Латвийский институт органического синтеза

Химия гетероциклических соединений **2018**, *54*(3), 320–328

Химия гетероциклических соединений

Sequentially rhodium-catalyzed enantioselective cycloisomerization–hydrogenation syntheses of alkylidene butyrolactone β-hydroxyethanes and alkylidene tetrahydrofuran β-aminoethanes

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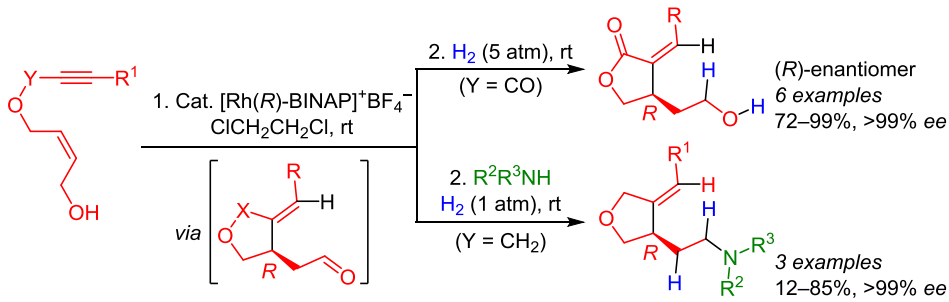
Submitted February 26, 2018
Accepted March 27, 2018



The enantioselective Rh-catalyzed Alder-ene cycloisomerization of ester- and ether-tethered alkyne allyl alcohols is an excellent entry to subsequent Rh-catalyzed one-pot hydrogenations in the sense of sequentially Rh-catalyzed processes to chiral alkylidene butyrolactone β-hydroxyethanes and alkylidene tetrahydrofuran β-aminoethanes, respectively, with excellent levels of enantioselectivity.

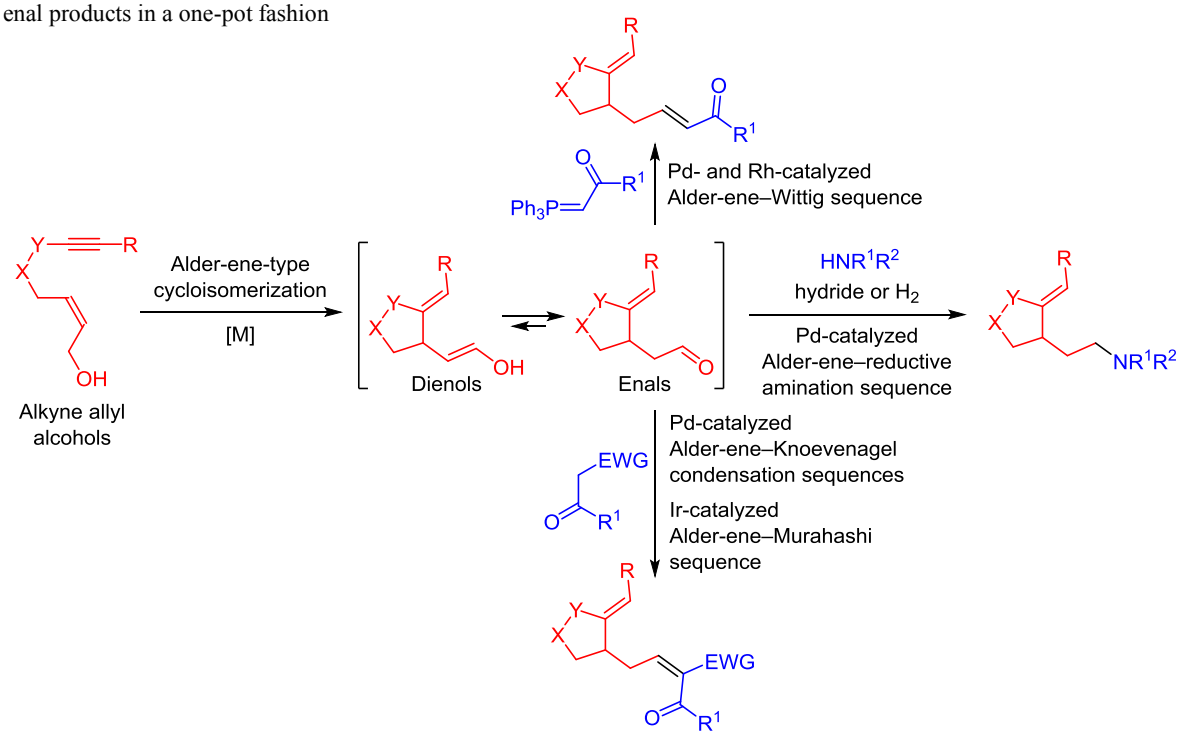
Keywords: furanones, rhodium, tetrahydrofurans, asymmetric catalysis, cycloisomerization, homogeneous catalysis, hydrogenation, one-pot reactions, sequential catalysis.

The invention of transition metal-catalyzed processes has considerably enhanced the generation of complex hetero- and carbocyclic structures starting from structurally simple linear precursors. A further twist in these types of cascading is the use of one catalyst for more than one transformation in a one-pot fashion. This type of one-pot methodology is generally referred to as sequential catalysis.[1–3] The catalytic cycloisomerization of enynes,[4–13] i.e., the intramolecular and transition metal-catalyzed version of the Alder-ene reaction,[14,15] enables formation of cycles bearing a diene functionality.

Rhodium(I)-catalyzed cycloisomerization processes,[16] firstly pioneered by Zhang,[17,18] allow enantioselective generation of a chiral center upon transformation of 1,6-enynes by a cationic rhodium complex with chelating enantiopure bisphosphane ligands furnishing five-membered rings.[19–22] Eventually rhodium–BINAP system turned out to be most practical and efficacious.[23] As a consequence Rh-catalyzed enantioselective cycloisomerizations of enyne substrates became increasingly important.[24–27]

As part of our program to design new sequentially catalyzed one-pot processes,[28–31] we are particularly interested in transition metal-catalyzed sequences initiated by intramolecular cycloisomerization. In case of cycloisomerization reactions with alkyne allyl alcohols, reactive aldehyde functionalities are generated by virtue of the tautomerism of the dienol intermediate. These resulting enals set the stage for consecutive transformations particularly in sequentially catalyzed one-pot processes (Scheme 1). While Pd-catalyzed cycloisomerization of TMS-substituted alkyne allyl alcohols proceeds smoothly, consecutive concatenation as cycloisomerization–Wittig,[32] cycloisomerization–Leuckart–Wallach,[33] and a cycloisomerization–Knoevenagel[34] sequences were conducted in a one-pot fashion. In the sense of a sequentially Pd-catalyzed process a cycloisomerization–reductive amination sequence was performed with hydrogen as the reductant.[35] Also a

Scheme 1. Metal-catalyzed cycloisomerization of alkyne allyl alcohols and *en route* transformation of the enal products in a one-pot fashion

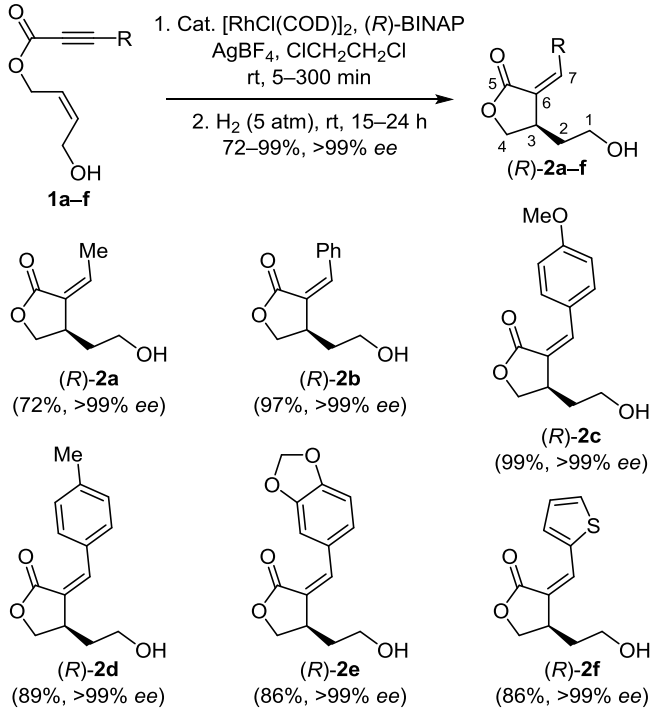


sequentially iridium-catalyzed version with aryl-substituted alkyne allyl alcohols furnished the corresponding condensation products in the sense of a cycloisomerization–Murahashi sequence under very mild reaction conditions in absence of acids and bases.[36] In addition, we could show that Rh-catalyzed Alder-ene cycloisomerizations can be successfully employed in one-pot sequences with Wittig olefinations, giving a straightforward access to chiral functionalized 4-alkyl 3-alkylidene tetrahydrofuran(on)es in an enantioselective fashion.[37]

Since rhodium has gained a superior role in catalytic hydrogenation reactions[38] sequential hydrogenation suggests an intriguing sequel after rhodium-catalyzed cycloisomerization. Recently, we observed that cationic Rh–(*R*)-BINAP complexes transform ether-tethered alkyne allyl alcohols elegantly and enantioselectively into 2,7-dioxabicyclo[3.2.1]octanes *via* a cycloisomerization–hydrogenation–isomerization–acetalization (CIHIA) sequence.[39] Inspired by these findings we herein report the enantioselective sequentially Rh-catalyzed cycloisomerization–hydrogenation syntheses of alkylidene butyrolactone β-hydroxyethanes and alkylidene tetrahydrofuran β-aminoethanes.

