22: yellow, amorphous solid; ^{1}H NMR (200 MHz, 1% TFA–Me_2SO-d_6) δ 5.20 (s, 2 H), 7.05 (dd, 1 H, J = 2.0, 8.8 Hz), 7.21 (m, 2 H), 7.40 (d, 1 H, J = 8.8 Hz), 7.3-7.6 (m, 6 H), 7.92 (d, 1 H, J = 2.0 Hz), 8.03 (s, 1 H), 8.03 (d, 1 H, J = 8.2 Hz), 8.10 (d, 1 H, J = 2.8 Hz), 8.82 (d, 1 H, J = 2.9 Hz), 11.63 (d, 1 H, J = 2.5 Hz), 12.40 (d, 1 H, J = 2.4 Hz).

23: yellow, amorphous solid; ^{1}H NMR (200 MHz, 1% TFA–Me_2SO-d_6) δ 5.21 (s, 2 H), 6.94 (dd, 1 H, J = 1.8, 8.8 Hz), 7.30 (d, 1 H, J = 8.8 Hz), 7.31 (m, 2 H), 7.3-7.6 (m, 5 H), 7.51 (d, 1 H, J = 1.8 Hz), 7.59 (m, 1 H), 8.03 (s, 1 H), 8.04 (d, 1 H, J = 3.5 Hz), 8.32 (m, 1 H), 8.88 (d, 1 H, J = 3.0 Hz), 11.49 (d, 1 H, J = 1.4 Hz), 12.46 (d, 1 H, J = 3.3 Hz).

Compound **22** (8.0 mg, 0.019 mmol) in methanol (8.0 mL) was stirred vigorously with 10% palladium on activated carbon (12 mg) under hydrogen at room temperature for 3 h. The reaction mixture was filtered through Celite and washed thoroughly with ethanol. Evaporation of ethanol gave **7** (5.7 mg, 0.017 mmol, 90%): bright-yellow, amorphous solid; ^{1}H NMR (300 MHz, 1% TFA–Me_2SO-d_6) δ 6.77 (dd, 1 H, J = 2.1, 8.7 Hz), 7.17 (m, 2 H), 7.35 (d, 1 H, J = 8.7 Hz), 7.47 (d, 1 H, J = 8.1 Hz), 7.70 (d, 1 H, J = 1.8 Hz), 7.97 (s, 1 H), 7.99 (d, 1 H, J = 7.8 Hz), 8.06 (d, 1 H, J = 2.1 Hz), 8.72 (br s, 1 H), 11.59 (br s, 1 H), 12.23 (d, 1 H, J = 1.2 Hz); LREIMS, m/z (relative intensity) 342 (100), 209 (49), 183 (12), 160 (8), 133 (37). Anal. Found for $C_{20}H_{14}N_4O_2$: M_r 342.1118 (HREIMS).

Compound **23** (5.7 mg, 0.013 mmol) in methanol (5.7 mL) was treated with 10% palladium on activated carbon (8.6 mg) under hydrogen for 3 h and worked up in the same manner as for **7** above to give **8** (3.9 mg, 0.011 mmol, 86%): bright-yellow, amorphous solid; ^{1}H NMR (300 MHz, 1% TFA–Me_2SO-d_6) δ 6.72 (dd, 1 H, J = 1.8, 8.4 Hz), 7.25 (d, 1 H, J = 1.8 Hz), 7.26 (d, 1 H, J = 8.4 Hz), 7.30 (m, 2 H), 7.56 (m, 1 H), 7.82 (s, 1 H), 7.95 (d, 1 H, J = 2.1 Hz), 8.29 (m, 1 H), 8.83 (d, 1 H, J = 1.8 Hz), 11.33 (br s, 1 H), 12.45 (d, 1 H, J = 1.8 Hz); LREIMS, m/z (relative intensity) 342 (100), 225 (56), 199 (13), 144 (16), 117 (53). Anal. Found for $C_{20}H_{14}N_4O_2$: M_r 342.1114 (HREIMS).

