

Synthesis and isomerization of enyne-group containing compounds in NaEDA/EDA media

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Dedicated to Professor Kalevi Pihlaja on the occasion of his 60th birthday

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Abstract

A series of conjugated enyne-group and isolated triple bond containing compounds were synthesized and their behavior in superbasic media NaEDA/EDA studied.

Keywords: Conjugated enynes, isomerization, superbases

Introduction

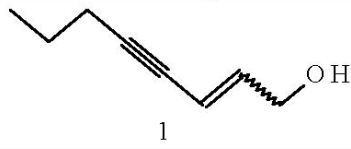
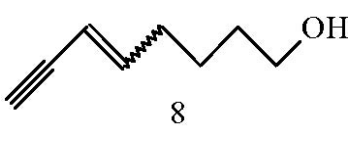

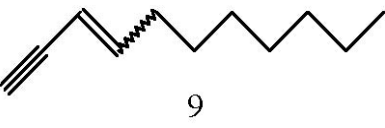
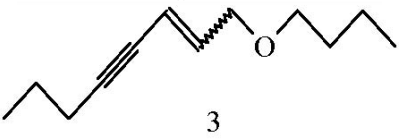

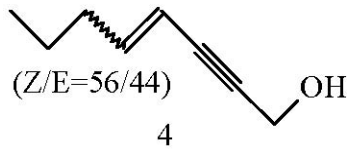
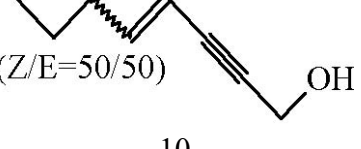
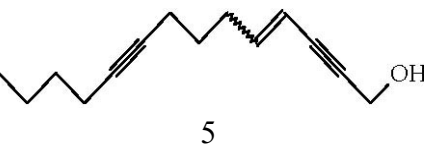
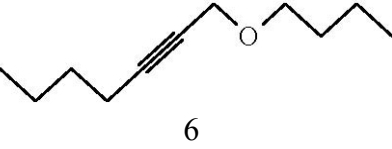
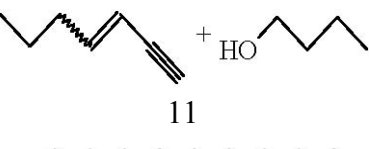
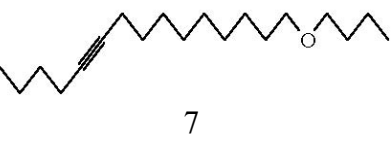
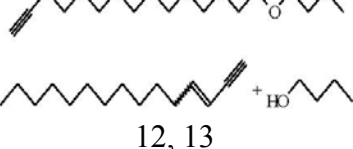
The multipositional migration of the triple bond along the carbon chain in hydrocarbons and alcohols by potassium 3-aminopropanamide was introduced by Brown¹. Later other superbasic systems based on different alkali metal amides of 1,2-diaminoethane and 1,3-diaminopropane for such processes were developed²⁻⁵. The triple bond usually migrates to the terminal position of carbon chain but in branched chain compounds⁶ and carboxylic acids^{7, 8}, several other compounds have been obtained. Remissive ET al.^{9, 10} have described the successful migration of conjugated diyne group in hydrocarbons and alcohols with LiEDA/EDA. The conjugated enyne group was still isomerized only at 1-position in (Z, E)-2-hexen-3-yn-1-ol by influence of KNH₂/NH₃¹¹. The lack of the data on multipositional isomerization of enyne-group inspired us to investigate this type of reaction on different model compounds to show the scope and limitations of this transformation.

