research from Ministero Pubblica Istruzione (MPI 60%) is gratefully acknowledged.

Registry No. **1a**, 90-02-8; **1b**, 148-53-8; **1c**, 673-22-3; **1d**, 672-13-9; **1e**, 24677-78-9; **1f**, 1194-98-5; **1g**, 1761-61-1; **1h**, 635-93-8; **1k**, 708-06-5; **2a**, 4986-28-1; **2b**, 124482-95-7; **2c**, 124482-96-8; **2d**, 124482-97-9; **2e**, 124482-98-0; **2f**, 38424-44-1; **2g**, 124482-99-1; **2h**, 124483-00-7; **2k**, 124483-17-6; **3a**, 54914-27-1; **3b**, 124483-03-0; **3c**, 124483-04-1; **3d**, 124483-05-2; **3g**, 124483-06-3; **3h**, 124483-07-4; **3k**, 124483-08-5; **4a**, 14227-12-4; **4g**, 124483-01-8; **4h**, 124483-02-9; **4k**, 120123-69-5; **5a**, 124483-09-6; **5e**, 124483-10-9; **5f**, 124483-11-0; *cis*-**6a'**, 124483-18-7; *trans*-**6a'**, 124483-20-1; **7a**, 124483-12-1; **7b**, 124483-13-2; **7d**, 124483-14-3; **7g**, 124483-15-4; **7h**, 124483-16-5; **8h**, 124483-19-8; $TiCl_3$, 7705-07-9; CH_3CHO, 75-07-0.

Formal 2 + 2 and 3 + 2 Cycloaddition Reactions of 2*H*-Chromenes with 2-Alkoxy-1,4-benzoquinones: Regioselective Synthesis of Substituted Pterocarpans

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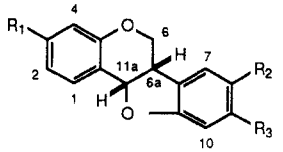
The titanium(IV)-catalyzed reaction of various 2*H*-chromenes and 2-alkoxy-1,4-benzoquinones stereoselectively yields the oxygenated pterocarpans **8** and/or the 2 + 2 adducts **7**, depending upon reaction conditions. Cyclobutanes **7** rearrange to **8** upon treatment with protic acids. Syntheses of the pterocarpan phytoalexins (±)-homopterocarpin (**2**), (±)-pterocarpin (**3**), and (±)-9-*O*-benzyl-3-*O*-methylsophoropterocarpan A (**4**) are presented, which demonstrates the synthetic utility of these formal cycloaddition reactions.

Introduction

Phytoalexins are antimicrobial compounds produced by plants in response to a stress.[1] The stress can be in a variety of forms such as attack by fungi or bacteria or by the application of an abiotic elicitor such as heavy metal salts or irradiation. It has been suggested that phytoalexins are crucial components in plant disease resistance and that they may be valuable in the development of new approaches to crop protection and perhaps in pharmaceutical applications as well.[2]

A large class of isoflavonoid phtoalexins possess a substituted pterocarpan ring system **1**. The structural requirements for biological activity and the mode of action of the pterocarpan phytoalexins have not been comprehensively studied, although oxygen-containing substituents at C_3 and C_9 appear to be necessary for potent activity, and the presence of prenyl substituents may also be important.[2a,3] For these reasons, methods for the synthesis of pterocarpans have received considerable interest recently.[4] We have developed an efficient synthesis of the structurally similar 2-aryl-2,3-dihydrobenzofurans via Lewis acid catalyzed reactions of styrenes with 1,4-benzoquinones.[5] We now report the details of the extension of this method to the regioselective preparation of substituted pterocarpan frameworks[6] including (±)-homopterocarpin (**2**), (±)-pterocarpin (**3**), and (±)-9-*O*-benzyl-3-*O*-methylsophoropterocarpan A (**4**). In addition, the method provides intermediates that should be useful in the synthesis of a number of other pterocarpan phytoalexins.



1, $R_1=R_2=R_3=H$
2, $R_1=R_3=OCH_3$, $R_2=H$
3, $R_1=OCH_3$, R_2-R_3=-OCH_2O-
4, $R_1=OCH_3$, $R_2=CH_2CH=C(CH_3)_2$, $R_3=OCH_2Ph$

† Lilly Grantee, 1989-1991.

Results and Discussion

Bicyclo[4.2.0]octenediones **7** and/or pterocarpans **8** are produced by Ti(IV)-catalyzed reactions of 2*H*-chromenes **5** and 2-alkoxy-1,4-benzoquinones **6** (Scheme I and Table I). The Ti(IV) employed was in the form of a premixed combination of titanium(IV) chloride and titanium(IV) isopropoxide, and the ratio of the products formed, **7**:**8**, is dependent upon the number of equivalents of Ti^{4+}, the ratio of $TiCl_4$ to $Ti(OiPr)_4$, and the reaction temperature. Thus, at -78 °C with 1-2 equiv of Ti(IV) as catalyst, formal 2 + 2 adducts **7** are formed exclusively in most cases. However, upon warming of the reaction mixture and/or utilization of catalyst systems with >2 equiv of Ti(IV) and enriched in $TiCl_4$, the formal 3 + 2 adducts **8** are the major, if not the exclusive, products found. Attempts to obtain cycloaddition products from **5** and **6** with stannic chloride

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(5) Engler, T. A.; Combrink, K. D.; Ray, J. E. *J. Am. Chem. Soc.* **1988**, *110*, 7931.

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0022-3263/90/1955-1248$02.50/0

Scheme I

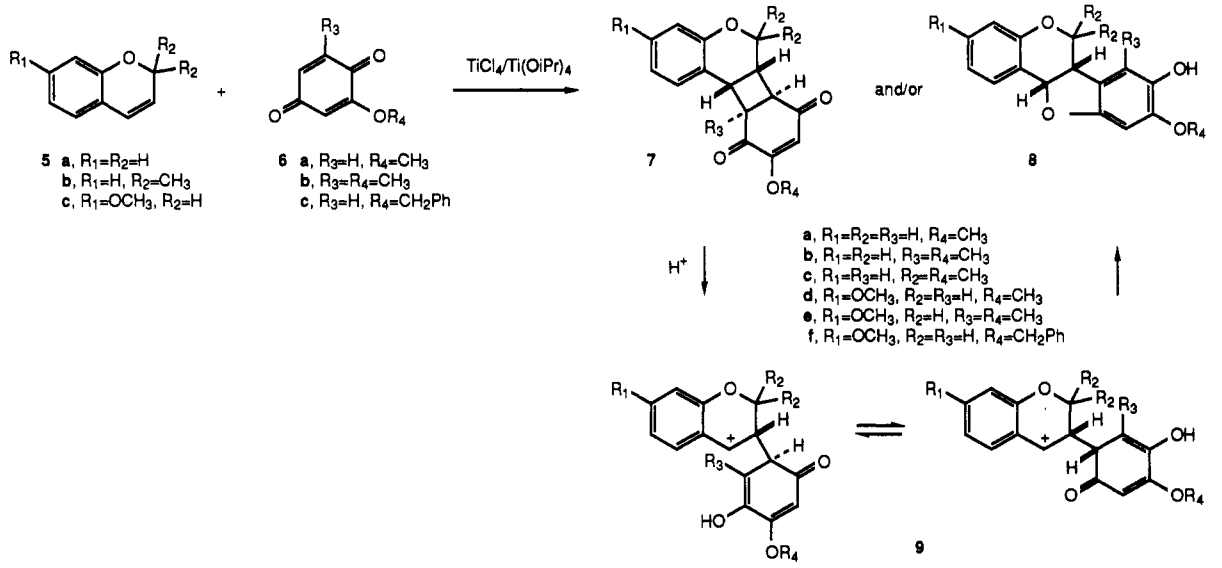

Table I. Titanium(IV)-Catalyzed Reactions of 2*H*-Chromenes and 2-Alkoxy-1,4-benzoquinones[a]

