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Cyclopropane Intermediates in the Synthesis of Chiral Alcohols with Methyl-Branched Carbon Skeleton. Application in the Synthesis of Insect Pheromones

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Abstract—Several chiral building blocks, (2*R*)-2-methylundec-10-en-1-ol, (3*R*)-3-methylheptan-1-ol, and (4*R*)-4-methyloctan-1-ol, have been synthesized using cyclopropane intermediate products. It has been shown that the obtained chiral alcohols can be used in the synthesis of insect pheromones.

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Methyl-branched optically active compounds are difficultly accessible but important intermediates in the synthesis of complex organic molecules. For this purpose, synthetic building blocks and optically active monoterpenoids (citronellal, pulegone, camphor, menthol, isomenthol, isolimonene, etc.) are used most frequently [1]. However, synthetic methyl-branched intermediate products are accessible in small amounts and are expensive, whereas the use of terpene compounds involves multistep transformations since methyl substituents therein are attached to the ring or are remote from the terminal parts of their molecules. In some cases, the use of natural compounds is limited by the optical purity of starting materials, multistep and complicated transformations, the use of expensive reagents and enzymes, and availability of only one optical enantiomer [1–3].

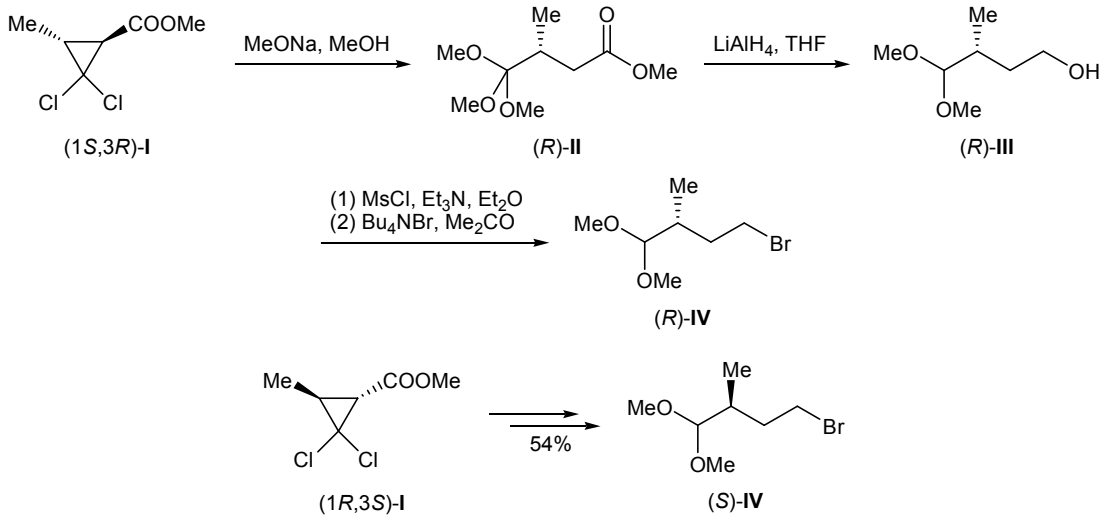
Apart from standard methylation procedures, cyclopropane derivatives are widely used to generate chiral centers bearing a methyl group. The synthesis of optically active cyclopropyl ketones as intermediate products was reported in numerous publications [4–10]. Methyl-branched compounds can be obtained from vinylcyclopropanes and divinylcyclopropanes [11–18]. In this respect, asymmetric [3+2]-cycloaddition reactions [19] and tandem transformations including cyclorpopanation and Cope rearrangement attract considerable interest [20, 21]. Such reactions ensure preparation of optically active substituted cyclopentenes and 1,4-cycloheptadienes without isolation of intermediate vinyl- and divinylcyclopropane derivatives.

A particular place is occupied by syntheses utilizing ring opening of hydroxycyclopropane derivatives [22–32]. Enantiopure methyl-branched compounds were synthesized by cyclopropanation of chiral amino and hydroxy acid esters, followed by cyclopropyl–allyl isomerization of the three-membered ring and diastereoselective reduction of the double bond in the resulting unsaturated compound [33–37].

Cyclopropane derivatives having no activated substituent in the ring can also undergo ring opening by the action of transition metal-based reagents [38] and strong electrophiles, e.g., lead(IV) [39], thallium(III) [40], and mercury(II) salts [41]. These reactions are generally characterized by high regio- and stereoselectivity, and the most interesting substrates are cyclopropylcarbinols which are readily accessible as optically active substances [42–48].

Thus, numerous examples of the use of cyclopropanes in stereoselective syntheses of methyl-branched natural compounds indicate their high synthetic potential. However, it is not always possible to obtain appropriate cyclopropane derivatives with a sufficiently high enantiomeric excess. Moreover, opening of the three-membered ring can be accompanied by reduction of the optical purity when the substrate contains a tertiary chiral center. Some procedures require difficultly accessible and toxic reagents. Therefore, development of new efficient methods for the synthesis of compounds possessing a methyl-branched carbon skeleton via transformations of cyclopropanes and cyclopropanols without loss of optical purity is an important problem of organic synthesis.

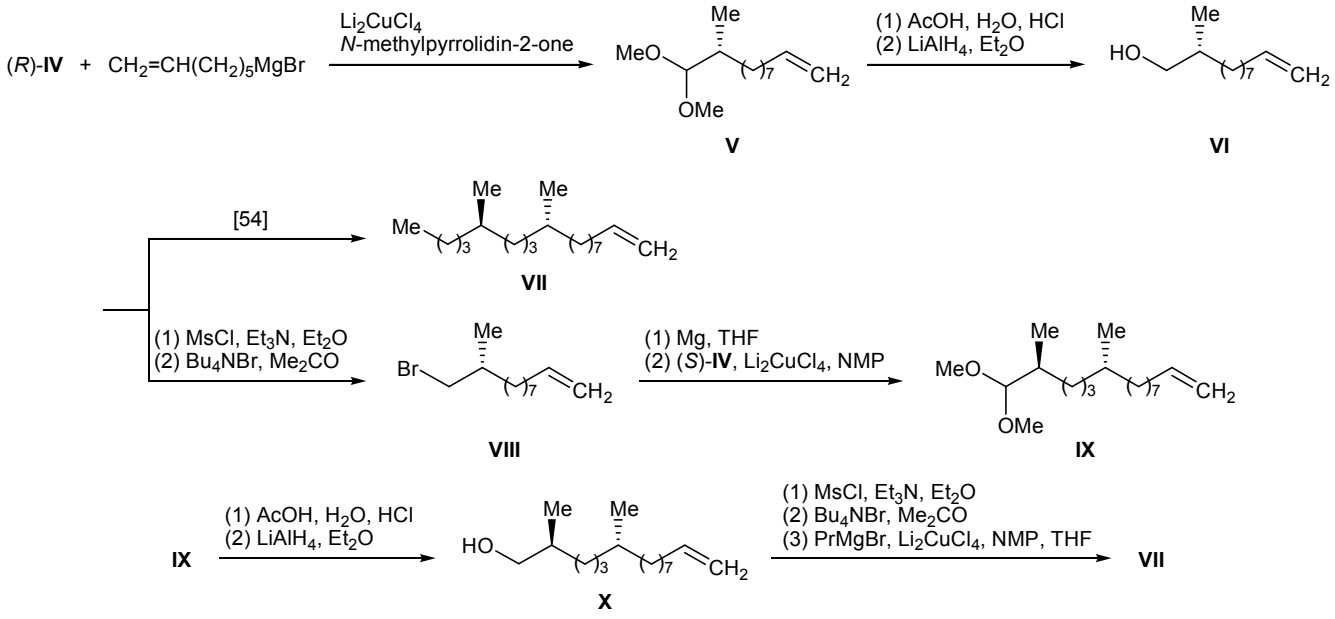
Scheme 1.



