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Reactions of Acenaphthenequinone and Aceanthrenequinone with Arenes in Superacid

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Abstract

The hydroxyalkylation reactions of aceanthrenequinone (**6**) and acenaphthenequinone (**7**) with a series of arenes have been studied. In reactions with the Brønsted superacid CF₃SO₃H (triflic acid), the condensation products are formed in good yields (58–99%, 10 examples) with high regioselectivity. Computational studies were also done to examine the structures and energies of mono- and diprotonated species from **6** and **7**. The results from the condensation reactions are consistent with the formation of superelectrophilic species involving protosolvation of carboxonium ion intermediates.

1. Introduction

The acid-catalyzed condensation of aromatic compounds and aldehydes or ketones is known as the hydroxyalkylation reaction.¹ Examples of this conversion date back to 1872, when it was reported that chloral condenses with benzene in sulfuric acid.² The hydroxyalkylation reaction is the basis for a number of industrially important synthetic conversions, including the preparation of bis-phenol monomers for polycarbonate resins, the preparation of dyes such as malachite green, and in the preparation of some pharmaceuticals. Recently, there have been several reports involving superacid-catalyzed condensations of 1,2-dicarbonyl compounds with benzene and other arenes. Shudo and Ohwada found that 2,3-butanedione (**1**) gives the condensation product (**3**) in high yield, and the diprotonated species (**2**) was proposed as an intermediate (eq 1).³ Similar reactions were used to prepare the anti-convulsant drug, phenytoin (**4**), from parabanic acid (eq 2) and the high molecular weight condensation polymer (**5**) from isatin (eq 3).^{4,5} In each of these examples, diprotonated or superelectrophilic intermediates are thought to be involved in the condensation reactions. The hydroxyalkylation reaction often requires the aromatic compound to be an activated system (i.e. nucleophilic) like phenol or an aryl ether. With non-activated or deactivated arenes (benzene, chlorobenzene, nitrobenzene), the condensation reaction can only occur with a highly electrophilic reactant. Superelectrophilic carboxonium ions and those substituted by strong electron withdrawing groups (–CF₃ or –CCl₃) have been shown to react with even deactivated arenes in the hydroxyalkylation reaction.⁶

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(1)

(2)

(3)

A survey of the literature shows that there are very few general examples of the hydroxyalkylation reaction involving quinones. An exception is the acid-catalyzed chemistry of aceanthrenequinone (**6**) and acenaphthenequinone (**7**). It has been shown in several studies that these quinone systems condense with pyrroles in good yields from CF₃CO₂H or BF₃-Et₂O.⁷ Pyrroles are reactive, electron-rich aromatic compounds and their condensation chemistry is well known in porphyrin synthesis. Recently two reports have described the syntheses of high molecular weight polymers based on this superacid-catalyzed condensation chemistry of **7**.⁸ In the following manuscript, we provide a full report of the chemistry aceanthrenequinone and acenaphthenequinone in superacid-catalyzed hydroxyalkylation reactions with arenes. We demonstrate that quinones **6** and **7** condense with benzene and related arenes in good to excellent yields, and a mechanism is proposed which invokes the formation of diprotonated, superelectrophilic quinones. The protonated structures are further characterized by theoretical calculations.

2. Experimental

2.1 General

Aceanthrenequinone (**6**), acenaphthenequinone (**7**), solid acid catalysts, trifluoroacetic acid, and 98% H₂SO₄ were purchased from commercial suppliers and used as received. Trifluoromethanesulfonic acid (triflic acid) was purchased from a commercial supplier and it was distilled from an Ar atmosphere prior to use.

