9-(2-Thienyl)-7-oxaspiro[5.4]decan-8-one (5i), a white, highly crystalline solid, was obtained in 77% yield; an analytical sample was obtained via recrystallization from hexane: mp 54–54.5 °C; IR (KBr) 2930, 1773, 1207, 1197, 1124, 730 cm^{-1}; NMR ($CDCl_3$) δ 7.33–6.92 (m, 3 H, thienyl C*H*), 4.30 (dd, *J* = 9,11 Hz, 1 H, C*H*C=O), 2.92–2.11 (m, 2 H, lactone CH_2), 2.05–1.31 (e, 10 H, cycloalkyl C*H*); TLC (CH_2Cl_2) R_f 0.67. Anal. Calcd for $C_{13}H_{16}O_2S$: C, 66.07; H, 6.82. Found: C, 66.02; H, 6.68.

9-(3,4-Dimethoxyphenyl)-7-oxaspiro[5.4]decan-8-one (5j), a white, powdery solid, was obtained in 90% yield; an analytical sample was obtained via column chromatography ($CHCl_3$): mp 88–88.5 °C; IR (KBr) 2937, 1760, 1522, 1269, 1121, 937 cm^{-1}; NMR ($CDCl_3$) δ 6.81 (s, 3 H, Ar *H*), 3.92 (s, 6 H, OCH_3), 3.93–3.65 (m, 1 H, C*H*C=O), 2.62–2.11 (m, 2 H, lactone CH_2), 1.81–1.29 (e, 10 H, cycloalkyl C*H*); TLC ($CHCl_3$) R_f 0.11. Anal. Calcd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.66; H, 7.77.

***trans,trans*-3-Phenyl-3a,4,5,6,7,7a-hexahydro-2(3*H*)-benzofuranone (9a)**, a white, crystalline solid, was obtained in 98% yield; an analytical sample was secured via recrystallization from hexane: mp 67–70 °C; IR (KBr) 2948, 2863, 1777, 1168, 1139 cm^{-1}; NMR ($CDCl_3$) δ 7.39–7.21 (m, 5H, Ar *H*), 3.92 (m, 1 H, C*H*OC=O), 3.44 (d, *J* = 12.91 Hz, 1 H, PhC*H*), 2.17–1.29 (e, 9 H, aliphatic C*H*); TLC (CH_2Cl_2) R_f 0.43. Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.50, H, 7.56.

***trans,trans*-3-Phenoxy-3a,4,5,6,7,7a-hexahydro-2(3*H*)-benzofuranone (9b)**, a white, crystalline solid, was obtained in 82% yield; an analytical sample was secured via recrystallization from hexane: mp 110–112 °C; IR (KBr) 2980, 2834, 1785, 1596, 1589 cm^{-1}; NMR ($CDCl_3$) δ 7.29–7.05 (m, 5 H, Ar *H*), 4.73 (d, *J* = 11.60 Hz, 1 H, PhOC*H*), 3.90 (m, 1 H, C*H*OC=O), 2.30–1.32 (e, 9H, aliphatic C*H*); TLC (CH_2Cl_2) R_f 0.46. Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.32; H, 7.17.

***trans,trans*-3-(Phenylthio)-3a,4,5,6,7,7a-hexahydro-2-(3*H*)-benzofuranone (9c)**, a beige oil, was obtained in 90% yield; an analytical sample was secured via chromatography using dichloromethane as eluent: IR (film) 2941, 1780, 1480, 1440, 1203, 1166 cm^{-1}; NMR ($CDCl_3$) δ 7.62–6.89 (m, 5 H, Ar *H*), 4.26–3.55 (m 2 H, PhSC*H* + OC*H*), 2.41–1.02 (e, 9 H, aliphatic C*H*); TLC (CH_2Cl_2) R_f 0.39. Anal. Calcd for $C_{14}H_{16}O_2S$: C, 67.71; H, 6.49. Found: C, 68.02; H, 6.55.

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this work. W.J.D. thanks the Dow Chemical Company Foundation for partial summer support. High-field NMR data were acquired with the assistance of the Molecular Spectroscopy Laboratory of the University of Illinois at Urbana–Champaign.

