Synthesis of Oligoethylene Glycol Ethers from the Seed Oil of *Vernonia anthelmintica*

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ABSTRACT: The seed oil of *Vernonia anthelmintica* on reaction with diols (mono-, di-, tri-, or tetraethylene glycols) in the presence of boron trifluoride etherate, followed by saponification and esterification (methanol/H$^+$), gives the oligoethylene glycol ethers: methyl 12(13)-hydroxy-13(12)[2-hydroxy-ethyl-1-oxy]-octadec-9-enoate; methyl 12(13)-hydroxy-13(12)-[5-hydroxy-3-oxapentyl-1-oxy]-octadec-9-enoate; methyl 12(13)-hydroxy-13(12)-[8-hydroxy-3,6-dioxaoctyl-1-oxy]-octadec-9-enoate; and methyl 12(13)-hydroxy-13(12)-[11-hydroxy-3,6,9-trioxaundecyl-1-oxy]-octadec-9-enoate. Methyl 12,13-dihydroxyoctadec-9-enoate is a co-product in all reactions.

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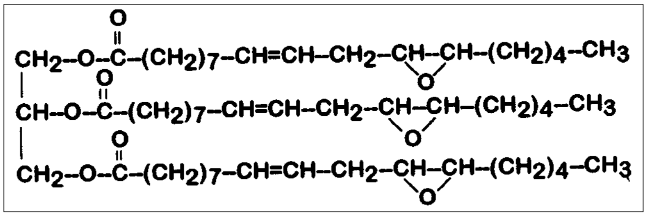
KEY WORDS: Boron trifluoride etherate, ethylene glycols (mono-, di-, tri-, and tetra-), methyl esters, seed oil, synthesis, trivernolein, *Vernonia anthelmintica.*

Oligoethylene glycols (1,2) are important building blocks in the synthesis of nonionic surfactants, crown ethers (3), di- and tetraester ligands (4), and aza-crown ethers (5).

Vernonia anthelmintica is an annual herb. Air-dried seeds of the plant contain about 30% oil, whose major fatty acid is vernolic (*cis*-12,13-epoxy-*cis*-9-octadecenoic) acid (70–80%) (6). The high vernolic acid content of this oil makes it a viable starting material in oligoethylene glycol synthesis.

Ayorinde *et al.* (7) reported that alkali-catalyzed transesterification of vernonia oil gave epoxy esters and that saponification of the oil with potassium hydroxide gave epoxy acids. In both reactions, the epoxy ring remained intact. In contrast, Kleiman *et al.* (8,9) reported that acid-catalyzed transesterification of the oil with methanol resulted in epoxide ring opening and gave the hydroxy methoxy methyl ester derivatives. Ayorinde and coworkers (10) also reported the synthesis of 12-hydroxy-13-alkoxy isomer as the major product in the acid-catalyzed alcoholysis of *V. galamensis* oil.

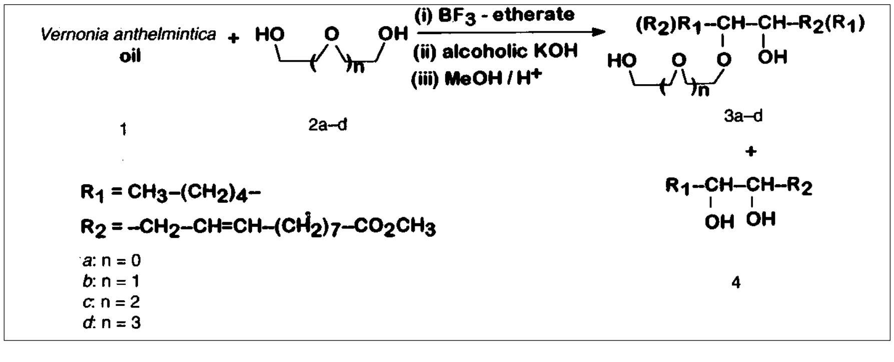


SCHEME 1

In the present study, *V. anthelmintica* oil has been used for the synthesis of oligoethylene glycol ethers. Scheme 1 represents the reactant trivernolein, which is the major triacylglycerol present in *V. anthelmintica* oil.

