Diels-Alder Reactions of 2-(2-Nitroethenyl)-1*H*-pyrroles and Their Oxygen and Sulfur Analogs with Quinones

Wayland E. Noland* and Gianluca Pardi

Department of Chemistry, University of Minnesota
207 Pleasant St. S. E.
Minneapolis, MN 55455
Received January 19, 2005

Diels-Alder reaction of 2-(*E*-2-nitroethenyl)-1*H*-pyrrole (**2a**) with 1,4-benzoquinone gave the desired benzo[*e*]indole-6, 9(3*H*)-dione (**4a**) in 10% yield versus a 26% yield (lit. 86% [5]) of the known *N*-methyl compound (**4b**) from the *N*-(or 1)-methyl compound (**2b**). Protection of the nitrogen of **2a** with a phenylsulfonyl group (**2c**) gave a 9% yield of the corresponding *N*-(or 3)-phenylsulfonyl compound (**4c**). The reaction of **2b** with 1,4-naphthoquinone gave in 6% yield (lit. 64% [5]) the known 3-methylnaphtho[2,3-*e*]-indole-6, 9(3*H*)-dione (**6**). The reaction of 2-(*E*-2-nitroethenyl)furan (**8a**) gave a small yield of the desired naphtho[2,1-*b*]furan-6, 9-dione (**9a**), recognized by comparing its NMR spectrum with that of **4b**. The corresponding reaction of 2-(*E*-2-nitroethenyl)thiophene (**8b**) gave a 4% yield of naphtho[2,1-*b*]thiophene-6,9-dione (**9b**), previously prepared in 24% yield [12] in a three-step procedure involving 2-ethenylthiophene. Introducing an electron-releasing 2-methyl substituent into **8a** and **8b** gave **12a** and **12b**, which, upon reaction with 1,4-benzoquinone, gave 2-methylnaphtho[2,1-*b*]furan-6, 9-dione (**13a**) and its sulfur analog (**13b**) in yields of 4 and 8%, respectively.

J. Heterocyclic Chem., **42**, 1149 (2005).

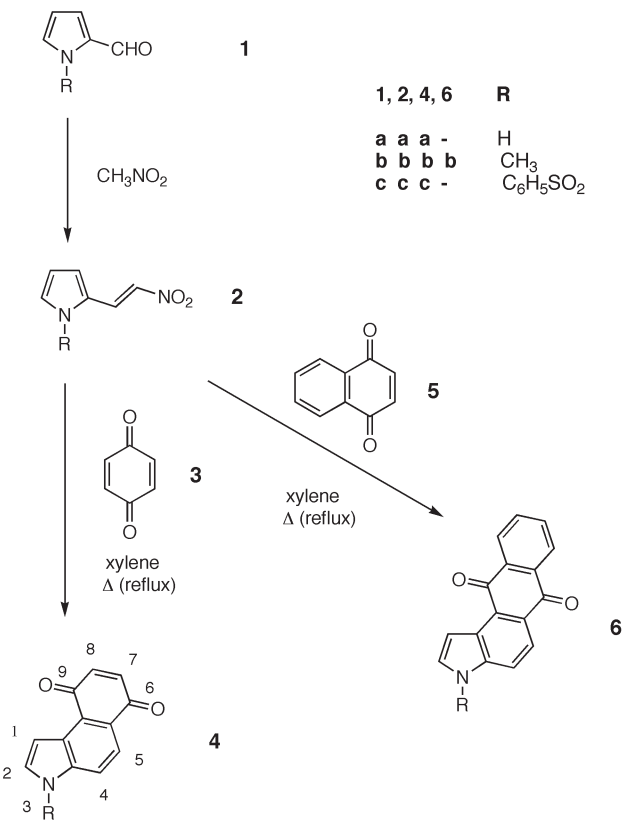
Introduction.

Quinoid heterocycles are of interest due to their potential DNA intercalating ability [la-d] and significant antitumor activity [la,2]. We have previously prepared benzo[*a*]carbazole-1,4-diones by normal electron demand [4+2] cycloadditions of 3-(2-nitroethenyl)indoles with 1,4-benzoquinones [3]. It has been reported from this laboratory that quinoid analogues can be formed by inverse electron demand [4+2] cycloadditions of nitroethenyl-substituted quinones with electron-rich heterocycles [4]. We are now reporting the formation of quinoid heterocycles by Diels-Alder reactions of 2-(2-nitroethenyl) derivatives of pyrrole, furan, and thiophene with 1,4-benzoquinone and 1,4-naphthoquinone. Electron-rich heterocycles having an ethenyl moiety in the 2-position represent a diene system which is effective in Diels-Alder reactions with various dienophiles such as 1,4-benzoquinone, 1,4-naphthoquinone, maleic anhydride, and maleimides. Although this method can be a route to polynuclear quinoid heterocyles, it suffers from limited applicability due to the instability of the ethenyl derivatives and the difficulty of preparing them. Nitroethenyl compounds, however, can serve as better dienes than their corresponding more reactive ethenyl analogues, because they are generally more readily available from a Knoevenagel condensation of the corresponding carboxaldehydes with nitromethane.

Results and Discussion.

