16.59. All yields are reported in Table I.

General Procedure B. Suspensions of **2a,b** in ethanol, with[4] and without the presence of 0.25 equiv of triethylamine, were heated under nitrogen in sealed glass tubes at 140 °C for 36–46 h. After this period, the reaction mixtures were cooled in an ice bath, and the resulting precipitate was collected by filtration to give the corresponding ICC products **4a,b** in pure form. For reactions with **2a**, the filtrates were evaporated under reduced pressure, and the residual material was purified by column chromatography (1:1 ethyl acetate/methylene chloride eluent) to provide additional ICC product **4a** and IDA product **3a**. Also isolated was 5-carbethoxy-6-ethoxy-2,3-dihydrothieno[2,3-*b*]-pyridine (**6**), R_f 0.75 (1:1 ethyl acetate/methylene chloride), mp 38–39 °C; ^{1}H NMR ($CDCl_3$) δ 7.88 (s, 1 H), 4.45 (q, J = 7.1 Hz, 2 H), 4.33 (q, J = 7.1 Hz, 2 H), 3.44 (t, J = 8.0 Hz, 2 H), 3.26 (t, J = 8.0, 2 H), 1.44–1.34 (m, 6 H); HRMS calcd for $C_{12}H_{15}NO_3S$ m/z 253.0772, found m/z 253.0783. For reactions with **2b**, the filtrates were evaporated under reduced pressure, and the residual material was purified by preparative TLC (5% methanol/methylene chloride eluent) to yield additional ICC product **4b** and the IDA product **3b**. Yields are reported in Table I. The spectral and physical properties of **3a,b** and **4a,b** derived from these reactions were identical with those described above in General Procedure A and elsewhere.[2]

General Procedure C. NMR tubes containing deuteriated dimethyl sulfoxide solutions of **2a,b** (~10 mg of the triazine in 1 mL of Me_2SO-d_6) were heated at 5–6-h intervals at 140 °C and at 1 h intervals at 170 °C. After each interval, the reaction mixture was analyzed by ^{1}H NMR to determine the extent of reaction. At 140 °C, the starting materials **2a,b** were consumed in ~20 h. At 170 °C, only 3 h were needed for complete disappearance of starting materials. Yields listed in Table I are based upon the ^{1}H NMR peak integration ratio of the pyridine C-4 proton of **3a,b** and one of the exocyclic vinyl methylene protons of **4a,b**.

6-Carbethoxy-5-ethoxy-3-(*p*-tolyl)-1,2,4-triazine (10). A stirred suspension of 6-carbethoxy-3-(*p*-tolyl)-1,2,4-triazin-5-(2*H*)-one[12] (**9**) (0.090 g, 0.35 mmol) in 10 mL of ethanol was heated to 140–145 °C for 43.5 h in a sealed glass tube. After this period, the reaction mixture was evaporated under reduced pressure. The residual material contained 20% of the desired product[12] along with unreacted starting material **10** as determined by ^{1}H NMR peak integration: ^{1}H NMR ($CDCl_3$) δ 1.44 (t, J = 7.0 Hz, 3 H), 1.52 (t, J = 7.0 Hz, 3 H), 2.44 (s, 3 H), 4.5 (q, J = 7.0 Hz, 2 H), 4.70 (q, J = 7.0 Hz, 2 H), 7.32 (d, J = 8.5 Hz, 2 H), 8.41 (d, J = 8.5 Hz, 2 H).

Registry No. **2a**, 115983-74-9; **2b**, 90997-83-4; **3a**, 115983-75-0; **3b**, 115983-76-1; **4a**, 116025-22-0; **4b**, 90997-87-8; *S*-(3-butynyl)-thiosemicarbazide hydroiodide, 109216-69-5; pyruvic acid, 127-17-3.

Supplementary Material Available: Tables of atomic coordinates, atomic thermal parameters, bond lengths and angles, and figures for **4a** (11 pages). Ordering information is given on any current masthead page.

Synthesis of the Left-Hand Ring of the Antitumor Antibiotic CC-1065 by an Intramolecular Carbenoid Addition Route. Synthesis and Reactivity of 4-Diazo-4,7-dihydroindol-7-ones and Related Compounds

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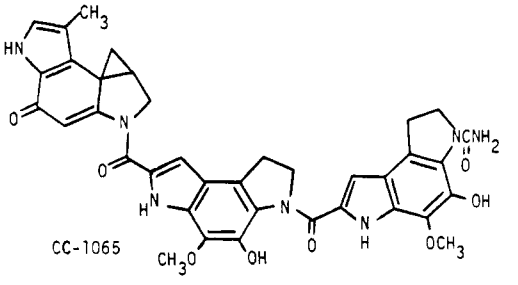
The synthesis of 4-diazo-4,7-dihydroindol-7-ones, which could serve as precursors of the A-ring structure of the antitumor antibiotic CC-1065 by intramolecular carbenoid addition, has been explored. Direct diazo transfer using 7-hydroxy-3-methyl-5-[*N*-(2-propenyl)acetamido]indole gave a 6-diazo-6,7-dihydroindol-7-one. Reduction and diazotiazation of 7-[(ethoxycarbonyl)oxy]-3-methyl-4-nitro-5-[*N*-(2-propenyl)sulfonamido]indole gave 4-diazo-3-methyl-5-[*N*-(2-propenyl)methanesulfonamido]-4,7-dihydroindol-7-one (**2b**). The 1-phenylsulfonyl analogue and a model diazocyclohexadienone, 2-acetamido-4-diazo-5-[*N*-(2-propenyl)methanesulfonamido]cyclohexa-2,5-dienone were also prepared. Photolysis, thermolysis, or transition metal catalyzed decomposition of the diazo compounds leads to mixtures of spirocyclopropanes by intramolecular carbenoid addition and sulfinamido quinones formed by oxygen-transfer from the sulfonyl group to the carbenoid intermediate. The best yields of cyclopropanation in the case of the 4-diazoindol-7-one (**2b**) were obtained with copper catalysts, which provided the methanesulfonyl derivative of the A-ring structure in 45–55% yield.

The highly potent antitumor antibiotic CC-1065 has attracted much attention.[1] The compound has been shown to covalently alkylate DNA in a site-selective manner by cyclopropane ring opening.[2] Beginning with Wierenga's synthesis reported in 1981,[3] a number of syntheses of the left-hand portion of the structure, which possesses the alkylating activity, have been developed.[4]



(1) Chidester, C. G.; Krueger, W. C.; Mizsak, S. A.; Duchamp, D. J.; Martin, D. G. *J. Am. Chem. Soc.* **1981**, *103*, 7629.

(2) Hurley, L. H.; Reynolds, V. L.; Swenson, D. H.; Petzold, G. L.; Scahill, T. A. *Science (Washington, D.C.)* **1984**, *226*, 843. Needham-Van Devanter, D. R.; Hurley, L. H.; Reynolds, V. L.; Theriault, N. Y.; Krueger, W. C.; Wierenga, W. *Nucleic Acids Res.* **1984**, *12*, 6159. Reynolds, V. L.; Molineux, I. J.; Kaplan, D. J.; Swenson, D. H.; Hurley, L. H. *Biochemistry* **1985**, *24*, 6228.

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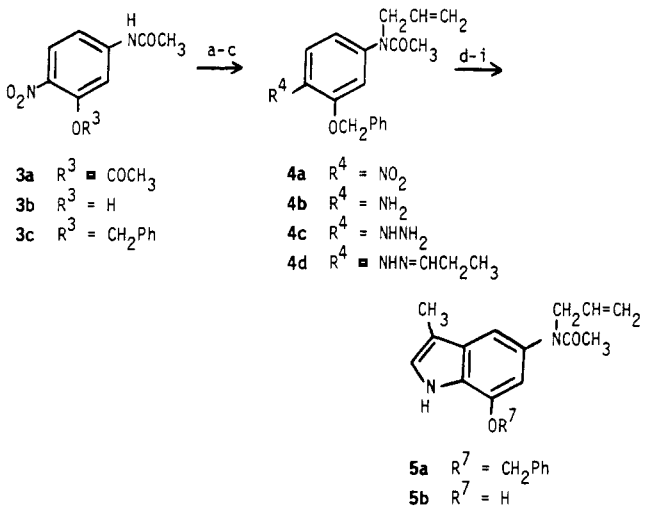
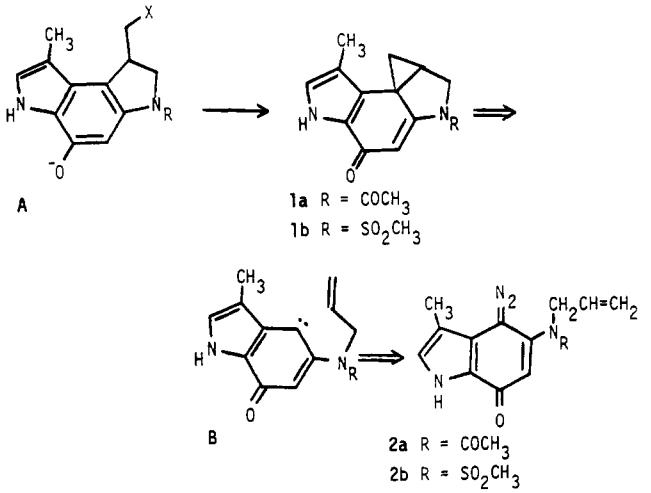
Scheme I[a]



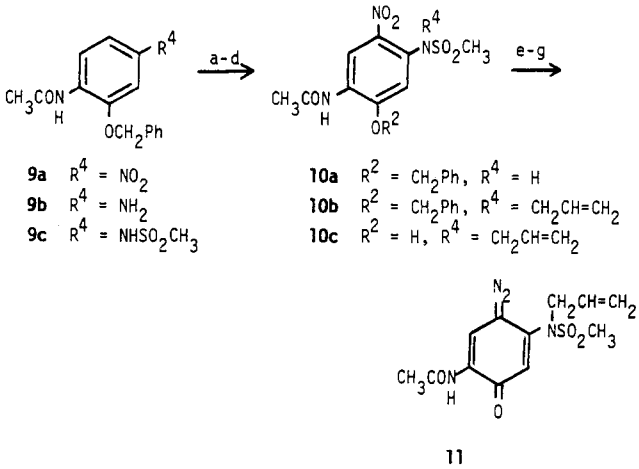
[a] (a) K_2CO_3, MeOH; (b) K_2CO_3, KI, $PhCH_2Cl$; (c) $KOC(CH_3)_3$, $CH_2{=}CHCH_2Br$; (d) Zn, $CaCl_2$; (e) $NaNO_2$, HCl; (f) $SnCl_2$; (g) $CH_3CH_2CH{=}O$; (h) TsOH; (i) BBr_3.

In all these syntheses, the cyclopropane ring is closed by an intramolecular phenolate alkylation (A → **1**). An alternative approach would be via an intramolecular carbenoid addition to an *N*-allyl intermediate as in **2** → B → **1**. Precedent for such a path exists in a number of pho-



tolysis of 4-diazocyclohexadienones[5] in the presence of alkenes, which have led to spirocyclopropane formation.[6]

Scheme II[a]



[a] (a) Zn, EtOH; (b) CH_3SO_2Cl; (c) HNO_3, $Hg(OAc)_2$, Ac_2O; (d) $KOC(CH_3)_2$, $CH_2CH{=}CH_2Br$; (e) BBr_3; (f) Zn, EtOH; (g) HCl, *i*-$C_5H_{11}ONO$.

When we began this work, no 4-diazoindol-7-ones such as **2** were known. Our objective was to develop syntheses of such compounds and examine their carbenoid decomposition.[7]

A. Synthesis of 4-Diazoindol-7-ones and Related Compounds. A number of studies have demonstrated that phenols or phenolate anions can be converted to diazocyclohexadienones by diazo transfer.[8] Arenesulfonyl azides have been used most frequently,[9] although other reagents are available.[10] Our initial approach to the synthesis of **2a** was to investigate diazo transfer reactions of **5b**.

The synthesis of **5b** is outlined in Scheme I. The nitration of 3-acetoxyacetanilide,[11] by which **3a** is prepared, also gives some of the 5-acetoxy-2-nitro isomer, but purification of **3a** can be accomplished by fractional crystallization. Subsequent steps in the synthesis are satisfactory. The overall yield of **5b** from **3a** is about 30%.

Diazo transfer under a number of conditions appropriate for phenols[9] were unsuccessful. The spectral properties of the crude products suggested that they might have resulted from attack at the indole 2-position,[12] a reaction which is known for nonphenolic indoles.[13] In a thesis from Kornblum's laboratory, the use of trifluoroethanol as solvent was reported to be advantageous in diazo transfer to naphthol.[14] By use of these conditions, we obtained a diazoindolone in 45% yield. This proved to be the 6-

(3) Wierenga, W. *J. Am. Chem. Soc.* **1981**, *103*, 5621. Warpehoski, M. A.; Gebhard, I.; Kelly, R. C.; Krueger, W. C.; Li, L. H.; McGovern, J. P.; Prairie, M. D.; Wicnienski, N.; Wierenga, W. *J. Med. Chem.* **1988**, *31*, 590.

