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Triflic acid promoted synthesis of polycyclic aromatic compounds

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ABSTRACT

The triflic acid (CF_3SO_3H) promoted cyclizations of 2-styrylbiaryls are found to be useful for the synthesis of polycyclic aromatic compounds, including functionalized derivatives of polycyclic aromatic compounds and heterocyclic systems. The reaction involves cationic cyclization followed by an elimination of benzene from the intermediate product.

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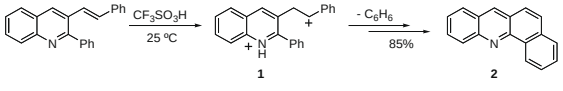
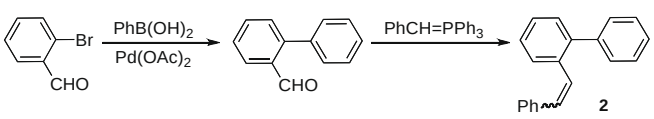
Polycyclic aromatic hydrocarbons and related compounds have been of great interest due to their relationships to chemical carcinogenesis.[1] Besides their biological activities, these substances have likewise been considered important components in material science applications. Due to their extended π-systems, they can exhibit novel optical properties.[2] Consequently, there is the continued need for new synthetic routes leading to these types of compounds and their functionalized derivatives.[3] We recently described a new superacid-promoted route to aza-polycyclic aromatic compounds (Eq. 1).[4,5] This chemistry involves the formation of superelectrophilic intermediates (i.e., **1**), followed by cyclization and elimination of benzene to give the condensed aromatic compounds (i.e., **2**). Because the precursor substrate possesses an N-heterocyclic ring that is fully protonated in acid, the cyclizations occur via the dicationic, superelectrophilic intermediates such as **1**. These results raised an interesting question: is it possible to achieve similar condensation reactions through monocationic reactions (without N-heterocyclic rings) to prepare polycyclic aromatic hydrocarbons? In the following Letter, we address this question and describe a new superacid-promoted synthetic route to polycyclic aromatic hydrocarbons, substituted derivatives, and heterocyclic systems.



(1)

In our initial investigation of this reaction, 2-styrylbiphenyl (**2**) was prepared and reacted with superacidic CF_3SO_3H.[6] This substrate (along with other olefins used in this study) was synthesized using Suzuki and Wittig coupling reactions (Eq. 2).[4] When compound **2** is reacted in superacid, the product mixture is complex, but some phenanthrene (**3**, ca. 5–10% yield) is detected by GCMS (Eq. 3). Other major products from the reaction include 9,10-dihydro-9-phenylphenanthrene (**4**) and 9-benzyl-9*H*-fluorene (**5**). With the formation of product **5**, it is clear that both possible carbocationic intermediates (**7a**,**b**) are generated in the acid. The phenanthrene (**3**) is formed by *ipso*-protonation of the phenyl group of compound **4** and elimination of benzene. Other minor products (ca. 5% yield) include biphenyl and dibenz[*a*,*c*]anthracene (**6**). Although it is not exactly clear how these products are formed, the presence of compound **6** suggests some type of dimerization and cleavage reaction steps. Compound **2** was also reacted in the gas-phase by flash vacuum pyrolysis (200 °C, 10^{-2} Torr) over the solid acid Nafion-H. Overall a similar product mixture was observed; however, the dibenz[*a*,*c*]anthracene (**6**) was not formed. Since intermolecular reactions are less likely in the gas-phase, this supports the idea that an intermolecular reaction gives compound **6** in the condensed phase.



