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ARTICLE

Acid-Catalyzed Reactions of *N*-Methyl-1,2,4-Triazoline-3,5-Dione (MeTAD) with Some Polyaromatic Hydrocarbons

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The acid-catalyzed reactions of *N*-methyl-1,2,4-triazoline-3,5-dione with naphthalene, anthracene, and phenanthrene have been studied using trifluoroacetic acid as catalyst. Quite different results between these reactions were ultimately observed. Reaction with naphthalene appears to be the result of a straightforward acid-catalyzed DA reaction. Reactions with anthracene and phenanthrene, however, are most consistent with formation of carbocation intermediates. The fate of the carbocation, and the nature of the products, depends upon the individual rates of competing inter- and intramolecular reactions.

KEYWORDS: *N*-Methyl-1,2,4-Triazoline-3,5-Dione, MeTAD, Trifluoroacetic Acid, Polycyclic Aromatic Hydrocarbons, 1-Aryl Urazoles, Diels-Alder Cycloaddition.

1. INTRODUCTION

We recently reported on the acid-catalyzed (CF_3CO_2H, TFA) reaction of *N*-methyl-1,2,4-triazoline-3,5-dione (MeTAD, **1**) with substituted benzenes to form 1-arylurazole products (**2**) (Scheme 1).[1] We considered extending these studies to the reactions of some polyaromatic hydrocarbons (PAHs) whose reactions with triazolinediones have been little-studied.

MeTAD is known to undergo a rapid thermal Diels-Alder (DA) reaction with anthracene to afford cycloadduct **3**, and a slower (reversible) DA reaction with naphthalene to give **4** (see Chart 1).[2,3] Similar DA reactivity takes place with substituted napthalenes.[3] The thermal reactions of *N*-phenyl-1,2,4-triazoline-3,5-dione (PhTAD) with perylene and benzo[ghi]perylene leads to heterocycles **5** and **6**, respectively, apparently resulting from DA cycloaddition followed by spontaneous dehydrogenation.[4] Interestingly, PhTAD reacts with dibenzo[a,e]pyrene and benzo[a]pyrene to afford 1-arylurazoles **7** and **8** (respectively) instead of products resulting from DA cycloaddition.[5] Finally, under visible light irradiation MeTAD reacts with naphthalene (and substituted naphthalenes), phenanthrene, and benzene to afford Diels-Alder adducts **4**, **9** and **10**, respectively.[3,6–8] To our knowledge, however, no studies on acid-catalyzed reactions of MeTAD with PAHs have been reported. Herein we report on the acid-catalyzed reactions of MeTAD with naphthalene, anthracene and phenanthrene.

2. EXPERIMENTAL DETAILS

All compounds and solvents other than MeTAD were obtained commercially and used without further purification. *N*-Methylurazole was obtained from Aldrich and oxidized to MeTAD using N_2O_4, and then purified by sublimation according to the literature.[11] NMR spectra were obtained on a JEOL ECS-400 instrument in $CDCl_3$ and referenced to TMS at 0.0 PPM unless otherwise specified.

Computational work was accomplished using Spartan '04. Structures were minimized using DFT B3LYP/6-31G* methods. Minima were confirmed by performing a vibrational analysis at the same computational level. No imaginary frequencies were found. A scaled zero-point correction was applied before calculating the molecular energies.

2.1. Reaction of MeTAD with Naphthalene in the Presence of Acid Catalyst

To a vial containing 25 mg (0.22 mmol) of MeTAD and 29 mg (0.23 mmol) of naphthalene in 0.5 mL of $CDCl_3$ was added 20 μL (0.22 mmol) of CF_3CO_2H via syringe. The resulting deep red solution was transferred to a clean, dry NMR tube which was then sealed and protected from the light. ^{1}H NMR spectra were run at regular intervals (5 min). The major product formed was that of cycloadduct

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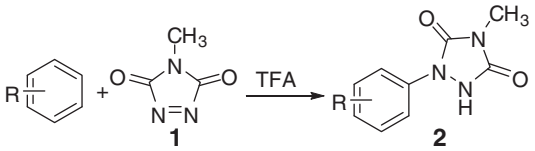


Scheme 1. Acid-catalyzed addition of MeTAD (**1**) with substituted benzenes to form 1-aryl urazoles (**2**).

