of 1 have been presented. Although carboxylic acid groups are generally more reactive toward borane than double bonds, decarboxylation and reduction of the 5,6 double bond occurred preferentially in pyrimidines 5 and 6. In contrast, an unusual lack of reactivity toward borane was observed for 9; both the carboxyl and double-bond functionalities were totally inert. The selectivity obtained in the borane reduction of the 5-carboxyethyl group of 8 conveniently provided 10. A separate debenzylation step readily affords 5-(hydroxymethyl)-2-thiouracil (1). Key structural features important for the successful reduction of the 5,6 double bond are the "ene-one" form[10] and an electron-withdrawing group of appropriate strength at the 5-position of the pyrimidine.

Experimental Section

All melting points were determined with a Thomas-Hoover apparatus and are uncorrected. ^{1}H NMR spectra were recorded with the use of a Varian Associates FT-80 instrument. Chemical shifts are reported on the scale in parts per million downfield from internal tetramethylsilane (Me_4Si), and apparent coupling constants (J) are given in hertz (Hz). Infrared spectra (IR) were obtained with the use of a Perkin-Elmer 257 grating infrared spectrophotometer. Ultraviolet spectra were recorded on a Cary Model 14 spectrophotometer. Elemental analyses were performed by Galbraith Laboratories, Inc.

The tetrahydrofuran was Fisher reagent grade and was freshly distilled from lithium aluminum hydride. Diethyl(ethoxymethylene)malonate, 2-thiouracil, uracil, and the borane–THF were obtained from Aldrich Chemical Company. Isoorotic acid, orotic acid, 5-chlorouracil, 5-fluorouracil, and 5-iodouracil were supplied by Sigma Chemical Company. All other chemicals were reagent grade.

Ethyl 4-Hydroxy-2-mercaptopyrimidine-5-carboxylate (7). The ester 7 was prepared by following a literature procedure:[7] mp 254–256 °C (lit.[5] mp 245 °C); IR (KBr) 3500 (NH), 1745 (ester carbonyl) 1670 (amide carbonyl) cm^{-1}; ^{1}H NMR (Me_2SO-d_6) 1.25 (3 H, t, J = 8, CH_3), 4.16 (2 H, q, J = 8, -CH_2-), 7.95 (1 H, s, H-6).

4-Hydroxy-2-mercaptopyrimidine-5-carboxylic Acid (5). The preceding ester 7 (5 g, 25 mmol) on hydrolysis by refluxing with an aqueous alcoholic KOH solution (2 N, 50 mL) gave the acid 5 (4.30 g, 100%); mp 297 °C dec; in its ^{1}H NMR spectrum only a singlet at 8.00 due to both carboxylic proton and H-6 could be observed; IR (KBr) 3520 (NH), 1700 (acid carbonyl), 1635 and 1580 (amide carbonyl) cm^{-1}. Anal. Calcd for $C_5H_4N_2O_3S$: C, 34.88; H, 2.34; N, 16.27. Found: C, 34.78; H, 2.30; N, 16.12.

Ethyl 4-Hydroxy-2-(benzylthio)pyrimidine-5-carboxylate (8). A mixture of 7 (1.0 g, 5 mmol), ethanolic NaOEt (1 N, 5 mL), and benzyl chloride (0.694 mL, 5.5 mmol) was refluxed in ethanol (25 mL) for 3 h, evaporated to dryness, triturated with water, and filtered. The precipitate on crystallization from ethanol afforded 8 (0.90 g, 62%); mp 174–175 °C (lit.[7] mp 174–179 °).

4-Hydroxy-2-(benzylthio)pyrimidine-5-carboxylic Acid (9). The above ester 8 (11.60 g, 40 mmol) was hydrolyzed by refluxing it in dilute alcohol (70%, 250 mL) containing KOH (8.96 g, 0.16 mol) to yield the acid 9 (9.2 g, 88%): mp 192–194 °C; λ_{max} (log ϵ) (EtOH) 302 (4.06), 258 (3.89) nm; (pH 2) 318 (4.06), 258 (3.84) nm, (pH 12) 294 (4.09), 252 (4.02) nm; ^{1}H NMR (Me_2SO-d_6) δ 4.50 (2 H, s, CH_2), 7.35 (5 H, m, C_6H_5), 8.60 (1 H, s, H-6) and 11.32 (2 H, bs, OH and COOH). Anal. Calcd for $C_{12}H_{10}N_2O_3S$: C, 54.95; H, 3.84; N, 10.68; S, 12.23. Found: C, 54.83; H, 3.93; N, 10.46; S, 12.06.