To our knowledge, there is only one paper reporting the Diels-Alder reaction of nitroethenyl derivatives with 1,4-benzoquinone **3** and 1,4-naphthoquinone **5** to afford the corresponding polynuclear quinoid heterocycles [5]. We were especially interested in repeating the reactions between the nitroethenylpyrrole **2b** and the quinones to obtain NMR spectra and samples for biological testing.

Scheme 1



We prepared the nitroethenylpyrrole **2b** by condensation of 1-methylpyrrole-2-carboxaldehyde **lb** with nitromethane, as previously reported [6a] (Scheme 1). Examination of the coupling constants for the vinyl protons in the ^{1}H NMR spectra of the 2-nitroethenyl derivatives reported in this paper show that they are in the range of 13-13.2 Hz, which is consistent with the values of 12-18 Hz assigned to the *E* stereochemistry of the protons on an ethenyl double bond [7]. We then allowed **2b** to react in refluxing xylene in the presence of two equivalents of 1,4-benzoquinone **3** as described [5]. We obtained the product **4b** (Scheme 1) in only 26% yield (versus 86% reported [5]) because **2b** partially oxidized and polymerized. We saw broad bands in the ^{1}H NMR spectrum of the corresponding polymer, and recovered some **2b** unchanged. All of our attempts to improve the procedure (use of three equivalents of **3** in refluxing xylene for 24 hours; two equivalents of **3** in refluxing acetic acid for 24 hours; two equivalents of **3** in refluxing toluene for 4 days; and two equivalents of **3** in refluxing dioxane for 7 days) were unsuccessful because we again collected oxidized polymer (which was the only product with acetic acid as a solvent) and variable amounts of unchanged **2b**; therefore, we decided to reflux the two reagents in xylene for 48 hours to obtain **4b** as reported, and modified the purification procedure to remove the polymeric material and unreacted **2b**. With **4b** there was a correlation in the ^{1}H-^{1}H COSY NMR spectrum between the *N*-methyl peak at 3.87 and the 2-H doublet at 7.70 ppm, which helped to anchor the assignments of the remaining protons.

When the nitroethenylpyrrole **2b** reacted in refluxing xylene in the presence of two equivalents of 1,4-naphthoquinone **5**, as reported [5], only a small amount of pure quinoid derivative **6** (6% yield versus 64% reported [5]) was obtained after 48 hours (Scheme 1). Work-up of the reaction mixture gave unchanged **2b** and **5** together with polymeric material, in a difficult-to-separate mixture which accounted for the low yield of pure product **6**. Prolonging the refluxing time in xylene to 5 days gave no improvement, as there was extensive polymerization of **2b**, leaving unreacted **5**, which was isolated together with a small amount of the desired product **6**. With **6** there was a correlation in the ^{1}H-^{1}H COSY NMR spectrum between the *N*-methyl peak at δ 3.91 and the 2-H doublet at 7.75 ppm, which helped to anchor the assignments of the remaining protons.

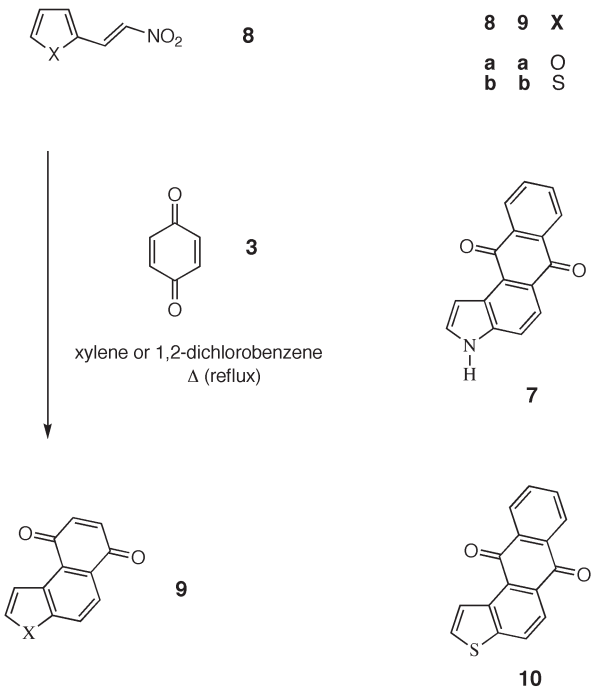
To prepare the new quinoid heterocycle **4a** (Scheme 1), we synthesized the nitroethenylpyrrole **2a** (Scheme 1) by modifying a reported procedure [8b] in which methylamine hydrochloride was replaced with ethylamine hydrochloride and, more importantly, in the work-up, vacuum (2 mm Hg) evaporation was applied, giving crude **2a** as a solid instead of an oil. The pyrrole derivative **2a** was allowed to react with two equivalents of 1,4-benzoquinone **3** in refluxing xylene for 5 days. The yield of compound **4a** was lower than with the corresponding methyl analogue **4b** (10 versus 26%) despite 3 more days of refluxing than in the case of **2b**. As with the product **4b**, we obtained complex mixtures containing considerable polymeric material and small molecules, including unreacted **2a** and **3**. With **4a** there were correlations in the ^{1}H-^{1}H COSY NMR spectrum between the NH singlet at δ 11.89 and the 2-H doublet at 7.75 and a weaker correlation with the 1-H peak at 7.27 ppm, which helped to anchor the assignments of the remaining protons.