Results and Discussion

Recently, we have described a successful isomerization of (Z, E)-2-octen-4-yn-1-ol (**1**) to (Z, E)-5-octen-7-yn-1-ol (**8**) by NaEDA/EDA¹². Here, we extend this study to other possible enynic substrates. The present results (cf. Table) indicate that the presence of functional groups in conjugated enynes influence substantially the isomerization. For example, (Z, E)-2-octen-4-yn-1-

ol (**1**) (Z/E=33/67) isomerizes by the influence of NaEDA/EDA to (Z, E)-5-octen-7-yn-1-ol (**8**) (Z/E=65/35) with high yield. On the other hand, the isomerization product of (Z, E)-4-undecen-6-yne (**2**) (Z/E=66/34) was contaminated with substantial amount of polymeric side products. After chromatographic separation on silica column, the (Z, E)-3-undecen-1-yne (**9**) (Z/E=52/48) was obtained with 44% yield. The change of the hydroxy group in compound (**3**) (Z/E=50/50) to butoxy group led even at the mildest reaction conditions (LiEDA/EDA) only to the polymeric product.

It appears that the order of double and triple bond with respect of the functional group in enynol also influences the isomerization. Thus, the position of enyne group in (Z, E)-4-octen-2-yn-1-ol (**4**) (Z/E=56/44) remained unchanged and only Z-E isomerization (**10**) (Z/E=50/50) was observed in NaEDA/EDA.

Initial compound	Isomerization product	Yield, %
 1	 8	98
 2	 9	44
 3	POLYMER + HO 	-
 (Z/E=56/44) 4	 (Z/E=50/50) 10	95
 5	POLYMER	-
 6	 11	65*
 7	 12, 13	60**

* Total yield, Compound (**11**)/1-butanol=1/1.

** Total yield, (**12**)/(13)=1/1, (**13**)/1-butanol=1/1.

By using this knowledge, we synthesized the compound (**5**) (Z/E=47/53) to test the stability of the enynol group and the reactivity of the isolated triple bond in its neighborhood. Unfortunately the product polymerized even using LiEDA/EDA.

Due to the polymerization of 1-butoxy-(Z,E)-2-octen-4-yne (**3**) (Z/E=50/50), the behavior of simple propargylic ether in NaEDA/EDA was tested. Such ethers are known as starting materials for the preparation of enynes by influence of $\text{NaNH}_2/\text{NH}_3$ ¹³. In our experiment with NaEDA/EDA, the corresponding (Z, E)-3-hepten-1-yne (**11**) was obtained with good yield (Z: E=1:2). In order to study the influence of the position of the triple bond with respect of the alkoxy group, we synthesized 1-butoxy-10-pentadecyne (**7**). By influence of NaEDA/EDA, two products containing triple bond were obtained as the 1:1 mixture with total yield of 60%. The mixture was separated by column chromatography on silica. One of these products was the terminal enyne (Z/E=50/50) whereas the other was determined as the butoxy derivative with terminal triple bond. According to those results, the triple bond can migrate to the both ends of carbon chain because several positions may be deprotonated and in equilibrium with each other. When the triple bond moves to the alkoxy group, the butanol is eliminated and after the isomerization the compound with the terminal enyne is formed¹³. Another terminal position for the triple bond migration can be localized at the other end of molecule because of higher acidity of the acetylenic proton.

It has to be concluded that Na and LiEDA/EDA are powerful superbases for the multipositional isomerization of enyne-group in hydrocarbons and alcohols. These superbases are though too strong in the case of some compounds and cause polymerization.

Experimental Section

General Procedures. ¹H and ¹³C NMR spectra were measured with Bruker AC 200P (Spektrospin AG, Switzerland) spectrometer at 200 and 50 MHz, respectively. IR spectra were recorded on Specord M82 Spectrometer (Carl Zeiss, Jena). GLC analyses: Chrom-5 (Laboratorni Pstroje, Praha), glass columns: 2.5*3mm, 20% Carbowax 20M, Chromosorb W/AW-DMCS, 100-120 mesh; 5% PDEAS, Chromosorb W/HP AW-DMCS, 100-120 mesh; and fused silica capillary column, 0.33*24m, SGE, BP10. For thin layer chromatography Silufol UV₂₅₄ (Chavalier) plates with silica gel were used. Preparative chromatography was carried out on columns packed with 40-63 μm silica gel. Reagents and chemicals were obtained from Aldrich Chemical Company (USA) and from REACHIM (USSR).