2.2. Procedure for the Preparation Condensation Products

Aceanthrenequinone (0.2 g, 0.86 mmol) is dissolved in 1 mL of arene and 3 mL CF₃SO₃H is added. After stirring for at least 4 hours at 25°C, the mixture is poured over ice. The resulting solution is then extracted twice with CHCl₃ and the organic phase is washed

thoroughly with water and then brine. The solution is then dried with MgSO_4 and concentrated *in vacuo* to give the product. The crude product is then purified by column chromatography (if necessary) or recrystallization. All new compounds have been completely characterized by ^1H and ^{13}C NMR spectroscopy, elemental analysis or high-resolution mass spectroscopy, and in the case of product 2,2-Diphenyl-2H-aceanthrylen-1-one (**8**), single crystal x-ray crystallography.⁹ With acenaphthenequinone, the products were sufficiently volatile for analysis by gas chromatography.

3. Results

When aceanthrenequinone (**6**) is reacted with C_6H_6 in the Brønsted superacid $\text{CF}_3\text{SO}_3\text{H}$, the condensation product (**8**) is formed in excellent yield (eq 4). Like the condensation of **6** with pyrrole,^{7b} nucleophilic attack by benzene occurs exclusively at 2-carbonyl group. A series of arenes were reacted with aceanthrenequinone (**6**) and $\text{CF}_3\text{SO}_3\text{H}$ and the expected condensation products (**8–12**) are formed regioselectively in good yields (Table 1). NMR analysis indicates that a single regioisomer is produced in the reactions of toluene and halobenzenes. In previous studies, other 1,2-dicarbonyl compounds have likewise shown good regioselectivity in hydroxyalkylation reactions.^{4,5b} The condensation reaction with benzene can be effected by as little as 3.0 equivalents of $\text{CF}_3\text{SO}_3\text{H}$. With 98% H_2SO_4 , product **8** is formed in just 26% yield from aceanthrenequinone (**6**) and benzene, while trifluoroacetic acid does not give any condensation product.

(4)

Acenaphthenequinone (**7**) also condenses with arenes in strongly acidic or superacidic media. When compound **7** is reacted with $\text{CF}_3\text{SO}_3\text{H}$ and a series of arenes, the condensation products (**13–17**) are also formed regioselectively in good yields (Table 1). Unlike aceanthrenequinone (**6**) however, the condensation reactions of acenaphthenequinone (**7**) generate some side-products, and the composition of the product mixtures varies considerably with the reaction conditions. For example with benzene, three types of products are formed in reactions with **7** in acidic media (Table 2). The optimal conditions for conversion to the hydroxyalkylation product (**13**) were found to be the reaction with a large excess (ca. 40 equivalents) of $\text{CF}_3\text{SO}_3\text{H}$ at 0°C . At higher temperatures, an increasing amount of product (**18**) is formed from a dehydrative cyclization reaction. An unusual acenaphthylene product (**19**) is also formed at 80°C , presumably from the reduction of cationic intermediates. Although H_2SO_4 gives some condensation product, none is obtained from $\text{CF}_3\text{CO}_2\text{H}$ or various solid acids (Table 2). If the hydroxyalkylation product (**13**) is isolated and reacted with $\text{CF}_3\text{SO}_3\text{H}$ (no C_6H_6), the dehydrative cyclization product (**18**) is formed in good yield (eq 5). Similar conversions were described involving dehydrative cyclizations of aryl-pinacols and 2,2,2-triphenylacetophenone (**20**).¹⁰ In the superacid promoted dehydrative cyclization of **20**, experimental evidence suggested the involvement of an *O,O*-diprotonated superelectrophile. An analogous diprotonated species (**21**) is proposed in the dehydrative cyclization (eq 5), with an initial step involving a phenyl migration to the carboxonium position.¹⁰

(5)