chromene	quinone	$TiCl_4$:$Ti(OiPr)_4$ (equiv of Ti^{4+})[b]	temp, °C	time, h	yields, % 7	yields, % 8
5a	**6a**	1:1 (1.0)	−78	0.5	85	–[c]
5a	**6a**	2:1 (3.0)	−78 → −30	2.5	–	46
5a	**6b**	3:1 (1.0)	−78	9	40	–
5a	**6b**	2:1 (3.0)	−78	2.5	–	67
5b	**6a**	3:1 (2.0)	−78	3	71	–
5b	**6a**	2:1 (3.0)	−78 → −20	5	–	47
5c	**6a**	1:1 (2.0)	−78	10	80	10
5c	**6a**	1:1 (2.0)	−78 → −30	5	–	58
5c	**6b**	1:1 (2.0)	−78 → −25	10	–	90
5c	**6c**	1:1 (2.0)	−78 → −25	5	–	94

[a] All reactions were conducted in CH_2Cl_2 under an N_2 atmosphere. [b] Equivalents with respect to quinone. [c] The dash indicates that none of this product was isolated.

Table II. Acid-Catalyzed Rearrangement of 7 to 8[a]

cyclobutane	acid catalyst	yield, %
7a	H_2SO_4	70
7b	H_2SO_4	65
7c	H_2SO_4	47
7d	*p*-TsOH	80

[a] All reactions were carried out in CH_2Cl_2 under an atmosphere of N_2.

or ethylaluminum dichloride as catalysts were not successful.[7] Cyclobutanes **7** are converted to pterocarpans **8** upon treatment with protic acids at room temperature (Table II), presumably via intermediate **9** (Scheme I).

Both **7** and **8** are produced regio- and stereoselectively. The stereochemistry of the dihydrobenzofurans **8** is established by their conversion to known compounds (vide infra) and by comparison of ^1H and ^{13}C NMR data with literature data which have been tabulated, and the assignments have been verified for a number of pterocarpans.[8] Further support for the assignment of a cis ring juncture in **8** is provided by $J_{H6a-11a} \cong 6–7$ Hz and by ^1H–^1H NOE experiments in which irradiation of H_{11a} in **8a** resulted in an 11% enhancement of the H_{6a} signal. In addition, irradiation of the C_7-methyl substituent in **8f** gave enhancements of the $H_{6\alpha}$, $H_{6\beta}$, and H_{6a} signals of 3.8%, 7.2%, and 3.8%, respectively. A summary of the NOE data appear in Figure 1.

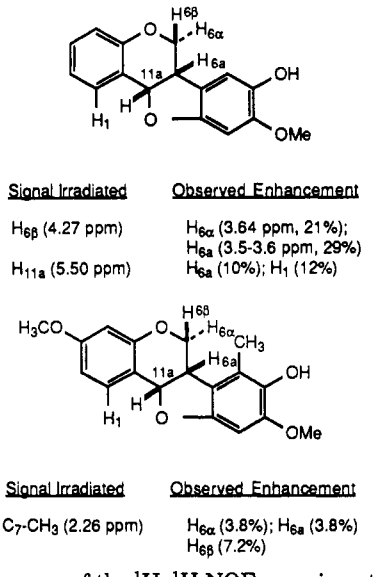

Figure 1. Summary of the ^1H–^1H NOE experiments on **8a** and **8e**.

(7) A 7% yield of **8a** was isolated in the $SnCl_4$ (1 equiv) catalyzed reaction of **5a** and **6a** at −78 °C to room temperature in CH_2Cl_2.

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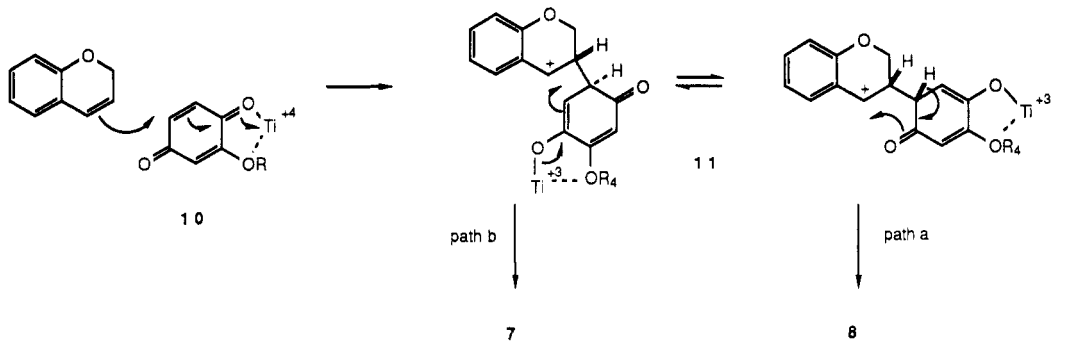
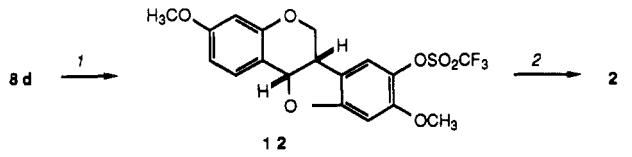
Scheme II



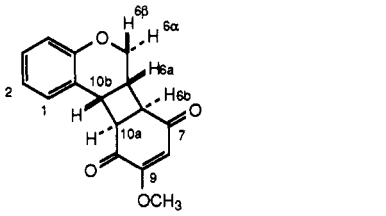
Scheme III[a]



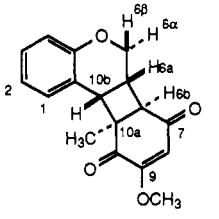
[a] Reagents and conditions: (1) $(CF_3SO_2)_2O$, pyridine, CH_2Cl_2, −78 °C to room temperature, 95%; (2) $Et_3NH^+{}^-O_2CH$, $Pd(OAc)_2$ (0.21 equiv), 1,1′-bis(diphenylphosphino)ferrocene (0.51 equiv), DMF, 75 °C, 93%.

The regiochemistry of cyclobutanes **7** is determined by chemical transformation to dihydrobenzofurans **8**, and the stereochemical assignments are made from ^1H NMR data. At 300 MHz, the methine and methylene hydrogens in **7** are observed as five distinct doublets of doublets and one multiplet. Specific resonances are assigned from selective ^1H–^1H decoupling and by ^1H NOE experiments, which are summarized in Figure 2. Thus, in **7a**, $H_{6\alpha}$ and $H_{6\beta}$ are coupled only to each other and H_{6a}; H_{10a} is coupled to H_{6b} and H_{10b}. A very small coupling (~1 Hz) between H_{6a} and H_{10a} is also observed in **7a**, **7c**, and **7d**. It was not possible to distinguish between H_{6b} and H_{10b} by decoupling experiments; however, they were assigned from NOE data. Irradiation of H_{10a} gave a 15% enhancement of the dd at 3.53 ppm, which is H_{6b}, and irradiation of the 3.70 ppm dd gave a 9% enhancement of H_{6a}. Therefore the signal at 3.70 ppm is assigned as H_{10b}. Results of other NOE experiments are summarized in Figure 2, and the cis-anti-cis stereochemistry of the ring fusions in **7** is evident from these experiments.