Registry No. **1a**, 103-82-2; **1b**, 122-59-8; **1c**, 103-04-8; **1d**, 107-92-6; **1e**, 86-87-3; **1f**, 79-09-4; **1g**, 104-01-8; **1h**, 1878-66-6; **1i**, 1918-77-0; **1j**, 93-40-3; **2**, 2043-61-0; **3a**, 114049-47-7; **3b**, 114049-48-8; **3c**, 114049-49-9; **3d**, 114049-45-5; **3e**, 117097-51-5; **3f**, 101972-51-4; **3g**, 117097-52-6; **3h**, 117097-53-7; **3i**, 117097-54-8; **3j**, 117097-55-9; **4a**, 114049-53-5; **4b**, 114049-54-6; **4c**, 114049-55-7; **4d**, 114049-51-3; **4e**, 117097-56-0; **4f**, 114049-50-2; **4g**, 117097-57-1; **4h**, 117097-58-2; **4i**, 117097-59-3; **4j**, 117097-60-6; **5a**, 77197-78-5; **5b**, 114049-58-0; **5c**, 53138-49-1; **5d**, 114049-56-8; **5e**, 117097-61-7; **5f**, 16149-84-1; **5g**, 117097-62-8; **5h**, 117097-63-9; **5i**, 117097-64-0; **5j**, 117097-65-1; **6**, 872-53-7; **7a**, 116491-82-8; **7b**, 116491-83-9; **7c**, 117097-66-2; **8a**, 116491-84-0; **8b**, 116491-85-1; **8c**, 117097-67-3; **9a**, 116491-86-2; **9b**, 116491-87-3; **9c**, 117097-68-4.

Formation of N–N and N–C Bond-Cleavage Products in Displacements with N,N-Disubstituted Hydrazines on 1-Halo- or 1,4-Dihaloanthracene-9,10-diones

A. Paul Krapcho* and Kenneth L. Avery, Jr.

Department of Chemistry, The University of Vermont, Burlington, Vermont 05405

Received March 11, 1987

The displacements of 1-halo- and 1,4-dihaloanthracene-9,10-diones by N,N-disubstituted hydrazines have been studied. These reactions proceed via N–N bond cleavages of the hydrazine to yield products with the regiospecific incorporation of an N,N-disubstituted amino group. In addition, pyrazoles which arise from intermediates which undergo N–C bond cleavage are also formed. The ratio of the N–N to N–C cleavage products is dependent on the reaction solvent, temperature, structure of the hydrazine, and the nature of the leaving group being displaced from the anthracene-9,10-dione. For example, treatment of **1a** with *N,N*-dimethylhydrazine in pyridine or dimethyl sulfoxide (DMSO) leads to **3a**:**2c** ratios of 6 and 3, respectively. Compound **1e** under comparable reaction conditions gives **3a**:**2c** product ratios of 49 and 4, respectively. The dichloro dione **1c** with *N,N*-dimethylhydrazine in pyridine or DMSO leads predominantly to **3b** in 76% and 72% yields, respectively, with relatively little pyrazole **2d**. The more reactive difluoro dione **1h** on reaction with *N,N*-dimethylhydrazine in pyridine leads to N–N bond-cleavage products **3c** (48%) and **3d** (40%). Treatment of **1e** with 1-piperidinamine in pyridine yields **3f**. The results will be discussed.

As part of a program dealing with the synthesis of hydrazino-substituted anthracene-9,10-diones for antitumor evalation, we have studied the displacement reactions of N,N-disubstituted hydrazines and halo-substituted anthracene-9,10-diones.[1,2] It has been reported that **1a** with hydrazine leads to the hydrazino dione **1b**.[3] On the other hand, when **1c** is heated with hydrazine the initially formed hydrazine **1d** undergoes a facile cyclization to yield pyrazole **2b**.[4]

The pyrazoles **2c** or **2d** are obtained when **1a** or **1c** is treated with methylhydrazine in pyridine, respectively.[4] The nitrogen atom bearing the methyl group initially displaces the chloride anion and the resultant hydrazines undergo cyclizations to the pyrazoles. In other reported

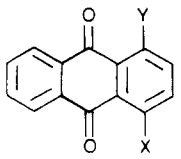
(1) (a) Krapcho, A. P.; Shaw, K. J.; Landi, J. J., Jr.; Phinney, D. G. *J. Org. Chem.* **1984**, *49*, 5253. (b) Krapcho, A. P.; Landi, J. J., Jr.; Hacker, M. P.; McCormack, J. J. *J. Med. Chem.* **1985**, *28*, 1124. (c) Krapcho, A. P.; Landi, J. J., Jr.; Shaw, K. J.; Phinney, D. G.; Hacker, M. P.; McCormack, J. J. *J. Med. Chem.* **1986**, *29*, 1370.

