A versatile approach to the synthesis of 9(*Z*)-unsaturated acyclic insect pheromones from undec-10-enoic acid

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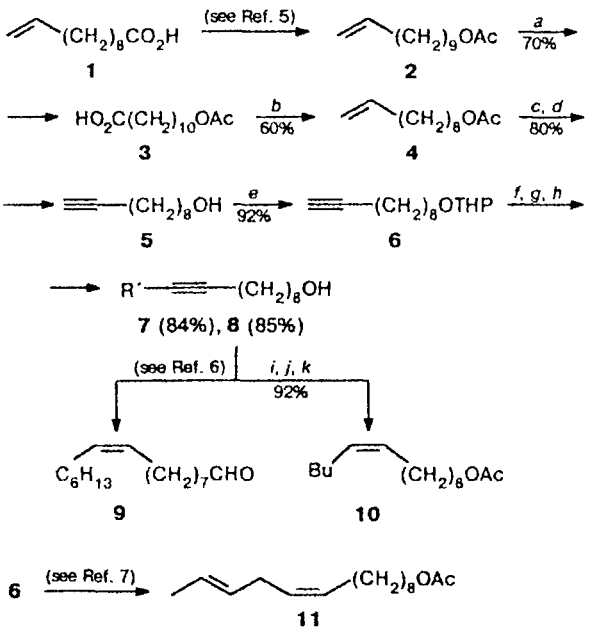
A general approach to the synthesis of 9(*Z*)-unsaturated acyclic insect pheromones from undec-10-enoic acid was developed. The method comprises the conversion of the acid into undec-10-enyl acetate, shortening of its carbon chain to afford dec-9-enyl acetate (*via* 11-acetoxyundecanoic acid), and a two-step transformation of the latter into the key intermediate, dec-9-yn-1-ol, by sequential bromination—dehydrobromination. The elimination of two HBr molecules from the dibromide is effectively performed using Bu^{t}OK in the presence of dibenzo-18-crown-6 as the catalyst.

Key words: 11-acetoxyundecanoic acid, dec-9-enyl acetate, dec-9-yn-1-ol, the Bu^{t}OK—dibenzo-18-crown-6 system, pheromones of *Lepidoptera*.

Undec-10-enoic acid (**1**), which is prepared by thermolysis of castor oil and used in food and chemico-perfumery industries, is finding increasing application in the chemistry of low-molecular-weight insect bioregulators.[1—5]

In this communication, we describe a general approach to the synthesis of alk-9(*Z*)-en-1-ols and their derivatives (Scheme 1) according to which acid **1** is the starting compound, and dec-9-yn-1-ol (**5**) is the key intermediate. The synthetic potential of this approach is demonstrated by the preparation of tetradec-9(*Z*)-en-1-yl acetate (**10**), a typical component of sex pheromones of many species of Lepidoptera of the *Pyralidae*, *Noctuidae*, and *Tortricidae* families, in particular, mill pyralid *Ephestia* (*Cadra*, *Anagasta*) *cautella*, cotton cutworm of the Spodoptera genus, and pine cutworm *Panolis flammea*. A similar synthetic scheme involving intermediate **5** can be used to prepare hexadec-9(*Z*)-enal, a component of the pheromone of cotton cutworm *Heliothis armigera*.[6] In addition, transformations reported in the literature[7] make it possible to convert alkynol **5** into yet another economically important pheromone, tetradeca-9(*Z*),12(*E*)-dien-1-yl acetate (**11**) produced by southern pyralid *Polidia interpunctella* and related *E. kuchniella*, as well as by cotton cutworms *Spodoptera exigua* and *S. littoralis*. Since pheromones of Lepidoptera often contain other functionalized 9(*Z*)-olefins as well, the proposed procedure appears to be a promising general method for the synthesis of many pheromones of insects of the Lepidoptera order. The method is based on the transformation of the initial acid **1** into undec-10-en-1-yl acetate (**2**);[5] the latter is converted into dec-9-en-1-yl acetate (**4**) by a two-step procedure comprising successive hydroboration of compound **2** and Jones oxidation to give acetoxy acid (**3**) and its oxidative decarboxylation. The key dec-9-yn-1-ol (**5**) is obtained in

Scheme 1



R′ = *n*-C_6H_{13} (**7**), Bu^n (**8**)

Reagents: *a.* (*1*) $BF_3 \cdot OEt_2/NaBH_4$, (*2*) H_2CrO_4/H_2SO_4; *b.* $Pb(OAc)_4/Cu(OAc)_2 \cdot H_2O$; *c.* Br_2/CH_2Cl_2; *d.* Bu^{t}OK/DB-18-C-6/*n*-C_6H_{14}; *e.* DHP/TsOH; *f.* $LiNH_2$; *g.* *n*-$C_6H_{13}Br$ (Bu^{n}Br); *h.* TsOH/H_2O—MeOH; *i.* $BuMgBr/Cp_2TiCl_2$; *j.* HCl; *k.* Ac_2O/Py.