The formation of **7** and **8** is rationalized as follows. Coordination of the Ti(IV) with the quinone produces



Signal Irradiated	Observed Enhancement
$H_{6\beta}$ (3.90 ppm)	$H_{6\alpha}$ (20%); H_{6a} (3.09 ppm, 11%)
$H_{6\alpha}$ (4.24 ppm)	H_{6b} (3.56 ppm, 7%); $H_{6\beta}$ (20%)
H_{10a} (3.14 ppm)	H_{6b} (15%)
H_{10b} (3.70 ppm)	H_{6a} (9%)

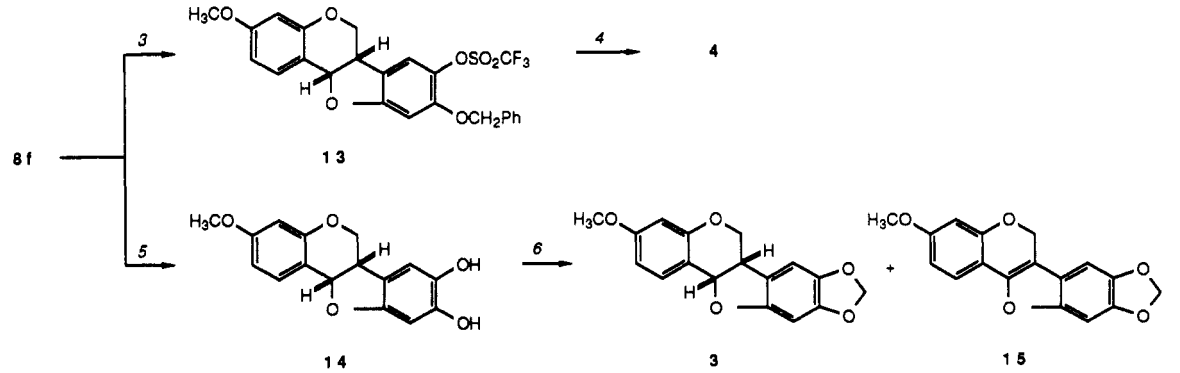


Signal Irradiated	Observed Enhancement
C_{10a}-CH_3 (0.83 ppm)	H_{6b} (3.24 ppm, 22.4%); H_1 (6.9%)
H_{6a} (2.98 ppm)	$H_{6\beta}$ (5.7%); H_{10b} (3.65-3.76 ppm, 12%)
$H_{6\alpha}$ (4.20 ppm)	$H_{6\beta}$ (3.65-3.76 ppm, 21%); H_{6b} (5.8%)

Figure 2. Summary of the ^1H–^1H NOE experiments on **7a** and **7b**.

complex **10** with a highly electrophilic center at C_5 (Scheme II). Alkylation of the complex by the chromene produces **11**, which then collapses via path a to give **8** or via path b to give **7**.[9] For reasons that are not yet clear, path b is

Scheme IV[a]



[a] Reagents and conditions: (3) $(F_3CSO_2)_2O$, pyridine, CH_2Cl_2, −78 °C to room temperature, 85%; (4) n-$Bu_3SnCH_2CH{=}C(CH_3)_2$, $(Ph_3P)_2PdCl_2$ (0.05 equiv), LiCl (4.4 equiv), DMF, 95–105 °C, 65%; (5) H_2, 10% Pd/C, acetone/95% EtOH/HOAc, room temperature or BF_3·Et_2O, $(CH_3)_2S/CH_2Cl_2$, room temperature, quantitative; (6) CH_2I_2, K_2CO_3, CuO, DMF, 80–90 °C, 46% of **3**, 6% of **15**.

apparently favored kinetically.

To demonstrate the synthetic utility of the methodology presently described, syntheses of **2–4** were carried out (Schemes III and IV). Thus, conversion of dihydrobenzofuran **8d** to triflate **12** followed by a palladium-catalyzed triethylammonium formate reduction[10] gave (±)-homopterocarpin (**2**) in 88% overall yield from **8d**. Similar methodology was utilized to convert phenol **8f** to triflate **13**, which gave (±)-9-*O*-benzyl-3-*O*-methylsophoropterocarpan A (**4**) upon palladium-catalyzed coupling[11] with $Bu_3SnCH_2CH{=}C(CH_3)_2$. It is notable that the carbon–carbon double bond of the prenyl unit did not migrate into conjugation in the latter reaction.

Finally, the benzyl moiety in dihydrobenzofuran **8f** was selectively removed via catalytic hydrogenation or upon treatment with $BF_3{\cdot}Et_2O$/dimethyl sulfide,[12] to give the chromatographically unstable catechol **14**, which was not purified but converted directly to (±)-pterocarpin (**3**) by the method of Tomita and Aoyagi.[13] A 46% overall yield of **3** was found, accompanied by small amounts (6%) of anhydropisatin (**15**).[14]

Summary and Conclusions

The titanium(IV)-catalyzed reaction of 2-alkoxy-1,4-benzoquinones and 2*H*-chromenes represents a direct route to the pterocarpan ring system. Notable features of the route are that (1) the pterocarpans produced incorporate oxygen substituents at the C_3 and C_9 positions; (2) the C_8 phenol moiety of the pterocarpans formed can be reductively removed or, more importantly, can be used to introduce a C_8 prenyl unit; and (3) with proper choice of alkoxy groups on the starting chromene and quinone, the pterocarpans produced possess differentiated oxygen substituents at C_3, C_8, and C_9 which can be selectively manipulated. The method should be applicable to the preparation of a wide variety of naturally occurring antimicrobial pterocarpan phytoalexins and analogues.

Experimental Section

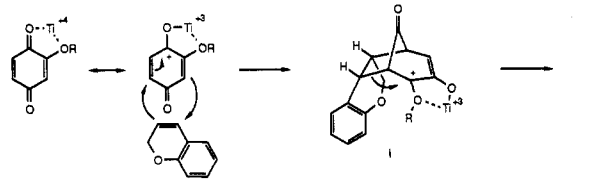
Solvents and Reagents. 2*H*-Chromene (**5a**),[15a] 2,2-dimethyl-2*H*-chromene (**5b**),[16] 7-methoxy-2*H*-chromene (**5c**),[15] and (benzyloxy)-1,4-benzoquinone (**6c**)[17] were prepared via literature procedures. 2-Methoxy-1,4-benzoquinone (**6a**) and 2-methoxy-6-methyl-1,4-benzoquinone (**6b**) were prepared via Fremy's salt oxidation[18] of 2-methoxyphenol and 2-methoxy-6-methylphenol.[19] Dichloromethane, diiodomethane, titanium(IV) chloride, triethylamine, boron trifluoride etherate, and dimethyl sulfide were distilled from calcium hydride under an N_2 atmosphere. Trifluoromethanesulfonic anhydride was distilled from phosphorus pentoxide and stored under nitrogen. Pyridine was distilled from potassium hydroxide and stored under argon. *N,N*-Dimethylformamide (DMF) was dried over barium oxide, distilled from potassium hydroxide, and stored over 4-Å molecular sieves. Titanium(IV) isopropoxide, 1,1-bis(diphenylphosphino)ferrocene (DPPF), anhydrous *N,N*-dimethylformamide, and formic acid were purchased from Aldrich and used without further purification. Bis(triphenylphosphine)palladium(II) chloride was prepared via a literature procedure.[25] Hexanes and acetone were fractionally distilled, and ethyl acetate was distilled from anhydrous potassium carbonate. All reactions were done in flame- or oven-dried glassware and were magnetically stirred under an atmosphere of dry nitrogen or argon. All compounds were prepared as racemic mixtures.

