than 30%, we may assume that (I) is isomerized to (II) during the consumption of (II) even though (I) is more stable than (II) (the methyl and isopropyl groups are in an equatorial position).

The modification of the cobalt catalyst by (+)-tartaric acid leads to the greatest content of axial alcohols (IV) + (VI) (up to 90%) with the predominant formation of (VI). This may serve as a convenient method for the preparation of this alcohol, which is the least stable and most difficult to synthesize of all the menthol isomers. The use of the modified binary Ni—Co catalyst is less effective: the content of (VI) is only 45-50%. The nickel catalyst under these conditions is nonselective, which is in accord with our previous work [3].

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SYNTHESIS OF ETHYL 3,7,11-TRIMETHYL-2,4-DODECADIENOATE (HYDROPRENE) FROM 4-METHYLTETRAHYDROPYRAN

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A new pathway has been proposed for the synthesis of the ethyl ester of 3,7,11-trimethyl-2,4-dodecadienoate (juvenoid hydroprene) from available 4-methyltetrahydropyran. The cleavage of the latter to 3-methyl-5-bromo-1-acetoxypentane and coupling with isobutylmagnesium bromide gave tetrahydrogeraniol, which was oxidized to the corresponding aldehyde. The reaction of this aldehyde with allylmagnesium chloride and subsequent oxidation by $O_2/PdCl_2$—CuCl led to 6,10-dimethyl-3E-undecen-2-one, which was converted by a known method to the desired product as a mixture of 70% 2E,4E- and 30% 2Z,4E-stereoisomers. The yield of hydroprene in the six-step synthesis was 32% relative to 4-methyltetrahydropyran.

Ethyl 3,7,11-trimethyl-2,4-dodecadienoate (hydroprene) (I) is one of the most active juvenoids [1]. The reported methods for its synthesis are based on transformations of citral [2], tetrahydrocitral derivatives [3-7], geraniol [8], and 1,5-dimethyl-1-cyclooctene [9].

We have developed a rational pathway for the synthesis of (I) from an available petrochemical product, namely, 4-methyltetrahydropyran (II) [10]. Its cleavage by the action of acetyl bromide in the presence of zinc chloride gives 3-methyl-5-bromo-1-acetoxypentane (III), whose coupling with isobutylmagnesium bromide in the presence of Kochi's catalyst [11] proceeds selectively and leads after alkaline hydrolysis to tetrahydrogeraniol (IV). A nontraditional pathway was used to convert (IV) to 6,10-dimethyl-2-oxo-3E-undecene (VII). This transformation was carried out in three steps with 46% total yield as follows.

The oxidation of alcohol (IV) by pyridinium chlorochromate gave the corresponding aldehyde (V), whose reaction with allylmagnesium chloride led to 6,10-dimethyl-4-hydroxy-1-un-

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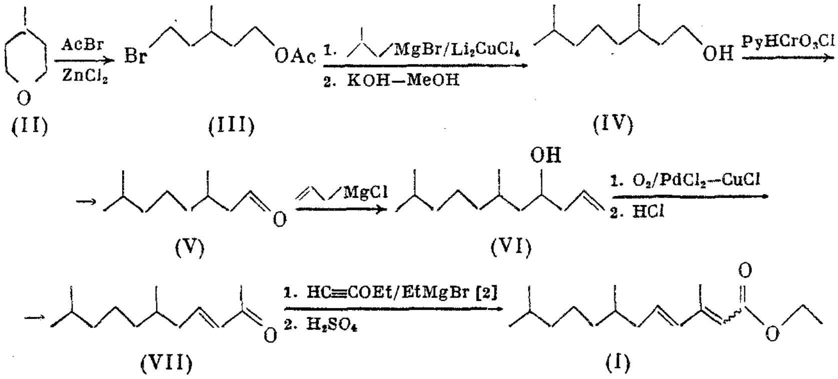
decene (VI). The oxidation of (VI) according to Tsuji et al. [12] with subsequent acid treatment gave ketone (VII). The reaction of (VII) with ethoxyethynylmagnesium bromide in ether at −10°C leads, according to Yanovskaya et al. [2], to the desired product (I) as a mixture of 70% 2E,4E- and 30% 2Z,4E-stereoisomers as indicated by gas-liquid chromatography. The total yield of hydroprene (I) in this six-step synthesis from methyltetrahydropyran (II) is 32%