General Procedure for Reduction with Diborane. BH_3–THF complex in THF (1.0 M) was used as the reducing agent. All the reductions were carried out in THF except in case of isoorotic acid where pyridine was used. The reagent, BH_3–THF solution (3 mL, 3 mmol), was added dropwise to a magnetically stirred and ice-cooled solution of the substrate (1 mmol) in THF or pyridine (40 mL) under nitrogen. After the addition was over, the reaction mixture was stirred at 0 °C for 30 min and at ambient temperature for 1 h. The solvent was then evaporated in a rotary evaporator. The residue was treated with aqueous acetic acid (50%, 8 mL) and the mixture was again evaporated to dryness. The residue was digested with hot water (10 mL) for 5 min and filtered, whereby most of the boric acid formed went into the filtrate. The precipitate was crystallized from either water or alcohol.

5,6-Dihydrouracil (12): mp and mmp 278–280 °C.

Ethyl 5,6-dihydro-4-hydroxy-2-mercaptopyrimidine-5-carboxylate (13): mp 142–143 °C λ_{max} (log ϵ) (H_2O, pH 7 and 2) 273 (4.46) and 226 (4.23) nm; in alkaline pH (12) the compound underwent some transformation showing UV absorption maximum at 237 (log ϵ 4.39) nm; IR (KBr) 3200, 1750, 1720 cm^{-1}, ^{1}H NMR (Me_2SO-d_6) δ 1.19 (3 H, t, J = 8, CH_3), 3.65 (3 H, m, -CH_2CHCO_2Et), 4.10 (2 H, q, J = 8, -CO_2CH_2-), 9.25 (1 H, bs, -NHCO-), and 11.02 (1 H, bs, -SCNHCO-). Anal. Calcd for $C_7H_{10}N_2O_3S$: C, 41.57; H, 4.98; N, 13.86. Found: C, 41.52; H, 4.94; N, 13.93.

4-Hydroxy-5-(hydroxymethyl)-2-(benzylthio)pyrimidine (10): mp 175 °C; λ_{max} (log ϵ) (aqueous ethanol, 50%) 285 (3.89), 289 (3.89) and 281 (3.93) nm at pH 7, 2, and 12, respectively, with isosbestic point at 286 nm; IR (KBr) 3400 (OH), 1660 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.40 (1 H, bs, OH), 4.30 (2 H, s, CH_2OH), 4.43 (2 H, s, $ArCH_2S$-), 7.85 (5 H, m, C_6H_5), 7.85 (1 H, s, H-6). Anal. Calcd for $C_{12}H_{12}N_2O_2S$: C, 58.04; H, 4.87; N, 11.28; S, 12.91. Found: C, 58.20; H, 4.86; N, 11.155; S, 12.75.

4-Hydroxy-5-(hydroxymethyl)-2-mercaptopyrimidine (1). To a solution of 10 (0.248 g, 1 mmol) in liquid ammonia (~30 mL) was added freshly cut sodium (0.086 g), affording a dark blue solution. The blue color was discharged by careful addition of ammonium chloride. The reaction was left in the hood to allow the ammonia to evaporate. The residue was dissolved in water (20 mL). Rotary evaporation to 5–6 mL followed by cooling gave needlelike crystals of final product 1 (0.076 g, 48% of theory). Physical data for 1: IR (KBr) 3300 (NH), 1650 and 1545 (amide carbonyl); ^{1}H NMR (Me_2SO-d_6) δ 4.17 (2 H, s, -CH_2-), 7.31 (1 H, s, vinyl), 8.80 (2 H, bs, D_2O exchangeable). Anal. Calcd for $C_5H_6N_2O_2S$: C, 37.96; H, 3.82; N, 17.72. Found: C, 38.05; H, 3.89; N, 17.62.

Acknowledgment. Thanks are due to Lloyd L. Brown for recording the NMR spectral data reported in this paper.

Registry No. 1, 93185-31-0; 5, 23945-50-8; 6, 23945-44-0; 7, 38026-46-9; 8, 93185-32-1; 9, 93185-33-2; 10, 93185-34-3; 11, 5366-11-0; 12, 504-07-4; 13, 93185-35-4.