Chromatography. Separations were carried out either by flash chromatography using MN-Kieselgel 60 silica gel (0.04–0.063-mm mesh size, VWR Scientific) or by radial chromatography on a Chromatotron (Harris Research 7924T) using Kieselgel 60 PF254 silica gel (VWR Scientific). Thin-layer chromatography (TLC) was done on precoated silica gel plates, which were developed in the indicated solvent systems. Compound visualization on TLC was done by UV irradiation and either *p*-anisaldehyde stain or phosphomolybdic acid stain.

Instrumentation. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on Bruker AM-500 Aspect 3000 (500 MHz), Varian XL-300 (300 MHz), and Varian FT-80A (80 MHz) spectrometers. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were obtained at 75 MHz on the Varian XL-300 spectrometer or at 125 MHz on the Bruker AM-500 spectrometer. All NMR samples were dissolved in deuteriochloroform unless otherwise specified, and chemical shifts are expressed in parts per million (δ) downfield from internal tetramethylsilane. Abbreviations for NMR multiplicities are as follows: s, singlet; d, doublet; t, triplet; m, multiplet; dd, doublet of doublets; dt, doublet of triplets. The coupling constants are abbreviated as *J* and are in hertz. High-resolution mass spectra (HRMS) were obtained on a VG Instruments ZAB double-focusing mass spectrometer. Melting points were obtained on a Mel-Temp apparatus and are uncorrected.

Cycloaddition of 2*H*-Chromenes 5a–c to 2-Alkoxy-1,4-benzoquinones 6a–c. General Procedure. Method A. Formation of 7a–d. With minor variations, the following general procedure was followed; detailed procedures for each experiment are included in the supplementary material. Titanium(IV) chloride and titanium(IV) isopropoxide (see Table I for ratios and equivalents) were combined in dichloromethane (~2 mL) at 0–5 °C, and the solution was stirred for 5–45 min and then cooled to −78 °C. A solution of the quinone in dichloromethane (1–6

(9) The formation of the cis-anti-cis ring fusions in **7** suggests that intermediate **11** is formed diastereoselectively. This selectivity may result from a mechanism in which complex **10** reacts with chromene **5** via a symmetry-allowed 5 + 2 ($4\pi + 2\pi$) cycloaddition to give **i** initially, which then proceeds to **11**.[5] The preference for the aryl unit of the chromene to occupy an endo position with respect to the pentadienyl cation moiety in **10** has been observed in related reactions; see: Engler, T. A.; Combrink, K. D.; Takusagawa, F. *J. Chem. Soc., Chem. Commun.*, in press.



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mL) was added, followed, after 5–15 min, by a solution of the 2*H*-chromene in dichloromethane (1–6 mL). The reaction mixtures were maintained at −78 °C. After the reactions were complete by TLC analysis (see Table I for the reaction times), the reaction mixtures were quenched either by the addition of isopropyl alcohol (4–5 mL) and solid sodium bicarbonate (1 g) followed by pouring into saturated aqueous sodium bicarbonate (for **7b–d**) or by direct pouring of the reaction mixture into saturated aqueous sodium bicarbonate (for **7a**). The aqueous layer was separated and extracted with dichloromethane. The organic extracts were combined, washed with water and brine, dried over sodium sulfate or magnesium sulfate, and concentrated.

Data for 7a. 2*H*-Chromene **5a** (0.15 mL, 1.5 mmol) and quinone **6a** (200 mg, 1.45 mmol) gave a crude orange residue, which was chromatographed on flash silica gel with 40% ethyl acetate in hexanes as eluent, to give **7a** (328 mg, 85%), mp 134.5–136 °C (isopropyl alcohol), as white needles: R_f (50% ethyl acetate/hexanes) 0.19; ^{1}H NMR (300 MHz) 3.09 [H_{6a} (m, J = 3, 8, 10)], 3.14 [H_{10a} (ddd, J = 1 (H_{6a}–H_{10a}), 4, 9)], 3.56 [H_{6b} (dd, J = 8, 9)], 3.70 [H_{10b} (dd, J = 4, 10)], 3.89 (s, 3 H), 3.90 [$H_{6\beta}$ (dd, J = 3, 12)], 4.24 [$H_{6\alpha}$ (dd, J = 3, 12)], 6.19 (s, 1 H), 6.95–7.10 (m, 2 H), 7.2–7.3 (m, 2 H); ^{13}C NMR (75 MHz) 37.2, 40.0, 42.8, 49.8, 56.4, 66.9, 114.2, 118.0, 122.6, 125.2, 128.2, 129.4, 155.3, 162.6, 192.4, 197.4; HRMS m/z 270.0888, calcd for $C_{16}H_{14}O_4$ 270.0892. Anal. Calcd for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 71.05; H, 5.50.

Data for 7b. 2*H*-Chromene **5a** (105 mg, 0.79 mmol) and quinone **6b** (104 mg, 0.68 mmol) gave a residue, which was purified by radial chromatography using 50% ethyl acetate/hexanes as eluent, to give **7b** (77 mg, 40%) as a yellow solid. Recrystallization from ethyl acetate/hexanes gave pale yellow needles, mp 127–128 °C: R_f (50% EtOAc/hexanes) 0.32; ^{1}H NMR (300 MHz) 0.83 (s, 3 H), 2.98 [H_{6a} (m, 1 H)], 3.24 [H_{6b} (d, J = 8.5)], 3.65–3.76 [$H_{6\beta}$ and H_{10b} (overlapping dd and d, J = 2.7, 12 for 1 H, J = 9.6 for 1 H)], 3.86 (s, 3 H), 4.20 [$H_{6\alpha}$ (dd, J = 1.2, 12)], 6.12 (s, 1 H), 7.00 (2 overlapping m, 2 H), 7.13 (d with higher order coupling, J = 7.7, 1 H), 7.21 (dt, J = 1.4, 7.7, 1 H); ^{13}C NMR (75 MHz) 197.7, 197.3, 161.9, 155.9, 131.1, 128.2, 121.9, 121.2, 117.9, 113.4, 65.7, 56.4, 50.1, 50.0, 39.6, 38.6, 21.6; HRMS m/z 284.1050, calcd for $C_{17}H_{16}O_4$ 284.1049. Anal. Calcd for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67. Found: C, 71.51; H, 5.60.

