A New Simple Method for the Preparation of Aryl Formates from Phenols

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Dedicated to Professor George A. Olah on the occasion of his 80th birthday

Aryl formates are prepared in a two step one-pot procedure from phenols. Firstly the formylating reagent triformamide (**1b**) is generated from sodium diformamide (**2**) and methanesulfonyl chloride *in situ*, which reacts with phenols **4a** – **f** to give aryl formates **5a** – **f** in good yields. Triformamide, prepared *in situ*, transforms anisole in the presence of aluminum chloride to the *N*-(diarylmethyl)formamide **7**.

Key words: Aryl Formates, Formylation, Hydroxyarenes

Introduction

Aryl formates are of significance in various fields of organic chemistry [1]. In recent papers [2, 3] a convenient method for the preparation of aromatic aldehydes from aryl formates by means of the Fries rearrangement has been described. Lewis acids, such as boron tribromide, boron trichloride and trifluoromethanesulfonic acid, were shown to be the most effective catalysts for this rearrangement. As starting compounds, several aryl formates of wide structural diversity were prepared in good yields [1] using a new method for *O*-formylation of hydroxyarenes by means of *N,N*-diformylacetamide (**1a**) or of triformamide (**1b**). The reaction can be catalyzed by sodium diformamide or by trifluoromethanesulfonic acid salts of some rare earth elements.

Actually aryl formates have attracted the attention of mechanistically and theoretically interested organic chemists. Despite the importance of the Fries reaction in synthetic organic chemistry, the details of its mechanism are still unclear. A few investigations dealing with the mechanism of the Fries rearrangement of aryl formates have appeared [4]. In the course of this work, it turned out that aryl formates can formylate phenols [4c]. If these observations can be generalized and confirmed on a preparative scale very likely aryl formates will attain significance as stable and easy to handle formylating reagents for aromatic compounds.

$$R-CON(CHO)_2 \quad \textbf{1a}\ R = CH_3 \qquad \textbf{1b}\ R = H$$

Results and Discussion

The *O*-formylation of hydroxyaromatic compounds has been performed with various formic acid derivatives [1]. In the present note we wish to report a new, even simpler method for the synthesis of aryl formates from phenols without isolating the formylating agent triformamide (**1b**) which could be prepared *in situ* (Scheme 1) starting from the very stable and easily obtainable sodium diformamide (**2**) and methanesulfonylchloride (**3**) in anhydrous acetonitrile at ambient temperature. Then, the corresponding hydroxyarene (**4a** – **f**) was added to the mixture and refluxed for 2 h to afford the known aryl formates **5a** – **f** in good yields (62 – 78 %). The substituents, yields, physical properties and some IR and NMR spectral data of products **5a** – **f** are summarized in Table 1.

In a series of papers [2, 5a – d], novel formylating agents and their formylating potential for aromatic compounds in electrophilic aromatic substitutions have been evaluated. A review article on new methods for direct aromatic formylation was published recently [3]. For example, triformamide (**1b**) in the presence of aluminum chloride was used for the preparation of numerous aromatic aldehydes [5a, b, d]. That is why we decided to explore whether the above described one-pot approach could also be applied to the direct formylation of aromatic compounds. Triformamide **1b** (Scheme 1) was prepared *in situ*, but in 1,2-dichloroethane instead of acetonitrile. Then, equimolar amounts of anisole (**6**) and anhydrous aluminum chloride were added, and the mixture was refluxed for 2 h (Scheme 2). The colorless crystalline diarylmethane

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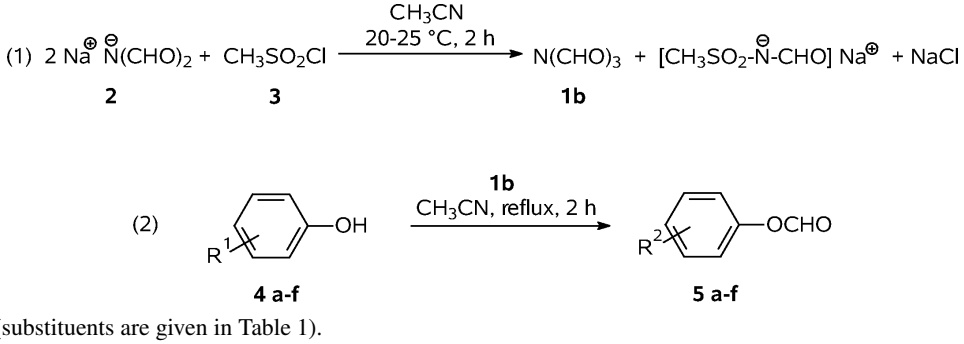
Table 1. Synthesis of aryl formates **5a – f** from phenols **4a – f**. IR and NMR spectral data for **5a – f**[a].

