stimulating discussions. We express our gratitude to G. J. J. Steghuis for his contribution to parts of the experimental work. We are indebted to J. M. Visser and J. L. M. Vrielink for recording the NMR and to T. W. Stevens for recording the mass spectra.

Registry No. **1b**, 14092-11-6; **1d**, 101471-70-9; **1e**, 101471-72-1; **1f**, 52919-64-9; **1g**, 101471-74-3; **1h**, 35595-58-5; **1i**, 101471-78-7; **1j**, 101471-80-1; **2a** (R = H), 82483-74-7; **3b** (R = H), 101493-68-9; **3c** (R = H), 101471-69-6; **3d** (R = H), 101471-71-0; **3f** (R = H), 101493-69-0; **3g** (R = H), 101471-75-4; **3h** (R = H), 101471-77-6; **3j** (R = H), 101471-81-2; **4b** (R = H), 98712-11-9; **4c** (R = H), 98728-15-5; **4d** (R = H), 98712-12-0; **4e** (R = H), 98712-09-5; **4f** (R = H), 98712-13-1; **4g** (R = H), 101471-76-5; **4h** (R = H), 98712-14-2; **4i** (R = H), 101471-79-8; **4j** (R = H), 101471-82-3; **5a** (R = H), 92196-97-9; **6b**, 98712-16-4; **6c**, 98712-17-5; **6d**, 99015-75-5; **6e**, 98712-10-8; **6f**, 98712-18-6; **6h**, 98712-19-7; **8b**, 101471-73-2; DMAD, 762-42-5; $HC{\equiv}CCO_2CH_3$, 922-67-8.

Supplementary Material Available: Tables of atomic coordinates, thermal parameters, bond distances, and bond angles for **5a** (R = H) and **3g** (R = H) (15 pages). Ordering information is given on any current masthead page.

Cycloaddition Routes to Azaanthraquinone Derivatives.[1] 1. Use of Azadienophiles

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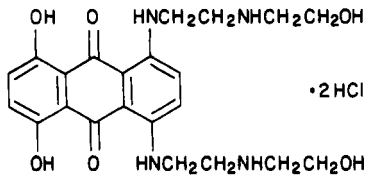
Received June 13, 1985

The mono- and diazanaphthoquinones underwent facile cycloaddition with cyclic and alicyclic dienes, and in the majority of these cycloadditions the initial 1:1-cycloadducts or their tautomers and intermediate products formed in the oxidation procedure leading to the final azaanthraquinones were isolated. Quinoline-5,8-dione and 1-methoxy-1,3-cyclohexadiene gave the 8-methoxy isomer in an essentially regiospecific cycloaddition; isoquinoline-5,8-dione, however, gave both the 5- and 8-methoxy isomers in a 2.8:1 ratio. These structural assignments were verified by alternative syntheses of the possible isomers using heteroatom-directed lithiation procedures.

Mitoxantrone (1) and related anthraquinones are of special interest in cancer chemotherapy, with mitoxantrone now undergoing clinical trials.[2] Mitoxantrone has been shown to be an intercalant[3] and, on the basis of a theoretical model[4] for intercalation, it was predicted that azaanthraquinone analogues of 1 would be very effective intercalants, and their study as potential antitumor agents is thus of considerable interest.[5] We now describe cycloaddition routes to a variety of azaanthraquinones, which establish the regiochemistry of the cycloadditions with asymmetric dienes and characterize the discrete intermediates involved in the overall reaction pathway.



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Several azaanthraquinones[6] have been described in the literature, and the synthetic routes employed have usually involved the classical Friedel–Crafts approach,[6g] introduction of the 9,10-carbonyl functions by oxidation of the corresponding hydrocarbon,[6h] or cycloaddition of an azanaphthoquinone with an appropriate diene.[6b-f] The present study establishes the Diels–Alder approach as a versatile method for introduction of substituents into the final azaanthraquinone.

Cycloadditions with Cyclic Dienes. These are expected to occur with formation of a 1:1-cycloadduct, followed by tautomerization and ready oxidation to yield a bridged ring system which can undergo thermal elimination of ethylene leading to the azaanthraquinone. Quinoline-5,8-dione (**2a**) underwent ready reaction with 1,3-cyclohexadiene (**3**: R = H) in boiling benzene over 24 h. The initial 1:1-cycloadduct separated from the cooled reaction mixture as its quinol tautomer **4a** (R = R^1 = H) (75%), and oxidation of **4a** (R = R^1 = H) with Ag_2O in DME gave the bridged-adduct 6,9-dihydro-6,9-ethanobenzo[*g*]quinoline-5,10-dione (**5a**: R = R^1 = H). The

(1) Partial support of this work by USPHS Grant CA 27241 and Lederle Laboratories is gratefully acknowledged; abstracted from the Ph.D. Thesis of E.B.W., Rensselaer Polytechnic Institute, Troy, NY, 1985.

(2) Von Hoff, D. D.; Pollard, E.; Kuhn, J.; Murray, E.; Coltman, C. A. *Cancer Res.* **1980**, *40*, 1516; for Phase II trials in breast cancer see: Coleman, R. E.; Maisey, M. N.; Knight, R. K.; Rubens, R. D. *Eur. J. Cancer Clin. Oncol.* **1984**, *20*, 771. Cornbleet, M. A.; Stuart-Harris, R. C.; Smith, I. E.; Coleman, R. E.; Rubens, R. D.; McDonald, M.; Mouridsen, H. T.; Rainer, H.; Van Osterom, A. T.; Smyth, J. F. *Eur. J. Cancer Clin. Oncol.* **1984**, *20*, 1141.

(3) Johnson, R. K.; Zee-Cheng, R. K.; Lee, W. W.; Acton, E. M.; Henry, D. W.; Cheng, C. C. *Cancer Treat. Rep.*, **1979**, *63*, 425.

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(5) For a discussion of this general topic see: Gale, E. F.; Cundliffe, E.; Reynolds, P. E.; Richmond, M. H.; Waring, M. J. "The Molecular Basis of Antibiotic Action", 2nd ed.; Wiley-Interscience: New York, 1981; pp 280–298.

(6) (a) For a review see: Baxter, I.; Davis, B. A. *Quart. Rev. Chem. Soc.* **1971**, *25*, 239. (b) Warren, J. D.; Lee, V. J.; Angier, R. B. *J. Heterocycl. Chem.* **1979**, *16*, 1617. (c) Birch, A. J.; Butler, D. N.; Siddal, J. B. *J. Chem. Soc.* **1964**, 2941. (d) Joullie, M. M.; Puthenpurayil, J. K. *J. Heterocycl. Chem.* **1969**, *6*, 697. Levy, M. R. W.; Joullie, M. M. *J. Heterocycl. Chem.* **1964**, *1*, 171. Gum, W. F.; Joullie, M. M. *J. Org. Chem.* **1965**, *30*, 2583; *Ibid.* **1967**, *32*, 53. (e) Adachi, J. *J. Chem. Soc. Jpn* **1955**, *76*, 311. (f) Munshi, J. F.; Joullie, M. M. *J. Heterocycl. Chem.* **1967**, *4*, 133. (g) Raudnitz, H. *Ber. Dtsch. Chem. Ges.* **1929**, *62*, 509. (h) Schofield, K.; Wright, D. E. *J. Chem. Soc.* **1965**, 6074.

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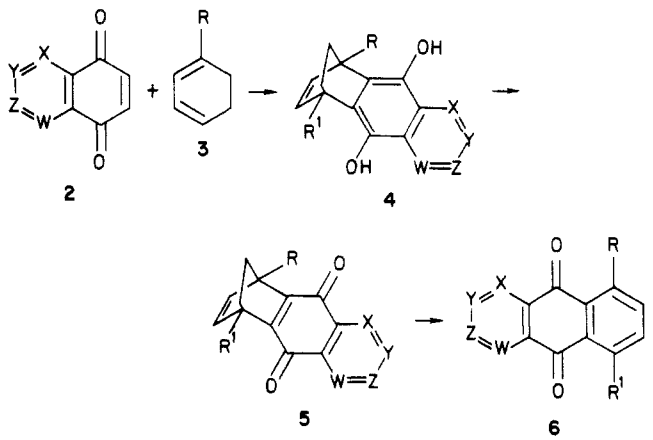
structures of these two products were readily determined from their analytical and spectral data, especially ν_{OH} 3500–3150 cm^{-1} in **4a** (R = R^1 = H) and ν_{CO} 1653 cm^{-1} in 5a (R = R^1 = H). Heating **5a** (R = R^1 = H) at 150–160 °C for 5–10 min resulted in an observable loss of ethylene to give **6a** (R = R^1 = H) which could be sublimed directly (72%) from the crude reaction melt. The overall conversion of **2a** into **6a** (R = R^1 = H) was 42%. The distinguishing ν_{CO} of **6a** (R = R^1 = H) 1680 cm^{-1}, together with other analytical data, were consistent with the assigned structure. In contrast to an earlier preparation[6c,f] of **6a** (R = R^1 = H), use of the above reaction conditions enables the initial 1:1-cycloadduct to be isolated as its tautomeric 5,10-diol **4a** (R = R^1 = H), now making these intermediate cycloadducts available for further study.

The ^1H NMR spectrum of the intermediate cycloadduct **5a** (R = R^1 = H) is of interest as it provides a reference point for others obtained in this study. The hydrogens at the 5 and 8 positions are two close-lying multiplets centered at δ 4.67 and 4.57, reflecting the electronic dissimilarity of the C-9 and C-10 carbonyl groups. Since H_8 is adjacent to the more electron deficient carbonyl group which has more π-bonding character, it is more deshielded than H_5 and is assigned the downfield chemical shift. The H_6 and H_7 hydrogens can be considered nearly equivalent and appear as a complex multiplet.

Cycloadditions of 1,3-cyclohexadiene (**3**: R = H) with the other heterocyclic quinones also yielded initial 1:1-cycloadducts **4b–e** which were isolated directly from the reaction mixture. Conversion into the oxidized quinone with silver oxide and thermal elimination of ethylene afforded the aza- and diazaanthraquinones in high yields.

Alternative syntheses of several of these azaanthraquinones were accomplished using 1-acetoxy-1,3-butadiene and 1,4-diacetoxy-1,3-butadiene. Quinoline-5,8-dione (**2a**) and 1-acetoxy-1,3-butadiene were refluxed in toluene for 24 h, affording 1-azaanthraquinone (**6a**: R = R^1 = H)



a: X = N; Y = CH; Z = CH; W = CH
b: X = N; Y = $C(CH_3)$; Z = $C(CH_3)$; W = N
c: X = N; Y = CH; Z = N; W = CH
d: X = N; Y = C(Cl); Z = CH; W = $C(CH_3)$
e: X = CH; Y = N; Z = CH; W = CH

directly (70%), the reaction proceeding by 1,4-elimination of acetic acid from the initial 1:1-cycloadduct and oxidative aromatization. Reaction of **2a** with 1,4-diacetoxy-1,3-butadiene in refluxing benzene (48 h) also afforded the azaanthraquinone **6a** (R = R^1 = H) directly (85%), the loss of 2 equiv of acetic acid by 1,2-eliminations giving the aromatized product. The other heterocyclic quinones and these dienes afforded the corresponding azaanthraquinones in 60–85% yield, and these cycloadditions are those of choice when the fully aromatic azaanthraquinones are desired.

1-Methoxy-1,3-cyclohexadiene (**3**: R = OCH_3) is also an efficient diene in Diels–Alder cycloadditions and, as an unsymmetrical diene, the regiochemistry of its cycloaddition product(s) must be considered. The C-4 carbon atom is the more nucleophilic terminus of the diene, and cycloaddition with the various heterocyclic quinones is expected to occur in a regioselective fashion, controlled by the electron distribution in the quinone used.

From the reaction of quinoline-5,8-dione (**2a**) and 1-methoxy-1,3-cyclohexadiene (**3**: R = OCH_3), Birch[6c] obtained a mixture of the 8- and 5-methoxy isomers **6a** (R = OCH_3; R^1 = H) and **6a** (R = H; R^1 = OCH_3) in a ratio of 3:2. We also isolated an analogous series of intermediate cycloadducts with the methoxy substituent in the 8-position, but the amount of the 5-methoxy product was essentially insignificant as shown by the ^1H NMR spectrum of the crude reaction mixture. The isomers occurred in a ratio of 8.9:1, but only the 8-methoxy isomer **6a** (R = OCH_3; R^1 = H) could be isolated in pure form.

This facile, highly regioselective cycloaddition may be attributed to the electron-withdrawing effect of the quinoline nitrogen atom making the C-8 carbonyl group more electron deficient, with subsequent attack of the more negative end of the diene occurring at the C-6 position. Similar effects of the pyridine ring nitrogen atom are observed in lithiation experiments described below and also in addition reactions to **2a**. Thus, aromatic amines add to **2a** to give a mixture of the 6- and 7-amino compounds, with the 6-amino product being the predominant isomer. In the presence of ceric ion, the 6-amino product is obtained exclusively.[7] Analogous rationalizations have been advanced to account for the regiochemistry observed in the cycloaddition of substituted naphthoquinones with asymmetric dienes.[8]

Isoquinoline-5,8-dione (**2e**) reacted with 1-methoxy-1,3-cyclohexadiene (**3**: R = OCH_3) in refluxing benzene to give the 1:1-cycloadduct as its quinol tautomer **4e** (R = H; R^1 = OCH_3), characterized by ν_{OH} 3400–3150 cm^{-1}. Facile oxidation with silver oxide in DME gave the bridged system **5e** (R = H; R^1 = OCH_3) which was inseparable into its regioisomers by HPLC. Heating the mixture above its melting point afforded the 5-methoxy- and 8-methoxy-2-azaanthraquinone **6e** (R = H; R^1 = OCH_3) and **6e** (R = OCH_3; R^1 = H), respectively, in a ratio of 2.8:1, this ratio being determined by ^1H NMR integration of the C-1 hydrogen in the crude reaction mixture. Based on the predicted regioselectivity of the isoquinoline-5,8-dione (**2e**), the 5-methoxy isomer was predominant as anticipated owing to the isoquinoline nitrogen decreasing the electron density at the C-5 carbonyl group. Fractional crystallization afforded the 5-methoxy isomer **6e** (R = H; R^1 = OCH_3) in pure form.