Data for 7c. 2*H*-Chromene **5b** (0.392 g, 2.45 mmol) and quinone **6a** (0.305 g, 2.21 mmol) gave a black solid, which was purified by radial chromatography with stepwise elution with 20%, 40%, and then 50% ethyl acetate/hexanes as eluent, to afford **7c** (0.464 g, 71%) as a pale brown solid. Recrystallization from ethyl acetate/hexanes gave an analytically pure sample as colorless needles, mp 155–156 °C: R_f (50% EtOAc/hexanes) 0.35; ^{1}H NMR (300 MHz) 1.07 (s, 3 H), 1.46 (s, 3 H), 2.82 (t, J = 9, 1 H), 2.96 (d, J = 9, 1 H), 3.61 (t, J = 9, 1 H), 3.67 (d, J = 9, 1 H), 3.84 (s, 3 H), 6.09 (s, 1 H), 6.89 (d, J = 8, 1 H), 6.98 (t, J = 8, 1 H), 7.17 (t, J = 8.0, 1 H), 7.25 (d, J = 8.0, 1 H); ^{13}C NMR (125 MHz) 197.0, 193.2, 162.2, 152.6, 129.3, 128.1, 123.7, 121.9, 118.5, 114.1, 73.8, 56.3, 49.1, 48.6, 42.9, 36.9, 25.2, 23.1; HRMS m/z 298.1200, calcd for $C_{18}H_{18}O_4$ 298.1205. Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.47; H, 6.08. Found: C, 72.35; H, 6.21.

Data for 7d. 2*H*-Chromene **5c** (93 mg, 0.57 mmol) and quinone **6a** (71 mg, 0.51 mmol) gave a residue, which was purified by flash chromatography with 30% and then 50% ethyl acetate/hexanes as eluent, to give pterocarpan **8d** (16 mg, 10%, identified as indicated below) and cyclobutane **7d** (123 mg, 80%) as pale yellow needles, mp 169–170 °C (EtOAc/hexanes): R_f (50% EtOAc/hexanes) 0.14; ^{1}H NMR (300 MHz) 3.02–3.14 [H_{6a} and H_{10a} (m)], 3.52 [H_{6b} (t with higher order coupling, J = 7.8)], 3.64 [H_{10b} (dd, J = 3.9, 9.4)], 3.79 (s, 3 H), 3.87 (s, 3 H), 3.89 [$H_{6\alpha}$ (dd, J = 3.5, 12)], 4.23 [$H_{6\beta}$ (dd, J = 3.0, 12)], 6.15 (s, 1 H), 6.52 (d, J = 1.9, 1 H), 6.59 (dd, J = 1.9, 8, 1 H), 7.09 (d, J = 8, 1 H); ^{13}C NMR (75 MHz) 197.5, 192.4, 162.6, 159.7, 156.2, 130.0, 117.2, 114.1, 109.4, 102.9, 66.9, 56.4, 55.3, 50.2, 42.8, 39.9, 36.8; HRMS m/z 300.1005, calcd for $C_{17}H_{16}O_5$ 300.0997. Anal. Calcd for $C_{17}H_{16}O_5$: C, 67.99; H, 5.37. Found: C, 67.83; H, 5.30.

Method B. Formation of 8a–f. The same procedure was followed as in method A with the exception that, after the addition of the 2*H*-chromene, the reaction mixtures were allowed to warm to the temperatures shown in Table I over the time period indicated. Detailed experimental procedures for each experiment are included in the supplementary material.

Data for 8a. 2*H*-Chromene **5a** (112 mg, 0.85 mmol) and quinone **6a** (100 mg, 0.72 mmol) produced a purple film, which was purified by flash chromatography with 15% ethyl acetate/hexanes as eluent, to give pterocarpan **8a** (89 mg, 46%), which was recrystallized from Et_2O/hexanes as a colorless solid, mp 120.7–121 °C: R_f (50% ethyl acetate/hexanes) 0.53; ^{1}H NMR (300 MHz) 3.5–3.6 [H_{6a} (m)], 3.64 [$H_{6\alpha}$ (dd, J = 11, 11)], 3.84 (s, 3 H), 4.27 [$H_{6\beta}$ (dd, $J_{H6a-6\beta}$ = 4, $J_{H6\alpha-6\beta}$ = 11)], 5.32 (s, 1 H), 5.50 [H_{11a} (d, $J_{H6a-11a}$ = 6)], 6.49 (s, 1 H), 6.85 (s, 1 H), 6.95 (d, J = 7, 1 H), 7.05 (ddd, J = 1, 7, 7, 1 H), 7.2–7.3 (m, 1 H), 7.52 (dd, J = 1, 8, 1 H); ^{13}C NMR (75 MHz) 40.5 (C_{6a}), 56.2, 66.5 (C_6), 78.0 (C_{11a}), 94.7, 110.4, 117.4, 117.9, 120.3, 121.6, 130.0, 131.0, 140.0, 146.9, 152.8, 155.5; HRMS m/z 270.0893, calcd for $C_{16}H_{14}O_4$ 270.0891. Anal. Calcd for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 71.40; H, 5.21.

Data for 8b. 2*H*-Chromene **5a** (105 mg, 0.79 mmol) and quinone **6b** (103 mg, 0.68 mmol) gave a brown oil, which upon radial chromatography with 20% ethyl acetate/hexanes as eluent gave **8b** (129 mg, 67%) as a pale yellow solid. A colorless analytical sample was obtained by recrystallization from ethyl acetate/hexanes, mp 156–158 °C: R_f (50% EtOAc/hexanes) 0.65; ^{1}H NMR (300 MHz) 2.26 (s, 3 H), 3.52 [H_{6a} and $H_{6\alpha}$ (m)], 3.81 (s, 3 H), 4.31 [$H_{6\beta}$ (m)], 5.37 (s, 1 H), 5.40 [H_{11a} (d, J = 6.1)], 6.37 (s, 1 H), 6.97 (d, J = 8, 1 H), 7.04 (t, J = 8, 1 H), 7.28 (t, J = 8, 1 H), 7.53 (d, J = 8, 1 H); ^{13}C NMR (75 MHz) 155.3, 151.8, 146.4, 138.0, 131.0, 130.0, 121.5, 120.4, 120.0, 117.7, 117.3, 92.3, 77.7 (C_{11a}), 65.5 (C_6), 56.2, 39.4 (C_{6a}), 12.3; HRMS m/z 284.1050, calcd for $C_{17}H_{16}O_4$ 284.1049. Anal. Calcd for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67. Found: C, 71.81; H, 5.68.

Data for 8c. 2*H*-Chromene **5b** (0.127 g, 0.79 mmol) and quinone **6a** (0.102 g, 0.74 mmol) gave, upon flash chromatography of the residue with 15% ethyl acetate/hexanes as eluent, pterocarpan **8c** (0.104 g, 47%) as a colorless oil: R_f (50% EtOAc/hexanes) 0.66; ^{1}H NMR (500 MHz) 0.88 (s, 3 H), 1.54 (s, 3 H), 3.34 [H_{6a} (d, J = 7.8)], 3.85 (s, 3 H), 5.31 (s, 1 H), 5.47 [H_{11a} (d, J = 7.8)], 6.50 (s, 1 H), 6.88 (s, 1 H), 6.90 (d, J = 8.0, 1 H), 7.00 (dt, J = 1.2, 7.5, 1 H), 7.26 (dt, J = 1.8, 8, 1 H), 7.52 (d, J = 7.6, 1 H); ^{13}C NMR (125 MHz) 153.6, 153.1, 146.8, 139.8, 129.9, 129.8, 121.2, 120.4, 119.0, 118.0, 110.9, 94.3, 78.6, 76.5, 56.1, 49.6, 27.5, 20.0; HRMS m/z 298.1202, calcd for $C_{18}H_{18}O_4$ 298.1205.

