SUMMARY

1. The direct bromination of NDPs or NTPs followed by catalytic dehalogenation of the bromine derivatives of gaseous tritium may be a convenient method for synthesizing nucleotides labeled in position 5 of the pyrimidine or position 8 of the purine nucleus.

2. The bromination of a mixture of the mono-, di-, and triphosphates of a given nucleoside followed by dehalogenation of the mixture of bromine derivatives and also isotope exchange of the mixture of nucleotides are effective methods which permit all three nucleotides with different degrees of phosphorylation to be obtained with fairly high molar activities.

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SYNTHESIS OF (Z)-TETRADEC-11-EN-1-OL AND (Z)-HEXADEC-11-EN-1-OL FROM DODECANE-1,12-DIOL

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A method has been developed for obtaining (Z)tetradec-11-en-1-ol and (Z)-hexadec-11-en-1-ol via dodec-11-yn-1-ol.

(Z)- and (E)-Tetradec-11-en-1-ols and (Z)- and (E)-hexadec-11-en-1-ol and also the (Z)- and (E)-tetradec-11-en-1-yl acetates, the (Z)- and (E)-tetradec-11-enals, the (Z)- and (E)-hexadec-11-en-yl acetates, and the (Z)-hexadec-11-enal obtained from them are sex attractants of a large number of butterflies and moths (*Lepidoptera*) [1]. Thus, a mixture of (Z)-hexadec-11-enal and (Z)-tetradec-11-enal in a ratio of 3:1 is the sex pheromone of the cotton bollworm (*Heliothis armigera*), which is widespread in Azerbaidzhan and Uzbekistan [2].

One of the commonest methods for the synthesis of the pheromones is the acetylene synthesis, where the main intermediate compound is dodec-11-yn-1-ol (I) [1, 3, 4]. We have developed the synthesis of (I) from dodecane-1,12-diol (II), easily obtained by the reduction of dodecane-1,12-dioic acid, which is produced on the industrial scale. The synthesis of (I) from (II) was performed by two routes:

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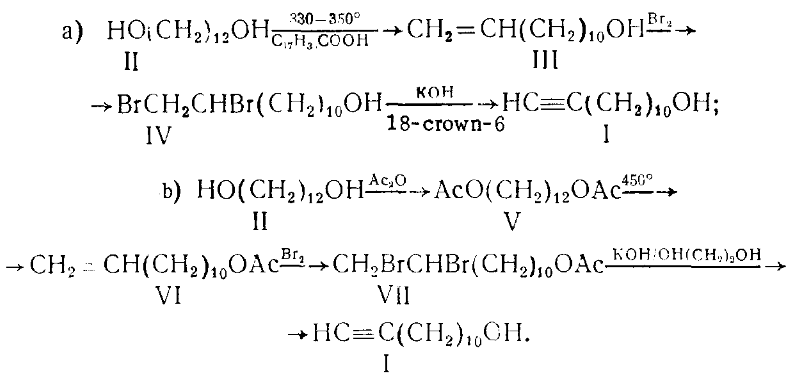
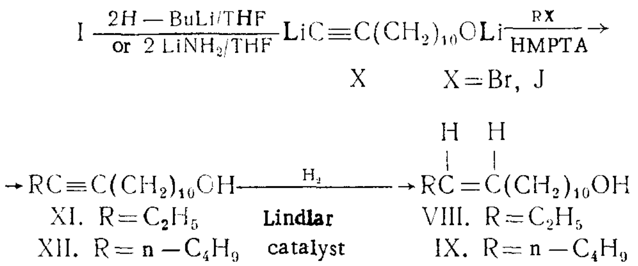


$$a)\ \underset{II}{HO(CH_2)_{12}OH} \xrightarrow[C_{17}H_{35}COOH]{330-350^\circ} \underset{III}{CH_2=CH(CH_2)_{10}OH} \xrightarrow{Br_2} \underset{IV}{BrCH_2CHBr(CH_2)_{10}OH} \xrightarrow[18\text{-crown-}6]{KOH} \underset{I}{HC\equiv C(CH_2)_{10}OH};$$

$$b)\ \underset{II}{HO(CH_2)_{12}OH} \xrightarrow{Ac_2O} \underset{V}{AcO(CH_2)_{12}OAc} \xrightarrow{450^\circ} \underset{VI}{CH_2=CH(CH_2)_{10}OAc} \xrightarrow{Br_2} \underset{VII}{CH_2BrCHBr(CH_2)_{10}OAc} \xrightarrow{KOH/OH(CH_2)_2OH} \underset{I}{HC\equiv C(CH_2)_{10}OH}.$$