(4) (a) Magnus, P.; Gallagher, T. *J. Chem. Soc., Chem. Commun.* **1984**, 389. Magnus, P.; Gallagher, T.; Schultz, J.; Or, Y.-S.; Anathanarayan, T. P. *J. Am. Chem. Soc.* **1987**, *109*, 2706. (b) Kraus, G. A.; Yue, S.; Sy, J. *J. Org. Chem.* **1985**, *50*, 283. (c) Moody, C. J.; Pass, M.; Rees, C. W.; Tojo, G. *J. Chem. Soc., Chem. Commun.* **1986**, 1062. Boger, D. L.; Coleman, R. S. *J. Am. Chem. Soc.* **1988**, *110*, 1321.

(5) 4-Diazocyclohexadienones are resonance structures of 4-oxyaryldiazonium zwitterions derived from *p*-aminophenols. In much of the literature the compounds are referred to as "quinone diazides." Other authors use the name "arene 1,4-diazo oxide." The structure, synthesis, and reactivity of these compounds have been reveiwed in Ershov, V. V.; Nikiforov, G. A.; de Jonge, C. R H. I. *Quinone Diazides*; Elsevier: Amsterdam, 1981.

(6) Koser, G. F.; Pirkle, W. H. *J. Org. Chem.* **1967**, *32*, 1992. Sriridov, B. D.; Nikiforov, G. A.; Stepanyants, A. U.; Lezina, V. P.; Ershov, V. V. *Izvest. Akad, Nauk SSSR, Ser. Khim., Engl. Transl.* **1973**, 1998. Fleming, J. C.; Schechter, H. *J. Org. Chem.* **1969**, *34*, 3962. Cauquis, G.; Reverdy, G. *Tetrahedron Lett.* **1972**, 3491. Nikiforov, G. A.; Sviridov, B. D.; Ershov, V. V. *Izvest. Akad, Nauk SSSR, Ser. Khim.* **1968**, 558. Ershov, V. V.; Nikiforov, G. A. *Uspekhi Khim., Engl. Transl.* **1975**, *44*, 816.

(7) Some aspects of this work have been published in preliminary form: (a) Sundberg, R. J.; Nishiguchi, T. *Tetrahedron Lett.* **1983**, *24*, 4773. (b) Sundberg, R. J.; Baxter, E. W. *Tetrahedron Lett.* **1986**, *27*, 2687.

(8) Regitz, M. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 733.

(9) Tedder, J. M.; Webster, B. *J. Chem. Soc.* **1960**, 4417. Regitz, M. *Chem. Ber.* **1964**, *97*, 2742. Raasch, M. *J. Org. Chem.* **1979**, *44*, 632.

(10) Viehe, H. G.; George, P. *Chimia* **1975**, *29*, 209. Kokel, B.; Viehe, H. G. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 716. Balli, H. *Justus Liebigs Ann. Chem.* **1961**, *647*, 11. Balli, H.; Muller, V.; Sezen-Gezgin, A. *Helv. Chim. Acta* **1978**, *61*, 104.

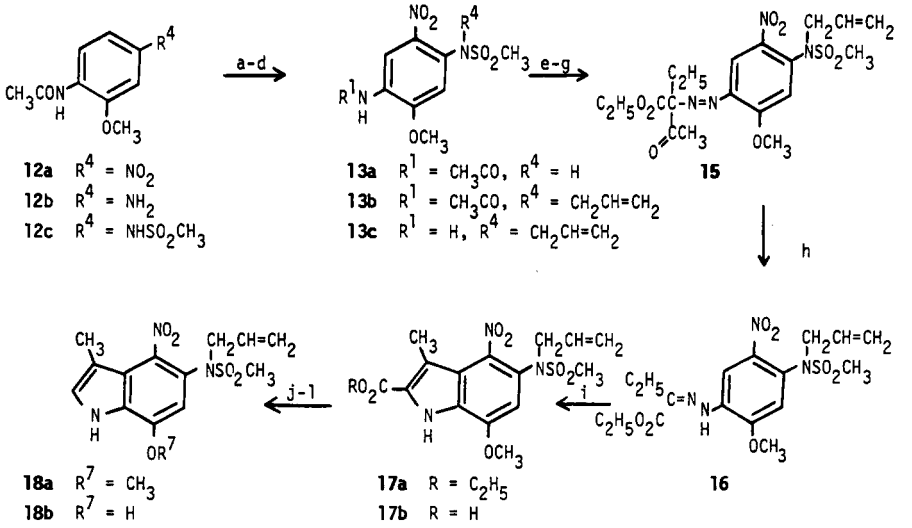
(11) Reverdin, F.; Widmer, K. *Ber. Dtsch. Chem. Ges.* **1913**, *46*, 4066. Reverdin, F. *Ber. Dtsch. Chem. Ges.* **1914**, *47*, 2216.

(12) The product from **5b** and (azidochloromethylene)dimethylammonium chloride has the formula $C_{17}H_{21}N_7O_2$. An analogous product is formed from **23**. The NMR spectra show that the indole 2-position is substituted but the 4- and 7-positions are not. Both products show that a dimethylamino group is present. Complete structural assignment has not been made.

(13) Bailey, A. S.; Hill, P. A.; Seager, J. F. *J. Chem. Soc., Perkin Trans. 1* **1974**, 967. Bailey, A. S.; Buckley, A. J. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1602. Bailey, A. S.; Buckley, A. J.; Warr, W. A. *J. Chem. Soc., Perkin Trans. 1* **1972**, 1626.

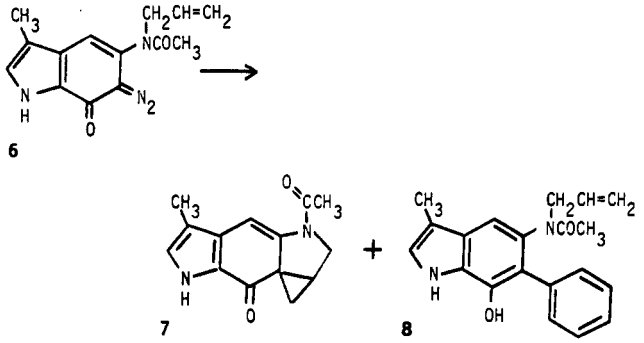
(14) Semenuk, N. S. *Dissert. Abstr., Sect. B* **1980**, 4308.

Scheme III[a]



[a] (a) H_2, Pd–C; (b) CH_3SO_2Cl; (c) HNO_3, $Hg(OAc)_2$, Ac_2O; (d) $KOC(CH_3)_3$, $CH_2{=}CHCH_2Br$; (e) NaOH, H_2O; (f) HCl, $NaNO_2$; (g) $CH_3C(OCH(C_2H_5)CO_2C_2H_5$, KOH; (h) Na_2CO_3, EtOH; (i) CF_3CO_2H, toluene; (j) NaOH, H_2O; (k) CuO, $AcN(Me)_2$; (l) PhSLi, HMPA.

diazoindol-7-one **6** on the basis of subsequent conversion to **7** and **8**, as will be discussed later.



An alternative route to diazocyclohexadienones involves diazotization of aminophenols.[5,15] We first investigated this method by preparing a model compound **11**, as in Scheme II. The overall nine-step sequence from 2-amino-5-nitrophenol proceeded in about 20% yield.[7b] The nitrophenol **10c** was reduced and diazotized with isoamyl nitrite to give the diazocyclohexadienone **11** in 60–70% yield. The product was purified by chromatography and characterized by its spectroscopic properties, including a strong diazo band at 2117 cm^{-1}. The compound was sensitive to ambient light but was stable at room temperature if protected from light and could be stored indefinitely under refrigeration.

The preparation **2b** by diazotization required **18b** as a reactant. Synthesis of **18b** was first done as shown in Scheme III.[7b]

Several stages in this sequence required extensive investigation to achieve acceptable yields. The conversion of aniline **13c** to the indole **17a** proceeds by Japp–Klingemann coupling and Fischer cyclization. The coupling with ethyl 2-ethyl-3-oxobutanoate (**14**) proceeds via the azo compound **15**. Frequently such compounds are spontaneously deacetylated under the alkaline conditions of the Japp–Klingemann reaction.[16] In this case, however, the azo compound was usually isolated, requiring a separate deacylation step using sodium carbonate in ethanol (step h). The Fischer cyclization step is ordinarily difficult with nitro substituents on the benzene ring,[17] and the current case was no exception. The best conditions found were adapted from a report by Danishefsky and Phillips,[18] who found trifluoroacetic acid in toluene to be favorable conditions for effecting mechanistically analogous sigmatropic rearrangements. These conditions resulted in the cyclization of **16** to **17a** in 50–65% yield. The decarboxylation of **17b** also required exploration of a number of conditions before finding that reaction with cuprous oxide in *N,N*-dimethylacetamide at 200 °C proceeded in 75% yield.[19] The final step in the synthesis, demethylation of **18a**, was accomplished with lithium thiophenoxide in HMPA.[20]

An alternative somewhat more convenient synthesis was developed as the work progressed. This sequence avoids the two most troublesome steps in the other route. This route is outlined in Scheme IV. The nitration step is delayed until after the indolization. The indole ring is then protected as a benzenesulfonyl derivative. The protected indole **20b** can be nitrated at C-4 with good selectivity in 55–60% yield. The use of the *O*-benzyl group also facilitated the deprotection of the phenolic oxygen, which was done with boron tribromide. Phenol **21b** was converted to **18b** in >90% yield by desulfonylation with sodium hydroxide. The overall yield of nitrophenol **18b** by this route is 10–15% from **9c**. Debenzylation of the intermediate **20b** by boron tribromide also provides access to phenol **23**.

After reduction of **18b** to **24a**, diazotization was attempted under the conditions that were successful for the model compound **11**. This resulted in the isolation of imine **25a**, which was readily hydrolyzed to the quinone **25b**. Nitrosation under other conditions, including nitrosylsulfuric acid at −40 °C,[21] and sodium nitrite in fluoroboric acid[22] resulted in the same product. Control experiments

(15) Kraus, G. A.; Nagy, J. O.; Delano, J. *Tetrahedron* **1985**, *41*, 2337. Puza, M.; Doestchman, D. *Synthesis* **1971**, 481. Ried, W.; Butz, M. *Justus Liebigs Ann. Chem.* **1968**, *716*, 190.

(16) Phillips, R. R. *Org. React. (N.Y.)* **1959**, *10*, 143.

(17) Robinson, B. *The Fischer Indole Synthesis*; Wiley: New York, 1982.

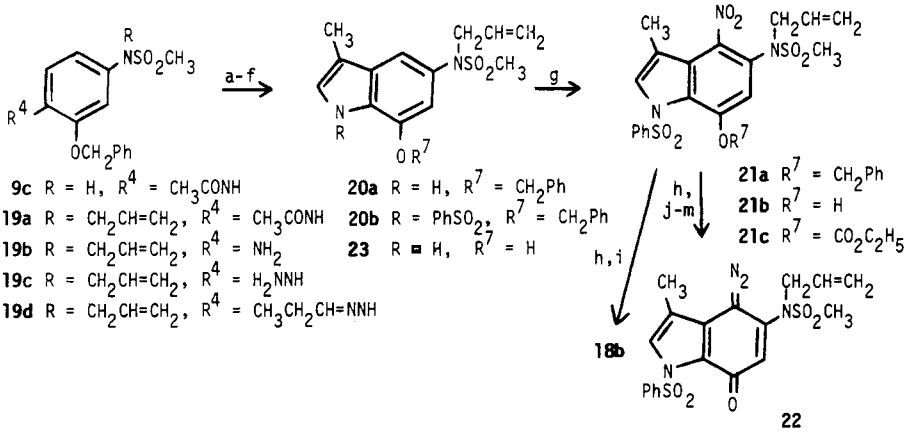
(18) Danishefsky, S.; Phillips, G. B. *Tetrahedron Lett.* **1984**, *25*, 3159.

(19) Kruse, L. I.; Meyer, M. D. *J. Org. Chem.* **1984**, *49*, 4761. Battey, P. K.; Crookes, D. L.; Smith, G. F. *Can. J. Chem.* **1979**, *57*, 1694. Schreier, E. *Helv. Chim. Acta* **1976**, *59*, 585.

(20) Bhatt, M. V.; Kulkarni, S. U. *Synthesis* **1983**, 249. McMurry, J. E.; Erion, M. D. *J. Am. Chem. Soc.* **1985**, *107*, 2712. Hansson, C.; Wickberg, B. *Synthesis* **1976**, 191.

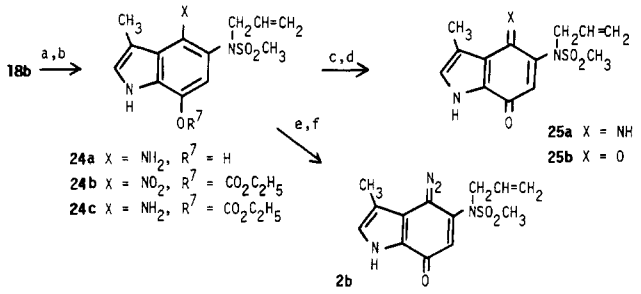
(21) Hayashi, S.; Ishikawa, N. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 2909.