Data for 8d. 2*H*-Chromene **5c** (61 mg, 0.38 mmol) and quinone **6a** (48 mg, 0.35 mmol) yielded a residue, which was purified by flash column chromatography using 25% ethyl acetate in hexane as eluent, to give **8d** (60 mg, 58%), which crystallized from ethyl acetate/hexanes as colorless needles, mp 136–138 °C: R_f (50% EtOAc/hexanes) 0.41; ^{1}H NMR[8d] (300 MHz) 3.47–3.56 [H_{6a} (m)], 3.64 [$H_{6\alpha}$ (t, J = 10.9)], 3.79 (s, 3 H), 3.84 (s, 3 H), 4.25 [$H_{6\beta}$ (dd, J = 10.9, 4.7)], 5.26 (s, 1 H), 5.47 [H_{11a} (d, J = 6.3)], 6.46–6.49 [H_4 and H_{10} (overlapping s and d)], 6.64 (dd, 1 H, J = 9, 2.8), 6.84 (s, 1 H), 7.40 (d, 1 H, J = 9); ^{13}C NMR (75 MHz) 161.0, 156.6, 152.8, 146.9, 139.8, 131.7, 117.9, 112.5, 110.3, 109.1, 101.6, 94.7, 78.0 (C_{11a}), 66.5 (C_6), 56.2, 55.3, 40.3 (C_{6a}); HRMS m/z 300.0999, calcd for $C_{17}H_{16}O_5$ 300.0997.

Data for 8e. 2*H*-Chromene **5c** (0.127 g, 0.78 mmol) and quinone **6b** (0.102 g, 0.67 mmol) gave a brown film, which was purified by radial chromatography using 20% ethyl acetate/hexanes as eluent, to give **8e** (0.191 g, 90%) as a white solid, which was recrystallized from ethyl acetate/hexanes, to give colorless needles, mp 151–152 °C: R_f (50% EtOAc/hexanes) 0.55; ^{1}H NMR (300 MHz) 2.26 (s, 3 H), 3.50 [H_{6a} and $H_{6\alpha}$ (2 overlapping m)], 3.80 (s, 3 H), 3.83 (s, 3 H), 4.30 [$H_{6\beta}$ (m)], 5.31 (s, 1 H), 5.37 [H_{11a} (d, J = 5.5)], 6.37 (s, 1 H), 6.50 (d, J = 2.4, 1 H), 6.64 (dd, J = 2.5, 8.6, 1 H), 7.42 (d, J = 8.6, 1 H); ^{13}C NMR (75 MHz) 161.0, 156.5, 151.9, 146.4, 138.0, 131.8, 120.4, 117.8, 112.3, 109.0, 101.6, 92.3, 77.8, 65.6, 56.2, 55.4, 39.2, 12.3; HRMS m/z 314.1152, calcd for $C_{18}H_{18}O_5$ 314.1154. Anal. Calcd for $C_{18}H_{18}O_5$: C, 68.78; H, 5.77. Found: C, 68.86; H, 5.76.

Data for 8f. 2*H*-Chromene **5c** (52 mg, 0.32 mmol) and quinone **6c** (54 mg, 0.25 mmol) gave a brown oil, which upon flash column chromatography using 18% ethyl acetate in hexanes as eluent yielded **8f** (89 mg, 94%) as an amorphous solid, mp 124–125 °C (ether): R_f (20% EtOAc/hexanes) 0.19; ^{1}H NMR (300 MHz) 3.45–3.53 [H_{6a} (m)], 3.63 [$H_{6\alpha}$ (t, J = 11)], 3.77 (s, 3 H), 4.24 [$H_{6\beta}$ (dd, J = 11, 4.9)], 5.04 (s, 1 H), 5.34 (s, 2 H), 5.44 [H_{11a} (d, J = 7.0)], 6.46 (d, 1 H, J = 2.6), 6.52 (s, 1 H), 6.62 (dd, 1 H, J = 8.5, 2.6), 6.85 (s, 1 H), 7.30–7.55 (m, 6 H); ^{13}C NMR (75 MHz) 161.0,

156.6, 152.7, 146.0, 140.1, 136.1, 131.7, 128.7, 128.4, 127.7, 118.5, 112.4, 110.5, 109.1, 101.6, 96.1, 78.1 (C_{11a}), 71.4, 66.5 (C_6), 55.3, 40.2 (C_{6a}); HRMS m/z 376.1310, calcd for $C_{23}H_{20}O_5$ 376.1309.

Acid-Catalyzed Rearrangement of 7 to 8. General Procedure. Concentrated sulfuric acid (1–2 drops from a Pasteur pipet) or *p*-toluenesulfonic acid (small amounts by spatula) was added to a dichloromethane solution of the cyclobutane **7** at room temperature. When starting **7** was no longer apparent by TLC analysis of the reaction mixture (2 min to 1 h), the mixture was poured into saturated aqueous sodium bicarbonate. Extraction of the mixture with dichloromethane followed by drying of the extracts over sodium sulfate, filtration, and concentration gave a crude product, which was purified by flash or radial chromatography, to give pterocarpan **8**, identified as previously described.

3,9-Dimethoxy-6a,11a-*cis*-dihydro-6*H*-benzofuro[3,2-*c*][1]benzopyran-8-ol Trifluoromethanesulfonate (12). To a solution of phenol **8d** (0.068 g, 0.226 mmol) in dichloromethane (3 mL) at −78 °C was added pyridine (0.06 mL, 0.742 mmol) followed, after 30 min, by trifluoromethanesulfonic anhyhdride (0.05 mL, 0.297 mmol). The mixture was stirred for 1 h at −78 °C, warmed to room temperature, and poured into water (10 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (2 × 10 mL). The combined dichloromethane solutions were washed with cold 10% aqueous sodium hydroxide (3 mL), cold 10% hydrochloric acid (3 mL), and water (3 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure, to give a brown oil. Radial chromatography using 15% ethyl acetate in hexane as eluent gave **12** (0.093 g, 95%) as a colorless oil: R_f (50% EtOAc/hexanes) 0.65; ^{1}H NMR (500 MHz), 3.56–3.61 (m, 1 H), 3.67 (t, J = 11, 1 H), 3.78 (s, 3 H), 3.84 (s, 3 H), 4.24 (dd, J = 5, 11, 1 H), 5.58 (d, J = 6.9, 1 H), 6.47 (d, J = 2.5, 1 H), 6.53 (s, 1 H), 6.64 (dd, J = 2.5, 8.5, 1 H), 7.10 (s, 1 H), 7.39 (d, J = 8.5, 1 H); ^{13}C NMR (125 MHz) 161.2, 160.0, 156.6, 152.6, 132.5, 131.7, 118.7 (q, J = 320 Hz, CF_3), 118.4, 111.7, 109.4, 101.6, 96.0, 79.3, 66.1, 56.3, 55.3, 39.7 (one aromatic quaternary signal is buried); HRMS m/z 432.0494, calcd for $C_{18}H_{15}O_7SF_3$ 432.0489.