1-Methoxy-1,3-cyclohexadiene (**3**: R = OCH_3) also underwent ready cycloaddition with the other heterocyclic quinones. Reaction with 2,3-dimethylquinoxaline-5,8-dione (**2b**) in refluxing benzene gave the initial 1:1-cycloadduct as its quinol tautomer **4b** (R = OCH_3; R^1 = H), characterized by ν_{OH} at 3420 cm^{-1}. Oxidation with silver oxide gave the bridged quinone **5b** (R = OCH_3; R^1 = H) with ν_{CO} 1665 cm^{-1} in 84% yield. The appearance of only one

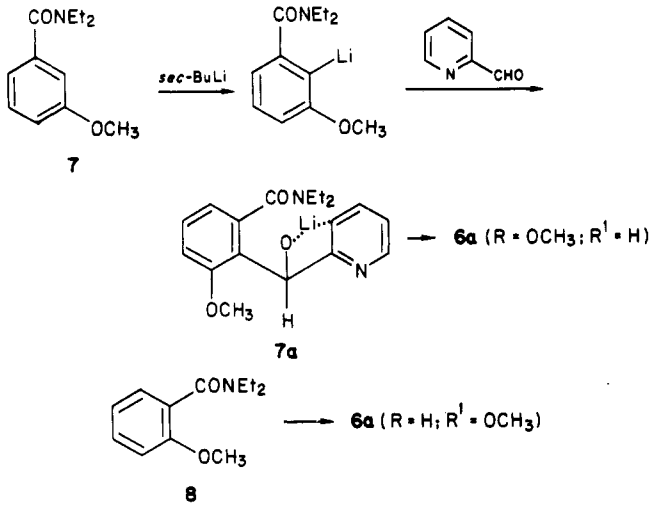
(7) Pratt, Y. T. *J. Org. Chem.* **1962**, *27*, 3905.

(8) (a) See, e.g., Manning, W. B.; Kelly, T. P.; Muschik, G. M. *Tetrahedron Lett.* **1980**, 2629. Kelly, T. R.; Montury, T. M. *Tetrahedron Lett.*, **1978**, 4311. Manning, W. B. *Tetrahedron Lett.*, **1979**, 1661. Boeckman, R. K.; Dolak, T. M.; Culos, C. O. *J. Am. Chem. Soc.*, **1978**, *100*, 7098. Rozeboom, M. D.; Teymo-Larsson, I. M.; Houk, K. N. *J. Org. Chem.* **1981**, *46*, 2338. (b) Determined by simple Hückel calculations in which the ω-technique was used to obtain self-consistency [Streitweiser, A. "Molecular Orbital Theory for Organic Chemists"; Wiley: New York, 1961; p 115].

carbonyl stretching frequency in **5b** is due to insufficient difference between the electronic character of the two carbonyl groups and is the average for the two groups. Loss of the ethylene bridge occurred upon heating **5b**, and 2,3-dimethyl-4-methoxy-1,4-diazaanthraquinone (**6b**: R = OCH_3; R^1 = H) was obtained directly by sublimation from the reaction melt. Spectral data of **6b** (R = OCH_3; R^1 = H) denoted two nonequivalent carbonyl groups with ν_{CO} at 1675 and 1650 cm^{-1}. Nonequivalency of the methyl groups in the ^1H NMR spectrum at δ 2.80 and 2.78 is also indicative of differences in the electron density at these positions.

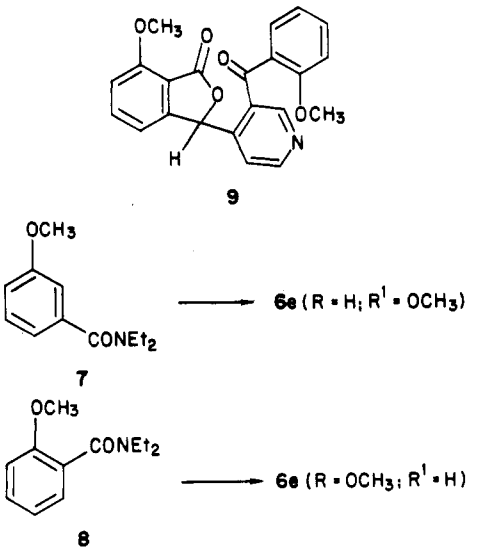
Reaction of the diene **3** (R = OCH_3) with quinazoline-5,8-dione (**2c**) proceeded in an analogous fashion. The discrete intermediates were not characterized; rather, oxidation and thermolysis were carried out consecutively. This afforded 8-methoxy-1,3-diazaanthraquinone **6c** (R = OCH_3; R^1 = H) in 55% overall yield. The regiochemistry in the cycloaddition is based on that observed with the quinoline- and isoquinoline-5,8-diones and frontier molecular orbital calculations.[8b]

In these cycloadditions with an unsymmetrical diene our initial structural assignment was based on the expected reactivity of quinoline-5,8-dione (**2a**) as indicated by molecular orbital calculations[8b] and was confirmed by an unambiguous synthesis of both isomers using a heteroatom-directed tandem lithiation procedure.[9] Lithiation of *m*-anisic acid *N,N*-diethylamide (**7**) with *sec*-BuLi in the presence of TMEDA occurred at −78 °C in ether under an argon atmosphere. Addition of pyridine-2-carbaldehyde and warming to 40 °C afforded a benzylalkoxide intermediate which, on lithiation with a second equivalent of *sec*-BuLi at −78 °C, resulted in **7a**. Cyclization and acid workup gave the 8-methoxy isomer **6a** (R = OCH_3; R^1 = H) in modest yield. 5-Methoxy-1-azaanthraquinone (**6a**: R = H; R^1 = OCH_3) was obtained in a similar manner by using *o*-anisic acid *N,N*-diethylamide (**8**) and pyridine-2-carbaldehyde.



^1H NMR and IR data were consistent with the designated structures and may be rationalized in terms of the methoxy substituent selectively increasing the electron density of the carbonyl group adjacent to it through resonance interaction and is reflected in a decrease in the carbonyl stretching frequency of this particular carbonyl group. In the 8-methoxy isomer the relative difference in the stretching frequencies of the two carbonyl groups is decreased, and absorptions at 1680 and 1670 cm^{-1} were observed. In the 5-methoxy isomer, the relative difference between the two carbonyl groups is increased with absorptions at 1685 and 1665 cm^{-1}. In both cases, the higher frequency corresponds to the carbonyl group adjacent to the nitrogen heteroatom.

The structures of the 5- and 8-methoxy-2-azaanthraquinones (**6e**, R = H; R^1 = OCH_3 and **6e**, R = OCH_3; R^1 = H) were established unambiguously by alternative syntheses of each isomer from *o*- and *m*-anisic acid *N,N*-diethylamides (**8**) and (**7**), respectively, and pyridine-4-carbaldehyde using the tandem-directed lithiation procedure employed previously. From *o*-anisic acid *N,N*-diethylamide (**8**) the 8-methoxy isomer **6e** (R = OCH_3; R^1 = H) and the lactone **9** were obtained. The structural

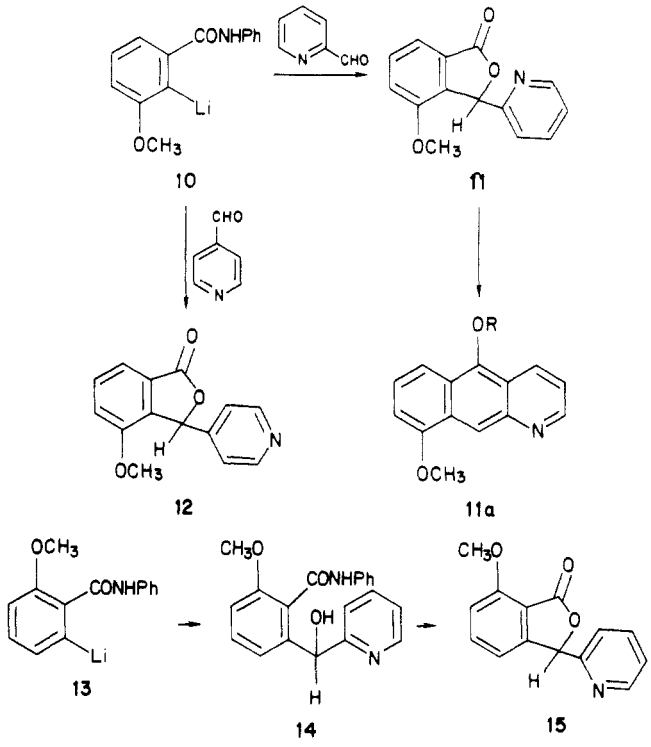


assignment of the latter was based on analytical and spectral data, especially its IR spectrum which showed ν_{CO} 1760, 1655 cm^{-1}.

The spectral data for the above two isomers are of importance for later structural assignments. The 8-methoxy isomer showed IR ν_{CO} of 1678 and 1670 cm^{-1} with the higher value corresponding to the more electron-deficient carbonyl group at C-10. The 5-methoxy isomer had ν_{CO} at 1678 cm^{-1} (C-9) and 1673 cm^{-1} (C-10). In this case the electron deficiency of the C-10 carbonyl group is reduced through resonance interaction with the methoxy substituent, and as the C-9 carbonyl group is no longer in conjugation with the methoxy group as in the 8-methoxy isomer, it would have a higher stretching frequency.

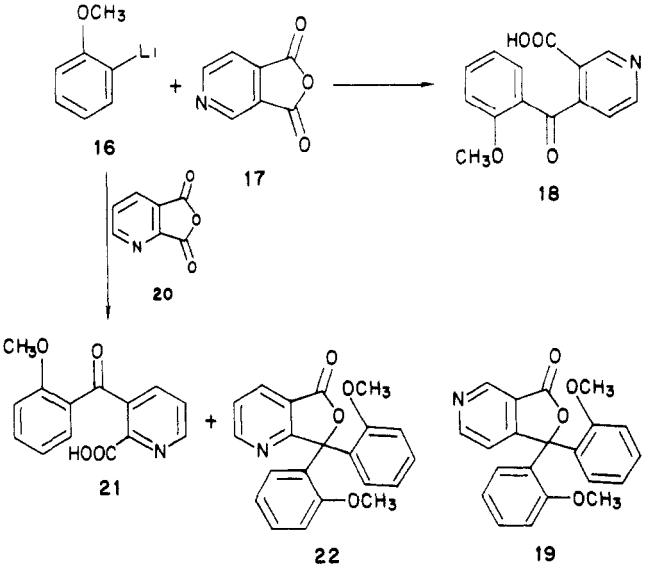
Variations of the above heteroatom-directed lithiation procedures were also studied in attempts to improve the yields of the final quinones. The lithio derivative **10**, when treated with pyridine-2- and -4-carbaldehydes, omitting the second equivalent of BuLi and using an oxalic acid workup procedure, gave rise to the phthalides **11** and **12**, respectively. In contrast, reaction of the lithio derivative **13** with pyridine-2-carbaldehyde gave the open-chain product **14**. Two factors may account for the formation of the open-chain product: reduced electrophilicity of the amide CO group due to the *o*-OCH_3 group or steric crowding in **14**. Cyclization of **14** to **15** occurred, however, when **14** was heated under reflux with *p*-toluenesulfonic acid in toluene for 6–7 h. The open-chain product **14** did not show a molecular ion in its mass spectrum, undergoing ring closure to **15** on heating in the spectrometer. The hydrogenolysis of these lactones using H_2/PdC/AcOH at 80 °C was not satisfactory; however, treatment of **11** with

(9) (a) de Silva, S. O.; Snieckus, V. *Tetrahedron Lett.* **1978**, 5103. (b) Watanabe, M.; Snieckus, V. *J. Am. Chem. Soc.* **1980**, *102*, 1457. (c) Snieckus, V. *Heterocycles*, **1980**, *14*, 1649. (d) Kende, A. S.; Rizzi, J. P. *J. Am. Chem. Soc.* **1981**, *103*, 4247.



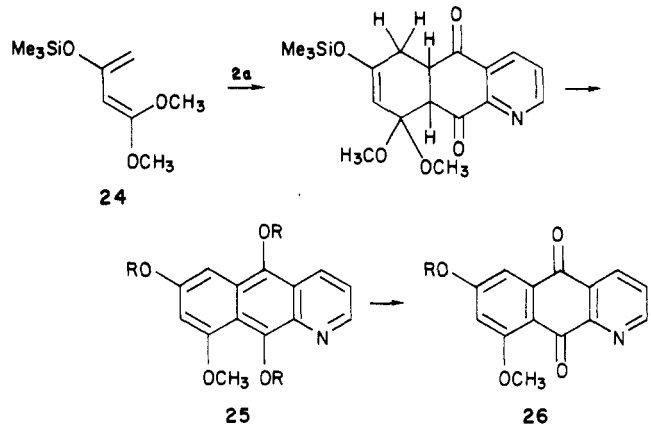
zinc and formic acid[9d] resulted in formation of **11a** (R = H) which was characterized as its trifluoroacetate **11a** (R = $COCF_3$).

Two additional methods were also studied. 2-Lithioanisole (**16**) was treated with pyridine-3,4-dicarboxylic acid anhydride (**17**) at −100 °C in THF. After the usual re-



action workup, the keto acid **18** together with the bis-adduct **19** were obtained. A similar, essentially regiospecific ring opening of **17** with 1-(phenylsulfonyl)-2-lithioindole, has been reported recently.[10] Attempts to convert **18** into the azaanthraquinone with a variety of cyclocondensation agents (e.g., concentrated H_2SO_4, PPA, $(CF_3CO)_2O$) were unsuccessful, although the ring closure of 2-chloro-3-(2,5-dimethoxybenzoyl)isonicotinic acid to 1-chloro-5,8-dihydroxy-2-azaanthracene-9,10-dione occurred in 57% yield with methanesulfonic acid at 120 °C. Sulfuric acid was found to be unsatisfactory.[10] Similarly, reaction of **16** with pyridine-2,3-dicarboxylic acid anhydride (**20**) at −100 °C/THF gave **21** and **22**. The keto acid **21** did not cyclize to the azaanthraquinone in more than trace amounts.

