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# Formation of Dichloromethyl Phenyl Ethers as Major Products in the Photo-Reimer-Tiemann Reaction without Base

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***Abstract***: Photolysis of phenols **1a-d** in chloroform or carbon tetrachloride afforded the corresponding di- or trichloromethyl phenyl ethers (**2a-d** or **6a-d**, respectively). In chloroform, hydroxybenzaldehydes **4a-d** or **5** and phenyl formates **3a-d** were obtained as minor photoproducts. In carbon tetrachloride, traces of salicyloyl chloride (**7**), phenyl salicylate (**8**) and phenyl *p*-hydroxybenzoate (**9**) were detected starting from the parent phenol (**1a**). The obtained results agree with the involvement of an electron transfer mechanism.

## INTRODUCTION

The Reimer-Tiemann reaction[1,2] involves formylation of phenols by means of dichlorocarbene, generated through base-induced HCl elimination from chloroform. In spite of being a very old reaction, it still remains the most general procedure for the synthesis of *o*- and *p*- hydroxybenzaldehydes. Since its discovery in 1876, the wide scope of this formylation procedure has been evidenced by a considerable number of applications. In this context, several variations have been devised, trying to optimize the product yields, as well as the *o*/*p* selectivity. Among them, the so-called photo-Reimer -Tiemann reaction[3,4] is based on the UV-irradiation of phenols in the presence of chloroform, using a large excess of diethylamine for removal of the resulting HCl. The mechanism probably involves electron transfer from excited phenol to chloroform,[3] giving dichloromethyl radical as key intermediate (instead of dichlorocarbene).

Dichloromethylphenols **IV** and **V** are necessary precursors of the final products **4** and **5**, not only in the base-catalyzed reaction, but also in its photochemical version. However, they have not been even detected because of their lability under the employed experimental conditions.

Very little is known about the formation of O-alkylation products **2**. Small amounts of orthoformic esters (1-3%) have been isolated in some cases, strongly suggesting that dichloromethyl ethers play a minor role in the classical process[1,2]. By contrast, such compounds do not appear to be formed during the photolysis of phenols in chloroform-containing media.

In the present work, we have tried to obtain direct evidences for the involvement of dichloromethyl compounds **2**, **IV** or **V** in the photo-Reimer-Tiemann reaction. For this purpose, the presence of added base has been avoided, in order to prevent elimination leading to decomposition of these intermediates.

## RESULTS AND DISCUSION

A series of four phenols (**1a-d**) were irradiated in chloroform solution (*ca.* $10^{-2}$M). The results are summarized in Table 1.

