Enantioselective synthesis of (1*E*,3*S*)-1-iodoundec-1-en-5-yn-3-ol, the eicosanoid synthon

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A synthesis of the title compound, the synthon for the constanolactones and other eicosanoids, has been developed from achiral starting compounds. The synthesis is based on the *S*-enantiodirected dihydroxylation of the double bond to introduce a chirality and on the use of conformational restriction of the triple bond (the latent *Z*-double bond) surroundings.

Key words: constanolactones, total synthesis, synthons, chiral catalysis, eicosanoids, enantioselective dihydroxylation.

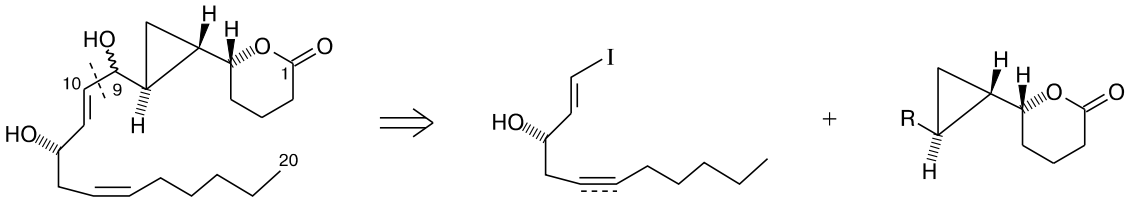
The so-called "marine" eicosanoids (ME), a vast family of polyunsaturated fatty acid oxidized metabolites isolated from marine aglae are of interest due to their possible biological activity (see review 1). Constanolactones (**CL**) **A** and **B** (Scheme 1) isolated from alga *Constantinea simplex*[2] are typical representatives of the ME family.

The ME samples for biological study are available virtually only by total chemical synthesis widely developed during the last 15 years (see review 3, for the recent synthesis of **CLA,B**, see Ref. 4). In the case of constanolactones, a convergent strategy is the most efficient and popular. It consists in the retrosynthetic cleavage of the structure into the two synthons **A** and **B**, the coupling of which by the Kishi—Nozaki[5] reaction is a relatively easy solving problem.[4–7]

Recently, we have developed an enantiodirected biomimetic method for the preparation of synthon of the type **B** (see Refs 8 and 9). Preparation of chiral synthons of the type **A** was the following problem. Note that such synthons have been used in the total syntheses of not only constanolactones, but also leukotrienes **B** [10] and 12-hydroxyeicosa-5(*Z*),8(*Z*),10(*E*),14(*Z*)-tetraenoic acids,[11] *i.e.*, they are the synthons for several types of eicosanoids. Scalemic and homochiral synthons of the type **A** are commonly obtained by a multi-step synthesis from malic acid[12] or carbohydrates[6] as the sources of chirality, as well as by kinetic resolution of late racemic intermediates.[10,11] This work describes more efficient way for the preparation of nonracemic synthon of the type **A** from achiral starting compounds using an enantioselective reaction for the introduction of chirality.

The *C*-allylation of hept-1-yne with allyl bromide under weakly basic conditions[13] smoothly led to dec-1-en-4-yne (**1**) (Scheme 2). The *S*-enantiodirected dihydroxylation of the double bond in enyne **1** using the Sharpless reagent AD-mix-α[14] afforded diol **2** in high yield, but in only 61% *ee*. The same low *ee*, not characteristic of the enantioselective dihydroxylation reaction of olefins (EDO),[15] was also obtained earlier in EDO of

