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THE ISOLATION AND SYNTHESIS OF A NOVEL TETRACYCLIC ETHER FROM EAST INDIAN SANDALWOOD OIL. A FACILE INTRAMOLECULAR PRINS REACTION

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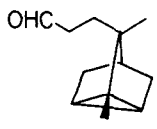
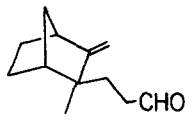
Through extensive efforts of numerous workers, particularly the Indian group headed by Bhattacharyya (1), the major components of the prized essential oil of East Indian sandalwood (Santalum album Linn) have been identified. Although various aldehydes (I) have been isolated from the oil, the presence of the aldehydes I and II in the essential oil has not been reported. We wish to report here the isolation of the aldehyde I and a novel tetracyclic ether, 11-methyl-7-oxa-tetracyclo[6.3.1.$0^{1,6}$.$0^{4,11}$]dodecane (III), from a commercial sample of East Indian sandalwood oil (2). The ether III was synthesized via II by an extraordinarily facile acid-catalyzed internal Prins cyclization, suggesting that II is the precursor of III in the oil.



I



II

III

Isolation. A commercial grade of sandalwood oil (2) was fractionally distilled from an 18-inch spinning band column and the portion distilling at 30-55° (0.35 mm) was collected. This fraction was subjected to gas chromatography (10 ft x 1/4 in. column packed with 20% DC-200 silicone oil on 60/80 mesh Chromosorb W-AW-DMCS at 150° and 60 ml/min helium flow) and the components with retention times between 16 and 20 min were collected.

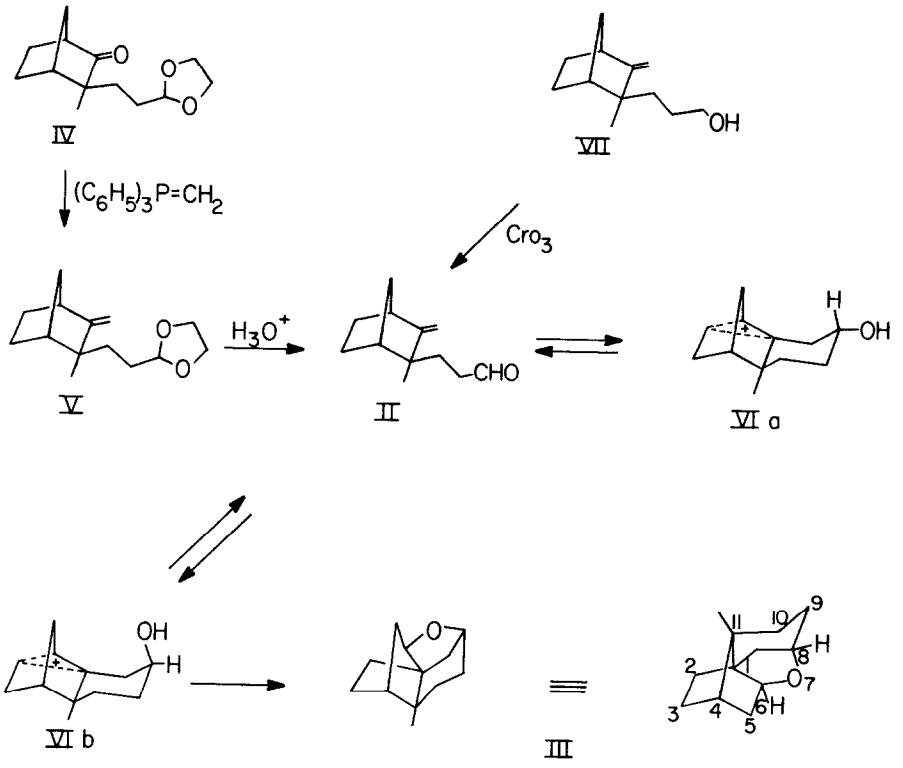
Tricycloekasantalal (I). Gas chromatography of the above fraction on a 10 ft x 1/4 in. column packed with 20% diethylene glycol succinate on 60/80 mesh Chromosorb W-AW-DMCS under the same conditions of temperature and flow listed above showed a complexity of peaks. The

component with a retention time of 35.8 min (relative to air) was collected as a colorless oil: ir (CS_2) 2833, 2725, 1722, 852 cm^{-1}; nmr ($CDCl_3$) τ 0.13 (triplet, 1H, J = 2 Hz, -CH=O; 7.55 (sextet, 2H, $J_1 = J_2 = 8$ Hz, $J_3 = 2$ Hz, $-CH_2CHO$), 9.02 (singlet, 2H, cyclopropyl H), 8.89, 9.09 (singlet, 3H each, CH_3); mass spectrum parent ion: m/e, 178.1356 (Calcd for $C_{12}H_{18}O$: 178.1358). The above data strongly suggested structure I for the isolate; this assignment was confirmed by comparison with an authentic sample (3).