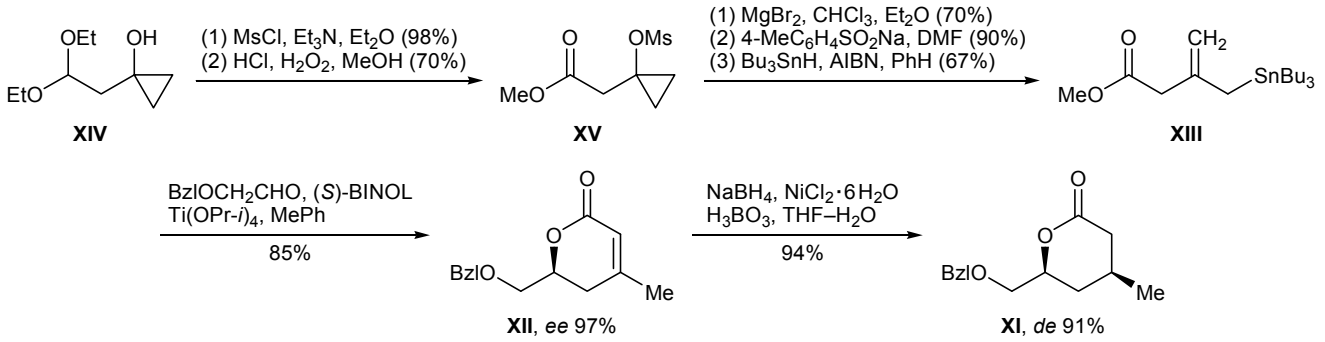
We previously demonstrated the possibility for the transformation of readily accessible methyl 2,2-dichlorocyclopropanecarboxylate (1*S*,3*R*)-(**I**) into chiral ortho ester (*R*)-**II** by the action of sodium methoxide via nucleophilic replacement of both chlorine atoms [49] and subsequent opening of the three-membered ring [50] (Scheme 1). It is known that ortho esters are readily hydrolyzed in acidic medium and are stable in basic medium and that they react with strong nucleophiles. By reduction of (*R*)-**II** with lithium tetrahydridoaluminate in boiling tetrahydrofuran we obtained compound (*R*)-**III** possessing hydroxy and protected aldehyde groups. The hydroxy group in (*R*)-**III** was replaced by bromine through intermediate methanesulfonate to obtain difunctional building block (*R*)-**IV**. Following an analogous scheme, from stereoisomeric ester (1*R*,3*S*)-**I** we synthesized bromide (*S*)-**IV** [51] (Scheme 1).

Coupling of (*R*)-**IV** with Grignard reagent afforded acetal **V** possessing a chiral center on C^2 (Scheme 2). It is known that removal of acetal protection can be accompanied by partial racemization of α-branched aldehyde [52]. However, no racemization was observed when compound **V** was hydrolyzed with aqueous acetic acid in the presence of a catalytic amount of HCl. Key alcohol **VI** was obtained by careful reduction of the reaction mixture obtained after removal of the acetal protection from **V**. The enantiomeric excess

Scheme 2.



Scheme 3.



XIV **XV** **XIII**

XII, *ee* 97% **XI**, *de* 91%

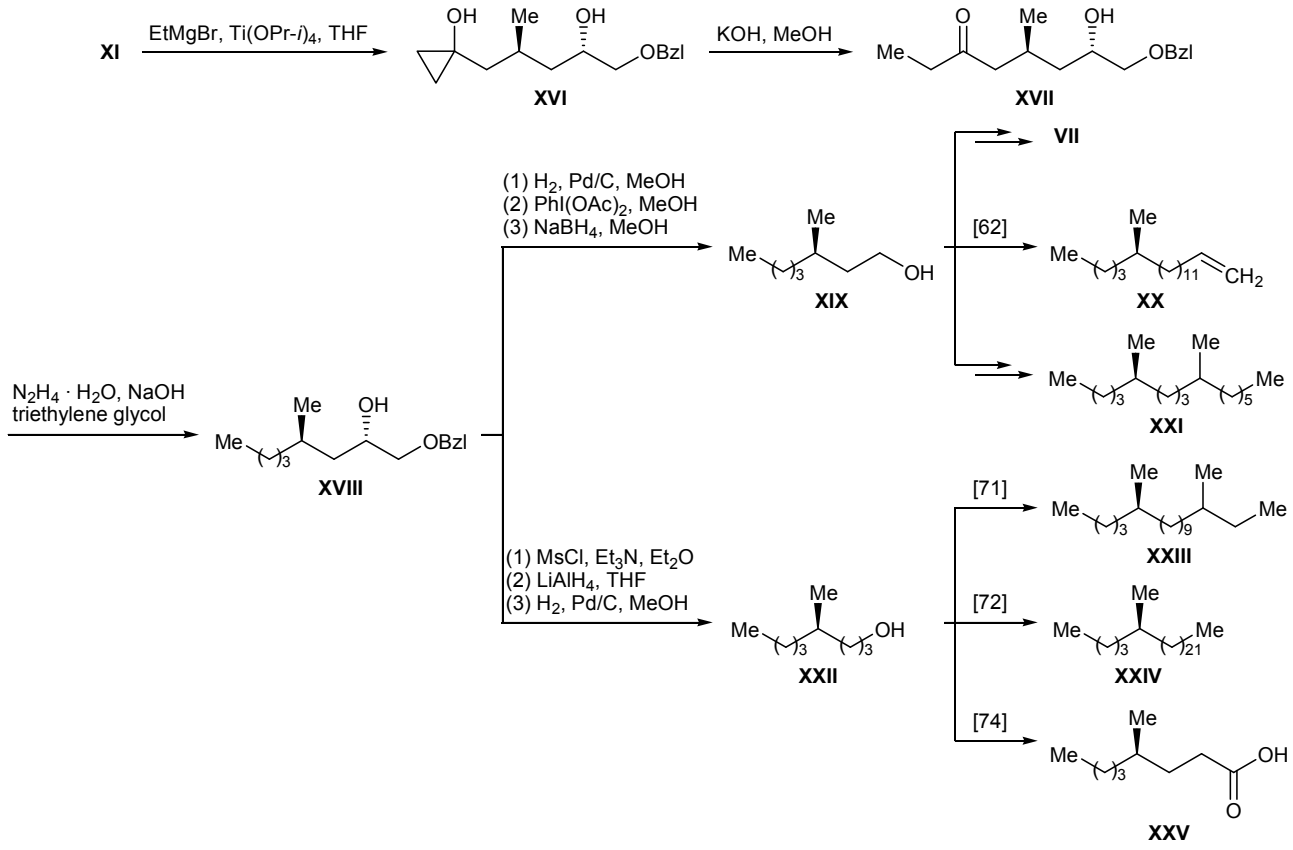
(*ee*) of alcohol **VI** was no less than 99%, as followed from the analysis of the ^{1}H NMR spectra of the corresponding Mosher ester [53]. The overall yield of **VI** starting from (1*S*,3*R*)-**I** was 43%.