According to the first route (II) was converted by selective dehydration at 330-350°C in the presence of a mixture of stearic and palmitic acids [5] into dodec-11-en-1-ol (III) with a yield of 71%. The bromination of (III) under the usual conditions led to 1,2-dibromododecan-12-ol (IV) which, on treatment with KOH in the presence of 18-crown-6 ether in petroleum ether smoothly gave (I). By the second route (II) was converted with acetic anhydride into 1,12-diacetoxydodecane (V), which, in pyrolysis at 450°C formed mainly dodec-11-en-1-yl acetate (VI), together with dodeca-1,11-diene. The alkaline hydrolysis of (VI) gave (III). The bromination of VI) at the double bond gave 1,2-dibromo-12-acetoxydodecane, the dehydrobromination of which with KOH in ethylen glycol led to (I). (Z)-Tetradec-11-en-1-ol (VIII) and (Z)-hexadec-11-en-1-ol (XIX) were synthesized from (I) by the following scheme:



$$I \xrightarrow[\text{or } 2\,LiNH_2/THF]{2H-BuLi/THF} \underset{X}{LiC\equiv C(CH_2)_{10}OLi} \xrightarrow[HMPTA]{RX} \quad X=Br,\ J$$

$$\to \underset{\substack{XI.\ R=C_2H_5\\ XII.\ R=n-C_4H_9}}{RC\equiv C(CH_2)_{10}OH} \xrightarrow[\text{Lindlar catalyst}]{H_2} \underset{\substack{VIII.\ R=C_2H_5\\ IX.\ R=n-C_4H_9}}{R\overset{H}{\overset{|}{C}}=\overset{H}{\overset{|}{C}}(CH_2)_{10}OH}$$

The action on (I) of two moles of n-C_4H_9Li in benzene—THF, or two moles of $LiNH_2$ in THF—liquid NH_3 led to the dilithium derivative (X), the alkylation of which with C_2H_5I and n-C_4H_9Br in the presence of HMPTA at 20°C smoothly yielded tetradec-11-yn-1-ol (XI) and hexadec-11-yn-1-ol (XII), respectively. The hydrogenation of (XI) and (XII) over Lindlar catalyst [6] in hexane solution at 15-20°C gave quantitative yields of (VIII) and (IX). On reduction with $LiAlH_4$ in THF—diglyme, the alcohol (XI) was converted into pure (E)-11-tetradec-11-en-1-ol.

EXPERIMENTAL

IR spectra were taken on a UR-20 spectrophotometer in KBr tablets. The individuality of the compounds obtained was determined with the aid of GLC using a Tsvet instrument with a katharometer, helium as the carrier gas at the rate of 40 ml/min, and a 2000 × 3 mm steel column containing 5% of SE-30 on Chromaton-H at a column temperature of 200-240°C. The dodecane-1,12-diol (II) was synthesized by a published method [7].

Dodec-11-en-1-ol (III). A mixture of 12 g of stearic acid, 15 g of palmitic acid, and 25 g of dodecane-1,12-diol was heated at 350°C in the instrument described in [5] at 260 nm Hg with simultaneous distillation of water and (III). Redistillation in vacuum yielded 16.2 g (71%) of (III) $C_{12}H_{24}O$, bp 117-118°C (2 mm).

1,12-Diacetoxydodecane (V). With stirring, 50 g of dodecan-1,12-diol was added to 65 ml of acetic anhydride containing three drops of H_2SO_4 at such a rate that the temperature did not rise above 50°C. After 1 h, the reaction mixture was poured onto 200 g of ice, and the precipitate was filtered off, washed with water to neutrality, and dried in a vacuum desiccator over P_2O_5 to constant weight. This gave 66 g (93%) of (V), $C_{16}H_{30}O_4$, mp 39-40°C (ethanol).

Dodec-11-en-1-yl Acetate (VI). At 450-470°C, 30 g of (V) in 40 ml of ethyl acetate was dripped into a quartz tube packed with glass. The product obtained in the receiver was treated with $NaHCO_3$ solution and extracted with ether, and the extract was dried with Na_2SO_4. After the ether had been driven off, the residue was distilled in vacuum. This gave 15.5 g (65%) of (VI), $C_{14}H_{26}O_2$, mp 108-109°C (1 mm), and 5 g of dodeca-1,11-diene, $C_{12}H_{22}$, bp 106-108°C (5 mm). Compound (VI) was boiled with a solution of 2.5 g of KOH in 20 ml of methanol and 3 ml of water for 8 h. The reaction mixture was diluted with water and extracted with ether, and the ethereal extracts were dried with Na_2SO_4. After elimination of the solvent, the residue was distilled in vacuum, giving 8 g (98%) of (III) with bp 115-116°C (2 mm).

Dodec-11-yn-1-ol (I). A. To a solution of 7.6 g of (III) in 30 ml of dry CCl_4 was slowly added 6.8 g of bromine in 10 ml of CCl_4 at 10-15°C, and the mixture was stirred at 20°C for 0.5 h. Then it was treated with $NaHCO_3$ solution and with water and was dried with Na_2SO_4. After the solvent had been driven off, the residue was distilled, giving 12.7 g (90%) of (IV), $C_{12}H_{23}Br_2O$, mp 175-176°C (1 mm) (with decomposition). A solution of 0.05 g of 18-crown-6-ether in 5 ml of high-boiling petroleum ether and 8 g of (IV) in 30 ml of petroleum ether were added to 4.85 g of powdered KOH. The mixture was stirred at 90-110°C for 10 h. Then it was diluted with water, and the organic layer was separated off and dried with Na_2SO_4. Distillation yielded 3.2 g (75%) of (I) with bp 111-112°C (1 mm), n_D^{20} 1.4900.