As previously reported, a subsequent Rh-catalyzed hydrogenation commences at a pressure of 5 bar, but in contrast to the sodium borohydride reduction, the alcohols were not isolated as products, and the isomeric 2,7-dioxabicyclo[3.2.1]octanes were obtained as a result of a CIHIA sequence.[15] For shutting down the Rh-catalyzed allyl ether–vinyl ether isomerization, which is considered to be responsible for the concluding acetalization, we employed (2*Z*)-4-hydroxybut-2-en-1-yl 3-(hetero)arylprop-2-ynoates **1a**–**f**[21] as substrates for the Rh–(*R*)-BINAP-catalyzed cycloisomerization followed by hydrogenation (5 atm) at room temperature for 24 h. Interestingly, instead of bicyclic products, we exclusively obtained alkylidene butyrolactone β-hydroxyethanes **2a**–**f** in good to excellent yield and excellent levels of enantioselectivity (Scheme 2). The

Scheme 2. Sequentially Rh–BINAP-catalyzed enantioselective cycloisomerization–hydrogenation synthesis of alkylidene butyrolactone β-hydroxyethanes **2a**–**f**



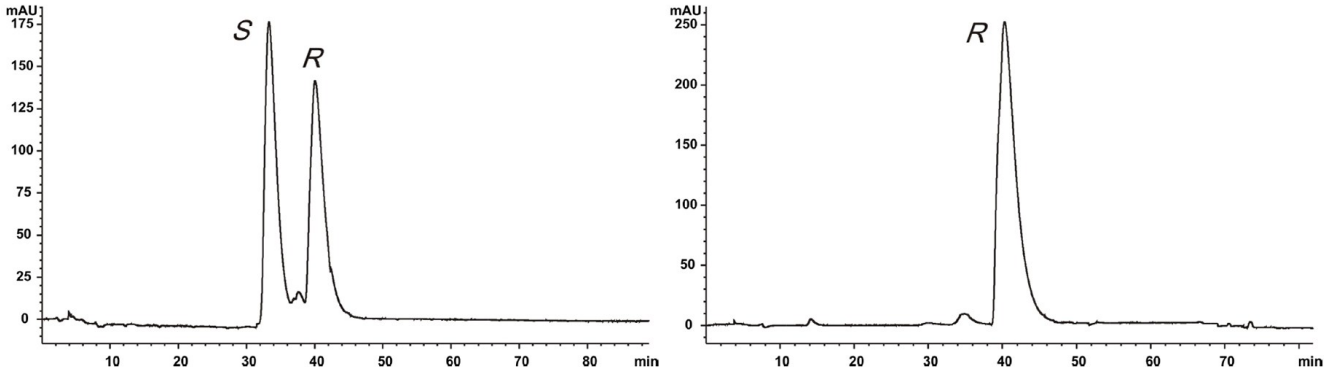


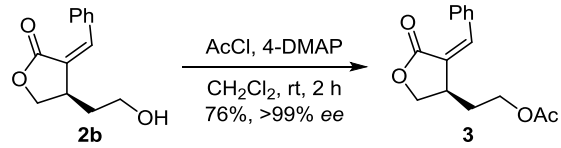
Figure 1. Analytical chiral HPLC chromatograms of (*rac*)-**3** (left) and (*R*)-**3** (right) (HPLC: *n*-hexane–2-PrOH, 95:5, 0.8 ml/min, λ_{exc} 254 nm, retention times: t_S 33.3 min (minor), t_R 40.2 min (major)).

structures of products **2** were unambiguously supported by ^{1}H, ^{13}C, DEPT-135, COSY, and NOESY NMR experiments as well as IR and mass spectrometry. The molecular composition was confirmed either by HRMS or elemental analysis.

The determination of the enantiomeric excesses by analytical chiral GC and analytical chiral HPLC was hampered by poor baseline separation for alcohol **2b**. Therefore, alcohol **2b** was acetylated with acetyl chloride in the presence of 4-(*N*,*N*-dimethylamino)pyridine (DMAP) to give the corresponding acetate **3** (Scheme 3), which was subjected to analytical chiral HPLC (Fig. 1).

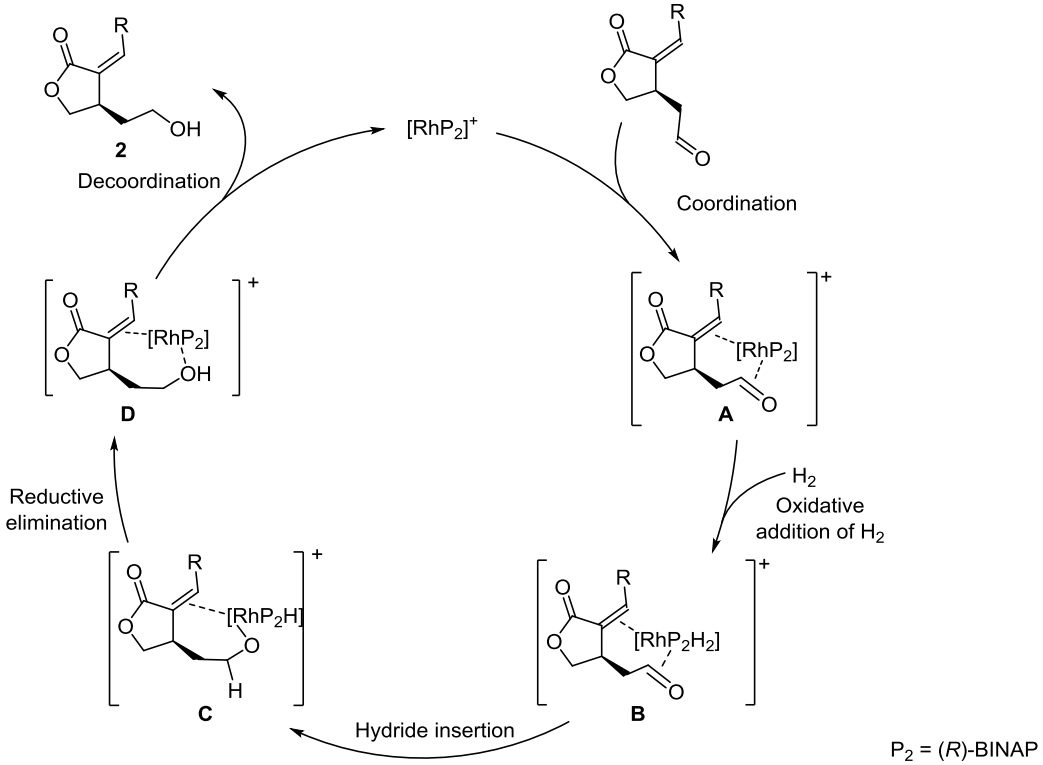
The mechanistic rationale of the Rh–(*R*)-BINAP-catalyzed cycloisomerization of alkyne allyl alcohols to cyclic enals and the assignment of absolute configuration

Scheme 3. Esterification of alcohol **2b** to give acetate **3**



of the new chiral center was presented and discussed previously.[39] The present cationic rhodium species further on catalyzes the hydrogenation of the aldehyde to alcohol **2** in the presence of the α,β-unsaturated double bond and various (hetero)aryl substituents of diverse electronic nature. The tentative mechanism is outlined in Scheme 4. After coordination of the enal intermediate to the cationic

Scheme 4. Mechanistic rationale for the Rh-catalyzed hydrogenation step in the sequentially Rh-catalyzed cycloisomerization–hydrogenation synthesis of alkylidene butyrolactone β-hydroxyethanes **2**



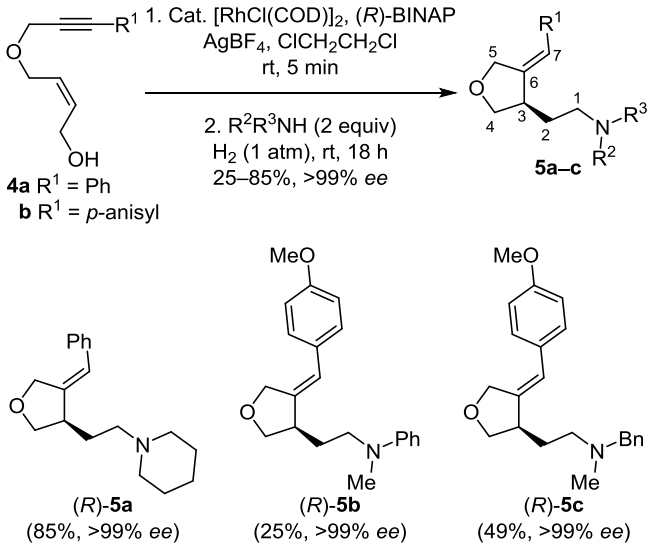
Rh–(*R*)-BINAP complex, the chelated complex **A** undergoes oxidative addition to give the dihydrido complex **B**. Hydride insertion furnishes the Rh-alcoholate **C**, which undergoes reductive elimination to generate the alcohol complex **D**. After decoordination of product **2**, the cationic Rh–(*R*)-BINAP complex is ready for a new catalytic cycle.

