Photochemical Conversion of 7-Methoxyhemigossypolone to the Lactone of 2,5,8Trihydroxy4-isopropyl-3-methoxy-6-methylnaphth-l-oic Acid

ARTICLE *in* JOURNAL OF NATURAL PRODUCTS · MARCH 1988

Impact Factor: 3.8 · DOI: 10.1021/np50056a038

2 AUTHORS, INCLUDING:

Noreen Mahoney
United States Department of…

71 PUBLICATIONS **1,591**
CITATIONS

SEE PROFILE

Journal of Natural Products
Vol. 51, No. 2, pp. 374-375, Mar-Apr 1988

PHOTOCHEMICAL CONVERSION OF 7-METHOXYHEMIGOSSYPOLONE TO THE LACTONE OF 2,5,8-TRIHYDROXY-4-ISOPROPYL-3-METHOXY-6-METHYLNAPHTH-1-OIC ACID

NOREEN E. MAHONEY* and BOCK G. CHAN

Western Regional Research Center, U.S. Department of Agriculture, Albany, California 94710

The resistance of glanded cotton varieties to insect attack has been attributed in part to the terpene aldehydes found in the pigment glands (1). The proposed mode of activity of these compounds is the condensation reaction of the aldehyde with the amino group of a protein resulting in disrupted protein digestion or enzyme deactivation (2,3). The terpene aldehyde gossypol has an ED_{50} (the concentration at which larval growth is reduced 50%) of 1.4 mmol/kg (wet wt) on the cotton pest *Heliothis zea*; however, its dianiline derivative, in which the aldehydes have been converted into imines, is inactive as a growth inhibitor (4).

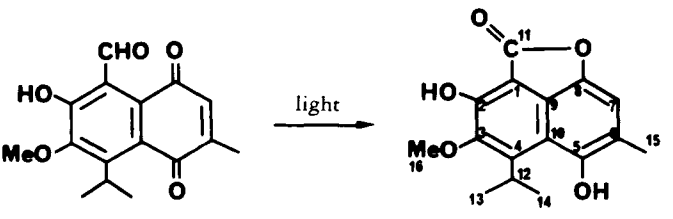
The gland constituent 7-methoxyhemigossypolone [**1**], however, shows no growth-inhibiting activity even though it contains the aldehyde moiety (5). A possible explanation is the observation that **1** undergoes a light-induced intramolecular lactonization to form the lactone of 2,5,8-trihydroxy-4-isopropyl-3-methoxy-6-methylnaphth-1-oic acid [**2**]. The photochemical conversion of similar quinones to lactones has been reported (6), but this reaction had not been previously reported for **1**. The conversion of **1** is slower than the lactonization of other, especially ortho, quinones, but this reaction begins immediately upon dissolution and is 98% complete in 24 h under normal room light.

Compound **1** and lactone **2** were separately incorporated into artificial diets at levels of up to 8 mmol/kg diet (wet wt), and neither produced any effect on the growth of *Pectinophora gossypiella* larvae. Lactone formation was not observed to occur for hemigossypolone, which had an ED_{50} of 4.1 mmol/kg on these larvae. The biological inactivity of **1** could be due to its conversion to lactone **2**, which is unable to undergo the condensation reaction with amines. This fact would provide additional evidence supporting the theory that the aldehyde is the active site of the cotton terpene aldehydes.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points were measured on a Thomas capillary melting point apparatus and are uncorrected. Ir and uv spectra were recorded on Perkin-Elmer 237B and Cary 219 spectrophotometers, respectively. ^1H- (200 MHz) and ^{13}C- (50 MHz) nmr spectra were obtained on a Nicolet NT-200 spectrometer using TMS as the internal standard. Mass spectra were determined on a VG 70/70 double focusing spectrometer at 70 eV with a source temperature of 120°. The diets for *P. gossypiella* larvae (7) were prepared in duplicate at concentrations of 1,2,4, and 8 mmol/kg diet (wet wt) for **1**, lactone **2**, and hemigossypolone.

ISOLATION OF 7-METHOXYHEMIGOSSYPO-



1 **2**

LONE.—Pima S-4 glanded cotton bracts were freeze-dried and extracted with EtOAc-hexane-HOAc (1:1:0.1%). The extract was concentrated and chromatographed successively on Biobeads SX-2 (Bio-Rad) eluted with EtOAc, Bio-Sil A (Bio Rad) eluted with hexane, and cyano bonded phase silica (J.T. Baker) eluted with hexane containing 2% HOAc. Compound **1** crystallized from this last eluent (mp 65–66°) and was identified from its nmr, ir, uv, and mass spectra, which were in good agreement with the published spectra (8).