Scheme IV[a]



[a] (a) $KOC(CH_3)_3$, $CH_2{=}CHCH_2Br$; (b) KOH, H_2O; (c) $NaNO_2$, HCl; (d) $SnCl_2$; (e) $CH_3CH_2CH{=}O$, H^+; (f) NaH, $PhSO_2Cl$; (g) NH_4NO_3, $(CF_3CO)_2O$; (h) BBr_3; (i) NaOH, H_2O; (j) $C_2H_5O_2CCl$; (k) Zn, EtOH; (l) i-$C_5H_{11}ONO$; (m) $NaHCO_3$.

Scheme V[a]



[a] (a) $C_2H_5O_2CCl$; (b) Zn, EtOH; (c) i-$C_5H_{11}ONO$ or $ONOSO_3H$; (d) H^+, H_2O; (e) i-$C_5H_{11}ONO$; (f) $NaHCO_3$.

argued against direct oxidation of **24a** being the cause for the formation of **25a**. Instead it appears that the *N*-nitroso intermediate in the diazotization undergoes a 1,6-elimination directly to **25a**. This problem was overcome by converting **18b** to the *O*-ethoxycarbonyl derivative **24b** prior to reduction. Diazotization then proceeded normally, and when the diazotized solution was exposed to sodium bicarbonate solution, the 4-diazoindol-7-one **2b** was obtained in 60–85% yield. These results are summarized in Scheme V.

The structure of **2b** was assigned on the basis of a strong diazo band at 2085 cm^{-1} in the infrared spectrum and a correct (unit resolution) atomic weight by mass spectrometry. The NMR spectrum was also consistent with the assigned structure but was found to exhibit variable chemical shifts. The conjugate acids of 4-diazocyclohexadienones have pK_a values around 3–4[5] while for 1-diazonaphthalen-4-one the pK_a is near 0. The pK_a of **2b** should be intermediate between these values, and we attribute the variable chemical shift to partial protonation by acid present in the NMR solvent. Addition of 1 equiv of trifluoroacetic acid shifted the indole NH (10.6 to 11.9), indole 2-H (7.08 to 7.32), indole 6-H (6.35 to 6.72) and indole 3-CH_3 (2.28 to 2.37) signals. By washing with sodium bicarbonate solution, the signals were shifted back to the original positions. The UV maxima of the neutral diazoindolone are at 262 (ϵ 7400) and 372 nm (ϵ 17 200).

The *N*-benzenesulfonyl derivative **21c** was also converted to the 4-diazoindol-7-one **22** by the same method as used for **24b**. The resulting product revealed a diazo band at 2110 cm^{-1}, and the NMR spectrum was consistent with the diazoindolone structure.

B. Carbenoid Decomposition. When **6** was photolyzed in benzene, two products, **7** and **8**, were formed. Compound **7** had the expected molecular weight for an intramolecular carbene addition product, but **8** had incorporated a benzene molecule. When the photolysis was done in methylene chloride, only **7** was formed. Direct comparison of **7** with the authentic acetyl derivative (**1a**) of the ring-A structure revealed they were different compounds.[23] The NMR spectrum of **7** was in agreement with the assigned structure. In particular, the signals due to the allyl group had disappeared and been replaced by high-field multiplets. Much of the 360-MHz spectrum of **7** is broad at room temperature but at 100 °C the spectrum is sharp, permitting assignment of coupling constants, as given in the Experimental Section. The NMR spectrum of the solvent incorporation product **8** also supported the assignment of **6** as a 6-diazoindol-7-one in that the indole C-3 methyl substituent appeared at nearly the same position in the NMR spectrum as in the precursors **5a** and **5b**. A phenyl substituent in the 4-position of the indole ring would have been expected to have a strong anisotropic shielding effect on this signal. Carbenoid decomposition of **6** under thermal and metal-catalyzed conditions was also briefly examined. 6-Diazoindolone **6** was only slowly decomposed at 110 °C in toluene. The reaction was moderately accelerated by bis[*N*-*tert*-butylsalicylaldiminato]Cu^{II}[24] or Cu^{II}(acetylacetonate)$_2$. Small amounts of **7** could be isolated, but the rate of decomposition of the product was comparable to that of its formation.

The model diazocyclohexadienone **11** was studied under a number of conditions including photolysis, thermolysis, and decomposition catalyzed by a variety of transition metal compounds.[24,25] Two major products were formed with the ratio being dependent on the conditions. These were identified as **26** and **27b** (Scheme VI). The cyclopropane ring in **26** was revealed by the upfield position and multiplicity of the aliphatic signals, which are very similar to those in **1b**.[23] Compound **27b** was identified on the basis

(22) Danek, O.; Snobl, D.; Knizek, J.; Nouzova, S. *Collect. Czech. Chem. Commun.* **1967**, *32*, 1642.

(23) Comparison spectra were kindly provided by Dr. W. Wierenga and Dr. M. Warpehoski of the Upjohn Co.

(24) Nozaki, H.; Takaya, S.; Moriuti, S.; Noyori, R. *Tetrahedron* **1968**, *24*, 3655. Corey, E. J.; Myers, A. G. *Tetrahedron* **1984**, *25*, 3559.

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Scheme VI

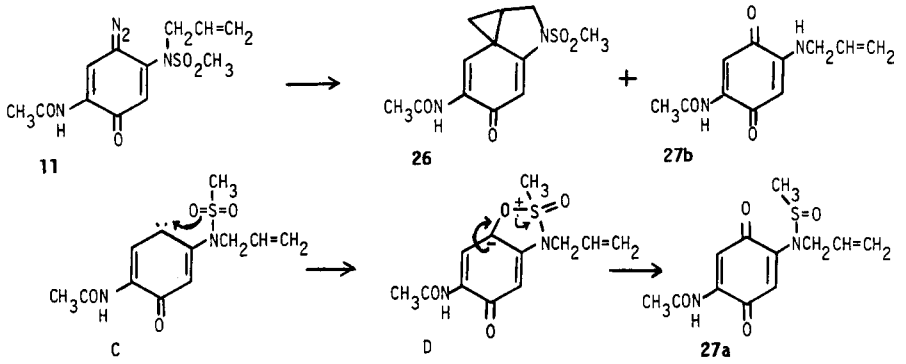


Table I

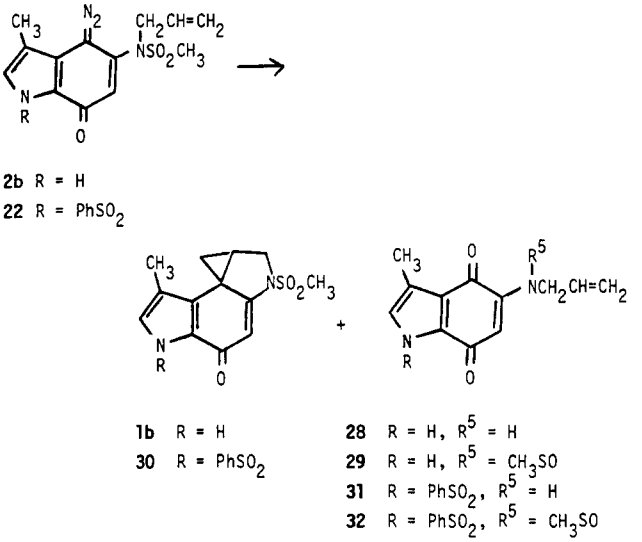
diazo compd	catalyst[a] (equiv)	temp, °C (time, h)	yield of cyclopropane, %	yield of quinone, %
11	none	110 (0.5)	37	52
11	photolysis	~30 (2.0)	26	56
11	$Rh_2(Oac)_4$ (0.175)	40 (24)	49	18
11	$Rh_2(Opiv)_4$ (0.1)	40 (2)	73	10
11	$Rh_2(Ooct)_4$ (0.1)	40 (2)	69	17
11	$Cu(sal)_2$ (0.1)	110 (0.5)	52	29
11	$Cu(sal)_2$ (0.5)	80 (0.5)	51	23
11	$Cu(sal)_2$ (1.0)	110 (0.5)	62	33
11	$Cu(acac)_2$ (0.15)	110 (0.5)	42	50
11	$Cu(acac)_2$ (1.0)	110 (0.5)	41	34
11	$Mo(CO)_6$ (0.1)	110 (2)	41	25
2b	none	110 (0.5)	30	68
2b	photolysis	~30 (1.0)	30	63
2b	$Rh_2(Oac)_4$ (0.1)	40 (24)	*b*	
2b	$Rh_2(Opiv)$ (0.1)	40 (*b*)	*c*	
2b	$Rh_2(Ooct)_4$ (0.1)	40 (0.6)	*c*	
2b	$Cu(sal)_2$ (0.1)	110 (0.5)	43	29
2b	$Cu(sal)_2$ (0.1)	80 (2.5)	45	32
2b	$Cu(sal)_2$ (0.3)	110 (0.5)	47	29
2b	$Cu(sal)_2$ (1.0)	110 (0.5)	44	10
2b	$Cu(sal)_2$ (1.0)	80 (1.5)	45	34
2b	$Cu(acac)_2$ (0.2)	110 (0.5)	56	38
2b	$Mo(CO)_6$ (0.35)	110 (2)	25	22
22	none	110 (0.5)	30	20
22	photolysis	~30 (0.25)	18	65
22	$Rh_2(Oac)_4$ (0.1)	40 (6)	*d*	
22	$Rh_2(Opiv)_4$ (0.1)	40 (6)	*c*	
22	$Rh(Ooct)_4$ (0.1)	40 (6)	*c*	
22	$Cu(sal)_2$ (0.1)	110 (0.5)	52	10
22	$Cu(acac)_2$ (0.1)	110 (0.5)	56	25
22	$Mo(CO)_6$ (0.1)	110 (2)	41	15

[a] Catalysts: $Rh_2(Oac)_4$ = dirhodium tetraacetate; $Rh_2(Opiv)_4$ = dirhodium tetrapivalate; $Rh_2(Ooct)_4$ = dirhodium tetraoctanoate; $Cu(sal)_2$ = bis[*N*-*tert*-butyl(salicylaldiminato)]copper(II); $Cu(acac)_2$ = bis(acetylacetonato)copper. [b] >50% recovery of starting material; **1b** and **28** can be isolated in ~1:1 ratio. Yields are estimated at ~25% from the reacted material. [c] Traces of product but primarily starting material. [d] 50% of starting material; 5% of **30**, 12% of **31**.

of its elemental composition and spectral features. The origin of the desulfonylated quinone **27b** was traced to an intramolecular oxygen transfer via the carbene C, which leads to the hydrolytically unstable sulfinamide **27a**. The intermediate **27a** could be detected by NMR and could be isolated by avoiding hydrolytic workup. The product ratio under various reaction conditions is given in Table I.

The quinone **27b** was the main product of both the thermal reaction and photolysis. With bis[*N*-*tert*-butylsalicylaldiminato]Cu^{II} at either 80 °C or 110 °C the ratio changed to favor the cyclopropane. The ratio was not dramatically effected by the amount of catalyst. We cannot rule out that some of the reaction is occurring by thermolysis in the presence of the catalyst, but the shift

Scheme VII



in product ratio is sufficient to establish that most of the cyclopropane is being formed by the catalyzed process. While reaction with rhodium acetate was rather slow, the more soluble rhodium octanoate and rhodium pivalate led to rapid reactions and improved cyclopropane:quinone ratios. (Acetylacetato)$_2Cu^{II}$ and molybdenum hexacarbonyl were only briefly examined and appeared to offer no advantages over the salicylaldimine catalyst.

The 4-diazoindol-7-one **2b** was also subjected to a similar range of conditions. Photolysis of **2b** with a low-intensity mercury lamp gave only **28**, but with a 450-W Hanovia lamp **1b** and **28** were obtained in a 1:2 ratio.[26] The cyclopropane **1b** and quinone **28** were also formed by thermolysis and by transition metal catalysis under various conditions (Scheme VII). The cyclopropane **1b** was identified by direct comparison with authentic material prepared at the Upjohn Co.[23] As was the case with photolysis of **11**, it was possible to observe the sulfinamide **29** prior to its hydrolytic conversion to **28**.

The product ratios are given in Table I. The thermolysis of **2b** resulted in excellent material balance. Photolysis was also a clean reaction when carried out with a filter that cut off near 300 nm. In both the thermal and photochemical reaction the product ratio was about 2:1 in favor of the quinone **28**. The salicylaldiminato copper catalyst improved the ratio to slightly favor the cyclopropane. The isolated yield of the cyclopropane was 47% on a 20-mg scale. Copper acetylacetonate also provided an improved

(26) This difference has not been investigated in detail but may reflect the relatively longer photolysis time with the low-intensity lamp. This may permit reaction with acidic impurities to destroy **1b** in situ.

ratio of cyclopropane. In contrast to the case of **11** none of the rhodium salts was an effective catalyst for cyclopropanation of **2b**. Cyclopropanation occurred in low yield with rhodium acetate, but most of the starting material was recover when the pivalate or octanoate salts were used. It appears that the additional steric bulk resulting from the indole ring and the 3-methyl substituent prevent effective interaction with the carboxylate-bridged rhodium species.

Carbenoid decomposition of **22** gave the analogous products **30** and **31**, and the yields are included in Table I.