Scheme 1



CLA,B **A** **B**

R = CHO, CH_2OH

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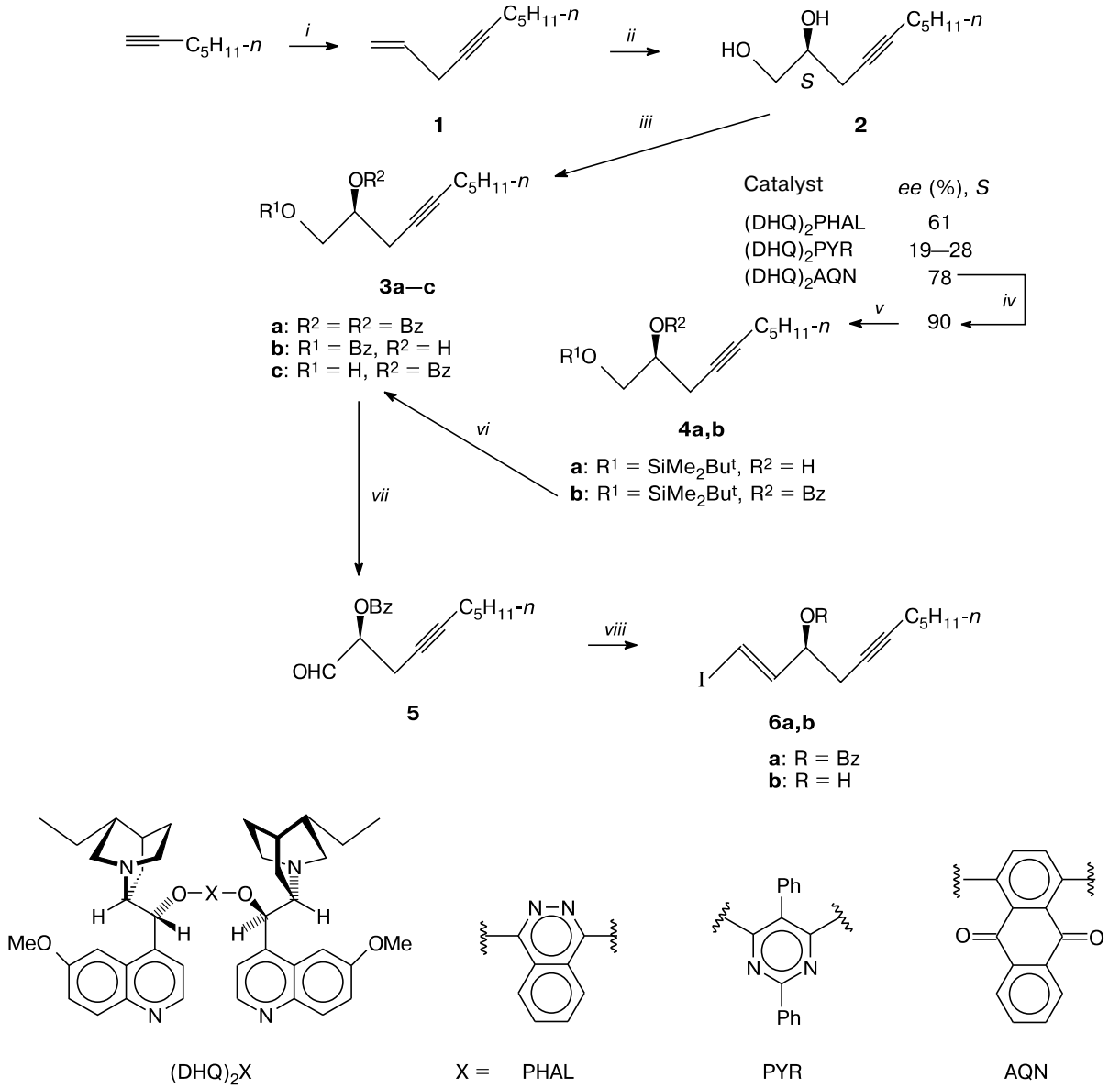
Scheme 2



Reagents and conditions: *i.* $H_2C{=}CHCH_2Br$, K_2CO_3, CuI, NaI, Cu, MeCN (92%); *ii.* $K_2OsO_2(OH)_4$, $(DHQ)_2X$ (X = AQN, PHAL, PYR), $K_3Fe(CN)_6$, K_2CO_3, $Bu^tOH—H_2O$ (92%); *iii. a*) BzCl, Py, PhMe; *b*) Et_3N, MeCN; *iv.* Recrystallization from Et_2O, –78 °C (65%); *v. a*) Bu^tMe_2SiCl, Py, Et_3N, C_6H_6; *b*) BzCl, Py, DMAP, C_6H_6; *vi.* AcOH—Pr^iOH—H_2O (92%); *vii.* PDC, AcOH, MS 3 Å, CH_2Cl_2 (79%); *viii. a*) CHI_3, $CrCl_2$, THF (47%); *b*) K_2CO_3, MeOH (84%).

analogous 1,4-enynes[9] and is apparently a specific feature of the substrates of this type.