Conversion of Phenol 8f to Triflate 13. In a manner similar to the preparation of **12**, phenol **8f** (0.105 g, 0.279 mmol) was converted to **13** by using pyridine (0.07 mL, 0.87 mmol) and trifluoromethanesulfonic anhydride (0.07 mL, 0.42 mmol), to give, after radial chromatography with 20% ethyl acetate/hexanes as eluent, the product (85%, 0.121 g) as a white solid, mp 142–144 °C dec (EtOAc/pentanes): R_f (50% EtOAc/hexanes) 0.69; ^{1}H NMR (500 MHz) 3.56–3.62 (m, 1 H), 3.67 (t, J = 11, 1 H), 3.76 (s, 3 H), 4.25 (dd, J = 4.9, 11, 1 H), 5.11 (s, 2 H), 5.57 (d, J = 6.9, 1 H), 6.47 (d, J = 2.5, 1 H), 6.57 (s, 1 H), 6.63 (dd, J = 2.5, 8.5, 1 H), 7.12 (s, 1 H), 7.30–7.44 (m, 6 H); ^{13}C NMR (125 MHz) 161.2, 159.6, 156.6, 151.6, 135.4, 132.7, 131.7, 128.6, 128.2, 127.2, 118.8, 118.7 (q, J = 321 Hz, CF_3), 118.4, 111.6, 109.4, 101.7, 97.3, 79.3, 71.2, 66.1, 55.4, 39.7; HRMS m/z 508.0813, calcd for $C_{24}H_{19}O_7SF_3$ 508.0804.

(±)-3,9-Dimethoxy-6a,11a-*cis*-dihydro-6*H*-benzofuro[3,2-*c*][1]benzopyran (2). Triflate **12** (84 mg, 0.19 mmol) was dissolved in *N*,*N*-dimethylformamide (1 mL) under argon at room temperature, and the trimer of palladium(II) acetate (27 mg, 0.04 mmol) was added followed by 1,1′-bis(diphenylphosphino)-ferrocene (55 mg, 0.099 mmol), triethylamine (0.54 mL, 3.9 mmol), and a 95–97% aqueous formic acid solution (0.15 mL, 3.8 mmol). The mixture was heated to 75 °C (oil bath temperature) and stirred for 17 h. The mixture was cooled, water (2 mL) was added, and the mixture was then poured into ethyl acetate (10 mL). The layers were separated, the aqueous layer was extracted with ethyl acetate (3 × 10 mL), and the combined organic extracts were washed with saturated aqueous ammonium chloride, saturated aqueous sodium bicarbonate, and water (15 mL each). The solution was dried over sodium sulfate, filtered, and concentrated. Filtration chromatography of the resulting brown film using dichloromethane as eluent followed by radial chromatography with 10% ethyl acetate in hexane as eluent gave **2** (51 mg, 93%): mp 126–127 °C (95% ethanol) (lit.[20] mp 123–125 °C and 129–130 °C); R_f (8% EtOAc/hexanes) 0.17; ^{1}H NMR[8b] (300 MHz) 3.49–3.58 [H_{6a} (m)], 3.64 [$H_{6\alpha}$ (t, J = 11)], 3.77 (s, 3 H), 3.79 (s, 3 H), 4.25 [$H_{6\beta}$ (dd, J = 4.5, 11)], 5.51 [H_{11a} (d, J = 6)], 6.43–6.49 (m, 3 H), 6.64 (dd, J = 2.8, 8.5, 1 H), 7.13 (d, J = 9.2, 1 H), 7.43 (d, J = 8.8, 1 H).

(3-Methyl-2-butenyl)tri-*n*-butyltin. The title compound was prepared by a method similar to one reported by Seyferth and Weiner.[21] To a suspension of magnesium turnings (2.43 g, 100 mmol) in dry THF (30 mL) was added 1,2-dibromoethane (0.5 mL), and the mixture was heated to reflux. A solution of 4-bromo-2-methyl-2-butene (5.0 mL, 43 mmol) and chlorotri-*n*-butyltin (6.8 mL, 25 mmol) in dry THF (25 mL) was added dropwise over 1 h, during which time heating was continued. After 15 h, the reaction mixture was cooled to room temperature and saturated aqueous ammonium chloride added carefully. The resulting mixture was extracted with ether (4 × 150 mL), and the combined extracts were washed with water (100 mL) and brine (100 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure. The pale green oil obtained was fractionally distilled, to give the title compound as a colorless oil (7.87 g, 87%), bp 92–96 °C/0.01 mm (lit. bp 114–116 °C/1 mm[22] and 90 °C/0.002 mm[23]): ^{1}H NMR[22,23] (300 MHz) 0.7–1.0 (m, 14 H), 1.2–1.8 (m, 21 H), 5.29 (t, J = 8.1, 1 H); ^{13}C NMR (75 MHz) 125.2, 122.9, 29.3, 27.4, 25.5, 17.3, 13.7, 10.7, 9.4.

(±)-9-*O*-Benzyl-3-*O*-methylsophoropterocarpan (4). Anhydrous lithium chloride (26 mg, 0.61 mmol) and bis(triphenylphosphine)palladium(II) chloride[25] (5 mg, 0.007 mmol) were dissolved in anhydrous DMF (0.5 mL), and a mixture of triflate **13** (70 mg, 0.14 mmol) and (3-methyl-2-butenyl)tri-*n*-butylstannane (71 mg, 0.20 mmol) in dry DMF (1 mL) was added via cannula. The resulting homogeneous pale yellow solution was heated to 95–105 °C for 24 h. The reaction mixture was cooled and poured into a two-phase mixture of 10% aqueous ammonium hydroxide (20 mL) and 1:1 ether/benzene (20 mL). The organic layer was separated, and the aqueous layer was extracted with 1:1 ether/benzene (4 × 40 mL). The combined organic solutions were washed with water (2 × 50 mL) and brine and dried over sodium sulfate. Concentration of the mixture gave a yellow-orange residue, which was purified by column chromatography (2×) with 10% ethyl acetate/hexanes as eluent, to give **4** (38 mg, 65%) as a colorless solid, mp 170–171 °C (EtOAc/hexanes): R_f (30% EtOAc/hexanes) 0.56; ^{1}H NMR (300 MHz) 1.67 (s, 3 H), 1.74 (s, 3 H), 3.22–3.40 (m, 2 H), 3.45–3.55 (m, 1 H), 3.63 (t, J = 11, 1 H), 3.78 (s, 3 H), 4.25 (dd, J = 4.4, 11.0, 1 H), 5.02 (s, 2 H), 5.31 (t with higher order coupling, J = 6.6, 1 H), 5.46 (d, J = 6.6, 1 H), 6.47 (d, J = 2.3, 1 H), 6.49 (s, 1 H), 6.63 (dd, J = 2.3, 8.3, 1 H), 7.00 (s, 1 H), 7.25–7.50 (m, 6 H); ^{13}C NMR (75 MHz) 161.0, 158.6, 157.2, 156.6, 137.1, 132.1, 131.8, 128.5, 127.7, 127.1, 124.8, 123.0, 122.7, 118.2, 112.5, 109.1, 101.6, 95.5, 78.4, 70.1, 66.7, 55.3, 39.9, 28.4, 25.8, 17.8; HRMS m/z 428.1998, calcd for $C_{28}H_{28}O_4$ 428.1988. Anal. Calcd for $C_{28}H_{28}O_4$: C, 78.48; H, 6.59. Found: C, 78.71; H, 6.66.

3-Methoxy-6a,11a-*cis*-dihydro-6*H*-benzofuro[3,2-*c*][1]-benzopyran-8,9-diol (14). Method A. From Debenzylation of 8f with Boron Trifluoride Etherate and Dimethyl Sulfide. To a solution of the benzyl ether **8f** (120 mg, 0.319 mmol) in dichloromethane (1.5 mL) and dimethyl sulfide (1.5 mL) at room temperature was added dropwise boron trifluoride etherate (0.23 mL, 1.87 mmol), and the mixture was stirred for 1 h. Water and ethyl acetate were added, and the aqueous layer was separated and extracted with ethyl acetate (4 × 15 mL). The combined ethyl acetate layers were washed with brine (30 mL), dried over anhydrous sodium sulfate, filtered, and concentrated to a reddish brown film, which was used without further purification.