Acknowledgment. We thank Dr. R. W. M. Van Soest, Amsterdam, for discussions about sponge identification; Drs. O. J. McConnell and F. E. Koehn for valuable discussions; and Dr. R. M. Milberg for mass spectra obtained in the Mass Spectrometry Laboratory of the School of Chemical Sciences. This is Harbor Branch Oceanographic Institution Contribution No. 670.

Registry No. 1, 112515-43-2; **2**, 112515-44-3; **3**, 116747-40-1; **4**, 116725-88-3; **5**, 116725-89-4; **6**, 112515-42-1; **7**, 116725-90-7; **8**, 116725-91-8; **9**, 116747-41-2; **10**, 28755-03-5; **11**, 116725-92-9; **12**, 2400-51-3; **13**, 116725-93-0; **14**, 7269-72-9; **15**, 116725-94-1; **16**, 116725-95-2; **17**, 116725-96-3; **18**, 116725-97-4; **19**, 37800-46-7; **20**, 116725-98-5; **21**, 116725-99-6; **22**, 116726-00-2; **23**, 116726-01-3; **24**, 116726-02-4; $Cu(OAc)_2$, 142-71-2; 6-(benzyloxy)indole, 15903-94-3; chloroacetyl chloride, 79-04-9; 5-(benzyloxy)indole, 1215-59-4.

Efficient Preparation of Some Biologically Active Substances from Natural and Nonnatural Aromatic Compounds by *m*-Chloroperbenzoic Acid Oxidation

Yoshinori Asakawa,* Reiko Matsuda, Motoo Tori, and Masakazu Sono

Faculty of Pharmaceutical Sciences, Tokushima Bunri University, Yamashiro-cho, Tokushima 770, Japan

Received April 12, 1988

Six naturally occurring aromatic terpenoids and six nonnatural aromatic compounds were oxidized by *m*-chloroperbenzoic acid in chloroform to give 1,2- and 1,4-quinones or hydroxylated products in which vitamin K_1, insecticidal, piscicidal, and antifungal compounds were included. The present method is advantageous for obtaining different types of natural or nonnatural aromatic products having biological activity from the starting aromatic compounds in a one-step reaction.

In previous papers,[1-6] we reported hydroxylation at nonactivated carbon atoms of mono-, sesqui- and triterpenoids by *m*-chloroperbenzoic acid (MCPBA). Workup of this reaction was very simple and various hydroxylated compounds were obtained in one step. We have applied this simple method to some natural and nonnatural aromatic compounds and obtained quinones, some of which possessed piscicidal, antifungal, and insecticidal activity. In this paper we report the structures of the oxidation products and their biological activity.

Results and Discussion

The aromatic substances dissolved in chloroform were oxidized by MCPBA at room temperature or under reflux with stirring. Each mixture, after filtration of excess MCPBA and *m*-chlorobenzoic acid, was chromatographed on silica gel to give oxidation products. Table I shows the starting materials, oxidation products, and reaction conditions. Known compounds (**2**,[7,8] **4**,[9,10] **6**,[11] **10**,[11] **12**,[11] **15**,[12-15] **16**,[12] **20**,[16] **29**,[17] and **31**[18]) had properties consonant with