Aqueous Intermolecular Diels–Alder Chemistry: Vernolepin Revisited

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Since the first synthesis of the potent cytotoxic sesquiterpene vernolepin (2) was recorded in 1976,[1] several ingenious approaches have been completed and published.[2] Notable among them is Schlessinger's[2d] route that proceeds via the intermediacy of bicyclic enone 1,[3] which was prepared in 11 steps from ethyl crotonate. We detail below an alternate, direct six-step synthesis of 1 that features an

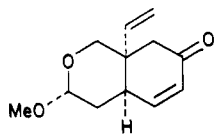
(1) Grieco, P. A.; Nishizawa, M.; Burke, S. D.; Marinovic, N. *J. Am. Chem. Soc.* **1976**, *98*, 1612. Grieco, P. A.; Nishizawa, M.; Oguri, T.; Burke, S. D.; Marinovic, N. *Ibid.* **1977**, *99*, 5773.

(2) (a) Danishefsky, S.; Schuda, P. F.; Kitahara, T.; Etheredge, S. J. *J. Am. Chem. Soc.* **1977**, *99*, 6066. (b) Iio, H.; Isobe, M.; Kawai, T.; Goto, T. *Ibid.* **1979**, *101*, 6076. (c) Zutterman, F.; DeWilde, H.; Mijngheer, R.; DeClercq, P.; Vandewalle, M. *Tetrahedron* **1979**, *35*, 2389. (d) Kieczykowski, G. R.; Quesada, M. L.; Schlessinger, R. H. *J. Am. Chem. Soc.* **1980**, *102*, 782.

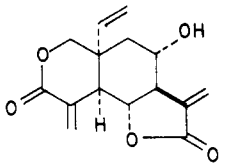
(3) The configuration about the anomeric carbon in bicyclic enone 1 was previously incorrectly assigned by the Schlessinger group. The structure of 1 has been unambiguously established by single-crystal X-ray analysis (unpublished results, Indiana University).

0022-3263/84/1949-5257$01.50/0

aqueous intermolecular Diels–Alder reaction.



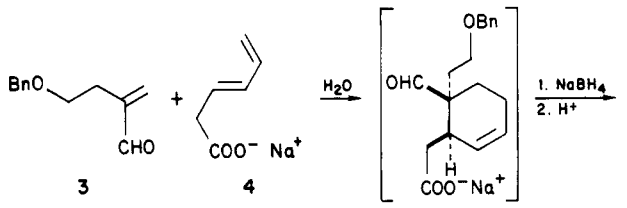
1



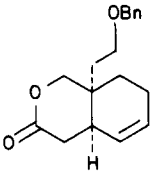
2

Previous results from our laboratory,[4] as well as data reported by Breslow's group,[5] have established that in several instances aqueous intermolecular Diels–Alder reactions, relative to their hydrocarbon counterparts, proceed with enhanced reaction rates. In view of our interest in applications of aqueous Diels–Alder chemistry to natural products syntheses, we examined the condensation of α-substituted acrolein **3** with sodium (*E*)-3,5-hexadienoate (**4**) in water. For comparison purposes we investigated the reaction of **3** with (*E*)-3,5-hexadienoic acid[6] and methyl (*E*)-3,5-hexadienoate[7] in both benzene and toluene (see Table I). Reaction of **3** with sodium (*E*)-3,5-hexadienoate (**4**) in water at 50 °C for 17 h provided after treatment with diazomethane a near quantitative yield of Diels–Alder adducts **5** (endo) and **6** (exo) in a ratio of 10:1. In contrast, the reaction of **3** with the corresponding acid (entry 2) proceeded much more slowly in benzene at 50 °C, requiring 96 h to give a 78% yield of adducts **5** and **6**. It is of interest to note that utilization of (*E*)-3,5-hexadienoic acid in benzene gave an improved endo/exo ratio relative to the aqueous Diels–Alder reaction. Use of the corresponding ester in benzene at 50 °C (entry 3) gave only a modest yield of **5** and **6** after 96 h. Utilization of toluene (reflux) as solvent (entries 4 and 5) gave poor yields along with reduced selectivity.

The ready availability of sodium carboxylate **7**, generated from the condensation of **3** with sodium (*E*)-3,5-hexadienoate (**4**), suggested the possibility of preparing



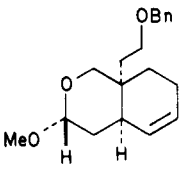
3 4 7



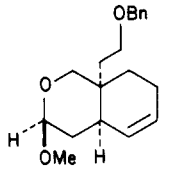
8

bicyclic enone **1**,[2d] a known precursor to vernolepin. Toward this end, Diels–Alder adduct **7**, generated in situ, was directly reduced with sodium borohydride and the resultant hydroxymethyl carboxylic acid upon acidification rapidly cyclized to the AB ring system **8** of vernolepin in 91% overall yield.