An attempt to make the known naphthoindole **7** [9] by our shorter and simpler procedure involving **2a** in a Diels-Alder reaction with 1,4-naphthoquinone **5** failed: reaction of **2a** with two equivalents of **5** in refluxing xylene for 7 days gave only the unchanged reagents and some polymeric material. Increasing the reflux temperature by using 1,2-dichlorobenzene as a solvent gave a complex dark black mixture indicated by ^{1}H NMR to contain **5** and its reduction product, 1,4-naphthohydroquinone, among other products.

In order to protect the 2-nitroethenylpyrrole from unwanted side reactions, we introduced the *N*-phenylsulfonyl protecting group by using the commercially available 1-phenylsulfonylpyrrole-2-carboxaldehyde **lc** as a starting material. It has been reported that reaction of **lc** with nitromethane in refluxing acetic acid gave the corresponding nitroethenylpyrrole **2c** [10]. In our hands, this procedure gave only unchanged **lc**; however, we obtained **2c** in good yield by refluxing the aldehyde **lc** in nitromethane in the presence of an excess of ammonium acetate, giving **2c** in 75% yield (Scheme 1). Reaction of **2c** with two equivalents of benzoquinone **3** in refluxing xylene for 5 days gave a new quinoid heterocycle **4c** in 9% yield (Scheme 1). Once again, the product was accompanied by unchanged reagents and polymeric material. Refluxing the diene **2c** and two equivalents of 1,4-naphthoquinone **5** in xylene for 7 days gave unchanged **2c**, **5**, and polymeric material.

The reported Diels-Alder reactions of *E*-2-nitroethenylfuran **8a** with acrylates and acrylonitrile to give benzofurans [11] prompted us to study the reaction of **8a** with 1,4-benzoquinone **3** and 1,4-naphthoquinone **5**. Refluxing the commercially available **8a** with two equivalents of **3** in xylene for 7 days, in an attempt to prepare the new quinoid heterocycle **9a**, gave only a tiny amount of impure **9a** (Scheme 2) and unchanged **8a**, **3**, and polymeric material. Refluxing the reagents in 1,2-dichlorobenzene for 7 days gave only a small amount of sticky oily material containing the quinoid derivative **9a** (Scheme 2). It was possible to characterize the product **9a** through ^{1}H NMR and assign peaks by comparison with the spectrum of **4b**. Refluxing **8a** and two equivalents of 1,4-naphthoquinone **5** in either xylene or 1,2-dichlorobenzene for 7 days gave only polymeric material and the unchanged reagents.

Scheme 2



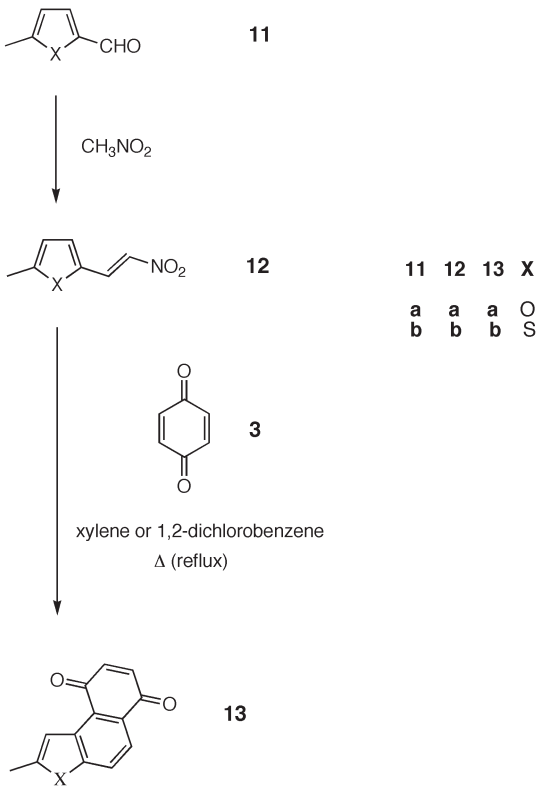
The naphthothiophene-6,9-dione **9b** (Scheme 2) was first prepared by a Diels-Alder reaction of 2-ethenylthiophene with 1,4-benzoquinone **3** in a three-step procedure starting from 2-iodothiophene, going to the ethenylthiophene diene, and then through reaction of the diene with **3**, giving **9b** in an overall yield of 24% [12]. The commercially available *E*-2-nitroethenylthiophene **8b** made it possible for us to carry out the preparation of **9b** in a single step (Scheme 2). Compound **8b** was allowed to react with two equivalents of 1,4-benzoquinone **3** in refluxing 1,2-dichlorobenzene, giving **9b** in only 4% yield, due to partial polymerization of **8b** and its low reactivity towards **3** (both reagents were detected). The product **9b** was characterized spectroscopically, and the ^{1}H NMR peaks were assigned by comparison with the spectrum of **4b**.

We attempted to prepare the known naphtho[2,3-*e*]benzothiophene-6,11-dione **10** [13] by our shorter and simpler procedure involving **8b** in a Diels-Alder reaction with 1,4-naphthoquinone **5**: reaction of **8b** with two equivalents of **5** in refluxing 1,2-dichlorobenzene for 7 days gave a mixture having a TLC analysis which showed eight spots and having a complex ^{1}H NMR spectrum which did not contain peaks which would be expected for the desired product **10**.