(1) Tori, M.; Matsuda, R.; Asakawa, Y. *Chem. Lett.* **1985**, 167.
(2) Tori, M.; Sono, M.; Asakawa, Y. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 2669.
(3) Tori, M.; Matsuda, R.; Asakawa, Y. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 2523.
(4) Asakawa, Y.; Matsuda, R.; Tori, M. *Experientia* **1986**, *42*, 201.
(5) Tori, M.; Matsuda, R.; Asakawa, Y. *Tetrahedron Lett.* **1985**, *26*, 227.
(6) Tori, M.; Matsuda, R.; Asakawa, Y. *Tetrahedron* **1986**, *42*, 1275.
(7) Smith, L. I.; Opie, J. W.; Wawzonek, S.; Prichard, W. W. *J. Org. Chem.* **1939**, *4*, 318.
(8) Jacob, P., III; Callery, P. S.; Shulgin, A. T.; Castagnoli, N., Jr. *J. Org. Chem.* **1976**, *41*, 3627.
(9) Makillop, A.; Swann, B. P.; Taylor, E. C. *Tetrahedron* **1970**, *26*, 4031.
(10) Wehrli, P. A.; Fryer, R. I.; Pigott, F.; Silverman, G. *J. Org. Chem.* **1972**, *37*, 2340.
(11) The spectral data of **6**, **10**, and **12** were identical with those of authentic samples.
(12) Zavarin, E.; Anderson, A. B. *J. Org. Chem.* **1955**, *20*, 82.
(13) Pilo, C.; Runeberg, J. *Acta Chem. Scand.* **1960**, *14*, 353.
(14) Runeberg, J. *Acta Chem. Scand.* **1960**, *24*, 1991.
(15) El-Dakhakhny, M. *Planta Med.* **1963**, *4*, 465.
(16) Matsuo, A.; Terada, I.; Nakayama, M.; Hayashi, S. *Tetrahedron Lett.* **1977**, 2821.
(17) Kashman, *Tetrahedron* **1979**, *35*, 263.
(18) Matsumoto, T.; Imai, S.; Yuki, S.; Katayama, A.; Furutani, M. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 527.

0022-3263/88/1953-5453$01.50/0

Table I. Oxidative Products from Naturally and Nonnaturally Occurring Aromatic Compounds by MCPBA Oxidation

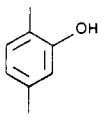
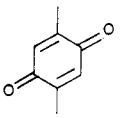
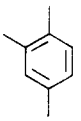
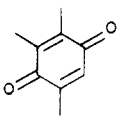
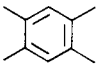
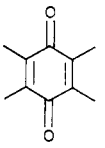
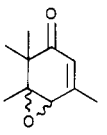
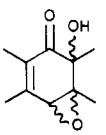
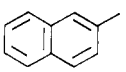
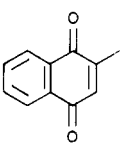
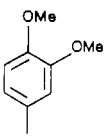
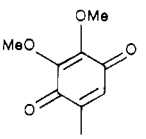
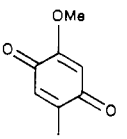
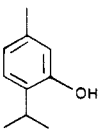
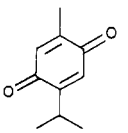
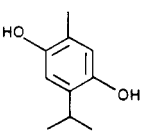
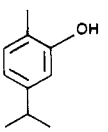
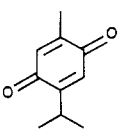
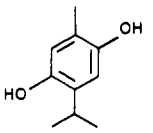
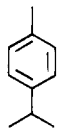
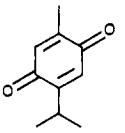
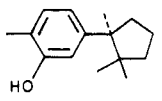
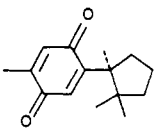
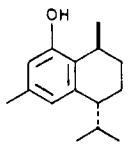
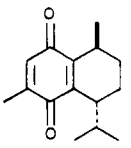
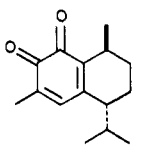
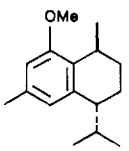
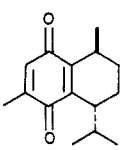
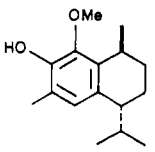
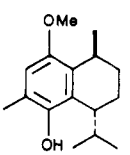
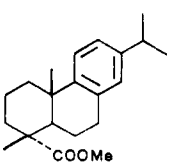
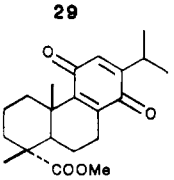
startng matrls (g)	products	yield,[a] %	MCPBA, equiv	reactn temp, °C	reactn time, min
 1 (2.0)	 2	32.7	2.2	rt[b]	30
 3 (3.0)	 4	16.5	2.2	60–70	30
 5 (5.5)	 6	20.0	2.2	60–70	30
	 7	6.0			
	 8	3.0			
 9 (2.0)	 10	21.0	1.2	rt	60
 11 (2.0)	 12	trace	2.2	rt	30
	 13	24.0			
 14 (5.0)	 15	47.0	1.2	rt	180[c]
	 16	30.0			
 17 (5.0)	 15	50.2	1.2	rt	180