Compound **VI** is a convenient building block for the synthesis of (10*R*,14*R*)-10,14-dimethyloctadec-1-ene (**VII**) [54], a component of the apple leafminer *Lyonetia prunifoliella* pheromone [55–57]. Only a few syntheses of **VII** and its stereoisomers have been reported [54, 57–59].

The key step in the synthesis of **VII** was coupling of (*S*)-**IV** with the Grignard compound prepared from 2 equiv of bromide **VIII**, which afforded acetal **IX**. Compound **VIII** was synthesized from alcohol **VI** according to the procedure described previously for bromide (*R*)-**IV**. Acetal **IX** was converted into chiral alcohol **X** (*ee* 99%) and then into the corresponding bromide, and reaction of the latter with propylmagnesium bromide gave target compound **VII** in an overall yield of 13% in 15 steps starting from methyl ester (1*R*,3*S*)-**I**.

Optically active lactone **XI** also turned out to be a convenient intermediate product for the preparation of methyl-branched building blocks for insect phero-

Scheme 4.



mones. Compound **XI** was synthesized according to the previously developed scheme which included diastereoselective reduction of chiral lactone **XII**. Lactone **XII** was obtained by Heck allylation of stannane **XIII** [34, 36] which is available on a gram scale through cyclopropanol intermediates **XIV** and **XV** [60, 61] (Scheme 3). The overall yield of compound **XII** in 7 steps was 23%.

Compound **XI** was smoothly subjected to cyclopropanation [30] (Scheme 4) to obtain hydroxyalkyl cyclopropanol **XVI** which was converted into ethyl ketone **XVII**. The Wolff–Kishner reduction of **XVII** gave alcohol **XVIII**, and a series of simple transformations of the latter (removal of the benzyl protection, oxidative cleavage of intermediate diol, and reduction of the resulting aldehyde) afforded known chiral alcohol **XIX** [62–69] with methyl-branched carbon skeleton. Compound **XIX** was used previously to build up a side-chain fragment of heptadepsipeptide HUN-7293 [66] and to synthesize (14*R*)-methyloctadec-1-ene (**XX**), sex pheromone of the peach leafminer moth *Lyonetia clerkella L*. [62]. Alcohol **XIX** may also be useful for the synthesis of other pheromones containing a similar structural fragment, e.g., of apple leafminer pheromone **VII** and 5,9-dimethylpentadecane stereoisomers (coffee leafminer moth *Perileucoptera coffeella* pheromone **XXI**) [70]. The overall yield of **XIX** starting from lactone **XI** (6 steps) was 34%, and its *ee* value was estimated at 97% with the aid of Mosher's acid [53]. The overall yield of chiral building block **XIX** was 8% in 13 steps starting from **XIV**.

Successive methanesulfonylation of **XVIII**, reduction of the resulting methanesulfonate, and removal of the benzyl protection afforded known alcohol **XXII** [71–73] which was also used in the synthesis of insect pheromones (Scheme 3). For example, compound **XXII** was converted into 3,13-dimethylheptadecane stereoisomers **XXIII** (components of the false hemlock looper *Nepytia freemani* sex pheromone [71]), (*R*)-5-methylheptacosane **XXIV** (characteristic component of the cuticular hydrocarbons of queen of the ant, *Diacamma* sp. [72]), and (*R*)-4-methyloctanoic acid (**XXV**, pheromone component of rhinoceros beetles of the genus *Oryctes* that are dangerous wood pests [74]). The overall yield of **XXII** was 39% starting from lactone **XI** (6 steps) and 9% starting from cyclopropanol **XIV** (13 steps).

In summary, we have described simple and convenient schemes for the synthesis of several optically active alcohols as methyl-branched chiral building blocks on the basis of halogen-substituted cyclopropanes, cyclopropanols, and products of their transformations and demonstrated broad potential of their use in the preparation of various biologically active compounds, primarily pest insect pheromones. In particular, we have synthesized (10*R*,14*R*)-10,14-dimethyloctadec-1-ene, a pheromone component of the apple leafminer moth *Lyonetia prunifoliella*. Formal schemes for the synthesis of pheromones of the peach leafminer moth *Lyonetia clerkella L*., false hemlock looper *Nepytia freemani*, and rhinoceros beetles of the genus *Oryctes* and a component of the cuticular secretion of the ant *Diacamma* sp. have been proposed.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded from solutions in chloroform-*d* on a Bruker AC 400 instrument at 400 and 100 MHz, respectively. The IR spectra were recorded from solutions in carbon tetrachloride on a Bruker Vertex 70 spectrometer. The optical rotations were measured at room temperature on an SM-3 polarimeter (scale division 0.05°). The products were isolated by chromatography on silica gel (70–230 mesh). Gas chromatographic/mass spectrometric analyses were carried out on a Hewlett Packard HP 5890 chromatograph coupled with an HP 5972 mass-selective detector (HP Innovax capillary column, 50 m × 0.2 mm; carrier gas helium; electron impact, 70 eV). The elemental compositions were determined by the semimicro method. All solvents were dried according to standard procedures and distilled just before use.

Methyl (3*R*)-4,4,4-trimethoxy-3-methylbutanoate (*R*)-(II). A solution of 90.0 mmol of sodium methoxide in 45 mL of anhydrous methanol was added dropwise under stirring to a solution of 7.50 g (41.0 mmol) of ester (1*S*,3*R*)-**I** [50] in 30 mL of anhydrous methanol on cooling with an ice bath. The cooling bath was removed, and the mixture was heated to 40°C and kept for 2 h at that temperature. The mixture was cooled to 0°C, diluted with 200 mL of water, and extracted with methylene chloride (5 × 50 mL). The extracts were combined, washed with brine, and dried over Na_2SO_4, the solvent was removed under reduced pressure, and the residue was distilled in a vacuum. Yield 6.93 g (82%), bp 48–50°C (1 mm), $[\alpha]_D = +9.2°$ (*c* = 7.5, Et_2O). IR spectrum: ν 1741 cm^{-1}. ^{1}H NMR spectrum, δ, ppm: 0.96 d (3H, C**H**$_3$CH, *J* = 6.8 Hz), 2.13 d.d (1H, CHC**H**$_2$, *J* = 15.4, 9.5 Hz), 2.45–2.54 m (1H, CH$_3$C**H**), 2.63 d.d (1H, CHC**H**$_2$, *J* = 15.4, 4.1 Hz), 3.29 s (9H, 4-OCH$_3$), 3.65 s (3H,

CO_2CH_3). ^{13}C NMR spectrum, δ_C, ppm: 14.2, 35.5, 36.4, 50.4 (3C), 51.4, 114.6, 173.8. Found, %: C 52.49; H 8.82. $C_9H_{18}O_5$. Calculated, %: C 52.41; H 8.80.