In the belief that a *C*-methyl group linked to a furan or thiophene ring might increase the reactivity of the corresponding 2-nitroethenyl compounds, we prepared the nitroethenyl derivatives **12a** and **12b** by a Knoevenagel condensation, as reported [14a,b,15a-c] (Scheme 3), and characterized them. The coupling constant of the ethenyl protons in the ^{1}H NMR spectrum of **12a** and **12b** enabled us to establish the *E* stereochemistry for their double bonds, which was consistent with what had previously been reported for **12b** [15a].

Refluxing of 2-(2-nitroethenyl)thiophene **12b** with two equivalents of 1,4-benzoquinone **3** in xylene for 5 days gave the new thiophene derivative **13b** in 8% yield (Scheme 3). The crude product also contained unreacted **12b** and polymeric material. Refluxing of **12b** with two equivalents of **3** at a higher temperature in 1,2-dichlorobenzene for 5 days also gave an 8% yield of **13b** (Scheme 3). Reaction of the nitroethenylfuran **12a** with two equivalents of 1,4-benzoquinone **3** in refluxing xylene for 7 days gave the new furan derivative **13a** in 4% yield (Scheme 3), which was recovered together with unreacted **12a** and polymeric material. Compounds **13a** and **13b** were characterized spectroscopically, and the ^{1}H NMR peaks were assigned by comparison with the spectrum of **4b**. Reactions of **12a** or **12b** with two equivalents of naphthoquinone **5** in refluxing 1,2-dichlorobenzene for 7 days gave black mixtures having TLC analyses, which showed several spots and complex ^{1}H NMR spectra, which

Scheme 3



revealed unchanged **5** but no peaks which would be expected for the desired products.

Conclusions.

The Diels-Alder reactions of 2-(2-nitroethenyl) derivatives of pyrroles, furans, and thiophenes with 1,4-benzoquinone and 1,4-naphthoquinone proceed in generally low yields. In the pyrrole cases especially, the main product was a dark or black amorphous polymer, the formation of which severely reduced the yield of Diels-Alder products. The presence of the built-in nitro group in the sidechain and the two molar equivalents of quinone dienophile may provide an oxidizing medium too strong for much of the sensitive pyrroles to withstand, in contrast to the relatively more stable indoles with which we have worked previously [3]. The best-yielding reactions were with the 1*H*-pyrrole (**2a**) and 1-methyl-1*H*-pyrrole (**2b**) derivatives, giving **4a** (10%) and **4b** (26%), respectively, allowing thorough characterization by IR, ^{13}C NMR, and high resolution mass spectroscopy. Products of the remaining reactions were analyzed similarly to the extent that available quantities permitted.

EXPERIMENTAL

General Methods.

Solvents and reagents were purchased and used as received. Reactions were monitored by TLC on precoated silica gel plates. Chromatography was performed with silica gel 60, 230-400 mesh. Melting points were uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively. ^{13}C NMR spectra were acquired proton-decoupled. Two dimensional ^{1}H-^{1}H COSY NMR experiments were run on a 300-MHz spectrometer. High resolution mass spectra were obtained using electron impact ionization (EI, 70 eV). Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ. 1-Methyl-2-(*E*-2-nitroethenyl)-1*H*-pyrrole **2b** was prepared in accordance with a reported method [6a].

2-(*E*-2-Nitroethenyl)-1*H*-pyrrole (**2a**).

Pyrrole-2-carboxaldehyde **1a** (3.0 g, 31.6 mmol) dissolved in absolute methanol (100 mL), containing nitromethane (4 mL, 73.9 mmol), sodium acetate (2.60 g, 31.7 mmol), and ethylamine hydrochloride (2.60 g, 31.9 mmol) was mixed and stirred at room temperature for 14 hours, giving a brown mixture. The insoluble material was filtered off and the solvent was removed *in vacuo* (2 mm Hg) without heating. The solid residue was suspended in methylene chloride (100 mL), and the still-insoluble material was collected and washed with water (200 mL), leaving **2a** as a yellow-brown solid (1.359 g, 31% yield); mp 105-107 °C (lit. mp 106 °C [6c], 98-103 °C [8a], 112-114 °C [8b]); IR (nujol, cm^{-1}) 3285 (NH), 1609 (C=C), 1545 (NO_2), 1323 (NO_2); ^{1}H NMR (methanol-d_4; δ, ppm) 7.97 (d, J= 13 Hz, 1H, 2'-H), 7.62 (d, J= 13 Hz, 1H, 1'-H), 7.14 (m, 1H, 5-H), 6.81 (m, 1H, 3-H), 6.33 (m, 1H, 4-H); ^{13}C NMR (methanol-d_4; δ, ppm) 128.72, 127.92, 124.65, 122.49, 117.74, 109.88; hrms m/z (M+) calcd for $C_6H_6N_2O_2$ 138.0429, found 138.0430.

2-(*E*-2-Nitroethenyl)-1-phenylsulfonyl-1*H*-pyrrole (**2c**).