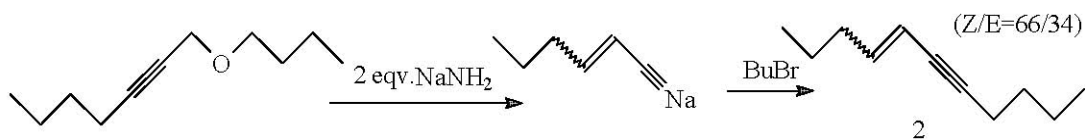
All isomerization experiments were done under dry and oxygen-free Ar-atmosphere. Ar was passed through the column (2.5*23 cm) with Ni (CrO₂)₂ granulated catalyst as oxygen bonding agent and through the column (4*18 cm) with molecular sieves 4Å to remove H₂O and CO₂. The batch of ethylenediamine (EDA) was distilled first from KOH and then two times above Na under Ar-atmosphere. For every experiment EDA was distilled freshly from Na under argon.

General Procedures. To a dry stirred EDA (3 mL) under Ar-atmosphere NaNH_2 (0.195g, 0.005 mol) was added and the mixture was stirred at room temperature until the gray colour changed to violet (0.5 h). The compound studied (0.001 mol) was added to 1.7M NaEDA/EDA solution. The stirring was continued and the reaction was monitored by GLC. When reaction was over, the mixture was hydrolyzed by ice water, extracted with ether and washed first with the 10% HCl solution, then with the saturated solutions of NaHCO_3 and NaCl. The organic phases were dried over MgSO_4 and concentrated *in vacuo*. The remaining brown liquid was purified using column chromatography on silica.

LiEDA/EDA (1.2M solution) was obtained by the reaction of EDA with Li (0.042g, 0.006 mol) during 0.5 hour until the colour of the mixture changed from blue to white.

(Z,E)-2-Octen-4-yn-1-ol (1). Described in ref. 12.

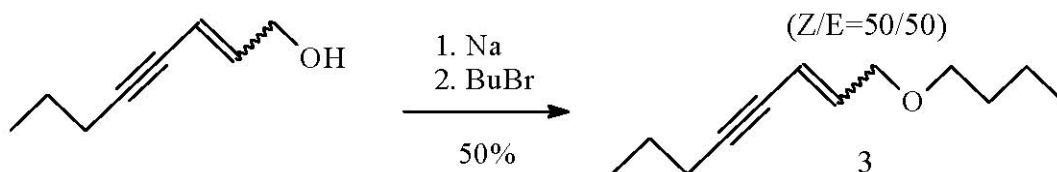
(Z, E)-4-Undecen-6-yne (2). Prepared analogously to the published method¹⁵ by the following scheme:



^1H NMR (CDCl_3) δ 6.15-5.75 (1H, m, $-\text{CH}_2-\text{CH}=\text{}$), 5.52-5.36 (1H, m, $=\text{CH}-\text{C}\equiv$), 2.20-1.98 (4H, m, $-\text{CH}_2-\text{C}\equiv$, $-\text{CH}_2-\text{CH}=\text{}$), 1.6-1.3 (6H, m, 3x $-\text{CH}_2-$), 0.98-0.82 (6H, m, 2x CH_3); ^{13}C NMR (CHCl_3) δ 142.9 (4- C_E), 142.1 (4- C_Z), 110.3 (5- C_E), 109.8 (5- C_Z), 94.38 (7- C_E), 88.62 (7- C_Z), 79.34 (6- C_E), 77.56 (6- C_Z), 35.11 (3- C_E), 32.17 (3- C_Z), 31.16 (9-C), 22.30 (2- C_Z), 22.19 (2- C_E), 22.09 (8- C_E), 22.05 (8- C_Z), 19.31 (10- C_Z), 19.15 (10- C_E), 13.75 (1-C), 13.62 (11-C); IR (KBr) 3024, 1660, 956, 733 cm^{-1} .