4 as described in the text, and its ^{1}H NMR spectrum was identical to the NMR data provided in the literature.[3]

2.2. Reaction of MeTAD with Anthracene in the Absence of Acid Catalyst

To a vial containing 25 mg (0.22 mmol) of MeTAD and 40 mg (0.22 mmol) of anthracene was added 2 mL of $CDCl_3$. The resulting solution was transferred to a clean, dry NMR tube which was then sealed and protected from the light. The deep red color of the solution rapidly decolorized (within 3 min). A ^{1}H NMR spectrum revealed the formation of cycloadduct **3**. Evaporation of the solvent afforded a white powder in quantitative yield. ^{1}H NMR (400 MHz) δ 7.44 (dd, $J = 5.3$, 3.2 Hz), 7.26 ($J = 5.3$, 3.2 Hz), 6.21 (s, 2H), 2.83 (s, 3H); ^{13}C NMR (100 MHz) δ 157.5, 136.6, 128.3, 124.0, 60.2, 25.5. The ^{1}H NMR data agreed with that provided in the literature.[2]

2.3. Reaction of MeTAD with Anthracene in the Presence of Acid Catalyst

To a vial containing 40 mg (0.22 mmol) of anthracene in 2 mL of $CDCl_3$ was added 20 μL (0.22 mmol) of CF_3CO_2H via syringe followed immediately by 25 mg (0.22 mmol) of MeTAD. The deep red color of the solution rapidly decolorized (within 0.5 min). The resulting solution was transferred to a clean, dry NMR tube which was then sealed. A ^{1}H NMR spectrum revealed the formation of a 60/40 mixture of cycloadduct **3** and 1-(9-anthryl)urazole **14** (see below).

2.4. Synthesis of 1-(9-anthryl)urazole (14) via BF_3-Catalyzed Isomerization of 3

To 100 mg (0.34 mmol) of **3** in 5 mL CH_2Cl_2 was added 50 μL of BF_3•Et_2O. The resulting solution was allowed to stand for 18 h. The solution was then diluted to 25 mL with CH_2Cl_2 and washed with 1 × 10 mL of water, dried over Na_2SO_4, filtered and concentrated to yield 100 mg of **14** as a white solid which was pure by ^{1}H NMR spectroscopy. The compound was recrystallized from ethanol to yield 74.3 mg of pale yellow plates, m.p. 272–274 °C: ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.35 (s, 1H, NH), 8.87 (s, 1H), 8.23 (d, $J = 8.4$ Hz, 2H), 7.99 (d, $J = 8.4$ Hz, 2H), 7.69–7.60 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 153.9, 152.4, 131.3, 129.8, 129.6, 128.7, 127.8, 126.0, 125.9, 122.9, 25.2.

2.5. Reaction of MeTAD with Phenanthrene in the Absence of Acid Catalyst

To a vial containing 25 mg (0.22 mmol) of MeTAD and 40 mg (0.22 mmol) of phenanthrene was added 1 mL of $CDCl_3$. The resulting deep red solution was transferred to a clean, dry NMR tube which was then sealed and protected from the light. ^{1}H NMR spectra were run at regular intervals. Over the course of 2 days, no change in the spectrum was noted.

2.6. Reaction of MeTAD with Phenanthrene in the Presence of Acid Catalyst

To a vial containing 25 mg (0.22 mmol) of MeTAD and 40 mg (0.22 mmol) of phenanthrene in 1 mL of $CDCl_3$

