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A Novel Oxidation Product Formed by the Oxidation of Di(1-propenyl)-tetramethoxybiphenyl with CrO_3–HBF_4–MeCN

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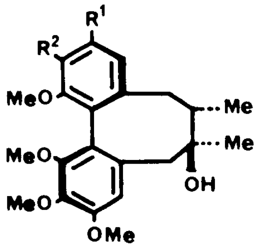
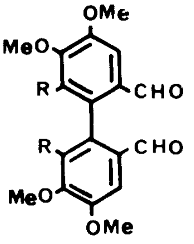
Oxidation of the di(1-propenyl)-biphenyl **3a** with the CrO_3–HBF_4–MeCN reagent system gave a novel oxidation product **4a**, which was subsequently transformed to the phenanthrenes **5** and **6**.

Keywords——oxidation; chromium trioxide; di(1-propenyl)-biphenyl; cross-conjugated dienone; phenanthrene

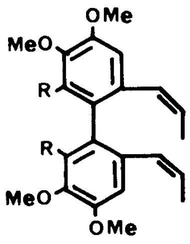
There is considerable interest in the synthesis of dibenzocyclooctadiene lignans, schizandrin **1a** and gomisins (**1b**: gomisin A), in connection with their interesting pharmacological activities,[1] namely, antitussive, tonic, inhibition of gastric ulceration, and tranquilizing activities. Although several syntheses of dibenzocyclooctadiene lignans have been reported already,[2] we investigated oxidation of the tetramethoxy-(*Z*)-di(1-propenyl)biphenyl **3a** with a new type of CrO_3 reagent system,[3] CrO_3–HBF_4–MeCN, continuing our previous work on the syntheses of the tetrahydronaphthalene and tetrahydrofuran neo-lignans[4] and podophyllum lignans[5] with the use of this reagent system, and we found that **3a** gives a novel oxidation product **4a** instead of the expected dibenzocyclooctenone.



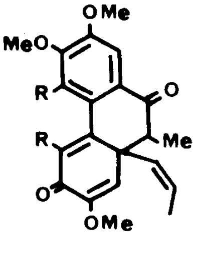
1a : $R^1 = R^2 = OMe$
1b : $R^1 + R^2 = OCH_2O$



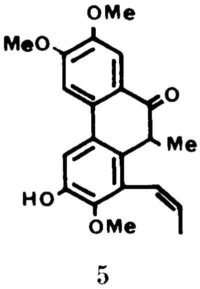
2a : R=H
2b : R=OMe



3a : R=H
3b : R=OMe



4a : R=H
4b : R=OMe



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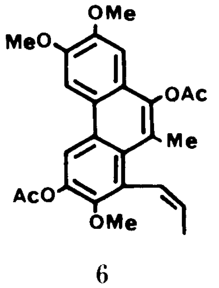

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Chart 1

The tetramethoxy-(*Z*)-di(1-propenyl)biphenyl **3a**, mp 90—92 °C, was synthesized from the corresponding dialdehyde **2a**, which was prepared by Ullmann reaction of 6-bromoveratraldehyde with ethyltriphenyl phosphonium bromide in the presence of K_2CO_3 and 18-crown-6.[6] Oxidation of **3a** with the CrO_3–HBF_4–MeCN system gave a cross-conjugated dienone **4a**, mp 115—117 °C, in 46% yield. The structure of **4a** was assigned from its spectral data and the following chemical transformations. Treatment of **4a** with $SnCl_4$ in AcOH gave the phenol **5**, mp 170—172 °C, by dienone–phenol rearrangement in 63% yield.[7] The phenol **5** gave the diacetate **6**, mp 157—159 °C, on acetylation with Ac_2O in pyridine. On the other hand, oxidation of hexamethoxy-(*Z*)-di(1-propenyl)-biphenyl **3b** with the same reagent system gave no identifiable products, presumably because of the instability of the corresponding dienone **4b** in acidic media, or *peri* interaction of the methoxy group.

Experimental

All melting points are uncorrected. Infrared (IR) spectra were recorded with a Hitachi 260-10 spectrometer, nuclear magnetic resonance (NMR) spectra with a JEOL JNM-FX 100 spectrometer with tetramethylsilane as an internal standard ($CDCl_3$ soln.) and mass spectra (MS) with a JEOL JMS-D 300 spectrometer. Elemental analyses were done by Ms. M. Takeda and Ms. S. Okamura, Kissei Pharmaceutical Company, Matsumoto, Japan. Mallinckrodt silica gel (100 mesh) and Merck Kieselgel 60 F_{254} were used for column chromatography and thin-layer chrometography (TLC), respectively.