11-Methyl-7-oxa-tetracyclo[6.3.1.$0^{1,6}$.$0^{4,11}$]dodecane (III). Under the same gas chromatographic conditions as for the isolation of IV, the component of retention time ca. 30.5 min was collected as a colorless solid: mp 178-180°; mass spectrum parent ion: m/e, 178.1354 (Calcd for $C_{12}H_{18}O$: 178.1358). The infrared and nmr spectra of this material were identical in every major respect with those of a sample of the synthetic material prepared below.

Synthesis of Ether III. Dropwise addition of 3-bromopropionaldehyde ethylene glycol acetal (5) at 130° to a xylene suspension of the sodium enolate of endo-3-methylnorcamphor (prepared by the action of sodium hydride on 3-endo-methylnorcamphor (6) in xylene solution maintained at 85-90° for a period of 4 hr) produced the acetal IV (4) [bp 110-115° (0.2 mm); ir (film) 1745 cm^{-1} (C=O), 1136, 1026 cm^{-1} (acetal); nmr (CCl_4) τ 5.30 (t, 1, J = 4 Hz, acetal methine H) τ 6.22 (m, 4, acetal methylene H), τ 7.54 and 7.71 (broad s, 2 bridgehead H), τ 9.06 (s, 3, endo-methyl H] in 50% yield. Treatment of IV with triphenylmethylene phosphorane in dimethylsulfoxide at 50° for 20 hr furnished the olefinic acetal V [bp 130-140° (0.12 mm); ir (neat) 3060, 1655, 815 cm^{-1}; nmr ($CDCl_3$) τ 5.34 (multiplet, 2, acetal methine and one olefinic H overlapping), 5.59 (singlet, 1, one olefinic H), 6.25 (multiplet, 4, acetal methylene H)] in 35% yield. Hydrolysis of the acetal V with 10 ml of 10% sulfuric acid in 25 ml of tetrahydrofuran at 60° afforded the ether III as the exclusive product. A sample of the ether collected by preparative glpc had mp 177-179° and showed the following spectral data: ir (CCl_4) 1050-1110 cm^{-1} (strong absorption); nmr (10% in $CDCl_3$) τ 5.71 (triplet, 1, J = 6 Hz, C-6 H), 6.34 (quartet, 1, $J_1 = 8.0$ Hz, $J_2 = 2.0$ Hz, C-8 H), 7.7-9.0 (multiplet, 11), 9.1 (singlet, 3, C-11 CH_3).

Presumably, V is hydrolyzed to the aldehyde II which undergoes an extraordinarily facile intramolecular Prins reaction to the cations VIa and VIb. The latter ion, VIb, is ideally disposed for cyclization to the ether III, thereby shifting the equilibrium in this direction.



Another example of the facility with which this cyclization occurs is exemplified by the chromic acid oxidation of the alcohol VII (7). Oxidation of VII under mild acid conditions (8) afforded the ether III as the major product with no evidence for the aldehyde II. Precursory studies suggest, in fact, that II cannot be prepared under acid conditions although its synthesis has been attained under basic or neutral conditions (9).

Acknowledgments. The technical assistance of Mr. Dennis Toepker and Miss Katherine Powell is acknowledged.

REFERENCES

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4. The stereochemical assignment is consistent with the observation that alkylation of sodium methylnorcamphorate occurs from the exo-face of the molecule: E. J. Corey, R. Hartmann, and P. A. Vatakencherry, J. Amer. Chem. Soc., 86, 2611 (1962).

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6. Prepared by the action of boron trifluoride etherate on endo-2-methyl-exo-2,3-epoxy-norbornane in benzene solution.

7. The synthesis of VII will be described in the complete paper.

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9. See the attendant paper by H. C. Kretschmar and W. F. Erman.