(2) Krapcho, A. P.; Avery, K. L., Jr.; Shaw, K. J., presented in part at the Northeast Regional Meeting of the American Chemical Society, SUNY Binghamton, June 1986, Abstract 188.

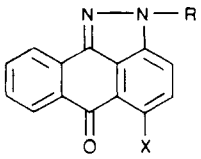
(3) (a) Mohlau, R. *Chem. Ber.* **1912**, *45*, 2244. (b) Our examination of the reaction products shows the presence of some **2a**.

(4) Bradley, W.; Geddes, K. W. *J. Chem. Soc.* **1952**, 1630.

0022-3263/88/1953-5927$01.50/0



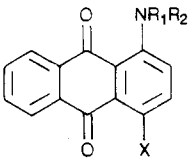
1a, X = H; Y = Cl
b, X = H; Y = $NHNH_2$
c, X = Y = Cl
d, X = Cl; Y = $NHNH_2$
e, X = H; Y = F
f, X = H; Y = $NHCH_3$
g, X = H; Y = $NHN(CH_3)_2$
h, X = Y = F



2a, R = H; X = H
b, R = H; X = Cl
c, R = CH_3; X = H
d, R = CH_3; X = Cl

examples of apparent SNAr displacements with monoalkylhydrazines on substituted anthracene-9,10-diones,[5] and halonitrobenzenes,[6] the nitrogen bearing the alkyl group is the nucleophilic site.

Our examination of the literature did not uncover any examples of reactions of haloanthracene-9,10-diones with N,N-disubstituted hydrazines. However, related studies that deal with reactions of 2-chlorobenzothiazoles (and similar systems)[7] and halonitrobenzenes[8,9] with *N,N*-dialkylhydrazines are pertinent. In the former case, products of dealkylation (N–C cleavage) and deamination (N–N cleavage) were obtained.[7] In the studies dealing with the halonitrobenzenes, it was shown that the products are highly dependent on the substrate structure.[8,9] It has been proposed that the different reaction pathways can be rationalized by the formation of charge-transfer complexes with highly π deficient (e.g., 2,4,6-trinitrochlorobenzene) polynitrohalo aromatics with the more substituted nitrogen of the hydrazine.[8] This complexation leads to attack on the ring by the unsubstituted nitrogen. For less π-electron-deficient aromatics (e.g., 2-nitrofluorobenzene) no charge-transfer complex is formed with the hydrazine and nucleophilic attack by the disubstituted nitrogen leads to an intermediate that eventually yields the N,N-disubstituted aniline via a N–N bond cleavage.



3a, X = H; $R_1 = R_2 = CH_3$
b, X = Cl; $R_1 = R_2 = CH_3$
c, X = F; $R_1 = R_2 = CH_3$
d, X = $N(CH_3)_2$; $R_1 = R_2 = CH_3$
e, X = Cl; R_1; $R_2 = —(CH_2)_5—$
f, X = H; R_1, $R_2 = —(CH_2)_5—$

A summary of displacements on **1a**, **1c**, and **1e** with *N,N*-dimethylhydrazine under different reaction conditions is tabulated in Table I.

The data presented in Table I shows that the **3a**:**2c** product ratios (from **1a** or **1e**) depend on the solvent and temperature. In pyridine the predominant product arises from an N–N cleavage while in DMSO the proportion of N–C bond-cleavage product increases. This same trend is seen for reactions of **1c**.

Table I. Products from Reactions of 1a, 1c, and 1e with *N,N*-Dimethylhydrazine

starting dione	product ratios **3a**:**2c**[a,b]	solvent (conditions)
1a	6:1	pyridine (4equiv, RT,[g] 308 h)
1a	24:1[c]	pyridine (4equiv, 65 °C, 42 h)
1a	3:1	DMSO (4equiv, RT, 308 h)
1a	2:1	DMSO (4equiv, 74 °C, 42 h)
1c	76:1	pyridine (8equiv, RT, 96 h)
1c	32:1	neat (RT, 27 h)
1c	6:1	DMSO (8equiv, RT, 96 h)
1e	49:1	pyridine (2equiv, RT, 43 h)
1e	6:1[d]	pyridine (4equiv, 96 °C, 48 h)
1e	4:1[e]	DMSO (2equiv, RT, 43 h)
1e	1:1[f]	DMSO (4equiv, 73 °C, 48 h)