EXPERIMENTAL

The IR spectra were taken neat on a UR-20 spectrometer. The PMR spectra were taken on a Tesla BS-467 spectrometer in CCl_4 at 60 MHz for (III)-(VII) and on a Tesla BS-567 spectrometer in $CDCl_3$ at 100 MHz for (I). The chemical shifts are given on the δ scale relative to HMDS as an internal standard. The gas-liquid chromatographic analysis was carried out on a Chrom-5 chromatograph using a column packed with 5% SE-30 on Chromaton N-AW-DMCS (0.16-0.20 mm) at 50-300°C. Helium was used as the gas carrier.

3-Methyl-5-bromo-1-acetoxypentane (III). A sample of 83.2 g (0.676 mole) acetyl bromide was added dropwise with stirring to a mixture of 71.2 g (0.71 mole) (II) and 1.57 g $ZnCl_2$ at 20°C. The temperature rose to 45°C. The reaction mixture was heated to 120°C, held for 2 h, cooled to 20°C, and diluted with 1 liter ether. The mixture was washed with saturated aq. $NaHCO_3$ and then with saturated aq. NaCl, dried over $MgSO_4$, and evaporated. Distillation gave 134.4 g (89%) bromoacetate (III), n_D^{23} 1.4660, bp 70-71°C (2 mm). IR spectrum (ν, cm^{-1}): 570 w, 610 w, 645 w, 1245 s, 1740 s. PMR spectrum (δ, ppm): 0.88 d (3H, J = 5 Hz, CH_3), 1.30-1.80 m (5H, CH_2, CH), 1.87 s (3H, CH_3CO), 3.32 t (2H, J = 7 Hz, $H-C^5$), 3.97 t (2H, J = 6.5 Hz, $H-C^1$). Found: C 42.82; H 6.71; Br 35.51%. Calculated for $C_8H_{15}O_2Br$: C 43.07; H 6.78; Br 35.82%.

3,7-Dimethyl-1-octanol (IV). A sample of 1.1 ml 0.1 M Li_2CuCl_4 [11] was added to a solution of 5.34 g (24.0 mmoles) (III) in 10 ml abs. THF at −10°C under argon and stirred for 10 min. Then, a solution of the Grignard reagent obtained from 3.13 g (134.5 mg-atom) magnesium and 15.36 g (112.1 mmoles) isobutyl bromide in 260 ml abs. THF was added dropwise at from −15 to −10°C, stirred for 1 h at −10°C and 15 h at about 20°C, and cooled to 5°C. Then, 50 ml saturated aq. NH_4Cl was added. The mixture was stirred for 0.5 h and extracted thrice with 200 ml ether. The extract was washed twice with 50 ml saturated aq. NaCl and evaporated. A sample of 24 ml methanol and 1.4 g KOH were added to the residue, heated at reflux for 1.5 h, and evaporated. The residue was extracted thrice with 150 ml ether. The extract was washed with saturated aq. NaCl, dried over Na_2SO_4, and evaporated. The residue was subjected to chromatography on silica gel using 7:3 hexane—ether as the eluent to give 3.50 g (92%) alcohol (IV), n_D^{22} 1.4350 [13]. IR spectrum (ν, cm^{-1}): 1070 s, 1385 m, 1470 s, 3200-3600 br. s. PMR spectrum (δ, ppm): 0.83 d (9H, J = 6.5 Hz, CH_3), 1.00-1.65 m (10H, CH_2, CH), 2.82 br. s (1H, OH), 3.50 t (2H, J = 7 Hz, $H-C^1$).