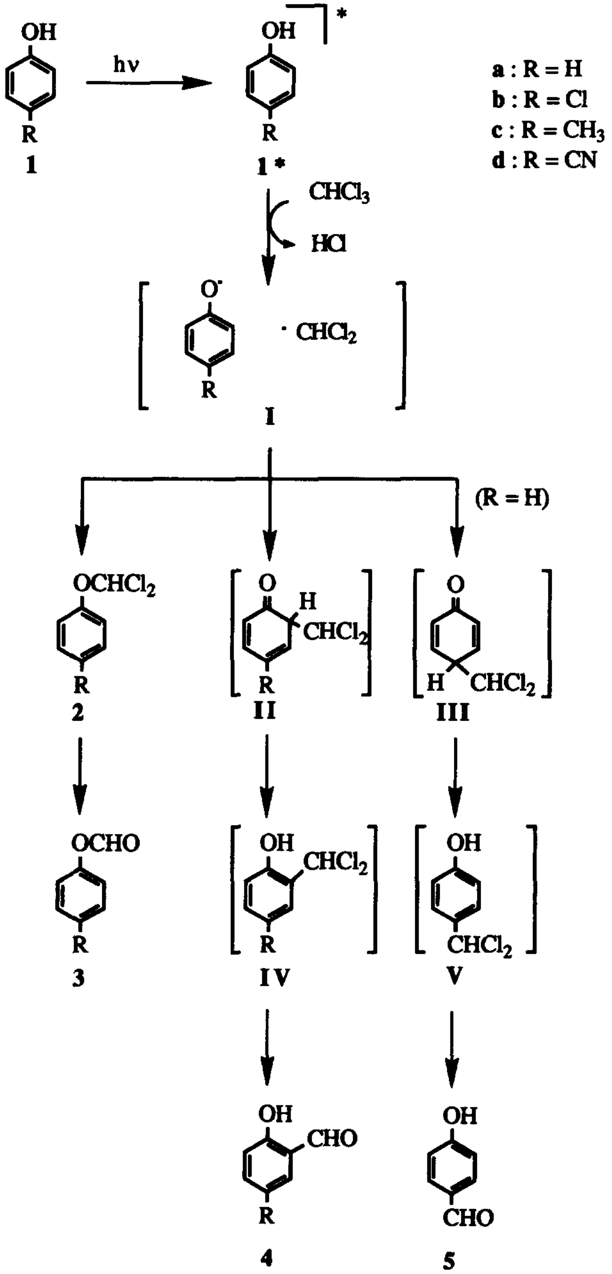


Table 1. Photolysis of Phenols in Chloroform and Carbon Tetrachloride.

| Entry | Phenol | Solvent | Conversion | Mass Balance[a] | Product Distribution (%) | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | 2 or 6[b] | 3 | 4 | 5 |
| 1 | **1a** | $CHCl_3$ | 92 | 36 | 75 | traces | 15 | 10 |
| 2 | **1b** | $CHCl_3$ | 89 | 38 | 78 | 7 | 15 | - |
| 3 | **1c** | $CHCl_3$ | 95 | 31 | 79 | 2 | 19 | - |
| 4 | **1d** | $CHCl_3$ | 55 | 68 | 87 | 8 | 5 | - |
| 5 | **1a** | $CCl_4$ | 98 | 30 | 88[c] | - | - | - |
| 6 | **1b** | $CCl_4$ | 99 | 28 | 100 | - | - | - |
| 7 | **1c** | $CCl_4$ | 100 | 31 | 100 | - | - | - |
| 8 | **1d** | $CCl_4$ | 66 | 41 | 100 | - | - | - |

[a] Large amounts of polymeric products were also obtained, [b] products **2** are formed in chloroform, while products **6** are formed in carbon tetrachloride, [c] traces of salicyloyl chloride (**7**), phenyl salicylate (**8**) and phenyl *p*-hydroxybenzoate (**9**) were also detected by GC/MS and GC/FTIR.

In general, the starting phenols were converted to a high extent into the corresponding dichloromethyl ethers (**2a-e**), *o*-hydroxybenzaldehydes (**4a-e**) and polymeric material. Minor amounts of the formates **3** were also obtained.

The major products were ethers **2**. Their unambiguous structural assignment was performed on the following bases: a) the mass spectral fragmentation, coupled with satisfactory HRMS measurements, b) the lack of OH stretching bands in the IR spectra and c) the presence of a characteristic singlet at $\delta$ about 7.4 ppm for the aliphatic methine proton, together with symmetric patterns for the aromatic multiplet.

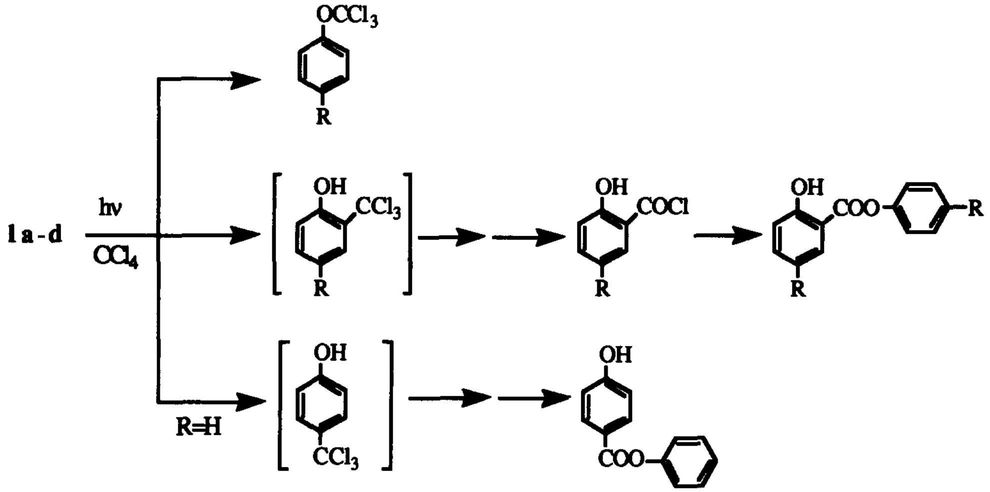
Previously, dichloromethyl phenyl ethers have been prepared by reaction of phenyl formates with $PCl_5$ or dichloromethyl methyl ether[5-8]. There is a limited number of data on these compounds. Most of them have appeared in chemical patents, where dichloromethyl phenyl ethers are synthetic intermediates for pharmaceuticals or agrochemicals.[9-13]