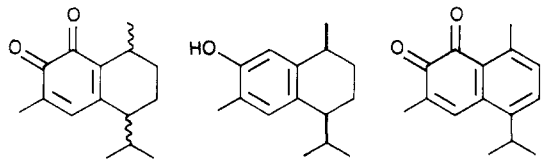
Table I (Continued)

startng matrls (g)	products	yield,[a] %	MCPBA, equiv	reactn temp, °C	reactn time, min
	 **16**	25.5			
 **18** (0.5)	 **15**	20.8 7.0	2.2	rt	180
 **19** (0.5)	 **20**	32.4	1.2	rt	30
 **21** (0.98)	 **22**	24.0	1.2	rt	30
	 **23**	19.2			
 **27** (1.2)	 **22**	9.2	1.2	rt	20
	 **28**	10.4			
	 **29**	10.1			
 **30** (1.75)	 **31**	25.0	2.2	70–75	720

[a] Yield is isolated yield. [b] rt = room temperature. [c] When MCPBA in $CHCl_3$ was added to the starting material, the reaction mixture instantenously boiled.

the literature; new compounds (**7**, **8**, **13**, **22**, **23**, and **28**) were identified as follows. The molecular formula of compound **7** was determined to be $C_{10}H_{14}O_2$ by high resolution mass spectrometry. The spectral data showed the presence of a β-substituted conjugated ketone group (1670 cm^{-1}; λ_{max} 247.5 nm; δ_C 200.42). The remaining one oxygen was ether oxygen since neither a hydroxyl nor an aldehyde absorption band was observed in the IR and NMR spectra.