Cycloadditions with Siloxyl Dienes. *trans*-1-Methoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene[11a] (**23**) (Danishefsky's diene) and 1,1-dimethoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene[11b] (**24**) underwent facile cycloaddition with the above quinones. Quinoline-5,8-dione (**2a**) and **24** in refluxing benzene under an inert atmosphere for $2^1/_2$ h gave, upon quenching in ice water, the quinol form **25** (R = H). This was converted into the triacetate **25** (R = Ac) (acetic anhydride in pyridine) for purification and characterization. Increasing the reaction time of the above cycloaddition to 16 h in the presence of air resulted in the oxidized product 6-hydroxy-8-methoxy-1-azaanthraquinone (**26**: R = H) being obtained directly and characterized by ν_{OH} 3400–3000 cm^{-1} and ν_{CO} 1660, 1655 cm^{-1}. Acetylation afforded the corresponding monoacetate **26** (R = Ac) in high yields. In both these cycloadditions, only



one isomer was obtained, and structural assignments were based on the established regioselectivity of the reacting components and spectral data.

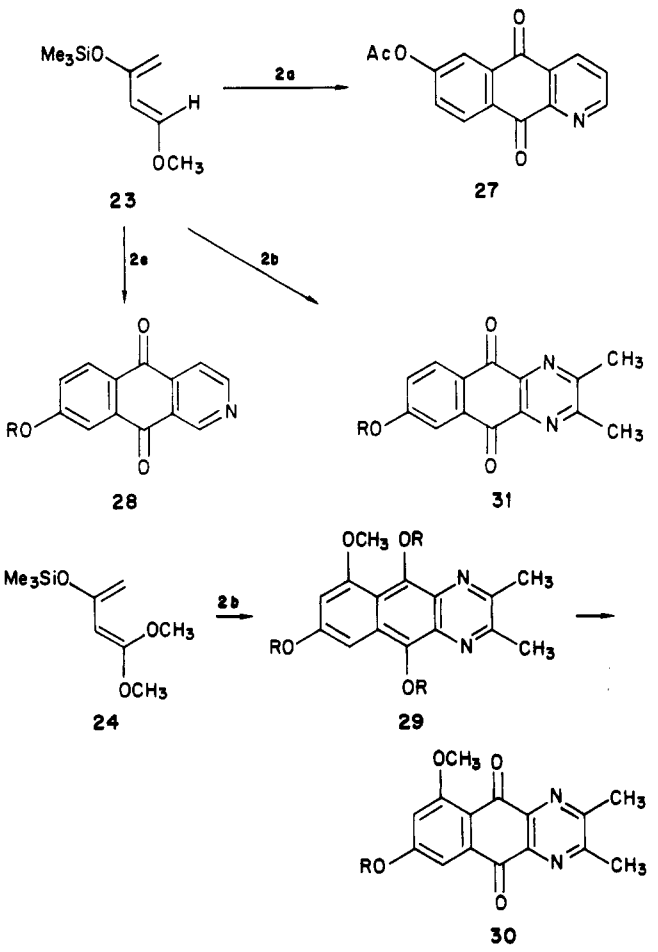
Quinoline-5,8-dione (**2a**) reacted with Danishefsky's diene **23** under similar conditions and gave, in a highly regioselective cycloaddition, the 6-acetoxy derivative **27** (75%) after acetylation of the reaction product. In contrast to the other cycloadditions with quinoline-5,8-dione, it was not possible to isolate any intermediates in this reaction.

The reaction of isoquinoline-5,8-dione (**2e**) and **23** also gave a regioselective cycloaddition. A single desilylated oxidized product **28** (R = H) with ν_{OH} 3500–3400 cm^{-1} and ν_{CO} 1655 cm^{-1} was obtained. This product was characterized further as its monoacetate **28** (R = Ac) with ν_{CO} 1740, 1665, and 1650 cm^{-1} and, based on the known reactivity patterns of the reagents, its structure was assigned as 7-acetoxy-2-azaanthraquinone (**28**: R = Ac).

Complete characterization of the intermediate cycloadducts from reactions of 2,3-dimethylquinoxaline-5,8-dione (**2b**) and the silyloxyl dienes was possible with the quinone **2b** and **24** in refluxing benzene giving the trihydroxy compound **29** (R = H) (90%), characterized by ν_{OH} 3490–3200 cm^{-1}. Acetylation of the trihydroxy compound afforded the corresponding acetate **29** (R = Ac), with ν_{CO} 1760 cm^{-1} and, after oxidation, compound **29** (R = H) was converted into the quinone **30**, identified by ν_{CO} 1680, 1650 cm^{-1} and ν_{OH} 3350–2950 cm^{-1}.

(10) (a) Sauliner, M. G.; Gribble, G. W. *J. Org. Chem.* **1982**, *47*, 2810. (b) Croisy-Delcey, M.; Bisagni, E. *J. Chem. Soc., Chem. Commun.* **1984**, 897.

(11) (a) Danishefsky, S.; Kihara, T. *J. Am. Chem. Soc.*, **1974**, *96*, 7807. (b) Banvile, J.; Brassard, P. *J. Chem. Soc., Perkin Trans. 1*, **1976**, 1985.



With Danishefsky's diene **23**, the quinone **2b** gave the oxidized cycloadduct **31** (R = H) directly (71%), with ν_{OH} 3550–3500 cm^{-1} and ν_{CO} 1655 cm^{-1}. This cycloadduct was further characterized as its acetate **31** (R = Ac), ν_{CO} 1755, 1655, and 1600 cm^{-1}.

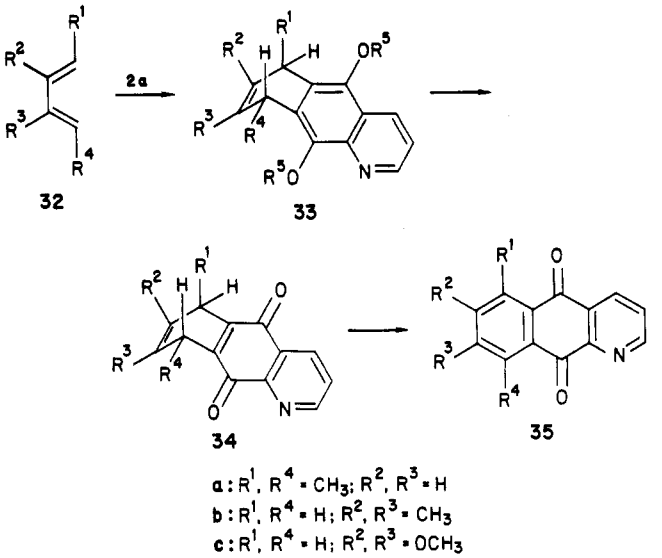
Cycloadditions with Alicyclic Dienes. In contrast to the above cycloadditions, aromatization of the intermediate cycloadducts obtained with this series of dienes involves a final dehydrogenation. Of the methods available for this transformation, oxidative aromatization in the presence of NaOH or KOH was found to be the most satisfactory.

Cycloaddition of 1,4-dimethyl-1,3-butadiene (**32a**), 2,3-dimethyl-1,3-butadiene (**32b**), and 2,3-dimethoxy-1,3-butadiene (**32c**) occurred readily with the quinones **2**. Thus, quinoline-5,8-dione (**2a**) and **32a** in boiling ethanol for 24 h gave in 80% yield the initial 1:1-cycloadduct (80%) as its tautomer **33a** (R^5 = H), ν_{OH} 3350–3100 cm^{-1}(s). Treatment of this cycloadduct with silver oxide resulted in a facile oxidation of the hydroquinone moiety to the quinone **34a**.

The methylene hydrogens H_5 and H_8 of the quinone **34a** appear as a broad multiplet in its ^1H NMR spectrum. The methyl groups are also not equivalent and are found as close-lying doublets centered at δ 1.32 and 1.29. Since the C-8 methyl group is adjacent to the more electron deficient carbonyl group which has more π-bonding character, this was assigned the downfield chemical shift. The C-6 and C-7 hydrogens are a doublet at δ 5.87 and are not affected by the dissimilar carbonyl groups.

Cycloaddition of 2,3-dimethyl-1,3-butadiene (**32b**) and quinoline-5,8-dione (**2a**) under similar reaction conditions resulted in the dihydro tautomer **33b** (R^5 = H) (87%) of the initial 1:1-cycloadduct. The diol was readily oxidized with Ag_2O in DME to 5,8-dihydro-6,7-dimethyl-1-azaanthraquinone (**34b**) in high yield, characterized by ν_{CO} 1670, 1660 cm^{-1}. The 5,8-methylene hydrogens were readily distinguishable appearing as a multiplet centered at δ 3.23 due to their nonequivalency. Treatment of **33b** (R^5 = H) with acetic anhydride afforded the corresponding diacetate **33b** (R^5 = Ac), the most convenient method of purification and characterization.

Oxidative aromatization of the quinol **33b** (R^5 = H) in the presence of KOH gave 6,7-dimethyl-1-azaanthraquinone (**35b**) (82%). Spectral and analytical data es-



a: R^1, R^4 = CH_3; R^2, R^3 = H
b: R^1, R^4 = H; R^2, R^3 = CH_3
c: R^1, R^4 = H; R^2, R^3 = OCH_3

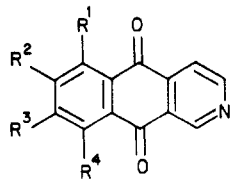
tablished this structure, especially ν_{CO} 1680, 1665 cm^{-1}, and the ^1H NMR data in which the nonequivalence of the C-5 and C-8 hydrogens resulted in them being well-separated singlets. This correlates with the variation in electron density associated with the carbonyl groups with the C-9 carbonyl group being more electron deficient than that at C-10. Consequently, the adjacent C-8 hydrogen is deshielded and occurs at δ 8.19. The C-5 hydrogen occurred slightly upfield at δ 8.08. The 6,7-methyl groups, a singlet at δ 2.47, were magnetically equivalent, indicating that there is no long-range shielding effect from the carbonyl groups.

2,3-Dimethoxy-1,3-butadiene (**32c**) and the quinone **2a** under similar reaction conditions did not afford any of the intermediate cycloadducts **33c** and **34c** in a pure state. The product initially isolated was oxidized directly with air in the presence of NaOH to give 6,7-dimethoxy-1-azaanthraquinone (**35c**) in 85% yield.

These alicyclic dienes also underwent ready reaction with isoquinoline-5,8-dione (**2e**); with **32a** in refluxing benzene (24 h) in the presence of air 5,8-dimethyl-2-azaanthraquinone (**36a**) was obtained directly (65%), oxidation of the intermediate cycloadducts occurring in the reaction mixture under these conditions. In the ^1H NMR spectrum of **36a** the 5,8-methyl substituents were nonequivalent and the 5-methyl group, being adjacent to the more electron deficient carbonyl group, was observed at δ 2.83, whereas the 8-methyl group was at δ 2.81. The C-6 and C-7 hydrogens had equivalent chemical shifts, appearing as a singlet at δ 7.41, and IR data were consistent with this structure.

2,3-Dimethoxy-1,3-butadiene (**32c**) and **2e** under analogous reaction conditions gave a mixture of the dihydro 1:1-cycloadduct and the fully oxidized product. Oxidation with air in methanolic NaOH converted the mixture into the fully oxidized 2,3-dimethoxy-2-azaanthraquinone (**36c**) (30%).

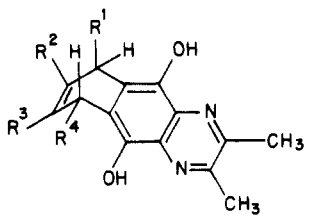
2,3-Dimethylquinoxaline-5,8-dione (**2b**) has been shown



36

a: R^1, R^4 = CH_3; R^2, R^3 = H
b: R^1, R^4 = H; R^2, R^3 = CH_3
c: R^1, R^4 = H; R^2, R^3 = OCH_3

by Joullie[6d] to react with 1,4-dimethyl-1,3-butadiene (**32a**) in refluxing ethanol (6 h) to give both the 1:1-cycloadduct and its quinol tautomer. By carrying out this reaction for 20 h, we obtained only the 1:1-cycloadduct as its quinol tautomer **37a** (90%). Spectral data established this structure, especially ν_{OH} 3500–3400 cm^{-1}. Also, the 5,8-methylene hydrogens appeared as a complex multiplet centered at δ 1.85 in the ^1H NMR spectrum. Oxidation occurred readily with silver oxide to give 5,8-dihydro-2,3,6,7-tetramethyl-1,4-diazaanthraquinone (**38a**) in 90% yield.



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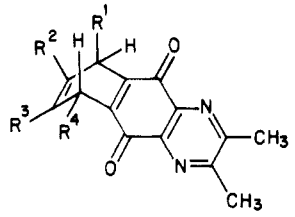


38

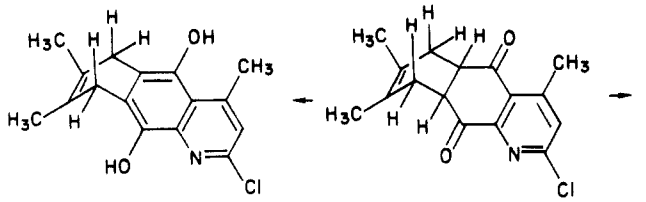
a: R^1, R^4 = CH_3; R^2, R^3 = H
b: R^1, R^4 = H; R^2, R^3 = CH_3

Reaction of the quinone **2b** with 2,3-dimethyl-1,3-butadiene (**32b**) under analogous conditions also gave the tautomeric form of the initial 1:1-cycloadduct **37b** in 90% yield. This quinol underwent ready oxidation with silver oxide to afford the corresponding quinone **38b**.

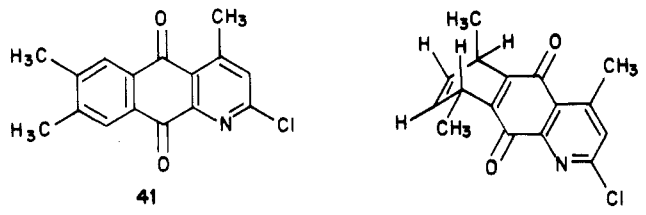
Our long-range interests in this area require the use of functionalized azaanthraquinones in these cycloadditions, and the cycloaddition of 2-chloro-4-methylquinoline-5,8-dione (**2d**) and 2,3-dimethyl-1,3-butadiene (**32b**) was thus of interest. In refluxing ethanol for 20 h the initial 1:1-cycloadduct **39** was obtained (95%). In contrast to the other reactions using this diene, none of the quinol tautomer was isolated. The ^1H NMR spectrum of **39** showed the ring junction hydrogens H_{8a} and H_{10a} as a complex multiplet at δ 3.55–3.25, with the methylene hydrogens appearing as a multiplet at δ 2.48–2.13. The C-6 and C-7 methyl groups were magnetically equivalent occurring as a singlet at δ 1.68.