Discussion and Conclusion

The results of this study demonstrate that 4-diazo-4,7-dihydroindol-7-ones and related diazocyclohexadienones can be prepared. Although the compounds are light sensitive, they are otherwise quite stable and can be stored without difficulty. The compounds have also been shown to undergo intramolecular carbenoid addition leading to spirocyclopropane–cyclohexadienone type structures. The main limitation on the yield spirocyclopropane–cyclohexadienones from **11**, **2b**, and **22** is the competing oxygen transfer from the methanesulfonyl group. It may be possible to avoid this problem by a change to an alternative protecting group.

The current results for transition metal catalyzed decompositions indicate that there are general similarities between the diazocyclohexadienones and α-diazo esters and α-diazo ketones, as could be expected on the basis of the vinylogous relationship.[27] Finer details of the mechanism are uncertain at this time. For example, we have no information on whether the allyl group becomes coordinated to the copper catalyst as part of the cyclopropanation process.

We are exploring potentially shorter syntheses of the diazocyclohexadienones since they appear to have significant promise as spirocyclopropane–cyclohexadienone precursors.

Experimental Section

General Procedures. Unless otherwise stated, chromatography was done using the "flash" procedure with M Kieselgel 60, 230–400 mesh. TLC was done with Kieselgel 60F. NMR spectra were run at 90, 300, or 360 MHz. Structurally significant coupling constants are given. All compounds with allyl substituents showed a typical set of multiplets with a CH_2 doublet, J = 6 Hz, CH_2=CH, J_{cis} = 10 Hz, J_{trans} = 16 Hz. These coupling constants are not given for the individual spectra. Mass spectra were recorded on a Finnigan 3200 quadrupole instrument, and the peak positions are reported to unit mass resolution as determined by the data system, which was calibrated periodically with tris(perfluorobutyl)amine. Either electron impact (EI) or chemical ionization (CI) ion sources were used.

Nitration of *m*-Acetoxyacetanilide. Preparation of 3a. Fuming nitric acid (225 mL) was cooled to −15 °C in an ice–salt bath. Solid *m*-acetoxyacetanilide (45 g, 0.23 mol) was added in portions, while the temperature of the solution was kept below −10 °C. After the addition was complete, the reaction mixture was stirred at −10 °C for 3 h and then poured on crushed ice. A sticky precipitate formed, and the entire mixture was extracted with ethyl acetate. The combined organic layers were washed with brine, dried, and evaporated. This crude product was a 4:1 mixture of the desired 3-acetoxy-4-nitroacetanilide (**3a**) and 5-acetoxy-2-nitroacetanilide. Pure **3a** crystallizes from ethyl acetate at room temperature (22.7 g, 42%), mp 149–151 °C (lit.[11] mp 149 °C). Refrigerating the solution then precipitates the isomeric 5-acetoxy-2-nitroacetanilide.

3-(Benzyloxy)-4-nitroacetanilide (3c). A mixture of **3a** (15.7 g, 66 mmol) and anhydrous K_2CO_3 (20 g, 0.145 mol) in methanol (150 mL) was stirred at room temperature for 5 h. The methanol was then removed at reduced pressure, and the residue suspended in water (200 mL). The suspension was made acidic with concentrated HCl, with the solid material being stirred and crushed as necessary until it was all light yellow in color. The solid was collected by filtration and identified as 3-hydroxy-4-nitroacetanilide (**3b**) by NMR analysis (yield 13.5 g, 98%). A small sample was recrystallized from water, mp 219–220 °C (lit.[28] mp 221 °C).

The dried material (8.4 g, 43 mmol) was mixed in DMF (50 mL) with finely pulverized K_2CO_3 (11.1 g, 80 mmol) and KI (14.6 g, 88 mmol). To this mixture benzyl chloride (10.1 mL, 88 mmol) was added slowly. The reaction mixture was stirred at room temperature for 4 h and then mixed with ethyl acetate (200 mL) and brine (200 mL). The layers were separated, and the aqueous layer was extracted with additional ethyl acetate. The combined organic layers gave **3c** (11.4 g, 98%), mp 131–132 °C after recrystallization from chloroform–hexane–benzene: 300-MHz NMR ($CDCl_3$) δ 2.23 (s, 3 H), 5.27 (s, 2 H), 6.80 (d of d, J = 12, 1 Hz, 1 H), 7.33–7.44 (m, 5 H), 7.51 (d, J = 12 Hz, 1 H), 7.94 (d, J = 12 Hz, 2 H).

***N*-(2-Propenyl)-*N*-[3-(benzyloxy)-4-nitrophenyl]acetamide (4a).** Solid **3c** (11.9 g, 41 mmol) and potassium *tert*-butoxide (4.75 g, 42 mmol) were weighed into a dry flask, and DMF (30 mL) was added all at once with external cooling (ice bath). To this solution was added allyl bromide (4.2 mL, 48 mmol), and the mixture was stirred for 1 day at room temperature. The reaction mixture was then poured into water. A precipitate was collected. Additional product was obtained by ethyl acetate extraction. The combined product was recrystallized from toluene and gave 10.2 g (83%) of **4a**, mp 156–157 °C: 300-MHz NMR ($CDCl_3$) δ 1.86 (s, 3 H), 4.23 (d, 2 H), 4.97–5.15 (m, 2 H), 5.24 (s, 2 H), 5.70–5.85 (m, 1 H), 7.0 (d of d, J = 12, 1 Hz, 1 H), 7.30–7.45 (m, 1 H), 7.87 (d, J = 12 Hz, 1 H). Anal. Calcd for $C_{18}H_{18}N_2O_4$: C, 66.25; H, 5.56; N, 8.58. Found: C, 66.31; H, 5.59; N, 8.53.

7-(Benzyloxy)-3-methyl-5-[*N*-(2-propenyl)acetamido]indole (5a). A mixture of **4a** (6.36 g, 19.5 mmol), acid-washed zinc powder (41.6 g), and $CaCl_2$ (1.4 g) in a solution of ethanol (110 mL) and water (30 mL) was refluxed for 1.5 h. The mixture was filtered to remove zinc, and the filtrate was evaporated. The residue was redissolved in ethyl acetate, washed with brine, and dried over $MgSO_4$. Evaporation of the residue left pure (NMR, TLC) 4-amino-3-(benzyloxy)-*N*-(2-propenyl)acetanilide, **4b**: 300-MHz NMR ($CDCl_3$) δ 1.85 (s, 3 H), 4.2 (d, 2 H), 4.98–5.05 (m, 2 H), 5.07 (s, 2 H), 5.74–5.88 (m, 1 H), 6.54–6.72 (m, 3 H), 7.33–7.45 (m, 5 H).

The amine (6.4 g) was dissolved in concentrated HCl (5.9 mL) and cooled to 0 °C. To the mixture was added slowly 1.58 g of $NaNO_2$ dissolved in 8 mL of water. After this was stirred at 0 °C, a clear solution was obtained. A solution of $SnCl_2 \cdot 2H_2O$ (17.6 g) dissolved in 18 mL of concentrated HCl was cooled in an ice–salt bath, and the chilled solution of the diazonium ion was added over 0.5 h, with vigorous shaking. A solid formed during the reduction. After the addition was complete, the solution was kept chilled in the ice bath for 2 h. The supernatant liquid was then decanted, and the solid was washed with additional ice water (40 mL). The residual solid was dissolved in DMF (150 mL), and propionaldehyde (1.4 mL) was added to the mixture, which was kept at 0 °C for 1 h. The solution was then neutralized with sodium acetate, and an additional 1.4 mL of propionaldehyde was added. This mixture was kept in a refrigerator overnight, diluted with aqueous NaH_2PO_4, and extracted with ethyl acetate. The extract was washed with brine, dried ($MgSO_4$), and evaporated to give the crude hydrazone. This material was subjected to flash chromatography (7:4 hexane ethyl–acetate) on silica gel, to give 5.4 g (79% from **4a**) of light yellow hydrazone **4d**, which was used directly in the Fischer cyclization.

The hydrazone **4d** (5.3 g, 15 mmol) and *p*-toluenesulfonic acid (10.3 g, 60 mmol) were dissolved in dry THF (100 mL) and stirred at room temperature for 8 h. The solvent was evaporated, and the residue was shaken with ethyl acetate (75 mL) and ice–water. The organic layer was collected, and the aqueous layer was

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neutralized with $NaHCO_3$ and again extracted with ethyl acetate (40 mL). The combined organic layers were washed with aqueous $NaHCO_3$, dried, and evaporated to a brown oil (4.8 g, 95%), which was of good purity by TLC, R_f = 0.4 with 1:1:1 hexane–CH_2Cl_2–ether, and NMR. This material was used without further purification in most subsequent preparations. Crystalline **5a**, mp 138–140 °C was obtained by flash chromatography on silica gel, followed by crystallization from ethyl acetate–hexane: 300-MHz NMR ($CDCl_3$) δ 1.83 (s, 3 H), 2.30 (s, 3 H), 4.31 (d, 2 H), 5.02–5.15 (m, 2 H), 5.17 (s, 2 H), 5.88–5.97 (m, 1 H), 6.44 (d, J = 2 Hz, 1 H), 6.97 (d, J = 2 Hz, 1 H), 7.00 (s, 1 H), 7.35–7.45 (m, 5 H), 8.22 (br s, 1 H); MS (EI) 334.

7-Hydroxy-3-methyl-5-[*N*-(2-propenyl)acetamido]indole (5b). A solution of **5a** (0.59 g, 1.8 mmol) in CH_2Cl_2 (25 mL) was cooled to −40 °C. To this solution was added 1 M BBr_3 in CH_2Cl_2 (3 mL, 3 mmol). The solution was stirred for 2.5 h and then quenched with saturated NaH_2PO_4 solution. The mixture was extracted with $CHCl_3$, washed with brine, and dried. The residue was chromatographed with 2:1 ethyl acetate–hexane to give **5b** (0.18 g, 40%), mp 181–183 °C after recrystallization from benzene–hexane: 300-MHz NMR ($CDCl_3$) δ 1.98 (s, 3 H), 2.30 (s, 3 H), 4.36 (d, 2 H), 5.14–5.23 (m, 2 H), 5.88–6.02 (m, 1 H), 6.47 (d, J = 2 Hz, 1 H), 6.90 (d, J = 2 Hz, 1 H), 6.98 (s, 1 H), 9.35 (br s, 2 H). Anal. Calcd for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.46. Found: C, 68.70; H, 6.62; N, 11.36.

6-Diazo-3-methyl-5-[*N*-(2-propenyl)acetamido]-6,7-dihydroindol-7-one (6). The phenol **5b** (110 mg, 0.45 mmol), K_2CO_3 (62 mg, 0.45 mmol), and *m*-nitrobenzenesulfonyl azide (109 mg, 0.45 mmol) in 2,2,2-trifluoroethanol (5 mL) were stirred for 12 h under nitrogen at room temperature. The mixture was then evaporated, and the residue was chromatographed with an ethyl acetate–hexane → 100% ethyl acetate gradient. There was obtained 54 mg (45%) of the diazo compound and 18 mg (16%) of unreacted starting material: 300-MHz NMR ($CDCl_3$) δ 2.07 (s, 3 H), 2.21 (s, 3 H), 4.29 (d, 2 H), 5.14–5.24 (m, 2 H), 5.83–5.97 (m, 1 H), 640, (s, 1 H), 7.06 (s, 1 H), 9.40 (br s, 1 H); MS (EI) 270, 242, 199; IR (KBr) 2108, 2089, 1674, 1669, 1630.

***N*-[2-(Benzyloxy)-4-nitrophenyl]acetamide (9a).** 2-Acetamido-5-nitrophenol[29] (10.0 g, 0.51 mmol) was dissolved in 100 mL of dry DMF. Then, KI (18.6 g, 0.112 mol) and K_2CO_3 (14.1 g, 0.112 mol) were added followed by benzyl chloride (12.9 mL, 0.112 mol). The reaction mixture was stirred for 4 h. Then, 100 mL of ethyl acetate and 100 mL of brine were added. The mixture was extracted with ethyl acetate, washed with brine, and dried. Evaporation of the solvent and recrystallization from ethyl acetate–hexanes afforded 10.1 g of beige needles. Two additional crops from the mother liquors yielded 2.14 g of additional product, giving a total yield of 12.3 g (84%): mp 125–126 ° (lit.[30] mp 127 °C); 90-MHz NMR ($CDCl_3$) δ 2.14 (s, 3 H) 5.16 (s, 2 H) 7.40 (s, 5 H), 7.82 (d, J = 2 Hz, 1 H), 7.90 (d of d, J = 10, 2 Hz, 1 H), 8.00 (br s, 1 H), 8.58 (d, J = 10 Hz, 1 H).