EXPERIMENTAL PROCEDURES

In Scheme 2, crude *V. anthelmintica* oil (**1**) was obtained by chloroform extraction of the crushed seeds. Mono-, di-, tri-, and tetraethylene glycols (**2a–d**) were procured from a commercial supplier (Sisco Chem., Bombay, India) and were dried in an oven at a temperature of 103 ± 2°C for 4 h and then cooled and stored in a dessicator. BF$_3$-etherate was ob-



tained from Fluka (Buchs, Switzerland) and was used without further purification. Thin-layer chromatography (TLC) was carried out on silica gel-G-coated (0.25-mm thick) plates with petroleum ether/diethyl ether/acetic acid (80:20:1) or (60:40:1) as mobile phase. Spots were visualized with iodine. Infrared (IR) spectra were recorded on a Pye-Unicam SP3-300 spectrophotometer (Cambridge, England) and ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra on a Bruker-AC 200 Fourier transform–NMR spectrometer (Gotthardstrasse, Switzerland) with tetramethylsilane as an internal standard. Mass spectra were recorded on a 2000 QP gas chromatograph–mass spectrophotometer from Shimadzu (Kyoto, Japan).

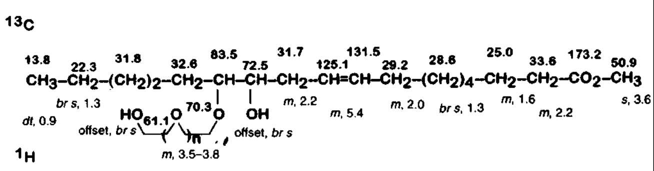
General procedure. To 10 mL of the diol in a 100-mL conical flask was added BF_3-etherate (*ca.* 0.5 mL). The diol solution was stirred at 80°C. *Vernonia anthelmintica* oil (5 g; 0.005 mole, based on an average molecular weight of 926) was added drop-wise to the BF_3-etherate–diol solution over a period of 30 min. The reaction was monitored by TLC and was completed within 3 h. Alcoholic sodium hydroxide (*ca.* 2 N, 50 mL) was added, and the mixture was refluxed for 1 h. The reaction mixture was cooled and acidified with dilute sulfuric acid (*ca.* 30%) and extracted with chloroform. The chloroform layer was washed with water (three times) and dried over anhydrous sodium sulfate. Evaporation of chloroform gave the crude product, which was esterified with dry methanol and concentrated H_2SO_4 (0.5 mL) as the catalyst. The esters, after the usual work-up, were fractionated in a silica gel column with petroleum ether (b.p. 60–80°C), followed by chloroform and chloroform/methanol mixture (98:2) as eluents to obtain the nonoxygenated fraction of *V. anthelmintica* oil, 12,13-dihydroxy ester (**4**), and the oligoethylene glycol ethers (**3a–d**), respectively.

RESULTS AND DISCUSSION

Vernonia anthelmintica seed oil, on reaction with diols (**2a–d**) in the presence of BF_3-etherate as catalyst, followed by saponification and esterification, yielded the oligoethylene glycol ethers (**3a–d**) and the diol (**4**) (Scheme 2), along with the nonoxygenated part of the oil. The oligoethylene glycol ethers (**3a–d**) and the diol (**4**) were obtained in almost equal amounts. However, the production of the glycol ethers showed an increasing pattern with increasing molecular weights of the respective diols. This behavior may be attributed to the decreasing hygroscopicity of the diols (**2a–d**) with increasing molecular weight, which results in the lower yield of **4**.

The IR spectra of all these products had characteristic absorptions at 3400–3500 cm^{-1} for –OH and 1740–1745 cm^{-1} for ester carbonyl stretchings. The ^{1}H and ^{13}C NMR spectra (Scheme 3) of the oligoethylene glycol ethers (**3a–d**) exhibited similar chemical shifts. In the ^{1}H NMR of these products, the methyl ester protons appeared as a singlet at $\delta = 3.6$ ppm, merged with a multiplet ($\delta = 3.5$ to 3.8 ppm) for the alkoxy protons.