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 8, pp. 1637—1639, August, 1998.

80% yield from alkene **4** *via* two steps, namely, successive exhaustive bromination and dehydrobromination (Bu^tOK), carried out in the presence of catalytic amounts of dibenzo-18-crown-6. The tetrahydropyranyl ether (**6**) of alkynol **5** was converted into the acetylenic precursors (**7**, **8**) of pheromones by alkylation of its lithium derivative with the corresponding *n*-alkyl bromides; the former of these products was converted into target compound **9** according to the procedure developed in our previous study.[6] The transformation of disubstituted acetylene **8** into (*Z*)-unsaturated acetate **10** with high (98%) configurational purity was carried out using the Cp_2TiCl_2-catalyzed hydromagnesation with Bu^iMgBr.

Experimental

IR spectra were recorded using a UR-20 instrument in thin films. ^1H NMR spectra were recorded on Tesla BS-567 (100 MHz) and Bruker AM-300 (300 MHz) instruments in $CDCl_3$. GLC analyses were carried out on a Chrom-5 chromatograph (Silicon SE-30 stationary phase, 1.2-m-long column, working temperature 50—300 °C) and on GC-9A Shimadzu instrument (PEG-20M stationary phase, a 25 m×0.2 mm quartz capillary column, working temperature 50—200 °C) using helium as the carrier gas.

11-Acetoxyundecanoic acid (3). A solution of $BF_3 \cdot Et_2O$ (20 mL) in 24 mL of anhydrous THF was added to a stirred suspension of $NaBH_4$ (4.0 g, 105 mmol) in 215 mL of anhydrous THF (0 °C, Ar). After 30 min (0 °C), a solution of unsaturated acetate **2** (45.4 g, 214 mmol) in 300 mL of anhydrous THF was added dropwise, and the reaction mixture was stirred for 1 h at 18—22 °C, allowed to stand for ~10 h, and cooled to 0 °C; then the Jones reagent prepared from CrO_3 (25.7 g, 257 mmol), conc. H_2SO_4 (36 mL), and H_2O (108 mL) was added with intense stirring. The mixture was stirred (0 °C, 1 h → 20 °C, 2 h), THF was evaporated, the residue was extracted with Et_2O (3×100 mL), and the extract was washed with a saturated solution of $NaHCO_3$ (3×100 mL). The combined aqueous solution was washed with Et_2O (2×50 mL), acidified with conc. HCl to pH 2, and extracted with Et_2O (3×100 mL). The extract was dried with $MgSO_4$ and evaporated to give 36.5 g (70%) of acetoxy acid **3**, m.p. 33.0—34.0 °C (*cf.* Ref. 8). IR, ν/cm^{-1}: 1050 (H_2C—O); 1265 (O—C—O); 1730, 1750 (C=O).

Dec-9-en-1-yl acetate (4). At 75 °C (Ar), $Pb(OAc)_4$ (86.7 g, 196 mmol) was added in portions to a suspension of acid **3** (30.0 g, 123 mmol), $Cu(OAc)_2 \cdot H_2O$ (2.85 g, 13.1 mmol), and Py (7 mL) in dry benzene (214 mL). The mixture was refluxed until gas evolution ceased (2—3 h), cooled, diluted with Et_2O (300 mL), and filtered through a layer of SiO_2 (100 g). The filtrate was washed successively with a saturated solution of $NaHCO_3$ and brine, dried with $MgSO_4$, and concentrated. Distillation of the residue gave 14.6 g (60%) of acetate **4**, b.p. 78—80 °C (4 Torr). The ^1H NMR and IR spectral parameters were identical with those described previously.[9]

Dec-9-yn-1-ol (5). At 10—15 °C, a solution of Br_2 (11.7 g, 73 mmol) in 5 mL of dry CH_2Cl_2 was slowly added to a solution of acetate **4** (14.1 g, 71 mmol) in 16 mL of dry CH_2Cl_2. The mixture was stirred at 20 °C for 0.5 h, diluted with 100 mL of CH_2Cl_2, washed successively with a saturated solution of $Na_2S_2O_3$ and brine, dried with $MgSO_4$, and concentrated. The residue (25.3 g) of 9,10-dibromodecan-1-yl acetate (IR, ν/cm^{-1}: 595, 650, 675 (C—Br); 1080 (H_2C—O); 1750 (C=O)) was dissolved in 71 mL of dry hexane, and Bu^tOK (15.8 g, 141 mmol) and dibenzo-18-crown-6 (37 mg) were added (Ar). The reaction mixture was refluxed with stirring until it no longer changed (~24 h, GLC monitoring), cooled, diluted with H_2O (50 mL), and extracted with Et_2O (3×100 mL). The combined extract was dried with Na_2SO_4, concentrated, and distilled to give 8.75 g (80%) of acetylenic alcohol **5**, b.p. 95 °C (0.8 Torr). The ^1H NMR and IR spectral parameters were identical with those described previously.[10]