Although the sequentially Rh-catalyzed cycloisomerization–hydrogenation of ether-tethered alkyne allyl alcohols led into the CIHIA sequence, we became curious to see what will happen in the presence of secondary amines, since we had observed reductive amination in the case of Pd-catalyzed sequences.[35] Indeed, after cycloisomerization of (*Z*)-4-[(3-arylprop-2-yn-1-yl)oxy]but-2-en-1-ols **4a**,**b**, the secondary amines were added to the reaction mixture, which turned brownish immediately. After purging the reaction mixture with hydrogen and stirring under an ambient pressure at room temperature for 4 to 18 h, alkylidene tetrahydrofuran β-aminoethanes **5a**–**c** were obtained in yields of 25, 49, and 85%, respectively (Scheme 5). The structures of products **5** were unambiguously supported by ^{1}H, ^{13}C, DEPT-135, and COSY NMR experiments as well as IR and mass spectrometry. The molecular composition was confirmed by HRMS. In addition, the molecular structure of compound **5a** was corroborated by an X-ray structure analysis (Fig. 2). The enantiomeric excesses of compounds **5** were directly determined by analytical HPLC with a chiral cyclodextrin column (Fig. 3).

The yields of alkylidene tetrahydrofuran β-aminoethanes **5** are definitely affected by the nucleophilicity of the secondary amines, i.e., morpholine is a stronger nucleophile than *N*-benzylmethylamine and *N*-methylaniline. Since alkylidene tetrahydrofuran β-aminoethanes are β-amino ethyl derivatives of heterocycles they are potentially interesting in pharmaceutical applications.

Sequentially Rh-catalyzed cycloisomerization–hydrogenation processes are ideally suited for rapid and enantioselective preparation of alkylidene butyrolactone β-hydroxyethanes from (2*Z*)-4-hydroxybut-2-en-1-yl 3-(hetero)arylprop-2-ynoates, whereas (*Z*)-4-[(3-arylprop-2-yn-1-yl)oxy]but-2-en-1-ols are good substrates for cycloisomerization–reductive amination sequences to give alkylidene tetrahydrofuran β-aminoethanes. Both substance classes are in their own right interesting as building blocks in the synthesis of lignans and their derivatives or as novel β-aminoethyl-substituted pharmacophores.

Scheme 5. Sequentially Rh–BINAP-catalyzed enantioselective cycloisomerization–hydrogenation synthesis of alkylidene tetrahydrofuran β-aminoethanes **5**



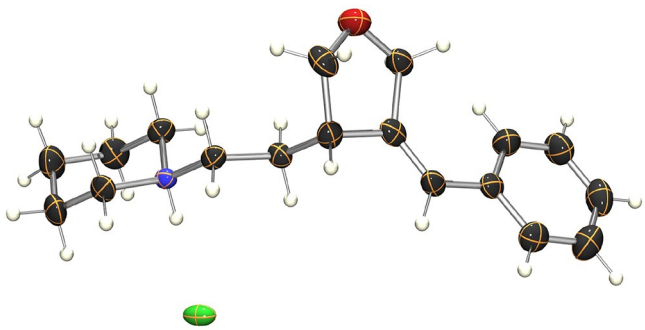


Figure 2. Molecular structure of compound (*R*)-**5a**·HCl (thermal ellipsoids shown at 50% probability).

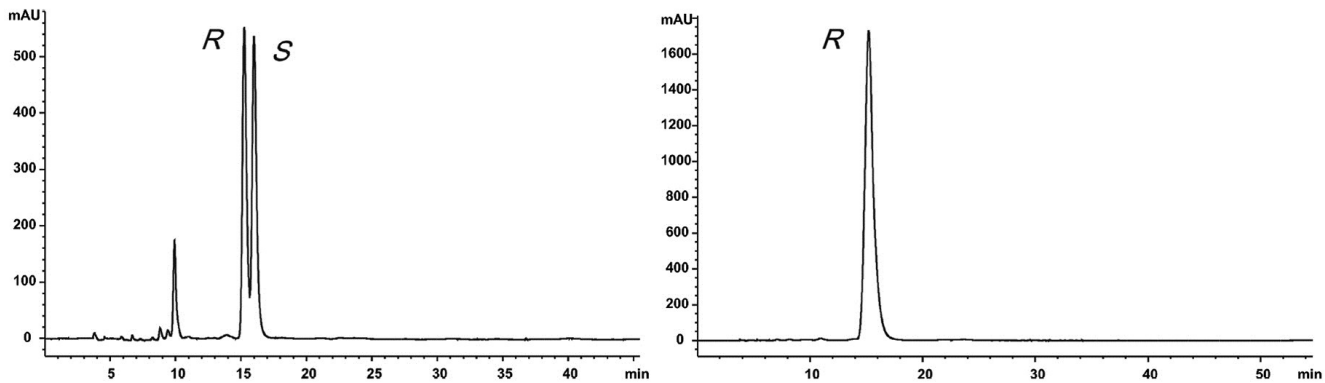


Figure 3. Analytical chiral HPLC chromatograms of (*rac*)-**5b** (left) and (*R*)-**5b** (right) (HPLC: *n*-hexane–2-PrOH 95:5, 0.8 ml/min, λ_{exc} 266 nm, retention times: t_R 15.2 min (major), t_S 16.0 min (minor)).

Experimental

IR spectra were recorded of solids as compressed KBr pellets and of oils as films on a Bruker Vector 22 FT-IR spectrometer. Optical rotation was measured on a PerkinElmer 341 polarimeter at λ_{max} 589 nm. UV-Vis spectra were recorded on a Hewlett Packard 84252 A diode array spectrophotometer. ^{1}H and ^{13}C NMR spectra were acquired on Bruker Avance III (300 and 75 MHz, respectively) and Bruker Avance DRX500 (500 and 126 MHz, respectively) spectrometers in $CDCl_3$ using the $CHCl_3$ resonance signal as internal standard (7.26 and 77.2 ppm, respectively). The assignments of C_{quat}, CH, CH_2, and CH_3 nuclei were based on DEPT spectra. Atom numbering used for assignment of NMR signals is shown on Schemes 2 and 3. Mass spectra were recorded on a Bruker FTICR APEX III spectrometer (EI, 70 eV). High-resolution mass spectra were recorded on Jeol JMS-700 (EI, 70 eV) and Finnigan TSQ 700 (EI, 70 eV) instruments and with Finnigan MAT 95 (ESI) mass spectrometer. Elemental analyses were performed on a PerkinElmer 2400 CHN elemental analyzer. TLC was performed with silica gel-coated aluminum plates 60 F154 (Merck) and visualization was achieved by a handheld UV lamp ($\lambda_{max,exc}$ 254 or 365 nm) or by immersion into an ethanolic solution of $KMnO_4$. The purification of products was performed on silica gel 60 (0.015–0.040 mm) by Macherey–Nagel using flash technique and under a pressure of 2 bar. The crude mixtures were adsorbed on Celite® 545 (0.02–0.10 mm) before chromatographic purification. The reaction progress was monitored qualitatively using TLC Silica gel 60 F254 aluminum sheets. Enantiomeric excesses were determined by chiral HPLC on an HP 1090 Liquid Chromatograph (Series II), Hewlett Packard, using a Chiralpak IA column (Daicel Chemical Industries Ltd.). The evaluation was performed with a HP ChemStations, Hewlett Packard.

The catalysis experiments were performed in degassed dichloroethane which was dried using an MBraun system MB-SPS-800. All rhodium-catalyzed cycloisomerization reactions were carried out in oven-dried Schlenk glassware using septa and syringes under argon atmosphere. All rhodium-catalyzed one-pot sequences based on the cycloisomerization reaction were performed in purpose-made Schlenk tubes (8 ml volume, 4 mm wall thickness to resist the excess hydrogen pressure). (2*Z*)-4-Hydroxybut-2-en-1-yl 3-(hetero)arylprop-2-ynoates (**1**) were synthesized according to the literature.[21] The synthesis of (*Z*)-4-[(3-arylprop-2-yn-1-yl)oxy]but-2-en-1-ols **4a**,**b** was previously reported.[39] Piperidine, *N*-methylaniline, and *N*-benzylmethylamine were purchased from Sigma-Aldrich and used without further purification.

