STEREOSPECIFIC SYNTHESIS OF TRANSOID MONO- AND 1,3-DIENE PHEROMONES OF LEPIDOPTERA FROM SECONDARY CYCLOPROPYLCARBINOLS

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The zinc halide-initiated homoallylic rearrangement of saturated or allylic cyclopropylcarbinols in the presence of trimethylsilyl halides has been employed as the key step in the total synthesis of seven behavioral regulators in twenty insects of the Lepidoptera family, namely 9E-tetradecenol and its acetate, 11E-hexadecenol and its acetate, 11E-hexadecenal, 5E, 7E-dodecadienol, and 3E,5E-tetradecadienyl acetate.

The great majority of currently known pheromones of the Lepidoptera are straight-chain acetogenides with a terminal hydroxy, acetate, or aldehyde group and one or two internal double bonds [1-3]. Until recently, the latter were regarded as generally having the Z-configuration, which is at least partly responsible for the interest of synthetic chemists in the development of stereospecific methods for the construction of cis-disubstituted olefins. The ever-increasing numbers of E-olefins in this group has made it just as necessary to find efficient methods for the generation of the trans-disubstituted double bond, currently effected for the most part by the transformation of acetylenes or the Wittig–Schlosser olefination of carbonyl compounds [1, 2, 4]. For this reason, it was decided to use our recently-discovered stereospecific homoallylic rearrangement of secondary alcohols, readily obtainable from acetylcyclopropane and trimethylsilyl halides in the presence of catalytic amounts of zinc halides, for this purpose [5]. This report describes the development of the synthetic potential of this version of the cyclopropylcarbinol rearrangement and its application to the synthesis of the pheromones (I)-(III), (XI), (XII), (XVI), and (XVIII), which have transoid monoene or diene groupings.

The first example to be considered here is the total synthesis of the 11E-C_{16} structures (I)-(III) (Scheme 1), which have been identified among the regulators of behavioral reactions in at least eight species of Lepidoptera. For example, the hexadecenol (I) and its acetate (II) are known to be components of the sex pheromone (SP) of the sweet potato moth Brachmia macroscopa [6], of which (II) is that of the aubergine beetle Leucinodes orbonalis [7], and the hexadecenol (III) of Caloptilia theivora [8]. The SP of the moth Diaphania nitidalis consists of a mixture of the alcohol (I) and the aldehyde (III) [9]. In addition, the alcohol (I) is attractive to the insect Eupsilia quadrilinea [10], and the acetate (II) to Diasemia litterata [9], Epiblema moza [10, 11], and Telorta edentata [10, 11].

Compounds (I)-(III) were obtained by two routes from the 3E-C_8 bromide (IV), obtained in five steps from propionaldehyde and acetylcyclopropane [5], or from the readily accessible octane-1,8-diols (V) and (VI) (Scheme 1). The first of these involved C-alkylation by the bromide (IV) of the dianion generated from the hydroxysulfone (V), followed by reductive desulfurization of the intermediate (VII) to the alcohol (I). The modest overall yields of the latter compound were improved considerably by using the second route, based on the Kochi reagent-catalyzed Wurtz cross-coupling of the same bromide (IV) with the Grignard reagent from the bromoether (VI), followed by removal of the tetrahydropyranyl (THP) protection from the intermediate (VIII). Acetylation of the alcohol (I), or its oxidation with pyridinium chlorochromate (XXII) afforded the required acetate (II) or aldehyde (III), the overall yields being high in both cases.

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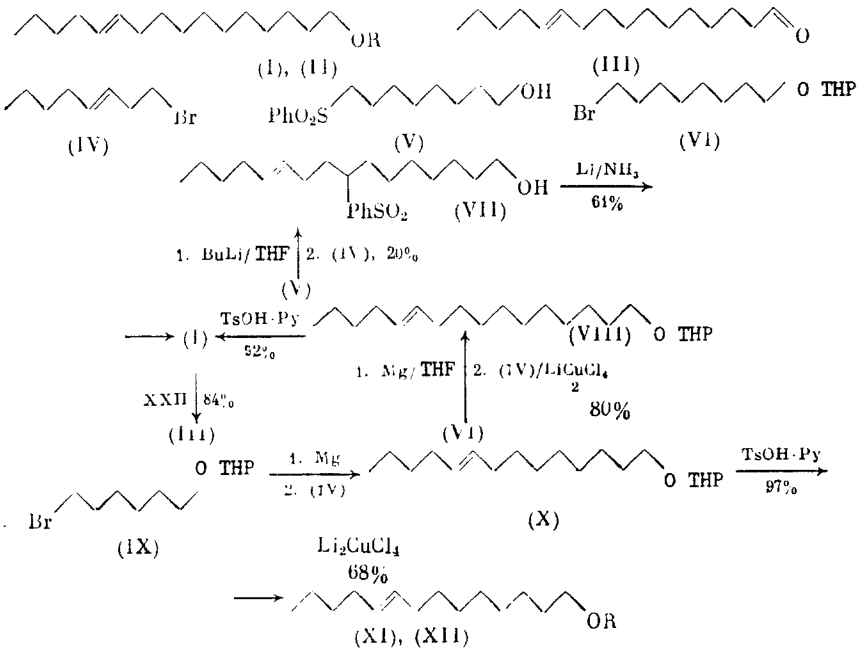
Scheme 1