***N*-[4-Acetamido-3-(benzyloxy)phenyl]methanesulfonamide (9c).** Acetanilide **9a** (5.00 g, 0.018 mol), acid-washed zinc powder (37.3 g), and $CaCl_2$ (1.26 g) were suspended in 125 mL of 95% ethanol. This suspension was refluxed for 90 min under nitrogen. After cooling, the reaction mixture was filtered through Celite. Evaporation of the solvent afforded the aminoacetanilide **9b** as a brown oil, which solidified under vacuum to a cream-color solid in quantitative yield: 300-MHz NMR ($CDCl_3$) δ 2.02 (, 3 H), 3.22 (br s, 2 H), 4.97 (s, 2 H), 6.23 (d of d, J = 10, 1 Hz, 1 H), 6.27 (d, J = 1 Hz, 1 H), 7.33 (s, 5 H), 7.48 (br s, 1 H), 8.02 (d, J = 10 Hz, 1 H). This material was used without further purification. The aminoacetanilide (4.4 g, 0.018 mol) was suspended in 125 mL of CH_2Cl_2. Pyridine (7.0 mL, 0.087 mol) was added, and the reaction mixture was cooled in ice. Methanesulfonyl chloride (4.0 g, 0.035 mol) was added dropwise. When addition was complete, the solution was warmed to 25 °C and stirred for 2 h. The extract was washed with 5% HCl solution and dried over anhydrous $NaSO_4$. Evaporation of the solvent afforded a red brown solid. Recrystallization from ethyl acetate–hexanes yielded 4.64 g (80%) of **9c** as sparkling brown crystals: mp 142–143 °C; 300-MHz NMR (DMSO) δ 2.00 (s, 3 H), 2.81 (s, 3 H), 5.10 (s, 2 H), 6.73 (d of d, J = 12, 2 Hz, 1 H), 6.92 (d, J = 2 Hz, 1 H), 7.25–7.50 (br m, 5 H), 7.65 (d, J = 12 Hz, 1 H), 9.08 (br s, 1 H), 9.57 (br s, 1 H). Anal. Calcd for $C_{16}H_{18}N_2O_4S$: C, 57.59; H, 5.39; N, 8.38. Found: C, 57.37; H, 5.47; N, 8.35.

***N*-[4-Acetamido-5-(benzyloxy)-2-nitrophenyl]methanesulfonamide (10a).** Acetanilide **9c** (5.00 g, 0.015 mol) and mercuric acetate (0.121 g, 0.38 mmol) were dissolved in 44 mL of acetic acid and 125 mL of acetic anhydride. This solution was heated at 90 °C for 15 min and then cooled to 0 °C. Nitric acid (70.3%, 0.037 mol, 2.4 mL diluted to 7.1 mL with water) was added dropwise over 30 min, and then the reaction mixture was stirred an additional 30 min at 0 °C. The crude reaction mixture was poured on to 250 mL of ice. This suspension was allowed to stand for 45 min and then the crude product was collected by filtration. Recrystallization of the precipitate from ethanol and water afforded 4.20 g (74%) of **10a** as a lemon yellow solid: mp 237–238 °C; 90-MHz NMR (DMSO) δ 2.08 (s, 3 H), 2.98 (s, 3 H), 5.27 (s, 2 H), 7.14 (s, 1 H), 7.10–7.60 (m, 5 H), 8.75 (s, 1 H), 9.51 (br s, 1 H), 9.73 (br s, 1 H). Anal. Calcd for $C_{16}H_{17}N_3O_6S$: C, 50.66; H, 4.49; N, 11.08. Found: C, 50.60; H, 4.52; N, 11.05.

***N*-[4-Acetamido-5-(benzyloxy)-2-nitrophenyl]-*N*-(2-propenyl)methanesulfonamide (10b).** Sulfonanilide **10a** (2.00 g, 5.28 mmol) was dissolved in 30 mL of dry DMF. The solution was cooled in an ice bath, potassium *tert*-butoxide (0.77 g, 6.86 mmol) was added, followed by the addition of allyl bromide (0.72 g, 6.0 mmol). The reaction mixture was warmed to 25 °C and stirred for 4 h and then poured into 50 mL of 5% HCl. The resulting suspension was extracted with ethyl acetate, washed with brine, and dried over $MgSO_4$. Evaporation of the solvent yielded a yellow solid. Recrystallization from $CHCl_3$–hexanes afforded 1.68 g (76%) of pale yellow crystals, mp 205–207 °C: 90-MHz NMR ($CDCl_3$) δ 2.16 (s, 3 H), 2.92 (s, 3 H), 3.90–4.40 (m, 2 H), 4.96 (m, 1 H), 5.01 (m, 1 H), 5.05 (s, 1 H), 5.18 (s, 2 H), 5.46–6.10 (br m, 1 H), 6.98 (s, 1 H), 7.38 (s, 5 H), 7.77 (br s, 1 H), 9.12 (s, 1 H).

***N*-(4-Acetamido-5-hydroxy-2-nitrophenyl)-*N*-(2-propenyl)methanesulfonamide (10c).** Sulfonanilide **10b** (0.24 g, 0.57 mmol) was dissolved in 15 mL of dry CH_2Cl_2 and cooled to −20 °C. In a separate flask, cyclohexene (0.35 mL, 3.44 mmol) was cooled to −20 °C, and a 1.0 M solution of boron tribromide in CH_2Cl_2 (3.44 mL, 3.44 mmol) was added. This solution was stirred 1 min and was then added to the solution of **10b**. The reaction mixture was stirred at −20 °C for 30 min and was then quenched at −20 °C with a few drops of absolute ethanol, followed by 10 mL of saturated NaH_2PO_4 solution. The product was then extracted with CH_2Cl_2. Evaporation afforded 0.16 g (83%) of **10c**: mp 214–215 °C; dec 360-MHz NMR (DMSO) δ 2.12 (s, 3 H), 3.04 (s, 3 H), 4.00–4.40 (br s, 2 H), 5.12 (m, 2 H), 5.80–5.95 (br m, 1 H), 6.80 (s, 1 H), 8.72 (s, 1 H) 9.48 (br s, 1 H). Anal. Calcd for $C_{12}H_{15}N_3O_6S$: C, 43.77; H, 4.56; N, 12.77. Found: C, 43.73; H, 4.62; N, 12.69.

2-Acetamido-5-[*N*-(2-propenyl)methanesulfonamido]-4-diazocyclohexadienone (11). Compound **10c** (0.310 g, 0.94 mmol), acid-washed zinc (2.2 g), and $CaCl_2$ (73 mg) were suspended in 6 mL of 95% ethanol. The reaction mixture was heated at 90 °C for 30 min. After cooling, the mixture was filtered through Celite into 7.7 mL of a 2.8 N HCl solution in methanol. Evaporation gave the hydrochloride of the amine as a brown solid: 90-MHz NMR (DMSO) δ 2.02 (s, 3 H), 2.95 (s, 3 H), 4.02 (d, 2 H), 4.45 (br s, 2 H), 5.35–6.10 (br m, 1 H), 7.03 (s, 1 H), 7.18 (br s, 1 H), 8.75 (s, 1 H), 9.15 (br s, 1 H); MS (EI) 299, 249, 227, 220, 215, 201, 187, 173, 148 amu. After this crude product was dried, it was dissolved in 5 mL of absolute ethanol. The solution was cooled in ice, and isoamyl nitrite (0.41 g, 3.5 mmol) was added. The solution was stirred at 0 °C for 15 min and then at 25 °C for 30 min. The solvent was evaporated to afford a reddish-brown semisolid. This material was dissolved in 15 mL of CH_2Cl_2, washed four times with saturated $NaHCO_3$, and dried over anhydrous Na_2SO_4. All extractions and evaporation were done with minimal exposure to light and without heating. Purification with flash column chromatography (ethyl acetate → 1:1 ethyl acetate–ethanol) afforded **11** as 0.206 mg (71%) of an orange-brown glass: 360-MHz NMR ($CDCl_3$) δ 2.21 (s, 3 H), 3.02 (s, 3 H), 4.21 (d, 2

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H), 5.22–5.31 (m, 2 H), 5.72–5.86 (br m, 1 H), 6.46 (s, 1 H), 8.57 (s, 1 H), 8.58 (br s, 1 H); MS (EI) 310, 282, 240, 203, 177, 161, 149, 133; IR (KBr) 2116, 1660.

***N*-(4-Acetamido-3-methoxyphenyl)methanesulfonamide (12c).** 2-Methoxy-4-nitroacetanilide (10.0 g, 47.6 mmol) was dissolved in 150 mL of ethyl acetate, and 5% palladium on charcoal (0.50 g) was added. The mixture was shaken under a hydrogen atmosphere for 3 h. The mixture was filtered and evaporated to give **12b** as a beige solid: 90-MHz NMR ($CDCl_3$) δ 2.08 (s, 3 H), 2.80–4.10 (br s, 1 H), 3.73 (s, 3 H), 6.10–6.45 (m, 2 H), 7.18–7.75 (br s, 1 H), 7.90–8.30 (d, 1 H). The crude product was dried under vacuum and dissolved in 200 mL of $CHCl_3$. Pyridine (28 mmol, 23 mL) was added, and the solution was cooled in ice. Methanesulfonyl chloride (6.0 g, 52 mmol) was added dropwise, and the solution was stirred at 0 °C for 15 min. After the mixture was stirred for another 2 h at 25 °C, 200 mL of saturated $NaHCO_3$ solution was added. The product was extracted with $CHCl_3$, washed with 5% HCl, dried, and evaporated. Recrystallization with decolorizing charcoal from ethyl acetate–hexanes yielded 6.94 g (57%) of **12c**: mp 159–160 °C; 90-MHz NMR (DMSO) δ 2.02 (s, 3 H), 2.92 (s, 3 H), 3.76 (s, 3 H), 6.71 (d of d, J = 8, 2 Hz), 6.84 (d, J = 2 Hz, 1 H), 7.77 (d, J = 8, 1 H), 9.02 (br, s, 1 H), 9.52 (br s, 1 H). Anal. Calcd for $C_{10}H_{14}N_2O_4S$: C, 46.51; H, 5.43; N, 10.85. Found: C, 46.53; H, 5.46; N, 10.82.

***N*-(4-Acetamido-5-methoxy-2-nitrophenyl)methanesulfonamide (13a).** Methanesulfonamide **12c** (10.0 g, 38.8 mmol) and mercuric acetate (0.314 g, 0.99 mmol) were dissolved in 112 mL of acetic acid and 324 mL of acetic anhydride. The solution was heated at 90 °C for 15 min and then cooled to 0 °C. A solution of 70% nitric acid (58 mmol, 3.7 mL) in water (11 mL) was added dropwise over 30 min. When addition was complete, the reaction mixture was stirred another 30 min at 0 °C and then poured into 500 mL of ice. After 30 min, the crude product was collected by filtration. Additional product was extracted with $CHCl_3$. Recrystallization from 95% ethanol–water afforded 8.35 g (71%) of **13a**: mp 219–222 °C; 90-MHz NMR (DMSO) δ 2.09 (s, 3 H), 3.17 (s, 3 H), 3.92 (s, 3 H), 7.12 (s, 1 H), 8.79 (s, 1 H), 9.46 (br s, 1 H), 9.75 (br s, 1 H). Anal. Calcd for $C_{10}H_{13}N_3O_6S$: C, 39.60; H, 4.29; N, 13.86. Found: C, 39.69; H, 4.34; N, 13.83.

***N*-(4-Acetamido-5-methoxy-2-nitrophenyl)-*N*-(2-propenyl)methanesulfonamide (13b).** A solution of sulfonanilide **13a** (8.50 g, 28.1 mmol) in 50 mL of dry DMF was cooled to 0 °C, and potassium *tert*-butoxide (3.78 g, 33.7 mmol) was added. Then, allyl bromide (3.73 g, 30.9 mmol) was added, and the reaction mixture was stirred at 0 °C for 15 min and at 15 °C for 4 h. The solution was diluted with 100 mL of water and worked up with $CHCl_3$ for extraction. Evaporation yielded an oil containing some DMF, which was removed under vacuum. The residue was crystallized from ethyl acetate–hexanes and gave **13b**, 8.74 g (91%), mp 162–163 °C: 90-MHz NMR ($CDCl_3$) δ 2.20 (s, 3 H), 2.99 (s, 3 H), 3.80 (s, 3 H), 3.90–4.50 (br m, 2 H), 5.05 (d, 1 H), 5.09 (m, 1 H), 5.50–6.28 (br m, 1 H), 6.88 (s, 1 H), 7.55 (br s, 1 H), 9.08 (s, 1 H). Anal. Calcd for $C_{13}H_{17}N_3O_6S$: C, 45.48; H, 4.96; N, 12.24. Found: C, 45.53; H, 5.00; N, 12.24.

***N*-(4-Amino-5-methoxy-2-nitrophenyl)-*N*-(2-propenyl)methanesulfonamide (13c).** Sulfonanilide **13b** (5.0 g, 0.015 mol) was added to 100 mL of a 1:1 (v/v) solution of 10% aqueous NaOH and 95% ethanol. This suspension was stirred at ambient temperature. After 12 h and 36 h elapsed time, an additional 0.50 g of solid NaOH was added. After 60 h, the crude yellow precipitate was collected and washed with cold water. Recrystallization from ethanol and water yielded 3.82 g (87%) of **13c**, mp 138–139 °C. A similar yield could be obtained by heating to 50 °C for 2 h: 90-MHz NMR (DMSO) δ 2.98 (s, 3 H), 3.85 (s, 3 H), 4.21 (br m, 2 H), 5.07 (m, 1 H), 5.11 (m, 1 H), 5.46 (s, 2 H), 5.62–6.24 (br m, 1 H), 6.82 (s, 1 H), 7.13 (s, 1 H). Anal. Calcd for $C_{11}H_{15}N_3O_5S$: C, 43.85; H, 4.98; N, 13.95. Found: C, 43.79; H, 5.03; N, 13.95.