1-Phenylsulfonylpyrrole-2-carboxaldehyde **1c** (1.00 g, 4.25 mmol), ammonium acetate (2.972 g, 38.6 mmol), and nitromethane (100 mL) were combined and the solution was refluxed with stirring for 24 hours. Evaporation of the solvent left a solid residue that was chromatographed on silica gel (chloroform:toluene 4:1, v/v), giving **2c** as yellow crystals (0.887 g, 75% yield); mp 132-133 °C (lit. mp 126-128 °C [10]); IR (nujol, cm^{-1}) 1628 (C=C), 1503 (NO_2), 1370 (SO_2N, partially nujol), 1328 (NO_2), 1152 (SO_2N); ^{1}H NMR (dimethyl sulfoxide-d_6; δ, ppm) 8.40 (d, J = 13 Hz, 1H, 2'-H), 8.10 (d, J = 13 Hz, 1H, 1'-H), 7.91 (m, 3H, *o*-H and 5-H), 7.80 (td, J = 7.6, 0.8 Hz, 1H, *p*-H), 7.69 (td, J= 7.6, 0.8 Hz, 2H, *m*-H), 7.40 (d, J = 3.6 Hz, 1H, 3-H), 6.60 (dd, J = 3.7, 3.6 Hz, 1H, 4-H); ^{13}C NMR (dimethyl sulfoxide-d_6; δ, ppm) 137.83, 137.31, 135.91, 130.92 (2C), 129.94, 127.21, 126.67 (2C), 126.03, 121.21, 115.13; hrms m/z (M^+) calcd for $C_{12}H_{10}N_2O_4S$ 278.0361, found 278.0344.

Benz[*e*]indole-6,9(3*H*)-dione (**4a**).

A solution of the diene **2a** (0.47 g, 3.4 mmol) and the dienophile **3** (0.75 g, 6.94 mmol) in xylene (20 mL) was refluxed with stirring for 5 days. After cooling, the suspension was filtered to collect the dark black material (0.393 g). This material was chromatographed on silica gel (hexane:ethyl acetate 6:4, v/v), giving **4a** (0.012 g) as a red powder. The solid which precipitated from the filtrate was collected and washed with a small volume of hexane, giving **4a** (0.032 g) as a red powder. The filtrate was evaporated to dryness *in vacuo* (2 mm Hg) without heating. Most of the unchanged **3** was sublimed away from a flask heated to its neck in warm water (85 °C). The sticky residue was chromatographed on silica gel (hexane:ethyl acetate 6:4, v/v), giving **4a** (0.027 g, 10% total yield) as a red powder; mp 241-244 °C; IR (nujol, cm^{-1}) 3294 (NH), 1649 (CO); ^{1}H NMR (dimethyl sulfoxide-d_6; δ, ppm) 11.89 (s, 1H, NH, exchanges in deuterium oxide), 7.82 (d, J = 8.6 Hz, 1H, 4-H), 7.77 (d, J = 8.6 Hz, 1H, 5-H), 7.75 (d, J = 2.7 Hz, 1H, 2-H), 7.27 (m, 1H, 1-H), 6.95 (s, 2H, 7-H and 8-H); ^{13}C NMR (dimethyl sulfoxide-d_6; δ, ppm) 187.65, 186.17, 140.89, 139.42, 138.22, 132.65, 125.91, 125.30, 123.85, 119.49, 117.67, 103.85; hrms m/z (M+) calcd for $C_{12}H_7NO_2$ 197.0477, found 197.0478.

3-Methylbenz[*e*]indole-6,9(3*H*)-dione (**4b**).

A solution of the diene **2b** (4.70 g, 30.9 mmol) and the dienophile **3** (7.10 g, 65.7 mmol) in xylene (200 mL) was refluxed with stirring for 48 hours. After cooling the dark black material (2.344 g) was filtered off, and the filtrate was evaporated to dryness *in vacuo* (2 mm Hg) without heating. Compound **3** and hydroquinone were sublimed away *in vacuo* (2 mm Hg) from a flask heated to its neck in warm water (75 °C). The residue was dissolved in methylene chloride (75 mL) and hexane (200 mL) was added, causing separation of sticky material, which was removed by filtration. Evaporation of the filtrate left a solid that was washed with carbon tetrachloride and crystallized from benzene (125 mL). The precipitated solid was collected and washed with hexane (100 mL), giving **4b** (1.384 g) as a red powder. The benzene mother liquor was slowly evaporated at room temperature. When the volume was about 5 mL, the precipitated solid was collected and washed with hexane (100 mL), giving **4b** as a red powder (0.348 g, 26% total yield); mp 167-168 °C (lit. 86%, mp 157 °C [5]); IR (nujol, cm^{-1}) 1653 (CO); ^{1}H NMR (dimethyl sulfoxide-d_6; δ, ppm) 7.88 (d, J= 8.5 Hz, 1H, 4-H), 7.76 (d, J =

8.5 Hz, 1 H, 5-H), 7.70 (d, J = 3 Hz, 1 H, 2-H), 7.23 (d, J = 3 Hz, 1H, 1H), 6.93 (s, 2H, 7-H and 8-H), 3.87 (s, 3H, CH_3); ^{13}C NMR (dimethyl sulfoxide-d_6; δ, ppm) 187.55, 186.09, 140.94, 139.41, 138.20, 136.74, 125.82, 125.54, 123.83, 119.34, 115.98, 103.17, 33.28; hrms m/z (M+) calcd for $C_{13}H_9NO_2$ 211.0633, found 211.0635.

Anal. Calcd. for $C_{13}H_9NO_2$: C, 73.93; H, 4.27; N, 6.64. Found: C, 73.81; H, 4.45; N, 6.58.