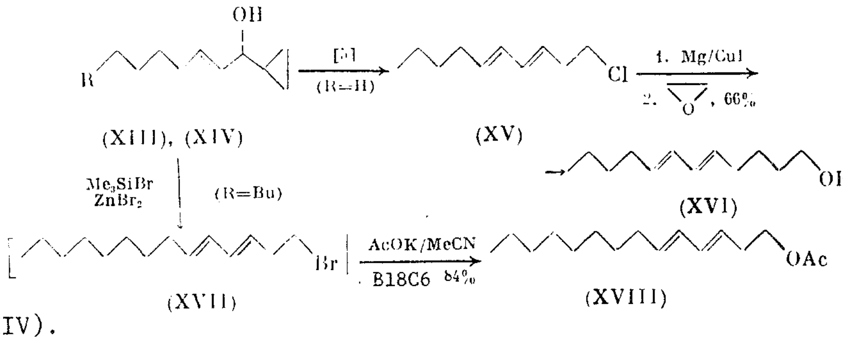


R = H(I), (XI), Ac(II), (XII).

Another example is the analogous synthesis (Scheme 1) of the 9E-tetradecenol (XI), (which has been identified as a component of the attractant mixture of Epiblema plaquifera [10]) and its acetate (XII), which are the SP or components of the SP for at least nine species of Lepidoptera [1, 12, 13]. Like its bis-homolog (VI), the bromoether (IX) undergoes Wurtz cross-coupling with the homoallyl bromide (IV) smoothly to give the THP ether (X), which is then converted in the usual way into the required (XI) and (XII).

The stereochemical purity of all the compounds obtained corresponded to that of the starting olefin (IV), the configuration of which (95-98% E [5]) was unaffected during the synthesis, as confirmed both by comparison of the spectral properties with those reported for (I)-(III) [14] and (XI), (XII) [15], and by examination of GLC data for samples of these compounds.

Scheme 2



R = H(XIII), Bu(XIV).

Basically the same method was used to prepare the two conjugated dienes (XVI) and (XVIII) (Scheme 2). Of these, the 5E,7E-dodecadienol (XVI) is a component of the SP of the pine moth Dendrolimus spectabilis [16] and the 3E,5E-tetradecadienyl acetate (XVIII) has been found to be a component of the attractant mixtures of the insects Accocus centerensis [1] and Prionoxystus robiniae [17]. The syntheis of the alcohol (XVI) was effected smoothly by the CuI-catalyzed C_2-homologization of ethylene oxide with the Grignard reagent from the homoallyl chloride (XV), which was in turn obtained in four steps from acetylcyclopropane and valeraldehyde via the intermediate allyl cyclopropyl carbinol (XIII) [5]. Replacement of the chloride (XV) by the labile homoallyl bromide obtained in the same way [5], or the use of copper salts as catalysts, resulted in considerable decreases in the yields of the required (XVI).

The starting material for the synthesis of the acetate (XVIII) was the carbinol (XIV), previously obtained by us from acetylcyclopropane and pelargonic aldehyde [5], $ZnBr_2$-initiated homoallyl rearrangement of which in the presence of Me_3SiBr [5] gave the extremely unstable bromide (XVII) which was therefore used without further purification. Acetolysis of the latter in the presence of dibenzo-18-crown-6 (DB18C6) gave the required 3E,5E-diene acetate in good yield. According to GLC and comparison of the spectral properties found with those reported for (XVI) [18] and (XVIII) [17, 19], the stereochemical purity of these dienes was 97-98% at both C=C bonds.