It was somewhat difficult to determine enantiomeric composition of diol **2**. The use of optical rotation values is not acceptable due to their low values for such terminal diols,[16] whereas running HPLC on chiral columns is difficult due to the high polarity and full UV transparency of the diol. Such disadvantages are absent in the cases of easily obtained dibenzoate **3a** and primary monobenzoate **3b** of diol **2**, but enantiomers of these benzoates were not resolved by chiral HPLC. Good separation was observed for enantiomers of secondary monobenzoate **3c**, which is formed as a small impurity (3—5%) during synthesis of monobenzoate **3b** by partial benzoylation. Increasing the fraction of benzoate **3c** up to 20—25% by equilibrating of the mixture **3b** + **3c** under basic conditions solved the problem of sensitive chiral analysis.

The reagent AD-mix-α contains $(DHQ)_2PHAL$ as a chiral catalyst. According to the literature data, the next generation analogous catalysts, $(DHQ)_2PYR$ (see Ref. 17) and $(DHQ)_2AQN$ (see Ref. 18)*, provide higher *ee* in EDO of terminal olefins. In the case of enyne **1**, a replacement of the catalyst in AD-mix-α with $(DHQ)_2PYR$ for unexplainable reasons led to a sharp decrease in the *ee* of diol **2** obtained (down to 19—28%) with retention of the high yield and *S*-enantiodirection. Such a dramatic drop in enantioselectivity during EDO with $(DHQ)_2PYR$ has not been earlier observed. Good result was obtained when $(DHQ)_2AQN$ was used, which led to diol **2** in significantly higher *ee* 78%. However, the intermediate product with such *ee* is not yet enantiopure enough to be efficiently used in the synthesis of the target enantiopure compounds, **CLA,B**.

Further increase in the *ee* of diol **2** was based on strategic use of the triple bond as a latent *Z*-double bond. In the synthesis of enyne **1**, this resulted in the easy creation of the C—C bond, while in the synthesis of diol **2**, this provided chemoselectivity of EDO. To increase the *ee* of diol **2**, it turned out possible to use a well known property of the triple bond, *viz.*, the higher tendency of acetylene compounds to crystallize as compared to the corresponding *Z*-olefin compounds. This is due to a sharp restriction in conformational mobility in the vicinity of the triple bond (as compared to the *Z*-double). Diol **2** easily crystallized near 0 °C and could be recrystallized from diethyl ether at −78 °C with simultaneous increase in the *ee* to 90%. A further increase in enantiomeric purity is possible by next recrystallization (with additional losses, too). However, this is not reasonable in the convergent scheme used for the synthesis of the final compounds, constanolactones. In fact, in such a scheme a coupling of the *S*-synthon of the type **A** with *ee* 90% with the *S*-synthon of the type **B**, which can be obtained with *ee* 98.4%, theoretically will lead to diastereomer *SS*-**AB** with *ee* 99.9% and with ~5% admixture of diastereomer *RS*-**AB** with *ee* 73%, which can be separated by chromatography.

In principle, now the triple bond in diol **2** can be converted to the *Z*-double by the Lindlar hydrogenation. However, because of the favorable influence of the triple bond on the properties of products indicated above (as well as an increase in stability), we decided to keep the triple bond almost until the end the synthesis. This additionally creates a possibility to obtain 14,15-dehydroconstanolactones as well.

To continue the synthesis, the secondary hydroxy group in diol **2** should be protected, for example, in the form of benzoate **3c**. Preparative synthesis of this benzoate is based on the use of very selective formation of *tert*-butyldimethylsilyl ether (**4a**) at the primary hydroxy group under mild conditions. The benzoylation of ether **4a** and desilylation of obtained compound **4b** under standard conditions and without purification of the intermediate compounds led to the desired benzoate **3c** in 92% overall yield on three steps.