Sequentially rhodium-catalyzed cycloisomerization–hydrogenation synthesis of alkylidene butyrolactone alcohols 2a–f (General method). Under an argon atmosphere [RhCl(COD)] (0.05 equiv) and (*R*)-BINAP ligand (0.1 equiv) were placed in a Schlenk tube with a magnetic stir bar. Then dried, degassed dichloroethane (4.0 ml) was added, and the solution was stirred for several minutes, until a dark-red solution was formed. Then, 3-substituted (2*Z*)-4-hydroxybut-2-en-1-yl prop-2-ynoate **1a–f** was added, the solution stirred for a few minutes, and finally the reaction was started by addition of a 0.05 M solution of $AgBF_4$ (0.1 equiv) in dry dichloroethane. Immediately, the solution turned yellow and a yellow precipitate of AgCl formed. The reaction was monitored by TLC and after full conversion (t_1), the reaction vessel was set under hydrogen pressure (5 bar) and stirred for the time t_2. Then, the solvent was removed *in vacuo* and the residue was chromatographed on silica gel (*n*-hexane – diethyl ether).

(3*Z*,4*R*)-3-Ethylidene-4-(2-hydroxyethyl)dihydrofuran-2(3*H*)-one (2a) was synthesized from (2*Z*)-4-hydroxybut-2-en-1-yl but-2-ynoate (**1a**) (154 mg, 1.00 mmol), t_1 5 min, t_2 18 h, eluent for flash chromatography *n*-hexane – diethyl ether, 1:5 to diethyl ether. Yield 113 mg (72%), yellow oil. R_f 0.39 (diethyl ether). (*R*)-enantiomer: $[\alpha]_D^{20}$ +55.1° (*c* 4.3 mg/ml, $CHCl_3$). IR spectrum (film), ν, cm^{-1}: 3433 (s), 2935 (s), 1751 (s), 1671 (m), 1439 (m), 1378 (m), 1211 (m), 1120 (m), 1020 (m), 864 (w), 776 (w). ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.69–1.74 (2H, m, OH, 2-CH); 1.84 (1H, dt, ^2J = 17.5, ^3J = 5.8, 2-CH); 2.16 (3H, dd, ^3J = 7.3, ^5J = 2.1, CH_3); 3.10–3.17 (1H, m, 3-CH); 3.69 (2H, dd, ^2J = 11.5, ^3J = 5.4, 1-CH); 3.99 (1H, dd, ^3J = 9.0, ^4J = 5.3, 4-CH); 4.42 (1H, dd, ^2J = 14.7, ^3J = 6.0, 4-CH); 6.26 (1H, qd, ^3J = 7.3, ^4J = 2.1, 7-CH). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ, ppm: 14.2 (CH_3); 36.6 (C-2); 37.8 (C-3); 60.1 (C-1); 71.3 (C-4); 129.0 (C-6); 139.1 (C-7); 170.7 (C-5). Mass spectrum (70 eV), *m*/*z* (I_{rel}, %): 156 $[M]^+$ (4), 139 $[M–OH]^+$ (9), 138 $[M–H_2O]^+$ (100), 130 (21), 112 (22), 111 $[M–C_2H_5O]^+$ (47), 110 (20), 109 (13), 95 (14), 93 (13), 85 (15), 83 $[C_4H_3O_2]^+$ (36), 82 (12), 81 (30), 79 (20), 71 (11), 69 (18), 67 $[C_4H_3O]^+$ (38), 55 (25), 53 (14), 43 $[C_2H_3O]^+$ (12). Found, *m*/*z*: 156.0786 $[M]^+$. $C_8H_{12}O_3$. Calculated, *m*/*z*: 156.0781.

(3*Z*,4*R*)-3-Benzylidene-4-(2-hydroxyethyl)dihydrofuran-2(3*H*)-one (2b)[39] was synthesized from (2*Z*)-4-hydroxybut-2-en-1-yl 3-phenylprop-2-ynoate (**1b**) (108 mg, 0.50 mmol), t_1 30 min, t_2 15 h, eluent for flash chromatography *n*-hexane – diethyl ether, 1:2. Yield 107 mg (97%), yellow oil. R_f 0.11 (*n*-hexane – diethyl ether, 1:2). (*R*)-enantiomer: $[\alpha]_D^{20}$ –2.2° (*c* 2.4 mg/ml, $CHCl_3$). IR spectrum (film), ν, cm^{-1}: 3418 (s), 3059 (m), 3027 (m), 2912 (s), 1747 (s), 1644 (s), 1576 (w), 1494 (m), 1451 (m), 1382 (s), 1177 (s), 1113 (w), 1068 (w), 1027 (w), 972 (w), 953 (w), 899 (w), 766 (m), 738 (m), 695 (s), 599 (m). ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.70–1.77 (1H, m, 2-CH); 1.83–1.89 (1H, m, 2-CH); 2.30 (1H, br. s, OH); 3.21–3.26 (1H, m, 3-CH); 3.65 (2H, t, ^3J = 6.0, 1-CH); 4.00 (1H, dd, ^3J = 9.0, ^4J = 4.8, 4-CH); 3.98–4.01 (1H, m, 4-CH); 6.85–6.87 (1H, m, 7-CH); 7.23–7.29 (3H, m, H Ar); 7.71 (2H, d, ^3J = 6.7, H Ar). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ, ppm: 36.5 (C-2); 39.4 (C-3); 59.4 (C-1); 70.8 (C-4); 127.9 (CH Ph); 128.0 (C_{quat} Ph); 129.4 (CH Ph); 130.5 (CH Ph); 133.4 (C-6); 139.8 (C-7); 169.4 (C-5). Mass spectrum (70 eV), *m*/*z* (I_{rel}, %): 218 $[M]^+$ (33), 200 $[M–H_2O]^+$ (35), 199 $[(M–H)–H_2O]^+$ (100), 185 (19), 182 (13), 181 (22), 173 $[M–CH_3O]^+$ (23), 172 $[M–CH_3OH]^+$ (34), 156 (19),

155 (95), 145 $[C_{10}H_9O]^+$ (31), 141 (63), 129 $[C_7H_{13}O_2]^+$ (87), 128 $[C_7H_{12}O_2]^+$ (91), 127 (41), 117 (84), 115 (76), 104 (14), 91 $[C_7H_7]^+$ (28), 77 (11). Found, *m*/*z*: 241.0835 $[M+Na]^+$. $C_{13}H_{14}NaO_3$. Calculated, *m*/*z*: 241.0835.

***rac*-(3*Z*)-3-Benzylidene-4-(2-hydroxyethyl)dihydrofuran-2(3*H*)-one ((*rac*)-2b)** was synthesized from (2*Z*)-4-hydroxybut-2-en-1-yl 3-phenylprop-2-ynoate (**1b**) (108 mg, 0.50 mmol) using (*rac*)-BINAP as ligand instead of (*R*)-BINAP, t_1 5 min, 24 h, eluent for flash chromatography *n*-hexane – diethyl ether, 1:2. Yield 38 mg (34%), yellow oil. IR spectrum (film), ν, cm^{-1}: 3416 (s), 3057 (m), 3025 (m), 2914 (s), 1746 (s), 1645 (s), 1575 (w), 1494 (m), 1450 (m), 1381 (s), 1178 (s), 1112 (w), 1069 (w), 1026 (w), 972 (w), 953 (w), 900 (w), 767 (m), 737 (m), 694 (s), 600 (m). ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.70–1.77 (1H, m, 2-CH); 1.82–1.89 (1H, m, 2-CH); 2.30 (1H, br. s, OH); 3.21–3.25 (1H, m, 3-CH); 3.65 (2H, t, ^3J = 6.0, 1-CH); 4.01 (1H, dd, ^3J = 9.0, ^4J = 4.8, 4-CH); 4.38–4.40 (1H, m, 4-CH); 6.85–6.87 (1H, m, 7-CH); 7.22–7.29 (3H, m, H Ar); 7.72 (2H, d, ^3J = 6.7, H Ar). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ, ppm: 36.5 (C-2); 39.3 (C-3); 59.4 (C-1); 70.8 (C-4); 127.9 (CH Ph); 128.0 (C_{quat} Ph); 129.3 (CH Ph); 130.4 (CH Ph); 133.4 (C-6); 139.9 (C-7); 169.5 (C-5). Mass spectrum (70 eV), *m*/*z* (I_{rel}, %): 218 $[M]^+$ (32), 200 $[M–H_2O]^+$ (34), 199 $[(M–H)–H_2O]^+$ (100), 185 (19), 182 (12), 181 (23), 173 $[M–CH_3O]^+$ (22), 172 $[M–CH_3OH]^+$ (33), 156 (19), 155 (94), 145 $[C_{10}H_9O]^+$ (30), 141 (62), 129 $[C_7H_{13}O_2]^+$ (87), 128 $[C_7H_{12}O_2]^+$ (90), 127 (41), 117 (85), 115 (75), 104 (14), 91 $[C_7H_7]^+$ (27), 77 (10). Found, *m*/*z*: 241.0835 $[M+Na]^+$. $C_{13}H_{14}NaO_3$. Calculated, *m*/*z*: 241.0835.