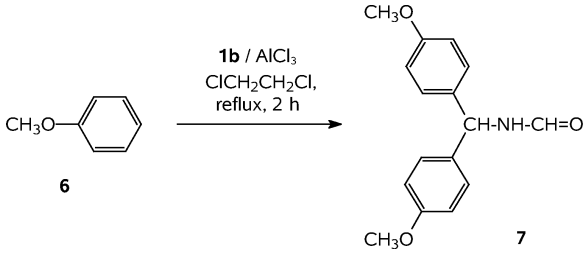
Starting phenol (**4a – f**)	R^1	Product name (**5a – f**)	R^2	Yield (%)	n_D^{20} (b. p., °C / hPa)	Lit. data n_D^{20} (b. p., °C / hPa)	IR (ATR) $\nu_{C=O}$ (cm^{-1})	NMR ($CDCl_3$)[a], δ (ppm)
4a	H	Phenyl formate **5a**	H	62	1.5088 (30/0.1 approx.)	1.5072 (35/0.1) [6]	1734	^{1}H NMR: δ = 7.12 (dd, ^3J = 7.8, ^4J = 2.1 Hz, 2H, 2-H, 6-H), 7.26 (t, J = 7.8 Hz, 1H, 4-H), 7.39 (t, J = 7.8 Hz, 2H, 3-H, 5-H), 8.28 (s, 1H, CHO). – ^{13}C NMR: δ = 121.1 (C-4), 126.4 (C-3, C-5), 129.7 (C-2, C-6), 149.9 (C-1), 159.4 (C=O).
4b	3-CH_3	3-Tolyl formate **5b**	3-CH_3	78	1.5008 (35/0.1 approx.)	1.508 (95.5 – 98.5 / 20.5 torr) [1]	1744	^{1}H NMR: δ = 2.36 (s, 3H, CH_3), 6.92 (d, J = 7.5 Hz, 1H, 4-H), 6.93 (s, 1H, 2-H), 7.08 (d, J = 7.5 Hz, 1H, 6-H), 7.30 (t, J = 7.5 Hz, 1H, 5-H), 8.28 (s, 1H, CHO). – ^{13}C NMR: δ = 21.3 (CH_3), 118.0 (C-3), 121.7 (C-4), 127.2 (C-5), 129.4 (C-6), 140.1 (C-2), 149.9 (C-1), 159.5 (CHO).
4c	3-OH	1,3-Phenylene diformate **5c**	3-OCHO	72	1.5189 (66/0.1 approx.)	1.5175 (70/0.1) [1]	1747	^{1}H NMR: δ = 7.01 (d, J = 2.1 Hz, 1H, 2-H), 7.08 (td, ^3J = 7.4 Hz, ^4J = 2.1 Hz, 1H, 4-H, 6-H), 7.41 (dd, J = 7.4 Hz, 1H, 5-H), 8.26 (s, 1H, CHO). – ^{13}C NMR: δ = 114.8 (C-2), 119.2 (2C, C-4, C-6), 130.3 (C-5), 150.4 (2C, C-1, C-3), 158.7 (2 × C=O).
4d	4-OH	1,4-Phenylene diformate **5d**	4-OCHO	78	1.5185 (55/0.1 approx.)	(m. p. 68 – 70) [7]	1724	^{1}H NMR: δ = 7.17 (s, $4H_{arom.}$), 8.28 (s, 2H, 2 × CHO). – ^{13}C NMR: δ = 122.4 (4 × $C_{arom.}$), 147.6 (2C, C-1, C-4), 158.9 (2 × C=O). (^{1}H NMR (CCl_4): δ = 8.60 (formyl H) [7]).
4e	3-OCH_3	3-Methoxy-phenyl formate **5e**	3-OCH_3	77	1.5188 (55/0.1 approx.)	1.5190 (57/0.1) [1]	1736	^{1}H NMR: δ = 3.78 (s, 3H, OCH_3), 6.68 (d, J = 2.3 Hz, 1H, 2-H), 6.68 (dd, ^3J = 8.2, ^4J = 2.3 Hz, 2H, 4-H), 6.73 (dd, ^3J = 8.2, ^4J = 2.3 Hz, 1H, 6-H), 7.28 (dd, J = 8.2 Hz, 1H, 5-H), 8.27 (s, 1H, CHO). – ^{13}C NMR: δ = 55.5 (OCH_3), 107.2 (C-3), 112.1 (C-4), 113.2 (C-5), 130.1 (C-6), 150.9 (C-2), 159.3 (C=O), 160.7 (C-1).
4f	3-Cl	4-Chloro-phenyl formate **5f**	3-Cl	68	1.5301 (42/0.1 approx.)	1.5277 (45/0.1) [1]	1741	^{1}H NMR: δ = 7.07 (dd, ^3J = 8.0 Hz, ^4J = 2.2 Hz, 2H, 2-H, 6-H), 7.35 (dd, ^3J = 8.0 Hz, ^4J = 2.2 Hz, 2H, 3-H, 5-H), 8.25 (s, 1H, CHO). – ^{13}C NMR: δ = 122.6 (2C, C-3, C-5), 129.7 (2C, C-2, C-6), 131.8 (C-4), 148.3 (C-1), 158.8 (C=O).