Treating **39** with 40% HCl in ethanol at 90 °C effected tautomerization to the quinol **40** (60% conversion) indicated by ν_{OH} 3500–3410 cm^{-1}. The acidic condition prevented concurrent oxidation. When the 1:1-adduct **39** was treated with ethanolic KOH and air bubbled through the solution, oxidative aromatization occurred affording 1-chloro-4,6,7-trimethyl-1-azaanthraquinone (**41**) (57% overall yield).

Reaction of the quinone **2d** with 1,4-dimethyl-1,3-butadiene (**32a**) in boiling ethanol for **24** h gave the partially oxidized cycloadduct, 2-chloro-5,8-dihydro-4,5,8-trimethyl-1-azaanthraquinone (**42**). This separated directly from the cooled reaction mixture and was characterized by ν_{CO} 1650 cm^{-1}.



40 39



41 42

Experimental Section[12]

Use of the following experimental conditions results in advantageous, reproducible syntheses of the following heterocyclic quinones.

Isoquinoline-5,8-dione (2e). Isoquinoline (43.0 g, 0.333 mol) was dissolved in concentrated H_2SO_4 (200 mL), a considerable amount of heat being evolved, and the solution was then cooled to 0 °C and stirred mechanically while KNO_3 (35.0 g, 0.347 mol) in H_2SO_4 (200 mL) was added dropwise over 2 h. After being kept below 50 °C for 6 h, the reaction was poured onto ice and neutralized with cold aqueous ammonia. Filtration and recrystallization from ethanol afforded 5-nitroisoquinoline as long yellow needles: 49.9 g (86%), mp 108–110 °C (lit.[13] mp 110 °C). A mixture of this 5-nitroisoquinoline (20.9 g, 0.115 mol), activated carbon (NuChar, 2.64 g), $FeCl_3 \cdot 6\ H_2O$ (0.20 g), and methanol (80 mL) was refluxed for 10 min with stirring. Anhydrous hydrazine (9.6 g, 0.30 mol) was added dropwise over 20 min, and the mixture was refluxed until TLC indicated that the nitro compound had been consumed (16 h). The mixture was cooled and filtered, and the filtrate was evaporated to dryness. The resultant solid was dissolved in a minimum volume of boiling $CHCl_3$, treated with decolorizing carbon and filtered, and the filtrate was poured into a large excess of petroleum ether (bp 30–60 °C). Filtration gave the desired amino compound as light yellow needles: 13.6 g (79%), mp 126–129 °C (lit.[14] mp 128–129 °C).

Formation of 5,8-diaminoisoquinoline required special attention to the following details. 5-Aminoisoquinoline (7.2 g, 0.05 mol) was dissolved in 1 N AcOH (100 mL), and a saturated Na_2CO_3 solution (100 mL) was added. A slurry of diazotized sulfanilic acid[15] (0.007 mol) was slowly added to this solution at 7–9 °C with stirring. After 30 min, the red azo dye was salted out with the

(12) Spectral characterizations were carried out on the following instruments: infrared spectra, Perkin-Elmer Model 298 or 337 spectrophotometers; ^1H NMR spectra, Perkin-Elmer R600 or Varian XL-200 spectrometer using Me_4Si as an internal standard; ^{13}C NMR, Varian XL-200 spectrometer at 50.3 MHz using Me_4Si as an internal standard: mass spectra, Hitachi Perkin-Elmer RMU-6E and Hewlett-Packard 5987A GC-MS System utilizing the direct insertion probe for solid samples with a variable leak gas/liquid inlet for perfluorokerosene standard. All melting points were determined in capillaries in a Thomas-Hoover capillary melting point apparatus or a Mel-Temp apparatus and are uncorrected. Evaporations were carried out under reduced pressure using a Buchi Rotovap apparatus. Microanalyses were performed by Galbraith Laboratories, Knoxville, TN and Atlantic Microlab, Inc., Atlanta, GA. Anhydrous solvents were prepared as follows: tetrahydrofuran (THF), stored over potassium hydroxide, refluxed and distilled with either metallic potassium or sodium/benzophenone; *N,N*-dimethylformamide (DMF), acetonitrile and methylene chloride, stored over 3-Å molecular sieves and decanted; toluene, benzene, hexane, and diethyl ether, stored over metallic sodium for a minimum of 12 h and decanted. Separations were performed using silica gel gravity or flash columns, preparative thin-layer plates, or a Waters Prep 500A HPLC system. Analytical data (±0.4% C, H, N) were obtained for products noted in Experimental Section.

(13) Le Fevre, C. G.; Le Fevre, R. J. W. *J. Chem. Soc.* **1935**, 1470.
(14) Joseph, P. K.; Joullie, M. M. *J. Med. Chem.* **1964**, *7*, 801.
(15) Fieser, L. F. "Experiments in Organic Chemistry", 3rd ed., Heath: Boston, MA, 1957; p 192.

addition of saturated sodium chloride solution (100 mL) and collected by filtration. It was then suspended in water (300 mL) containing sodium hydroxide (8.0 g), heated to 50 °C, and treated with sodium dithionite (30.0 g). The red solution turned green and the temperature spontaneously rose to 60 °C. It was kept at 60 °C for 30 min and finally cooled to room temperature. The solution was made strongly alkaline with sodium hydroxide (15.0 g) and was *rapidly extracted with* $CHCl_3$ (*5 × 150 mL*). The combined $CHCl_3$ solution was washed with saturated sodium chloride (2 × 100 mL), dried (Na_2SO_4), filtered, and evaporated to dryness. The diamino compound was obtained as light brown needles: 1.89 g (24%), mp 132–133 °C (lit.[14] mp 138–140 °C) and was satisfactory for the next step.

5,8-Diaminoisoquinoline (5.0 g, 0.003 mol) was dissolved in a mixture of 12 N H_2SO_4 (4 mL) and H_2O (200 mL). A mixture of 10% w/v potassium dichromate solution (20 mL) and 12 N H_2SO_4 (17 mL) was added with stirring, followed by a mixture of dichromate solution (80 mL) and 12 N H_2SO_4 (17 mL), and finally by fresh $CHCl_3$ (190 mL). After 10 min, stirring was discontinued and the $CHCl_3$ layer removed. The stirring was resumed with the addition of fresh $CHCl_3$ (190 mL). After another 10 min the $CHCl_3$ layer was withdrawn and replaced by two additional portions of $CHCl_3$ (95 mL) which were drawn off after 40 and 60 min total reaction time. The combined chloroform solutions were washed twice with saturated NaCl solution and once with H_2O, dried (Na_2SO_4), treated with decolorizing carbon, and filtered. The solution was concentrated and poured into petroleum ether (500 mL, bp 30–60 °C). The quinone precipitated as a fine yellow powder which was collected by filtration and dried to yield 2.0 g (40%), mp 136–138 °C, dec (lit.[14] mp 135–138 °C, dec).

Quinazoline-5,8-dione (2c). A stirred solution of 5,8-dimethoxyquinazoline[16] (2.0 g, 0.01 mol) in acetonitrile (30 mL) was treated with ceric ammonium nitrate (23.0 g, 4 equiv.) in water (30 mL) over a 5-min period. After stirring for an additional hour, the reaction mixture was extracted with $CHCl_3$ (3 × 100 mL), and the $CHCl_3$ extract was washed with water, dried (anhydrous Na_2SO_4), and then evaporated. The oily residue was triturated with ether yielding the quinone as yellow irregular prisms: 0.8 g (48%), mp > 300 °C dec (lit.[16] mp > 350 °C dec); IR ν_{CO} (KBr) 1685, 1670 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$–Me_2SO-d_6) δ 9.15 (s, 1, H_4), 8.74 (s, 1, H_2), 6.75 (d, 1, J = 8.0 Hz, H_7), 6.31 (d, 1, J = 8.0 Hz, H_6).

2-Chloro-4-methylquinoline-5,8-dione (2d). (a) 2-Chloro-5,8-dihydroxy-4-methylquinoline. A mixture of 2-chloro-5,8-dimethoxy-4-methylquinoline[17] (9.0 g, 0.04 mol) and anhydrous $AlCl_3$ (25 g) in dry benzene (250 mL) was heated under reflux with vigorous stirring for 7 h, during which appreciable solid separated. The cooled reaction mixture was poured into ice water (500 mL), and the separated material was collected, washed thoroughly with water, and dried. It crystallized from EtAc–hexane as light yellow irregular prisms: 5.5 g (70%), mp 190–191 °C; anal. for $C_{10}H_8ClNO_2$: IR ν_{OH} (KBr) 3500–2900 (b), $\nu_{C=N}$ 1615 cm^{-1}; ^1H NMR δ (60 MHz, Me_2SO-d_6) δ 7.25 (s, 1, H_3), 6.87 (overlapping d, 2, J = 9.0 Hz, H_6, H_7), 2.83 (s, 3, CH_3); MS, M^+· 209 (100), [M + 1] 210 (20), [M + 2] 211 (35).

(b) Oxidation to the Quinone. A mixture of the above dihydroxy compound (2.0 g, 0.001 mol) and purified[18] Ag_2O (2.7 g, 1.2 equiv) in DME (10 mL) was stirred at room temperature in the dark for 6 h. The reaction mixture was filtered through a sintered glass funnel, the residue was washed with hot $CHCl_3$, and the combined filtrates were evaporated to yield the quinone as yellow needles when recrystallized from CH_2Cl_2–hexane: 1.8 g (93%), mp 145–146 °C dec; anal. for $C_{10}H_6ClNO_2$; IR ν_{CO} (KBr) 1680, 1655 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 7.54 (s, 1, H_3), 7.08 (s, 2, H_6, Hz), 2.81 (s, 3, CH_3); MS, M^+· 207 (100), [M + 2] 209 (42), [M + 3] 210 (8).

The following general procedures for the reaction of the various azanaphthoquinones with dienes allow the isolation of the intermediate cycloadducts as well as the azaanthraquinones.

Cycloaddition with Cyclic Dienes. (a) Isolation of the Tautomeric Initial 1:1-Cycloadduct. Quinoline-5,8-dione[19] (**2a**) (6.1 g, 0.038 mol) and 1,3-cyclohexadiene (**3**: R = H) (16.0 g, mol) in anhydrous benzene (100 mL) were heated under reflux for 24 h. The solid that separated from the cooled reaction mixture crystallized from benzene giving 5,10-dihydroxy-6,9-dihydro-6,9-ethanobenzo[*g*]quinoline (**4a**: R^1 = R = H) as yellow needles (benzene): 6.9 g (75%), mp 182–184 °C; anal. for $C_{15}H_{13}NO_2$; IR ν_{OH} (KBr) 3500–3150 cm^{-1}; MS, M^+· 239 (27); ^1H NMR (60 MHz, $CDCl_3$) δ 9.72 (dd, 1, $J_{2,3}$ = 5.5 Hz, $J_{2,4}$ = 2.0 Hz, H_2), 8.57 (dd, 1, $J_{4,3}$ = 8.0 Hz, $J_{4,2}$ = 2.0 Hz, H_4), 7.38 (dd, 1, $J_{3,4}$ = 8.0 Hz, $J_{3,2}$ = 5.5 Hz, H_3), 6.64 (d, 1, $J_{6,7}$ = 4.0 Hz, H_6 or H_7), 4.58 (m, 2, H_5 and H_8), 1.56 (m, 4, CH_2). The following compounds were obtained by this procedure: **4b** [(R = H; R^1 = H), yellow needles (CH_2Cl_2/EtOH), 84%: mp 240–241 °C; IR ν_{OH} (KBr) 3500–3070 cm^{-1}; MS, M^+· 268 (17); ^1H NMR δ (200 MHz, $CDCl_3$) 7.04 (br s, 2, OH), 6.62–6.47 (m, 2, H_6 and H_7), 4.56–4.51 (m, 2, H_5 and H_8), 2.69 (s, 6, CH_3), 1.66–1.58 (m, 4, CH_2)]; **4b** [(R = OCH_3; R^1 = H), yellow microneedles (EtOH) 94%: mp 209–210 °C dec; anal. for $C_{17}H_{18}N_2O_3$; IR ν_{OH} (KBr) 3350–3100 cm^{-1}; MS, M^+· 298 (12); ^1H NMR δ (60 MHz, $CDCl_3$) 7.27 (d, 1, $J_{6,7}$ = 7.0 Hz, H_6), 6.65 (d, 1, $J_{6,7}$ = 7.0 Hz, H_7), 4.52 (br s, 1, H_8), 3.77 (s, 1, OCH_3), 2.77 (s, 1, CH_3), 2.69 (s, 1, CH_3), 1.95–1.65 (m, 4, CH_2)].