(2)

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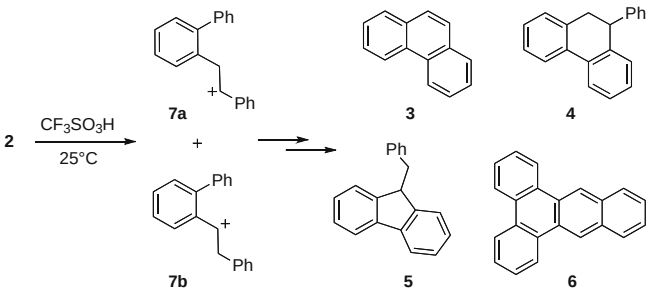
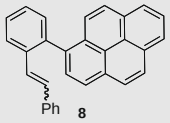
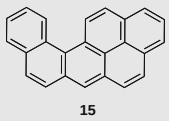
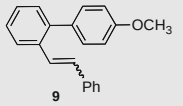
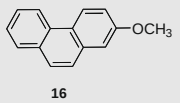
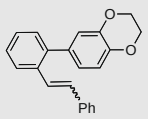
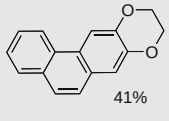
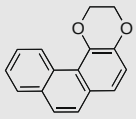
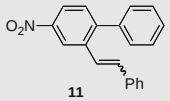
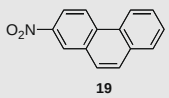
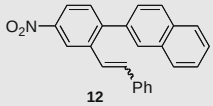
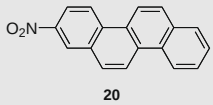
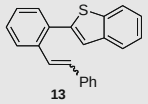
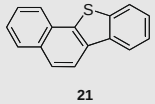
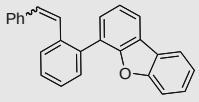
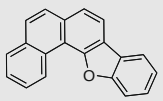


(3)

The formation of some phenanthrene (**3**) from 2-styrylbiphenyl (**2**) was a promising initial result, so a number of styryl-substituted arenes were prepared and reacted with CF_3SO_3H (Table 1). Substrate **8** gives naphtho[1,2-*a*]pyrene (**15**) as the major product in fair yield. This system (**8**) differs from 2-styrylbiphenyl (**2**) most notably by the increased nucleophilic character of the pyrenyl group versus the phenyl group (in **2**). Similarly, reactions of the aryl ether derivatives **9** and **10** provide good yields of the condensation products (entries 2 and 3). In the case of substrate **9**, the reaction with CF_3SO_3H gives 2-methoxyphenanthrene (**16**), while compound **10** produces two regioisomers (**17** and **18**) from reaction at the 5- and 8-positions of the benzodioxane ring. Nitro-functionalized substrates give the polycyclic aromatic compounds in good yields, with the preparation of 2-nitrophenanthrene (**19**) and 2-nitrochrysene (**20**). Cyclization of **12** occurs regioselectively at the 1-position of the naphthyl ring. Although the yields were low, heterocyclic systems (**21** and **22**) were prepared from cyclization of a benzothiophene derivative (**13**) and the dibenzofuran derivative (**14**). Most of the condensation reactions were done by reacting a $CHCl_3$ solution the substrate with CF_3SO_3H at 25 °C. However, in some cases, the reaction conditions needed to be tailored for particular substrates. For example, compound **12** gave complex product mixtures when the reaction was done at temperatures warmer than 0 °C.

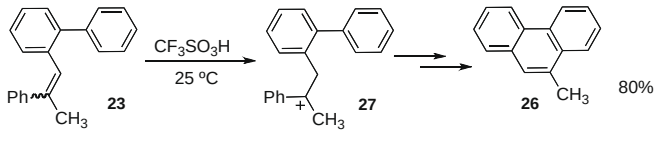
In order to obtain better yields for the conversions, we reasoned that the 2-phenyl-1-propenyl system should lead to regioselective protonation and more efficient cyclizations. Several 2-phenyl-1-propenyl derivatives were prepared and reacted with superacid (Eqs. 4,5,6). When compounds **23** and **24** were reacted with CF_3SO_3H, the polycyclic aromatic hydrocarbons (**26** and **28**) are formed in reasonably good yields. The conversion of compound **23** to 9-methylphenanthrene (**26**) is a marked improvement over the analogous reaction of 2-styrylbiphenyl (**2**) to give phenanthrene (**3**, Eq. 2). This improvement may be understood by considering the regioselectivity of protonation. Compounds **23** and **24** are