By analogy with other schemes for obtaining synthons of the type **A**, the creation of the iodovinylic group was performed by the Takai reaction.[19] For this, the corresponding aldehyde **5** was obtained by oxidation of the primary hydroxy group in benzoate **3c**, the reaction of which with CHI_3 and $CrCl_2$ led to vinylic iodide **6a** in satisfactory yield. Its mild debenzoylation smoothly gave alcohol **6b**, a desired synthon of the type **A**. Alcohol **6b** has also proved easy to crystallize, which at necessity can be used for its enantiomeric purification.

The scheme developed for the preparation of synthon **6b** has relatively low number of steps, *viz.*, six starting from hept-1-yne. Based on this synthon, it is possible to synthesize not only natural eicosanoids, but also their monoacetylenic and isotopically labeled (with deuterium, tritium) analogs. The same scheme without considerable changes can be applied for the synthesis of the corresponding synthon with *R*-configuration, only by replacement of reagent AD-mix-α with AD-mix-β.

Experimental

^1H NMR spectra were recorded on a Bruker VM-250 (250.13 MHz) and Bruker AM-300 (300.13 MHz) spectrometers at 303 K using $SiMe_4$ as an internal standard. Mass spectra were recorded on a Kratos MS-30 instrument using direct injection of compounds into the ions source at 200 °C, EI, 60 eV. Optical rotation was measured on a PU-07 universal polarimeter (GNIITs NP, Russia). Analytical TLC was performed on Sorbfil silica gel plates (Sorbpolimer, Russia), visualization was performed by spraying with aqueous phosphomolybdic acid with subsequent heating. Column chromatography was performed on Kieselgel 60 silica gel (Merck), 230—400 mesh activated at 150 °C (30 min). Unless otherwise stated, the extracts were dried with anhydrous $MgSO_4$, concentrated to dryness first on a rotary evaporator *in vacuo* of a water-jet pump, then under pressure <1 Torr until the weight was constant.

Reagents AD-mix-α, $(DHQ)_2AQN$, CHI_3, $CrCl_2$ (Aldrich), $(DHQ)_2PHAL$, PDC, hept-1-yne (Fluka), $(DHQ)_2PYR$ (Chemika), Bu^tMe_2SiCl (Sigma) were used as purchased; $K_2OsO_2(OH)_4$ was obtained according to the procedure described earlier.[20] Other reagents were produced in Russia.

Dec-1-en-4-yne (1). Hept-1-yne (15.0 g, 156 mmol) was added in one portion to a stirred suspension of K_2CO_3 (38.8 g, 280 mmol), CuI (29.7 g, 150 mmol), and copper powder (1.98 g, 31 mmol) in solution of NaI (42 g, 280 mmol) in MeCN (75 mL) at 20 °C, followed by a dropwise addition of $CH_2{=}CHCH_2Br$ (22.64 g, 187 mmol). After 12 h of stirring, the mixture was poured into saturated aq. NH_4Cl (700 mL) and hexane (300 mL), the layers were separated, the aqueous layer was extracted with hexane (2×100 mL). Combined organic layers

* $(DHQ)_2PHAL$, $(DHQ)_2PYR$, and $(DHQ)_2AQN$ are 1,4-phthalazinediyl, 2,5-diphenylpyrimidine-4,6-diyl, and 9,10-anthraquinone-1,4-diyl ethers of dihydroquinine, respectively.

were stirred with 10% aq. NH_4OH (50 mL) for 15 min, the organic layer was separated, dried, and concentrated by distillation of volatile components using a distillation column under atmospheric pressure. The residue was distilled *in vacuo* to obtain enyne **1** (19.51 g, 92%) as a colorless mobile liquid, b.p. 72—78 °C (30 Torr), R_f 0.69 (hexane—EtOAc, 9 : 1). ^{1}H NMR (250 MHz, $CDCl_3$), δ: 0.90 (t, 3 H, Me, J = 7.0 Hz); 1.25—1.43 (m, 4 H, C(8)H_2 + C(9)H_2); 1.51 (m, 2 H, C(7)H_2); 2.18 (tt, 2 H, C(6)H_2, J = 2.3 Hz, 7.0 Hz); 2.94 (m, 2 H, C(3)H_2); 5.09 (dq, 1 H, H(1A), J = 10.0 Hz, 1.7 Hz); 5.31 (dq, 1 H, H(1B), J = 16.9 Hz, 1.7 Hz); 5.83 (ddt, 1 H, H(2), J = 16.9 Hz, 10.0 Hz, 5.2 Hz).