1-(2-Tetrahydropyranyloxy)dec-9-yne (6). At 10—15 °C, 3,4-dihydro-2*H*-pyran (22.1 g, 263 mmol) was added to a solution of alcohol **5** (8.7 g, 56.5 mmol) and TsOH (0.12 g, 0.7 mmol) in anhydrous Et_2O (167 mL), and the mixture was stirred (20 °C, 20 h), diluted with 200 mL of Et_2O, washed successively with a saturated solution of $NaHCO_3$ and brine, dried with Na_2SO_4, and concentrated to give 12.37 g (92%) of ether **6**. The ^1H NMR and IR spectral parameters were identical with those described previously.[11]

Hexadec-9-yn-1-ol (7). Alkyne **6** (8.5 g, 35.7 mmol) was added to a suspension of lithium amide prepared from Li (0.5 g, 71 mg-at.), $FeCl_3$ (0.05 g), and distilled liquid NH_3 (240 mL). The mixture was stirred (−33 °C, 1 h), then a solution of *n*-hexyl bromide (7.46 g, 45.2 mmol) in anhydrous THF (24 mL) was added, and, immediately after that, distilled DMSO (24 mL) was added. The reaction mixture was stirred until NH_3 completely evaporated, 40 mL of H_2O was added, and the product was extracted with hexane (3×100 mL). The extract was washed with brine and concentrated. The residue (14.55 g) was dissolved in a mixture of MeOH (143 mL) and H_2O (14 mL), TsOH (2.86 g) was added, and the mixture was stirred at 20 °C for 20 h. The solvent was evaporated, the residue was extracted with Et_2O (3×100 mL), and the combined extract was successively washed with a saturated solution of $NaHCO_3$ and brine, dried with Na_2SO_4, and concentrated. Chromatography of the residue on SiO_2 using a 7 : 3 hexane—Et_2O mixture as the eluent gave 9.03 g (84%) of acetylenic alcohol **7**. The ^1H NMR and IR spectral parameters were identical with those described previously.[6]

Tetradec-9-yn-1-ol (8). Alkyne **6** (8.5 g, 35.7 mmol) was added to a suspension of lithium amide prepared from Li (0.5 g, 71 mg-at.), $FeCl_3$ (0.05 g), and distilled liquid NH_3 (240 mL), the mixture was stirred (−33 °C, 1 h), and a solution of Bu^nBr (6.2 g, 45.2 mmol) in 24 mL of anhydrous THF and, immediately thereafter, 24 mL of distilled DMSO were added. The subsequent workup similar to that described above for compound **7** gave 6.37 g (85%) of acetylenic alcohol **8**. The ^1H NMR and IR spectral parameters were identical with those described previously.[12]

Tetradec-9*Z*-en-1-yl acetate (10). At 0 °C (Ar), a 1.5 *N* ethereal solution of Bu^iMgBr (99 mL, 148 mmol) was added to a solution of alkynol **8** (4.5 g, 21.4 mmol) in 66 mL of anhydrous Et_2O, the mixture was stirred for 15 min, heated to ~20 °C, and Cp_2TiCl_2 (0.33 g) was added. After stirring for 3 h, the mixture was cooled to 0 °C, a saturated solution of NH_4Cl (30 mL) and 10% HCl (100 mL) were added successively, and the product was extracted with Et_2O (3×100 mL). The combined extract was washed successively with a saturated solution of $NaHCO_3$ and brine, dried with Na_2SO_4, and concentrated. A 2 : 3 mixture of Ac_2O and Py (19 mL) was added to the residue (4.45 g), and the mixture was stirred for 24 h, diluted with 300 mL of CH_2Cl_2, and washed successively with saturated solutions of $CuSO_4$ and $NaHCO_3$ and with brine, dried with $MgSO_4$, and concentrated. The residue was chromatographed on a column with SiO_2 using a 15 : 1 hexane—Et_2O mixture as the eluent to give 4.96 g (92%) of

acetate **10**. The ^{1}H NMR and IR spectral parameters of the product were identical with those described previously.[13]

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Received February 2, 1998