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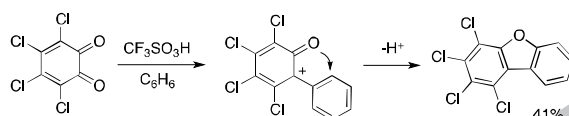
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Superacid-promoted synthesis of polychlorinated dibenzofurans

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ABSTRACT

Polychlorinated dibenzofurans have been prepared in one step by the condensations of *o*-chloranil with arenes in triflic acid. A mechanism is proposed involving formation of a monoprotonated quinone (carboxonium ion), electrophilic attack at the arene, and cyclization of a carbocation intermediate. The chemistry is further examined by spectroscopic and theoretical studies.

Keywords: heterocycles; superacid; condensation; dioxins; dibenzofurans

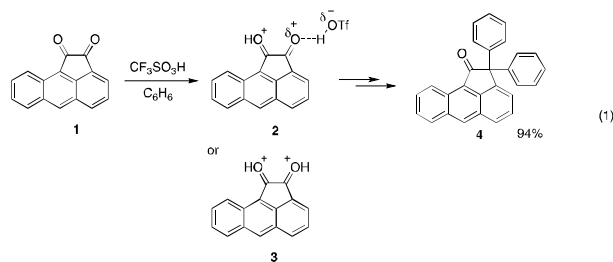
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Introduction

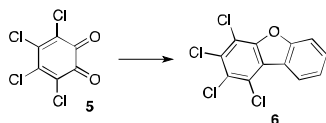
Polychlorinated dibenzofurans are a persistent and highly toxic environmental pollutant.¹ They are released into the environment by a variety of means - often the result of poorly controlled industrial processes,² waste incineration,³ and other routes. The polychlorinated dibenzofurans have been the subject of a vast number of studies related to their toxicology,⁴ detection and analytical chemistry,⁵ and environmental impact.⁶ Despite the significance of these substances, they are difficult to synthesize in a controlled manner. Several approaches have been made towards their directed chemical synthesis, including the chlorination of dibenzofuran,⁷ diazocoupling of chlorinated arenes,⁸ and the pyrolysis of chlorinated precursors.⁹ Each of these synthetic methods suffers from either low yields or poor regiocontrol. Given the importance of this class of compounds, new synthetic methods are highly desirable. New chemistry leading to polychlorinated dibenzofurans may improve access to the substances, and moreover, it may provide insights into the formation of these compounds during industrial processes and in other environments.

Results

Over the years, our research group has studied the reactions of several types of 1,2-dicarbonyl compounds and their chemistry in superacidic media.¹⁰ These compounds often form exceedingly reactive electrophiles, or superelectrophiles, in highly acidic media.¹¹ This can occur from double protonation of the carbonyl groups. For example, acenaphthenequinone and aceanthrenequinone were shown to condense with benzene in high yields in superacid CF₃SO₃H (triflic acid, eq 1).¹² It was



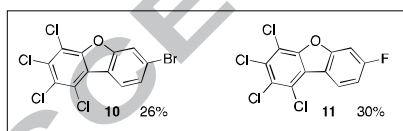
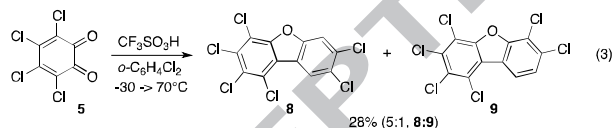
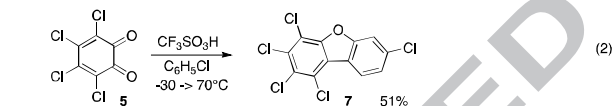
proposed that the superelectrophile **2** or **3** is involved in the transformation. During the course of our studies, we examined the chemistry of 1,2-benzoquinones. 1,2,3,4-Tetrachloro-1,2-benzoquinone (*o*-chloranil, **5**) is an inexpensive 1,2-benzoquinone reagent which is used in a variety of organic transformations.¹³ When *o*-chloranil (**5**) is mixed with benzene in superacid, the chlorinated dibenzofuran (**6**) is formed as the major product in 17% yield (Table 1). The balance of the starting material (**5**) is assumed to be lost in polymeric byproduct. Numerous attempts were made to limit the amount of resinous byproduct, however, the highest obtained yield was 41% of 1,2,3,4-tetrachlorodibenzofuran **6**. Despite the low yield of this route, it is a direct synthetic route and competitive with other published methods for preparing compound **6**. It was observed that initiating the conversion at low temperature provides a modest improvement in the yield of product. We reasoned that the low temperature might suppress polymerization and side-reactions at the initial stage. Weaker acids (H₂SO₄ and CF₃CO₂H) were also used as the acid catalyst, however useful yields of product **6** were not obtained.