3,7-Dimethyoxyoctanal (V). A solution of 3.16 g (20 mmoles) alcohol (IV) in 15 ml abs. CH_2Cl_2 was added with stirring to a suspension of 6.46 g (30 mmoles) pyridinium chlorochromate in 65 ml abs. CH_2Cl_2 at 20°C under argon. Stirring was continued for 2 h. The mixture was diluted with 200 ml ether and filtered through silica gel. The residue on the filter was washed with 200 ml ether and the filtrate was evaporated. The residue was subjected to chromatography on silica gel using CH_2Cl_2 as the eluent to give 2.84 g (91%) aldehyde (V), n_D^{20} 1.4265 [8]. IR spectrum (ν, cm^{-1}): 1390 m, 1470 m, 1725 s, 2730 m.

4-Hydroxy-6,10-dimethyl-1-undecene (VI) A sample of 5 ml abs. ether and several drops of allyl chloride was added consecutively to 1.35 g (57 mg-atoms) magnesium activated by iodine, and then a mixture of 3.66 g (23.5 mmoles) aldehyde (V) and 3.6 g (47.0 mmoles) allylchloride in 20 ml abs. ether was added at a rate such that ether boiled at a gentle reflux. Stirring was continued for 15 h at about 20°C and cooled to 5°C. Then, 10 ml saturated aq. NH_4Cl was added and stirred for 15 min. The mixture was extracted thrice with 100 ml ether. The extract was washed twice with 30 ml saturated aq. NaCl, dried over Na_2SO_4, and evaporated. The residue was subjected to chromatography on silica gel with 4:1 hexane–ether as the eluent to give 3.86 g (83%) alcohol (VI), n_D^{23} 1.4485. IR spectrum (ν, cm^{-1}): 915 s, 995 m, 1070 m, 1385 m, 1470 s, 1645 m, 3085 m, 3200-3600 br. s. PMR spectrum (δ, ppm): 0.70-0.92 (0.78 and 0.88) m (9H, CH_3), 1.00-1.65 m (10H, CH_2, CH), 1.90-2.20 m (2H, $H{-}C^3$), 3.40-3.76 m (1H, $H{-}C^4$), 4.95-5.16 m (2H, $H{-}C^1$), 5.39-6.00 m (1H, $H{-}C^2$). Found: C 78.52; H 13.18%. Calculated for $C_{13}H_{26}O$: C 78.72; H 13.21%.

6,10-Dimethyl-3E-undecen-2-one (VII). A mixture of 0.38 g (2.1 mmoles) $PdCl_2$, 2.19 g (22.0 mmoles) CuCl, 11.4 ml dimethylformamide, and 1.4 ml water was stirred for 1 h in an oxygen atmosphere, and, then, 3.98 g (20.1 mmoles) alcohol (VI) was added and stirred until 270 ml oxygen was absorbed (about 6 h). Then, 11 ml 10% hydrochloric acid was added. The mixture was heated at reflux for 1 h and extracted with four 100-ml portions of ether. The extract was washed consecutively with saturated aq. NaCl, saturated aq. $NaHCO_3$, and saturated aq. NaCl, dried over Na_2SO_4, and evaporated. The residue was subjected to chromatography on silica gel using 10:1 hexane–ether as the eluent to give 2.40 g (61%) enone (VII), n_D^{20} 1.4540 [2]. The IR and PMR spectra of this sample were identical to those described by Yanovskaya et al. [2].

Ethyl Ester of 3,7,11-Trimethyl-2,4-dodecadienoic acid (I). A solution of 0.71 g (3.6 mmoles) ketone (VII) in 8 ml abs. ether was added dropwise with stirring to a solution of ethoxyethynylmagnesium bromide at −10°C under argon obtained from 0.26 g (10.8 mg-atoms) magnesium, 1.21 g (11.1 mmoles) ethyl bromide, and 0.74 g (10.6 mmoles) ethoxyacetylene in 8 ml abs. ether. The mixture was stirred for 3 h and then warmed to about 20°C over 1 h. A sample of 18 ml 10% sulfuric acid was added, and, after 1 h, 200 ml ether was added. The organic layer was separated, washed consecutively with saturated aq. $NaHCO_3$ and aq. NaCl, dried over $MgSO_4$, and evaporated. The residue was subjected to chromatography on silica gel with CH_2Cl_2 as the eluent to give 0.76 g (84%) hydroprene (I), n_D^{20} 1.4850 [2]. The IR and PMR spectra of this sample were identical to those described by Yanovskaya et al. [2].

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