[a] For **1a** and **1e** the ratio of **3a**:**2c** was determined by ^1H NMR analysis of methyl group integrals. [b] For **1c** the ratio of **3b**:**2d** was obtained from isolated percentage yield data. [c] Some **1f** and **1g** were also present. [d] Isolation led to **3a** (53%), **2c** (10%), **1f** (12%), and **1g** (3%). [e] Isolation gave **3a** (36%), **2c** (14%), some starting material, and **1f** and **1g**. [f] Isolation led to **3a** (19%), **2c** (49%), **1f** (5%), and **1g** (6%). Some **3a** was lost in workup. [g] RT = room temperature.

The more reactive difluoro dione **1h** on treatment with *N,N*-dimethylhydrazine in pyridine at room temperature (73 h) led to the N–N bond-cleavage products **3c** (48%) and **3d** (40%). Reactions of **1c** and **1e** with 1-piperidinamine in pyridine led predominantly to the N–N bond-cleavage products **3e** (85%) and **3f** (61%), respectively.

Discussion

Displacement rates for similar halides from 1- and 2-haloanthracene-9,10-diones and *o*- or *p*-halonitrobenzenes by various nucleophiles differ only by a factor of 2 in a variety of solvents.[10,11] This rate similarity is suggestive of comparable π-electron deficiencies in these systems.

In the reactions reported here, no charge-transfer complexation would be expected to occur between the disubstituted end of the hydrazine and the haloanthracene-9,10-diones.[8] For example, treatment of **1a** with *N,N*-dimethylhydrazine would lead to intermediate **4**, which on loss of chloride anion would give intermediate **5**. This intermediate could then partition into the products via two S_N2 pathways. Dimethylamino adduct **3a** would derive from an N–N bond cleavage and pyrazole **2c** from an initial C–N bond cleavage to intermediate **6** followed by cyclodehydration.

The N–N versus N–C cleavage ratio is expected to be dependent on the reaction solvent,[12] the temperature, and the nature of the halide anion present in the intermediate (Table I, entries 5 and 8).

Similar mechanistic arguments explain the products derived from reaction of **1e** with 1-piperidinamine. The formation of **1f** via demethylation of **3a** has been previously noted.[13]

Experimental Section

Melting points were determined on a Thomas-Hoover apparatus and are uncorrected. Proton NMR spectra were run on a Bruker

(5) (a) Showalter, H. D. H.; Johnson, J. L.; Werbel, L. M.; Leopold, W. K.; Jackson, R. C.; Elslager, E. F. *J. Med. Chem.* **1984**, *27*, 253. (b) Showalter, H. D.; Berman E. M.; Johnson, J. L.; Atwood, J. L.; Hunter, W. E. *Tetrahedron Lett.* **1985**, *26*, 157. (c) Showalter, H. D. H.; Johnson, J. L.; Hoftiezer, J. M. *J. Heterocycl. Chem.* **1986**, *23*, 1491. (d) Showalter, H. D. H.; Johnson, J. L.; Hoftiezer, J. M.; Turner, W. R.; Leopold, W. R.; Shillis, J. L.; Jackson, R. C.; Elslager, E. F. *J. Med. Chem.* **1987**, *30*, 121.

(6) Blanksma, J. J.; Wackers, M. L. *Recl. Trav. Chim. Pays-Bas* **1936**, *55*, 655, 661.

(7) Nagarajan, K.; Kulkarni, C. L.; Shah, R. K. *Ind. J. Chem.* **1971**, *9*, 748.

(8) (a) Latham, D. W. S.; Meth-Cohn, O.; Suschitzky, H. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2216. (b) Latham, D. W. S.; Meth-Cohn, O.; Suschitzky, H. *Tetrahedron Lett.* **1972**, 5365.

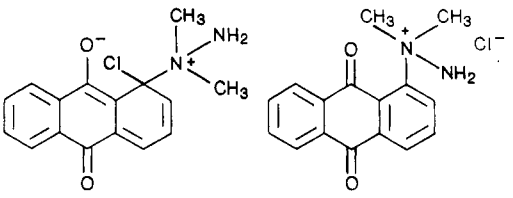
(9) (a) Vis, B. *Recl. Trav. Chim. Pays-Bas* **1939**, *58*, 747. (b) Poirier, R. H.; Benington, F. *J. Org. Chem.* **1954**, *19*, 1157.