In their ^{13}C NMR spectra, the C_{12} and C_{13} compounds with hydroxyl and alkoxy groups were observed at $\delta = 72.5 \pm 0.3$ and 83.5 ± 0.3 ppm, respectively. The ethereal carbons of the alkoxy part were observed at $\delta = 70.3 \pm 0.3$ ppm. The $-CH_2-OH$ carbon appeared at $\delta = 61.1$ ppm, and methyl ester carbon was observed at $\delta = 50.9$ ppm. The olefinic (C_9 and C_{10}) and carbonyl carbons appeared at $\delta = 131.5$, 125.1, and 173.2 ppm, respectively.



SCHEME 3

In the mass spectra of (**3b–d**), the parent ion was invariably absent (Fig. 1). The α cleavage through path b gave an ion at *m/z* 227 (5, 5.2, and 4.3% of the base peak, respectively) and supported the presence of a hydroxyl group at C_{12}. For **3b** and **3c** the presence of alkoxy groups at C_{12} for other positional isomers was indicated by the ions at *m/z* 315 (0.5%) and 359 (0.8%).

In the mass spectra of compounds **3b** and **3c**, the presence of α-cleavage ions (through path d) at *m/z* 189 (4.7%) and 233 (4.6%), respectively, indicates the presence of an alkoxy group at C_{13}, and the ion at *m/z* 101 (1.8, 4.2, and 19.0%) shows the presence of a positional isomer with an hydroxyl group at C_{13} (**3b–d**). The relative intensity of ions due to isomers possessing alkoxy groups at C_{12} was lower than that of alkoxy groups at C_{13}. This indicates the presence of the 13-alkoxy isomer as the major product and the 12-alkoxy isomer as the minor, which could be explained by the lower steric hindrance toward nucleophilic attack at C_{13}. These results are similar to the observations made by Ayorinde *et al.* (10).

The α cleavage through path e gave ions at *m/z* 219 (3.6%) and 263 (1.9%) for **3b** and **3c**. In **3d**, the absence of mass ions

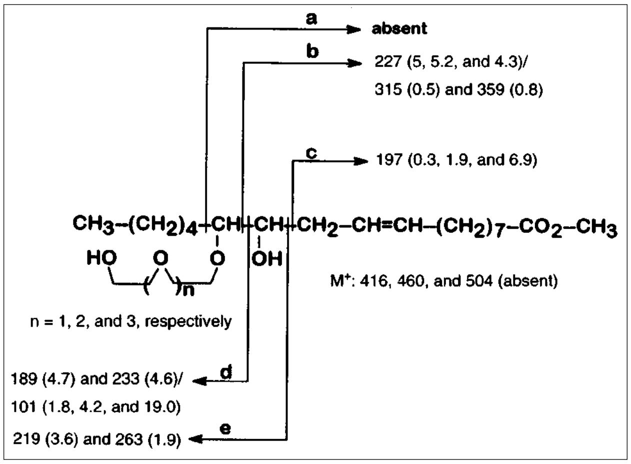


FIG. 1. Resultant mass spectra of α-cleavage ions of oligoethylene glycol ethers (**3b–d**). Numbers represent *m/z* (percentage of the base peak).

at *m/z* 277 (cleavage path d) and 307 (cleavage path e) can be attributed to their higher molecular ion size and is supported by further loss of mass 88 from these α-cleavage ions, leading to ions at *m/z* 189 (7.2%) and 219 (9.1%), respectively. Other major ions resulting from the loss of water, acetate ion, acetic acid, methanol, etc. were also observed in all analyses.

The base peak was observed at *m/z* 45 for **3b** (arising from the ion CH_2–CH_2=^+OH), at *m/z* 89 for the product **3c** (HO^+=CH_2–CH_2–O–CH_2–CH_2), and at *m/z* 56 (HC=CH–CH=^+OH) for the product **3d**. These ion peaks establish the positions of alkoxy and hydroxyl groups in all products.

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