This variant of the homoallyl rearrangement of secondary cyclopropyl carbinols [5] can therefore be used advantageously as the key step in the stereospecific total synthesis of transoid monoene and 1,3-diene pheromones of acetogenic origin.

EXPERIMENTAL

IR spectra were obtained on a UR-20 instrument in chloroform, and the UV spectra of alcoholic solutions on a Specord UV-VIS spectrophotometer. The PMR spectra of $CDCL_3$ solutions were measured relative to TMS on a Bruker WM-250 spectrometer and mass spectra at an ionizing voltage of 70 eV on a Varian MAT CH-6. GLC was carried out with an LKhM-80 chromatograph (column 3 m × 3 mm, with 15% Carbowax 20M on Chromatone N-AW-DMCS), and TLC on Silufol plates.

8-Phenylsulfonyl-11E-hexadecen-1-ol (VII). To a solution of 0.54 g (2 mmoles) of (V) [20] and 3 ml of HMPA in 15 ml of THF was added with stirring at −65°C under argon over 20 min 3.5 ml of a 1.15 M solution of BuLi (4 mmoles) in hexane. The mixture was kept for 1 h at −50°C, then treated over 10 min with a solution of 0.38 g (2 mmoles) of (IV) [5]. After 30 min, the reaction mixture was warmed to 20°C, kept for 1 h, then decomposed with saturated ammonium chloride solution and extracted with ether. The extract was washed with saturated NaCl solution, dried over $MgSO_4$, evaporated under reduced pressure, and the residue (0.7 g) chromatographed on 20 g of SiO_2. Gradient elution from hexane to ether (up to 50% of the latter) gave 0.15 g (20%) of (VII) as a colorless oil, R_f 0.2 (ether), n_D^{21} 1.5118. IR spectrum (ν, cm^{-1}): 600, 690, 910, 970, 1085, 1145, 1220, 1305, 1450, 1470, 1585, 2860, 2940, 3005, 3520, 3620. UV spectrum (λ_{max}, nm (ε)): 218 (8600), 267 (1010). PMR spectrum (δ, ppm, J, Hz): 0.88t (3H, CH_3, J = 7), 1.2-2.2m (22H, CH_2), 2.93m (1H, CHS), 3.61t (2H, HC^1, J = 7), 5.20d.t (1H, HC^{12}, J = 15 and 7), 5.37d.t (1H, HC^{11}, J = 15 and 7), 7.5-7.9m (5H, C_6H_5). Mass spectrum, m/z (I, %): M^+ 380(5), 239(14), 238(27), 143(20), 110(25), 109(27), 103(35), 95(36), 81(50), 69(50), 67(47), 55(84), 43(100). Found: C, 69.20; H, 9.50; S, 7.95%. $C_{22}H_{36}O_3S$. Calculated: C, 69.43; H, 9.53; S, 8.42%.

1-(2-Tetrahydropyranyloxy)-11E-hexadecene (VIII). To a suspension of the Grignard reagent, freshly prepared from 1.15 g (3.9 mmoles) of (VI) [21] and 0.24 g (9.9 mg-atom) of Mg in 15 ml of THF, was added with stirring at −70°C under argon over 10 min a solution of 0.30 g (1.6 mmoles) of (IV) in 3 ml of THF and 0.5 ml of a 0.1 M solution of Li_2CuCl_4 [22] in THF. The mixture was warmed to 20°C over 45 min, kept for 2 h, then treated with saturated ammonium chloride solution and extracted with ether. The extract was washed with saturated NaCl solution, dried over $MgSO_4$, evaporated under reduced pressure, and the residue (~1.2 g) chromatographed on 100 g of SiO_2. Gradient elution from hexane to ether (up to 2% of the latter) gave 0.41 g (80%) of (VIII) as a colorless oil, R_f 0.6 (hexane:ether, 3:1), n_D^{21} 1.4602. IR spectrum (ν, cm^{-1}): 810, 875, 970, 1030, 1075, 1120, 1135, 1240, 1355, 1380, 1440, 1455, 1470, 2860, 2930, 3005. PMR spectrum (δ, ppm, J, Hz): 0.89t (3H, CH_3, J = 7), 1.2-2.1m (30H, CH_2), 3.3-3.9m (4H, OCH_2), 3.59br.t (1H, OCHO, J = 4), 5.39m (2H, HC=CH). Mass spectrum, m/z (I, %): M^+ 324(0.6), 251(0.9), 213(3), 141(2), 115(5), 101(14), 86(12), 85(100), 84(29), 71(25), 69(13), 67(10), 57(57), 56(43), 55(29), 43(31), 41(30). Found: C, 77.81; H, 12.53%. $C_{21}H_{40}O_2$. Calculated: C, 77.72; H, 12.42%.