(Z, E)-3-Undecen-1-yne (9). ^1H NMR (CDCl_3) δ 6.15-5.90 (1H, m, $=\text{CH}-\text{CH}_2-$), 5.55-5.35 (1H, m, $\equiv\text{C}-\text{CH}=\text{}$), 3.06/2.76 (1H, 2x d, $\text{HC}\equiv$, cis/trans), 2.40-1.95 (2H, m, $-\text{CH}_2-\text{CH}=\text{}$), 1.55-1.10 (10H, m, 5x $-\text{CH}_2-$), 0.93 (3H, t, CH_3); ^{13}C NMR (CHCl_3) δ 146.9 (4- C_E), 146.1 (4- C_Z), 108.6 (3- C_E), 108.1 (3- C_Z), 81.12 (1- C_E), 82.66 (2- C_Z), 80.66 (2- C_E), 75.49 (1- C_Z), 33.03 (5- C_E), 31.83 (5- C_Z), 29.76 (6-C, 7-C, 8-C), 29.12 (9-C), 22.68 (10-C), 14.06 (11-C); IR (KBr) 3320, 3024, 2110, 1656, 962, 764, 641 cm^{-1} .

1-Butoxy-(Z, E)-2-octen-4-yne (3). Obtained by the scheme¹⁴:

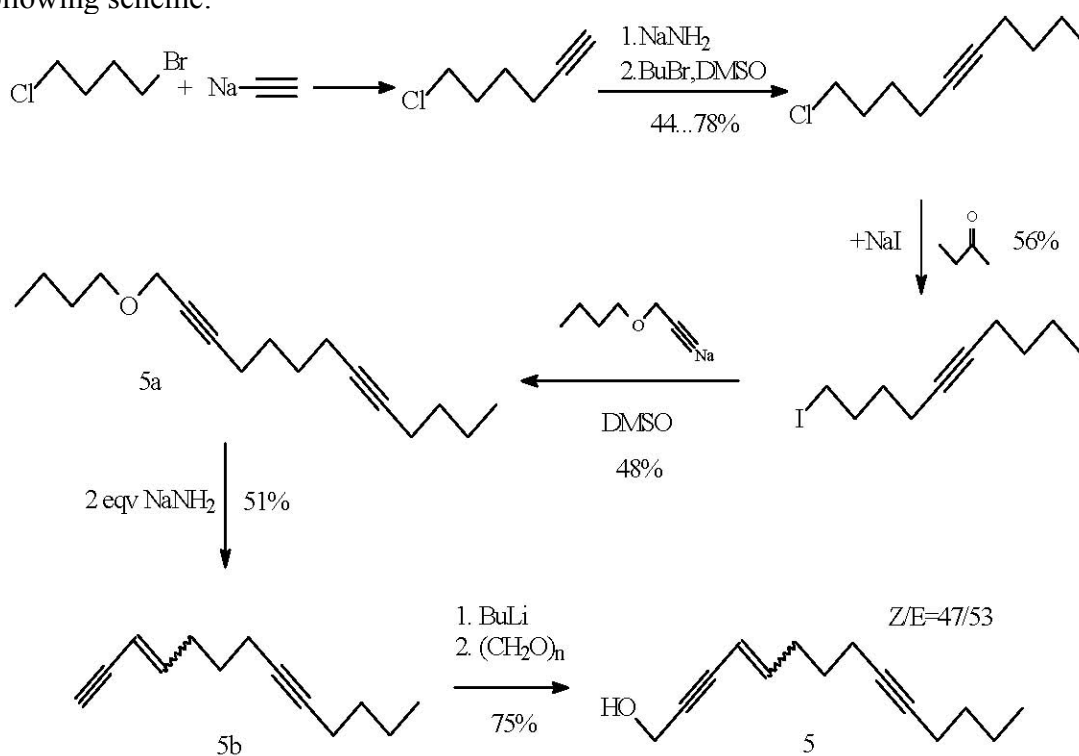


^1H NMR (CDCl_3) δ 6.15-5.55 (2H, m, $=\text{CH}-\text{CH}_2-$, $\equiv\text{C}-\text{CH}=\text{}$), 4.22/3.97 (2H, 2x d, $=\text{CH}-\text{CH}_2-$, cis/trans), 3.55-3.35 (2H, m, $-\text{O}-\text{CH}_2-\text{CH}_2-$), 2.35-2.20 (2H, m, $-\text{CH}_2-\text{C}\equiv$), 1.7-1.2 (6H, m, 3x $-\text{CH}_2-$), 1.10-0.82 (6H, m, 2x CH_3); ^{13}C NMR (CHCl_3) δ 138.4 (2- C_E), 138.3 (2- C_Z), 112.2 (3-