Table 1
Cyclizations of styryl-substituted precursors **8**–**14** to the condensed products **15**–**22** in CF_3SO_3H

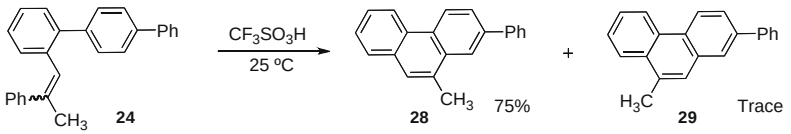
Entry	Starting material	Product(s)	Yield[d] (%)
1	 **8**	 **15**	52[a]
2	 **9**	 **16**	71[a]
3	 **10**	 41% **17**  **18**	34[a]
4	 **11**	 **19**	81[a]
5	 **12**	 **20**	78[b]
6	 **13**	 **21**	42[c]
7	 **14**	 **22**	12[a]

[a] Reaction done at 25 °C.
[b] Reaction done at 0 °C.
[c] Reaction done at 65 °C.
[d] Isolated yields of pure products. Products were characterized by ^1H and ^{13}C NMR and by high resolution and low resolution mass spectra.

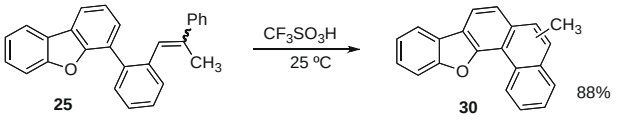
protonated exclusively at the 1-carbon position of the olefinic groups, leading to the stable 3° carbocations (i.e., **27**). This leads to efficient conversions to the phenanthrenes. In the case of compound **24,** however, the product mixture also contains a small amount of 9-methyl-2-phenylphenanthrene (**29**; visible by NMR),



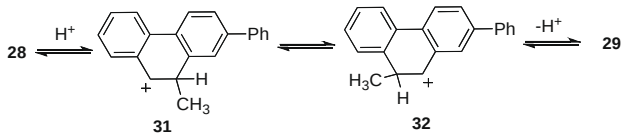
(4)



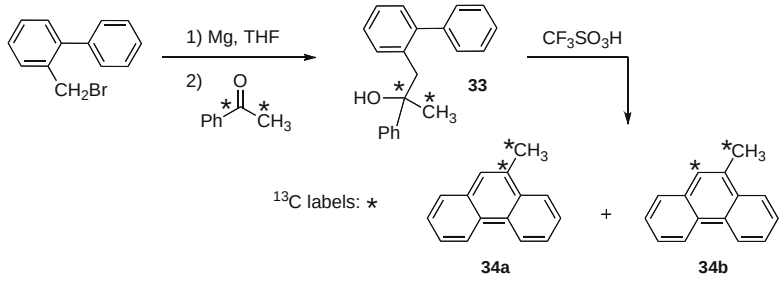
(5)



(6)



(7)

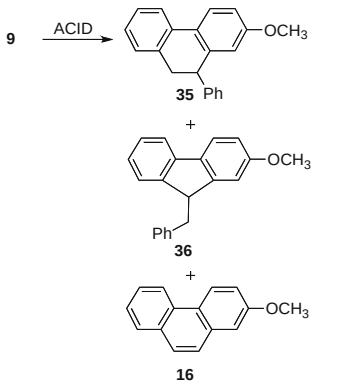


(8)

which can be removed from the 10-methyl-2-phenylphenanthrene (**28**) by recrystallization. In a similar respect, reaction of compound **25** gives a high yield of the cyclization product **30**; however, it is formed as an inseparable pair of structural isomers (ca. 1:1 ratio). Presumably, these isomeric products are formed by migration of the methyl group in product **30** as a result of protonation in superacid. The same isomerization evidently occurs with compound **28** (Eq. 6).[8] To verify that methyl migration can occur in these systems, a doubly ^{13}C labeled derivative was also prepared and the precursor alcohol was reacted in CF_3SO_3H (Eq. 8). 2-Bromomethylbiphenyl gave the Grignard reagent, which reacted with doubly labeled acetophenone to provide alcohol **33**. Upon reaction with CF_3SO_3H, the expected 9-methylphenanthrene (**34a**,**b**) was produced quantitatively. NMR analysis showed that the product 9-methylphenanthrene had undergone extensive ^{13}C scrambling, presumably through methyl migration. The acid-catalyzed migration of methyl-substituents on arenes is a well-known process, for example, in the industrial-scale isomerization of xylene isomers.[7] In the present case, the isomerization may, however, lead to undesirable product isomers of the polycyclic aromatic compounds.