1-(2-Tetrahydropyranyloxy)-9E-tetradecene (X). Similarly, from 5.05 g (19 mmoles) of (IX) [23], 1.14 g (46.9 mg-atom) Mg, and 1.04 g (5.4 mmoles) of (IV) in 65 ml of THF and 2 ml of 0.1 M Li_2CuCl_4 in THF there was obtained 1.09 g (68%) of (X) as a colorless oil, R_f 0.5 (hexane:ether, 3:1), n_D^{21} 1.4580. IR spectrum (ν, cm^{-1}): 810, 870, 905, 970, 1030, 1080, 1120, 1135, 1260, 1325, 1355, 1380, 1440, 1470, 2860, 2930, 3005. PMR spectrum (δ, ppm, J, Hz): 0.89t (3H, CH_3, J = 7), 1.2-2.1m (26H, CH_2), 3.3-3.9m (4H, OCH_2), 4.58br.t (1H, OCHO, J = 4), 5.39m (2H, HC=CH). Mass spectrum, m/z (I, %): M^+ 296(1.6), 278(0.8), 223(3), 124(3), 110(6), 101(8), 97(8), 96(12), 95(7), 85(100), 84(15), 83(14), 69(18), 67(16), 57(16), 56(18), 55(36), 45(19), 43(15), 41(19). Found: C, 76.61; H, 12.25%. $C_{19}H_{36}O_2$. Calculated: C, 76.97; H, 12.24%.

11E-Hexadecenol (I). To a solution of 40 mg (5.7 mg-atom) of Li in 5 ml of ammonia was added with stirring at −70°C under argon over 5 min a solution of 0.13 g (0.34 mmole) of (VII) in 2 ml of THF. The mixture was kept for one hour at −60°C, then decomposed with ammonium chloride, the ammonia evaporated, and the residue treated with water and extracted with ether. The extract was washed with 5% HCl and saturated NaCl, dried over $MgSO_4$, evaporated under reduced pressure, and the residue (~0.1 g) chromatographed on 10 g of SiO_2. Gradient elution from hexane to ether (up to 10% of the latter) gave 50 mg (61%) of (I) [14] as a colorless oil, bp 104°C (0.05 mm), n_D^{22} 1.4570. PMR spectrum (δ, ppm, J, Hz): 0.89t (3H, CH_3, J = 7), 1.2-1.4m (18H, CH_2), 1.57m (2H, HC^2), 1.9-2.1m (4H, HC^{10}, HC^{13}), 3.64t (2H, HC^1, J = 7), 5.39m (2H, HC=CH).

A solution of 0.47 g (1.45 mmoles) of (VIII) and 40 mg (0.16 mmole) of TsOH·Py [24] in 15 ml of methanol was kept for 3 h at 45°C, then evaporated under reduced pressure and the residue (~0.5 g) chromatographed on 15 g of SiO_2 under the conditions described in the preceding preparation, to give 0.32 g (92%) of (I), identical with the sample obtained above.

Acetate (II) [14] – colorless oil, bp 120°C (bath) (0.02 mm), n_D^{22} 1.4476. PMR spectrum (δ, ppm, J, Hz): 0.89t (3H, CH_3, J = 7), 1.2-1.4m (18H, CH_2), 1.62m (2H, HC^2), 1.9-2.1m (4H, HC^{10}, HC^{13}), 2.06s (3H, CH_3CO), 4.06t (2H, HC^1, J = 7), 5.39m (2H, HC=CH).

9E-Tetradecenol (XI). Obtained as described for (VIII), from 0.50 g (1.7 mmole) of (X) and 40 mg (0.16 mmole) of TsOH·Py in 15 ml of methanol, yield 0.35 g (97%) of (XI) [15] as a colorless oil, bp 89°C (0.03 mm), n_D^{20} 1.4555. PMR spectrum (δ, ppm, J, Hz): 0.89t (3H, CH_3, J = 7), 1.2-1.4m (14H, CH_2), 1.57m (2H, HC^2), 1.9-2.1m (4H, HC^8, HC^{11}), 3.65t (2H, HC^1, J = 7), 5.39m (2H, HC=CH).

