A BRIEF SYNTHESIS OF 3-HYDROXYEICOS-4(*E*)-EN-1-YNE, A COMPONENT OF MARINE SPONGE, *Cribrochalina vasculum*

Bhimashnkar A. KULKARNI, Angshuman CHATTOPADHYAY and Vasant R. MAMDAPUR*

Bio-Organic Division, Mod. Labs., Bhabha Atomic Research Centre, Bombay-400 085, India

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In the recent years considerable attention has been focused on organic compounds of marine origin. Consequently a large array of marine compounds possessing diverse biological activities have been isolated. However, very low natural abundance of these precluded systematic studies of their metabolism and unerroneous bioassay. Stereoselective/specific syntheses of these might be handy in this respect. One such compounds viz. 3-hydroxyeicos-4(*E*)-en-1-yne (*I*), has been recently isolated[1] along with other related acetylenic alcohols from the marine sponge *Cribrochalina vasculum*. The immunosuppressive[2,3] and antitumor properties exhibited by *I* has prompted us to report a short approach to its synthesis from easily accessible starting materials (see Scheme 1). To the best of our knowledge, this constitutes the first report of the synthesis of *I*.

Palmitic acid on decarboxylative bromination[4] furnished the bromide *II* in excellent yield. Alkylation of protected propargyl alcohol *III* with bromide *II* and subsequent deprotection produced the acetylenic alcohol *V* in high yield. This alcohol on oxidation with pyridinium chlorochromate afforded the aldehyde *VI* which on reaction with lithium acetylide gave the required alcohol *VII* in good yield. The latter when subjected to sodium and liquid ammonia reduction without proton donor resulted in the stereoselective reduction of internal alkyne thus providing compound *I*. The spectral data (NMR, IR) of the purified sample were in good agreement with those reported[1].

EXPERIMENTAL

All the boiling points were uncorrected. IR spectra (films) were recorded on a Perkin–Elmer infracord spectrophotometer model 783; wavenumbers in cm^{-1}. ^1H NMR spectra were recorded in deuterio-

* The author to whom correspondence should be addressed.

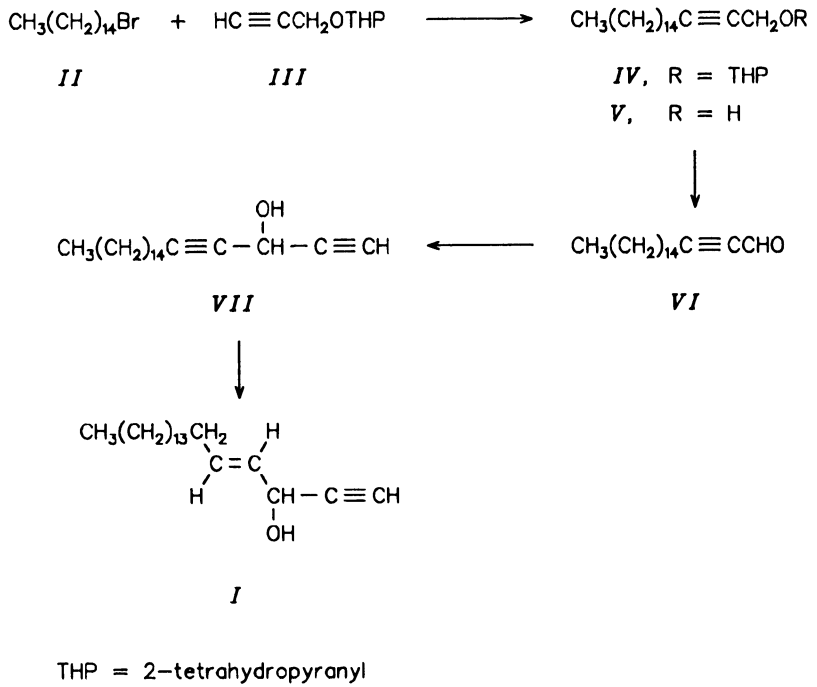
chloroform on a Bruker AC200 (200 MHz) instrument using tetramethylsilane as internal standard. Chemical shifts are given in ppm (δ-scale), coupling constants (*J*) in Hz. All anhydrous reactions were carried out under argon atmosphere with freshly dried solvents. Unless otherwise mentioned, the organic extracts were dried over anhydrous sodium sulfate.

1-Bromopentadecane (*II*)

To a stirred mixture of palmitic acid (32 g, 0.125 mol) and mercury(II) oxide (21 g, 0.097 mol) in carbon tetrachloride (75 ml) at room temperature was added dropwise bromine (6.5 ml; 0.126 mmol) over a period of 30 min. Then the mixture was refluxed for 2 h, cooled, filtered and the solid cake washed with carbon tetrachloride. Concentration of the extract and subsequent column chromatography of the residue over silica gel (hexane) afforded pure *II* (29.3 g, 80%). B.p. 159 – 60 °C/5 mm; IR spectrum: 2 940, 2 860. ^{1}H NMR spectrum: 0.90 bt, 3 H (CH_3); 1.30 bs, 26 H (13 × CH_2); 3.60 t, 2 H (CH_2Br, J = 6).