The transformation of bicyclic lactone **8** into bicyclic enone **1** was carried out via a five-step sequence. Reduction (*i*-Bu_2AH, $PhCH_3$, −78 °C) of the lactone carbonyl, followed by exposure of the crude lactol to methanol containing a trace of sulfuric acid, provided a 3:2 mixture of protected lactols **9** and **10** in 97% yield that were readily

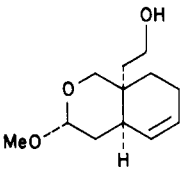


9

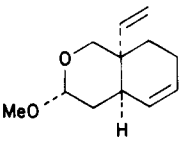


10

separated and characterized. The structures of **9** and **10** were easily derived from their ^1H NMR spectra. Cleavage (Li, NH_3, THF, −78 °C) of the benzyl ether in **9** provided the corresponding hydroxyethyl compound **11** that per-

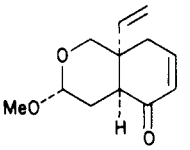


11



12

mitted introduction of the angular vinyl group via organoselenium chemistry. Treatment of **11** with *o*-nitrophenyl selenocyanate and freshly distilled tri-*n*-butylphosphine in tetrahydrofuran[8] followed by oxidation (H_2O_2) of the primary selenide generated in 72% overall yield from **9** the bicyclic compound **12**. Allylic oxidation employing chromium trioxide/3,5-dimethylpyrazole[9] afforded, in addition to approximately 5% of the undesired enone **13**, crystalline enone **1**, mp 52.0–52.2 °C (lit.[2d] mp 51.0–52.5 °C) which was identical in all respects (IR, NMR) with an authentic sample provided by Professor Schlessinger.



13

Experimental Section

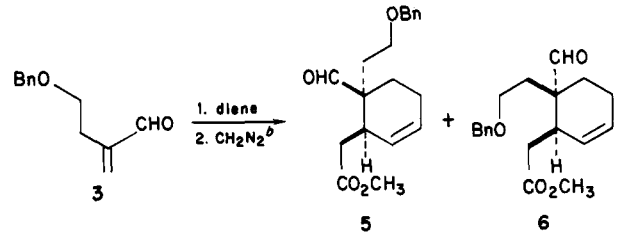
Melting points were determined on a Fisher-Johns hot-stage melting point apparatus and are uncorrected. Infrared spectra (IR) were determined on a Perkin-Elmer 298 grating infrared spectrometer, and nuclear magnetic resonance (NMR) spectra were recorded at either 220 (Varian HR-220) or 360 MHz (Nicolet NT-360) as indicated. Chemical shifts are reported in parts per million (δ) relative to Me_4Si (δ 0.00) as an internal standard. High-resolution mass spectra were recorded on a Kratos MS-80 spectrometer.

All solvents are reagent grade unless otherwise stated. "Dry" solvents were dried immediately before use. Tetrahydrofuran was distilled from sodium benzophenone ketyl. Methylene chloride was dried by passing through a column of alumina (Woelm, basic activity I) and was stored over molecular sieves (type 3A). Thin-layer chromatography (TLC) was carried out on Analtech (Uniplate) glass plates precoated with silica gel GF (250 μm). Column chromatographic separations were performed on silica gel (Merck silica gel 60, 70–230 mesh ASTM).

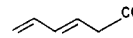
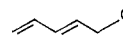
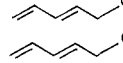
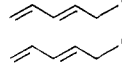
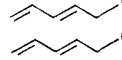
2-Methylene-4-(phenylmethoxy)butanal (3). A mixture of 4-(benzyloxy)butanal[10] (712 mg, 4.0 mmol), 37% formalin (650

(4) Grieco, P. A.; Garner, P.; He, Z. *Tetrahedron Lett.* **1983**, *24*, 1901. Grieco, P. A.; Garner, P.; Yoshida, K.; Huffman, J. C. *Ibid.* **1983**, *24*, 3087. Grieco, P. A.; Yoshida, K.; Garner, P. *J. Org. Chem.* **1983**, *48*, 3137.
(5) Rideout, D. C.; Breslow, R. *J. Am. Chem. Soc.* **1980**, *102*, 7816. Breslow, R.; Maitra, U.; Rideout, D. *Tetrahedron Lett.* **1983**, *24*, 1901.
(6) Boeckman, R. K., Jr.; Demko, D. M. *J. Org. Chem.* **1982**, *47*, 1789.
(7) Stevens, R. V.; Cherpeck, R. E.; Harrison, B. L.; Lai, J.; Lapalme, R. *J. Am. Chem. Soc.* **1976**, *98*, 6317.
(8) Grieco, P. A.; Gilman, S.; Nishizawa, M. *J. Org. Chem.* **1976**, *41*, 1485.
(9) Salmond, W. G.; Barta, M. A.; Havens, J. L. *J. Org. Chem.* **1978**, *43*, 2057.