Acetate (XII) [15] – colorless oil, bp 94°C (0.05 mm), n_D^{21} 1.4460. PMR spectrum (δ, ppm, J, Hz): 0.89t (3H, CH_3, J = 7), 1.2-1.4m (14H, CH_2), 1.62m (2H, HC^2), 1.9-2.1m (4H, HC^8, HC^{11}), 2.06s (3H, CH_3CO), 4.06t (2H, HC^1, J = 7), 5.39m (2H, HC=CH).

11E-Hexadecenal (III). To a suspension of 0.22 g (1 mmole) of (XXII) [25] in 3 ml of dichloromethane was added all at once with stirring at 20°C under argon a solution of 0.12 g (0.5 mmole) of (I) in 0.5 ml of dichloromethane. After 1 h, the mixture was diluted with ether, filtered through a layer (~3 cm) of silica, the filtrate evaporated and the residue distilled in vacuo to give 0.10 g (84%) of (III) [14] as a colorless oil, bp 110°C (bath) (0.01 mm), n_D^{21} 1.4562. PMR spectrum (δ, ppm, J, Hz): 0.89t (3H, CH_3, J = 7), 1.2-1.4m (16H, CH_2), 1.62m (2H, HC^3), 1.9-2.1m (4H, HC^{10}, HC^{13}), 2.3-2.5m (2H, HC^2), 5.39m (2H, HC=CH), 9.78t (1H, HC^1, J = 2).

5E,7E-Dodecadienol (XVI). To a suspension of the Grignard reagent, freshly prepared from 0.34 g (2.0 mmoles) of (XV) [5] and 70 mg (2.9 mg-atom) of Mg in 2 ml of THF, was added with stirring at −70°C under argon 40 mg (0.2 mmole) of CuI. The mixture was warmed to −10°C over 20 min, stirred at this temperature for 15 min, and treated at −20°C with a solution of 0.13 g (2.9 mmoles) of ethylene oxide in 3 ml of THF. The mixture was warmed to 20°C over 30 min, and after one hour it was decomposed at 0°C with saturated aqueous NH_4Cl and extracted with ether. Working up in the usual way gave 0.4 g of product, which was chromatographed on 20 g of SiO_2. Gradient elution from hexane to ether (up to 15% of the latter) gave 0.28 g (77%) of (XVI) [18] as a colorless oil, bp 98°C (1 mm), n_D^{20} 1.4875. PMR spectrum (δ, ppm, J, Hz): 0.90t (3H, CH_3, J = 7), 1.2-1.7m (8H, CH_2), 2.0-2.2m (4H, HC^4, HC^9), 3.66t (2H, HC^1, J = 7), 5.56 and 5.59d.t (2H, HC^5, HC^8, J = 15 and 7), 5.9-6.1m (2H, HC^6, HC^7).

3E,5E-Tetradecadienyl Acetate (XVIII). To a suspension of 0.1 g (0.47 mmole) of (XIV) [5] and 20 mg (0.1 mmole) of $ZnBr_2$ in 5 ml of dichloromethane was added with stirring at −20°C under argon over 5 min a solution of 0.16 g (1 mmole) of Me_3SiBr in 1 ml of dichloromethane. After 30 min, the mixture was treated with saturated aqueous $NaHCO_3$ and extracted with ether. The extract was washed with saturated aqueous NaCl, dried over $MgSO_4$, evaporated under reduced pressure, and the residual bromide (XVII) (0.13 g) dissolved in 6 ml of acetonitrile containing 0.23 g (2.4 mmoles) of potassium acetate and 10 mg of DB18C6. The mixture was boiled for 6 h (the reaction being followed by GLC), then filtered and the filtrate diluted with water and extracted with ether. The usual workup of the extract gave 0.15 g of product, which was chromatographed on 10 g of SiO_2. Gradient elution from hexane to 2% of ether in hexane gave 0.1 g (84%) of (XVIII) [17, 19] as a colorless oil, bp 97°C

(0.03 mm), n_D^{23} 1.4679. PMR spectrum (δ, ppm, J, Hz): 0.89t (3H, CH_3, J = 7), 1.2-1.5m (12H, CH_2), 2.06s (3H, CH_3CO), 2.08m (2H, HC^7), 2.40q (2H, HC^2, J = 7), 4.10t (2H, HC^1, J = 7), 5.51d.t (1H, HC^3, J = 15 and 7), 5.62d.t (1H, HC^6, J = 15 and 7), 5.9-6.2m (2H, HC^4, HC^5).

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