Methyl (3*S*)-4,4,4-trimethoxy-3-methyl-butanoate (*S*)-(II) was synthesized in a similar way from ester (1*R*,3*S*)-**I**. Yield 82%, $[\alpha]_D$ = –9.2° (*c* = 7.5, Et_2O). The spectral parameters of (*S*)-**II** were identical to those of (*R*)-**II**.

(3*R*)-4,4-Dimethoxy-3-methylbutan-1-ol (*R*)-(III). Lithium tetrahydridoaluminate, 7.40 g (195.0 mmol), was added in portions under stirring to a solution of 20.00 g (97.0 mmol) of ester (*R*)-**II** in 100 mL of THF, and the mixture was heated for 8 h under reflux in an argon atmosphere. The mixture was cooled and treated in succession with 7 mL of water, 7 mL of 15% aqueous sodium hydroxide, and 20 mL of water, 100 mL of methylene chloride was then added, and the mixture was filtered. The filtrate was dried over Na_2SO_4 and evaporated under reduced pressure, and the residue was subjected to chromatography using petroleum ether–diethyl ether (2:1) as eluent. Yield 11.95 g (83%), $[\alpha]_D$ = +5.5° (*c* = 3.2, Et_2O). IR spectrum: ν 3487 cm^{-1}. ^1H NMR spectrum, δ, ppm: 0.94 d (3H, C**H**$_3$CH, *J* = 6.9 Hz), 1.41–1.49 m and 1.70–1.78 m (1H each, CHC**H**$_2$), 1.89–1.99 m (1H, CH_3C**H**), 2.07 br.s (1H, OH), 3.36 s and 3.39 s (3H each, OCH_3), 3.59–3.75 m (2H, C**H**$_2$OH), 4.08 d [1H, C**H**$(OCH_3)_2$, *J* = 6.0 Hz]. ^{13}C NMR spectrum, δ_C, ppm: 15.4, 33.4, 35.0, 53.8, 54.9, 61.0, 109.0. Found, %: C 56.75; H 10.85. $C_7H_{16}O_3$. Calculated, %: C 56.73; H 10.88.

(3*S*)-4,4-Dimethoxy-3-methylbutan-1-ol (*S*)-(III) was synthesized in a similar way from ester (*S*)-**II**. Yield 83%, $[\alpha]_D$ = –5.5° (*c* = 3.0, Et_2O). The spectral parameters of the product were identical to those of (*R*)-**III**.

(2*R*)-4-Bromo-1,1-dimethoxy-2-methylbutane (*R*)-(IV). A solution of 7.59 g (51.3 mmol) of alcohol (*R*)-**III** and 16.0 mL (115.0 mmol) of triethylamine in 50 mL of anhydrous diethyl ether was cooled to 0°C, a solution of 6.0 mL (77.5 mmol) of methanesulfonyl chloride in 25 mL of diethyl ether was added, and the mixture was stirred for 1 h at 0°C. The mixture was then treated with a saturated aqueous solution of sodium hydrogen carbonate (100 mL), the organic layer was separated, the aqueous layer was extracted with ethyl acetate (3×30 mL), the extracts were combined with the organic phase, dried over Na_2SO_4, and evaporated under reduced pressure, the residue was dissolved in 50 mL of benzene, and the solution was evaporated under reduced pressure. The residue was dissolved in 80 mL of acetone, 24.6 g (76.9 mmol) of tetrabutylammonium bromide and 0.7 mL (5.1 mmol) of triethylamine were added, and the mixture was heated for 2 h at 50–55°C. The mixture was cooled and evaporated under reduced pressure, the residue was treated with 200 mL of water, and the product was extracted into diethyl ether (4×50 mL). The combined extracts were washed with water and brine, dried over Na_2SO_4, and evaporated under reduced pressure, and the residue was purified by chromatography using petroleum ether–diethyl ether (20:1) as eluent. Yield 8.77 g (81%), $[\alpha]_D$ = –14.5° (*c* = 5.0, Et_2O). IR spectrum, ν, cm^{-1}: 2935, 2831. ^1H NMR spectrum, δ, ppm: 0.92 d (3H, C**H**$_3$CH, *J* = 6.8 Hz), 1.63–1.71 m (1H, CH_3C**H**), 1.94–2.12 m (2H, CHC**H**$_2$), 3.35 s and 3.36 s (3H each, CH_3O), 3.39–3.58 m (2H, CH_2Br), 4.06 d [1H, C**H**$(OCH_3)_2$, *J* = 6.0 Hz]. ^{13}C NMR spectrum, δ_C, ppm: 14.1, 32.1, 34.5, 34.9, 54.0, 54.5, 108.4. Found, %: C 39.90; H 7.19. $C_7H_{15}BrO_2$. Calculated, %: C 39.83; H 7.16.

(2*S*)-4-Bromo-1,1-dimethoxy-2-methylbutane (*S*)-IV was synthesized in a similar way from (*S*)-**III**. Yield 79%, $[\alpha]_D$ = +14.0° (*c* = 5.0, Et_2O). The spectral parameters of the product coincided with those of (*R*)-**IV**.

(10*R*)-11,11-Dimethoxy-10-methylundec-1-ene (V). The Grignard reagent prepared from 4.43 g (25.0 mmol) of 7-bromohept-1-ene and 0.91 g (37.5 mmol) of magnesium in 30 mL of THF [59] was added under stirring at room temperature to a solution of 2.25 g (10.7 mmol) of bromide (*R*)-**IV**, 8.92 g (90.0 mmol) of *N*-methylpyrrolidin-2-one (NMP), 40 mg (0.94 mmol) of LiCl, and 63 mg (0.47 mmol) of $CuCl_2$ in 20 mL of THF. The mixture was stirred for 1 h at room temperature, treated with 40 mL of a saturated aqueous solution of ammonium chloride, and the aqueous phase was extracted with petroleum ether (3×20 mL). The combined extracts were washed with a saturated aqueous solution of $NaHCO_3$ and dried over Na_2SO_4, the solvent was distilled off under reduced pressure, and the residue was subjected to chromatography using petroleum ether–ethyl acetatate (30:1) as eluent. Yield 2.30 g (94%), $[\alpha]_D$ = +13.1° (*c* = 1.8, hexane). IR spectrum: ν 3081 cm^{-1}. ^1H NMR spectrum, δ, ppm: 0.88 d (3H, C**H**$_3$CH, *J* = 6.8 Hz), 1.02–1.51 m [12H, (C**H**$_2$)$_6$CH$_2$CH=], 1.66–1.76 m (1H, CH_3C**H**), 2.00–2.06 m (2H, C**H**$_2$CH=CH_2), 3.34 s (6H, CH_3O), 4.01 d [1H, C**H**$(OCH_3)_2$, *J* = 6.5 Hz], 4.90–5.00 m (2H, CH=C**H**$_2$), 5.81 d.d.t (1H, C**H**=CH_2, *J* = 17.0, 10.2, 6.7 Hz). ^{13}C NMR spectrum, δ_C, ppm:

14.3, 26.9, 28.9, 29.1, 29.4, 29.8, 31.6, 33.8, 35.6, 53.8, 54.0, 108.9, 114.1, 139.2. Found, %: C 73.55; H 12.35. $C_{14}H_{28}O_2$. Calculated, %: C 73.63; H 12.36.