3-Phenylsulfonylbenz[*e*]indole-6,9(3*H*)-dione (**4c**).

A solution of the diene **2c** (0.278 g, 1.00 mmol) and the dienophile **3** (0.216 g, 2.00 mmol) in xylene (20 mL) was refluxed with stirring for 5 days. After cooling, the resulting suspension was filtered to remove a tiny amount of dark black solid. The filtrate was evaporated to dryness *in vacuo* (2 mm Hg) without heating; the sticky residue was chromatographed on silica gel (methylene chloride:toluene 1:1, v/v), giving **4c** as an orange solid (0.029 g, 9% yield); mp 247-250 °C; IR (nujol, cm^{-1}) 1665 (CO), 1374 (SO_2N, partially nujol), 1138 (SO_2N); ^1H NMR (dimethyl sulfoxide-d_6; δ, ppm) 8.42 (d, J= 8.8 Hz, 1H, 4-H), 8.21 (d, J= 3.7 Hz, 1H, 2-H), 8.07 (d, J = 8.1 Hz, 2H, *o*-H), 7.98 (d, J = 8.8 Hz, 1H, 5-H), 7.73 (t, J = 7.5 Hz, 1H, *p*-H), 7.62 (m, 2H, *m*-H), 7.58 (d, J= 3.7 Hz, 1H, 1-H), 7.01 (s, 2H, 7-H and 8-H); ^{13}C NMR (dimethyl sulfoxide-d_6; δ, ppm) 186.67, 185.29, 139.69, 138.35, 138.26, 137.10, 135.80, 132.82, 130.67 (2C), 128.76, 128.33, 127.46 (2C), 124.67, 123.11, 118.86, 109.92; hrms m/z (M+) calcd for $C_{18}H_{11}NO_4S$ 337.0409, found 337.0390.

3-Methylnaphtho[2,3-*e*]indole-6,11(3*H*)-dione (**6b**).

A solution of the diene **2b** (0.456 g, 3.00 mmol) and the dienophile **5** (0.982 g, 6.00 mmol) in xylene (20 mL) was refluxed with stirring with for 48 hours. After cooling, the resulting suspension was filtered to remove a small amount of dark black material. The filtrate was concentrated to half volume *in vacuo* (2 mm Hg) without heating; a small amount of dark black precipitate formed within a day and was filtered off. The filtrate was evaporated to dryness *in vacuo* (2 mm Hg) without heating; the remaining sticky residue was suspended in acetone (5 mL) and the insoluble material was collected. This solid was heated at 90 °C (warm water) *in vacuo* (2 mm Hg) to sublime away unchanged **5**, leaving **6** (0.047 g, 6% yield) as a brown powder; mp 179-182 °C (lit. 67%, mp 197 °C [5]); IR (nujol, cm^{-1}) 1663 (CO); ^1H NMR (dimethyl sulfoxide-d_6; δ, ppm) 8.17 (m, 2H, 7-H and 10-H), 8.04 (d, J= 8.7 Hz, 1H, 4-H), 7.98 (d, J= 8.7 Hz, 1H, 5-H), 7.88 (m, 2H, 8-H and 9-H), 7.75 (d, J= 2.8 Hz, 1H, 2-H), 7.43 (d, J= 2.8 Hz, 1H, 1-H), 3.91 (s, 3H, CH_3); ^{13}C NMR (dimethyl sulfoxide-d_6; δ, ppm) 184.77, 183.50, 140.99, 136.52, 134.56, 134.42, 134.18, 133.34, 127.42, 126.90, 126.74, 126.12, 125.40, 120.16, 116.59, 104.10, 33.33; hrms m/z (M+) calcd for $C_{17}H_{11}NO_2$ 261.0790, found 261.0781.

Naphtho[2,1-*b*]furan-6,9-dione (**9a**).

A. Reaction in Xylene.

A solution of the diene **8a** (0.417 g, 3.00 mmol) and dienophile **3** (0.648 g, 6.00 mmol) in xylene (20 mL) was refluxed with stirring for 7 days. After cooling, the suspension was filtered to remove the dark black solid (0.132 g). Evaporation of the filtrate left a sticky residue that was chromatographed on silica gel (chloroform:toluene 4:1, v/v), giving a small amount of dark red, sticky, oily material containing **9a**; ^1H NMR (dimethyl sulfoxide-d_6; δ, ppm) 8.33 (d, J= 2.2 Hz, 1H, 2-H), 8.02 (d, J = 8.7 Hz, 1H, 4-H), 7.92 (d, J = 8.7 Hz, 1H, 5-H), 7.56 (d, J= 2.2 Hz, 1H, 1-H), 7.02 (s, 2H, 7-H and 8-H).

B. Reaction in 1,2-Dichlorobenzene.

A solution of the diene **8a** (0.417 g, 3 mmol) and the dienophile **3** (0.648 g, 6.00 mmol) in 1,2-dichlorobenzene (20 mL) was refluxed with stirring for 7 days. After cooling, the suspension was filtered to remove the dark black solid (0.456 g). Evaporation of the filtrate left a small amount of dark red sticky oily material containing **9a**; the ^1H NMR spectrum was identical with that of the material obtained in part A.

Naphtho[2,1-*b*]thiophene-6,9-dione (**9b**).