C_E), 111.8 (3- C_Z), 96.19 (5- C_E), 90.77 (5- C_Z), 78.81 (4- C_E), 76.80 (4- C_Z), 70.68 (1- C_E), 70.35 (1- C_Z), 68.48 (1'- C), 31.98 (2'- C), 22.29 (7- C), 21.61 (6- C_Z), 21.47 (6- C_E), 19.44 (3'- C), 13.90 (4'- C), 13.48 (8- C); IR (KBr) 3024, 1658, 1103, 974, 764 cm^{-1} .

(Z, E)-4-Octen-2-yn-1-ol (4). Prepared according to the literature¹¹. Bp: 118-121 °C/5-6 mmHg. ^1H NMR (CDCl_3) δ 6.25-5.85 (1H, m, =CH- CH_2 -), 5.55-5.45 (1H, m, $\equiv\text{C-CH=}$), 4.41/4.36 (2H, 2x s, - $\text{CH}_2\text{-O-}$, cis/trans), 2.76 (1H, s, -OH), 2.35-2.0 (2H, m, $\text{CH}_3\text{-CH}_2\text{-CH}_2$ -), 1.55-1.30 (2H, m, $\text{CH}_3\text{-CH}_2$ -), 1.0-0.85 (3H, m, CH_3 -); ^{13}C NMR (CHCl_3) δ 145.3 (5- C_E), 144.4 (5- C_Z), 109.2 (4- C_E), 108.6 (4- C_Z), 91.51 (3- C_Z), 85.89 (3- C_E), 84.55 (2- C_E), 82.59 (2- C_Z), 51.58 (1- C_Z), 51.48 (1- C_E), 35.12 (6- C_E), 32.32 (6- C_Z), 22.13 (7- C_Z), 21.95 (7- C_E), 13.88 (8- C_Z), 13.55 (8- C_E); IR (KBr) 3321, 3018, 1660, 1011, 956, 733, 616 cm^{-1} .

(Z, E)-4-Tetradecen-2,9-diyn-1-ol (5). Prepared according to the literature¹¹ in a similar way by the following scheme:



Intermediates and final products were purified by column chromatography (EtAc/Hexane=1/3) and characterized by NMR and IR spectra:

1-Butoxy-2,8-tridecadiyne (5a). ^1H NMR (CDCl_3) δ 4.09 (2H, t, $J=2.2$, -O- $\text{CH}_2\text{-C}\equiv$), 3.48 (2H, t, $J=6.6$, - $\text{CH}_2\text{-CH}_2\text{-O-}$), 2.30-2.08 (6H, m, - CH_2 -), 1.65-1.52 (2H, m, - CH_2 -), 1.48-1.32 (10H, m, 5x - CH_2 -), 0.97-0.85 (6H, m, 2x CH_3 -); ^{13}C NMR (CHCl_3) δ 86.13 (3- C), 80.54 (2- C), 79.57 (9- C), 76.74 (8- C), 69.65 (1'- C), 58.57 (1- C), 31.81 (2'- C), 31.42 (11- C), 28.39 (5- C), 27.91 (6- C), 22.03 (12- C), 19.46 (4- C), 18.52 (7- C), 18.45 (10- C), 18.41 (3'- C), 13.88 (4'- C), 13.62 (13- C); IR (KBr) 1141, 1098 cm^{-1} .