Chart I



24 25 26

The ^1H NMR spectrum had the signals of two tertiary methyls (δ 1.17 and 1.33), one vinyl methyl (δ 2.10, d, J = 2 Hz), coupled with one vinylic proton (δ 5.80, d, J = 2 Hz), and one additional tertiary methyl group (δ 1.55) on carbon (δ 55.43) bearing an ether oxygen and one proton (δ 3.17, s) on carbon (δ 68.91) bearing an ether oxygen. The ^{13}C NMR spectrum further contained the signals of four methyls, a trisubstituted double bond, and one quaternary carbon. On the basis of the above data, the structure of the epoxide was determined to be **7**. Compound **8**, $C_{10}H_{14}O_3$, (M^+ 182.0950) showed the presence of a tertiary hydroxyl group (3500 cm^{-1}; δ_C 76.36, s) and a conjugated carbonyl group (1683 cm^{-1}; λ_{max} 255 nm; δ_C 200.13). The ^1H NMR spectrum disclosed the presence of two vinylic methyl groups (δ 1.82 and 2.10 each, d, J = 2 Hz), two tertiary methyl groups (δ 1.25 and 1.55 each s), one of which might be attached on a carbon (δ 61.06) bearing an ether oxygen, and a methine proton (δ 3.25, s) on a carbon (δ 60.03) bearing an ether oxygen and one hydroxyl group (δ 3.80, br s), which disappeared on addition of D_2O. The ^{13}C NMR further contained the signals of four methyls and a tetrasubstituted double bond. These evidences led to the conclusion that the structure of the epoxy alcohol was **8**. It is noteworthy that the methyl rearranged product **7** was obtained from durene (**5**) by MCPBA oxidation. 2,3-Dimethoxy-5-methyl-1,4-benzoquinone (**12**) is an important starting material for the synthesis of coenzyme, ubiquinones. MCPBA oxidation of 3,4-dimethoxytoluene (**11**) gave primarily 2-methoxy-5-methyl-1,4-benzoquinone (**13**), whose structure was easily determined by the spectral data (see Experimental Section). The minor compound was confirmed to be **12**, by comparison of R_f values on TLC with an authentic sample. In this case, only a trace amount of the desired compound **12** was obtained. From the sesquiterpene phenol **21**,[19] two quinone derivatives **22** and **23** were obtained. The former compound **22**, $C_{15}H_{20}O_2$ (M^+ 232.1467), contained a para quinone moiety (λ_{max} 260 nm; 1650 cm^{-1}) indicating that **22** was the 5,8-quinone derivative and the latter compound **23**, $C_{15}H_{20}O_2$ (M^+ 232.1455, showed the presence of an ortho quinone group (λ_{max} 430 nm; 1680, 1660, 1650 cm^{-1}), meaning that **23** was 7,8-quinone derivative. The spectral data of **23** was closely related to those of the sesquiterpene ortho quinone, mansonone A (**24**)[20,21] (Chart I). However, the melting point of **23** was 34° lower than that of **24**, indicating that **23** and **24** were the stereoisomers of the secondary methyl and/or isopropyl groups on the cyclohexane ring. As the stereochemistry of the secondary methyl and isopropyl groups of **21** has been established as *S* and *R*, respectively,[19] compound **23** was determined to be (1*S*,4*R*)-mansonone A. The same groups on the cyclohexane ring of **24** should be arranged to be cis. The co-occurrence of (1*S*,4*S*)-7-hydroxycalamenene (**25**) and mansonone C (**26**) in Ulmaceae[22] supports the above assumption. A new hydroxycalamenene (**28**) and the previously known hydroxycalamenene (**29**)[17] were obtained from 8-methoxycalamenene (**27**) together with the para quinone **22**. Compound **28** had the same molecular formula, $C_{15}H_{24}O_2$ (M^+ 248.1787), as that of **29**, indicating that **28** was 7-hydroxylated calamenene. This fact was further supported by the NOE difference spectra of both compounds. In compound **28**, the NOE was observed between OMe (δ 3.78) and 7-OH (δ 5.54) and in **29**, between OMe (δ 3.76) and H-7 (δ 6.49), respectively.

The oxidation products **2** and **4** showed potent insecticidal activity against the adult of *Chrysolina aurichalcea*, which was killed on filter paper (125 mm diameter) impregnated with 1 mg of each quinone. Compounds **15** and **16** possess antifungal properties against various wood-destroying fungi.[12] Compounds **15** and **29** showed piscicidal activity against killie fish, which were killed within 40–47 min at a concentration of 6.62 ppm.

The present method is one pot and has a short-time reaction, and the workup is very simple, not dangerous, and nontoxic, in comparison with the oxidation reaction using dry ozone and heavy metals, and the yield of oxidation products is satisfactory. Application of the present method to flavonoids, bibenzyls, and alkanoids is under progress.

Experimental Section

Melting points are uncorrected. The solvents used for the spectral measurements were $CDCl_3$ (400-MHz and 60-MHz ^1H NMR; 100-MHz and 22.5-MHz ^{13}C NMR), $CHCl_3$ (IR and $[\alpha]_D$), and MeOH (UV). TLC: spots were visualized by UV (254 and 360 nm) and spraying (0.5% of (2,4-dinitrophenyl)hydrazine–2 N HCl, 1% $FeCl_3$–H_2O, 30% H_2SO_4 or 2% $Ce(SO_4)_2$–2 N H_2SO_4) and heating at 120 °C on a hot plate. All the starting materials were checked by TLC, GC, and ^{13}C NMR and impurities were not detected. Commercial MCPBA (70–80%) was used for the oxidation reaction.