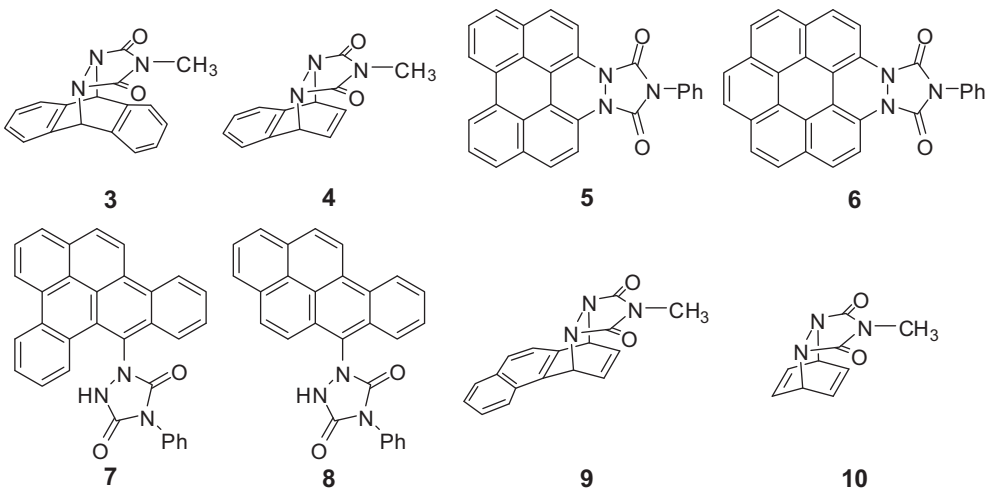


Chart 1. Structures of various MeTAD and PhTAD adducts with polyaromatic compounds.

was added 20 μL (0.22 mmol) of CF_3CO_2H via syringe. The resulting deep red solution was transferred to a clean, dry NMR tube which was then sealed and protected from the light. ^1H NMR spectra were run at regular intervals (10 min). The signals attributed to adduct **15** (see below) slowly grew in intensity and reached a maximum (~43% yield) over 2 h.

2.7. Synthesis of Adduct 15

To a stirring solution of 1.26 g (7.08 mmol) of phenanthrene in 20 mL $CHCl_3$ (filtered through Al_2O_3 to remove ethanol stabilizer) at 0 °C was added 1.63 mL (3 eq) of trifluoroacetic acid via syringe. Immediately following, 0.8 g (7.08 mmol) of MeTAD was added as a solid at once. The resulting deep red solution was stirred for 15 min and then removed from the ice bath and allowed to warm to room temperature. After 5 h, most of the deep red color had been discharged and the reaction mixture was diluted with 50 mL CH_2Cl_2. The resulting solution was washed 3 × 5 mL H_2O, 1 × 25 mL sat. aq. NaCl, dried over Na_2SO_4, filtered and concentrated to a pale yellow foam. Column chromatography (SiO_2, 3 : 1 hexane/ethyl acetate) afforded 1.15 g (40% yield) of **15** as a white solid. This compound could be further purified by recrystallization by dissolving 0.135 g of **15** in a minimum of ethyl acetate at room temperature, adding hexane until cloudy, and chilling in a refrigerator overnight. Colorless needles (0.11 g) were obtained, m.p. 134.0–134.5 °C. ^1H NMR (400 MHz) δ 7.81 (d,$J = 7.7$ Hz, 1H), 7.79 (d, $J = 7.7$ Hz, 1H), 7.49–7.44 (m, 2H), 7.38–7.29 (m, 4H), 6.50 (br s, 1H, NH), 6.29 (d, $J = 4.8$ Hz, 1H), 5.75 (d, $J = 4.8$ Hz, 1H), 2.95 (s, 3H); ^{13}C NMR (100 MHz) δ 156.6 (q, $J = 43.4$ Hz), 154.5, 154.4, 133.6, 132.2, 130.4, 130.0, 129.25, 129.21, 129.1, 129.0, 128.9, 127.7, 125.8, 124.5, 114.3 (q, $J = 286$ Hz), 74.4, 54.7, 25.2. Anal Calcd for $C_{19}H_{13}N_3O_4F_3$: C, 56.42; H, 3.24; N, 10.40; F, 14.10. Found: C, 56.75; H, 3.55; N, 10.33; F, 13.89.