2-Methoxy-5-nitro-4-[*N*-(2-propenyl)methanesulfonamido]phenylhydrazone of Ethyl 2-Oxobutanoate (16). Aniline **13c** (2.00 g, 6.64 mmol) was stirred in 2.8 mL of concentrated HCl. When the mixture had developed a homogeneous creamy consistency, the flask was cooled in an ice bath. Then a solution of sodium nitrite (0.495 g, 7.17 mmol) in 4.2 mL of water was added, and the resulting mixture was vigorously stirred at 0 °C for 5 min. In a separate flask, ethyl 2-ethylacetoacetate (1.05 g, 6.65 mmol) was dissolved in 7.0 mL of ethanol and cooled to 0 °C. A 50% KOH solution (2.4 mL) was added followed by the addition of 11.9 mL of water. Then, the diazonium solution was added all at once, and the reaction mixture was stirred for 5 min at 0 °C. The solution was diluted with 25 mL water, and the pH was adjusted to 5–6. This solution was extracted with $CHCl_3$. Evaporation of the dried $CHCl_3$ yielded **15** as a red oil: 90-MHz NMR ($CDCl_3$) δ 1.00 (t, J = 7 Hz, 3 H), 1.28 (t, J = 7 Hz, 3 H), 1.88 (m, 2 H), 2.28 (s, 3 H), 3.03 (s, 3 H), 3.99 (s, 3 H), 3.70–4.60 (br m, 4 H), 5.08 (m, 1 H), 5.20 (m, 1 H), 5.58–6.35 (br m, 1 H), 7.12 (s, 1 H), 7.99 (s, 1 H). After vacuum drying, the oil was dissolved in 25 mL of ethanol, and Na_2CO_3 (1.41 g, 13.3 mmol) was added. This solution was stirred at ambient temperature for 8 h and then diluted with 50 mL of water. After acidification, the solution was extracted with $CHCl_3$. Evaporation afforded a dark red solid, which was purified with a short flash chromatography column (2:1 hexanes–ethyl acetate) to remove the polar red impurities. There was obtained 1.66 g (58%) of **16** (typically yields ranged from 50–60%): 90-MHz NMR ($CDCl_3$) δ 1.20 (t, J = 7 Hz, 3 H), 1.35 (t, J = 7 Hz, 3 H), 2.58 (m, 2 H), 2.97 (s, 3 H), 3.93 (s, 3 H), 3.75–4.70 (br m, 2 H), 4.30 (q, 2 H), 5.16 (m, 1 H), 5.18 (m, 1 H), 5.50–6.30 (br m, 1 H), 6.83 (s, 1 H), 8.10 (s, 1 H). This material was sufficiently pure for the subsequent Fischer cyclization. Recrystallization from ethyl acetate–hexanes afforded orange-yellow crystals of analytical purity, mp 140–143 °C. Anal. Calcd for $C_{17}H_{24}N_4O_7S$: C, 47.66; H, 5.61; N, 13.08. Found: C, 47.72; H, 5.66; N, 13.03.

Ethyl 7-Methoxy-3-methyl-4-nitro-5-[*N*-(2-propenyl)methanesulfonamido]indole-2-carboxylate (17a). Crude hydrazone **16** (1.6 g, 3.7 mmol) was dissolved in 25 mL of dry toluene followed by the addition of trifluoroacetic acid (1.44 mL, 18.7 mmol), and the solution was refluxed under nitrogen for 8 h. The reaction mixture was cooled, and the solvent was removed under reduced pressure to afford a black gum. Flash chromatography (hexanes-ethyl acetate) afforded 1.54 g (66%) of **17a**: 90-MHz NMR ($CDCl_3$) δ 1.38 (t, J = 7 Hz, 3 H), 2.39 (s, 3 H), 2.97 (s, 3 H), 3.80–4.50 (br m, 2 H), 3.99 (s, 3 H), 4.39 (q, J = 7 Hz, 2 H), 5.05 (d, J = 12 Hz, 1 H), 5.19 (s, 1 H), 5.70–6.30 (br m, 1 H), 6.67 (s, 1 H), 9.20 (br s, 1 H); MS (EI) 411, 365, 286, 240, 207, 199 amu.

7-Methoxy-3-methyl-4-nitro-5-[*N*-(2-propenyl)methanesulfonamido]indole (18a). Indole **17a** (0.36 g, 0.88 mmol) was added to 8.6 mL of water. After the addition of 3.5 mL of 10% NaOH solution, the suspension was heated to reflux for 4 h. The reaction mixture was cooled in an ice bath and acidified. The resulting precipitate was collected to give **17b**, 0.34 g (88%): mp 298–302 °C dec; 300-MHz NMR (DMSO) δ 2.29 (s, 3 H), 3.15 (s, 3 H), 4.00 (s, 3 H), 4.25 (d, J = 7 Hz, 2 H), 5.04–5.16 (m, 2 H), 5.82–5.92 (m, 1 H), 6.87 (s, 1 H), 12.20 (s, 1 H).

Acid **17b** (0.091 g, 0.24 mmol) was dissolved in 1.0 mL of freshly distilled *N,N*-dimethylacetamide. After the addition of copper(I) oxide (0.018 g, 20 weight %), the reaction flask was put in an oil bath preheated to 200 °C. The reaction mixture was vigorously stirred for 2.5 h at this temperature. After cooling, the reaction mixture was filtered through Celite, rinsing with ethyl acetate. The filtrate was washed with 5% HCl, dried, and evaporated to a brown glass, which was purified by flash chromatography (2:1 hexanes–ethyl acetate). Compound **18a** was obtained as a glass, 0.058 g (75%). Crystallization from $CHCl_3$ and hexanes afforded yellow crystals: mp 162–163 °C; 300-MHz NMR ($CDCl_3$) δ 2.15 (s, 3 H), 3.05 (s, 3 H), 3.90 (s, 3 H), 4.05–4.40 (br m, 2 H), 5.09 (d, J = 7 Hz, 1 H), 5.11 (m, 1 H), 5.88–6.02 (m, 1 H), 6.54 (s, 1 H) 7.01 (br s, 1 H), 8.58 (br s, 1 H). Anal. Calcd for $C_{14}H_{17}N_3O_5S$: C, 49.56; H, 5.01; N, 12.39. Found: C, 49.28; H, 5.04; N, 12.33.

7-Hydroxy-3-methyl-4-nitro-5-[*N*-(2-propenyl)methanesulfonamido]indole (18b). Indole **18a** (0.087 g, 0.26 mmol) was dissolved in 2 mL of hexamethylphosphoramide. In a separate flask, thiophenol (90 μL, 0.88 mmol) was dissolved in 1.66 mL of hexamethylphosphoramide under nitrogen. To the thiophenol solution was added a solution of 1.55 M *n*-butyllithium in hexanes (0.53 mL, 0.82 mmol). This solution was stirred for 1–2 min at ambient temperature. The lithium thiophenoxide solution was added to the solution of **18a**. The reaction mixture was heated to 180 °C. Heating was continued for 7–8 h while the reaction was monitored by thin-layer chromatography. The reaction mixture was cooled to 25 °C and diluted with 10 mL of ethyl

acetate. This solution was extracted with 5% NaOH solution. The aqueous extracts were combined, acidified, and extracted with ethyl acetate. The extract was washed extensively with water and dried over $MgSO_4$. Evaporation of the solvent under reduced pressure afforded a red-orange oil. Purification by flash column chromatography (1:1 hexanes–ethyl acetate) afforded 0.056 g (67%, generally yields ranged from 60–70%) of **18b**. Recrystallization from ethanol and water afforded an analytical sample: mp 179–180 °C dec; 300-MHz NMR ($CDCl_3$) δ 2.03 (s, 3 H), 3.19 (s, 3 H), 4.20 (br d, 2 H), 5.15 (m, 2 H), 5.87 (m, 1 H), 6.52 (s, 1 H), 6.93 (br s, 1 H), 7.08 (br s, 1 H), 8.72 (br s, 1 H). Anal. Calcd for $C_{13}H_{15}N_3O_5S$: C, 48.00; H, 4.62; N, 12.92. Found: C, 47.78; H, 4.68; N, 12.81.

***N*-[4-Acetamido-3-(benzyloxy)phenyl]-*N*-(2-propenyl)-methanesulfonamide (19a).** Compound **9c** (0.50 g, 1.5 mmol) was dissolved in 5 mL of DMF and cooled to 0 °C. Potassium *tert*-butoxide (0.20 g, 1.8 mmol) was then added, followed by allyl bromide (0.20 g, 1.7 mmol). The reaction mixture was then warmed to room temperature and stirred for 3 h. The reaction was quenched with 15 mL of water and extracted with ethyl acetate. Removal of the solvent yielded a gray solid. Recrystallization from ethyl acetate–hexanes afforded 0.45 g (80%) of a fluffy white solid, mp 114–116 °C: 90-MHz NMR ($CDCl_3$) δ 2.13 (s, 3 H), 2.83 (s, 3 H), 4.24 (d, 2 H), 4.95–5.30 (m, 2 H), 5.08 (s, 2 H), 5.35–6.15 (br m, 1 H), 6.89 (d of d, J = 10, 1 Hz, 1 H), 7.00 (d, J = 1 Hz, 1 H), 7.38 (s, 5 H), 7.75 (br s, 1 H), 8.40 (d, J = 10 Hz, 1 H). Anal. Calcd for $C_{19}H_{22}N_2O_4S$: C, 60.96; H, 5.88; N, 7.49. Found: C, 60.85; H, 5.93; N, 7.47.

***N*-[4-Amino-3-(benzyloxy)phenyl]-*N*-(2-propenyl)-methanesulfonamide (19b).** Sulfonanilide **19a** (0.68 g, 1.81 mmol) was dissolved in 3 mL of a 1:1 (v/v) solution of 95% ethanol and 50% aqueous KOH solution and refluxed for 8 h. The reaction flask was cooled to 0 °C. The crude product was collected by suction filtration. Recrystallization from ethanol–water afforded 0.60 g (82%) of **19b** as white needles, mp 125–127 °C: 90-MHz NMR ($CDCl_3$) δ 2.80 (s, 3 H), 3.92 (br s, 2 H), 4.14 (d, 2 H), 5.05 (s, 2 H), 4.90–5.30 (m, 2 H), 5.52–6.18 (br m, 1 H), 6.67 (m, 1 H), 6.78 (m, 1 H), 7.31 (s, 5 H). Anal. Calcd for $C_{17}H_{20}N_2O_3S$: C, 61.45; H, 6.02; N, 8.43. Found: C, 61.48; H, 6.09; N, 8.43.

7-(Benzyloxy)-3-methyl-5-[*N*-(2-propenyl)methanesulfonamido]indole (20a). Aniline **19b** (2.00 g, 6.02 mmol) was suspended in 7 mL of concentrated HCl and cooled in an ice–salt bath. A solution of $NaNO_2$ (0.500 g, 7.25 mmol) in 2 mL of water was added dropwise with constant stirring and checked against potassium iodide–starch indicator paper. When diazotization was complete, the diazonium solution was added in small portions with vigorous stirring to a precooled solution of $SnCl_2$ (2.86 g, 15.1 mmol) in 3 mL of concentrated HCl. A precipitate formed immediately. The reaction mixture was placed in the refrigerator for 2 h. The precipitate was filtered and redissolved in 20 mL of cold DMF. Propionaldehyde (0.38 g, 6.62 mmol) was added dropwise, and the reaction mixture was stirred at room temperature, under nitrogen for 12 h. The reaction mixture was poured into 20% NaH_2PO_4 solution and extracted with ethyl acetate. The crude product was purified by flash column chromatography (hexane–ethyl acetate 7:2) to yield 1.04 g (47%) of white solid: mp 152–154 °C; 300-MHz NMR ($CDCl_3$) δ 2.30 (s, 3 H), 2.93 (s, 3 H), 4.30 (d, 2 H), 5.07–5.15 (m, 2 H), 5.18 (s, 2 H), 5.89 (m, 1 H), 6.67 (d, J = 2 Hz, 1 H), 6.95 (s, 1 H), 7.15 (d, J = 2 Hz, 1 H), 7.42 (m, 5 H), 8.30 (s, 1 H); MS (EI) 370, 291, 200, 199, 91. Anal. Calcd for $C_{20}H_{22}N_2O_3S$: C, 64.84; H, 5.98; N, 7.56. Found: C, 64.90; H, 6.01; N, 7.56.