(2*R*)-2-Methylundec-10-en-1-ol (VI). A mixture of 11.49 g (50.4 mmol) of acetal **V**, 100 mL of acetic acid, 100 mL of water, and 1.0 mL of 5% aqueous HCl was stirred for 5 h at room temperature under argon. The mixture was diluted with 150 mL of water, neutralized with solid $NaHCO_3$, and extracted with diethyl ether (4×80 mL). The combined extracts were washed with brine and dried over Na_2SO_4, the solvent was removed under reduced pressure, the residue was dissolved in 50 mL of diethyl ether, and the solution was added dropwise under stirring to a suspension of 1.00 g (26.3 mmol) of $LiAlH_4$ in 50 mL of anhydrous diethyl ether on cooling to –20°C. The mixture was allowed to warm up to 0°C and treated with 100 mL of 10% aqueous H_2SO_4. The organic phase was separated, the aqueous phase was extracted with diethyl ether (3×50 mL), the extracts were combined with the organic phase and washed in succession with water and saturated aqueous solutions of $NaHCO_3$ and NaCl, the solvent was distilled off under reduced pressure, and the residue was subjected to chromatography using petroleum ether–ethyl acetate (40:1) as eluent. Yield 7.79 g (84%), $[\alpha]_D$ = +8.4° (*c* = 4.6, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3508, 3078. ^{1}H NMR spectrum, δ, ppm: 0.90 d (3H, C**H**$_3$CH, *J* = 6.8 Hz), 1.05–1.64 m [14H, (C**H**$_2$)$_6$CH$_2$CH=, CH$_3$C**H**, OH], 2.00–2.06 m (2H, C**H**$_2$CH=CH$_2$), 3.41 d.d (1H, C**H**$_2$OH, *J* = 10.4, 6.5 Hz), 3.50 d.d (1H, C**H**$_2$, *J* = 10.4, 5.7 Hz), 4.91–5.01 m (2H, CH=C**H**$_2$), 5.81 d.d.t (1H, C**H**=CH$_2$, *J* = 17.0, 10.2, 6.7 Hz). ^{13}C NMR spectrum, δ_C, ppm: 16.5, 26.9, 28.9, 29.1, 29.4, 29.8, 33.1, 33.8, 35.7, 68.3, 114.1, 139.2. Found, %: C 78.22; H 13.09. $C_{12}H_{24}O$. Calculated, %: C 78.20; H 13.12.

(10*R*)-11-Bromo-10-methylundec-1-ene (VIII) was synthesized from alcohol **VI** according to the procedure described above for compound (*R*)-**IV**. The product was isolated by chromatography using petroleum ether as eluent. Yield 93%. IR spectrum: ν 3078 cm^{-1}. ^{1}H NMR spectrum, δ, ppm: 1.00 d (3H, C**H**$_3$CH, *J* = 6.7 Hz), 1.17–1.51 m [12H, (C**H**$_2$)$_6$CH$_2$CH=], 1.75–1.82 m (1H, CH$_3$C**H**), 2.00–2.06 m (2H, C**H**$_2$CH=CH$_2$), 3.32 d.d (1H, CH$_2$Br, *J* = 9.7, 6.4 Hz), 3.40 d.d (1H, CH$_2$Br, *J* = 9.7, 5.0 Hz), 4.91–5.01 m (2H, CH=C**H**$_2$), 5.81 d.d.t (1H, C**H**=CH$_2$, *J* = 17.0, 10.2, 6.7 Hz). ^{13}C NMR spectrum, δ_C, ppm: 18.7, 26.8, 28.9, 29.1, 29.4, 29.6, 33.8, 34.8, 35.2, 41.6, 114.1, 139.2. Found, %: C 58.36; H 9.35. $C_{12}H_{23}Br$. Calculated, %: C 58.30; H 9.38.

(10*R*,14*S*)-15,15-Dimethoxy-10,14-dimethylpentadec-1-ene (IX). A solution of 0.89 g (3.60 mmol) of bromide **VIII** in 4.5 mL of THF was added dropwise under argon to 0.18 g (7.40 mmol) of magnesium. The mixture was stirred for 1 h at 45°C and cooled to room temperature, and the resulting solution of Grignard reagent was added dropwise under stirring in an argon atmosphere to a solution of 0.38 g (1.80 mmol) of bromide (*S*)-**IV**, 1.45 g (14.6 mmol) of NMP, 4.2 mg (0.10 mmol) of LiCl, and 6.7 mg (0.05 mmol) of $CuCl_2$ in 5 mL of THF. The mixture was stirred for 1 h at room temperature, treated with 10 mL of a saturated aqueous solution of ammonium chloride, and extracted with petroleum ether (3×10 mL). The combined extracts were washed with a saturated solution of $NaHCO_3$ and dried over Na_2SO_4, the solvent was removed under reduced pressure, and the product was isolated by chromatography using petroleum ether–ethyl acetate (30:1) as eluent. Yield 0.46 g [85%, calculated on (*S*)-**IV**], $[\alpha]_D$ = –10.3° (*c* = 1.9, hexane). IR spectrum: ν 3079 cm^{-1}. ^{1}H NMR spectrum, δ, ppm: 0.83 d (3H, C**H**$_3$CH, *J* = 6.5 Hz), 0.88 d [3H, C**H**$_3$CHCH(OCH$_3$)$_2$, *J* = 6.8 Hz], 1.02–1.48 m [19H, (C**H**$_2$)$_6$CH$_2$CH=, CH(C**H**$_2$)$_3$CH, C**H**CH$_3$], 1.66–1.76 m [1H, CH$_3$C**H**CH(OCH$_3$)$_2$], 2.00–2.06 m (2H, C**H**$_2$CH=CH$_2$), 3.34 s (6H, CH$_3$O), 4.01 d [1H, C**H**(OCH$_3$)$_2$, *J* = 6.5 Hz], 4.90–5.00 m (2H, CH=C**H**$_2$), 5.81 d.d.t (1H, C**H**=CH$_2$, *J* = 17.0, 10.2, 6.7 Hz). ^{13}C NMR spectrum, δ_C, ppm: 14.3, 19.6, 24.3, 27.1, 28.9, 29.1, 29.5, 29.9, 31.9, 32.7, 33.8, 35.6, 37.1, 37.2, 53.8, 54.0, 109.0, 114.1, 139.2. Found, %: C 76.54; H 12.85. $C_{19}H_{38}O_2$. Calculated, %: C 76.45; H 12.83.

(2*S*,6*R*)-2,6-Dimethylpentadec-14-en-1-ol (X) was synthesized from acetal **IX** according to the procedure described above for alcohol **VI**. Yield 82%. The spectral parameters of the product coincided with those reported in [56].