(*S*)-Dec-4-yne-1,2-diol (2). A solution of enyne **1** (1.00 g, 7.35 mmol), $K_3Fe(CN)_6$ (7.25 g, 22 mmol), K_2CO_3 (3.04 g, 22 mmol), $(DHQ)_2AQN$ (31.5 mg, 36.7 μmol), and $K_2OsO_2(OH)_4$ (5.5 mg, 15 μmol) in Bu^tOH (35 mL) and water (35 mL) (a two-layer mixture) was stirred at 0 °C until complete transformation of the starting reactant (TLC control). The mixture was filtered, a precipitate was washed with EtOAc on the filter. In the filtrate, the organic layer was separated, the aqueous layer was extracted with EtOAc (3×25 mL). Combined organic layers were washed with 20% aq. H_2SO_4 (20 mL) and then with water to neutrality, dried, and concentrated to dryness. The residual yellow oil was the diol **2** (1.17 g, 92%), *ee* 78%, m.p. (−1)—(−0.5) °C, R_f 0.49 (EtOAc; the starting **1**: R_f 0.78). Repeated recrystallizations from Et_2O at −78 °C gave diol **2** in 65% yield with *ee* 90%, m.p. 3—7 °C, $[\alpha]_D^{18}$ +8.4° (*c* 1.6, EtOH). ^{1}H NMR (250 MHz, $CDCl_3$), δ: 0.90 (t, 3 H, Me, J = 7.0 Hz); 1.23—1.40 (m, 4 H, C(8)H_2 + C(9)H_2); 1.49 (m, 2 H, C(7)H_2); 2.15 (tt, 2 H, C(6)H_2, J = 2.3 Hz, 6.9 Hz); 2.39 (m, 2 H, C(3)H_2); 2.98 (br.s, 2 H, 2 OH); 3.57 (dd, 1 H, H(1A), J = 6.6 Hz, 11.3 Hz); 3.75 (dd, 1 H, H(1B), J = 3.3 Hz, 11.3 Hz); 3.82 (m, 1 H, H(2)). ^{13}C NMR (50.32 MHz, $CDCl_3$), δ: 14.03, 18.74, 22.25, 23.83, 28.67, 31.15, 65.67, 70.65, 75.35, 83.43.

Analysis of enantiomeric composition of diol 2. Pyridine (19 μL, 0.24 mmol) and BzCl (14 μL, 0.12 mmol) were sequentially added to a solution of diol **2** (10 mg, 0.06 mmol) in toluene (600 μL) at 0 °C. The mixture was kept for 15 h at 4 °C, followed by addition of MeOH (20 μL) and concentration to dryness after 15 min. The residue was dissolved in benzene, the solution was filtered and concentrated to dryness. The residue was dissolved in a mixture of MeCN (60 μL) and Et_3N (60 μL) and kept for 48 h at 20 °C, concentrated to dryness, the residue was analyzed by HPLC without additional work-up to obtain a mixture of products containing monobenzoates **3b** and **3c** in the ratio **3b** : **3c** = (75—80) : (20—25) and small variable quantities of dibenzoate **3a**; the retention times were: 1.83 (**3a**), 7.60 (**3b**), 9.75 (*R*-**3c**) and 10.82 (*S*-**3c**) min (HPLC: a 250×4.6 mm Kromasil 100-5-TBB column (Eka Chemicals, Sweden) with the copolymer of L-*O*,*O*′-bis(*p*-*tert*-butylbenzoyl)tartaric acid *N*,*N*′-diallyldiamide with hydrosilane immobilized on silica gel as a chiral phase, 0.5% Pr^iOH in *n*-hexane as a mobile phase, 2 mL min^{-1}, UV detector at λ = 280 nm). For spectroscopic analysis, a mixture of monobenzoates **3b** + **3c** was isolated by column chromatography on silica gel. ^{1}H NMR (300 MHz, $CDCl_3$), δ for component **3b**: 0.89 (t, 3 H, Me, J = 6.9 Hz); 1.25—1.40 (m, 4 H, C(8)H_2 + C(9)H_2); 1.50 (m, 2 H, C(7)H_2); 2.16 (m, 2 H, C(6)H_2); 2.54 (m, 2 H, C(3)H_2); 4.10 (m, 1 H, H(2)); 4.40 (dd, 1 H, H(1A), J = 6.1 Hz, 11.4 Hz); 4.44 (dd, 1 H, H(1B), J = 4.4 Hz, 11.4 Hz); 7.44 (t, 2 H, 2 *m*-H_{Bz}, J = 7.4 Hz); 7.57 (t, 1 H, *p*-H_{Bz}, J = 7.3 Hz); 8.06 (d, 2 H, 2 *o*-H_{Bz}, J = 7.4 Hz); component **3c** exhibits characteristic signals at δ 3.94, 3.97, and 5.20 (the full spectrum see below). The ratios of **3b** : **3c**, measured using NMR and HPLC, agreed within the experimental error.