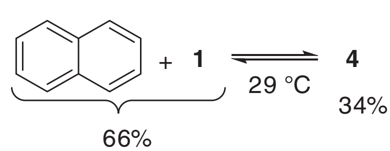
2.8. Conversion of 15 to 18

A solution of **15** in DMSO-d_6 was allowed to stand in a sealed NMR tube, protected from the light. Periodic ^1H NMR spectra were obtained which saw gradual loss of the signals from **15** and a concomitant increase in signals due to formation of 1-(9-phenanthryl)urazole **18** over 6 days. At the end of this time, the DMSO was removed via rotary evaporation and the urazole purified by preparative TLC (SiO_2, EtOAc) to afford a solid which was recrystallized from a mixture of ethyl acetate and hexane to afford a white powdery solid, m.p. 200–202.5 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 1.2 (br s, 1H, NH), 8.93 (d, $J = 8.1$ Hz, 1H), 8.89 (d, $J = 8.1$ Hz, 1H), 8.08 (dd, $J = 8.1$, 1.2 Hz, 1H), 8.07 (s, 1H), 8.03 (dd, $J = 8.1$ Hz, 1.2 Hz, 1H), 7.82–7.68 (m, 4H), 3.08 (s, 3H). ^{13}C NMR (100 MHz, d_6) δ 154.1, 153.0, 131.8, 130.7, 130.6, 129.6, 128.9, 128.2, 128.0, 127.7, 127.5, 127.3, 125.2, 124.4, 123.3, 123.1, 25.1. Anal Calcd for $C_{17}H_{13}N_3O_2$: C, 70.08; H, 4.50; N, 14.43. Found C, 70.48; H, 4.48; N, 14.24.

3. RESULTS AND DISCUSSION

3.1. Reaction of MeTAD with Naphthalene

As mentioned previously, MeTAD is known to react with naphthalene via a DA cycloaddition to afford cycloadduct **4**.[3] In $CDCl_3$, as monitored by ^1H NMR spectroscopy, the reaction between MeTAD and naphthalene establishes an equilibrium between **4** (34%) and starting materials at 29 °C over an 18 hour period (Scheme 2).[3] When MeTAD was added to a pre-mixed solution of naphthalene and one equivalent of TFA at room temperature in $CDCl_3$, monitoring by ^1H NMR spectroscopy demonstrated that the same equilibrium between **4** and starting materials was established as that in the uncatalyzed reaction, but at a much faster rate (within 0.5 hr). Upon standing, however, the MeTAD underwent acid-catalyzed decomposition over the course of 24 h to ultimately yield a complicated mixture of products and recovered naphthalene.[9] In his studies on the TFA-catalyzed mechanism of reaction of PhTAD with electron-rich aromatic polymers, Stadler suggested that protonation by TFA markedly increases the electrophilicity of the TAD.[9] Stadler further suggested that protonation occurs at one of the azo nitrogen atoms rather than the carbonyl oxygen atom of the TAD ring. To test this theory, we modeled the structures of neutral MeTAD (Fig. 1) and also the two isomeric compounds resulting from protonation of MeTAD at the oxygen atom (Fig. 1, compound **11**) and at one of the azo nitrogen atoms (Fig. 1, compound **12**) at the DFT B3LYP/6-31G* level. The structural impact of *O*-protonation is much greater than that of *N*-protonation as can be seen by the bond lengths provided in Figure 1. Much of the symmetry is retained in **12** with an observed slight shortening of the N=N bond relative to neutral MeTAD. The *N*-protonated isomer **12** was indeed found to be 5.5 kcal/mol lower in energy than the *O*-protonated isomer **11** as predicted. The effect of protonation should be to enhance the electrophilicity (and thus the reactivity) of the azo group. In support of this, Nelsen has shown that acids can be used to promote DA reactions of azo compounds (acting as dienophiles) with cyclic dienes (where thermal reaction does not take place) via protonation at one of the azo nitrogen atoms.[10] In the reaction with naphthalene, therefore, the effect of added TFA



Scheme 2. Equilibrium estabilished between naphthalene and MeTAD with DA cycloadduct **4**.