In view of the failure to detect the ethers **2** upon the reported photochemical Reimer-Tiemann conditions (irradiation of phenols in aqueous methanol or acetonitrile, in the presence of chloroform and bases such as diethylamine, potassium carbonate, potassium hydroxide or tetraethylammonium hydroxide) the following control experiment was performed: the photomixture obtained from *p*-clorophenol (**1b**) was concentrated under reduced pressure and the resulting oil was treated with methanol/water/diethylamine (10:10:1, v/v/v). This led to the quantitative conversion of **2b** back to the phenol **1b**. The above result allows to rule out the possible formation of hydroxybenzaldehydes **4** or **5** *via* rearrangement of the corresponding ethers **2** in the employed solvent system and explains the lack of these products under the conditions reported in the literature.

Further control experiments consisted in the irradiation of ethers **2** and formates **3** in chloroform. The former remained essentially unreacted after 2 hours, while the latter underwent efficient decarbonylation to the corresponding phenols **1**.

Table 1 also shows that the degree of conversion and the mass balance depended upon the nature of ring substituents. The introduction of an electron-donating methyl group (entry 3) resulted in a slightly enhanced conversion, although the amount of polymeric material was higher. The reverse was true for electron-withdrawing substituents, as evidenced with *p*-cyano- or *p*-chlorophenol (entries 4 and 2, respectively). These observations are in good agreement with the involvement of an electron transfer mechanism.

In order to ascertain whether phenyl trichloromethyl ethers **6** can be obtained in an analogous way, the four phenols (**1a-d**) were irradiated in carbon tetrachloride. As expected, compounds **6a-d** were the almost exclusive photoproducts, together with large amounts of polymer. In the case of the parent phenol (**1a**), traces of salicyloyl chloride (**7**), phenyl salicylate (**8**) and phenyl *p*-hydroxybenzoate (**9**) were also detected.



Finally, the photolysis of **1a-d** was carried out in equimolar mixtures of chloroform and carbon tetrachloride, in order to compare the relative yields of both ethers (**2** *versus* **6**), and thus establish the possible predominance of one of the involved competing processes. As a general rule, formation of phenyl trichloromethyl ethers **6** was overwhelmingly preferred, while the dichloromethyl analogues were found in the photomixtures in very small amounts (less than 1%). Again, this fact agrees well with an electron transfer mechanism involving reductive cleavage of the halogenated solvent. According to the reduction potentials of chloroform (-1.67 V *vs.* SCE) and carbon tetrachloride (-0.78 V *vs.* SCE),[14] generation of the corresponding radical anions by trapping of the electron ejected upon photoionization of **1a-d** would be favoured in the latter solvent by *ca.* 20 kcal/mol.

## EXPERIMENTAL SECTION

### *General*

IR-Spectra were obtained by means of a GC/FTIR Hewlett Packard HP 5965 instrument; $\nu_{max}$ (cm$^{-1}$) is given for the main absorption bands. $^1$H NMR Spectra were measured in $CDCl_3$ at 400 MHz with a VXR-400S Varian Instrument; chemical shifts are reported in δ (ppm) values, using TMS as internal standard. High resolution mass spectra were conducted on a VG AUTOSPEC instrument under electron impact; the ratios m/z, the assignments and the relative intensities (%) are indicated for the significant peaks.

*General irradiation procedure*

Solutions of 0,2 mmol of the substrates in 20 ml of chloroform or carbon tetrachloride were placed into pyrex test tubes surrounding a centrally positioned quartz cooling jacket containing a 125 W medium pressure Hg lamp, and irradiated for 5 h. Argon was bubbled through the solutions prior to and during irradiation. The photomixtures were analysed by GC, GC/MS, GC/FTIR and $^1$H-NMR spectroscopy using *p*-dimetoxybenzene as standard for integration.