General Method of MCPBA Oxidation Reaction (Table I). (1) To a $CHCl_3$ (30 mL) solution of MCPBA (1.2–2.2 equiv) was added the substrate in $CHCl_3$ (8 mL) dropwise in 30 min. The mixture was stirred for 30 min at room temperature. The reaction mixture was cooled and filtered to remove excess MCPBA and *m*-chlorobenzoic acid, and the filtrate was directly chromatographed on silica gel by using a C_6H_6–EtOAc gradient to isolate the oxidation products or washed with 5% Na_2SO_3, 5% $NaHCO_3$, and saturated NaCl, and the solvent was evaporated in vacuo. The resulting residue was chromatographed on silica gel by using a C_6H_6–EtOAc gradient to give pure compounds.

(2) To a $CHCl_3$ (16 mL) solution of MCPBA (1.2–2.2 equiv) was added the starting material in the same solvent, and the mixture was stirred for 30 min–9 h under reflux. The reaction mixture was treated in the same manner as described above to give quinones and/or hydroxylated compounds.

Epoxy ketone 7: mp 47–49 °C; UV 200 nm (log ϵ 3.64), 247.5 (3.73); IR ν 1670, 1380, 1210, 880 cm^{-1}; ^1H NMR (400 MHz) δ 1.17, 1.33, 1.55 (each s, 3 H), 2.10 (d, J = 2 Hz, 3 H), 3.16 (s, 1 H), 5.80 (d, J = 2 Hz, 1 H); ^{13}C NMR (100 MHz) δ 18.91, 21.11, 21.19, 24.63 (each q, Me), 43.09 (s, C), 55.43 (s, -OC), 68.91 (d, -OCH), 126.12 (d, =CH), 157.65 (s, =C), 200.42 (s, C=O); HREIMS, m/z 166.1007, calcd for $C_{10}H_{14}O_2$ 166.0994; EIMS, m/z (relative intensity) 166 (M^+) (6), 151 (30), 123 (100), 95 (44), 83 (26), 67 (67), 55 (25), 43 (67), 41 (48), 39 (43).

Epoxy alcohol 8: mp 50–52.5 °C; UV 200 nm (log ϵ 3.53), 255 (3.79); IR ν 3500, 1685, 1645, 1235, 1172, 1107, 1070, 1015, 935, 875, 845 cm^{-1}; ^1H NMR (400 MHz) δ 1.25, 1.55 (each s, 3 H), 1.83 (d, J = 2 Hz, 3 H), 2.10 (d, J = 2 Hz, 3 H), 3.23 (s, 1 H), 3.80 (br s, 1 H, OH); ^{13}C NMR (100 MHz) δ 12.43, 15.21, 19.70, 20.06 (each q, Me) 60.03 (d, -OCH), 61.06 (s, -OC), 76.36 (s, COH), 130.42,

(19) Nishizawa, M.; Inoue, A.; Sastrapradje, S.; Hayashi, Y. *Phytochemistry* **1983**, *22*, 2083.
(20) MariniBettolo, G. B.; Casinovi, C. G.; Galeffi, C. *Tetrahedron Lett.* **1966**, 4857.
(21) Tanaka, N.; Yasue, M.; Imamura, H. *Tetrahedron Lett.* **1966**, 2767.
(22) Rowe, J. W.; Deikel, M. K.; Roy, D. N.; Jorgensen, E. *Phytochemistry* **1972**, *11*, 2513.

149.13 (each s, =C), 200.13 (s, C=O); HREIMS, m/z 182.0950, calcd for $C_{10}H_{14}O_3$ 182.0943; EIMS, m/z (relative intensity) (M^+ not appeared), 167 (2), 139 (24), 137 (21), 67 (9), 55 (10), 43 (100).