(b) Isolation of the Oxidized Initial 1:1-Cycloadduct. 5,10-Dihydroxy-6,9-dihydro-6,9-ethanobenzo[*g*]quinoline **4a** (R = R^1 = H) (2.4 g, 0.01 mol) in DME (30 mL) was stirred with Ag_2O (2.8 g, 0.012 mol) at room temperature in the dark for 6 h. The reaction mixture was filtered through a sintered glass funnel, and the residue was washed well with hot $CHCl_3$. Evaporation of the $CHCl_3$ and recrystallization of the residue from ethanol afforded 6,9-dihydro-6,9-ethanobenzo[*g*]quinoline-5,8-dione (**5a**: R = R^1 = H) as light brown needles, changing to yellow at 160–165 °C and finally melting at 283–284 °C: 1.85 g (78%); anal. for $C_{15}H_{11}NO_2$; MS, M^+· 237 (12%); IR ν_{CO} (KBr) 1653 cm^{-1}; ^1H NMR δ (200 MHz, $CDCl_3$) 9.00 (dd, 1, $J_{2,4}$ = 1.82 Hz, $J_{2,3}$ = 4.71 Hz, H_2), 8.43 (dd, 1, $J_{4,3}$ = 7.87 Hz, $J_{4,2}$ = 1.82 Hz, H_4), 7.65 (dd, 1, $J_{3,2}$ = 4.71 Hz, $J_{3,4}$ = 7.87 Hz, H_3), 6.44–6.46 (m, 2, H_6 and H_7), 4.69–4.54 (m, 2, H_5 and H_8), 1.64–1.43 (m, 4, CH_2). The following compounds were obtained by this procedure: **5b** [(R = R^1 = H), yellow needles (CH_2Cl_2/EtOH), 76%; IR ν_{CO} (KBr) 1675 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.62–6.48 (m, 2, H_6 and H_7), 4.61–4.49 (m, 2, H_5 and H_8), 2.75 (s, 6, CH_3), 1.62–1.58 (m, 4, CH_2)], **5b** [(R = OCH_3; R^1 = H), yellow needles (EtOH), 87%, mp 238–240 °C: anal. for $C_{17}H_{16}N_2O_3$; MS, M^+· 296 (7); IR ν_{CO} (KBr) 1665 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.65 (d, 1, $J_{6,7}$ = 7.93 Hz, H_6), 6.44 (m, 1, $J_{7,8}$ = 5.96 Hz, $J_{6,7}$ = 7.93 Hz, H_7), 4.60–4.56 (m, 1, H_8), 3.70 (s, 3, OCH_3), 2.77 (s, 3, CH_3), 2.76 (s, 3, CH_3), 1.88–1.60 (m, 4, CH_2)], **5c** [(R = R^1 = H), yellow irregular prisms ($CHCl_3$/EtOH), 86%, mp 225–227 °C dec: anal. for $C_{14}H_{10}N_2O_2$: IR ν_{CO} (KBr) 1655, 1645 cm^{-1}; M^+· 238 (6); NMR (200 MHz, $CDCl_3$) δ 9.51 (s, 1, H_4), 9.65 (s, 1, H_2), 6.53–6.47 (m, 2, H_6 and H_7), 4.67–4.56 (m, 2, H_5 and H_8), 1.66–1.43 (m, 4, CH_2)], **5d** [(R = R^1 = H), yellow irregular prisms (CH_2Cl_2/EtOH), 42%, mp 221–223 °C dec: anal. for $C_{16}H_{12}ClNO_2 \cdot {}^1/_4\ H_2O$: IR ν_{CO} (KBr) 1670, 1648 cm^{-1}; MS, M^+· 285 (16); ^1H NMR (60 MHz, $CDCl_3$) δ 7.42 (s, 1, H_3), 6.49 (d, 1, J = 7.5 Hz, H_6 or H_7), 6.42 (d, 1, J = 7.5 Hz, H_6 or H_7), 4.57 (br m, 2, H_8 and H_5), 2.79 (s, 3, CH_3), 1.49 (m, 4, CH_2)], **5e** [(R = R^1 = H), bright yellow needles[20] (CH_2Cl_2/EtOH), 68%, mp 155 °C, resolidifying and melting at 177–178 °C: anal. for $C_{15}H_{11}NO_2$; IR ν_{CO} (KBr) 1663, 1648 cm^{-1}; MS, M^+· 237 (15); ^1H NMR (200 MHz, $CDCl_3$) δ 9.33 (d, 1, $J_{1,4}$ = 0.76 Hz, H_1), 9.02 (dd, 1, $J_{4,3}$ = 4.95 Hz, $J_{1,3}$ = 0.76 Hz, H_3), 7.87 (dd, 1, $J_{3,4}$ = 4.95 Hz, H_4), 6.55 (d, 1, $J_{6,7}$ = 7.60 Hz, H_6), 6.46 (d, 1, $J_{6,7}$ = 7.60 Hz, H_7), 4.57–4.54 (m, 2, H_5 and H_8), 1.60–1.42 (m, 4, CH_2)].

(c) Isolation of the Azaanthraquinone. (i) 6,9-Dihydro-6,9-ethanobenzo[*g*]quinoline-5,8-dione (**5a**: R = R^1 = H) (1.0 g, 0.004 mol) was heated at 150–160 °C for 5–10 min. An observable

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loss of ethylene occurred and the residue was sublimed directly from the sublimation apparatus in vacuo affording 1-azaanthracene-9,10-dione (**6a**: R = R^1 = H) as pale yellow needles: 0.6 g (72%), mp 272–275 °C (lit.[6c] mp 273–275 °C). The overall yield to **6a** (R = R^1 = H) from the quinone **2a** was 42%: anal. for $C_{13}H_7NO_2$; IR ν_{CO} (KBr) 1680 cm^{-1}; MS, M$^+$· 209 (100); ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.14 (dd, 1, $J_{2,3}$ = 4.46 Hz, $J_{2,4}$ = 1.34 Hz, H_2), 8.56 (dd, 1, $J_{4,3}$ = 7.94 Hz, $J_{4,2}$ = 1.34 Hz, H_4), 8.46–8.32 (m, 2, aromatic), 7.92–7.83 (m, 2, aromatic), 7.77 (dd, 1, $J_{3,2}$ = 4.46 Hz, $J_{3,4}$ = 7.94 Hz, H_3). **6a** (R = OCH_3; R^1 = H), yellow needles (EtOAc), 54%, mp 198–199 °C: anal. for $C_{14}H_9NO_3$; IR ν_{CO} (KBr) 1680, 1665 cm^{-1}; MS, M$^+$· 239 (100); ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.16 (dd, 1, $J_{3,2}$ = 4.46 Hz, $J_{2,4}$ = 2.50 Hz, H_2), 8.61 (dd, 1, $J_{4,3}$ = 7.84 Hz, $J_{2,4}$ = 2.50 Hz, H_4), 8.00 (dd, 1, $J_{5,6}$ = 8.05 Hz, $J_{5,7}$ = 1.11 Hz, H_5), 7.80 (overlapping dd, 1, $J_{5,6}$ = 8.05 Hz, $J_{6,7}$ = 8.05 Hz, H_6), 7.72 (dd, 1, $J_{4,3}$ = 7.84 Hz, $J_{3,2}$ = 4.46 Hz, H_3), 7.44 (dd, 1, $J_{5,6}$ = 1.11 Hz, $J_{6,7}$ = 8.05 Hz, H_7), 4.08 (s, 3, OCH_3). **6b** (R = R^1 = H) yellow needles (EtOH), 63%, mp 243–244 °C: anal. for $C_{14}H_{10}N_2O_2$; IR ν_{CO} (KBr) 1670 cm^{-1}; MS, M$^+$· 238 (100); ^{1}H NMR (60 MHz, $CDCl_3$) δ 8.49–8.35 (m, 2, aromatic), 7.96–7.81 (m, 2, aromatic), 2.84 (s, 6, CH_3). **6b** (R = OCH_3; R^1 = H), yellow microneedles by sublimation, 68%, mp 278–279 °C: anal. for $C_{15}H_{12}N_2O_3$; IR ν_{CO} (KBr) 1675, 1650 cm^{-1}; MS, M$^+$· 268 (100); ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.04 (dd, 1, $J_{8,7}$ = 8.5 Hz, $J_{8,6}$ = 2.3 Hz, H_8), 7.77 (overlapping dd, $J_{7,8}$ = 8.5 Hz, $J_{7,6}$ = 8.5 Hz, H_7), 7.41 (dd, 1, $J_{6,8}$ = 2.3 Hz, $J_{6,7}$ = 8.5 Hz, H_6), 4.04 (s, 3, OCH_3), 2.80 (s, 3, CH_3), 2.78 (s, 3, CH_3). **6c** (R = R^1 = H), bright yellow needles (CH_2Cl_2/EtOH), 65%, mp 231–232 °C: anal. for $C_{12}H_6N_2O_2$: IR ν_{CO} (KBr) 1670, 1650 cm^{-1}; MS, M$^+$· 210 (100); ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.77 (br s, 2, H_2 and H_4), 8.48–8.33 (m, 2, aromatic), 7.99–7.90 (m, 2, aromatic). **6c** (R = OCH_3; R^1 = H), yellow needles (CH_2Cl_2/EtOH), 54%, mp 227–228 °C: anal. for $C_{13}H_8N_2O_3$; IR ν_{CO} (KBr) 1687 cm^{-1}; MS, M$^+$· 240 (100); ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.73 (s, 1, H_4), 9.67 (s, 1, H_2), 7.98 (dd, 1, $J_{5,6}$ = 7.65 Hz, $J_{5,7}$ = 1.19 Hz, H_5), 7.85 (overlapping d, 1, $J_{6,7}$ = 7.65 Hz, $J_{6,5}$ = 7.65 Hz, H_6), 7.44 (dd, 1, $J_{6,7}$ = 7.65 Hz, $J_{5,7}$ = 1.19 Hz, H_7), 4.10 (s, 3, OCH_3). **6d** (R = R^1 = H), yellow needles (CH_2Cl_2/EtOH), 92%, mp 215–216 °C: anal. for $C_{14}H_8ClNO_2$; IR ν_{CO} (KBr) 1685, 1665 cm^{-1}; MS, M$^+$· 257 (100); ^{1}H NMR (60 MHz, $CDCl_3$) δ 8.43–8.16 (m, 2, H_5 and H_8), 7.91–7.73 (m, 2, H_6 and H_7), 7.54 (s, 1, H_3), 2.89 (s, 3, CH_3). **6e** (R = R^1 = H), light yellow needles (CH_2Cl_2/EtOH), 80%, mp 178–180 °C: anal. for $C_{13}H_7NO_2$; IR ν_{CO} (KBr) 1676 cm^{-1}; MS, M$^+$· 209 (100); ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.57 (s, 1, H_1), 9.10 (d, 1, $J_{3,4}$ = 5.04 Hz, H_3), 8.36–8.29 (m, 2, aromatic), 8.07 (d, 1, $J_{4,3}$ = 5.04 Hz, H_4), 7.92–7.83 (m, 2, aromatic). **6e** (R = H; R^1 = OCH_3), yellow needles (EtOAc), 41%, mp 203–205 °C: anal. for $C_{14}H_9NO_3$: IR ν_{CO} (KBr) 1678, 1673 cm^{-1}; MS, M$^+$· 239 (100); ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.57 (d, 1, $J_{1,4}$ = 0.53 Hz, H_1), 9.15 (dd, 1, $J_{3,4}$ = 5.25 Hz, $J_{3,1}$ = 0.53 Hz, H_3), 8.13 (d, 1, $J_{4,3}$ = 5.25 Hz, $J_{4,1}$ = 0.53 Hz, H_4), 8.04 (dd, 1, $J_{7,8}$ = 8.02 Hz, $J_{6,8}$ = 1.10 Hz, H_8), 7.86 (overlapping dd, 1, $J_{6,7}$ = 8.02 Hz, $J_{7,8}$ = 8.02 Hz, H_7), 7.45 (dd, 1, $J_{6,7}$ = 8.02 Hz, $J_{6,8}$ = 1.10 Hz, H_6), 4.11 (s, 3, OCH_3).

Two convenient alternates to the overall transformation which utilize alicyclic dienes are described below.

(ii) A solution of quinoline-5,8-dione (**2a**) (1.0 g, 0.006 mol) and 1-acetoxy-1,3-butadiene (1.4 g, 0.013 mol) in toluene (20 mL) was heated under reflux for 24 h. The reaction mixture was cooled and concentrated under reduced pressure, and the material that had separated was collected. It crystallized from CH_2Cl_2 as pale yellow needles, 0.9 g (69%), mp 272–273 °C, identical with 1-azaanthracene-9,10-dione (**6a**: R = R^1 = H) prepared above.

(iii) A solution of quinoline-5,8-dione (**2a**) (0.42 g, 0.003 mol) and 1,4-diacetoxy-1,3-butadiene (0.38 g, 0.002 mol) in dry benzene (20 mL) was heated under reflux for 48 h. After concentration of the benzene solution, addition of a small amount of ethanol caused the 1-azaanthracene-9,10-dione (**6a**: R = R^1 = H) to separate as a yellow solid which crystallized from EtOH–CH_2Cl_2 as yellow needles: 0.39 g (85%), mp 272–275 °C. Compound **6e** (R = R^1 = H) was also obtained by this procedure.

Cycloaddition with Alicyclic Dienes. (a) Silylated Dienes. (i) Isolation of the Tautomeric Form of the Initial 1:1-Cycloadduct. A mixture of quinoline-5,8-dione (**2a**) (1.13 g, 0.007 mol) and freshly distilled 1,1-dimethoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene (**24**) (2.4 g, 0.014 mol) in anhydrous benzene (25 mL) was heated under reflux in a N_2 atmosphere for 2.5 h. The reaction mixture was then poured into ice-water and the resultant precipitate collected, an additional amount being obtained by CH_2Cl_2 extraction of the aqueous filtrate. The organic fractions were dissolved in CH_2Cl_2, and the solution was washed with H_2O and dried (Na_2SO_4). Evaporation of the CH_2Cl_2 gave a residue which crystallized from ethanol giving 5-methoxy-7,9,10-trihydroxy-1-azaanthracene (**25**: R = H) (1.63 g, 89%) as a light brown amorphous solid. Treatment of this product (1.0 g) with Ac_2O (10 mL) and pyridine (10 mL) for 12 h followed by quenching with ice water afforded 5-methoxy-7,9,10-triacetoxy-1-azaanthracene (**25**: R = Ac) as pale yellow needles from ethanol: 0.82 g (58%), mp 219–222 °C; anal. for $C_{20}H_{17}NO_7 \cdot {}^1/_2\ H_2O$; IR ν_{CO} (KBr) 1725, 1660 cm^{-1}; MS, M$^+$· 383 (6); ^{1}H NMR (60 MHz, $CDCl_3$) δ 8.95 (dd, 1, $J_{2,3}$ = 6 Hz, $J_{2,4}$ = 2 Hz, H_2), 8.15 (dd, 1, $J_{4,3}$ = 6 Hz, $J_{4,2}$ = 2 Hz, H_4), 7.48 (d, 1, $J_{6,8}$ = 4 Hz, H_8), 7.35 (d, 1, $J_{6,8}$ = 4 Hz, H_6), 6.66 (dd, 1, $J_{3,4}$ = 6 Hz, $J_{3,2}$ = 2 Hz, H_3), 4.00 (s, 1, OCH_3), 2.58 (s, 3, $OCOCH_3$), 2.57 (s, 3, $OCOCH_3$), 2.35 (s, 3, $OCOCH_3$). The following compounds were prepared in this manner: **29** [(R = H), light red microneedles (EtOH), 90%, mp >300 °C dec; IR ν_{OH} (KBr) 3350–2950 cm^{-1}; MS, M$^+$· 286 (100); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.47 (d, 1, $J_{6,8}$ = 2.22 Hz, H_8), 6.83 (d, 1, $J_{6,8}$ = 2.22 Hz, H_6), 4.00 (s, 3, OCH_3), 2.80 (s, 6, CH_3)] and **29** [(R = Ac) prepared from **29** (R = H) and Ac_2O/pyridine, bright yellow irregular prisms (CH_2Cl_2/EtOH), 78%, mp 251–252 °C: anal. for $C_{21}H_{20}N_2O_7$; IR ν_{CO} (KBr) 1760 cm^{-1}; MS, M$^+$· 412 (9); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.48 (d, 1, $J_{8,6}$ = 1.80 Hz, H_8), 6.65 (d, 1, $J_{6,8}$ = 1.80 Hz, H_6), 4.01 (s, 3, OCH_3), 2.73 (s, 6, CH_3), 2.61 (s, 3, $OCOCH_3$), 2.55 (s, 3, $OCOCH_3$), 2.37 (s, 3, $OCOCH_3$)].