(10*R*,14*R*)-10,14-Dimethyloctadec-1-ene (VII). Following the procedure described above for the synthesis of (*R*)-**IV**, mesylation of 0.28 g (1.10 mmol) of alcohol **X**, followed by replacement of the sulfonate group by bromine, gave the corresponding bromide which was dissolved (without additional purification) in 3 mL of THF, 2.20 g (22.2 mmol) of NMP, 19 mg (0.45 mmol) of LiCl, and 30 mg (0.22 mmol) of $CuCl_2$ were added, and 5.0 mL (5.0 mmol) of a 1.0 M solution of propylmagnesium bromide in THF was added dropwise under stirring in an argon atmosphere. The mixture was stirred for 1 h at room temperature and treated with 10 mL of a saturated aqueous solution of

ammonium chloride, and the aqueous phase was extracted with petroleum ether (3×10 mL). The combined extracts were washed with a saturated aqueous solution of $NaHCO_3$ and dried over Na_2SO_4, the solvent was removed under reduced pressure, and the residue was subjected to chromatography using petroleum ether as eluent. Yield 0.28 g (91%). The spectral parameters of the product coincided with those given in [54, 56, 59]. According to the GLC data, compound **VII** contained >98% of the main substance. Mass spectrum: *m*/*z* 280 (I_{rel} 0.4%) $[M]^+$.

1-[(2*S*,4*S*)-5-Benzyloxy-3-hydroxy-2-methylpentyl]cyclopropanol (XVI). A solution of 45.0 mmol of ethylmagnesium bromide in 45 mL of THF was added under stirring over a period of 4.5 h to a solution of 2.34 g (10.0 mmol) of lactone **XI** and 2.8 mL (10.0 mmol) of Ti(OPr-*i*)$_4$ in 10 mL of THF, and the mixture was stirred for 12 h. The solvent was removed under reduced pressure, and 50 mL of methylene chloride and 6 mL of a saturated aqueous solution of ammonium chloride were added to the residue under efficient cooling. The mixture was filtered, the precipitate was washed with methylene chloride (3×20 mL), and the organic phase was separated, washed with a saturated aqueous solution of $NaHCO_3$ (50 mL), and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the product was isolated by chromatography using petroleum ether–ethyl acetate (10:1) as eluent. Yield 2.14 g (81%), $[\alpha]_D$ = –3.2° (*c* = 1.2, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3392, 1076, 1028. ^{1}H NMR spectrum, δ, ppm: 0.98 d (3H, C**H**$_3$CH, *J* = 6.7 Hz), 0.33–0.43 m and 0.68–0.78 m (2H each, CH_2 in cyclopropane), 0.95–1.09 m and 1.24–1.36 m (1H each, CC**H**$_2$CHCH$_3$), 1.60–1.69 m (1H, CH$_3$C**H**), 1.73–1.82 m and 2.10–2.17 m (1H each, C**H**$_2$CHOH), 3.29–3.34 m and 3.43–3.47 m (1H each, C**H**$_2$OBzl), 3.91–3.98 m (1H, C**H**OH), 4.54 br.s (2H, C**H**$_2$Ph), 7.27–7.38 m (5H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 12.9, 14.5, 20.7, 27.0, 39.2, 45.9, 53.5, 68.8, 73.30, 75.3, 127.7 (2C), 128.4 (2C), 137.9. Found, %: C 72.73; H 9.13. $C_{16}H_{24}O_3$. Calculated, %: C 72.69; H 9.15.

(5*S*,7*S*)-8-Benzyloxy-7-hydroxy-5-methyloctan-3-one (XVII). Potassium hydroxide, 0.17 g (3.0 mmol), was added to a solution of 0.40 g (1.5 mmol) of cyclopropanol **XVI** in 3 mL of methanol, and the mixture was heated for 1 h under reflux. The mixture was diluted with water and extracted with diethyl ether (3×10 mL), the combined extracts were dried over Na_2SO_4, the solvent was removed under reduced pressure, and the residue was subjected to chromatography using petroleum ether–ethyl acetate (25:1) as eluent. Yield 0.36 g (90%), $[\alpha]_D$ = –4.2° (*c* = 1.8, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3430, 1712, 1196, 1093. ^{1}H NMR spectrum, δ, ppm: 0.91 d (3H, CHC**H**$_3$, *J* = 6.7 Hz), 0.95 t (3H, CH$_2$C**H**$_3$, *J* = 7.5 Hz), 1.58–1.74 m (3H, C**H**CH$_3$, CHC**H**$_2$CHOH), 1.89 br.s (1H, OH), 1.90–2.06 m (2H, CH$_3$C**H**$_2$CO), 2.27–2.46 m (2H, COC**H**$_2$CH), 3.41 d.d (1H, C**H**$_2$OBzl, *J* = 10.0, 4.4 Hz), 3.47 d.d (1H, C**H**$_2$OBzl, *J* = 10.0, 6.4 Hz), 4.09–4.15 m (1H, C**H**OH), 4.57 br.s and 4.59 br.s (1H each, C**H**$_2$Ph), 7.27–7.38 m (5H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 7.5, 22.1, 25.1, 26.0, 35.9, 40.6, 50.2, 69.6, 73.2, 73.7, 127.5, 126.6, 127.7, 128.3, 128.5, 138.5, 211.3. Found, %: C 72.72; H 9.13. $C_{16}H_{24}O_3$. Calculated, %: C 72.69; H 9.15.

(2*S*,4*R*)-1-Benzyloxy-4-methyloctan-2-ol (XVIII). Powdered potassium hydroxide, 0.30 g (5.4 mmol), was added to a solution of 0.24 g (0.9 mmol) of ketone **XVII** and 0.2 mL of hydrazine hydrate in 4.5 mL of triethylene glycol. The mixture was carefully heated in a stream of argon to 180°C over a period of 1 h and then to 210°C, cooled to room temperature, and diluted with 20 mL of water, and the aqueous phase was extracted with diethyl ether (3×10 mL). The combined extracts were washed with brine (15 mL) and dried over Na_2SO_4, the solvent was removed under reduced pressure, and the product was isolated by chromatography using petroleum ether–ethyl acetate (25:1) as eluent. Yield 0.16 g (70%), $[\alpha]_D$ = –6.3° (*c* = 1.6, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3460, 1103, 1029. ^{1}H NMR spectrum, δ, ppm: 0.87 d (3H, CHC**H**$_3$, *J* = 6.9 Hz), 0.88 t (3H, CH$_2$C**H**$_3$, *J* = 6.9 Hz), 1.06 d.d.d (1H, CHC**H**$_2$CHOH, *J* = 13.3, 9.4, 3.8 Hz), 1.12–1.34 m [6H, CH$_3$(C**H**$_2$)$_3$CH], 1.49 d.d.d (1H, CHC**H**$_2$CHOH, *J* = 13.3, 9.4, 4.4 Hz), 1.61–1.70 m (1H, C**H**CH$_3$), 2.28 br.s (1H, OH), 3.30 d.d (1H, C**H**$_2$OBzl, *J* = 9.4, 7.9 Hz), 3.43 d.d (1H, C**H**$_2$OBzl, *J* = 9.4, 2.8 Hz), 3.90–3.94 m (1H, C**H**OH), 4.56 br.s (2H, C**H**$_2$Ph), 7.24–7.38 m (5H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 14.1, 19.2, 22.9, 28.9, 29.2, 37.5, 40.3, 68.3, 73.4, 75.3, 127.7 (3C), 128.5 (2C), 138.6. Found, %: C 76.79; H 10.45. $C_{16}H_{26}O_2$. Calculated, %: C 76.75; H 10.47.