A solution of the diene **8b** (0.465 g, 3.00 mmol) and the dienophile **3** (0.648 g, 6.00 mmol) in 1,2-dichlorobenzene (20 mL) was refluxed with stirring for 5 days. After cooling, the suspension was filtered to remove the dark black solid (0.083 g). Evaporation of the filtrate left a sticky material that was suspended in toluene (5 mL) and the suspension was filtered to remove the solid. Evaporation of the filtrate left a sticky residue that was chromatographed on silica gel (chloroform:toluene 4:1, v/v), giving **9b** as a brown solid (0.025 g, 4% yield); mp 152-155 °C (lit. mp 167-168 °C [12]); IR (nujol, cm^{-1}) 1654 (CO); ^1H NMR (dimethyl sulfoxide-d_6; δ, ppm) 8.52 (d, J = 8.4 Hz, 1H, 4-H), 8.48 (d, J = 5.7 Hz, 1H, 2-H), 8.21 (d, J = 5.7 Hz, 1H, 1-H), 7.96 (d, J = 8.4 Hz, 1H, 5-H), 7.06 (s, 2H, 7-H and 8-H); ^{13}C NMR (dimethyl sulfoxide-d_6; δ, ppm) 186.85, 185.81, 146.83, 139.79, 137.94, 136.61, 134.86, 130.07, 129.27, 125.94, 124.46, 121.52; hrms m/z (M+) calcd for $C_{12}H_6O_2S$ 214.0088, found 214.0076.

Analyses of Compounds **12a** and **12b**.

Compounds **12a** and **12b** were prepared as reported [15c].

2-Methyl-5-(*E*-2-nitroethenyl)furan (**12a**).

This compound was obtained as a brown solid (3.605 g, 71% yield); mp 70-74 °C (lit. mp 75 °C [14a], 75-76 °C [14b]); IR (nujol, cm^{-1}) 1636 (C=C), 1522 (NO_2), 1328 (NO_2); ^1H NMR (dimethyl sulfoxide-d_6; δ, ppm) 7.95 (d, J= 13.2 Hz, 1H, 2'-H), 7.63 (d, J= 13.2 Hz, 1H, 1'-H), 7.21 (d, J = 3.3 Hz, 1H, 3-H), 6.43 (d, J = 3.3 Hz, 1H, 4-H), 2.38 (s, 3H, CH_3); ^{13}C NMR (dimethyl sulfoxide-d_6; δ, ppm) 159.11, 145.73, 133.40, 126.74, 124.09, 111.38, 14.31; hrms m/z (M+) calcd for $C_7H_7NO_3$ 153.0426, found 153.0434.

2-Methyl-5-(E-2-nitroethenyl)thiophene (**12b**).

This compound was obtained as a yellow solid (1.203 g, 21% yield); mp 81-82 °C (lit. mp 82-82.5 °C [15b], 79-81 °C [15c]; IR (nujol, cm^{-1}) 1611 (C=C), 1377 or 1329 (NO_2); ^1H NMR (dimethyl sulfoxide-d_6; δ, ppm) 8.28 (d, J= 13.2 Hz, 1H, 2-H), 7.84 (d, J= 13.2 Hz, 1H, 1'-H), 7.65 (d, J= 4.2 Hz, 1H, 3-H), 6.97 (d, J= 4.2 Hz, 1H, 4-H), 2.52 (s, 3H, CH_3); ^{13}C NMR (dimethyl sulfoxide-d_6; δ, ppm) 148.96, 137.32, 134.98, 133.62, 132.11, 128.57, 16.14; hrms m/z (M+) calcd for $C_7H_7NO_2S$ 169.0197, found 169.0203.

2-Methylnaphtho[2,1-*b*]furan-6,9-dione (**13a**).

A solution of the diene **12a** (0.459 g, 3.00 mmol) and the dienophile **3** (0.648 g, 6 mmol) in xylene (20 mL) was refluxed with stirring for 7 days. After cooling, the suspension was filtered to remove the dark black solid (0.326 g). Evaporation of

the filtrate left a sticky residue that was chromatographed on silica gel (chloroform:toluene 4:1, v/v), giving **13a** as a brown solid (0.029 g, 4% yield); mp 167-170 °C; IR (nujol, cm^{-1}) 1660 (CO); ^1H NMR (dimethyl sulfoxide-d_6; δ, ppm) 7.95 (d, J = 8.4 Hz, 1H, 4-H), 7.87 (d, J= 8.4 Hz, 1H, 5-H), 7.30 (s, 1H, 1-H), 7.04 (s, 2H, 7-H and 8-H), 2.56 (s, 3H, CH_3); ^{13}C NMR (dimethyl sulfoxide-d_6; δ, ppm) 186.38, 185.32, 162.56, 158.28, 139.48, 138.66, 128.21, 127.89, 122.35, 116.43, 104.28, 14.47; hrms m/z (M+) calcd for $C_{13}H_8O_3$ 212.0473, found 212.0477.

2-Methylnaphtho[2,1-*b*]thiophene-6,9-dione (**13b**).