(ii) Isolation of the Oxidized Form of the Initial 1:1-Cycloadduct. Quinoline-5,8-dione (**2a**) (4.5 g, 0.03 mol) and 1,1-dimethoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene (**24**) (10.3 g, 0.05 mol) in anhydrous benzene (80 mL) was heated under reflux for 16 h, solution occurring in ca. 10 min. The reaction mixture was cooled and concentrated under reduced pressure, and the material that separated was collected. This was washed with benzene and dried, giving 3.83 g of 5-methoxy-7-hydroxy-1-azaanthracene-9,10-dione (**26**: R = H) as a pale yellow solid mp >300 °C with decomposition. Evaporation of the filtrate afforded an additional gram of product; total yield 4.8 g (67%), separating from EtOH as yellow irregular prisms, mp >300 °C dec: anal. for $C_{14}H_9NO_4 \cdot {}^1/_4\ H_2O$; IR ν_{OH} (KBr) 3400–3000 cm^{-1}; ν_{CO} (KBr) 1660, 1655 cm^{-1}; MS, M$^+$· 255 (100); (200 MHz, Me_2SO-d_6) δ 9.05 (dd, 1, $J_{2,3}$ = 4.62 Hz, $J_{2,4}$ = 1.73 Hz, H_2), 8.46 (dd, 1, $J_{4,3}$ = 7.92 Hz, $J_{4,2}$ = 1.73 Hz, H_4), 7.82 (dd, 1, $J_{3,2}$ = 4.62 Hz, $J_{3,4}$ = 7.92 Hz, H_3), 7.22 (d, 1, $J_{6,8}$ = 2.32 Hz, H_8), 6.89 (d, 1, $J_{8,6}$ = 2.32 Hz, H_6), 3.92 (s, 3, OCH_3). Treatment of the above product (1.0 g) with Ac_2O (10 mL) and 4 drops of pyridine overnight at room temperature and quenching the reaction mixture by pouring into ice water gave a yellow solid, 0.7 g, and an additional 0.2 g was recovered by $CHCl_3$ extraction of the aqueous phase. Recrystallization from ethanol afforded 5-methoxy-7-acetoxy-1-azaanthracene-9,10-dione (**26**: R = Ac), 1.0 g, 86%, as light yellow needles, mp 194–195 °C: anal. for $C_{16}H_{11}NO_5 \cdot {}^1/_4\ H_2O$; IR ν_{CO} (KBr) 1785, 1675 and 1670 cm^{-1}; MS, M$^+$· 297 (45); ^{1}H NMR (60 MHz, $CDCl_3$) δ 9.16 (dd, 1, $J_{2,3}$ = 6 Hz, $J_{2,4}$ = 2 Hz, H_2), 8.61 (dd, 1, $J_{4,3}$ = 8 Hz, $J_{4,2}$ = 2 Hz, H_4), 7.75 (dd, 1, $J_{4,3}$ = 8 Hz, $J_{3,2}$ = 6 Hz, H_3), 7.66 (d, 1, $J_{5,7}$ = 3 Hz, H_5), 7.21 (d, 1, $J_{7,5}$ = 3 Hz, H_7), 4.08 (s, 3, OCH_3), 2.40 (s, 3, $OCOCH_3$).

Compound **30** (R = H) was also obtained by the procedure a.ii above: deep yellow irregular prisms (EtOH), mp >310 °C dec: anal. for $C_{15}H_{12}N_2O_4$; IR ν_{OH} (KBr) 3450–2950 cm^{-1}; ν_{CO} (KBr) 1680, 1650 cm^{-1}; M$^+$· 284 (100); ^{1}H NMR (60 MHz, $CDCl_3$) δ 7.50 (d, 1, $J_{6,8}$ = 3 Hz, H_8), 6.85 (d, 1, $J_{6,8}$ = 3 Hz, H_6), 4.01 (s, 3, OCH_3), 2.77 (s, 3, CH_3).

The same procedure is also applicable to 1-methoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene (**23**). Thus, isoquinoline-5,8-dione (**2e**) (2.7 g, 0.017 mol) and **23** (5.0 g, 0.030 mol) in anhydrous benzene (70 mL) after 16 h of reflux and evaporation of the solvent, gave a residue which was dissolved in pyridine (25 mL) and Ac_2O (10 mL) and stirred at room temperature overnight. The reaction was quenched by pouring into ice water (600 mL), followed by $CHCl_3$ extraction. The $CHCl_3$ extract was washed with H_2O, dried (Na_2SO_4), and evaporated leaving a residue which crystallized from ethanol (charcoal) as light yellow flakes of 7-acetoxy-2-azaanthracene-9,10-dione (**28**: R = Ac), 2.3 g (66%), mp 164.5–165.5 °C: anal. for $C_{15}H_9NO_4$; IR ν_{CO} (KBr) 1740, 1655,

1650 cm^{-1}; MS, M$^{+\cdot}$ 267 (4); ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.62 (d, 1, $J_{1,4}$ = 1.2 Hz, H_1), 9.18 (d, 1, $J_{4,3}$ = 5.6 Hz, $J_{3,1}$ = 1.2 Hz, H_3), 8.41 (d, 1, $J_{5,6}$ = 8.4 Hz, H_5), 8.13 (dd, 1, $J_{3,4}$ = 5.6 Hz, H_4), 8.09 (d, 1, $J_{6,8}$ = 2.6 Hz, H_8), 7.61 (dd, 1, $J_{6,5}$ = 8.4 Hz, $J_{6,8}$ = 2.6 Hz, H_6), 2.41 (s, 3, CH_3).

The following compounds were prepared by the above procedure: compound **27** [yellow irregular prisms (EtOH), 75%, mp 194–195 °C: anal. for $C_{15}H_9NO_4$; IR ν_{CO} (KBr) 1765, 1688, 1668 cm^{-1}; MS, M$^{+\cdot}$ 267 (18); ^{1}H NMR δ 9.18 (dd, 1, $J_{2,3}$ = 4.8 Hz, $J_{4,2}$ = 1.4 Hz, H_2), 8.72 (dd, 1, $J_{3,4}$ = 5.3 Hz, $J_{4,2}$ = 1.4 Hz, H_4), 8.19 (d, 1, $J_{5,7}$ = 2.2 Hz, H_5), 7.82 (dd, 1, $J_{3,2}$ = 4.8 Hz, $J_{3,4}$ = 5.3 Hz, H_3), 7.64 (dd, 1, $J_{5,7}$ = 2.2 Hz, $J_{7,8}$ = 5.0 Hz, H_7), 2.11 (s, 3, CH_3)], **31** [(R = H), bright yellow microneedles (EtOH), 71%, mp 298–302 °C; anal. for $C_{14}H_{10}N_2O_3$; IR ν_{OH} (KBr) 3550–2500 cm^{-1}; ν_{CO} (KBr) 1655 cm^{-1}; ^{1}H NMR (60 MHz, $CDCl_3$–Me_2SO-d_6) δ 8.24 (d, 1, $J_{5,6}$ = 9 Hz, H_5), 7.74 (d, 1, $J_{8,6}$ = 2 Hz, H_8), 7.29 (dd, 1, $J_{5,6}$ = 9 Hz, $J_{6,8}$ = 2 Hz, H_6), 2.81 (s, 6, CH_3)] and **31** [(R = Ac), colorless needles (EtOH), 98%, mp 208–209 °C: anal. for $C_{16}H_{12}N_2O_4$; IR ν_{CO} (KBr) 1755, 1655, 1600 cm^{-1}; MS, M$^{+\cdot}$ 296 (9); ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.51 (d, 1, $J_{8,7}$ = 7.5 Hz, H_8), 8.13 (d, 1, $J_{5,7}$ = 2.8 Hz, H_5), 7.63 (dd, 1, $J_{7,8}$ = 7.5 Hz, $J_{7,5}$ = 2.8 Hz, H_7), 2.84 (s, 6, CH_3), 2.41 (s, 3, OCH_3).].

(b) Symmetrical 1,3-Dienes. (i) Isolation of the Tautomeric Form of the Initial 1:1-Cycloadduct. 2,3-Dimethylquinoxaline-5,8-dione[6d] (**2b**) (1.0 g, 0.012 mol) and 2,3-dimethyl-1,3-butadiene (**32b**) (0.5 g, 0.003 mol) in absolute ethanol (10 mL) were heated under reflux for 20 h. After cooling, 5,8-dihydro-2,3,6,7-tetramethyl-9,10-dihydroxy-1,4-diazaanthracene (**37b**) separated. An additional 0.2 g was recovered from the mother liquor on standing. Crystallization from EtOH afforded yellow needles: 1.2 g (90%), mp 208–210 °C dec; anal. for $C_{16}H_{18}N_2O_2$: IR ν_{OH} (KBr) 3500–3400 cm^{-1}; MS, M$^{+\cdot}$ 270 (100); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.71 (s, 6, Ar–CH_3), 1.85 (m, 4, 2 × H_5 and 2 × H_8), 1.59 (s, 6, CH_3).

An alternative method of isolation was to convert a dihydroxy tautomer into its acetate, illustrated as follows: quinoline-5,8-dione (**2a**) (1.6 g, 0.01 mol) and 2,3-dimethyl-1,3-butadiene (**32b**) (1.64 g, 0.02 mol) in absolute EtOH after 24 h reflux and subsequent cooling gave a precipitate of the dihydroxy compound. This crude product (0.5 g) was treated with Ac_2O (1 mL) and 3 drops of pyridine and, after warming at 40–50 °C for 3 h, it was poured onto ice water (30 mL). Recrystallization of the separated material from EtOH–CH_2Cl_2 afforded 5,8-dihydro-6,7-dimethyl-9,10-diacetoxy-1-azaanthracene (**33b**: R^5 = Ac) as colorless needles: 0.59 g (87%), mp 236–237 °C; anal. for $C_{19}H_{19}NO_4$; IR ν_{CO} (KBr) 1760–1740 cm^{-1}; MS, M$^{+\cdot}$ 325 (10); ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.86 (dd, 1, $J_{2,3}$ = 4.22 Hz, $J_{2,4}$ = 1.63 Hz, H_2), 8.03 (dd, 1, $J_{4,3}$ = 8.52 Hz, $J_{4,2}$ = 1.63 Hz, H_4), 7.38 (dd, 1, $J_{3,4}$ = 8.52 Hz, $J_{3,2}$ = 4.22 Hz, H_3), 3.43–3.37 (br s, 2, CH_2), 3.32–3.28 (br s, 2, CH_2), 2.55 (s, 3, $OCOCH_3$), 2.51 (s, 3, $OCOCH_3$), 1.81 (br s, 6, CH_3).

The following compounds were obtained by this procedure: **37a**, yellow needles (EtOH), 89%, mp 217–218 °C; anal. for $C_{16}H_{18}N_2O_2$; IR ν_{OH} (KBr) 3490–3300 cm^{-1}; MS, M$^{+\cdot}$ 270 (67); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.20 (s, 2, OH), 5.99 (m, 2, H_6 and H_7), 3.89–3.84 (m, 2, H_5 and H_8), 2.71 (s, 6, Ar CH_3), 1.41 (d, 6, J = 6.95 Hz, C_5-CH_3, C_8-CH_3).

(ii) Isolation of the Oxidized Form of the Initial 1:1-Cycloadduct. 5,8-Dihydro-2,3,6,7-tetramethyl-9,10-dihydroxy-1,4-diazaanthracene (**37a**) (0.6 g, 0.002 mol) in DME (20 mL) was stirred with Ag_2O (0.56 g) at room temperature in the dark for 5 h. The reaction mixture was filtered, the residue was washed with hot $CHCl_3$, and the solvent was evaporated. The residue crystallized from EtOH–CH_2Cl_2, affording 5,8-dihydro-2,3,6,7-tetramethyl-1,4-diazaanthracene-9,10-dione (**38b**) as pink needles: 0.43 g (67%), mp 286–288 °C after turning yellow at 200 °C; anal. for $C_{16}H_{16}N_2O_2$; IR ν_{CO} (KBr) 1660 cm^{-1}; MS, M$^{+\cdot}$ 268 (100); ^{1}H NMR (60 MHz, $CDCl_3$) δ 3.26 (s, 4, 2 × H_5, 2 × H_8), 2.73 (s, 6, Ar CH_3), 1.78 (s, 6, C_6-CH_3 and C_7-CH_3).

The following compounds were obtained by the above procedure: **34a** [yellow needles (EtOH/CH_2Cl_2), 76%, mp 153–154 °C: anal. for $C_{15}H_{13}NO_2$; IR ν_{CO} (KBr) 1650 cm^{-1}; MS, M$^{+\cdot}$ 239 (56); ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.03 (dd, 1, $J_{2,3}$ = 4.70 Hz, $J_{2,4}$ = 1.73 Hz, H_2), 8.44 (dd, 1, $J_{4,2}$ = 1.73 Hz, $J_{4,3}$ = 7.93 Hz, H_4), 7.67 (dd, 1, $J_{2,3}$ = 4.70 Hz, $J_{4,3}$ = 7.93 Hz, H_3), 5.88–5.86 (m, 2, H_6 and H_7), 3.73–3.61 (m, 2, H_5 and H_8), 1.32 (d, 3, J = 3.53 Hz, CH_3), 1.29 (d, 3, J = 3.59 Hz, CH_3)], **34b** [pink needles (EtOH), 82%, mp 254–256 °C with color change to yellow at 200 °C: anal. for $C_{15}H_{13}NO_2$; IR ν_{CO} (KBr) 1670, 1660 cm^{-1}; MS, M$^{+\cdot}$ 239 (38); ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.02 (dd, 1, $J_{2,3}$ = 4.69 Hz, $J_{2,4}$ = 1.80 Hz, H_2), 8.44 (dd, 1, $J_{4,3}$ = 7.93 Hz, $J_{4,2}$ = 1.80 Hz, H_4), 7.66 (dd, 1, $J_{3,4}$ = 7.93 Hz, $J_{3,2}$ = 4.69 Hz, H_3), 3.34–3.12 (m, 4, CH_2), 1.78 (s, 6, CH_3)], **38a** [light brown needles (EtOH), 78%, mp 164–166 °C: anal. for $C_{16}H_{16}N_2O_2$; IR ν_{CO} (KBr) 1660 cm^{-1}; MS, M$^{+\cdot}$ 268 (92); ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.87 (d, 1, J = 3.81 Hz, H_6 and H_7), 3.71–2.82 (m, 2, H_5 and H_8), 2.79 (s, 6, Ar CH_3), 1.31 (d, 6, J = 6.95 Hz, C_5-CH_3 and C_8-CH_3)].