(3*R*)-3-Methylheptan-1-ol (XIX). Alcohol **XVIII**, 3.00 g (12.0 mmol), was dissolved in 50 mL of methanol, 0.30 g of 5% Pd(OH)$_2$/C was added, and the mixture was vigorously stirred for 3 h in a hydrogen atmosphere. The mixture was diluted with 50 mL of methylene chloride, the catalyst was filtered off and washed with 30 mL of methylene chloride, and the

filtrate was combined with the washings and evaporated under reduced pressure. The residue was dissolved in 20 mL of methanol, 4.67 g (14.5 mmol) of $PhI(OAc)_2$ was added, the mixture was stirred for 10 min and cooled to 0°C, 0.46 g (12.0 mmol) of $NaBH_4$ was added, and the mixture was stirred for 1 h. It was then treated with a saturated aqueous solution of NH_4Cl (40 mL) and extracted with diethyl ether (3× 15 mL), the combined extracts were dried over $MgSO_4$ and evaporated under reduced pressure, and the product was isolated by chromatography on silica gel using petroleum ether–ethyl acetate (20:1) as eluent. Yield 1.03 g (66% in 3 steps). The spectral parameters of **XIX** coincided with those given in [62].

(4*R*)-4-Methyloctan-1-ol (XXII). A solution of 1.00 g (4.0 mmol) of alcohol **XVIII** in 10 mL of anhydrous diethyl ether was cooled to 0°C, 0.9 mL (6.3 mmol) of triethylamine and a solution of 0.5 mL (5.0 mmol) of methanesulfonyl chloride in 5 mL of anhydrous diethyl ether were added in succession, and the mixture was stirred for 2 h and treated with a saturated aqueous solution of $NaHCO_3$ (15 mL). The organic phase was separated, the aqueous phase was extracted with diethyl ether (3×10 mL), and the extracts were combined with the organic phase, washed with brine (15 mL), and dried over Na_2SO_4. Removal of the solvent under reduced pressure quantitatively afforded intermediate methanesulfonate which was dissolved in 3 mL of anhydrous THF, and the solution was added under stirring to a boiling suspension of 0.15 g (4.0 mmol) of $LiAlH_4$ in 4 mL of anhydrous THF. After 1 h, the mixture was diluted with 30 mL of diethyl ether and treated with 1 mL of water on cooling, and the organic layer was separated and dried over Na_2SO_4. The solvent was removed under reduced pressure, the residue was dissolved in 20 mL of methanol, 0.10 g of 5% $Pd(OH)_2/C$ was added, and the mixture was vigorously stirred for 3 h in a hydrogen atmosphere. The mixture was then diluted with 50 mL of methylene chloride, the catalyst was filtered off and washed with 30 mL of methylene chloride, and the filtrate was combined with the washings and evaporated under reduced pressure. The product was isolated by chromatography on silica gel using petroleum ether–ethyl acetate (30:1) as eluent. Yield 0.44 g (76% in 3 steps). The spectral parameters of **XXII** coincided with those given in [73].

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REFERENCES

1. Yakovleva, M.P., Khasanova, E.F., Talipov, R.F., and Ishmuratov, G.Yu., *Vestn. Bashkir. Univ*., 2009, vol. 14, p. 1072.
2. Mori, K., *Tetrahedron*, 1989, vol. 45, p. 3233.
3. Ishmuratov, G.Yu., Kharisov, R.Ya., Odinokov, V.N., and Tolstikov, G.A., *Russ. Chem. Rev*., 1995, vol. 64, p. 541.
4. Abdallah, H., Gree, R., and Carrie, R., *Tetrahedron*, 1985, vol. 41, p. 4339.
5. Cid, M.M., Eggnauer, U., Weber, H.P., and Pombo-Villar, E., *Tetrahedron Lett*., 1991, vol. 32, p. 7233.
6. Oppolzer, W. and Radinov, N., *J. Am. Chem. Soc*., 1993, vol. 115, p. 1593.
7. Srikrishna, A., Anebouselvy, K., and Reddy, T.J., *Tetrahedron Lett*., 2000, vol. 41, p. 6643.
8. Honma, M., Sawada, T., Fujisawa, Y., Utsugi, M., Watanabe, H., Umino, A., Matsumura, T., Hagihara, T., Takano, M., and Nakada, M., *J. Am. Chem. Soc*., 2003, vol. 125, p. 2860.
9. Takano, M., Umino, A., and Nakada, M., *Org. Lett*., 2004, vol. 6, p. 4897.
10. Hodgson, D.M., Chung, Y.K., Nuzzo, I., Freixas, G., Kulikievicz, K.K., Cleator, E., and Paris, J.-M., *J. Am. Chem. Soc*., 2007, vol. 129, p. 4456.
11. Goldschmidt, Z. and Crammer, B., *Chem. Soc. Rev*., 1988, vol. 17, p. 229.
12. Harada, S., Kiyono, H., Nishio, R., Taguchi, T., and Hanzawa, Y., *J. Org. Chem*., 1997, vol. 62, p. 3994.
13. Barrett, A.G.M. and Tam, W., *J. Org. Chem*., 1997, vol. 62, p. 7673.
14. Davies, H.M.L., Kong, N., and Churchill, M.R., *J. Org. Chem*., 1998, vol. 63, p. 6586.
15. Cossy, J., Blanchard, N., and Meyer, C., *Synthesis*, 1999, p. 1063.
16. Rubin, M., Rubina, M., and Gevorgyan, V., *Chem. Rev*., 2007, vol. 107, p. 3117.
17. Connor, D.T., Kluthko, S., and Strandtman, M., *J. Antibiot*., 1979, vol. 32, p. 368.
18. Davies, H.M.L., *Tetrahedron*, 1993, vol. 49, p. 5203.
19. Davies, H.M.L., Xiang, B., Kong, N., and Stafford, D.G., *J. Am. Chem. Soc*., 2001, vol. 123, p. 7461.
20. Davies, H.M.L., Stafford, D.G., Doan, B.D., and Houser, J.H., *J. Am. Chem. Soc*., 1998, vol. 120, p. 3326.
21. Müller, P., Allenbach, Y.F., and Grass, S., *Tetrahedron: Asymmetry*, 2005, vol. 16, p. 2007.
22. Nakamura, E., Sekiya, K., and Kuwajima, I., *Tetrahedron Lett*., 1987, vol. 28, p. 337.