(3*Z*,4*R*)-4-(2-Hydroxyethyl)-3-(4-methoxybenzylidene)-dihydrofuran-2(3*H*)-one (2c) was synthesized from (2*Z*)-4-hydroxybut-2-en-1-yl 3-(4-methoxyphenyl)prop-2-ynoate (**1c**) (123 mg, 0.50 mmol), t_1 300 min, t_2 24 h, eluent for flash chromatography diethyl ether. Yield 122 mg (99%), yellow oil. R_f 0.27 (diethyl ether). (*R*)-enantiomer: $[\alpha]_D^{20}$ –16.9° (*c* 2.0 mg/ml, $CHCl_3$). IR spectrum (film), ν, cm^{-1}: 3426 (s), 2934 (s), 2840 (w), 2048 (w), 1732 (s), 1634 (m), 1602 (s), 1573 (w), 1514 (s), 1429 (m), 1385 (m), 1304 (m), 1259 (s), 1172 (m), 1077 (m), 953 (w), 912 (w), 834 (m), 777 (w), 529 (m), 506 (w). ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.75–1.77 (1H, m, OH); 1.83–1.88 (1H, m, 2-CH); 1.92–1.98 (1H, m, 2-CH); 3.28–3.34 (1H, m, 3-CH); 3.77–3.83 (5H, m, CH_3, 1-CH); 4.10 (1H, dd, ^2J = 9.0, ^3J = 4.5, 4-CH); 4.48 (1H, dd, ^2J = 9.0, ^3J = 7.8, 4-CH); 6.84–6.94 (3H, m, 7-CH, H Ar); 7.85–7.93 (2H, m, H Ar). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ, ppm: 37.2 (C-2); 39.9 (C-3); 55.5 (OCH_3); 60.0 (C-1); 71.0 (C-4); 113.8 (CH Ar); 114.7 (C_{quat} Ar); 125.5 (C_{quat} Ar); 126.7 (C-6); 132.4 (CH Ar); 140.0 (C-7); 160.9 (C-5). Mass spectrum (70 eV), *m*/*z* (I_{rel}, %): 248 $[M]^+$ (47), 246 (10), 230 $[M–H_2O]^+$ (10), 229 (13), 203 (74), 202 (10), 199 $[M–H_2O–OCH_3]^+$ (10), 185 (21), 175 (28), 159 $[C_{10}H_7O_2]^+$ (31), 158 (17), 148 (14), 147 $[C_9H_7O_2]^+$ (100), 145 $[C_{10}H_9O]^+$ (17), 144 (26), 141 $[C_7H_9O_3]^+$ (12), 135 (17), 134 (31), 132 (13), 131 (15), 129 $[C_7H_{13}O_2]^+$ (16), 128 $[C_6H_8O_3]^+$ (18), 127 (16), 121 (69), 115 (59), 108 $[C_7H_8O]^+$ (15), 91 $[C_7H_7]^+$ (56), 77 (24). Found, *m*/*z*: 248.1049 $[M]^+$. $C_{14}H_{16}O_4$. Calculated, *m*/*z*: 248.1043.

(3*Z*,4*R*)-4-(2-Hydroxyethyl)-3-(4-methylbenzylidene)-dihydrofuran-2(3*H*)-one (2d) was synthesized from (2*Z*)-4-hydroxybut-2-en-1-yl 3-(4-methylphenyl)prop-2-ynoate (**1d**) (115 mg, 0.50 mmol), t_1 60 min, t_2 24 h, eluent for flash chromatography diethyl ether. Yield 103 mg (89%), yellow oil. R_f 0.16 (diethyl ether). (*R*)-enantiomer: $[\alpha]_D^{20}$ –3.3° (*c* 1.7 mg/ml, $CHCl_3$). IR spectrum (film), ν, cm^{-1}: 3417 (s), 2924 (s), 1747 (s), 1645 (m), 1607 (m), 1514 (m), 1380 (m), 1177 (m), 1080 (w), 814 (w). ^{1}H NMR spectrum (200 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.59 (1H, s, OH); 1.79–1.89 (2H, m, 2-CH); 2.34 (3H, s, CH_3); 3.25–3.39 (1H, m, 3-CH); 3.78 (2H, t, ^3J = 6.1, 1-CH); 4.11 (1H, dd, ^2J = 9.0, ^3J = 3.5, 4-CH); 4.49 (1H, dd, ^2J = 9.0, ^3J = 7.6, 4-CH); 6.89 (1H, d, ^4J = 1.9, 7-CH); 7.16 (2H, d, ^3J = 8.0, H Ar); 7.74 (2H, d, ^3J = 8.2, H Ar). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ, ppm: 21.7 (CH_3); 37.0 (C-2); 39.8 (C-3); 60.1 (C-1); 71.0 (C-4); 127.1 (C-6); 129.1 (CH Ar); 130.0 (C_{quat} Ar); 130.5 (C_{quat} Ar); 131.0 (CH Ar); 140.2 (C-7); 169.5 (C-5). Mass spectrum (70 eV), *m*/*z* (I_{rel}, %): 232 $[M]^+$ (94), 217 $[M–CH_3]^+$ (52), 199 (84), 187 $[M–C_2H_5O]^+$ (12), 141 $[C_7H_9O_3]^+$ (89), 116 (82), 112 $[C_6H_8O_2]^+$ (51) 108 $[C_7H_8O]^+$ (100). Found, *m*/*z*: 255.0992 $[M+Na]^+$. $C_{14}H_{16}NaO_3$. Calculated, *m*/*z*: 255.0992.

(3*Z*,4*R*)-3-(1,3-Benzodioxol-5-ylmethylidene)-4-(2-hydroxyethyl)dihydrofuran-2(3*H*)-one (2e) was synthesized from (2*Z*)-4-hydroxybut-2-en-1-yl 3-(1,3-benzodioxol-5-yl)prop-2-ynoate (**1e**) (130 mg, 0.50 mmol), t_1 15 min, t_2 66 h, eluent for flash chromatography diethyl ether. Yield 113 mg (86%), yellow oil. R_f 0.29 (diethyl ether). (*R*)-enantiomer: $[\alpha]_D^{20}$ –16.3° (*c* 2.25 mg/ml, $CHCl_3$). IR spectrum (film), ν, cm^{-1}: 3528 (s), 2914 (s), 1737 (s), 1706 (m), 1633 (m), 1597 (m), 1503 (s), 1448 (s), 1398 (m), 1341 (m), 1264 (s), 1210 (m), 1183 (m), 1108 (m), 1035 (s), 960 (w), 926 (m), 811 (m), 776 (m), 668 (w), 607 (w), 541 (w). ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.61 (1H, s, OH); 1.82–2.00 (2H, m, 2-CH); 3.23–3.37 (1H, m, 3-CH); 3.78 (2H, t, ^3J = 6.0, 1-CH); 4.10 (1H, dd, *J* = 9.0, *J* = 4.5, 4-CH); 4.48 (1H, dd, *J* = 9.0, *J* = 7.5, 4-CH); 5.97 (2H, s, OCH_2O); 6.73–6.82 (2H, m, 7-CH, H Ar); 7.20 (1H, dd, *J* = 8.1, *J* = 1.5, H Ar); 7.77 (1H, d, *J* = 1.8, H Ar). ^{13}C NMR spectrum (125 MHz, acetone-d_6), δ, ppm: 38.0 (C-2); 40.9 (C-3); 59.8 (C-1); 71.6 (C-4); 102.5 (CH_2 dioxole); 108.6 (CH Ar); 111.4 (CH Ar); 127.9 (CH Ar); 128.0 (C-6); 129.6 (C_{quat} Ar); 139.6 (C-7); 148.4 (C_{quat} Ar); 149.7 (C_{quat} Ar); 170.0 (C-5). Mass spectrum (70 eV), *m*/*z* (I_{rel}, %): 262 $[M]^+$ (67), 217 $[M–C_2H_5O]^+$ (34), 192 (18), 171 $[C_{11}H_7O_2]^+$ (2) 159 (20), 143 (10), 136 (12), 125 $[C_7H_9O_2]^+$ (100), 131 (17), 115 (11), 77 $[C_6H_5]^+$ (10), 45 $[C_2H_5O]^+$ (14). Found, *m*/*z*: 262.0841 $[M]^+$. $C_{14}H_{14}O_5$. Calculated, *m*/*z*: 262.0836.