A. Reaction in Xylene.

A solution of the diene **12b** (0.507 g, 3.00 mmol) and the dienophile **3** (0.648 g, 6.00 mmol) in xylene (20 mL) was refluxed with stirring for 5 days. After cooling, the suspension was filtered to remove the dark black solid (0.041 g). Evaporation of the filtrate left a sticky residue that was chromatographed on silica gel (chloroform:hexane 4:1, v/v), giving **13b** as a brown-yellow solid (0.054 g, 8% yield); mp 158-160 °C; IR (nujol, cm^{-1}) 1660 (CO); ^1H NMR (dimethyl sulfoxide-d_6; δ, ppm) 8.35 (d, J= 8.1 Hz, 1H, 4-H), 8.18 (s, 1H, 1-H), 7.85 (d, J = 8.1 Hz, 5-H), 7.02 (s, 2H, 7-H and 8-H), 2.67 (s, 3H, CH_3); ^{13}C NMR (dimethyl sulfoxide-d_6; δ, ppm) 186.63, 185.75, 148.89, 146.79, 139.74, 137.87, 137.42, 129.87, 128.53, 124.86, 122.55, 120.92, 16.82; hrms m/z (M+) calcd for $C_{13}H_8O_2S$ 228.0245, found 228.0233.

B. Reaction in 1,2-Dichlorobenzene.

A solution of the diene **12b** (0.507 g, 3.00 mmol) and the dienophile **3** (0.648 g, 6.00 mmol) in 1,2-dichlorobenzene (20 mL) was refluxed with stirring for 5 days. After cooling, the suspension was filtered to remove the dark black solid (0.489 g). Evaporation of the filtrate left a sticky residue that was chromatographed on silica gel (chloroform: hexane 4:1, v/v), giving **13b** as a brown-yellow solid (0.053 g, 8% yield); the spectroscopic data were identical with those of the material obtained in part A.

Acknowledgements.

We thank the Wayland E. Noland Research Fellowship Fund of the University of Minnesota Foundation for a postdoctoral fellowship for G. P.

REFERENCES AND NOTES

[1a] M. Rogge, G. Fischer, U. Pindur and D. Schollmeyer, *Monatsh. Chem*., **127**, 97 (1996); [b] M. Dräger, M. Haber, H. Erfanian-Abdoust, U. Pindur and K. Sattler, *Monatsh. Chem*., **124**, 559 (1993); [c] U. Pindur, L. Pfeuffer, M. Eitel, M. Rogge and M. Haber, *Monatsh. Chem*., **122**, 291 (1991); [d] S. P. Hiremath and M. G. Purohit, *Indian J. Chem*., **12**, 493 (1974).

[2] Wayland E. Noland, University of Minnesota, unpublished results received from the National Cancer Institute.

[3] W. E. Noland, M. J. Konkel, M. S. Tempesta, R. D. Cink, D. M. Powers, E. O. Schlemper and C. L. Barnes, *J. Heterocyclic Chem*., **30**, 183 (1993).

[4] W. E. Noland and B. L Kedrowski, *J. Org. Chem*., **64**, 596 (1999).

[5] R. S. Hosmane, S. P. Hiremath and S. W. Schneller, *J. Chem. Soc., Perkin Trans. I*, 2450 (1973).

[6a] S. A. F. Rostom, A. M. Farghaly, F. S. G. Soliman, M. M. El-Semary, S. Elz and J. Lehmann, *Arch. Pharm. Pharm. Med. Chem*., **334**, 241 (2001); [b] J. Bourguignon, G. Le Nard and G. Queguiner, *Can. J. Chem*., **63**, 2354 (1985); [c] A. S. Polyanskaya, V. V. Perekalin, N. I. Aboskalova, Z. I. Demireva, L. N. Sokolova and Z. A. Abdulkina, *J. Org. Chem. USSR* (Engl. Transl.), **15**, 1859 (1979).

[7] R. M. Silverstein, G. C. Bassler and T. C. Morrill, Spectrometric Identification of Organic Compounds, John Wiley and Sons, New York, NY, 1981, p 235.

[8a] G. J. T. Kuster, R. H. J. Steeghs and H. W. Scheeren, *Eur. J. Org. Chem*., 553 (2001); [b] J. P. Strachan, D. F. O'Shea, T. Balasubramanian, and J. S. Lindsey, *J. Org. Chem*., **65**, 3160 (2000).

[9] S. L. Vorob'eva, V. N. Buyanov, I. I. Levina, and N. N. Suvorov, *Chem. Heterocycl. Compd*. (Engl. Transl.), 58 (1989).

[10] A. Hamdan and J. W. F. Wasley, *Synth. Commun*., **15**, 71 (1985).

[11] R. S. Kusurkar and D. K. Bhosale, *Synth. Commun*., **20**,101 (1990).

[12] W. Davies and Q. N. Porter, *J. Chem. Soc*., 4958 (1957).

[13] Y. Tominaga, M. L. Lee, and R. N. Castle, *J. Heterocyclic Chem*., **18**, 967 (1981), and references therein.

[14a] Y. K. Yur'ev, N. S. Zefirov and R. A. Ivanova, *J. Gen. Chem. USSR* (Engl. Transl.), **33**, 3444 (1963); [b] E. W. Scott and J. R. Johnson, *J. Am. Chem. Soc*., **54**, 2549 (1932).

[15a] H. Satonaka and M. Watanabe, *Bull. Chem. Soc. Jpn*., **58**, 3651 (1985); [b] M. L. Dressler and M. M. Joullie, *J. Heterocyclic Chem*., **7**, 1257 (1970); [c] W. J. King and F. F. Nord, *J. Org. Chem*., **14**, 405 (1949).