Table I[a]



3 5 6

entry	diene	solv	temp, °C	time, h	ratio endo/exo[c]	yield,[d] %	recovered dienophile, %
1		water	50	17	10:1	98	0
2		benzene	50	96	12:1	78	5
3		benzene	50	96	12:1	32	53
4		toluene	110	24	8:1	66	0
5		toluene	110	48	7:1	59	0

[a] All reaction were carried out 2.0 M in diene. A fivefold excess of diene was employed. [b] Products were characterized as their methyl ester. [c] Ratios were determined by NMR (360 MHz). [d] Yields reported are for chromatographically pure endo/exo mixtures.

μL, 8.0 mmol), diethylamine hydrochloride (660 mg, 6.0 mmol), and hydroquinone (1 mg) was heated at 70 °C. After 13.5 h at 70 °C, the reaction mixture was diluted with 10 mL of water. The product was isolated by extraction with methylene chloride. The extracts were washed with brine and dried over anhydrous magnesium sulfate. Evaporation of the solvent in vacuo gave a colorless oil that was purified by chromatography on silica gel. Elution with ether/hexane, 1:4, afforded 380 mg (50%) of **3** as a colorless oil: IR (film) 3080, 3055, 3025, 2920, 2850, 2700, 1685, 1628, 1490, 1475, 1450, 1360, 1325, 1305, 1270, 1235, 1201, 1104, 1096, 1070, 1060, 1035, 1005, 946, 904, 855, 830, 780, 730, 690 cm^{-1}; NMR (90 MHz) 2.55 (t, 2 H, H = 7.0 Hz), 3.58 (t, 2 H, J = 7.0 Hz), 4.50 (s, 2 H), 6.03 (s, 1 H), 6.34 (s, 1 H), 7.31 (s, 5 H), 9.53 (s, 1 H); high-resolution mass spectrum, calcd for $C_{12}H_{18}O_2$ 190.0994, found 190.0990.

(±)-*cis*-1,4,4a,7,8,8a-Hexahydro-8a-[2-(phenylmethoxy)-ethyl]-3*H*-2-benzopyran-3-one (8). To a suspension of (*E*)-3,5-hexadienoic acid (2.37 g, 21.2 mmol) in 10.6 mL of water was added solid sodium bicarbonate (1.69 g, 20.1 mmol). After 30 min, 2-methylene-4-(phenylmethoxy)butanal (**3**) (806 mg, 4.24 mmol) and a catalytic amount of 2,6-di-*tert*-butyl-4-methylphenol were added. The reaction mixture was heated at 50 °C for 19 h with vigorous stirring. The reaction mixture was cooled to 0 °C with an ice bath and was treated with sodium borohydride (170 mg, 4.5 mmol). After 30 min the reaction mixture was carefully acidified with sulfuric acid and the product was isolated by extraction with ether. The ether extracts were allowed to stand at room temperature for 1 h to complete lactonization. The organic layer was washed with saturated sodium bicarbonate and brine. The crude product was purified by chromatography on silica gel. Elution with ether/hexane, 2:3, gave 1.10 g (91%) of lactone **8** as a colorless oil: IR ($CHCl_3$) 3020, 2950, 2910, 2850, 1733, 1490, 1475, 1445, 1425, 1395, 1380, 1360, 1285, 1255, 1230, 1170, 1145, 1090, 1060, 1040, 970, 940, 905, 815 cm^{-1}; NMR (360 MHz) ($CDCl_3$) δ 1.53 (t, 2 H, J = 6.9 Hz), 1.77 (m, 2 H), 2.03 (m, 2 H), 2.31 (m, 2 H), 2.68 (m, 1 H), 3.59 (t, 2 H, J = 6.9 Hz), 4.14 (AB q, 2 H, J = 11.9 Hz, $\Delta\nu_{AB}$ = 83.2 Hz), 4.48 (s, 2 H), 5.51 (m, 1 H), 5.82 (m, 1 H), 7.25–7.45 (m, 5 H); high-resolution mass spectrum, calcd for $C_{18}H_{22}O_3$ 286.1569, found 286.1566.