1-(Phenylsulfonyl)-7-(benzyloxy)-3-methyl-5-[*N*-(2-propenyl)methanesulfonamido]indole (20b). Compound **20a** (250 mg, 0.68 mmol) was dissolved in 5 mL of dry THF and stirred under N_2 in an ice bath. Sodium hydride (70 mg, 2.9 mmol) was added. The reaction mixture was stirred at 0 °C for 1 h. Benzenesulfonyl chloride (282 mg, 1.6 mmol) was added dropwise. The reaction mixture was removed from the ice bath and was stirred at room temperature for 8 h, during which time a colorless precipitate formed. The reaction mixture was poured into 20 mL of cold 20% NaH_2PO_4 solution and extracted with ethyl acetate. The crude product was purified by chromatography (hexanes–ethyl acetate, 3:1) to yield 286 mg, 83%, of a white solid, which was recrystallized from ethyl acetate–hexane to yield needles: mp 134–135 °C; 300-MHz NMR ($CDCl_3$) δ 2.25 (s, 3 H), 2.74 (s, 3 H), 4.17 (d, 2 H), 5.02 (s, 2 H), 5.07–5.09 (m, 2 H), 5.67–5.80 (m, 1 H), 6.60 (d, J = 2 Hz, 1 H), 7.05 (d, J = 2 Hz, 1 H), 7.30 (m, 6 H), 7.47 (m, 2 H), 7.62 (m, 3 H); MS (CI, isobutane) 511, 371, 143. Anal. Calcd for $C_{26}H_{26}N_2O_5S$: C, 61.16; H, 5.13; N, 5.49. Found: C, 61.05; H, 5.20; N, 5.50.

7-Hydroxy-3-methyl-5-[*N*-(2-propenyl)methanesulfonamido]indole (23). Indole **20a** (500 mg, 1.35 mmol) was dissolved in 5 mL of dry CH_2Cl_2 and cooled to −20 °C under nitrogen. In a separate flask cyclohexene (0.55 g, 6.8 mmol) was cooled under nitrogen. Boron tribromide (1 M in CH_2Cl_2, 2.9 mL, 2.9 mmol) was added to the cyclohexene and allowed to stir for approximately 1 min. This mixture was added dropwise to the indole solution and stirred for 1 h. The reaction was quenched by the addition of a few drops of absolute ethanol followed after 5 min by the addition of 15 mL of 20% NaH_2PO_4. The reaction mixture was extracted with CH_2Cl_2, dried, and evaporated. The product was purified by flash column chromatography (hexanes–ethyl acetate) to yield 130 mg (34%) of **23**: 300-MHz NMR ($CDCl_3$) δ 2.30 (s, 3 H), 3.00 (s, 3 H), 4.30 (d, J = 6 Hz, 2 H), 5.10–5.20 (m, 2 H), 5.82–5.95 (m, 1 H), 6.60 (s, 1 H), 6.97 (s, 1 H), 7.07 (s, 1 H), 8.20 (s, br, 1 H); MS (EI) 290, 239, 201, 186, 160.

1-(Phenylsulfonyl)-7-(benzyloxy)-3-methyl-4-nitro-5-[*N*-(2-propenyl)methanesulfonamido]indole (21a). A flask containing indole **20b** (445 mg, 0.87 mmol) and ammonium nitrate (70 mg, 87 mmol) was dissolved in 3 mL of trifluoroacetic anhydride and 3 mL of dry $CHCl_3$. The reaction mixture was stirred under nitrogen until all of the inorganic material dissolved (6 h). The reaction mixture was poured into 20 mL of ice water and extracted with $CHCl_3$. The crude product was purified by flash chromatography (hexane–ethyl acetate, 7:2) to yield **21a**, 276 mg, (57%) as a yellow solid contaminated with the 4,6-dinitro derivative. NMR integration shows the ratio to be approximately 6:1. Recrystallization from ethyl acetate–ether afforded pure **21a**, mp 172–174 °C: 300-MHz NMR ($CDCl_3$) δ 2.15 (s, 3 H), 2.88 (s, 3 H), 4.05 (s, br, 2 H), 4.88–4.98 (m, 2 H), 5.03 (s, 2 H), 5.60–5.75 (m, 1 H), 6.59 (s, 1 H), 7.22 (m, H), 7.35 (m, 4 H), 7.52 (d, J = 9 Hz, 2 H), 7.59 (d, J = 9 Hz, 2 H), 7.78 (s, br, 1 H); MS (EI) 555, 509, 495, 476, 429, 414, 402, 368, 355, 339, 305, 289, 91. Anal. Calcd for $C_{26}H_{25}N_3O_7S_2$: C, 56.20; H, 4.54; N, 7.56. Found: C, 56.28; H, 4.57; N, 7.50.

1-(Phenylsulfonyl)-7-hydroxy-3-methyl-4-nitro-5-[*N*-(2-propenyl)methanesulfonamido]indole (21b). Indole **21a** (170 mg, 0.31 mmol) was dissolved in 5 mL of dry CH_2Cl_2 and cooled to −20 °C under nitrogen. In a separate flask, cyclohexene (125 mg, 1.52 mmol) was cooled under nitrogen. Boron tribromide (1 M in CH_2Cl_2, 0.75 mL, 0.75 mmol) was added to the cyclohexene and allowed to stir for approximately 1 min. This mixture was added dropwise to the indole solution. The reaction mixture was stirred for 0.5 h. The reaction was quenched by the addition of a few drops of absolute ethanol, followed after 5 min by the addition of 15 mL of 20% NaH_2PO_4 solution. The reaction mixture was extracted with CH_2Cl_2, dried, and evaporated to yield a yellow glass, which was purified by flash chromatography (hexanes–ethyl acetate) to yield 114 mg (80%) of **21b** as yellow foam. Recrystallization from ethyl acetate–benzene afforded needles: mp 130–131 °C; 300-MHz NMR ($CDCl_3$) δ 2.07 (s, 3 H), 3.00 (s, 3 H), 4.17 (s, br, 2 H), 5.15 (m, 2 H), 5.89 (m, 1 H), 6.92 (s, 1 H), 7.37 (br s, 1 H), 7.54 (t, J = 9 Hz, 2 H), 7.65 (t, J = 9 Hz, 1 H), 7.82 (d, J = 9 Hz, 2 H), 9.26 (s, 1 H); MS (EI) 465, 448, 419, 405, 340, 278, 228, 215, 199, 141, 91, 77. Anal. Calcd for $C_{19}H_{19}N_3O_2S_2$: C, 52.37; H, 4.39; N, 8.32. Found: C, 52.33; H, 4.28; N, 8.32.

7-Hydroxy-3-methyl-4-nitro-5-[*N*-(2-propenyl)methanesulfonamido]indole (18b). Compound **21b** (156 mg, 335 mmol) was dissolved in 10 mL of 10% NaOH (1:1 water–methanol). The reaction mixture was refluxed under nitrogen for 20 min, during which time the starting material dissolved and the solution took on a deep red color. The reaction mixture was allowed to cool to room temperature and then chilled, acidified, and extracted with $CHCl_3$. The crude product was purified by column chromatography (hexane–ethyl acetate) to yield 102 mg, 94%, of **18b**. Crystallization from ethanol–water afforded **18b**, mp 181–182 °C dec, identical with **18b** prepared by the alternative route.

7-[(Ethoxycarbonyl)oxy]-3-methyl-4-nitro-5-[*N*-(2-propenyl)methanesulfonamido]indole (24b). Indole **18b** (0.018 g, 0.054 mmole) was dissolved in 1 mL of CH_2Cl_2. After the

addition of pyridine (0.022 g), the reaction mixture was cooled in an ice bath. Ethyl chloroformate (0.009 g) was added. After 15 min, the cooling bath was removed, and the reaction mixture was stirred at 25 °C for 3 h. The reaction mixture was diluted with CH_2Cl_2, washed with 5% aqueous hydrochloric acid, and dried over Na_2SO_4. Evaporation afforded a yellow oil. Purification by flash chromatography afforded 0.015 g (69%) of **24a** as an orange solid: 90-MHz NMR ($CDCl_3$) δ 1.38 (t, J = 7 Hz, 3 H), 2.07 (s, 3 H), 3.01 (s, 3 H), 4.00–4.70 (m, 4 H), 5.09 (m, 1 H), 5.15 (m, 1 H), 5.60–6.30 (br m, 1 H), 7.02 (br s, 1 H), 7.15 (s, 1 H), 8.65 (br s, 1 H); MS (EI) 379, 351, 319, 300, 272, 243, 227, 199.

4-Diazo-3-methyl-5-[*N*-(2-propenyl)methanesulfonamido]-4,7-dihydroindol-7-one (2b). Indole **24b** (0.015 g, 0.038 mmol), acid-washed zinc (0.17 g), and calcium chloride (3 mg) were suspended in 2 mL of 95% ethanol. This suspension was heated under nitrogen at 90 °C for 30 min. The reaction mixture was cooled to 25 °C and filtered through Celite into 2 mL of a 3.6 M HCl in methanol. Evaporation under reduced pressure afforded a reddish glass, which was dried under vacuum. This material was dissolved in 5 mL of absolute ethanol in a round-bottom flask wrapped in aluminum foil and cooled under nitrogen to 0 °C. Isoamyl nitrite (0.02 mL, 0.10 mmol) was added, and the solution was stirred at 0 °C for 30 min. After the cooling bath was removed, stirring was continued another 60 min at 25 °C. The reaction mixture was then diluted with 10 mL of dichloromethane and washed with saturated $NaHCO_3$ solution. The extract was dried over anhydrous sodium sulfate and evaporated under reduced pressure to afford a reddish-brown oil. Purification of this material by flash column chromatography (1:1 hexanes–ethyl acetate) afforded 0.4 mg of quinone imine **25a** and 10 mg (85%) of the diazoindolone **2b** as a cream-color solid: 300-MHz NMR ($CDCl_3$) δ 2.28 (s, 3 H)8, 3.07 (s, 3 H), 4.25 (br s, 1 H), 5.22–5.32 (m, 2 H), 5.77–5.87 (m, 1 H), 6.35 (s, 1 H), 7.08 (br s, 1 H), 9.75 (br s, 1 H), IR (KBr) 2082, 1577 cm^{-1}.

1-(Phenylsulfonyl)-7-[(ethoxycarbonyl)oxy]-4-nitro-5-[*N*-(2-propenyl)methanesulfonamido]indole (21c). Indole **21b** (156 mg, 0.34 mmol) was dissolved in 2 mL of dry methylene chloride. Pyridine (80 mg, 1.0 mmol) was added, and the mixture was cooled to 0 °C in an ice bath, under nitrogen. Ethyl chloroformate (82 mg, 0.67 mmol) was added dropwise. The reaction mixture was stirred for 10 min at 0 °C and then at room temperature for 1 h. The reaction mixture was diluted with 15 mL of CH_2Cl_2 and washed with 5% HCl solution. The organic layer was dried and evaporated. The crude product was purified by flash chromatography (2:1 hexane–ethyl acetate) to yield 140 mg, 78%, of a yellow foam: 300-MHz NMR ($CDCl_3$) δ 1.47 (t, J = 7 Hz, 3 H), 2.15, (s, 3 H), 2.98 (s, 3 H), 4.15 (br s, 2 H), 4.42 (q, J = 7 Hz, 2 H), 5.10–5.22 (m, 2 H), 5.80–5.95 (m, 1 H), 7.09 (s, 1 H), 7.54 (t, J = 9 Hz, 2 H), 7.72 (br s, 1 H), 7.99 (d, J = 9 Hz, 2 H); MS (EI) 537, 509, 491, 447, 419, 386, 340, 199, 141, 77.

1-(Phenylsulfonyl)-4-diazo-3-methyl-5-[*N*-(2-propenyl)-methanesulfonamido]-4,7-dihydroindol-7-one (22). Indole **21c** (155 mg, 0.29 mmol) and $CaCl_2$ (23 mg, 0.20 mmol) were suspended in 8 mL of 95% ethanol. Acid-washed zinc (500 mg, 7.68 mmol) was added, and the reaction mixture was refluxed under nitrogen for 1 h. The reaction mixture was cooled to room temperature and then chilled and filtered through Celite into cold 3 N methanolic HCl. The filtrate was evaporated and dried to a solid under vacuum. The solid was dissolved in 12 mL of absolute ethanol and cooled in an ice–salt bath, under nitrogen. Isoamyl nitrite (202 mg, 1.73 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 15 min and then at room temperature for 1 h, while being protected from light. The reaction mixture was then poured into 10 mL of chilled saturated $NaHCO_3$ solution. The mixture was extracted with CH_2Cl_2. The crude product was purified by flash chromtography (1:1 hexane–ethyl acetate) to yield 62 mg (48%) of product: 300-MHz NMR ($CDCl_3$) δ 2.26 (s, 3 H), 2.96 (s, 3 H), 4.15 (br s, 2 H), 5.19–5.27 (m, 2 H), 5.68–5.83 (m, 1 H), 6.20 (s, 1 H), 7.55 (m, 3 H), 7.70 (br s, 1 H), 8.09 (d, J = 9 Hz, 2 H); IR (KBr) 2110, 1690 cm^{-1}.

Photolysis of 6-Diazo-3-methyl-5-[*N*-(2-propenyl)acetamido]-6,7-dihydroindol-7-one. (a) In Methylene Chloride. A solution of **6** (25 mg) in methylene chloride (20 mL) was photolyzed through a $CuSO_4$–$NaNO_2$ filter system for 50 min. The product was chromatographed with ethyl acetate to give **7** (10 mg, 45%) and **5b** (6 mg). **7**: 360-MHz NMR (DMSO, 110 °C) δ 1.32 (d of d, J = 2.9, 5.4 Hz, 1 H), 1.72 (d of d, J = 2.8, 7.6 Hz, 1u H), 2.08 (s, 3 H), 2.15 (s, 3 H), 2.70 (d of t, J = 7.2, 5.2 Hz, 1 H), 3.90 (d of d, J = 4.6, 10.7 Hz, 1 H), 4.01 (d, J = 10.7 Hz, 1 H), 6.88 (br s, 1 H), 6.97 (s, 1 H); MS (EI) 242, 199, 185, 183, 170, 157, 144, 130, 115, 84.