(*S*)-2-Benzoyloxydec-4-yn-1-ol (3c). *a*. A solution of diol **2** (1.00 g, 5.88 mmol, *ee* 90%), Bu^tMe_2SiCl (1.31 g, 8.82 mmol), pyridine (475 μL, 5.9 mmol), and Et_3N (1.52 mL, 11.0 mmol) in anhydrous benzene (7 mL) was stirred for 48 h at ~20 °C with TLC monitoring, then, another portions of Bu^tMe_2SiCl (442 mg, 2.9 mmol) and Et_3N (510 μL, 3.7 mmol) were added, and after 24 h the starting compound disappeared. The mixture was diluted with benzene (20 mL) and water (10 mL), the aqueous layer was extracted with benzene (3×5 mL), combined organic layers were washed with water, dried, and concentrated to dryness to obtain crude silyl ether **4a** (1.85 g, 110%) as a light brown oil, R_f 0.60 (hexane—EtOAc, 7 : 3; the starting **2**: R_f 0.09), which was further used without additional purification.

b. A solution of obtained ether **4a** (5.88 mmol), BzCl (1.02 mL, 8.83 mmol), DMAP (108 mg, 0.88 mmol), and pyridine (1.42 mL, 17.7 mmol) in anhydrous benzene (15 mL) was stirred for 72 h at ~20 °C with TLC monitoring. Then, another portions of BzCl (339 μL, 2.93 mmol) and pyridine (469 μL, 5.9 mmol) were added, and after 24 h the starting compound was consumed. Methanol (0.5 mL) was added to the mixture, which was stirred for 30 min, diluted with benzene (20 mL) and water (10 mL), the aqueous layer was extracted with benzene (3×5 mL). The combined organic layers were sequentially washed with 10% aq. HCl (10 mL), saturated aq. $NaHCO_3$ (10 mL), water until neutrality, dried, and concentrated to dryness to obtain crude product **4b** (2.81 g, 123%) as a light brown oil, R_f 0.48 (hexane—EtOAc, 95 : 5; the starting **4a**: R_f 0.19), which was further used without additional purification. The sample for spectroscopic analysis was purified by chromatography. ^{1}H NMR (250 MHz, $CDCl_3$), δ: 0.05, 0.06 (both s, 3 H each, Me_2Si); 0.86 (t, 3 H, C(10)H_3, J = 6.9 Hz); 0.88 (s, 9 H, Bu^tSi); 1.31 (m, 4 H, C(8)H_2 + C(9)H_2); 1.45 (m, 2 H, C(7)H_2); 2.12 (tt, C(6)H_2, J = 2.3 Hz, 6.9 Hz); 2.62 (ddt, 1 H, H(3A), J = 16.5 Hz, 5.9 Hz, 2.3 Hz); 2.65 (ddt, 1 H, H(3B), J = 16.5 Hz, 6.2 Hz, 2.3 Hz); 3.89 (d, 2 H, C(1)H_2, J = 4.9 Hz); 5.17 (tt, 1 H, H(2), J = 4.9 Hz, 6.0 Hz); 7.43 (tt, 2 H, 2 *m*-H_{Bz}, J = 1.3 Hz, 7.2 Hz); 7.55 (tt, 1 H, *p*-H_{Bz}, J = 1.3 Hz, 7.2 Hz); 8.04 (m, 2 H, 2 *o*-H_{Bz}).

