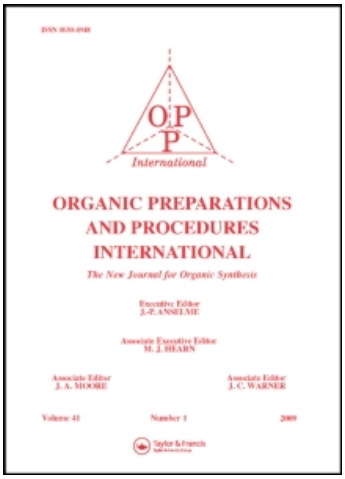

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PREPARATION OF THE PALMITATES OF KAHWEOL AND CAFESTOL

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ethyl acetate-chloroform gave 2.49 g (63%) of white crystals. By raising the temperature rapidly (~20°/min), the unusually broad melting range could be narrowed to 193-200°. The clear melt soon solidified at this temperature and remelted to a yellow liquid at 255-290° similar to that obtained by slowly heating the substance (~2°/min) to these temperatures. NMR ($CDCl_3$): δ 5.20 (s, 2H) and 7.1-7.8 (m, 20 H); MS (70 eV): m/e 349 (M-45), 272 (M-122), 242 (M-152), 212 (M-182), and 167 (M-227).

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PREPARATION OF THE PALMITATES OF KAHWEOL AND CAFESTOL

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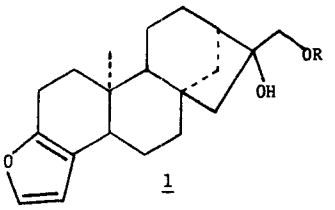
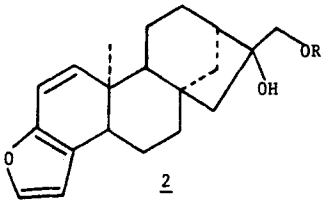
The diterpene esters, kahweol palmitate (1a) and cafestol palmitate (2a), isolated from green coffee beans have been found to induce increased activity of the detoxifying enzyme system, glutathione S-transferase.[1] Administration of compounds 1a and 2a to Sprague-Dawley rats treated with 7,12-dimethylbenz(a)anthracene, resulted in a decrease in the incidence of mammary tumor formation.[2] To study further the effects of 1a and 2a as inhibitors of chemically-induced tumorigenesis, large quantities were required. The yield of 1a and 2a isolated from green coffee beans was less

than 0.02%. Large scale isolation of these two compounds from green coffee beans by the extraction and fractionation method is not efficient. We now describe a semi-synthetic method to obtain 1a and 2a and their corresponding acetates (1b and 2b) in gram quantity.



1



2

a) R = $C(CH_2)_{14}CH_3$ (O)

b) R = $-CCH_3$ (O)

In addition to the palmitates, kahweol and cafestol exist as esters of other fatty acids as well in green coffee beans. The total diterpene esters were extracted into petroleum ether along with other lipid soluble substances. After removal of the solvent, the petroleum ether extract was saponified with ethanolic potassium hydroxide to give the free alcohols, 1 and 2. The diterpene alcohols were then separated from the other unsaponified material by preparative LC. Esterification with palmitoyl chloride in pyridine followed by preparative LC separation gave the pure palmitates, 1a and 2a in good yield.

EXPERIMENTAL SECTION

Esters of Kahweol (1) and Cafestol (2).- Ground green coffee beans (1 kg Colombia Supremo) were extracted with petroleum ether in a modified Sohxlet extracter (Curtin Matheson Scientific, Inc.) for 10 days. The solvent was removed and the extract weighed 80-90 g. The combined extracts from several extractions (200 g) were saponified with 600 ml of ethanolic KOH (10% KOH in 80% aq. ethanol) at room temperature for 3 days. The reaction mixture was poured into ice water and the unsaponified material was extracted into ether. The crude product (18-23 g) which contained kahweol,

cafestol, phytosterols and other lipid soluble substances was fractionated by normal phase preparative LC [2X silica gel prepPAK 500 column, hexane:ethyl acetate (1:2 v/v)]. The mixture of kahweol and cafestol was collected as a single peak. The solvent was removed. The yield of the diterpene mixture was 5-7 g.

To a cooled (0°) solution containing 10 g (0.032 mol) of a mixture of kahweol and cafestol in 100 ml of pyridine was added dropwise 0.035 mol of palmitoyl chloride or acetyl chloride with stirring. The mixture was then allowed to warm up to room temperature and stirring was continued overnight. The reaction mixture was poured onto ice and the aqueous solution extracted three times with 150 ml of ether. The ethereal extracts were combined, washed with 6N HCl until all the pyridine was neutralized. The organic layer was washed with saturated $NaHCO_3$ solution and water. Evaporation of the solvent left the palmitates which were separated by preparative LC with silver nitrate impregnated silica gel collumns [hexane:ethyl acetate (2:1 v:v); flow rate - 200 ml/min].[3] The yield of 1a and 2a were 3.5 g (20%) and 2.5 g (14%) respectively; the acetates of kahweol and cafestol (1b and 2b) were similarly obtained in 28% (3.2 g) and 20% (2.3 g) yields respectively. These esters were identical to those previously reported by NMR, IR, and MS determinations.[1,4,5]

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SYNTHESIS OF 3,4-DIPHENYL-1,2,3,4-TETRAHYDROISOQUINOLINES

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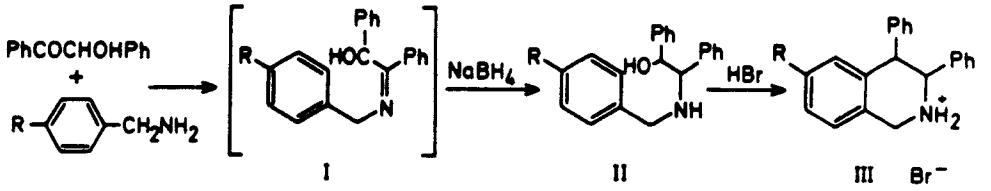
Earlier a convenient synthesis of 1,2,3,4-tetrahydroisoquinolines[1] was developed from ω-bromoalkylamino compounds and aluminium chloride.[2] Still many mono as well as disubstituted tetrahydroisoquinolines are lacking.[3] This note describes a synthesis of 3,4-diphenyl-1,2,3,4-tetrahydroisoquinolines (III) by cyclizationnn of 2-benzylamino-1,2-diphenylethanols (II) in boiling hydrobromic acid which may be obtained from benzoins.[4] The structure of III is supported by elemental anallysis as well as IR and NMR evidence.



I II III

a) R = H b) R = CH_3 c) R = Cl

EXPERIMENTAL SECTION

Melting points are uncorrected. Infrared spectra (KBr pellet) were recorded by using a Perkin-Elmer Model 580 spectrometer. Proton NMR spectra ($CDCl_3$ solvent) were obtained with A-60 A instrument using Me_4Si as internal standard.

2-Benzylamino-1,2-diphenylethanol (II). Typical Procedure.- Benzoin (10.0 g) and freshly distilled benzylamine (10.0 g), were boiled under reflux in