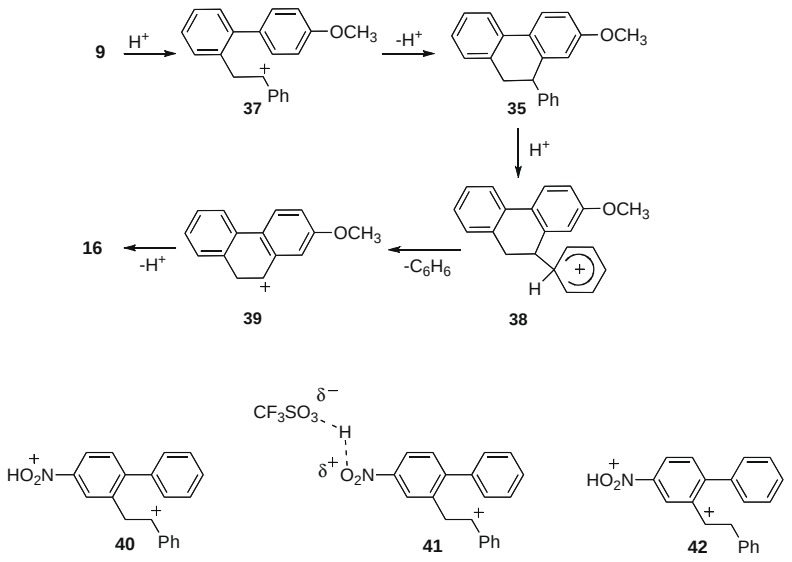
Although it was shown that compound **2** may produce phenanthrene by flash vacuum pyrolysis at 200 °C over Nafion-H catalyst, CF_3SO_3H is the only acid catalyst found to produce the polycyclic aromatic compounds at modest temperatures in the condensed phase. A series of solid acids, electrophilic metals, and other catalysts were tested for their activities in the cyclization of compound **9** (Fig. 1). Several of the catalytic systems induced cyclization, although none gave benzene elimination. Some of the electrophilic metal catalysts, such as $PtCl_2$, isomerized the olefin group in **9**, but did not give the cyclized products (**35** and **36**).

The cyclization of styryl-substituted biaryl systems is a new general synthetic route to polycyclic aromatic systems. This superacid-promoted conversion in most cases is thought to involve monocationic cationic intermediates. For example, in the conversion of compound **9** to 2-methoxyphenanthrene (**16**), protonation of the styryl group begins a series of reaction steps involving three carbocationic species (**37**–**39**, Eq. 9). Benzene elimination requires *ipso*-protonation of intermediate **35**. Thus, very strong acids (or high temperatures) are required to complete the condensation reaction. Mechanistically, the overall conversion is similar to the methoxy-vinyl cyclization strategy developed by the Harvey group, although in the later case mild acids could be employed.[8] In the case of the nitro-substituted compounds (**11** and **12**), the reaction may involve superelectrophilic, diprotonated species. Nitro-substituted arenes are known to be protonated in CF_3SO_3H at the nitro group and they can participate in superelectrophilic reactions.[9] This suggests either the dication **40** or the protosolvated species **41** as the initial intermediate. Both **40** and **41** are expected to possess enhanced electrophilic reactivities compared to related monocationic species (i.e., **7b**). Moreover, protonation of the nitro group should tend to disfavor the undesired intermediate **42** due to electrostatic repulsive effects.[10]