c. A solution of compound **4b** (5.88 mmol) in 10% aq. AcOH and Pr^iOH (1 mL) was kept at ~20 °C until the starting compound disappeared (72 h, TLC monitoring). The solution was concentrated to dryness and from the oil obtained (2.09 g) pure benzoate **3c** was isolated (1.78 g, 92%) by column chromatography on silica gel (benzene—EtOAc, 95 : 5 and 90 : 10) as a light yellow oil, R_f 0.28 (hexane—EtOAc, 80 : 20; the starting **4b**: R_f 0.72), $[\alpha]_D^{18}$ −5.43° (*c* 1.1, EtOH). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.87 (t, 3 H, Me, J = 7.0 Hz); 1.20—1.40 (m, 4 H, C(8)H_2 + C(9)H_2); 1.45 (quint, 2 H, C(7)H_2, J = 6.9 Hz); 2.13 (tt, 2 H, C(6)H_2, J = 2.4 Hz, 7.0 Hz); 2.65 (dt, 2 H, C(3)H_2, J = 6.4 Hz, 2.4 Hz); 3.94 (dd, 1 H, H(1A), J = 5.4 Hz, 12.1 Hz); 3.97 (dd, 1 H, H(1B), J = 3.9 Hz, 12.1 Hz); 5.20 (tdd, 1 H, H(2), J = 6.4 Hz, 5.4 Hz, 3.9 Hz); 7.45 (t, 2 H, 2 *m*-H_{Bz}, J = 7.6 Hz); 7.58 (t, 1 H, *p*-H_{Bz}, J = 7.4 Hz); 8.06 (d, 2 H, 2 *o*-H_{Bz}, J = 7.8 Hz).

(*S*)-2-Benzoyloxydec-4-yn-1-al (5). A suspension of PDC (790 mg, 2.11 mmol) and freshly calcined finely ground molecular sieves 3 Å (1.07 g) in the solution of benzoate **3c** (579 mg, 2.11 mmol) and AcOH (60 μL, 1.05 mmol) in CH_2Cl_2 (22 mL) was intensively stirred for 1 h. Then, activated charcoal was added (~100 mg), after 30 min the mixture was filtered through

silica gel (20 g) with subsequent washing with CH_2Cl_2 (150 mL). Aldehyde **5** (454 mg, 79%) was isolated by concentration of the filtrate as a light yellow oil, which contained (NMR data) up to 20% nonaldehyde impurity, presumably "dimeric" ester[21] (a formal product of the Cannizzaro reaction), R_f 0.46 (CH_2Cl_2, two developments; impurity: R_f 0.56, the starting **3c**: R_f 0.22). This sample of aldehyde **5** was used in the subsequent step without additional purification. The sample for spectroscopic analysis was isolated by chromatography. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.85 (t, 3 H, Me, J = 7.1 Hz); 1.20—1.40 (m, 4 H, C(8)H_2 + C(9)H_2); 1.44 (m, 2 H, C(7)H_2); 2.12 (tt, 2 H, C(6)H_2, J = 2.4 Hz, 7.0 Hz); 2.83 (dt, 2 H, C(3)H_2, J = 6.2 Hz, 2.4 Hz); 5.31 (t, 1 H, H(2), J = 6.2 Hz); 7.47 (tt, 2 H, 2 m-H_{Bz}, J = 1.5 Hz, 7.5 Hz); 7.60 (tt, 1 H, p-H_{Bz}, J = 1.5 Hz, 7.4 Hz); 8.12 (dt, 2 H, 2 o-H_{Bz}, J = 7.0 Hz, 1.5 Hz); 9.72 (s, 1 H, CHO).