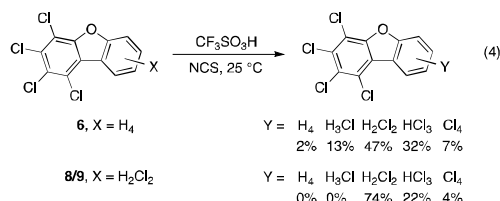
conditions		yield ^a
CF ₃ SO ₃ H (30 equiv) C ₆ H ₆	25°C	17%
CF ₃ SO ₃ H (65 equiv) CH ₂ Cl ₂ /C ₆ H ₆	-50°C → 25°	35%
CF ₃ SO ₃ H (65 equiv) CF ₃ CH ₂ OH/C ₆ H ₆	-30°C → 80°	41%
CF ₃ SO ₃ H (16 equiv) C ₆ H ₆	-30°C → 80°	36%
CF ₃ SO ₃ H (1.6 equiv) C ₆ H ₆	-30°C → 80°	22%

^a18 hr reaction

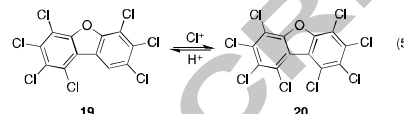
With chlorinated arene nucleophiles, some polychlorinated dibenzofurans could be prepared. For example, chlorobenzene provides product **7** in good yield (eq 2). Again, temperature is found to be an important factor. If the reaction is started at low temperature, then the yield of product **7** is over 50%, but reaction at room temperature gives just 22% yield of the product. Products **8** and **9** are formed as an inseparable mixture in 28% overall yield from *o*-dichlorobenzene (eq 3). We also attempted the condensation chemistry with 1,2,3-trichlorobenzene and 1,2,3,4-tetrachlorobenzene, but no polychlorinated dibenzofuran products could be isolated. Both bromobenzene and fluorobenzene also give the expected condensation products (**10** and **11**) from *o*-chloranil (**5**).



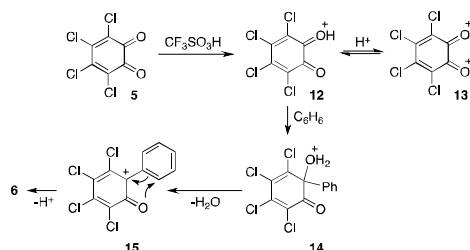
In an effort to produce more highly chlorinated products, the dibenzofurans **6** and **8/9** were subjected to electrophilic chlorination. Olah and co-workers have previously shown that *N*-chlorosuccinimide (NCS) is capable of halogenating even nitro-substituted arenes in the presence of superacid.¹⁴ When compound **6** is combined with an excess of NCS (6 equivalents) and triflic acid (20 equivalents), more highly chlorinated dibenzofurans are obtained (eq 4). Analysis by GC-MS and GC-FID indicated that both the heptachloro and octachlorodibenzofurans are formed (relative yields reported). In the case of heptachlorodibenzofuran, two isomers are obtained in a 3:1 ratio (see Supporting Information). Even in the presence of excess NCS, however, there remained some starting material **6** (2%). When compounds **8** or **9** are subjected to chlorination, a



significant amount of the starting material remains but the heptachloro and octachlorodibenzofurans are again formed. Despite using an excess of the chlorinating reagents, complete halogenation is not obtained. This suggests an equilibrium involving chlorination and protolytic dechlorination between heptachlorodibenzofuran (**19**) and octachlorodibenzofuran (**20**, eq 5).