Reaction Products and Catalyst Systems
Starting Materials Only
Catalyst Systems:
1. $PtCl_2$, 50 °C, 24 hr
2. $AuCl_3$, 50 °C, 24 hr
3. AuCl, 50 °C, 24 hr
4. CF_3CO_2H, 25 °C, 24 hr
5. Sulfated zirconia
Products 35 and 36 Formed
Catalyst Systems:
1. $PtCl_2$/AgOTf, 50 °C, 24 hr
2. $AuCl_3$/AgOTf, 50 °C, 24 hr
3. Phosphotungstic acid, 50 °C, 24 hr
4. Montmorillonite KSF, 50 °C, 24 hr
5. Nafion SCA-13, 50 °C, 24 hr
Product 16 Formed
Catalyst System:
1. CF_3SO_3H, 25 °C, 24 hr

Figure 1. Reactions of olefin **9** with various acids.



(9)

In summary, we have found that reactions of olefinic substrates with superacid can give polycyclic aromatic products.[11] Substituted derivatives may also be prepared. An addition–elimination mechanism is proposed for this condensation reaction, including a superacid-promoted benzene elimination. Most of the conversions are thought to involve monocationic species; however, the nitro-substituted systems may react via dicationic superelectrophiles (with protonated nitro groups). The condensations were found to be most successful when the olefin group tends to be regioselectively protonated. Good conversions were also observed with activated (nucleophilic) aryl groups, such pyrenyl and 4-methoxyphenyl groups.

Acknowledgments

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11. *General procedure for cyclization of the olefins to the polycyclic aromatic compounds*: The olefin (1 mmol) is dissolved in 1 mL of $CHCl_3$ and the solution is cooled to 0 °C. Triflic acid (3 mL, 30 mmol) is slowly added to the solution. Depending on the substrate, the mixture is stirred from 2 to 18 h at reaction temperatures from 0 °C to 65 °C. The solution is then poured over ca. 15 g of ice and it is made slightly basic by dropwise addition of 10 M NaOH. The mixture is then extracted twice with $CHCl_3$ and the organic phase is washed with water, followed by two brine washes. The chloroform solution is then dried over Na_2SO_4, filtered, and concentrated to yield crude product. Products are then purified by column chromatography (silica gel, hexanes–ether). Benzo[*b*]phenanthro[3,4-*d*]furan (**22**): White solid, mp: 135–140 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ, ppm: 7.45–7.49 (m, 1H), 7.56–7.59 (m, 1H), 7.72–7.75 (m, 1H), 7.85–7.93 (m, 5H), 8.00–8.02 (d, J = 7.8 Hz, 1H), 8.09–8.10 (d, J = 7.6 Hz, 1H), 8.15–8.17 (d, J = 8.1 Hz, 1H), 9.84–9.86 (d, J = 8.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ, ppm: 111.9, 117.9, 118.8, 120.4, 122.1, 123.1, 124.0, 124.3, 126.7, 127.1, 127.2, 127.9, 128.3, 138.7, 132.5, 153.5, 156.1. High resolution MS (EI), $C_{20}H_{12}O$ calcd: 268.08882, found: 268.09060. 10-Methyl-2-phenylphenanthrene (**28**): White solid, mp: 105–107 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ, ppm: 2.80 (s, 3H), 7.45–7.47 (t, J = 7.4 Hz, 1H), 7.55–7.58 (t, J = 7.7 Hz, 1H), 7.68–7.74 (m, 3H), 7.82–7.82 (d, J = 8.1 Hz, 2H), 7.88–7.90 (dd, J_1 = 8.6 Hz, J_2 = 1.5 Hz, 1H), 8.07 (d, J = 1.5 Hz, 1H), 8.11–8.13 (m, 1H), 8.73–8.75 (d, J = 8.6 Hz, 1H), 8.76–8.78 (m, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ, ppm: 20.1, 123.1, 124.8, 125.1, 125.9, 126.4, 126.6, 127.0, 127.4, 127.6,129.0, 130.3, 132.2, 132.4, 133.0, 139.2, 141.0. High resolution MS (EI), $C_{21}H_{16}$ calcd: 268.12520, found: 268.12415.