(iii) Isolation of the Fully Oxidized Azaanthraquinone. Quinoline-5,8-dione (**2a**) (1.6 g, 0.01 mol) and 2,3-dimethyl-1,3-butadiene (**32b**) (1.64 g, 0.02 mol) in absolute EtOH (20 mL) were heated under reflux for 24 h. The solid that separated from the cooled reaction mixture was dissolved in ethanolic KOH (25 mL, 5% solution), and air was passed through the mixture for 24 h during which time the initial green solution turned yellow. After cooling to ca. −10 °C the separated product was collected and washed with cold water followed by cold EtOH, and 6,7-dimethyl-1-azaanthracene-9,10-dione (**35b**) crystallized from EtOH:CH_2Cl_2 as greenish yellow needles: 1.94 g (82%), mp 261–262 °C; anal. for $C_{15}H_{11}NO_2$; IR ν_{CO} (KBr) 1680, 1665 cm^{-1}; MS, M$^{+\cdot}$ 237 (100); ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.11 (dd, 1, $J_{2,3}$ = 4.63 Hz, $J_{2,4}$ = 1.59 Hz, H_2), 8.64 (dd, 1, $J_{4,3}$ = 8.00 Hz, $J_{4,2}$ = 1.59 Hz, H_4), 8.19 (s, 1, H_8), 8.08 (s, 1, H_5), 7.73 (dd, 1, $J_{3,4}$ = 8.00 Hz, $J_{3,2}$ = 4.63 Hz, H_3), 2.47 (s, 6, CH_3).

The following compounds were prepared by this procedure: **36a** [yellow needles (EtOAc), 65%, mp 191–192 °C; anal. for $C_{15}H_{11}NO_2$; IR ν_{CO} (KBr) 1660, 1650 cm^{-1}; MS M$^{+\cdot}$ 239 (54) ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.48 (d, 1, $J_{1,4}$ = 0.53 Hz, H_1), 9.05 (dd, 1, $J_{3,4}$ = 5.08 Hz, $J_{3,1}$ = 0.53 Hz, H_3), 7.98 (d, 1, $J_{3,4}$ = 5.08 Hz, H_4), 7.51 (s, 2, H_7 and H_6), 2.83 (s, 3, CH_3), 2.81 (s, 3, CH_3)], **41** [light yellow needles (EtOH/CH_2Cl_2), 57%, mp 262–263 °C: anal. for $C_{16}H_{12}NO_2Cl$; IR ν_{CO} (KBr) 1675, 1660 cm^{-1}; MS M$^{+\cdot}$ 285 (100); ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.09 (s, 1, H_8), 7.99 (s, 1, H_5), 7.51 (s, 1, H_3), 2.89 (s, 3, C_4-CH_3), 2.48 (s, 6, C_6-CH_3 and C_7-CH_3)].

In an alternative oxidation procedure the initial precipitate from the cycloaddition of quinoline-5,8-dione (**2a**) (0.7 g, 0.004 mol) and 2,3-dimethoxy-1,3-butadiene (**32c**) (2.4 g, 0.021 mol) was dissolved in CH_3OH (3 mL), CH_2Cl_2 (1 mL), and NaOH solution (2 mL, 1 N solution). After the reaction mixture had been stirred at room temperature for 30 min, it was neutralized with dilute HCl and then extracted with $CHCl_3$, the $CHCl_3$ extract was dried (Na_2SO_4) and evaporated. Crystallization of the residue from EtOH–CH_2Cl_2 afforded 6,7-dimethoxy-1-azaanthracene-9,10-dione (**35c**) as yellow irregular prisms: 0.41 g, (85%), mp 272–274 °C dec; anal. for $C_{15}H_{11}NO_4$; IR ν_{CO} (KBr) 1675, 1655 cm^{-1}; MS, M$^{+\cdot}$ 269 (100); ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.07 (dd, 1, $J_{2,3}$ = 4.69 Hz, $J_{2,4}$ = 1.65 Hz, H_2), 8.60 (dd, 1, $J_{4,3}$ = 7.99 Hz, $J_{4,2}$ = 1.65 Hz, H_4), 7.82 (s, 1, H_8), 7.72 (s, 1, H_5), 7.70 (dd, 1, $J_{3,2}$ = 4.69 Hz, $J_{3,4}$ = 7.99 Hz, H_3), 4.09 (s, 3, OCH_3), 4.08 (s, 3, OCH_3).

Compound **36c** was also obtained by this procedure: yellow irregular prisms (EtOAc/CH_2Cl_2), 30%, mp 242–244 °C; anal. for $C_{15}H_{11}NO_4$; IR ν_{CO} KBr 1650 cm^{-1}; MS, M$^{+\cdot}$ 269 (100); ^{1}H NMR (60 MHz, $CDCl_3$) δ 9.55 (s, 1, H_1), 9.10 (d, 1, $J_{3,4}$ = 7 Hz, H_3), 8.07 (d, 1, $J_{4,3}$ = 7 Hz, H_4), 7.75 (s, 2, H_5 and H_8), 4.10 (s, 6, OCH_3).

5-Methoxy-1-azaanthracene-9,10-dione (6a; R = H, R^1 = OCH_3). A stirred solution of *o*-anisic acid diethylamide (**8**) (5.60 g, 0.03 mol) in anhydrous ether at −78 °C under an argon atmosphere and TMEDA (3.4 g, 0.03 mol) was treated with 1 equiv *sec*-BuLi (26.36 mL of a 1.1 M solution, 0.03 mol). The reaction was allowed to stir for 1 h after which time pyridine-2-carbaldehyde (3.07 g, 0.03 mole) was added. Stirring was continued for 2 h at −40 °C. The mixture was recooled to −78 °C and a second equivalent of *sec*-BuLi (26.36 mL of a 1.1 M solution, 0.03 mol) was added slowly. The reaction mixture was warmed slowly to room temperature, and stirring was continued for an additional 16 h. The mixture was poured into ice H_2O, made slightly acidic with 10% aqueous HCl, and extracted with $CHCl_3$ (3 × 150 mL). The chloroform fractions were combined, washed with a 30% solution of sodium bisulfite and once with H_2O, dried (anhydrous Na_2SO_4), and evaporated. The oily residue was passed twice through a silica packed column eluting with EtOAc to give **6a** (R = H; R^1 = OCH_3) as yellow irregular prisms, mp 218–219 °C: anal. for $C_{14}H_9NO_3 \cdot {}^1/_2\ H_2O$; IR ν_{CO} (KBr) 1685, 1663 cm^{-1}; MS, M$^{+\cdot}$ 239 (100); ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.10 (dd, 1, $J_{2,3}$ = 4.04

Hz, $J_{2,4}$ = 2.50 Hz, H_2), 8.64 (dd, 1, $J_{4,2}$ = 2.50 Hz, $J_{4,3}$ = 7.84 Hz, H_4), 8.10 (dd, 1, $J_{6,8}$ = 1.04 Hz, $J_{7,8}$ = 8.03 Hz, H_8), 7.82 (overlapping dd, 1, $J_{6,7}$ = $J_{7,8}$ = 8.03 Hz, H_7), 7.76 (dd, 1, $J_{3,2}$ = 4.04 Hz, $J_{3,4}$ = 7.84 Hz, H_3), 7.43 (dd, 1, $J_{6,7}$ = 8.03 Hz, $J_{6,8}$ = 1.04 Hz, H_6), 4.08 (s, 3, OCH_3).

8-Methoxy-1-azaanthracene-9,10-dione (6a; R = OCH_3, R^1 = H) was obtained in the same manner as the 5-methoxy isomer **6a** (R = H, R^1 = OCH_3) using *m*-anisic acid diethylamide (**7**) (5.6, 0.03 mol) and pyridine-2-carboxaldehyde (3.07 g, 0.03 mol). The product was isolated by column chromatography and found to be identical with that above prepared via the cycloaddition reaction.

8-Methoxy-2-azaanthracene-9,10-dione (6e; R = H, R^1 = OCH_3). A stirred solution of *o*-anisic acid diethylamide (**8**) (5.6 g, 0.04 mol) in anhydrous THF at −78 °C under an argon atmosphere and TMEDA (3.4 g, 0.03 mole) was treated with *sec*-BuLi (26.36 mL of a 1.1 M solution, 0.03 mol). The reaction mixture was allowed to stir for 1 h and pyridine-4-carbaldehyde (3.07 g, 0.03 mol) was added slowly. The mixture was warmed to −40 °C, stirred for 2 h, and again cooled to −78 °C. A second equivalent of *sec*-BuLi (26.36 mL of a 1.1 M solution) was added slowly. The mixture was allowed to warm slowly to room temperature and, after being stirred for an additional 16 h, it was poured into ice H_2O. The resultant mixture was made slightly acidic with 10% aqueous HCl and extracted with $CHCl_3$ (3 × 150 mL). The organic fractions were combined, washed with a 30% aqueous solution of sodium bisulfite followed by water, dried (anhydrous Na_2SO_4), and evaporated, yielding a dark brown oil. Column chromatography (silica gel) eluting with a solvent gradient of EtOAc/hexanes and crystallization from EtOAc afforded the quinone **6e** (R = H; R^1 = OCH_3) as yellow needles, mp 202–204 °C (10%). This was identical with **6e** (R = H; R^1 = OCH_3) made via the cycloaddition sequence.

5-Methoxy-2-azaanthracene-9,10-dione (6e; R = OCH_3, R^1 = H). This was prepared in the same manner as the 8-methoxy isomer **6e** (R = H; R^1 = OCH_3) using m-anisic acid diethylamide (**7**) (5.6 g, 0.03 mol) and pyridine-4-carbaldehyde. Recrystallization from MeOH afforded yellow needles, mp 203–205 °C.

Reaction of *o*-Lithioanisole (16) with (A) Pyridine-3,4-dicarboxylic Anhydride (17). A solution of *o*-bromoanisole (18.7 g, 11.6 mL, 0.10 mol) in pentane (100 mL) was treated with *n*-BuLi in hexane (63 mL, 1.6 mol). The solution was stirred overnight under argon. The *o*-anisyllithium (**16**), thus formed, was added to pyridine-3,4-dicarboxylic acid anhydride (**17**) (14.9 g, 0.10 mol) in anhydrous THF (200 mL) cooled to −100 °C. After the addition was completed, the solution was warmed to room temperature, stirred overnight, and poured carefully into water (300 mL). The colorless solid that precipitated was recrystallized from ethanol giving the bis-adduct **19** as colorless needles: mp 190–192 °C (8%). Anal. for $C_{21}H_{17}NO_4$: IR ν_{CO} (KBr) 1750 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.22 (d, 1, $J_{3,5}$ = 1.90 Hz, H_3), 8.72 (d, 1, $J_{6,5}$ = 4.10 Hz, H_6), 7.85 (dd, 1, $J_{5,6}$ = 4.10 Hz, $J_{5,3}$ = 1.90 Hz, H_5), 7.46–7.32 (m, 4, aromatic), 7.04–6.91 (m, 4, aromatic), 3.57 (s, 6, 2 × OCH_3); MS, M^+· 346 (49%).

The above filtrate was brought to pH 4–5 by addition of dilute HCl. A colorless solid crystallized and was recrystallized from ethanol giving the keto carboxylic acid **18** as colorless needles, 54%, mp 270–274 °C dec: anal. for $C_{14}H_{11}NO_4$; IR ν_{OH} (KBr) 2990–2800, ν_{CO} (KBr) 1700, 1650 cm^{-1}; MS, M^+· 257 (12); ^1H NMR (200 MHz, Me_2SO-d_6/$CDCl_3$) δ 9.22 (d, 1, $J_{1,3}$ = 0.60 Hz, H_1), 8.78 (d, 1, $J_{4,3}$ = 5.01 Hz, H_4), 7.99–7.78 (m, 1, aromatic), 7.58–7.49 (m, 1, aromatic), 7.19–6.88 (m, 3, aromatic), 3.51 (s, 3, OCH_3).

(B) Pyridine-2,3-dicarboxylic Anhydride (20). Using the same procedure and quantities as in A above resulted in isolation of the bis-adduct **22** as colorless needles from CH_2Cl_2/EtOH, mp 208–209 °C, 8%: anal. for $C_{21}H_{17}NO_4$; IR ν_{CO} (KBr) 1750 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.86 (dd, 1 $J_{5,6}$ = 4.90 Hz, $J_{5,7}$ = 1.66 Hz, H_5), 8.24 (dd, 1, $J_{7,6}$ = 7.71 Hz, $J_{7,5}$ = 1.66 Hz, H_7), 7.46 (dd, 1, $J_{6,5}$ = 4.90 Hz, $J_{6,7}$ = 7.71 Hz, H_6), 7.38–7.30 (m, 2, aromatic), 7.19–7.14 (m, 2, aromatic), 6.94–6.83 (m, 4, aromatic), 3.95 (s, 6, 2 × OCH_3); MS, M^+· 347 (44%).