(3*Z*,4*R*)-4-(2-Hydroxyethyl)-3-(thiophen-2-ylmethylidene)dihydrofuran-2(3*H*)-one (2f) was synthesized from (2*Z*)-4-hydroxybut-2-en-1-yl 3-(thiophen-2-yl)prop-2-ynoate (**1f**) (111 mg, 0.50 mmol), t_1 5 min, t_2 24 h, eluent for flash chromatography diethyl ether. Yield 96 mg (86%), yellow oil. R_f 0.21 (diethyl ether). $[\alpha]_D^{20}$ +19.8° (*c* 2.4 mg/ml, $CHCl_3$). IR spectrum (film), ν, cm^{-1}: 3419 (s), 3104 (w),

2914 (s), 1732 (s), 1633 (s), 1479 (w), 1422 (w), 1392 (s), 1330 (m), 1247 (m), 1174 (s), 1111 (m), 1026 (m), 859 (w), 776 (m), 717 (m), 609 (w), 503 (w). ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.62 (1H, s, OH); 1.76–1.98 (2H, m, 2-CH); 3.23–3.42 (1H, m, 3-CH); 3.78 (2H, t, ^3J = 6.1, 1-CH); 4.12 (1H, dd, ^2J = 9.0, ^3J = 4.7, 4-CH); 4.51 (1H, dd, ^2J = 9.0, ^3J = 7.7, 4-CH); 7.02–7.07 (2H, m, 7-CH, H thienyl); 7.50 (1H, d, ^3J = 5.2, H thienyl); 7.55 (1H, d, ^3J = 3.6, H thienyl). ^{13}C NMR spectrum (125 MHz, acetone-d_6), δ, ppm: 38.0 (C-2); 39.8 (C-3); 59.9 (C-1); 72.0 (C-4); 125.4 (C-6); 127.6 (CH thienyl); 131.5 (CH thienyl); 132.6 (CH thienyl); 136.0 (C-7); 138.3 (C_{quat} thienyl); 170.4 (C-5). Mass spectrum (70 eV), *m*/*z* (I_{rel}, %): 224 $[M]^+$ (22), 206 $[M–H_2O]^+$ (6), 205 (15), 179 $[M–C_2H_5O]^+$ (15), 167 (18), 161 (9), 151 (18), 123 (11), 111 (10), 97 $[C_5H_5O_2]^+$ (18), 93 (12), 83 $[C_4H_3S]^+$ (14), 73 (61), 71 (17), 45 $[C_2H_5O]^+$ (100). Found, *m*/*z*: 247.0399 $[M+Na]^+$. $C_{11}H_{12}O_3NaS$. Calculated, *m*/*z*: 247.0399.

2-((3*R*,4*Z*)-4-Benzylidene-5-oxotetrahydrofuran-3-yl)-ethyl acetate (3). Compound **2b** (218 mg, 1.00 mmol), acetyl chloride (0.1 ml, 1.4 mmol), and DMAP (170 mg, 1.40 mmol) were dissolved in dry dichloromethane (10 ml) under argon atmosphere and stirred at room temperature for 2 h. After extraction with water (3 × 10 ml), the solvents were removed *in vacuo* and the residue was purified by flash chromatography on silica gel (*n*-hexane – diethyl ether, 1:1). Yield 198 mg (76%), yellow solid. R_f 0.56 (*n*-hexane – diethyl ether, 1:2). (*R*)-enantiomer: $[\alpha]_D^{20}$ –61.3° (*c* 2.0 mg/ml, MeOH). HPLC: *n*-hexane–*i*-PrOH, 95:5, 0.8 ml/min, 254 nm, t_S 33.3 min (minor), t_R 40.2 min (major): *ee* >99%. IR spectrum (KBr), ν, cm^{-1}: 2964 (m), 2911 (m), 1747 (s), 1644 (m), 1576 (w), 1494 (w), 1453 (w), 1368 (m), 1243 (s), 1177 (s), 1092 (m), 1063 (m), 1030 (m), 767 (m), 738 (w), 695 (m), 602 (w), 516 (w), 503 (w). ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.91–1.99 (1H, m, 2-CH); 2.02–2.10 (4H, m, 2-CH, CH_3); 3.11–3.26 (1H, m, 3-CH); 4.09 (1H, dd, ^2J = 9.0, ^3J = 4.7, 4-CH); 4.13–4.28 (1H, m, 1-CH); 4.23 (1H, ddd, ^2J = 12.0, ^3J = 6.6, ^3J = 5.6, 1-CH); 4.48 (1H, dd, ^2J = 9.0, ^3J = 7.6, 4-CH); 6.91 (1H, d, ^4J = 2.0, 7-CH); 7.28–7.38 (3H, m, H Ar); 7.81 (2H, dd, ^3J = 7.7, ^4J = 1.6, H Ar). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ, ppm: 21.1 (CH_3); 33.3 (C-2); 39.9 (C-3); 61.6 (C-1); 70.4 (C-4); 127.7 (C_{quat} Ph); 128.4 (CH Ph); 129.9 (CH Ph); 130.9 (CH Ph); 133.5 (C-6); 140.3 (C-7); 168.8 (C-5); 171.0 (C_{quat} acetyl). Mass spectrum (70 eV), *m*/*z* (I_{rel}, %): 260 $[M]^+$ (8), 201 $[M–CH_3CO_2]^+$ (7), 200 $[M–CH_3CO_2H]^+$ (57), 199 (39), 185 $[M–C_2H_3O_3]^+$ (22), 182 (17) 181 (12), 172 $[C_{11}H_8O_2]^+$ (48), 171 (11), 156 (21), 155 $[M–CH_3–C_7H_7]^+$ (100), 154 (17), 153 (10), 143 (22), 142 (21), 141 (56), 129 (41), 128 $[C_6H_8O_3]^+$ (59), 127 (22), 117 (52), 116 (15), 115 (62), 102 (13), 91 $[C_7H_7]^+$ (43), 78 (11), 77 $[C_6H_5]^+$ (19), 65 (10), 51 (13). Found, %: C 69.04, H 6.45. $C_{15}H_{16}O_4$. Calculated, %: C 69.22, H 6.20.

***rac*-2-((4*Z*)-4-Benzylidene-5-oxotetrahydrofuran-3-yl)-ethyl acetate ((*rac*)-3)**. Compound (*rac*)-**2b** (110 mg, 0.50 mmol), acetyl chloride (50 μl, 0.7 mmol), and 4-DMAP (85 mg, 0.7 mmol) were dissolved in dry dichloromethane (5 ml) under argon atmosphere and stirred at room temperature for 2 h. After extraction with water (3 × 6 ml), the solvents were removed *in vacuo* and the residue was purified by flash chromatography on silica gel (*n*-hexane – diethyl ether, 1:1). Yield 90 mg (69%), yellow solid. R_f 0.56 (*n*-hexane – diethyl ether, 1:2). HPLC: *n*-hexane–*i*-PrOH, 95:5, 0.8 ml/min, 254 nm, t_S 33.3 min, t_R 40.2 min. IR spectrum (KBr), ν, cm^{-1}: 2962 (m), 2912 (m), 1745 (s), 1643 (m), 1577 (w), 1492 (w), 1453 (w), 1367 (m), 1244 (s), 1177 (s), 1093 (m), 1063 (m), 1030 (m), 768 (m), 737 (w), 695 (m), 601 (w), 515 (w), 502 (w). ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.91–1.98 (1H, m, 2-CH); 2.01–2.09 (4H, m, 2-CH, CH_3); 3.10–3.25 (1H, m, 3-CH); 4.09 (1H, dd, ^2J = 9.0, ^3J = 4.6, 4-CH); 4.12–4.28 (1H, m, 1-CH); 4.23 (1H, ddd, ^2J = 11.9, ^3J = 6.6, ^3J = 5.6, 1-CH); 4.47 (1H, dd, ^2J = 9.0, ^3J = 7.5, 4-CH); 6.91 (1H, d, ^4J = 2.0, 7-CH); 7.28–7.38 (3H, m, H Ar); 7.82 (2H, dd, ^3J = 7.6, ^4J = 1.6, H Ar). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ, ppm: 21.1 (CH_3); 33.3 (C-2); 39.9 (C-3); 61.5 (C-1); 70.4 (C-4); 127.6 (C_{quat} Ph); 128.4 (CH Ph); 129.9 (CH Ph); 130.8 (CH Ph); 133.5 (C-6); 140.2 (C-7); 168.8 (C-5); 171.1 (C_{quat} acetyl). Mass spectrum (70 eV), *m*/*z* (I_{rel}, %): 260 $[M]^+$ (7), 201 $[M–CH_3CO_2]^+$ (6), 200 $[M–CH_3CO_2H]^+$ (56), 199 (40), 185 $[M–C_2H_3O_3]^+$ (22), 182 (17), 181 (11), 172 $[C_{11}H_8O_2]^+$ (49), 171 (11), 156 (20), 155 $[M–CH_3–C_7H_7]^+$ (100), 154 (17), 153 (11), 143 (23), 142 (21), 141 (55), 129 (41), 128 $[C_6H_8O_3]^+$ (59), 127 (23), 117 (51), 116 (15), 115 (62), 102 (13), 91 $[C_7H_7]^+$ (44), 78 (11), 77 $[C_6H_5]^+$ (19), 65 (10), 51 (12). Found, %: C 69.04, H 6.45. $C_{15}H_{16}O_4$. Calculated, %: C 69.22, H 6.20.