(b) In Benzene. A solution of **6** (25 mg) in benzene (20 mL) was irradiated through a $CuSO_4$–$NaNO_2$ filter for 0.5 h. The solvent was evaporated, and the product was chromatographed to give **7** (3 mg) and **8** (6 mg): 360-MHz NMR ($CDCl_3$) δ 1.94 (s, 3 H), 2.32 (s, 3 H), 3.17 (d of d, J = 7.3, 14.6 Hz, 1 H), 4.47 (d of d, J = 5.4, 14.6 Hz, 1 H), 5.02 (d of d, J = 1.0, 10.5 Hz, 1 H), 5.05 (d of d, J = 1.0, 10.5 Hz, 1 H), 5.80 (m, 1 H), 5.95 (s, 1 H), 6.93 (s, 1 H), 7.02 (s, 1 H), 7.27 (d, 2 H), 7.38 (t, 1 H), 7.48 (t, 2 H), 8.58 (br s, 1 H); MS (EI) 320, 278, 277, 249, 238, 223, 82.

Photolysis of Diazocyclohexadienone 11. Compound **11** (0.020 g, 0.064 mmol) was dissolved in 2 mL of dry CH_2Cl_2. This solution was photolyzed with a filter containing aqueous solutions of $CuSO_4$ and $NaNO_2$. Thin-layer chromatography indicated that the diazocyclohexadienone had completely reacted after 1 h. The crude reaction mixture was evaporated under reduced pressure to afford a bright red glass. Purification by flash chromatography (ethyl acetate) afforded two fractions. The less polar fraction gave 5.3 mg of a purple solid identified as quinone **27b**: 360-MHz NMR ($CDCl_3$) δ 2.24 (s, 3 H), 3.80 (t, J = 5.8 Hz, 2 H), 5.25–5.34 (m, 2 H), 5.44 (s, 1 H), 5.78–5.91 (br m, 1 H), 6.28 (br s, 1 H), 7.37 (s, 1 H), 8.59 (br s, 1 H); MS (EI) 220, 178, 177, 161, 149, 133. Anal. Calcd for $C_{11}H_{12}N_2O_3$: C, 59.99; H, 5.49; N, 12.72. Found: C, 59.92; H, 5.51; N, 12.71.

The more polar fraction, 9.5 mg, was the spirocyclopropyl compound **26**: 360-MHz NMR ($CDCl_3$) δ 1.50 (t, J = 5.4 Hz, 1 H), 1.86 (d of d, J = 7.2, 3.6 Hz, 1 H), 2.17 (s, 3 H), 2.64–2.72 (m, 1 H), 3.06 (s, 3 H), 3.97 (d of d, J = 9.7, 5.4 Hz, 1 H), 4.09 (d, J = 10 Hz, 1 H), 6.42 (s, 1 H), 7.48 (s, 1 H), 8.35 (br s, 1 H); MS (EI) 282, 264, 240, 185, 161, 131, 116. Anal. Calcd for $C_{12}H_{14}O_4N_2S$: C, 51.05; H, 5.00; N, 9.92. Found: C, 50.94; H, 5.03; N, 9.91.

In some runs small amounts of a third product identified as 5-acetamido-3-(chloromethyl)-7-hydroxy-1-(methylsulfonyl)-2,3-dihydroindole was obtained: 360-MHz NMR ($CDCl_3$) δ 2.26 (s, 3 H), 2.92 (s, 3 H), 3.57–3.75 (m, 3 H), 3.94 (d of d, J = 10.8, 4.0 Hz, 1 H), 4.03–4.13 (m, 1 H), 7.08 (s, 1 H), 7.14 (s, 1 H), 7.43 (br s, 1 H), 8.26 (br s, 1 H); MS (EI) 320, 318, 300, 275, 239, 241, 221, 199, 197, 185, 177, 161, 147.

Thermal Decomposition of Diazocyclohexadienone 11. A suspension of **11** (30 mg, 0.097 mmol) in 3 mL of anhydrous toluene was kept at 110 °C for 0.5 h. Upon cooling and concentration in vacuo, the crude product mixture was subjected to flash chromatography and yielded 10 mg (37%) of cyclopropane **26** and 11 mg (52%) of quinone **27b**.

Detection of Sulfinamide 27a as an Intermediate. A sample of **11** (20 mg, 0.064 mmol) was dissolved in $CDCl_3$ in a sealed NMR tube, and a 90-MHz NMR spectrum was recorded. The solution was thermolyzed at 80 °C in the NMR tube, and 90-MHz NMR spectra were recorded periodically to follow the progress of the reaction. The total time of thermolysis was 3.5 h, at which time a 360-MHz NMR spectrum was recorded. Analysis of the spectrum indicated the presence of two compounds in addition to a little starting material. The compounds were the intermediate sulfinamide **27a** and the spirocyclopropane **26** in a ratio of 1.4 to 1.

Decomposition of Diazocyclohexadienone 11 Catalyzed by Transition-Metal Compounds. The diazocyclohexadienone (0.05–0.10 mmol) in solvent with the catalysts added was maintained at the temperatures and times listed in Table I. The solvent was then evaporated, and the crude residue was subjected to flash chromatography with use of ethyl acetate for elution. The identity of the products **26** and **27b** was established by NMR.

Photolysis of Diazoindolone 2b. A sample of diazoindolone **2b** (14.0 mg, 0.046 mmol) was dissolved in 2 mL of anhydrous CH_2Cl_2, and the solution purged with nitrogen for 2 min. The sample was photolyzed for 1.0 h with a 450-W Hanovia lamp with $CuSO_4$ and $NaNO_2$ solutions as filters. The resulting orange solution was washed with saturated $NaHCO_3$, dried, and evaporated. The crude product was purified by flash column chromatography (hexane–ethyl acetate (3:1) → ethyl acetate) to give two products. The less polar fraction was isolated as 6.2 mg (63%)

of a deep purple solid identified as quinone **28**: 360-MHz NMR ($CDCl_3$) δ 2.30 (s, 3 H), 3.80 (t, J = 6 Hz, 2 H), 5.20 (s, 1 H), 5.24–5.34 (m, 2 H), 5.78–5.92 (m, 1 H), 6.15 (br s, 1 H), 6.63 (s, 1 H), 9.23 (br s, 1 H); MS (EI) 216, 199, 187, 175, 159, 154, 108.

The more polar fraction was isolated as 3.8 mg of off-white solid and identified as spirocyclopropane **1b** by direct spectral comparison (NMR, IR) with an authentic sample.[23]

Photolysis of Diazoindolone 2b with Detection of 29. A sample of **2b** was dissolved in $CDCl_3$ in an NMR tube to afford an orange-brown solution, and a 360-MHz NMR spectrum was recorded. The solution was photolyzed for 15 min with aqueous $CuSO_4$ and $NaNO_2$ solutions as filters. After the photolysis, the solution was bright red. The major product at this point was **29** identified by its NMR spectrum: 360-MHz NMR ($CDCl_3$) δ 2.33 (s, 3 H), 2.93 (s, 1 H), 3.73–3.83 (m, 2 H), 4.53–4.63 (m, 1 H), 5.21–5.30 (m, 2 H), 5.73 (s, 1 H), 5.69–5.88 (br m, 1 H), 6.77 (br s, 1 H), 9.68 (br s, 1 H), 9.89 (br s, 1 H). If the photo product was subjected to flash chromatography prior to hydrolytic workup, **29** could be isolated.

Thermal Decomposition of Diazoindolone 2b. A suspension of diazoindolone **2b** (8.3 mg, 0.027 mmol) in 2 mL of toluene was heated to 110 °C for 0.5 h. Upon cooling and concentration in vacuo, the crude product mixture was subjected to flash chromatography and yielded 4 mg (68%) of quinone **28** and 2.3 mg (30%) of cyclopropane **1b**.

Catalyzed Decomposition of Diazoindolone 2b. The diazoindolone (0.05–0.1 mmol) with the solvent and catalyst were heated at the temperature and time specified in Table I. The solvent was then evaporated, and the residue was separated by flash chromatography and identified by NMR. The yields are given in Table I.

Photolysis of Diazoindolone 22. The diazoindolone (10 mg, 0.013 mmol) was dissolved in dry CH_2Cl_2 under nitrogen in a Pyrex tube. The reaction mixture was photolyzed for 30 min with a 450-W Hanovia lamp with $CuSO_4$ and $NaNO_2$ solutions as filters. The reaction mixture was washed with saturated $NaHCO_3$, dried, and evaporated. The crude reaction mixture was purified by flash column chromatography (hexane–dichloromethane–ether, 1:1:1) to yield 4.5 mg (55%) of a purple solid identified as quinone **31**: 360-MHz NMR ($CDCl_3$) δ 2.33 (s, 3 H), 3.70 (t, 2 H), 5.15 (s, 1 H), 5.20–5.27 (m, 2 H), 5.75–5.85 (m, 1 H), 7.47 (s, 1 H), 7.51–7.67 (m, 3 H), 8.11 (d, 2 H); MS (CI) 357, 217, 143. The second fraction yielded 1.0 mg (10%) of bright orange solid identified as sulfinamide **32**: 360-MHz NMR ($CDCl_3$) δ 2.35 (s, 3 H), 2.88 (s, 3 H), 3.70 (d of m, J_{gem} = 16 Hz, 1 H), 4.50 (d of m, J_{gem} = 16 Hz, 1 H), 5.20 (m, 2 H), 5.67 (m, 1 H), 5.68 (s, 1 H), 7.55 (m, 3 H), 7.66 (m, 1 H), 8.13 (d, J = 9 Hz); MS (CI) 419, 357, 64. The final fractions yielded 2.0 mg (20%) of the spirocyclopropane **30**.

Thermolysis of Diazoindolone 22. Diazoindolone **22** (14 mg) was dissolved in 3 mL of toluene. The reaction mixture was refluxed for 0.5 h. The solvent was evaporated and the residue was separated by flash chromatography (hexane–ethyl acetate (3:1) → ethyl acetate) to yield 1.2 mg (11%) of quinone **31**, 1.0 mg (8%) of sulfinamide **32**, and 4.0 mg (30%) of the spirocyclopropane **30**. Recrystallization from ethyl acetate–hexane afforded an analytical sample of **30**: mp 208–210 °C dec; 300-MHz NMR ($CDCl_3$) δ 1.40 (t, J = 4.9 Hz, 1 H), 1.94–2.04 (m, 1 H), 2.02 (s, 3 H) 2.95–3.02 (m, 1 H), 2.97 (s, 3 H), 3.92 (q, J = 5.5 Hz, 1 H), 4.08 (d, J = 10.1 Hz, 1 H), 6.16 (s, 1 H), 7.47–7.62 (m, 4 H), 8.07 (d, J = 9.0 Hz, 2 H); MS (CI) 419, 279, 143, 89. Anal. Calcd for $C_{19}H_{18}N_2O_5S_2$: C, 54.53; H, 4.34; N, 6.69. Found: C, 54.57; H, 4.35; N, 6.65.

Catalyzed Decomposition of Diazoindolone 22. The diazoindolone **22** (0.05–0.1 mmol) with the solvent and catalyst was heated as specified in Table I. The solvent was evaporated, and the residue was separated by flash chromatography and identified by NMR.

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A Selective Cleavage of the Oxazole Moiety in Noviosylcoumarin Antibiotics: A New Process to Key Intermediates for Coumermycin Analogue Synthesis

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The oxazole moiety of the noviosylcoumarinooxazole **6** was found to be cleaved selectively under mild acidic conditions to produce 3-amino-4-hydroxycoumarins **3** without destruction of the glycosidic bond. By use of this selective oxazole cleavage reaction, a new process to key intermediates for the synthesis of coumermycin analogues PNC-amine[1] **3a** and 2′-acetyl PNC-amine **3b** has been developed by starting from coumermycin A_1 (**1**). This process was also applied to the novobiocin series, establishing the first chemical transformation of novobiocin (**2**) to novenamine (**8a**).

Coumermycin A_1 (**1**) is an antibiotic, isolated from fermentation broths of several different species of streptomyces almost 20 years ago.[2] Coumermycin A_1 (**1**) and the structurally related coumarin antibiotic novobiocin (**2**)[3] have recently been receiving much attention because of their potent antibacterial activity against methicillin-resistant strains of Staphylococci species, which have become clinically important pathogens over the last several years.[4] Coumermycin A_1 (**1**) and novobiocin (**2**) have also been

(1) PNC-amine stands for 3-amino-4-hydroxy-8-methyl-7-[[3-*O*-[(5-methyl-2-pyrrolyl)carbonyl]novisoyl]oxy]coumarin (**3a**). The coumermycin subunits are referred to as P, 5-methylpyrrole; N, noviose; and C, 4-hydroxy-8-methylcoumarin, see ref 6.

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