The keto acid **21** was isolated in a similar fashion, crystallizing from EtOH as colorless needles, mp 182–183 °C, 53%: anal. for $C_{14}H_{11}NO_4$; IR ν_{OH} (KBr) 3600–3400, ν_{CO} (KBr) 1700, 1650 cm^{-1}; ^1H NMR (200 MHz, Me_2SO-d_6/$CDCl_3$) δ 8.67 (dd, 1, $J_{6,5}$ = 4.87 Hz, $J_{6,4}$ = 1.66 Hz, H_6), 8.34 (dd, 1, $J_{5,6}$ = 4.87 Hz, $J_{4,5}$ = 7.83 Hz, H_5), 8.01 (dd, 1, $J_{4,5}$ = 7.83 Hz, $J_{4,6}$ = 1.66 Hz, H_4), 7.57–7.41 (m, 2, $H_{4'}$, $H_{3'}$), 7.07 (sextet, 1, $J_{5',6'}$ = 7.62 Hz, $J_{5',4'}$ = 7.62 Hz, $J_{5',3'}$ = 0.95 Hz, $H_{5'}$), 3.46 (s, 3, OCH_3); MS, M^+· 257 (9%).

Reaction of *m*-Anisic Acid Anilide (10) with (A) Pyridine-2-carbaldehyde in Et_2O. A suspension of the anilide **10** (2.27 g, 0.01 mol) in anhydrous ether (225 mL) and TMEDA (2.32 g, 0.02 mol) was cooled in a dry ice–acetone bath to −78 °C. Under an argon atmosphere, *n*-BuLi (12.5 mL of a 1.65 M solution in hexane) was added dropwise. A light yellow color slowly developed. The solution was allowed to warm to −20 °C during a 5-h period. It was recooled to −78 °C and pyridine-2-carbaldehyde (1.07 g, 0.01 mol) in ether (30 mL) was added affording a colorless solid. Crystallization from ethanol gave the lactone **11** as colorless needles: 1.64 g, 68%, mp 130–132 °C; anal. for $C_{14}H_{11}NO_3$: IR ν_{CO} (KBr) 1735 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.68–8.62 (m, 1, $H_{6'}$), 7.78–6.12 (m, 6, aromatic), 6.49 (s, 1, H_7), 3.74 (s, 3, OCH_3); MS, M^+· 241 (48%).

(B) Pyridine-4-carbaldehyde. Using the above reaction conditions and quantities gave the lactone **12** which crystallized from ethanol as fluffy, colorless plates, 1.71 g, 71%, mp 157–158 °C: anal. for $C_{14}H_{11}NO_3$; IR ν_{CO} (KBr) 1775 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.62 (d, 2, $J_{2',3'}$ = $J_{6',5'}$ = 6.18 Hz, $H_{2'}$, $H_{6'}$), 7.58–7.55 (m, 2, H_5, H_7), 7.27 (d, 2, $J_{3',2'}$ = $J_{5',6'}$ = 6.18 Hz, $H_{3'}$, $H_{5'}$), 7.12 (dd, 1, $J_{6,7}$ = 3.78 Hz, $J_{6,5}$ = 5.13 Hz, H_6), 6.38 (s, 1, H_3), 2.81 (s, 3, OCH_3); MS, M^+· 241 (90%).

(C) Pyridine-2-carbaldehyde in THF. Under the same reaction conditions, except that THF was used as solvent, the initial adduct **14** was obtained as colorless needles from ethanol, 1.86 g, 55%, mp 160–162 °C: anal. for $C_{20}H_{18}N_2O_3$: IR ν_{OH} (KBr) 3500–3100, ν_{CO} (KBr) 1645 cm^{-1}; ^1H NMR (200 MHz, Me_2SO-d_6) δ 8.49–8.46 (m, 1, aromatic), 7.75–7.53 (m, 3, aromatic), 7.38–7.20 (m, 3, aromatic), 7.11–6.97 (m, 3, aromatic), 6.11–6.09 (d, 1, aromatic), 5.84–5.82 (d, 1, aromatic), 3.77 (s, 3, CH_3); MS [M^+· − C_6H_7N] 241 (100%).

The above product **14** was converted into the lactone **15** when the hydroxyamide (3.34 g, 0.01 mol) in toluene (100 mL) and *p*-toluenesulfonic acid (0.5 g) were refluxed for 6 h. The solution was concentrated, cooled, and filtered. Crystallization of the separated product from benzene–hexane gave the lactone **15** as colorless granules, 2.2 g, 91%, mp 120–121 °C: anal. for $C_{14}H_{11}NO_3$; IR ν_{CO} KBr 1749 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.65 (dd, 1, $J_{6',5'}$ = 4.87 Hz, $J_{6',4'}$ = 1.32 Hz, $H_{6'}$), 7.74–7.63 (m, 2, aromatic), 7.59–7.55 (m, 1, aromatic), 7.40–7.22 (m, 2, aromatic), 6.96–6.92 (m, 1, aromatic), 6.44 (s, 1, H_3), 4.02 (s, 3, OCH_3); MS, M^+· 241 (26%).

Conversion of the Phthalide 11 into 10-(Trifluoroacetoxy)-8-methoxy-1-azaanthracene (11a). A mixture of the phthalide **11** (1.2 g, 0.005 mol), activated Zn dust[21] (2.4 g), formic acid (35 mL, 88%), and water (2.4 mL) was heated under reflux for 12 h. After neutralization and extraction (CH_2Cl_2) of the reaction mixture the colorless solid that was obtained was treated with $(CF_3CO)_2O$ (2 mL) in CH_2Cl_2 (10 mL) at 0 °C for 4 h. The reaction mixture was concentrated, treated with 5% aqueous $NaHCO_3$ solution, and extracted with CH_2Cl_2. The CH_2Cl_2 extract was washed with H_2O, dried (anhydrous Na_2SO_4), and evaporated. The residue crystallized from CH_2Cl_2/CH_3OH as yellow needles, 0.41 g, 26%, mp 170–171 °C. Anal. for $C_{16}H_{10}NF_3O_3$: IR ν_{CO} (KBr) 1655 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.96 (dd, 1, $J_{2,3}$ = 7.58 Hz, $J_{2,4}$ = 0.88 Hz, H_2), 8.26 (dd, 1, $J_{4,3}$ = 8.29 Hz, $J_{4,2}$ = 0.88 Hz, H_4), 7.55–7.13 (m, 4, aromatic), 6.84–6.47 (m, 1, aromatic), 3.95 (s, 3, OCH_3); MS, M^+· 321 (62%).

Registry No. **2a**, 10470-83-4; **2b**, 2768-63-0; **2c**, 24271-82-7; **2e**, 50-46-4; **3** (R = H), 592-57-4; **3** (R = OMe), 2161-90-2; **4a** (R = R^1 = H), 101402-59-9; **4b** (R = R^1 = H), 2759-04-8; **4b** (R = OMe, R^1 = H), 101402-60-2; **4c** (R = R^1 = H), 101402-63-5; **4d** (R = R^1 = H), 101402-65-7; **5a** (R^1 = R^1 = H), 13785-27-8; **5b** (R = R^1 = H), 2759-10-6; **5b** (R = OMe, R^1 = H), 101402-61-3; **5c** (R = R^1 = H), 101402-62-4; **5d** (R = R^1 = H), 101402-64-6; **5e** (R = R^1 = H), 96937-79-0; **6a** (R = R^1 = H), 3712-09-2; **6a** (R = OMe, R^1 = H), 90381-59-2; **6a** (R = H, R^1 = OMe), 101402-88-4; **6b** (R = R^1 = H), 7029-88-1; **6b** (R = OMe, R^1 = H), 101402-66-8; **6c** (R = R^1 = H), 6537-59-3; **6c** (R = OMe, R^1 = H), 101402-67-9; **6d** (R = R^1 = H), 101402-68-0; **6e** (R = R^1 = H), 46492-08-4; **6e**

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(R = H, R[1] = OMe), 90381-62-7; **6e** (R = OMe, R[1] = H), 90381-63-8; **7**, 62924-93-0; **8**, 51674-10-3; **10**, 101402-93-1; **11**, 101402-94-2; **11a**, 101402-98-6; **12**, 101402-95-3; **14**, 101402-96-4; **15**, 101402-97-5; **17**, 4664-08-8; **18**, 101402-90-8; **19**, 101402-89-5; **20**, 699-98-9; **21**, 101402-92-0; **22**, 101402-91-9; **23**, 59414-23-2; **24**, 61539-61-5; **25** (R = H), 101402-69-1; **25** (R = Ac), 101402-70-4; **26** (R = H), 101402-73-7; **26** (R = Ac), 101402-74-8; **27**, 101402-77-1; **28** (R = Ac), 101402-76-0; **29** (R = H), 101402-71-5; **29** (R = Ac), 101402-72-6; **30** (R = H), 101402-75-9; **31** (R = H), 101402-78-2; **31** (R = Ac), 101402-79-3; **32b**, 513-81-5; **32c**, 3588-31-6; **33b** (R[5] = Ac), 101402-80-6; **33b** (R[5] = H), 101402-81-7; **34a**, 101402-83-9; **34b**, 13785-28-9; **35b**, 101402-85-1; **35c**, 101402-87-3; **36a**, 101402-86-2; **37a**, 101402-82-8; **37b**, 2768-65-2; **38a**, 101402-84-0; **38b**, 2893-08-5; **41**, 101402-99-7; isoquinoline, 119-65-3; 5-nitroisoquinoline, 607-32-9; 5-aminoisoquinoline, 1125-60-6; 5,8-diaminoisoquinoline, 1127-49-7; 5,8-dimethoxyquinazoline, 17944-05-7; 2-chloro-5,8-dimethoxy-4-methylquinoline, 58868-27-2; 2-chloro-5,8-dihydroxy-4-methylquinoline, 101402-57-7; 2-chloro-4-methyl-5,8-quinolinedione, 101402-58-8; 1-acetoxy-1,3-butadiene, 1515-76-0; 1,4-diacetoxy-1,3-butadiene, 3817-40-1; pyridine-2-carboxaldehyde, 1121-60-4; pyridine-4-carboxaldehyde, 872-85-5; *o*-bromoanisole, 578-57-4.

A Facile Synthesis of 7-Halo-5*H*-indeno[1,2-*b*]pyridines and -pyridin-5-ones

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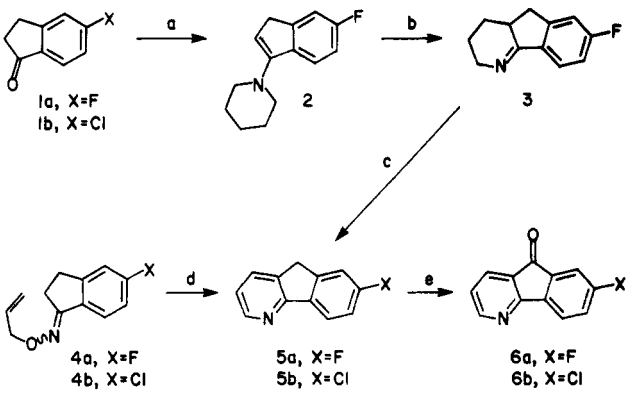
Received November 26, 1985

The 2-aryl-3-methylpyridines **7a–c** were obtained in good yield by the addition of the corresponding aryllithium to 2-fluoro-3-methylpyridine. Permanganate oxidation provided the 2-aryl-3-pyridinecarboxylic acids **8a–c** which were cyclized to 5*H*-indeno[1,2-*b*]pyridin-5-ones **6a–c** in hot polyphosphoric acid. The 5*H*-indeno[1,2-*b*]pyridines **5a–c** were readily obtained from the ketones **6a–c** by treatment with hydrazine in hot diethylene glycol.

Recently, we required as intermediates various 7-halo-5*H*-indeno[1,2-*b*]pyridines and the corresponding pyridin-5-ones. While the bromo-substituted compounds are readily obtained by bromination of 5*H*-indeno[1,2-*b*]-pyridin-5-one,[1] to our knowledge the 7-chloro and 7-fluoro compounds have not been reported. Our attempts to chlorinate either the unsubstituted azafluorene or the ketone with a variety of chlorinating agents were unsatisfactory, as were our efforts to introduce a fluoro substituent proceeding from the 7-nitro ketone by reduction to the amine followed by a Schiemann reaction. Thus, our attention turned to finding a route of synthesis that would be applicable to both the 7-chloro and the 7-fluoro compounds. A review of the reported syntheses[2] of 4-azafluorene and 4-azafluorenone suggested several routes that might be modified to provide the 7-halo derivatives.

The procedure described by Parcell and Hauck for the preparation of 4-azafluorene from 1-indanone[2b] provided the first sample of 7-fluoro-5*H*-indeno[1,2-*b*]pyridine (**5a**). Thus, the piperidine enamine **2** of 5-fluoro-1-indanone[3] (**1a**) was reacted with 3-bromopropylamine hydrobromide to furnish the tetrahydroindenopyridine **3** which was then dehydrogenated to provide **5a** in 75% yield (Scheme I). It proved necessary to purify **3** by distillation prior to the dehydrogenation reaction, as attempts using crude or only partially purified material failed. The yield of **3** from the distilled enamine **2** was 46%; however, the enamine was obtained in only 29% yield as distillation resulted in substantial decomposition. Therefore, **2** was typically used without purification, increasing the overall yield of **3** from **1a** to 28%. Oxidation of **5a** to the azafluorenone **6a** was

Scheme I[a]



[a] (a) Piperidine, catalytic TSOH, toluene, reflux; (b) $Br(CH_2)_3NH_2 \cdot HBr$, DMF, 100 °C; (c) 10% Pd/C, nitrobenzene, xylene, reflux; (d) sealed tube, 190–200 °C; (e) O_2, Triton B, pyridine.

accomplished in 36% yield by bubbling oxygen into a pyridine solution of the azafluorene and Triton B.[4] Unfortunately, the 7-chloro compounds were not readily accessible via this route as the chloro-substituted tetrahydroindenopyridine decomposed upon distillation.

A second route from 5-halo-1-indanones investigated was based on Irie's synthesis of substituted pyridines by the thermolysis of *O*-allyl oxime ethers.[5] Both 5-fluoro- (**1a**) and 5-chloro-1-indanone (**1b**) were readily converted to the oxime ethers **4a** and **4b** by O-alkylation (NaOEt/EtOH, allyl bromide, 95%) of the corresponding oxime ($H_2NOH \cdot HCL$, EtOH, pyridine, 72–86%). Thermolysis of **4a** and **4b** at 190–200 °C in a sealed tube did indeed produce **5a** and the first sample of **5b**, but the yields (14% and 15%, respectively) were too low to be useful. As with **5a**, oxidation of **5b** with oxygen and Triton B in pyridine furnished the azafluorenone **6b** in 33% yield.

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