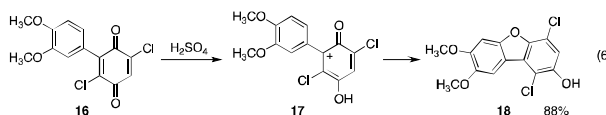


Although the yields of these condensation reactions are low, the conversions are quite novel. For the reaction leading to product **6**, a mechanism is proposed involving carbonyl protonation and subsequent electrophilic attack at benzene (Scheme 1). Thus, the quinone (**5**) is protonated at the carbonyl group to provide the carboxonium ion **12**. Although other 1,2-dicarbonyl compounds are thought to undergo diprotonation in superacid-promoted reactions with benzene,¹⁰ the involvement of a supelectrophilic dication (**13**) is probably not necessary. It has



Scheme 1.

been shown that monocationic carboxonium ions may react with benzene when electron-withdrawing substituents are present.¹⁵ In the case of **12**, the inductive effects of the chloro substituents and the adjacent carbonyl group should provide a high level of electrophilic reactivity at the carboxonium ion center. Reaction with benzene leads to the oxonium ion **14** which undergoes loss of water to give the carbocation **15**. Intermediate **15** provides a simple route to the dibenzofuran ring system – cyclization involving the carbonyl oxygen. The proposed mechanism is not without precedent. Recently, Lemal and coworkers described heteroaryl adducts of **5** in which an indole and a pyrrole have reacted at the carbonyl carbon.¹⁶ Musgrave and Webster also described a remarkably similar cyclization in 70% H₂SO₄ - as quinone **16** provides the dibenzofuran **18** in high yield (eq 6). This type of transformation was also found to be catalyzed by AlCl₃. The exact nature of the proposed cyclization mechanism is not clear, but there are two likely scenarios: cyclization of **15** or **17** involves the oxygen lone pair electrons to form the new carbon-oxygen bond, or cyclization of **15** or **17** involves a concerted 4π-electron electrocyclovelization. In the later case, the



transformation would be remarkably similar to the Nazarov reaction, and as such, the present chemistry would be a rare example of an oxo-Nazarov cyclization.

In order to further characterize the nature of the electrophilic intermediate for *o*-chloranil **5**, NMR studies were done (Table 2). The quinone was dissolved in solutions of increasing acidity and the ^{13}C NMR spectra recorded. In the progression from chloroform to $\text{CF}_3\text{CO}_2\text{H}$ (H_o -2.7) to $\text{CF}_3\text{SO}_3\text{H}$ (H_o -14), the carbonyl carbons move increasingly downfield. While this is consistent with a greater degree of protonation, the extent of protonation is difficult to determine. Interestingly, the superacid solution produces extra sets of peaks at a significantly higher chemical shift. These downfield peaks may arise from the fully protonated species, perhaps with *cis/trans* isomerism.

Table 2. ^{13}C NMR signals from *o*-chloranil **5** in varied solutions (25°C).

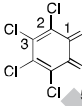
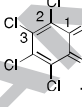
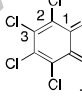
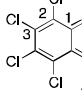
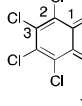
solvent	^{13}C NMR, δ
CDCl_3	131.1, 143.2, 168.1
$\text{CF}_3\text{CO}_2\text{H}$	131.1, 145.6, 170.1
$\text{CF}_3\text{SO}_3\text{H}$	130.8, 148.3, 170.8 minor peaks {182.2, 180.0, 168.6, 168.3, 140.3, 137.9}