(10) Shein, S. M.; Shternshis, M. V. *J. Org. Chem. USSR (Engl. Ed.)* **1971**, *7*, 1278.

(11) (a) Crampton, M. R. *Organic Reaction Mechanisms*; Knipe, A. C., Watts, W. E., Eds.; John Wiley and Sons, Ltd.: New York, 1986; pp 249–268. (b) Bunnett, J. F.; Zahler, R. E. *Chem. Rev.* **1951**, *49*, 273–412.

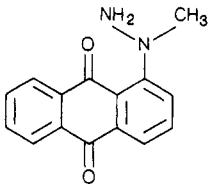
(12) Parker, A. J. *Adv. Phys. Org. Chem.* **1967**, *5*, 173.

(13) Lord, W. M.; Peters, A. T. *J. Chem. Soc. C* **1968**, 783.



4

5



6

WP270SY or WM-250 pulsed Fourier transform spectrometer. TLC precoated silica and alumina sheets (Eastman Chromagram sheets with fluorescent indicator) were used to monitor reactions. Chromatography was performed on a preparative centrifugally accelerated, radial thin layer chromatograph Chromatotron Model 7924 (Harrison Research, 840 Moana Court, Palo Alto, CA) using plates of Merck silica gel 60 PF 254 containing gypsum. Baker analyzed 80–200-mesh silica gel was utilized for column chromatography. Microanalyses were performed by Robertson Laboratories, Madison, NJ. Mass spectra were run on a Finnigan Mat 4610 mass spectrometer (70 ev, electron impact). All pyrazoles fluoresce yellow under long and short wavelength radiation.

The hydrazines and **1a** were purchased from the Aldrich Chemical Co. Dione **1e** was prepared from 1-aminoanthracene-9,10-dione.[14] The diones **1c**[15] and **1h**[15] as well as the pyrazoles **2b**[4] and **2c**[4] were prepared by literature routes.

The product ratios of **3b** (3.04 ppm) and **2d** (4.22 ppm) were in most cases determined by integration of methyl peaks in the ^{1}H NMR spectrum. The reliability of this method was determined by ^{1}H NMR spectral analysis of a standardized solution of **3b** and **2d**.

General Displacement Procedure. All room temperature reactions were performed in a stoppered flask or a flask equipped with a drying tube. The reactions at elevated temperatures were performed with reflux condensers purged with nitrogen and connected to a bubbler. The stoichiometry, temperature, and reaction times are given in Table I. The reactions were quenched with cold water and the products filtered. Some of the reactions led to oils that were extracted with CH_2Cl_2 or $CHCl_3$. The products were analyzed by ^{1}H NMR or chromatographed.

Typical Procedures. (1) (Table I, Entry 8). Fluoro dione **1e** (107 mg, 0.47 mmol), *N,N*-dimethylhydrazine (56.9 mg, 0.95 mmol), and pyridine (5 mL) were placed in a stoppered flask. The resulting red solution was stirred at room temperature for 43 h. Quenching with water, filtration, and analysis by NMR ($CDCl_3$) of the crude sample gave **3a** and **2c** in a 49:1 ratio. ^{1}H NMR ($CDCl_3$) of the crude: δ 3.03 (s, 6 H), 4.26 (very minor singlet, pyrazolo), 7.31 (m, 1 H), 7.56 (m, 1 H), 7.78 (m, 3 H), 8.24 (m, 2 H). The mixture was recrystallized from ethyl alcohol, mp 137–138 °C, lit.[13] mp 138–139 °C.

(2) (Table I, Entry 9). Chromatography (silica gel, $CHCl_3$) gave the following products in order of elution: **1f**[13] (12%) [^{1}H NMR ($CDCl_3$) δ 3.05 (d, 3 H), 7.05 (m, 1 H), 7.57 (m, 2 H), 7.75 (m, 2 H), 8.24 (m, 2 H), 8.64 (s, 1 H)], **1g** (3%) [^{1}H NMR ($CDCl_3$) δ 2.67 (s, 6 H), 7.70 (m, 5 H), 8.25 (m, 2 H), 10.01 (s, 1 H); mass spectrum, *m/z* (relative intensity) 266.03 (53, M^+), 222.91 (100). Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 71.82; H, 5.50; N, 10.33], **3a** (61.8 mg, 53%), **2c** (11.7 mg, 10%), and two unidentified yellow compounds.