B. At 0-1°C, 5.5 g of bromine in 10 ml of CCl_4 was slowly added to a solution of 7.6 g of (VI) in 50 ml of dry CCl_4, and after being stirred for 0.5 h, the reaction mixture was shaken with a solution of $NaHCO_3$, washed with water, and dried. The solvent was distilled off, to give 12.8 g of the 1,2-dibromo derivative (VII), which was stirred with a solution of 10 g of KOH in 50 ml of ethylene glycol first at 50-60°C for 2 h and then at 120-130°C for 12 h. The mixture was diluted with 200 ml of water and was twice extracted with ether, and the ethereal extracts were washed with water and dried with Na_2SO_4. After the solvent had been driven off, the residue was distilled. This gave 4.2 g (70%) of (I), $C_{12}H_{22}O$, bp 105-106°C (0.5 mm), n_D^{20} 1.4901. According to the literature [8]: bp 83-86°C (0.05 mm), n_D 1.4899.

Tetradec-11-yn-1-ol (XI). At 0°C, 35 ml of a 1.24 N solution of n-BuLi in benzene was added to 3.5 g of (I) in 10 ml of absolute THF. Then the temperature was raised to 20°C, and, after 1 h, 3 g of C_2H_5I in 5 ml of HMPTA was added and the mixture was stirred at 20°C for 6 h. Then it was treated with 40 ml of 3 N solution of HCl and extracted with ether–hexane (1:1), and the extract was dried with Na_2SO_4. After the solvent had been driven off, 3.4 g (85%) of (XI), $C_{14}H_{26}O$, was obtained with bp 133-135°C (2 mm), n_D^{20} 1.4646.

Tetradec-11-yn-1-ol (XII). To lithium amide in THF obtained from 1.4 g of lithium and a mixture of 100 ml of liquid ammonia and 40 ml of TF followed by the evaporation of the NH_3 was added 5 g of (I) in 10 ml of THF, and the mixture was stirred at 30-35°C for 0.5 h. Then it was cooled to 10°C and 4 g of n-C_4H_9Br in 5 ml of HMPTA was added and the resulting mixture was stirred at 20°C for 2 h. It was worked up in the usual way, giving 6.1 g (93%) of (XII), with mp 151-153°C (1 mm Hg); n_D^{20} 1.4675.

(Z)-Tetradec-1-en-1-ol (VIII). A solution of 2 g of the alcohol (Xi) in 30 ml of hexane was added to 0.5 g of 5% $Pd/BaSO_4$ with five drops of quinoline, and hydrogenation was carried out at 20°C, until one equivalent of hydrogen had been absorbed. The catalyst was filtered off and the solution was treated with 1% HCl and extracted with ether, the extract was dried with Na_2SO_4 and, after the solvent had been driven off, the residue was distilled. This gave 1.9 g (95%) of (VIII), bp 120-121°C (1.0 mm), n_D^{20} 1.4587. According to the literature [9]: bp 115-118°C (0.5 mm), n_D 1.4577.

(Z)-Hexadec-11-en-1-ol (IX). The hydrogenation of (XII) was carried out as for the preparation of (VIII). This gave (IX), $C_{16}H_{30}O$, mp 137-138°C (1.0 mm), n_D^{20} 1.4590. According to the literature [9]: bp 128-129°C (0.5 mm), n_D^{20} 1.4593.

(E)-Tetradec-11-en-1-ol. At 20-25°C, in a current of argon, 4.6 g (22 mmole) of (IX) was added to a mixture of 40 ml of diglyme, 8 ml of absolute THF, and 1.4 g (37 mmole) of $LiAlH_4$, and the mixture was heated with the distillation of the THF until the temperature had reached 140°C, after which heating was continued for 10 h. Then the mixture was cooled and was carefully poured into ice water, the mixture was acidified with 10% HCl and extracted with ether, and the extracts were washed with water and dried with Na_2SO_4. After the solution had been driven off, the residue was distilled. This gave 4.5 g (97%) of (E)-tetradec-11-en-1-ol with mp 133-134°C (2 mm). n_D^{20} 1.4575. According to the literature [10]: bp 120-122°C (0.2 mm).

SUMMARY

The synthesis has been performed of the sex pheromones (Z)- and (E)-tetradec-11-en-1-ols and (Z)-hexadec-11-en-1-ol by the acetylene scheme from dodec-11-yn-1-ol, for which a simple method of production from dodecane-1,12-diol has been developed.

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