In order to further explore these superacid-catalyzed condensation reactions, DFT calculations were done to determine the structures and energies of likely protonated intermediates from aceanthrenequinone (**6**) and acenaphthenequinone (**7**).¹¹ A recent manuscript reported the structures and energies for mono and diprotonated acenaphthenequinone (**7**) with geometry calculations done at the B3LYP/6–31G* level of theory and single point energy calculations done at the aug-ccpvtz(-f) level.⁹ Even with solvation taken into account however, these calculations suggested that diprotonated, superelectrophilic intermediates were unlikely based on the energies of these intermediates. Our calculations at the B3LYP/6–311G**//B3LYP/6–311G** level¹² are in partial agreement with the earlier study: the most stable diprotonated structures (**22c** and **23c**) arise from sequential protonation at each of the carbonyl oxygens (Figure 2). Stationary points were also found at several C,O-diprotonated structures and at structures in which protonation occurs twice on the same carbonyl group, but in each of these cases the dicationic structures are significantly less stable than the global minima. Interestingly, the most stable monoprotonated species from aceanthrenequinone (**6**) is found at structure **22a** in which the 1-carbonyl group is protonated. In the acid-catalyzed condensation reactions however, nucleophilic attack occurs at the 2-carbonyl group to give product **8** (eq 4). In order for the acid-catalyzed reaction to give product **8**, the reaction must involve the 2-carbonyl-protonated species (**22b**) or a superelectrophilic intermediate. Based on the calculations, however, ion **22b** is 5 kcal/mol less stable than **22a**. This suggests that a diprotonated species (i.e. **22c,d**) is the reacting electrophile in the condensation reaction.

4. Discussion

The widely accepted mechanism for the hydroxyalkylation reaction involves formation of a carboxonium ion by protonation of a carbonyl group, followed by nucleophilic attack by the arene. For the condensation reactions of aceanthrenequinone (**6**) and acenaphthenequinone (**7**), there are three possibilities: the condensations occur through only monoprotonated intermediates and transition states, the condensations occur through monoprotonated intermediates with protosolvation of the transition states (and partial dicationic character), or the condensations occur by the involvement of discrete, fully formed, dicationic superelectrophiles. In this study, there are several lines of evidence to suggest that superelectrophiles with partial or full dicationic character are involved in the condensation reactions of aceanthrenequinone (**6**) and acenaphthenequinone (**7**). Benzene and chlorobenzene are arenes with relatively low strength as nucleophiles. With these arenes, electrophilic reactions require an activated carboxonium ion electrophile. This is consistent with the formation of diprotonated intermediates, such as **22c,d** and **23c,d**. The condensation reactions are also shown to be sensitive to acid strength and this is often a hallmark of superelectrophilic activation. It is particularly striking that CF₃CO₂H will give hydroxyalkylation products with aceanthrenequinone (**6**) and pyrrole (a strong nucleophile),^{7b} but the same reaction conditions give no condensation product with the less nucleophilic benzene. Furthermore, the formation of the dehydrative cyclization product (**18**) from acenaphthenequinone (**7**) very likely involves the gitionic superelectrophile **21** (eq 5). This suggests that the superacidic reaction conditions are capable of forming

carboxonium ion-based superelectrophiles. The previously reported direct observation of diprotonated acEnapthenequinone (**23c,d**) in superacid further supports the possibility that it is a viable reactive intermediate in these conversions.¹³ Finally, the computational results suggest that the regiochemistry of nucleophilic attack on aceanthrenequinone (**6**) is best explained by invoking a diprotonated species. Although these lines of evidence suggest that diprotonated species are involved in the hydroxyalkylation reactions of compounds **6** and **7**, it is not possible to determine if these are fully formed dicationic, superelectrophilic intermediates (**23a,b**), or if they are species with only partial proton transfer.¹⁴

5. Conclusions

In summary, we have found that aceanthrenequinone (**6**) and acenapthenequinone (**7**) condense with moderately deactivated arenes in generally good yields in the presence of the Brønsted superacid, CF₃SO₃H. It is proposed that the condensations reactions occur through superelectrophilic species involving protosolvation of carboxonium ion intermediates. While the extent of protosolvation is not known, the results suggest considerable dicationic character.