Sequentially rhodium-catalyzed cycloisomerization–reductive amination synthesis of alkylidene tetrahydrofuran β-aminoethane 5a–c (General method). Under an argon atmosphere [RhCl(cod)] and (*R*)-BINAP ligand were placed into a Schlenk tube with a magnetic stirring bar. Then dried, degassed dichloroethane was added and the solution was stirred for several minutes, until a dark-red solution was formed. Then (*Z*)-4-[(3-arylprop-2-yn-1-yl)-oxy]but-2-en-1-ol (**4**) was added, the solution stirred for a few minutes and finally the reaction was started by addition of a 0.05 M solution of $AgBF_4$ in dry dichloroethane. Immediately, the solution turned yellow and a yellow precipitate of AgCl formed. After 5 min, the secondary amine was added to the reaction mixture and the reaction vessel was flushed with hydrogen (1 atm) and stirred at room temperature under hydrogen for 18 h. The reaction mixture was then diluted with diethyl ether (100 ml), and potassium carbonate (1 g) was added. After filtration, the solvents were removed *in vacuo* and the residue was chromatographed on alumina (basicity level IV) to give the analytically pure alkylidene tetrahydrofuran β-amino-ethanes **5a**–**c**.

1-{2-[(3*R*,4*Z*)-4-Benzylidenetetrahydrofuran-3-yl]ethyl}-piperidine (5a) was synthesized from (*Z*)-4-[(3-phenylprop-2-yn-1-yl)oxy]but-2-en-1-ol (**4a**) (202 mg, 1.00 mmol) using [RhCl(cod)] (12.3 mg, 0.03 mmol), (*R*)-BINAP (31.1 mg, 0.05 mmol), dichloroethane (4.0 ml), 0.05 M solution of $AgBF_4$ in dry dichloroethane (1.0 ml, 0.05 mmol),

and piperidine (0.2 ml, 2.0 mmol). Eluent for flash chromatography *n*-hexane – diethyl ether, 1:2 + 5 vol % of NEt_3. Yield 230 mg (85%), yellow oil. R_f 0.86 (diethyl ether). (*R*)-enantiomer: $[\alpha]_D^{20}$ –31.4° (*c* 4.5 mg/ml, $CHCl_3$). HPLC: *n*-hexane–*i*-PrOH, 0.8 ml/min, 266 nm, t_R 18.2 min (major), t_S 25.5 min (minor): *ee* >99%. IR spectrum (film), ν, cm^{-1}: 2933 (s), 2851 (s), 2802 (m), 1468 (m), 1059 (m), 738 (m), 694 (m). ^1H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.38–1.47 (2H, m, CH_2 piperidinyl); 1.54–1.63 (5H, m, CH_2 piperidinyl, 2-CH); 1.64–1.74 (1H, m, 2-CH); 2.28–2.46 (6H, m, CH_2 piperidinyl, 1-CH); 2.80–2.90 (1H, m, 3-CH); 3.55 (1H, dd, ^2J = 8.5, ^3J = 6.3, 4-CH); 4.03 (1H, dd, ^2J = 8.5, ^3J = 6.8, 4-CH); 4.62–4.63 (2H, m, 5-CH); 6.34–6.36 (1H, m, 7-CH); 7.11–7.22 (3H, m, H Ph); 7.30–7.35 (2H, m, H Ph). ^{13}C NMR spectrum (75 MHz, $CDCl_3$), δ, ppm: 24.5 (CH_2 piperidinyl); 26.0 (CH_2 piperidinyl); 30.4 (C-2); 44.0 (C-3); 54.7 (C-1); 57.4 (CH_2 piperidinyl); 70.1 (C-5); 72.8 (C-4); 120.7 (C-7); 126.5 (CH Ph); 127.9 (CH Ph); 128.5 (CH Ph); 137.4 (C_{quat} Ph); 145.2 (C-6). Mass spectrum (70 eV), *m*/*z* (I_{rel}, %): 271 $[M]^+$ (1), 141 (14) 131 (15), 129 (23), 128 (35), 98 (100), 91 $[C_7H_7]^+$ (100), 77 $[C_6H_5]^+$ (8), 55 (19), 41 (16). Found, *m*/*z*: 271.1916 $[M]^+$. $C_{18}H_{25}NO$. Calculated, *m*/*z*: 271.1931.

***N*-{2-[(3*R*,4*Z*)-4-(4-Methoxybenzylidene)tetrahydrofuran-3-yl]ethyl}-*N*-methylaniline (5b)** was synthesized from (*Z*)-4-{[3-(4-methoxyphenyl)prop-2-yn-1-yl]oxy}but-2-en-1-ol (**4b**) (116 mg, 0.50 mmol) using [RhCl(cod)] (6.2 mg, 0.01 mmol), (*R*)-BINAP (15.6 mg, 0.03 mmol), dichloroethane (2.0 ml), 0.05 M solution of $AgBF_4$ in dry dichloroethane (0.5 ml, 0.03 mmol), and *N*-methylaniline (0.11 ml, 1.0 mmol). Eluent for flash chromatography *n*-hexane – diethyl ether, 1:1 + 5 vol % of NEt_3. Yield 40 mg (25%), yellow oil. R_f 0.76 (*n*-hexane – diethyl ether, 1:1 + + 5 vol % of NEt_3). $[\alpha]_D^{20}$ –30.5° (*c* 1.4 mg/ml, $CHCl_3$). HPLC: (*n*-hexane–*i*-PrOH) 0.8 ml/min, 266 nm, t_R 15.2 min (major), t_S 16.0 min (minor): *ee* >99%. IR spectrum (film), ν, cm^{-1}: 2933 (s), 2858 (s), 1603 (s), 1575 (w), 1509 (s), 1464 (m), 1367 (m), 1296 (m), 1252 (s), 1179 (m), 1116 (m), 1066 (m), 1034 (s), 992 (w), 910 (w), 826 (m), 750 (s), 733 (s), 693 (m), 531 (m). UV/Vis spectrum (CH_2Cl_2), λ_{max}, nm (ε): 262 (22600), 304 (2800). ^1H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.67–1.80 (1H, m, 2-CH); 1.93–2.04 (1H, m, 2-CH); 2.79–2.87 (1H, m, 3-CH); 2.93 (3H, s, NCH_3); 3.33–3.46 (2H, m, 1-CH); 3.61 (1H, dd, ^2J = 8.4, ^3J = 5.6, 4-CH); 3.79 (3H, s, OCH_3); 4.04 (1H, dd, ^2J = 8.4, ^3J = 6.7, 4-CH); 4.60–4.61 (2H, m, 5-CH); 6.28 (1H, dd, ^3J = 4.5, ^4J = 2.2, 7-CH); 6.62–6.73 (3H, m, H aniline); 6.85–6.90 (2H, m, H *p*-anisyl); 7.03–7.08 (2H, m, H aniline); 7.19–7.26 (2H, m, H *p*-anisyl). ^{13}C NMR spectrum (75 MHz, $CDCl_3$), δ, ppm: 29.8 (C-2); 38.3 (N-CH_3); 43.3 (C-3); 50.8 (C-1); 55.2 (O-CH_3); 70.0 (C-5); 72.6 (C-4); 112.4 (CH aniline); 114.0 (CH *p*-anisyl); 116.3 (CH aniline); 120.3 (C-7); 129.1 (CH *p*-anisyl); 129.2 (CH aniline); 130.0 (C_{quat} aniline); 142.3 (C_{quat} *p*-anisyl); 149.1 (C-6); 158.3 (C_{quat} *p*-anisyl). Mass spectrum (70 eV), *m*/*z* (I_{rel}, %): 323 $[M]^+$ (9), 216 $[C_{14}H_{16}O_2]^+$ (1), 188 $[C_{12}H_{12}O_2]^+$ (2), 162 $[C_{10}H_{10}O_2]^+$ (2), 149 (20), 146 $[C_{10}H_{10}O]^+$ (4), 132 $[C_9H_8O]^+$ (4), 121 $[C_8H_9O]^+$ (10), 120 $[C_8H_8O]^+$ (100). Found, *m*/*z*: 323.1890 $[M]^+$. $C_{21}H_{25}NO_2$. Calculated, *m*/*z*: 323.1880.