Octadec-2-yn-1-ol (*V*)

To a stirred solution of 1-(2′-tetrahydropyranyloxy)-2-propyne (*III*; 1.4 g, 0.01 mol) in THF was added 1.5 M solution of n-butyllithium in hexanes (6.6 ml) at −70 °C. After stirring for 1 h the mixture was brought to



SCHEME 1

-50 °C and hexamethylphosphoramide (5 ml) was added. A solution of bromide *II* (2.91 g, 0.01 mol) in THF (10 ml) was introduced into it after 30 min and stirring continued for 5 h. The reaction was quenched with saturated aqueous NH_4Cl solution and the mixture worked up as usual. Removal of solvent led to a residue (crude *IV*) which was dissolved in methanol (100 ml) and a drop of conc. hydrochloric acid added and refluxed for 6 h. Methanol was removed and the product isolated by extracting with ether. This on column chromatography over silica gel (0 – 20% ethyl acetate in hexane) afforded alcohol *V* as crystalline solid (2.03 g 76%). M.p. 58 – 59 °C; IR spectrum: 3 200. ^{1}H NMR spectrum: 0.90 bt, 3 H (CH_3); 1.33 bs, 26 H (13 × CH_2); 1.53 s, 1 H (OH, D_2O exchangeable); 1.9 – 2.3 m, 2 H ($CH_2C{\equiv}C$); 4.30 bs, 2 H (CH_2OH).

Octadec-2-yn-1-al (*VI*)

To a stirred suspension of pyridinum chlorochromate (1.2 g, 5.5 mmol) in dichloromethane (20 ml) at room temperature was added *V* (1.0 g, 3.7 mmol). The mixture was stirred for 2 h and pure aldehyde *VI* was isolated by usual work-up. Yield 0.64 g (65%). IR spectrum: 2 700, 2 280, 2 200, 1 720. ^{1}H NMR spectrum: 0.88 bt, 3 H (CH_3); 1.32 bs, 26 H (13 × CH_2); 1.9 – 2.3 m, 2 H ($CH_2C{\equiv}C$); 9.23 s, 1 H (CHO).

3-Hydroxyeicosa-1,4-diyne (*VII*)

To a suspension of lithium acetylide (7.3 mmol) in liquid ammonia (40 ml) was added a solution of aldehyde *VI* (0.64 g, 2.4 mmol) in THF (10 ml) while passing acetylene gas continuously. After 3 h the reaction was stopped by careful addition of solid ammonium chloride. Usual work-up followed by column chromatography of the residue over silica gel (0 – 15% ethyl acetate in hexane) afforded pure *VII* (0.38 g, 54%). IR spectrum: 3 400, 3 320, 2 200. ^{1}H NMR spectrum: 0.86 bt, 3 H (CH_3); 1.34 bs, 26 H (13 × CH_2); 1.7 s, 1 H (OH, D_2O exchangeable); 1.9 – 2.1 m, 2 H ($CH_2C{\equiv}C$); 2.52 s, 1 H ($C{\equiv}CH$); 4.3 m, 1 H (CH–OH).

3-Hydroxyeicos-4(*E*)-en-1-yne (*I*)

To a solution of Na (0.15 g, 6.5 mol) in liquid ammonia (40 ml) was added a solution of *VII* (0.3 g, 1 mmol) in ether (20 ml). After stirring for 2 h ammonium chloride and ice water were added and the mixture extracted with ether. Solvent removal and column chromatography over silica gel (0 – 15% ethyl acetate in hexane) gave pure *I*. Yield 0.17 g (58 %); IR spectrum: 3 400, 3 310, 960. ^{1}H NMR spectrum: 0.88 bt, 3 H (CH_3, J = 6); 1.30 bs, 26 H (13 × CH_2); 1.56 s, 1 H (OH, D_2O exchangeable); 2.0 – 2.3 m, 2 H ($CH_2C{\equiv}C$); 2.55 s, 1 H ($C{\equiv}CH$); 4.85 m, 1 H (CH–OH); 5.60 dd, 1 H (=CH–CHOH, J = 15; J' = 6); 5.90 dt, 1 H (CH_2–CH=, J = 15; J' =7). GLC: 3% OV-17 column, 200 – 40 °C (temp. prog., 4 °C/min), 40 ml N_2/min, R_t = 10.15 min, 95% purity.

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