₆ H ₄	2/95	9-Anthracenecarbaldehyde 13	63 ⁷
	2 /CH ₂ Cl ₂	48/37		98
Phenanthrene 7	1	—	No reaction ³	
	2 /—	168/130	3-Phenanthrenecarbaldehyde 14	25
Anisole 8	1	15/95	4-Methoxybenzaldehyde 15 + 2-Methoxybenzaldehyde 16	70 ⁹
	2 /toluene	24/110	15 (78%) + 16 (22%) ^b	80
Pyrrole 9	1 /(CH ₂) ₂ Cl ₂	0.25/70	2-Pyrrolecarbaldehyde 17	79 ¹⁰
	2 /CH ₂ Cl ₂	12/—10		75

^a Yield of isolated products. All products are known^{4–10} and were fully characterized by comparing the spectral data with an authentic sample. ^b The *o/p* ratio was determined by GC (Column OV-101, 50 m, temp. 120 °C).

A definite advantage of our method is the easy work-up that avoids any necessity to remove high-boiling solvents. Toluene and cumene do not react under our reported conditions.

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