2-Methoxy-5-methyl-1,4-benzoquinone (13): mp 158–160 °C; UV 203 nm (log ϵ 3.74), 260 (4.30); IR ν 1675, 1655, 1605 cm^{-1}; ^1H NMR (400 MHz) δ 2.07 (d, J = 2 Hz, 3 H), 3.85 (s, 3 H), 5.93 (s, 1 H), 6.55 (q, J = 2 Hz, 1 H); HREIMS, m/z 152.0471, calcd for $C_8H_8O_3$ 152.0474; EIMS, m/z (relative intensity) 152 (M^+) (52), 122 (24), 69 (100), 66 (24), 39 (20).

5,6,7,8-Tetrahydro-8-isopropyl-2,5-dimethyl-1,4-naphthoquinone (22): mp 52–53 °C; $[\alpha]_D$ -77.8° (c 2.38); UV 205 nm (log ϵ 3.60), 260 (4.04); IR ν 1650 cm^{-1}; ^1H NMR (100 MHz) δ 0.87 (d, J = 7 Hz, 6 H, C_8 isopropyl Me), 1.05 (d, J = 7 Hz, 3 H, C_5 Me), 1.98 (d, J = 2 Hz, 3 H, C_2 Me), 2.70 (m, 1 H, H-8), 2.90 (m, 1 H, H-5), 6.42 (q, J = 2 Hz, H-3); ^{13}C NMR (100 MHz) δ 15.9, 20.5, 21.1, 21.9 (each q, Me), 18.7, 25.4 (each, t, CH_2), 26.4, 31.8, 36.6 (each, d, CH), 133.3 (d, Ph CH), 144.5, 145.6, 147.1 (each s, Ph C), 187.3, 188.5 (each s, C=O); HREIMS, m/z 232.1467, calcd for $C_{15}H_{20}O_2$ 232.1463; EIMS, m/z (relative intensity) 232 (M^+) (46), 205 (21), 189 (100), 175 (76), 161 (40), 149 (61), 91 (30), 43 (40).

5,6,7,8-Tetrahydro-5-isopropyl-3,8-dimethyl-1,2-naphthoquinone (23): mp 84–85 °C; $[\alpha]_D$ -87.5° (c 0.33); UV 212 nm (log ϵ 4.09), 430 (3.10); IR ν 1680, 1660, 1650 cm^{-1}; ^1H NMR (400 MHz) δ 0.88, 1.07, 1.08 (each d, J = 6.6 Hz, C_5 isopropyl Me and C_8 Me), 1.94 (br s, 3 H, C_3 Me), 2.85 (m, 1 H, H-8), 6.70 (s, 1 H, H-4); ^{13}C NMR (100 MHz) δ 15.1, 19.3, 20.6, 21.9 (each q, Me), 18.5, 26.5 (each t, CH_2), 26.6, 30.6, 44.0 (each d, CH), 135.4, 140.6, 150.2 (each s, Ph C), 140.4 (d, Ph CH), 180.0, 181.6 (each s, C=O); HREIMS, m/z 232.1455, calcd for $C_{15}H_{20}O_2$ 232.1463; EIMS, m/z (relative intensity) 232 (M^+) (5), 204 (13), 191 (36), 161 (100).

8-Methoxy-7-hydroxycalamenene (28): mp 62–63 °C; $[\alpha]_D$ +23° (c 0.21); UV 220 nm (log ϵ 3.78), 270 (4.11), 280 (3.15); IR ν 3550, 1420, 1060 cm^{-1}; ^1H NMR (400 MHz) δ 0.80, 0.96, 1.20 (each d, J = 7 Hz, C_4 isopropyl Me and C_1 Me), 2.21 (s, 3 H, C_6 Me), 3.06 (td, J = 6.5, 2.9 Hz, 1 H, H-1), 3.78 (s, 3 H, C_8 OMe), 5.54 (br s, 1 H, C_7 OH), 6.69 (s, 1 H, H-5); ^{13}C NMR (100 MHz) δ 15.5, 19.3, 22.0, 23.3 (each q, Me), 15.5, 27.5 (t, CH_2), 27.9, 33.0, 42.8 (each d, CH), 60.9 (q, OMe), 121.4, 131.6, 132.9, 144.7, 145.1 (each s, Ph C), 127.1 (d, Ph CH), HREIMS, m/z 248.1787, calcd for $C_{16}H_{24}O_2$ 248.1776; EIMS, m/z (relative intensity) 248 (M^+) (9), 223 (26), 205 (100), 173 (21).