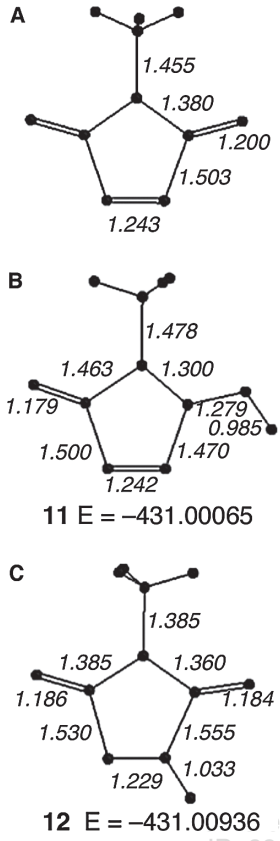
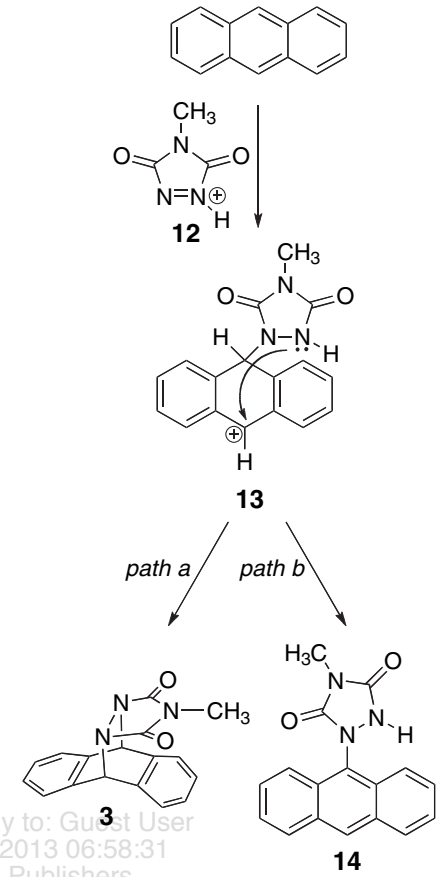


Fig. 1. Computed structures and energies for (A) MeTAD, (B) *O*-protonated MeTAD (**11**) and (C) *N*-protonated MeTAD **12** as calculated at the DFT B3LYP/6-31G* level. Bond lengths are in units of Angstroms. Energies are in Hartrees.



Scheme 3. Potential pathways for initially formed carbocation intermediate **13**. *Path a*: intramolecular trapping of the carbocation by the free lone pair on nitrogen followed by proton loss. *Path b*: loss of a proton to reform the aromatic ring.

appears to be simply that of a catalyst for the previously observed DA cycloaddition by enhancing the electrophilicity of the MeTAD.

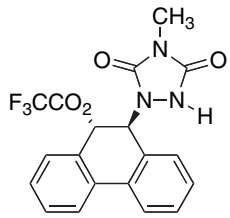
3.2. Reaction of MeTAD with Anthracene

In the absence of an acid catalyst, the reaction of MeTAD with anthracene proceeds quickly at room temperature (within a few minutes) to afford only DA adduct **3**.[2] When MeTAD was added to a premixed solution of anthracene and CF_3CO_2H in $CDCl_3$, in addition to formation of the expected cycloadduct **3**, 1-aryl urazole **14** was also formed (Scheme 3) in a ratio of 1.5 : 1, respectively. Urazole **14** did not arise via acid-catalyzed isomerization of **3** since control studies established that **3** was stable to TFA. A mechanism that accounts for formation of both compounds is provided in Scheme 3. In this case, protonated MeTAD (**12**) initially reacts with anthracene to form carbocation intermediate **13**. Intermediate **13** may then either (i) collapse to ultimately form **3** (*path a*), or (ii) lose a proton to form the urazole product **14** (*path b*). Urazole **14** could be independently synthesized by treatment of **3** with the strong Lewis acid BF_3•Et_2O.

3.3. Reaction of MeTAD with Phenanthrene

Unlike naphthalene and anthracene, phenanthrene does not react thermally with MeTAD as determined by monitoring an equimolar solution in $CDCl_3$ by ^{1}H NMR spectroscopy over several days. However, Sheridan reported that photochemical reaction between MeTAD and phenanthrene affords DA adduct **9**.[7] We wondered whether TFA would catalyze the DA reaction as it did with naphthalene. Addition of one equivalent of TFA to a mixture of MeTAD and phenanthrene in $CDCl_3$ resulted in the slow formation of an adduct over the course of 2 hours in about 43% yield as observed by ^{1}H NMR spectroscopy. The observed adduct was not the same as the photochemical DA adduct **9**, however. The DA adduct is reported to exhibit (in addition to aromatic proton signals) three doublet of doublets signals at 6.9 (1H), 6.7 (1H), and 6.0 (1H) ppm along with an *N*-Me signal at 2.75 (3H) ppm.[7] The adduct we observed exhibited (in addition to aromatic proton signals) two doublets at 6.29 (1H, $J = 4.8$ Hz) and 5.75 (1H, $J = 4.8$ Hz) ppm along with an *N*-Me signal at 2.95 (3H) ppm. The adduct appeared to be the result of reaction at the 9,10-positions of the phenanthrene ring, consistent with

structure **15**. We were able to successfully isolate this new compound via addition of excess