[a] ^{1}H NMR at 250.1 MHz; ^{13}C NMR at 62.9 MHz.



Scheme 1. (substituents are given in Table 1).

derivative **7** was isolated after hydrolysis as main product (yield: 40 %). Its ^{1}H NMR spectrum shows a singlet for the two methoxy groups at δ = 3.78 ppm, a singlet at δ = 8.23 for the formyl proton and at δ = 6.33 for the methine proton. The ^{13}C NMR spectrum of **7** also confirms this structure. The product **7** has been prepared earlier [5a] from anisole and diformamide in the presence of aluminum chloride.



Scheme 2.

Experimental Section

General procedure for the O-formylation of phenols

Sodium diformamide (**2**) (38.0 g, 0.4 mol) is dissolved in 100 mL of anhydrous acetonitrile and 22.9 g (0.2 mol) of methanesulfonyl chloride (**3**) is added at 0 °C. After completion of the addition the reaction mixture is stirred at room temperature for 2 h. Afterwards, 0.1 mol of the corresponding phenol is added, and the mixture is refluxed under stirring for further 2 h. Completion of reaction is monitored by means of TLC (silica gel pre-coated plastic sheets Polygram SIL G/UV_{254}, Macherey-Nagel GmbH; solvent system : toluene-acetone (8 : 2); detection by UV irradiation at 254 nm). The mixture is then filtered to remove the insoluble salts, and acetonitrile is evaporated in vacuum. Finally, the crude product is distilled to give the corresponding pure aryl formates **5a – f** as colorless liquids (Table 1).

N-[Bis(4-methoxyphenyl)methyl]-formamide (7)

Sodium diformamide (**2**) (38.0 g, 0.4 mol) is dissolved in 100 mL of 1,2-dichloroethane, and 22.9 g (0.2 mol) of methanesulfonyl chloride (**3**) is added at 0 °C under stirring. After completion of the addition, the reaction mixture is stirred at r. t. for 2 h. Afterwards, 42.5 g (0.39 mol) of anisole (**6**) and 51.9 g (0.39 mol) of $AlCl_3$ are added, and the mixture is refluxed for further 2 h. Completion of the reaction is monitored by TLC. The reaction mixture is then filtered to remove insoluble salts, and the filtrate is evaporated under reduced pressure to afford the crude formamide **7** which is then recrystallized from ethanol. Yield 26.0 g (40 %), colorless crystals with m. p. 148 – 149 °C (149 – 150 °C [4a]). – ^{1}H NMR ($CDCl_3$, 500.16 MHz): δ = 3.78 (s, 6H, 2 × OCH_3), 6.21 (d, 1H, J = 8.17 Hz, CH–N), 6.33 (br, d, 1H, NH), 6.84 (d, 4H, J = 8.7 Hz, 2 × $2H_{arom.}$), 7.13 (d, 4H, J = 8.7 Hz, 2 × $2H_{arom.}$), 8.23 (br, 1H, CHO). – ^{13}C NMR ($CDCl_3$, 125.78 MHz): δ = 54.5 (CH–N), 55.3 (2 × OCH_3), 114.0 (2 × 3-$C_{arom.}$ and 5-$C_{arom.}$), 128.4 (2 × 2-$C_{arom.}$ and 6-$C_{arom.}$), 133.4 (2 × 1-$C_{arom.}$), 158.9 (2 × 4-$C_{arom.}$), 160.1 (CHO).

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