23. Sugimura, T., Futagawa, T., and Tai, A., *Tetrahedron Lett*., 1988, vol. 29, p. 5775.
24. Imai, T., Mineta, H., and Nishida, S., *J. Org. Chem*., 1990, vol. 55, p. 4986.
25. Scott, R.W. and Heathcock, C.H., *Carbohydr. Res*., 1996, vol. 291, p. 205.
26. Ramana, C.V., Murali, R., and Nagarajan, M., *J. Org. Chem*., 1997, vol. 62, p. 7694.
27. Schumacher, R., Dammast, F., and Reiβig, H.-U., *Chem. Eur. J*., 1997, vol. 3, p. 614.
28. Beyer, J. and Madsen, R., *J. Am. Chem. Soc*., 1998, vol. 120, p. 12137.
29. Luithle, J.E.A. and Pietruszka, J., *Eur. J. Org. Chem*., 2000, p. 2557.
30. Kulinkovich, O.G., *Chem. Rev*., 2003, vol. 103, p. 2597.
31. Li, X., Li, J., and Mootoo, D.R., *Org. Lett*., 2007, vol. 9, p. 4303.
32. Konik, Y.A., Kananovich, D.G., and Kulinkovich, O.G., *Tetrahedron*, 2013, vol. 69, p. 6673.
33. Lysenko, I.L. and Kulinkovich, O.G., *Russ. J. Org. Chem*., 2005, vol. 41, p. 70.
34. Bekish, A.V., Prokhorevich, K.N., and Kulinkovich, O.G., *Eur. J. Org. Chem*., 2006, p. 5069.
35. Mineyeva, I.V. and Kulinkovich, O.G., *Tetrahedron Lett*., 2010, vol. 51, p. 1836.
36. Mineeva, I.V., *Russ. J. Org. Chem*., 2013, vol. 49, p. 253.
37. Mineeva, I.V., *Russ. J. Org. Chem*., 2013, vol. 49, p. 979.
38. Bishop, K.C., *Chem. Rev*., 1976, vol. 76, p. 461.
39. Ouellette, R.J. and Shaw, D.L., *J. Am. Chem. Soc*., 1964, vol. 86, p. 1651.
40. Ouellette, R.J., Shaw, D.L., and South, A., Jr., *J. Am. Chem. Soc*., 1964, vol. 86, p. 2744.
41. Meyer, C., Blanchard, N., Defosseux, M., and Cossy, J., *Acc. Chem. Res*., 2003, vol. 36, p. 766.
42. Collum, D.B., Mohamadi, F., and Hallock, J.S., *J. Am. Chem. Soc*., 1983, vol. 105, p. 6882.
43. Collum, D.B., Still, W.C., and Mohamadi, F., *J. Am. Chem. Soc*., 1986, vol. 108, p. 2094.
44. Charette, A.B. and Marcoux, J.-F., *Synlett*, 1995, p. 1197.
45. Cossy, J., Blanchard, N., and Meyer, C., *Org. Lett*., 2001, vol. 3, p. 2567.
46. Cossy, J., Blanchard, N., Defosseux, M., and Meyer, C., *Angew. Chem., Int. Ed*., 2002, vol. 41, p. 2144.
47. Lebel, H., Marcoux, J.-F., Molinaro, C., and Charette, A.B., *Chem. Rev*., 2003, vol. 103, p. 977.
48. Fox, J.M. and Yan, N., *Curr. Org. Chem*., 2005, vol. 9, p. 719.
49. Tishchenko, I.G., Kulinkovich, O.G., and Glazkov, Yu.V., *Zh. Org. Khim*., 1975, vol. 11, p. 581.
50. Kovalenko, V.N. and Kulinkovich, O.G., *Tetrahedron: Asymmetry*, 2011, vol. 22, p. 26.
51. Kovalenko, V.N. and Matiushenkov, E.A., *Tetrahedron: Asymmetry*, 2012, vol. 23, p. 1393.
52. Hosokawa, T., Yamanaka, T., Itotani, M., and Murahashi, S.-I., *J. Org. Chem*., 1995, vol. 60, p. 6159.
53. Byström, S., Högberg, H.-E., and Norin, T., *Tetrahedron*, 1981, vol. 37, p. 2249.
54. Yadav, J.S., Gayathri, K.U., Trimurtulu, N., and Prasad, A.R., *Tetrahedron*, 2009, vol. 65, p. 3536.
55. Gries, R., Gries, G., King, G.G.S., and Maier, C.T., *J. Chem. Ecol*., 1997, vol. 23, p. 1119.
56. Tamagawa, H., Takikawa, H., and Mori, K., *Eur. J. Org. Chem*., 1999, p. 973.
57. Nakamura, Y. and Mori, K., *Eur. J. Org. Chem*., 2000, p. 2745.
58. Mori, K., *Pure Appl. Chem*., 2001, vol. 73, p. 601.
59. Van Summeren, R.P., Reijmer, S.J.W., Feringa, B.L., and Minnaard, A.J., *Chem. Commun*., 2005, p. 1387.
60. Mineeva, I.V. and Kulinkovich, O.G., *Russ. J. Org. Chem*., 2008, vol. 44, p. 1261.
61. Mineeva, I.V. and Kulinkovich, O.G., *Russ. J. Org. Chem*., 2009, vol. 45, p. 1623.
62. Mori, K. and Kato, M., *Justus Liebigs Ann. Chem*., 1985, p. 2083.
63. Castle, G.H. and Ley, S.V., *Tetrahedron Lett*., 1994, vol. 35, p. 7455.
64. King, G.G.S., Gries, R., Gries, G., abd Slessor, K.N., *J. Chem. Ecol*., 1995, vol. 21, p. 2027.
65. Norsikian, S., Marek, I., and Normant, J.-F., *Tetrahedron Lett*., 1997, vol. 38, p. 7523.
66. Boger, D.L., Keim, H., Oberhauser, B., Schreiner, E.P., and Foster, C.A., *J. Am. Chem. Soc*., 1999, vol. 121, p. 6197.
67. Norsikian, S., Marek, I., Klein, S., Poisson, J.F. and Normant, J.F., *Chem. Eur. J*., 1999, vol. 5, p. 2055.
68. Tai, A., Syouno, E., Tanaka, K., Fujita, M., Sugimura, T., Higashiura, Y., Kakizaki, M., Hara, H., and Naito, T., *Bull. Chem. Soc. Jpn*., 2002, vol. 75, p. 111.
69. Burger, B.V. and Petersen, W.G.B., *J. Chem. Ecol*., 2002, vol. 28, p. 501.
70. Liang, T., Kuwahara, S., Hasegawa, M., and Kodama, O., *Biosci. Biotechnol. Biochem*., 2000, vol. 64, p. 2474.
71. Takikawa, H., Shirai, Y., Kobayashi, M., and Mori, K., *Justus Liebigs Ann. Chem*., 1996, p. 1965.
72. Marukawa, K., Takikawa, H., and Mori, K., *Biosci. Biotechnol. Biochem*., 2001, vol. 65, p. 305.
73. Munoz, L., Bosch, M.P., Guerrero, A., and Rosell, G., *Tetrahedron: Asymmetry*, 2009, vol. 20, p. 420.
74. Song, S., Zhu, S.-F., Yu, Y.-B., and Zhou, Q.-L., *Angew. Chem., Int. Ed*., 2013, vol. 52, p. 1556.