(±)-(3α,4aα,8aα)-3,4,4a,7,8,8a-Hexahydro-3-methoxy-8a-[2-(phenylmethoxy)ethyl]-1*H*-2-benzopyran (9). To a solution of lactone **8** (143 mg, 0.50 mmol) in 2 mL of toluene cooled to −78 °C was added dropwise 1.1 mL of a 1.0 M solution of diisobutylaluminum hydride in toluene. The reaction was stirred at −78 °C for 45 min. The reaction was quenched by the careful addition of methanol (0.5 mL). The product was isolated by extraction with ether. The combined organic extracts were successively washed with water and brine and dried over anhydrous magnesium sulfate. After removal of the solvent in vacuo, the crude residue was dissolved in 10 mL of methanol and was treated with 1 drop of concentrated sulfuric acid. After 1 h, the reaction was quenched by the addition of 0.2 mL of pyridine. After removal of the solvent under reduced pressure, the crude residue was chromatographed on silica gel. Elution with ether/hexane, 1:6, afforded in order of elution 88 mg (58%) of **9** [R_f 0.68 (ether/hexane, 1:1); IR (film) 3055, 3010, 2920, 2860, 1490, 1480, 1450, 1360, 1270, 1245, 1195, 1125, 1095, 1048, 1025, 1015, 1000, 980, 895, 885, 825, 725, 609 cm^{-1}; NMR (360 MHz) ($CDCl_3$) δ 1.34 (dt, 1 H, J = 14.8, 5.2 Hz), 1.52–1.63 (m, 2 H), 1.78 (ddd, 1 H, J = 14.1, 4.7, 2.9 Hz), 1.87 (dt, J = 14.8, 6.5 Hz), 1.98 (m, 1 H), 2.07 (m, 2 H), 2.17 (m, 1 H), 3.36 (s, 1 H), 3.54 (AB q, 1 H, J = 11.9 Hz, $\Delta\nu_{AB}$ = 117.4 Hz), 3.52 (t, 2 H, J = 6.9 Hz), 4.48 (s, 2 H), 4.58 (t, 1 H, J = 3.2 Hz), 5.5–5.6 (m, 2 H), 7.23–7.38 (m, 5 H); high-resolution mass spectrum, calcd for $C_{19}H_{26}O_3$ 302.1882, found 302.1881] and 59 mg (39%) of **10** [R_f 0.55; IR (film) 3020, 2950, 2925, 2850, 1650, 1490, 1480, 1445, 1382, 1360, 1300, 1235, 1180, 1125, 1095, 1065, 1050, 980, 970, 950, 895, 880, 825, 690 cm^{-1}; NMR (360 MHz) ($CDCl_3$) δ 1.34 (dt, 1 H, J = 14.4, 4.3 Hz), 1.40 (dt, 1 H, J = 10.8, 2.2 Hz), 1.54 (dt, 1 H, J = 14.4, 7.2 Hz), 1.8–2.0 (m, 4 H), 2.03 (m, 2 H), 3.43 (s, 3 H), 3.53 (t, 1 H, J = 6.9 Hz), 3.59 (AB q, 2 H, J = 11.9 Hz, $\Delta\nu_{AB}$ = 124.7 Hz), 4.34 (dd, 1 H, J = 7.9, 2.9 Hz), 4.48 (s, 2 H), 5.5–5.7 (m, 2 H), 7.2–7.4 (m, 5 H); high-resolution mass spectrum, calcd for $C_{19}H_{26}O_3$ 302.1882, found 302.1876].

(±)-(3α,4aα,8aα)-8a-Ethenyl-3,4,4a,7,8,8a-hexahydro-3-methoxy-1*H*-2-benzopyran (12). To a solution of lithium (107 mg, 15.5 mmol) in 50 mL of liquid ammonia cooled to −78 °C was added a solution of benzyl ether **9** (310 mg, 1.03 mmol) in 10 mL of tetrahydrofuran. After being stirred for 0.5 h, the reaction was quenched by the addition of solid ammonium chloride. After evaporation of ammonia, the residue was extracted with ether. The combined ether extracts were successively washed with water and brine and dried over magnesium sulfate. Evaporation of the solvent under reduced pressure gave 210 mg (96%) of alcohol **11** as a colorless oil that was employed directly in the next reaction.