(3) (Table I, Entry 5). A mixture of **1c** (300 mg, 1.08 mmol), *N,N*-dimethylhydrazine (522 mg, 8.69 mmol), and pyridine (8 mL) was stirred at room temperature for 96 h. The resultant deep purple reaction mixture was poured into ice–water and a red solid (285 mg) was collected by filtration. Chromatography on silica gel with $CHCl_3$/toluene (1:4 v/v) gave three products in the following elution order: (a) an unidentified purple compound (16 mg, 5.6% w/w); (b) **3b**, a red solid (237 mg, 76%), crystallized from ethanol [mp 168–170 °C; ^{1}H NMR δ 3.04 (s, 6 H), 7.2 (d, 1 H), 7.47 (d, 1 H), 7.72 (m, 2 H), 8.2 (m, 2 H); mass spectrum, *m/z* (relative intensity) 285 (100, M^+). Anal. Calcd for $C_{16}H_{12}ClNO_2$: C, 67.26; H, 4.23; N, 4.90. Found: C, 67.00; H, 4.49; N, 4.70] and (c) **2d**, a fluorescent yellow solid (3.5 mg, 1.2%) [^{1}H NMR ($CDCl_3$) δ 4.22 (s, 3 H), 7.57 (m, 3 H), 7.70 (m, 1 H), 8.16 (d, 1 H), 8.46 (d, 1 H)].

(4) Dione **1c** (200 mg, 0.721 mmol), 1-piperidinamine (580 mg, 5.79 mmol), and pyridine (5 mL) were stirred at room temperature for 96 h. The solution was poured into ice–water and extracted with chloroform to yield a deep purple oil. The oil was taken up in $CHCl_3$ and chromatographed ($CHCl_3$, silica gel); **3f** eluted first as an oil (85%): ^{1}H NMR ($CDCl_3$) δ 1.75 (m, 6 H), 3.2 (m, 4 H), 7.27 (d, 1 H), 7.52 (d, 1 H), 7.72 (m, 2 H), 8.2 (m, 2 H). The oil was recrystallized from MeOH/$CHCl_3$ to give purple needles, mp 100–102 °C. Anal. Calcd for $C_{19}H_{16}NClO_2$: C, 70.04; H, 4.95; N, 4.30. Found: C, 69.76; H, 4.97; N, 4.11.

(5) Dione **1h** (100 mg, 0.41 mmol) was combined with *N,N*-dimethylhydrazine (0.25 mL, 197 mg, 3.3 mmol) in pyridine (5 mL). Collection of the major compounds by chromatography ($CHCl_3$, silica gel) yielded a red compound identified as **3c** (53.8 mg, 48%). The sample was recrystallized from ethyl acetate, mp 150–151.5 °C: ^{1}H NMR ($CDCl_3$) δ 3.01 (s, 6 H), 7.30 (m, 2 H), 7.73 (m, 2 H), 8.20 (m, 2 H); mass spectrum, *m/z* (relative intensity, chemical ionization, methane) 270.1 (100, M + 1). Anal. Calcd for $C_{16}H_{12}FNO_2$: C, 71.36; H, 4.49; N, 5.20. Found: C, 71.14; H, 4.39; N, 4.91. A blue compound was collected and identified as **3d** (49.2 mg, 40%). The sample was recrystallized from ethyl acetate, mp 171–172 °C: ^{1}H NMR ($CDCl_3$) δ 2.98 (s, 12 H), 7.30 (s, 2 H), 7.65 (m, 2 H), 8.20 (m, 2 H); mass spectrum, *m/e* (relative intensity) 294.12 (100, M^+). Anal. calcd for $C_{18}H_{18}N_2O_2$: C, 73.44; H, 6.16; N, 9.52. Found: C, 73.39; H, 5.99; N, 9.71.

Acknowledgment. This research was supported by Grant PHS 24543 from the National Cancer Institute.

(14) Valkanas, G.; Hopff, H. *J. Org. Chem.* **1962**, *27*, 3680.
(15) Krapcho, A. P.; Getahun, Z. *Synth. Commun.* **1985**, *15* (10), 907.