(1*E*,3*S*)-3-Benzoyloxy-1-iodoundec-1-en-5-yne (6a). Chromium(II) chloride (1.22 g, 9.9 mmol) was quickly added in one portion to a solution of aldehyde **5** (448 mg, 1.65 mmol) and CHI_3 (571 mg, 1.45 mmol) in anhydrous THF (45 mL) at 0 °C and with stirring. After 15 min, an initially yellowish green suspension turned dark brown, the cooling was removed, and the reaction mixture was stirred at ~20 °C until the starting compound disappeared (1.5 h, TLC data). The mixture was diluted with water (30 mL) and extracted with diethyl ether (3×15 mL), the extract was washed with 10% aq. $Na_2S_2O_3$ (10 mL), dried, and concentrated to dryness. Vinylic iodide **6a** (308 mg, 47%) was isolated as a light yellow oil from the residue by chromatography on silica gel eluting with toluene, R_f 0.52 (toluene; the starting **5**: R_f 0.18), $[\alpha]_D^{17}$ +15.6° (*c* 1.2, EtOH). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.88 (t, 3 H, Me, J = 6.8 Hz); 1.25—1.36 (m, 4 H, C(9)H_2 + C(10)H_2); 1.46 (m, 2 H, C(8)H_2); 2.14 (tt, 2 H, C(7)H_2, J = 2.4 Hz, 7.0 Hz); 2.62 (m, 2 H, C(4)H_2); 5.10 (q, 1 H, H(3), J = 6.3 Hz); 6.60 (d, 1 H, H(1), J = 14.6 Hz); 6.73 (dd, 1 H, H(2), J = 6.3 Hz, 14.6 Hz); 7.45 (t, 2 H, 2 m-H_{Bz}, J = 7.6 Hz); 7.60 (t, 1 H, p-H_{Bz}, J = 7.4 Hz); 8.12 (d, 2 H, 2 o-H_{Bz}, J = 7.1 Hz). MS, m/z, I_{rel} (%): 287 [M − (C(4)—C(11))] (11), 274 [M − BzOH] (2), 218 (4), 147 [M − BzOH—I] (45), 105 [PhCO] (100), 91 (64), 77 (70).

(1*E*,3*S*)-1-Iodoundec-1-en-5-yn-3-ol (6b). A solution of benzoate **6a** (292 mg, 0.735 mmol) and K_2CO_3 (60 mg, 0.44 mmol) in MeOH (5 mL) was kept for 1 h at ~20 °C, diluted with water (5 mL), neutralized with 5% aq. H_3PO_4, and MeOH was evaporated. The aqueous residue was extracted with EtOAc (3×3 mL), the extract was washed with water, dried, and concentrated to dryness. Alcohol **6b** (180 mg, 84%) was isolated as a light yellow oil from the residue by chromatography on silica gel (eluent, hexane—EtOAc, 9 : 1), crystallizing at −18 °C, R_f 0.35 (hexane—EtOAc, 8 : 2; the starting **6a**: R_f 0.46), $[\alpha]_D^{18}$ +35.2° (*c* 1.56, EtOH), $[\alpha]_D^{17}$ −22.6° (*c* 1.68, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$), δ: 0.91 (t, 3 H, Me, J = 7.1 Hz); 1.25—1.36 (m, 4 H, C(9)H_2 + C(10)H_2); 1.50 (m, 2 H, C(8)H_2); 2.17 (tt, 2 H, C(7)H_2, J = 2.5 Hz, 6.9 Hz); 2.40 (ddt, 1 H, H(4A), J = 16.4 Hz, 6.2 Hz, 2.3 Hz); 2.46 (ddt, 1 H, H(4B), J = 16.4 Hz, 5.3 Hz, 2.7 Hz); 2.70 (br.d, 1 H, OH); 4.21 (dddd, 1 H, H(3), J = 1.2 Hz, 5.3 Hz, 5.6 Hz, 6.2 Hz); 6.45 (dd, 1 H, H(1), J = 1.2 Hz, 14.4 Hz); 6.62 (dd, 1 H, H(2), J = 5.6 Hz, 14.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 14.05, 18.78, 22.27, 27.43, 28.62, 31.11, 72.61, 74.69, 78.23, 84.34, 146.59.

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