*Spectral data of the compounds*

*Dichloromethyl phenyl ether (2a).*[7] FTIR ν 3081, 1594, 1491, 1318, 1205, 1070, 1003, 845, 718; $^1$H NMR δ 7.50 (s, 1H, $OCHCl_2$), 6.84-7.58 (m, 5H, $C_6H_5$); HRMS m/z (assignment, %) 179.9743 ($C_7H_6{}^{37}Cl_2O$, 5), 177.9774 ($C_7H_6{}^{35}Cl^{37}ClO$, 31), 175.9797 ($M^+$, 46; required for $C_7H_6{}^{35}Cl_2O$, 175.9796), 140.9933 ($C_7H_6{}^{35}ClO$, 100), 94.0416 ($C_6H_6O$, 13), 84.9389 ($CH^{35}Cl^{37}Cl$, 9), 82.9415 ($CH^{35}Cl_2$, 13), 77.0356 ($C_6H_5$, 80), 65.0406 ($C_5H_5$, 16), 51.0234 ($C_4H_3$, 19).

*4-Chlorophenyl dichloromethyl ether (2b).*[7] FTIR ν 1589, 1489, 1319, 1210, 1166, 1061, 1014, 855, 793, 721; $^1$H NMR δ 7.44 (s, 1H, $OCHCl_2$), 7.13-7.40 (m, 4H, $C_6H_4$); HRMS m/z (asignment, %) 213.9346 ($C_7H_5{}^{35}Cl^{37}Cl_2O$, 17), 211.9372 ($C_7H_5{}^{35}Cl_2{}^{37}ClO$, 52), 209.9413 ($M^+$, 54; required for $C_7H_5{}^{35}Cl_3O$ 209.9406), 176.9670 ($C_7H_5{}^{35}Cl^{37}ClO$, 67), 174.9704 ($C_7H_5{}^{35}Cl_2O$, 100), 128.0047 ($C_6H_5{}^{35}ClO$, 28), 126.9979 ($C_6H_4{}^{35}ClO$, 28), 110.9881 ($C_6H_4{}^{35}Cl$, 63), 84.9432 ($CH^{35}Cl^{37}Cl$, 15), 82.9464 ($CH^{35}Cl_2$, 27).

*Dichloromethyl 4-methylphenyl ether (2c).*[7] FTIR ν 3039, 2937, 1606, 1508, 1319, 1207, 1168, 1070, 857, 716; $^1$H NMR δ 2.34 (s, 3H, $CH_3$), 7.43 (s, 1H, $OCHCl_2$), 7.03-7.25 (m, 4H, $C_6H_4$); HRMS m/z (assignment, %) 191.9914 ($C_8H_8{}^{35}Cl^{37}ClO$, 23), 189.9943 ($M^+$, 37; required for $C_8H_8{}^{35}Cl_2O$ 189.9952), 157. 0223 ($C_8H_8{}^{37}ClO$, 22), 155.0257 ($C_8H_8{}^{35}ClO$, 71), 108.0572 ($C_7H_8O$, 25), 107.0494 ($C_7H_7O$), 91.0545 ($C_7H_7$, 100), 79.0550 ($C_6H_7$, 25), 77.0389 ($C_6H_5$, 35), 65.0395 ($C_5H_5$, 27), 51.0231 ($C_4H_3$, 14).

*4-Cyanophenyl dichloromethyl ether (2d).* FTIR ν 2235, 1603, 1504, 1318, 1219, 1169, 1056, 857, 727; $^1$H NMR δ 7.53 (s, 1H, $OCHCl_2$), 7.30-7.73 (m, 4H, $C_6H_4$); HRMS m/z (assignment, %) 202.9770 ($C_8H_5{}^{35}Cl^{37}ClNO$, 9), 200.9742 ($M^+$, 15; required for $C_8H_5{}^{35}Cl_2NO$ 200.9748), 166.0046 ($C_8H_5{}^{35}ClNO$, 14), 102.0330, ($C_7H_4N$, 52), 84.9407 ($CH^{35}Cl^{37}Cl$, 48), 82.9456 ($CH^{35}Cl_2$, 100).