The structure of *o*-chloranil **5** and its protonated ions – was further studied using computational methods. The quinone and its ions were studied at the B3LYP 6-311G(d,p) level of theory using the Gaussian 09 program suite.¹⁸ Additional calculations were done with the MP2 6-31G and HF 6-311G+(d,p) models for comparison. Relative energies are for isomeric structures and they represent the differences in ZPE-corrected energies of the optimized structures. Among the observations from these calculations, the LUMO level is found to drop considerably with each protonation. The quinone (**5**) itself has a LUMO at -0.17 eV, while the monoprotonated ions (**12a,b**) have LUMOs in the range of -0.3 eV and the diprotonated ions (**13a,b**) have LUMOs in the range of -0.5 eV. These data are consistent with the experimental observation that superacidic conditions are required for reaction with benzene or halogen-substituted benzene. As a weak nucleophile, benzene (B3LYP 6-311G(d,p) calculated HOMO at -0.26 eV) requires a fairly reactive electrophile in order to react. The calculations show that the LUMOs of the monoprotonated ions (**12a,b**) are at a comparable level to the HOMO of benzene. This likely facilitates the initial steps of the conversion. The lowering of the LUMO is the most significant effect of quinone protonation, but modest structural effects are also seen. The C-O bond is shown to lengthen and the C-Cl bond shortens with protonation of the carbonyl. This is consistent with delocalization of the cationic charge, even to the extent that $n \rightarrow \pi$ donation may be occurring at the chloro substituent. Regarding isomeric structures, **12a,b** and **13a,b**, the endo stereoisomers (**12a** and **13a**) exhibit modest stabilization over the exo stereoisomers (**12b** and **13b**). This may be the result of favorable hydrogen bonding available in the endo structures.

Summary

We have found the polychlorodibenzofurans may be prepared in fair yields by the condensations of *o*-chloranil with arenes in the presence of superacid. The chemistry represents a direct route to a class of compounds of great interest. The condensation begins with protonation of the carbonyl group – significantly lowering the LUMO of the quinone structure. The key step in the transformation involves the cyclization of a carbocation with a carbonyl group – leading to the dibenzofuran ring system. Polychlorodibenzofurans have been detected as impurities in *o*-chloranil, this study may suggest a possible mechanism of formation for these impurities.

Table 3. B3LYP 6-311G(d,p) calculated parameters for *o*-chloranil **5** and related ions.^a

	rel. E, kcal/mol	HOMO, eV	LUMO, eV	C1-O distance, Å	C1-C2 distance, Å	C2-C3 distance, Å	C3-Cl distance, Å
	N/A	-0.28 (-0.38) [-0.37]	-0.17 (-0.06) [-0.03]	1.20 (1.26)	1.48 (1.48)	1.36 (1.37)	1.73 (1.81)
	0.0	-0.43 (-0.55) [-0.53]	-0.36 (-0.27) [-0.24]	1.29 (1.32)	1.39 (1.40)	1.41 (1.40)	1.68 (1.76)
	+3.5	-0.44 (-0.55) [-0.53]	-0.36 (-0.26) [-0.23]	1.29 (1.32)	1.39 (1.40)	1.41 (1.41)	1.68 (1.76)
	+1.6	-0.59 (-0.70) [-0.69]	-0.54 (-0.47) [-0.43]	1.29 (1.33)	1.39 (1.40)	1.41 (1.41)	1.66 (1.75)
	0.0	-0.59 (-0.71) [-0.69]	-0.54 (-0.46) [-0.43]	1.27 (1.31)	1.41 (1.42)	1.39 (1.40)	1.67 (1.74)

^aAdditional data: (MP2 6-31G) calculated values; [HF 6-31+G(d,p)] calculated values.

Acknowledgments

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Supplementary Material

Experimental procedures, characterization data for new compounds, computational methods and results.

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Highlights:

- A one step procedure has been developed for the synthesis of polychlorinated dibenzofurans.
- The chemistry involves a superacid-promoted condensation reaction of *o*-chloranil and arenes.
- An unusual carbocation cyclization is proposed for the conversion.