***rac*-*N*-{2-[(4*Z*)-4-(4-Methoxybenzylidene)tetrahydrofuran-3-yl]ethyl}-*N*-methylaniline ((*rac*)-5b)** was synthesized from (*Z*)-4-{[3-(4-methoxyphenyl)prop-2-yn-1-yl]oxy}but-2-en-1-ol (**4b**) (116 mg, 0.50 mmol), using [RhCl(cod)] (6.1 mg, 0.01 mmol), (*rac*)-BINAP (15.5 mg, 0.03 mmol) as ligand instead of (*R*)-BINAP, dichloroethane (2.0 ml), 0.05 M solution of $AgBF_4$ in dry dichloroethane (0.5 ml, 0.03 mmol), and *N*-methylaniline (0.11 ml, 1.0 mmol). Eluent for flash chromatography *n*-hexane – diethyl ether, 1:1 + 5 vol % of NEt_3. Yield 132 mg (78%), yellow oil. HPLC: (*n*-hexane–*i*-PrOH) 0.8 ml/min, 266 nm, t_R 15.2 min, t_S 16.0 min. IR spectrum (film), ν, cm^{-1}: 2932 (s), 2858 (s), 1602 (s), 1576 (w), 1509 (s), 1464 (m), 1368 (m), 1295 (m), 1253 (s), 1180 (m), 1115 (m), 1065 (m), 1033 (s), 991 (w), 909 (w), 825 (m), 750 (s), 731 (s), 692 (m), 532 (m). ^1H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.66–1.80 (1H, m, 2-CH); 1.93–2.03 (1H, m, 2-CH); 2.79–2.86 (1H, m, 3-CH); 2.92 (3H, s, NCH_3); 3.33–3.45 (2H, m, 1-CH); 3.62 (1H, dd, ^2J = 8.3, ^3J = 5.6, 4-CH); 3.79 (3H, s, OCH_3); 4.03 (1H, dd, ^2J = 8.3, ^3J = 6.7, 4-CH); 4.59–4.61 (2H, m, 5-CH); 6.27 (1H, dd, ^3J = 4.5, ^4J = 2.2, 7-CH); 6.62–6.72 (3H, m, H aniline); 6.85–6.91 (2H, m, H *p*-anisyl); 7.03–7.07 (2H, m, H aniline); 7.19–7.25 (2H, m, H *p*-anisyl). ^{13}C NMR spectrum (75 MHz, $CDCl_3$), δ, ppm: 29.8 (C-2); 38.3 (N-CH_3); 43.2 (C-3); 50.7 (C-1); 55.2 (O-CH_3); 70.0 (C-5); 72.5 (C-4); 112.4 (CH aniline); 114.0 (CH *p*-anisyl); 116.2 (CH aniline); 120.3 (C-7); 129.1 (CH *p*-anisyl); 129.2 (CH aniline); 130.0 (C_{quat} aniline); 142.4 (C_{quat} *p*-anisyl); 149.1 (C-6); 158.2 (C_{quat} *p*-anisyl). Mass spectrum (70 eV), *m*/*z* (I_{rel}, %): 323 $[M]^+$ (8), 216 $[C_{14}H_{16}O_2]^+$ (1), 188 $[C_{12}H_{12}O_2]^+$ (2), 162 $[C_{10}H_{10}O_2]^+$ (2), 149 (19), 146 $[C_{10}H_{10}O]^+$ (4), 132 $[C_9H_8O]^+$ (4), 121 $[C_8H_9O]^+$ (10), 120 $[C_8H_8O]^+$ (100). Found, *m*/*z*: 323.1890 $[M]^+$. $C_{21}H_{25}NO_2$. Calculated, *m*/*z*: 323.1880.

***N*-Benzyl-2-[(3*R*,4*Z*)-4-(4-methoxybenzylidene)tetrahydrofuran-3-yl]-*N*-methylethanamine (5c)** was synthesized from (*Z*)-4-{[3-(4-methoxyphenyl)prop-2-yn-1-yl]oxy}but-2-en-1-ol (**4b**) (232 mg, 1.00 mmol) using [RhCl(cod)] (25 mg, 0.05 mmol), (*R*)-BINAP (63 mg, 0.1 mmol), dichloroethane (10.0 ml), 0.05 M solution of $AgBF_4$ in dry dichloroethane (2.0 ml, 0.1 mmol), and *N*-benzylmethylamine (0.26 ml, 2.0 mmol). Eluent for flash chromatography *n*-hexane – diethyl ether, 1:1 + 5 vol % of NEt_3. Yield 166 mg (49%), yellow oil. R_f 0.37 (*n*-hexane – diethyl ether, 1:2 + 5 vol % of NEt_3). $[\alpha]_D^{20}$ –23.9° (*c* 2.8 mg/ml, $CHCl_3$). IR spectrum (film), ν, cm^{-1}: 3028 (w), 2940 (m), 2837 (m), 2790 (m), 1607 (s), 1511 (s), 1495 (w), 1454 (m), 1296 (m), 1251 (s), 1179 (m), 1113 (w), 1060 (m), 1035 (s), 933 (w), 872 (w), 825 (w), 739 (m), 700 (m), 531 (w). UV/Vis spectrum (CH_2Cl_2), λ_{max}, nm (ε): 266 (23200), 276 (17400). ^1H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.60–1.72 (1H, m, 2-CH); 1.85–1.97 (1H, m, 2-CH); 2.21 (3H, s, NCH_3); 2.36–2.48 (2H, m, 1-CH); 2.81–2.93 (1H, m, 4-CH); 3.44–3.56 (3H, m, CH_2 benzyl, 4-CH); 3.74–3.76 (1H, m, 5-CH); 3.79 (3H, s, OCH_3); 3.97 (2H, dd, ^2J = 8.4, ^3J = 6.7, 5-CH); 6.23–6.25 (1H, m, 7-CH); 6.87 (2H, d, ^3J = 8.8, H *p*-anisyl); 7.04 (2H, d, ^3J = 8.7, H Ph); 7.24–7.32 (5H, m, H *p*-anisyl, H Ph). ^{13}C NMR spectrum (75 MHz, $CDCl_3$), δ, ppm: 30.9 (C-2);

42.3 (N-CH_3); 43.4 (C-3); 55.3 (O-CH_3); 62.5 (CH_2 benzyl); 70.0 (C-5); 72.8 (C-4); 113.9 (CH *p*-anisyl); 120.0 (C-7); 127.0 (CH Ph); 128.2 (CH Ph); 128.3 (CH Ph); 129.1 (CH *p*-anisyl); 130.2 (C_{quat} Ph); 139.2 (C_{quat} *p*-anisyl); 142.9 (C-6); 158.2 (C_{quat} *p*-anisyl). Mass spectrum (70 eV), *m*/*z* (I_{rel}, %): 337 $[M]^+$ (15), 216 $[C_{14}H_{16}O_2]^+$ (1), 188 $[C_{12}H_{12}O_2]^+$ (2), 146 $[C_{10}H_{10}O]^+$ (5), 135 (12), 134 $[C_9H_{10}O]^+$ (100), 121 $[C_8H_9O]^+$ (7), 120 (5), 91 $[C_7H_7]^+$ (63). Found, *m*/*z*: 337.2056 $[M]^+$. $C_{22}H_{27}NO_2$. Calculated, *m*/*z*: 337.2036.

X-ray structural study of compound (*R*)-5a·HCl. The single crystal of compound (*R*)-**5a**·HCl suitable for X-ray crystallography was obtained by evaporation of the solution of compound (*R*)-**5a**·HCl in dichloromethane kept at room temperature for 7 days. The data were collected on a Bruker SMART APEX diffractometer (radiation Mo*K*a, λ 0.71073 Å, 0.3 deg ω-scans with CCD area detector, covering a whole sphere in reciprocal space) using a colorless crystal (polyhedron), dimensions 0.36 × 0.16 × 0.05 mm^3. Crystal system orthorhombic; space group $P2_12_12_1$; *Z* 4; *a* 6.059(3), *b* 10.745(6), *c* 26.18(2) Å; α 90, β 90, γ 90°; *V* 1704.3(19) $Å^3$; ρ 1.200 g/cm^3; *T* 200(2) K; θ_{max} 28.54°; 17724 reflections measured, 4288 (*R*(int) 0.0741), observed 3623 ($I > 2(I)$), intensities were corrected for Lorentz and polarization effects, an empirical absorption correction was applied using the SADABS software[40] based on the Laue symmetry of the reciprocal space, μ 0.224 mm^{-1}, T_{min} 0.99, T_{max} 0.92. The structure was solved by direct methods and refined against F_2 with a full-matrix least-squares algorithm using the SHELXTL-PLUS (5.10) software package,[41] 194 parameters refined, hydrogen atoms were treated using appropriate riding models, goodness of fit 1.31 for observed reflections, final residual values $R_1(F)$ 0.104, $wR(F_2)$ 0.164 for observed reflections, residual electron density –0.33 to 0.59 $eÅ^{-3}$. Crystallographic data of compound **5a** is deposited at the Cambridge Crystallographic Data Center (deposit CCDC 1825476).

Financial support of the Deutsche Forschungsgemeinschaft (SFB 623) and Fonds der Chemischen Industrie is gratefully acknowledged. We also cordially thank the BASF SE for the generous donation of chemicals.

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