*Phenyl trichloromethyl ether (6a).*[8] FTIR ν 3081, 1592, 1490, 1191, 1066, 1001, 918, 868, 759, 690, 573; $^1$H NMR δ 7.35-7.52 (m, 5H, $C_6H_5$); HRMS m/z (assignment, %) 213.9353 ($C_7H_5{}^{35}Cl^{37}Cl_2O$, 16), 211.9379 ($C_7H_5{}^{35}Cl_2{}^{37}ClO$, 52), 209.9412 ($M^+$, 50; required for $C_7H_5{}^{35}Cl_3O$ 209.9406), 176.9681 ($C_7H_5{}^{35}Cl^{37}ClO$, 65), 174.9716 ($C_7H_5{}^{35}Cl_2O$, 100), 118.9029 ($C^{35}Cl_2{}^{37}Cl$, 82), 116.9014 ($C^{35}Cl_3$, 84), 77.0409 ($C_6H_5$, 74), 65.0401 ($C_5H_5$, 29), 51.0230 ($C_4H_3$, 38).

*4-Chlorophenyl trichloromethyl ether (6b).*[15] FTIR ν 1426, 1193, 1164, 1054, 1015, 887, 764; $^1$H NMR δ 7.33-7.43 (m, 4H, $C_6H_4$); HRMS m/z (assignment, %) 249.8924 ($C_7H_4{}^{35}Cl^{37}Cl_3O$, 7), 247.8967 ($C_7H_4{}^{35}Cl_2{}^{37}Cl_2O$, 36), 245.8987 ($C_7H_4{}^{35}Cl_3{}^{37}ClO$, 79), 243.9018 ($M^+$, 58; required for $C_7H_4{}^{35}Cl_4O$ 243.9016), 210.9288 ($C_7H_4{}^{35}Cl_2{}^{37}Cl$, 72), 208.9321 ($C_7H_4{}^{35}Cl_3O$, 74), 126.9976 ($C_6H_4{}^{35}ClO$, 59), 118.9031 ($C^{35}Cl_2{}^{37}Cl$, 95), 116.9036 ($C^{35}Cl_3$, 100), 75.0208 ($C_6H_3$, 45), 62.9707 ($C^{35}ClO$, 37).

*4-Methylphenyl trichloromethyl ether (6c).*[15] FTIR ν 3041, 2937, 1505, 1284, 1194, 1165, 1064, 883, 761; $^1$H NMR δ 2.37 (s, 3H, $CH_3$), 7.19-7.40 (m, 4H, $C_6H_4$): HRMS m/z (assignment, %) 227.9479 ($C_8H_7{}^{35}Cl^{37}Cl_2O$), 225.9530 ($C_8H_7{}^{35}Cl_2{}^{37}ClO$, 91), 223.9563 ($M^+$, 91; required for $C_8H_7{}^{35}Cl_3O$ 223.9562), 190.9915 ($C_8H_7{}^{35}Cl^{37}ClO$, 70), 188.9934 ($C_8H_7{}^{35}Cl_2O$, 100), 152.9990 ($C_8H_6{}^{35}ClO$, 60), 107.0501 ($C_7H_7O$, 49), 91.0533 ($C_7H_7$, 16).

*4-Cyanophenyl trichloromethyl ether ( 6d).*[16] FTIR ν 2236, 1603, 1501, 1204, 1169, 1048, 890, 770; $^1$H NMR δ 6.90-7.75 (m, 4H, $C_6H_4$); HRMS m/z (assignment, %) 238.9299 ($C_8H_4{}^{35}Cl^{37}Cl_2NO$, 6), 236.9329 ($C_8H_4{}^{35}Cl_2{}^{37}ClNO$, 20), 234.9364 ($M^+$, 21; required for $C_8H_4{}^{35}Cl_3NO$ 234.9358), 199.9676 ($C_8H_4{}^{35}Cl_2NO$, 22), 120.9010 ($C^{35}Cl^{37}Cl_2$, 30), 118.9034 ($C^{35}Cl_2{}^{37}Cl$, 91), 116.9056 ($C^{35}Cl_3$, 100), 62.9695 ($C^{35}ClO$).

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