The above alcohol and *o*-nitrophenyl selenocyanate (267 mg, 1.18 mmol) were dissolved in 5 mL of tetrahydrofuran. To this solution at room temperature was added dropwise freshly distilled tri-*n*-butylphosphine (238 mg, 1.18 mmol). After 1 h the solvent was removed in vacuo. Chromatography of the residue on silica gel using ether/hexane (2:3) gave almost pure selenide as a yellow oil. The selenide was dissolved in 10 mL of tetrahydrofuran and was treated at 0 °C with 0.35 mL of 50% hydrogen peroxide. The reaction mixture was stirred at room temperature for 15 h. The reaction mixture was concentrated in vacuo, and the residue was dissolved in ether and was washed with water. The aqueous layer was extracted exhaustively with ether. The combined extracts were dried over anhydrous magnesium sulfate. The solvent was

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removed under reduced pressure. The crude olefin was purified by chromatography on silica gel. Elution with ether/hexane (1:8) gave 148 mg (75%) of pure **12** as an oil: IR (film) 3075, 3010, 2990, 2940, 2920, 2890, 2860, 2830, 1635, 1460, 1450, 1435, 1414, 1360, 1338, 1315, 1275, 1250, 1225, 1195, 1176, 1125, 1075, 1055, 1010, 990, 975, 945, 910, 900, 885, 865, 850, 830, 732, 690 cm^{-1}; NMR (360 MHz) ($CDCl_3$) δ 1.40 (m, 1 H), 1.57 (ddd, 1 H, J = 14.1, 11.2, 3.6 Hz), 1.82 (ddd, J = 14.1, 5.1, 2.5 Hz), 1.97–2.19 (m, 3 H), 2.39 (m, 1 H), 3.35 (s, 3 H), 3.41 (AB q, 2 H, J = 11.2 Hz, $\Delta\nu_{AB}$ = 152.6 Hz), 4.60 (t, 1 H, J = 2.9 Hz), 5.09 (d, 1 H, J = 11.2 Hz), 5.10 (d, 1 H, J = 17.7 Hz), 5.61 (m, 2 H), 5.68 (dd, 1 H, J = 17.7, 11.2); high-resolution mass spectrum, calcd for $C_{12}H_{18}O_2$ 194.1307, found 194.1298.

(±)-(3α,4aα,8aα)-8a-Ethenyl-4,4a,8,8a-tetrahydro-3-methoxy-1*H*-2-benzopyran-7(3*H*)-one (1). To 200 mg (2.0 mmol) of chromium trioxide in 2.0 mL of dry methylene chloride at −20 °C was added 193 mg (2.0 mmol) of 3,5-dimethylpyrazole in one portion. After being stirred at −20 °C for 15 min, a solution of olefin **12** (19.4 mg, 0.10 mmol) in 2.0 mL of methylene chloride was added dropwise. The mixture was stirred at −20 °C for 1 h and at 0 °C for 4 h. The reaction was quenched at 0 °C by the addition of 2 mL of a 1.0 M solution of sodium hydroxide. The organic layer was separated and successively washed with 5% hydrochloric acid, water, sodium bicarbonate solution, and brine and dried over magnesium sulfate. Evaporation of the solvent under reduced pressure gave a crude product that was purified on silica gel. Elution with ether/hexane, 2:3, afforded in order of elution 1.0 mg (5%) of enone **13** [R_f 0.58, ether/hexane, 2:1; IR ($CHCl_3$) 2990, 2920, 2830, 1670, 1445, 1420, 1390, 1360, 1290, 1265, 1210, 1125, 1095, 1055, 995, 975, 925, 905, 835 cm^{-1}; NMR (360 MHz) ($CDCl_3$) δ 1.75 (ddd, 1 H, J = 13.4, 12.3, 3.6 Hz), 1.81 (ddd, 1 H, J = 13.4, 5.4, 1.1 Hz), 2.22 (dd, 1 H, J = 19.5, 5.8 Hz), 2.86 (dd, 1 H, J = 12.3, 5.4 Hz), 3.04 (ddd, 1 H, J = 19.5, 2.9, 2.2 Hz), 3.36 (ABq, 1 H, J = 11.6 Hz, $\Delta\nu_{AB}$ = 126.5 Hz), 3.36 (s, 3 H), 4.74 (dd, 1 H, J = 3.6, 1.1 Hz), 5.06 (d, 1 H, J = 17.7 Hz), 5.13 (d, 1 H, J = 11.2 Hz), 5.55 (dd, 1 H, J = 17.7, 11.2 Hz), 5.95 (dd, 1 H, J = 10.1, 2.9 Hz), 6.88 (ddd, 1 H, J = 10.1, 5.8, 2.2 Hz)] and 10 mg (48%) of pure enone **1** as colorless plates, mp 52.0–52.5 °C (lit.[2d] 51.0–52.5 °C) [R_f 0.52; IR ($CHCl_3$) 2995, 2950, 2930, 2905, 2870, 2840, 1675, 1445, 1410, 1380, 1360, 1125, 1088, 1050, 1010, 995, 970, 925, 915, 890, 850 cm^{-1}; NMR (360 MHz) ($CDCl_3$) δ 1.63 (ddd, 1 H, J = 14.1, 12.3, 3.2 Hz), 1.96 (ddd, 1 H, J = 14.1, 4.7, 1.1 Hz), 2.71 (AB q, 2 H, J = 17.0 Hz, $\Delta\nu_{AB}$ = 211.9 Hz), 2.74 (dt, 1 H, J = 12.3, 5.8 Hz), 3.38 (AB q, 2 H, J = 11.9 Hz, $\Delta\nu_{AB}$ = 208.2 Hz), 3.39 (s, 3 H), 4.77 (dd, 1 H, J = 3.2, 1.1 Hz), 5.08 (d, 1 H, J = 17.6 Hz), 5.14 (d, 1 H, J = 10.9 Hz), 5.56 (dd, 1 H, J = 17.6, 10.9 Hz), 5.95 (d, 1 H, J = 10.0 Hz), 6.79 (dd, 1 H, J = 10.0, 5.8 Hz)].