Method B. From Hydrogenolysis of 8f. To a solution of the benzyl ether **8f** (0.127 g, 0.337 mmol) in 95% ethanol (17 mL) and acetone (17 mL) were added 10% palladium on carbon (0.0230 g) and 8 drops of glacial acetic acid from a Pasteur pipet. This mixture was shaken for 1 h under H_2 pressure (17 psi) in a Parr hydrogenation apparatus. The mixture was filtered through Celite, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to a greenish black film, which was used as is in the next experiment: R_f (30% EtOAc/hexanes) 0.16; ^{1}H NMR (acetone-d_6, 300 MHz) 3.47–3.55 (m, 1 H), 3.58 (t, J = 10, 1 H), 3.78 (s, 3 H), 4.27 (dd, J = 4, 10, 1 H), 5.41 (d, J = 6.7, 1 H), 6.34 (s, 1 H), 6.43 (d, J = 2.6, 1 H), 6.62 (dd, J = 2.6, 8.7, 1 H), 6.85 (s, 1 H), 7.37 (d, J = 8.7, 1 H), 7.6–7.80 (br s, 2 H).

(±)-3-Methoxy-6a,11a-*cis*-dihydro-6*H*-[1,3]dioxolo[5,6]-benzofuro[3,2-*c*][1]benzopyran (3).[8b,f] The crude product from the above debenzylation reactions (assumed quantitative) was dissolved in DMF (5 mL) and placed in a resealable glass tube.

Cupric oxide (0.007 g, 0.08 mmol) and anhydrous potassium carbonate (0.094 g, 0.68 mmol) were added. The tube was flushed with argon, and diiodomethane (82 μL, 1.02 mmol) was added. The tube was sealed and heated to 80–90 °C (oil bath temperature) for 24 h. After the mixture had been cooled to room temperature, aqueous HCl (4 mL of 1 N HCl in 20 mL of H_2O) was added and the solution extracted with ethyl acetate (5 × 20 mL). The combined extracts were washed with water (1 × 50 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure, to give a brown solid. Radial chromatography with 10% ethyl acetate/hexanes as eluent yielded (±)-pterocarpin (**3**) (35 mg, 35%), anhydropisatin (**15**, 1.5 mg, 2%), and a mixture of **3** and **15** (14.6 mg, 11% and 4%, respectively, by ^{1}H NMR). Flash column chromatography using silver nitrate impregnated silica gel (prepared by swirling SiO_2 in 4% $AgNO_3/CH_3CN$ and then evaporating the solvent under reduced pressure) gave pure (±)-pterocarpin (**3**) and anhydropisatin (**15**). Recrystallization of **3** from ethyl acetate/hexanes gave cylindrical colorless crystals: mp 190–192 °C (lit. mp 168–169 °C[24a] and 185–186 °C[24b]). Physical data for **3**: R_f (30% EtOAc/hexanes) 0.52; R_f [10% Et_2O/hexanes on $AgNO_3$ impregnated silica gel plate (made by dipping in 4% $AgNO_3/CH_3CN$ solution)] 0.14; ^{1}H NMR[8b,f] (300 MHz) 3.44–3.53 (m, 1 H), 3.66 (t, 1 H, J = 11), 3.79 (s, 3 H), 4.23 (dd, 1 H, J = 11, 4.4), 5.49 (d, 1 H, J = 6.7), 5.90 (2 overlapping d, 2 H), 6.43 (s, 1 H), 6.47 (d, 1 H, J = 2.6), 6.64 (dd, 1 H, J = 8.0, 2.5), 6.72 (s, 1 H), 7.40 (d, 1 H, J = 8.0). Physical data for **15**:[14] R_f [10% Et_2O/hexanes on $AgNO_3$ impregnated silica gel plate (made by dipping in 4% $AgNO_3/CH_3CN$ solution and then drying] 0.18; ^{1}H NMR (300 MHz) 3.80 (s, 3 H), 5.52 (s, 2 H), 5.99 (s, 2 H), 6.53 (d, J = 2.2, 1 H), 6.56 (dd, J = 2.2, 8, 1 H), 6.73 (s, 1 H), 7.02 (s, 1 H), 7.37 (d, J = 8, 1 H); EIMS m/z (relative intensity) 296 (100), 147 (12), 139 (13), 69 (12).

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Supplementary Material Available: Experimental details for the preparation of **7a–d** and **8a–f** and IR, UV (if relevant), and low-resolution electron-impact mass spectral data for **7**, **8**, **12**, **13**, and **4** (6 pages). Ordering information is given on any current masthead page.

Chemistry of Oxaziridines. 13.[1] Synthesis, Reactions, and Properties of 3-Substituted 1,2-Benzisothiazole 1,1-Dioxide Oxides

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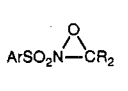
The synthesis, properties, and reactions of 3-substituted 1,2-benzisothiazole 1,1-dioxide oxides **8**, highly stable examples of 3,3-disubstituted *N*-sulfonyloxaziridines **3**, are described. These new *N*-sulfonyloxaziridines are prepared in high yield by oxidation of the corresponding sulfonimines **7**. The bicyclic sulfonimines were prepared by treatment of saccharin (**5**) or preferably pseudosaccharin ethyl ether **6** with organolithium reagents. Kinetic studies of the oxidation of sulfoxides to sulfones and the epoxidation of limonene reveal that these new oxidizing reagents exhibit reduced reactivity, but greater selectivity, compared to oxaziridines of type **1**, in their oxygen-transfer reactions due to greater steric hindrance of the active-site oxygen. This is reflected in lower rates of oxidation and in improved cis/trans selectivity for the epoxidation of (+)-limonene.

The *N*-sulfonyloxaziridines **1** and **2** are an important class of highly selective, neutral aprotic oxidizing reagents that are finding increased utility in organic synthesis.[2] Enantiomerically pure examples of these compounds are useful asymmetric oxidizing reagents affording high stereoselectivities for the asymmetric oxidation of sulfides (selenides) to sulfoxides (selenoxides) (66 to ≥95% ee),[3] for the epoxidation of alkenes (up to 65% ee),[4] and for the asymmetric oxidation of enolates to optically active α-hydroxy carbonyl compounds (55–95% ee).[5]

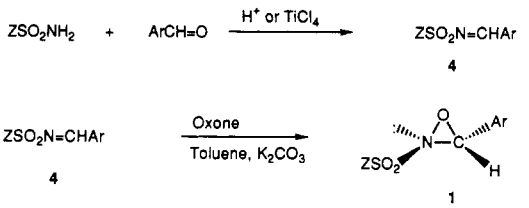
1a, Z= Alkyl, Aryl
b, Z= (-)(S)-N-(α-methylbenzyl)-N-benzylamine

(+)-**2**



3

Scheme I



For the past several years our studies have focused on the oxygen-transfer reactions of *N*-sulfonyloxaziridines **1a** and *N*-sulfamyloxaziridines **1b**.[6] More recently studies have been concerned with the properties of (camphorylsulfonyl)oxaziridines **2** because they are conveniently prepared, enantiomerically pure, without the need for diastereomer separation as is required for oxaziridines of

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