ISOLATION AND IDENTIFICATION OF THE LACTONE OF 2,5,8-TRIHYDROXY-4-ISOPROPYL-3-METHOXY-6-METHYLNAPHTH-1-OIC ACID [2].—Compound **1** (100 mg) was added to MeCN (10 ml) and allowed to stand at room temperature under normal room light. The rate of lactone **2** formation was monitored by hplc (9); lactone **2** and **1** have retention times of 3.8 and 7.8 min, respectively. Conversion to lactone **2** was approximately 50% after 2 h, 80% after 5 h, and 98% after 24 h. Lactone **2** was purified on a Bio-Sil A silica column eluted with hexane-EtOAc (4:1) and formed yellow crystals from EtOAc/hexane, mp 205–206°; ms *m/z* (rel. int. %) $[M]^+$ 288.0995 ($C_{16}H_{16}O_5$ requires 288.0997) (100), 273 (98), 245 (14); ir ν max ($CHCl_3$) cm^{-1} 3600, 3510 (OH); 1750 (C=O); uv λ max (MeOH) nm (log ϵ) 218 (4.61), 279 (4.42), 350 (3.74), 389 (3.70); ^1H nmr ($CDCl_3$, room temperature) δ 1.50 (6H, d, $J=7$ Hz, H-13,14), 2.42 (3H, s, H-15), 3.98 (3H, s, H-16), 4.58 (1H, br, OH-5), 5.22 (1H, br, OH-2), 6.94 (1H, s, H-7); ^1H nmr (DMSO-d_6, 80°), δ 1.46 (6H, d, $J=7$ Hz, H-13,14), 2.36 (3H, s, H-15), 3.20 (1H, br, OH-5), 3.84 (3H, s, H-16), 4.68 (1H, sept, $J=7$ Hz, H-12), 6.99 (1H, s, H-7), 8.54 (1H, br, OH-2); ^{13}C nmr (DMSO-d_6, room temperature), δ 17.8 (C-15), 21.7 (C-13,14), 27.5 (C-12), 61.5 (C-16), 109.3 (C-7), 115.4 (C-10), 119.5 (C-9), 125.0 (C-6), 140.3 (C-4), 146.7 (C-3), 152.1 (C-2), 165.2 (C-11); ^{13}C nmr (DMSO-d_6, 80°), 17.1 (C-15), 21.4 (C-13,14), 27.0 (C-12), 61.1 (C-16), 101.1 (C-1), 108.6 (C-7), 115.4 (C-10), 119.4 (C-9), 124.6 (C-6), 140.3 (C-4), 146.4 (C-3), 146.5 (C-8), 149.9 (C-5), 151.6 (C-2), 164.7 (C-11).

ACKNOWLEDGMENTS

We thank Dr. Robert Lundin and Ms. Mabry Benson for the nmr spectra and Mr. Roger England for the mass spectra. The cotton plant material was kindly provided by Dr. Doug Wilson of the USDA Western Cotton Research Laboratory in Phoenix, Arizona.

LITERATURE CITED

1. B.G. Chan, A.C. Waiss, Jr., R.G. Binder, and C.A. Elliger, *Entomol. Exp. Appl.*, **24**, 94 (1978).
2. C.M. Cater and C.M. Lyman, *J. Am. Oil Chem. Soc.*, **46**, 649 (1969).
3. A.G. Appu Rao, *Int. J. Pept. Protein Res.*, **27**, 380 (1986).
4. B.G. Chan, N. Mahoney, A.C. Waiss, Jr., and J. Baker, "Proceedings," Beltwide Cotton Products Research Conference, Jan. 2–6, San Antonio, TX, 1983, p. 74.
5. R.D. Stipanovic, A.A. Bell, and M.J. Lukefahr, in: "Host Plant Resistance to Pests." Ed. by P.A. Hedin, American Chemical Society, Washington, DC, 1977, p. 197.
6. M.A. Ferreira, T.J. King, S. Ali, and R.H. Thomson, *J. Chem. Soc., Perkin Trans. 1*, 249 (1980).
7. B.G. Chan, A.C. Waiss, Jr., W.L. Stanley, and A.E. Goodban, *J. Econ. Entomol.*, **71**, 366 (1978).
8. A.A. Bell, R.D. Stipanovic, D.H. O'Brien, and P.A. Fryxell, *Phytochemistry*, **17**, 1297 (1978).
9. N.E. Mahoney and B.G. Chan, *J. Chromatogr.*, **329**, 91 (1985).

Received 23 October 1987