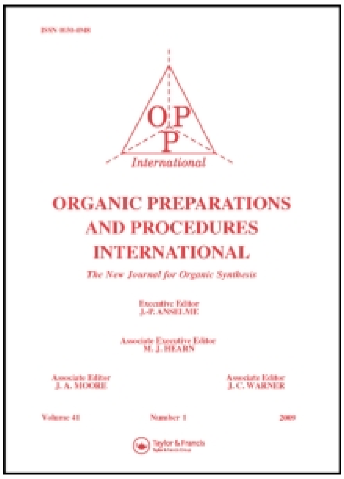

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SYNTHESIS OF dl-2-METHYL-2-(4-METHYL-3-PENTENYL) 5-OXYMETHYLENEMETHOXY-2H-BENZOPYRAN. A CANNABICHROMENE HOMOLOGUE

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(0.15 mole) thiophosgene in 50 ml acetone is added dropwise over 10 min. After stirring for another 30 min, the volatiles are removed by rotatory evaporation at room temperature, and the residue is triturated with water. Crude yields: 65-71%, mp. 168-170°. Recrystallization from acetonitrile raises the mp. to 170.5-173.4°, lit.[1] mp. 170.5-173.0°, (yield 43%). NMR ($CDCl_3$, TMS): δ 5.88 (s, 1H), 7.3-8.2 (m, 15H).

S-[(Bis-p-toluenesulfonyl)-methyl] p-toluenethiosulfonate (I, R = 4-MeC_6H_4).- From sodium p-toluenesulfinate dihydrate according to the preceding procedure. Crude yield: 90%, mp. 159-164.5°. Recrystallization as above yields 59% of pure product, mp. 165.9-168.0°. NMR ($CDCl_3$, TMS): δ 2.46 (s, 9H), 5.83 (s, 1H), 7.2-7.9 (m, 12H).

Anal. Calcd. for $C_{22}H_{22}O_6S_4$: S, 25.11. Found: S, 25.07

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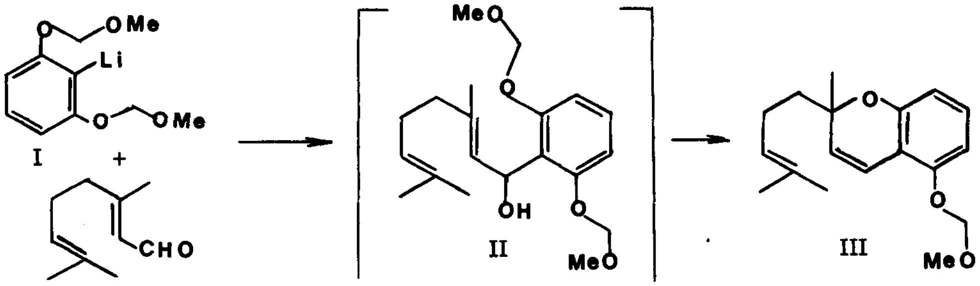
The benzopyran ring system has previously been synthesized in the case of cannabichromene by the pyridine catalyzed reaction of olivetol with citral.[1] However this method gives a low yield of complicated mixture of products which is very difficult to separate. Other indirect methods involve tedious dehydrogenation and cyclization procedures.[2-4]



We now report that citral can be successfully converted to the previously unreported title compound by treatment with 1,3-bis(oxymethylenemethoxy)benzene-2-lithium derivative I in anhydrous ether. It turned out that the expected intermediate condensation product II cyclized during work up (silica gel/chromatography) to yield the chromene III.

EXPERIMENTAL

Infrared spectra were recorded on a Perkin Elmer 567 spectrophotometer. Nmr spectra were obtained using a Varian A-60A spectrometer with $CDCl_3$ as solvent and TMS as internal standard. Chemical shifts are reported in δ values in parts per million (ppm) downfield from TMS signal. Mass spectra were determined on a Hitachi-Perkin-Elmer RMU-7H mass spectrometer. Elemental analysis was determined at Dr. F. Pasher's Laboratory, Bonn (Germany).

2-Methyl-2-(4-methyl-3-pentenyl)5-oxymethylenemethoxy-2H-benzopyran III.- To a solution of 1,3-bis(oxymethylenemethoxy)benzene (3 g. 0.015 mole)[5] in 100 ml of anhydrous ether under nitrogen atmosphere, with magnetic stirring and ice-bath cooling, was added a 24.76% solution (3.7 ml, 0.014 mole) of *n*-butyllithium in benzene by means of a hypodermic syringe through a septum inlet during 30 min. The mixture was stirred at 0° for 20 hrs. and allowed to stand at RT for 0.5 hrs. to complete the reaction. After this period, the flask was cooled to -70° and a solution of 2.5 g (0.014 mole) of citral in 20 ml of ether was added and stirred for 4 hrs. more. The mixture was treated with a saturated ammonium chloride solution as the temperature slowly became ambient. The reaction was conveniently monitored by tlc (silica gel/benzene). The aqueous layer was extracted with ether (3 x 25 ml). The combined organic phase was dried over anhydrous sodium sulfate and the solvent was evaporated leaving a yellow oil. The residue was chromatographed on silica gel (Merck 60) column. The product was eluted with benzene and the first fraction yielded III which was distilled _in vacuo_ to yield 1.61 g. (37%) of product, bp. 110°/0.5 mm.

IR (film): 3100-2940, 2900, 1665, 1600, 1465, 1380, 1280, 1000 cm^{-1}

NMR ($CDCl_3$): δ 1.4 (3 H, s, CH_3), 1.6 (6 H, d, $(CH_3)_2C=$), 1.8 (2 H, m, CH_2), 2.1 (2 H, m, CH_2), 3.45 (3 H, s, CH_3O), 5.10 (1 H, m, $HC=C(CH_3)_2$), 5.15 (2 H, s, $O-CH_2-O$), 5.52 (1 H, d, J = 10 Hz, HC=), 6.4 - 7.1 (3 H, m, Ar), 6.7 (1 H, d, J = 10Hz, =CHAr); MS, m/e: 288, 273, 205, 175, 161, 160. 144, 132, 129.

Anal. Calcd. for $C_{16}H_{24}O_3$: C, 74.97; H, 8.39; O. 16.64.

Found: C, 75.11; H, 8.32; O, 16.74.

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