(Z, E)-3-Tridecen-1,8-diyn-1-ol (5b). ^1H NMR (CDCl_3) δ 6.32-5.92 (1H, m, =CH- CH_2 -), 5.55-5.40

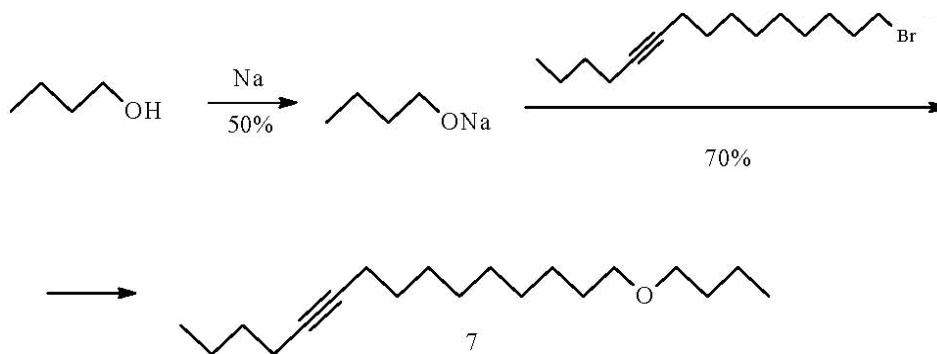
(1H, m, $\equiv\text{C}-\text{CH}=\text{}$), 3.08/2.78 (1H, 2x d, $\text{HC}\equiv$, cis/trans), 2.55-2.05 (6H, m, 3x $-\text{CH}_2-$), 1.7-1.2 (6H, m, 3x $-\text{CH}_2-$), 1.02-0.80 (3H, m, CH_3 -); ^{13}C NMR (CHCl_3) δ 145.7 (4- C_E), 144.9 (4- C_Z), 109.4 (3- C_E), 108.8 (3- C_Z), 82.46 (2- C_Z), 81.51 (1- C_E), 80.98 (2- C_E), 80.73 (8- C_E), 80.39 (8- C_Z), 79.52 (9- C_Z), 79.25 (9- C_E), 75.84 (1- C_Z), 32.02 (11- C_E), 31.33 (11- C_Z), 29.76 (5- C_E), 29.54 (5- C_Z), 28.46 (6- C_E), 28.08 (6- C_Z), 21.99 (12-C), 18.50 (7-C), 18.24 (10-C), 13.61 (13-C); IR (KBr) 3308, 3024, 2110, 1656, 962, 746, 635 cm^{-1} .

(Z, E)-4-Tetradecen-2.9-diyne-1-ol (5). ^1H NMR (CDCl_3) δ 6.22-5.83 (1H, m, $=\text{CH}-\text{CH}_2-$), 5.6-5.45 (1H, m, $\equiv\text{C}-\text{CH}=\text{}$), 4.40/4.35 (2H, 2x s, $-\text{O}-\text{CH}_2-\text{C}\equiv$, cis/trans), 3.20 (1H, s, $\text{HO}-$), 2.50-2.05 (6H, m, 3x $-\text{CH}_2-$), 1.70-1.23 (6H, m, 3x $-\text{CH}_2-$), 1.02-0.82 (3H, m, CH_3 -); ^{13}C NMR (CHCl_3) δ 144.3 (5- C_E), 143.4 (5- C_Z), 109.8 (4- C_E), 109.3 (4- C_Z), 92.00 (3- C_Z), 86.32 (2- C_E), 84.22 (3- C_E), 82.22 (9- C_E), 81.00 (10- C_Z), 80.77 (9- C_Z), 79.77 (5- C_E), 79.38 (2- C_Z), 51.39 (1- C_E), 51.31 (1- C_Z), 32.06 (12- C_E), 31.34 (12- C_Z), 29.52 (6- C_E), 28.55 (6- C_Z), 28.21 (7-C), 22.00 (13-C), 18.49 (8-C), 18.24 (11-C), 13.61 (14-C); IR (KBr) 3364, 3024, 1660, 1017, 962, 740, 628 cm^{-1} .

1-Butoxy-2-heptyne (6). Prepared from propargyl alcohol according to the literature¹¹. Bp: 75-80 $^\circ\text{C}/3-4$ mmHg.