4,5,4′,5′-Tetramethoxy-(*Z*)-2,2′-di(1-propenyl)biphenyl (3a)——Ethyltriphenyl phosphonium bromide (111 g, 0.3 mol), anhydrous K_2CO_3 (41.4 g, 0.3 mol), and 18-crown-6 (1 g) were added to a solution of **2a** (33 g, 0.1 mol), which was prepared from 6-bromoveratraldehyde by means of usual Ullmann reaction, in dry dioxane (150 ml), and the mixture was stirred at 100 °C for 48 h. The precipitates were separated from the solution by filtration and the filtrate was concentrated under a vacuum. The residue was taken up in ether. The ether solution was washed with water, dried and concentrated. The residue was subjected to silica gel chromatography. The eluate with 40% hexane in chloroform gave 31.9 g (90%) of **3a** as colorless crystals (ethanol), mp 90—92 °C. IR (Nujol): 1600 cm^{-1}. NMR ($CDCl_3$) δ: 1.80 (6H, dd, J=6.5 and 1.5 Hz, 2 × -C=C-Me), 3.80, 3.85 (each 6H, s, 4 × OMe), 5.42 (2H, dq, J=11.5 and 6.5 Hz, olefinic H), 5.95 (2H, dd, J=11.5 and 1.5 Hz, olefinic H), 6.60 (2H, s, aromatic H), 6.80 (2H, s, aromatic H). *Anal.* Calcd for $C_{22}H_{26}O_4$: C, 74.54; H, 7.39: MS *m/e*: 354.1830. Found: C, 74.31; H, 7.49. MS *m/e*: 354.1820.

Oxidation of 3a with CrO_3–HBF_4–MeCN——A solution which was prepared by adding MeCN (17.6 ml) to a mixture of CrO_3 (220 mg, 2.2 mmol) and aqueous 42% HBF_4 (4.4 ml) was added at room temperature to a solution of **3a** (354 mg, 1 mmol) in MeCN (12 ml), and the whole was stirred at room temperature for 30 s. The reaction mixture was poured into ice-water and extracted with ether. The organic layer was washed with sat. $NaHCO_3$ and H_2O, then dried and concentrated. The residue was subjected to silica gel chromatography. The eluate with 40% hexane in chloroform gave 162.8 mg (46%) of 2,6,7-trimethoxy-10-methyl-10a-(*Z*)-(1-propenyl)phenanthrene-3,9(10*H*, 10a*H*)-dione **4a** as colorless crystals (chloroform–ether), mp 115—117 °C. IR (Nujol): 1680, 1650, 1630, 1590 cm^{-1}. NMR ($CDCl_3$) δ: 1.36 (3H, d, J=5.61 Hz, C=C-Me), 1.52 [3H, d, J=6.59 Hz, C(10)-Me], 2.62 [1H, q, J=6.59 Hz, C(10)-H], 3.78, 3.97, 4.00 (each 3H, s, 3 × OMe), 5.22—5.57 (2H, m, olefinic H), 5.99 (1H, s, C(1)-H), 6.77, 7.04, 7.52 (each 1H, s, C(4)-H, and aromatic H). *Anal.* Calcd for $C_{21}H_{22}O_5$: C, 71.17; H, 6.26. MS *m/e*, 354.1468. Found: C, 71.08; H, 6.24. MS *m/e*: 354.1496.

3-Hydoxy-2,6,7-trimethoxy-10-methyl-(*Z*)-1-(1-propenyl)phenanthrene-9(10*H*)-one (5)——$SnCl_4$ (624 mg, 2.4 mmol) was added to a solution of **4a** (213 mg, 0.6 mmol) in AcOH (15 ml), and the whole was stirred overnight at room temperature. The reaction mixture was poured into ice-water and extracted with chloroform. The organic layer was washed with sat. $NaHCO_3$ and H_2O, then dried and concentrated. The residue was subjected to silica gel chromatography. The eluate with 10% hexane in chloroform gave 134 mg (63%) of **5** as colorless crystals (chloroform–ether), mp 170—172 °C. IR (Nujol): 3400, 1660, 1600 cm^{-1}. NMR ($CDCl_3$) δ: 1.29 (3H, d, J=7.32 Hz, C(10)-Me), 1.60 (3H, dd, J=6.59 and 1.46 Hz, -C=C-Me), 3.74 (1H, q, J=7.32 Hz, C(10)-H), 3.75, 3.97, 4.05 (each 3H, s, 3 × OMe), 5.97 (1H, dq, J=11.23 and 6.59 Hz, olefinic H), 6.41 (1H, dd, J=11.23 and 1.46 Hz, olefinic H), 7.30, 7.44, 7.50 (each 1H, s, aromatic H). *Anal.* Calcd for $C_{21}H_{22}O_5$. MS *m/e*: 354.1466. Found: 354.1461.

3,9-Diacetoxy-2,6,7-trimethoxy-10-methyl-(*Z*)-1-(1-propenyl)phenanthrene (6)——Ac_2O (1.5 ml) was added to a solution of **5** (45 mg, 0.127 mmol) in dry pyridine (0.5 ml) and the whole was stirred overnight at room temperature. The reaction mixture was worked up in the usual manner to yield 52.9 mg (95%) of **6** as colorless crystals from ethanol, mp 157—159 °C. IR (Nujol): 1740 cm^{-1}. NMR ($CDCl_3$) δ: 1.37 (3H, dd, J=6.84 and 1.71 Hz, -C=C-Me), 2.42, 2.47, 2.49 (each 3H, s, C(10)-Me and 2 × OCOMe), 3.73, 4.00, 4.08 (each 3H, s, 3 × OMe), 5.88 (1H, dq, J=11.23 and 6.84 Hz, olefinic H), 6.96 (1H, dd, J=11.23 and 1.71 Hz, olefinic H), 7.08, 7.77, 8.16 (each 1H, s, aromatic H). *Anal.* Calcd for $C_{25}H_{26}O_7$: C, 68.48; H, 5.98. MS *m/e*: 438.1676. Found: C, 68.42; H, 5.95. MS *m/e*: 438.1669.

References and Notes

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