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Registry No. (±)-**1**, 93111-71-8; (±)-**2**, 59598-29-7; **3**, 61700-12-7; **4**, 86668-91-9; (±)-**5**, 93111-72-9; (±)-**6**, 93111-73-0; (±)-**8**, 93111-74-1; (±)-**9**, 93111-75-2; (±)-**10**, 93111-76-3; (±)-**11**, 93111-77-4; (±)-**12**, 93111-78-5; (±)-**13**, 93111-79-6; methyl (*E*)-3,5-hexadienoate, 32775-94-3; 4-(benzyloxy)butanal, 5470-84-8; (*E*)-3,5-hexadienoic acid, 32775-95-4.

Observation of a Sterically Hindered Hydroxyarenesulfenyl Chloride: Novel Base-Catalyzed Dimerization to a Diphenoquinone

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The chemistry of the sulfur–chlorine bond continues to be an active area of interest from both a mechanistic and synthetic point of view.[1] The preparation of sulfenate esters and sulfenamides by the reaction of sulfenyl halides with alcohols and amines, respectively, is well documented in the literature.[2] Sulfenyl derivatives have been used to protect amines, alcohols, and thiols in organic synthesis and have, for example, been used in the synthesis of peptides, penicillins, and nucleosides.[3] Little is known, however, about the chemistry of hydroxy-substituted arenesulfenyl halides, which is no doubt due to their propensity for rapid self-condensation.[4] Hydroxyarenesulfenyl halides are proposed as intermediates in the reaction of phenols with sulfur dichloride leading to the formtion of bisphenol sulfides.

A report in the patent literature[5] claims the preparation of 2,6-dialkyl-4-hydroxybenzenesulfenyl chlorides, although their existence was based solely upon the analysis of the reaction products.

The kinetic stabilization of both reactive intermediates and strained molecules[6] by sterically large substituents is a well-known tool which recently has been used effectively to study the chemistry of phosphorus doubly bonded to itself and other elements.[7] These reports suggested that arenesulfenyl chlorides prepared from hindered phenols may be kinetically stable and capable of study. This paper reports the first spectroscopic observation of a hindered 4-hydroxybenzenesulfenyl chloride and a novel base-catalyzed dimerization to a diphenoquinone.

Results and Discussion

The reaction of a disulfide with elemental chlorine is a standard method for the preparation of a sulfenyl chloride.[2a] The reaction of a solution of **1** in heptane at −30 °C with chlorine gas gave a reddish orange solution characteristic of a sulfenyl chloride. After the addition of 2 equiv of dibutylamine to the solution of **2** at −50 °C, the reaction mixture rapidly turned dark red. Surprisingly, the diphenoquinone **3** was isolated (56% yield) rather than the expected sulfenamide. The diphenoquinone **3** was characterized by its MS, IR, ^1H and ^{13}C NMR spectra, and elemental analysis.

The course of the reaction was monitored by both ^1H NMR (200 MHz) and IR spectroscopy. An equivalent of chlorine gas was introduced to a solution of **1** in carbon tetrachloride at −10 °C. The ^1H NMR spectrum of the reaction mixture had a new singlet resonance at δ 1.12,

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