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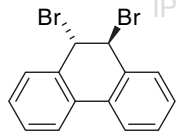
TFA (3 equivalents) to a mixture of phenanthrene and MeTAD to afford the adduct in 40% yield (after column chromatography) as a stable crystalline compound. A ^{13}C NMR spectrum quickly verified the structure of **15** since two of the carbon signals were obviously coupled to fluorine atoms (i.e., the carbonyl signal of the trifluoroacetate group at 157 ppm was a quartet with coupling constant of 43.4 Hz, and the CF_3 carbon at 114 ppm was a quartet with coupling constant of 286 Hz). Furthermore, the relatively small coupling constant (4.8 Hz) between the two saturated C–H's at the 9 and 10 positions is consistent with the observed small coupling constant between the C–H bonds of *trans*-dibromide **16** of 2.6 Hz (using the ^{13}C satellite signals to obtain the coupling constant).



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Formation of adduct **15** may be explained using a mechanism similar to that invoked for the anthracene reaction (Scheme 4). Reaction of *N*-protonated MeTAD (**12**) with phenanthrene at the vulnerable 9-position leads to carbocation intermediate **17**. Three subsequent reaction pathways are available to **17**:

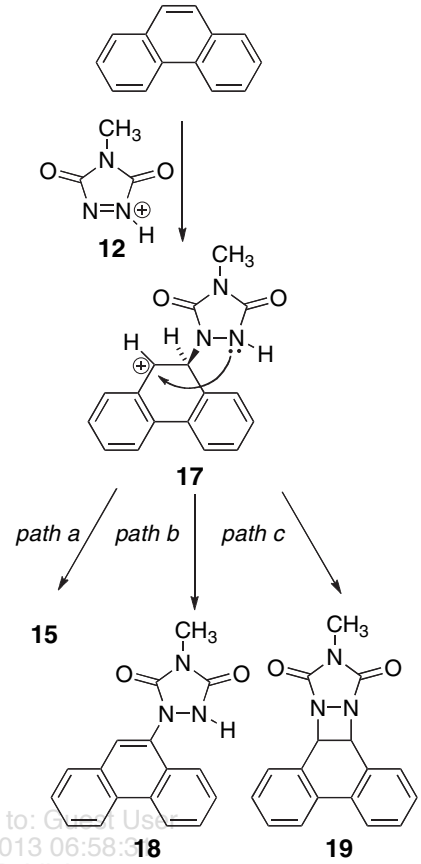
(i) trapping by a nearby TFA molecule to form observed adduct **15** (*path a*),

(ii) loss of a proton to form 1-aryl urazole **18** (*path b*), or

(iii) intramolecular attack of the lone pair on the nitrogen atom of the urazole to form (after loss of H^+) the strained diazetidine compound **19** (*path c*).

In this case, preferential trapping of carbocation intermediate **17** by TFA occurs (opposite the side of the bulky urazole heterocycle).

Interestingly, however, we found that upon prolonged standing in DMSO solutions, adduct **15** spontaneously converted to urazole **18** over about 6 days presumably via slow heterolytic loss of the trifluoroacetate group to yield carbocation **17** followed by deprotonation. Thus, *path b* is favored in the absence of sufficient concentrations of free TFA to capture the carbocation.



Scheme 4. Potential pathways for initially formed carbocation intermediate **17**. *Path a*: Trapping of the carbocation by backside attack of a free TFA molecule. *Path b*: Loss of a proton to reform the aromatic ring. *Path c*: Intramolecular trapping of the carbocation by the free lone pair on nitrogen followed by proton loss.

4. CONCLUSIONS

In summary, acid-catalyzed reactions of MeTAD with polyaromatics may yield a host of products depending upon the structure of the starting PAH. Reaction with naphthalene appears to be the result of a straightforward acid-catalyzed DA reaction. Reactions with anthracene and phenanthrene, however, are most consistent with formation of carbocation intermediates. The fate of the carbocation depends upon the individual rates of competing inter- and intramolecular reactions.

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