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- (a) **2,2-Diphenyl-2H-aceanthrylen-1-one (8)**. Yellow solid MP 210–214°C (C₆H₆); ¹H NMR (300 MHz, CDCl₃) δ, ppm: 7.20–7.36 (m, 10 H), 7.45 (d, *J*=6.9 Hz, 1H), 7.59–7.65 (m, 2H), 7.72–7.79 (m, 1H), 7.96 (d, *J*=8.4 Hz, 1H), 8.17 (d, *J*=8.4 Hz, 1H), 8.74 (s, 1H), 9.22 (d, *J*=8.7 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ, ppm: 67.7, 122.4, 124.5, 124.8, 125.2, 126.6, 127.0, 127.9, 128.3, 128.6, 128.7, 128.9, 129.3, 133.0, 133.8, 142.7, 143.3, 143.5, 203.8; EI MS: 370 (M⁺), 339, 265, 168; HRMS C₂₈H₁₈O *m/z* calcd 370.135765, found 370.135781. Crystal data: C₂₈H₁₈O, MW 370.42, yellow crystals, triclinic, space group *P*-1, *a* = 8.6398(18) Å, *b* = 9.744 (2) Å, *c* = 11.667 (2) Å, α = 93.702 (4)°, β = 96.937 (4)°, γ = 94.812 (4)°, *U* 968.9 (3) Å³, *Z* = 2, *D*_c = 1.270 g/cm³, *F*(000) 388, μ (MoKα) 0.075 mm⁻¹, graphite monochromated Mo Kα λ = 0.71073 Å, *T* = 293(2) K. Final discrepancy factors: *R*1 = 0.0504 and *wR*2 = 0.1323 for 10125 reflections with *F*_o > 4σ_F.

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Figure 1.
 Structures and energies for mono- and diprotonated structures from aceanthrenequinone (**6**) and acenaphthenequinone (**7**).^a

^aCalculations done at the B3LYP/6-311G**//B3LYP/6-311G** level

Table 1

Products and yields from the reactions of aceanthrenequinone (**6**) or acenathenequinone (**7**) with arenes and $\text{CF}_3\text{SO}_3\text{H}$.^a

Products/Yields
8 94% ^b	13 99% ^c
9 82% ^b	14 58% ^c
10 78% ^b	15 96% ^b
11 84% ^b	16 99% ^b
12 86% ^b	17 62% ^b

^a Isolated yields of pure product.

^b Reaction done at 25°C.

^c Reaction done at 0°C.

Table 2
Products and yields from reactions of acenaphthenequinone (**7**) with C₆H₆ in acidic media.^a

entry	acid	temp	18	19	13	7
(1)	5 mL CF ₃ SO ₃ H	0°C	0%	0%	100%	0%
(2)	1 mL CF ₃ SO ₃ H	25°C	1%	0%	99%	0%
(3)	5 mL CF ₃ SO ₃ H	25°C	13%	0%	86%	0%
(4) ^b	5 mL CF ₃ SO ₃ H	80°C	19%	81%	0%	0%
(5)	5 mL H ₂ SO ₄	25°C	0%	0%	75%	25%
(6) ^c	5 mL CF ₃ CO ₂ H	25°C	0%	0%	0%	100%
(7) ^c	0.1 g acidic Al ₂ O ₃	25°C	0%	0%	0%	100%
(8) ^c	0.1 g ZrO ₂ •H ₂ SO ₄	25°C	0%	0%	0%	100%
(9) ^c	0.1 g Amberlite-H	25°C	0%	0%	0%	100%
(10) ^c	0.1 g Nafion SAC-13	25°C	0%	0%	0%	100%
(11) ^c	0.1 g Nafion SAC-13	80°C	0%	0%	0%	100%
(12) ^c	0.1 g Montmorill. KSF	25°C	0%	0%	0%	100%

^aReported as relative yields based on GC-FID analysis; 250 mg of quinone **7**, 1 mL C₆H₆ used (4 mL for solid acids); 18 hr reaction.

^bConsiderable amount of insoluble polymer or oligomer formed under these conditions (ca. 100 mg).

^cComplete recovery of starting material.