Acknowledgment. We thank Prof. M. Nishizawa, Tokushima Bunri University, for his generous gift of (1*S*,4*R*)-8-hydroxycalamenene. Thanks are also due to Arakawa Co. Ltd. for the gift of dehydroabietic acid. This work was supported in part by Grant-in Aids for Cancer Research (Y.A.) from the Ministry of Health and Welfare.

Antiinsectan Aflavinine Derivatives from the Sclerotia of *Aspergillus flavus*

James B. Gloer,* Mark R. TePaske, and John S. Sima

Department of Chemistry, University of Iowa, Iowa City, Iowa 52242

Donald T. Wicklow and Patrick F. Dowd

Agricultural Research Service, Northern Regional Research Center, United States Department of Agriculture, Peoria, Illinois 61604

Received July 12, 1988

Four natural products with the aflavinine ring system (1 and 3–5) have been isolated as major components of the sclerotia (key survival structures) produced by several isolates of the common fungus *Aspergillus flavus*. These metabolites are selectively allocated to the sclerotia and exhibit antifeedant activity against fungivorous insects which commonly encounter sclerotia in nature. All four compounds were characterized and identified by NMR and mass spectral analysis, and three of them (3–5) have not been previously reported, despite extensive chemical studies of *Aspergillus* spp.

Many species of higher fungi produce specially adapted propagules called sclerotia as a means of surviving harsh climates or nutrient-poor conditions.[1] These relatively large resting bodies can survive for several months to several years in the soil, but the factors that permit the long-term survival of sclerotia are not fully understood. It has been suggested that sclerotial metabolites that would prevent or reduce predation by detritivorous, fungivorous insects could make a significant contribution to sclerotial longevity.[2-4] Some sclerotium-producing species of the widespread genus *Aspergillus* are known to produce significant amounts of a variety of important mycotoxins, including aflatoxins.[5] However, to our knowledge, *Aspergillus* sclerotia have not been specifically surveyed for unique bioactive metabolites.

Our studies of the sclerotia of a non-aflatoxigenic strain of *Aspergillus flavus* have led to the isolation of four sclerotial metabolites that deter feeding by the fungivorous beetle *Carpophilus hemipterus* (nitidulidae), a common crop insect that encounters *A. flavus* sclerotia under natural conditions. The antiinsectan activity of one of these compounds, 20,25-dihydroxyaflavinine (1), has been described earlier.[4] We report here details of the characterization of these metabolites.

Results and Discussion

Sclerotia of a non-aflatoxigenic isolate of *A. flavus* (NRRL 6541) produced in solid-substrate fermentation

(1) Willets, H. J. *Biol. Rev. Cambridge Philos. Soc.* **1971**, *46*, 387.
(2) Wicklow, D. T.; Cole, R. J. *Can. J. Bot.* **1982**, *60*, 525.
(3) Wicklow, D. T.; Shotwell, O. L. *Can. J. Microbiol.* **1983**, *29*, 1.
(4) Wicklow, D. T.; Dowd, P. F.; TePaske, M. R.; Gloer, J. B. *Trans. Br. Mycol. Soc.*, in press.
(5) Cole, R. J.; Cox, R. H. *Handbook of Toxic Fungal Metabolites*; Academic: New York, 1981.

0022-3263/88/1953-5457$01.50/0