(Z, E)-3-Hepten-1-yne (11). ^1H NMR (CDCl_3) δ 6.35-5.90 (1H, m, $=\text{CH}-\text{CH}_2-$), 5.53-5.38 (1H, m, $\equiv\text{C}-\text{CH}=\text{}$), 3.06/2.76 (1H, 2x d, $\text{HC}\equiv$, cis/trans), 2.4-2.0 (2H, m, $-\text{CH}_2-\text{CH}=\text{}$), 1.55-1.30 (2H, m, $-\text{CH}_2-$), 0.93 (3H, t, CH_3 -); ^{13}C NMR (CHCl_3) δ 146.5 (4- C_E), 145.8 (4- C_Z), 108.9 (3- C_E), 108.4 (3- C_Z), 82.66 (2- C_E), 81.20 (1- C_E), 80.66 (2- C_E), 75.59 (1- C_Z), 35.14 (5- C_E), 32.35 (5- C_Z), 22.14 (6- C_E), 21.92 (6- C_Z), 13.68 (7- C_Z), 13.57 (7- C_E); IR (KBr) 3302, 3024, 2104, 1660, 962, 616 cm^{-1} .

15-Butoxy-5-pentadecyne (7). Prepared according to the literature¹⁴ by following scheme:



^1H NMR (CDCl_3) δ 3.40/3.39 (4H, 2x t, $-\text{CH}_2-\text{O}-\text{CH}_2-$, cis/trans), 2.22-2.08 (4H, m, 2x $-\text{CH}_2-\text{C}\equiv$), 1.65-1.22 (22H, m, 11x $-\text{CH}_2-$), 0.98-0.85 (6H, m, 2x CH_3 -); ^{13}C NMR (CHCl_3) δ 80.18 (5-C, 6-C), 71.02 (1'-C), 70.70 (15-C), 32.04 (2'-C), 31.42 (3-C), 29.92 (11-C), 29.58 (12-C), 29.54 (9-C), 29.30 (10-C), 29.19 (8-C), 28.92 (14-C), 26.32 (13-C), 21.99 (2-C), 19.49 (3'-C), 18.84 (7-C), 18.53 (4-C), 13.92 (4'-C), 13.61 (1-C); IR (KBr) 1092 cm^{-1} .

15-Butoxy-1-pentadecyne (12). ^1H NMR (CDCl_3) δ 3.40/3.39 (4H, 2x t, $-\text{CH}_2-\text{O}-\text{CH}_2-$, cis/trans), 2.23-2.12 (4H, m, 2x $-\text{CH}_2-\text{C}\equiv$), 1.93 (1H, t, $J=2.4$, $\text{HC}\equiv$), 1.63-1.18 (26H, m, 11x $-\text{CH}_2-$), 0.92 (3H, t, $J=7.2$, CH_3 -); ^{13}C NMR (CHCl_3) δ 85.68 (2-C), 71.95 (1'-C), 71.61 (15-C),

68.98 (1-C), 32.91 (2'-C), 30.81 (7-C), 30.57 (9-C, 10-C, 11-C, 12-C), 30.48 (14-C, 8-C), 30.09 (6-C), 29.75 (4-C), 29.52 (5-C), 27.21 (13-C), 20.37 (3'-C), 19.39 (3-C), 14.86 (4'-C); IR (KBr) 3315, 1116 cm^{-1} .

(Z,E)-3-Pentadecen-1-yne (13). ^1H NMR (CDCl_3) δ 6.23-5.90 (1H, m, =CH-CH₂-), 5.55-5.35 (1H, m, $\equiv\text{C}-\text{CH}=\text{}$), 3.06/2.76 (1H, 2x d, HC \equiv , cis/trans), 2.4-2.0 (2H, m, -CH₂-CH=), 1.55-1.05 (18H, m, 9x -CH₂-), 0.91 (3H, t, CH₃-); ^{13}C NMR (CHCl_3) δ 146.8 (4-C_E), 146.1 (4-C_Z), 108.6 (3-C_E), 108.1 (3-C_Z), 82.42 (2-C_E), 81.12 (1-C_E), 80.44 (2-C_E), 75.48 (1-C_Z), 33.03 (5-C_E), 31.84 (5-C_Z), 29.76 (6-C, 7-C, 8-C, 9-C, 10-C), 29.45 (11-C), 29.22 (12-C), 29.10 (13-C), 22.62 (14-C), 14.12 (15-C); IR (KBr) 3315, 3024, 2104, 1656, 962, 758, 616 cm^{-1} .

Acknowledgements

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