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Conformational control on remote stereochemistry in the intramolecular Pauson–Khand reactions of enynes tethered to homoallyl and homopropargyl alcohols

Serdar Sezer,[a] Devrim Özdemirhan,[b] Ertan Şahin[c] and Cihangir Tanyeli[a,*]

[a]*Department of Chemistry, Middle East Technical University, 06531 Ankara, Turkey*
[b]*Department of Chemistry, Abant İzzet Baysal University, 14280 Bolu, Turkey*
[c]*Department of Chemistry, Ataturtk University, 25240 Erzurum, Turkey*

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Abstract—An intramolecular Pauson–Khand reaction of enynes derived from homoallyl and homopropargyl alcohols is described. 2-Furyl substituted homoallyl and homopropargyl alcohols are easily and efficiently resolved through enzymatic resolution in a high ee (93–99%) with a known stereochemistry. Each enantiomerically enriched enyne affords the conformationally most stable diastereomeric cyclopenta[*c*]pyran ring system.

1. Introduction

Heterocyclic natural products having α-heterocyclic carbinol moieties, are exceptionally valuable compounds for biomedical and pharmaceutical research, owing to their structural features and diverse medicinal values. A number of heterocyclic natural products exhibiting useful biological activities have been isolated from natural sources.[1] Brown et al.[2] accomplished the highly stereoselective synthesis of furyl-, thiophenyl-, pyridyl-, and other heterocyclic carbinols, which are useful for the stereoselective synthesis of many other important heterocyclic compounds,[3] by the asymmetric allylboration of heterocyclic aldehydes with diterpenylallylboranes. However, catalytic enantioselective methods hold tremendous appeal in synthetic organic chemistry. A significant progress in the development of catalytic enantioselective allylation and propargylation has been recorded in recent years.[4]

Since biocatalysts have become popular and powerful in organic synthesis,[5] enzymatic resolution can sometimes be very useful if it works well for individual alcohols. In 1997, we reported the first enzyme-catalyzed resolution of racemic furylcarbinols with high enantiomeric purity and in good total yields.[6] This approach was used recently by some other groups.[7]

The Pauson–Khand reaction (PKR)[8] has been established as a powerful method for the synthesis of the cyclopentenone framework by a cobalt-mediated reaction performed by joining an alkyne, an olefin, and carbon monoxide. The intramolecular version of the reaction has gained much popularity because it can afford cyclopentenone-fused ring systems, which are difficult to construct.[9] Although the application of this useful method to the construction of chiral cyclopentenone–pyran ring skeletons using carbohydrate templates has been well documented,[10] little attention has been focused on the PKR of chiral enyne systems.[11] Recent reports from our laboratory have demonstrated the utility of biocatalysts in the resolution of racemic α-heterocyclic carbinols[6,12] as a potentially useful scaffold for carrying out intramolecular PKRs. The important characteristics of this scaffold are the availability of the starting material, easy enzymatic resolution of the products, and the easy construction of enyne systems on it. Herein we report, a brief study on the PKR of enyne systems tethered to a chiral 2-furylcarbinol scaffold affording chiral cyclopenta-pyran fused ring systems with an excellent diastereoselectivity.

* Corresponding author. Tel.: +90 312 210 3222; fax: +90 312 210 3200; e-mail: tanyeli@metu.edu.tr

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2. Results and discussion

The parent homoallylic alcohol (±)-**1** and homopropargylic alcohol (±)-**2** were prepared by the addition of allylmagnesium bromide and propargyl bromide in the presence of a zinc–copper couple to the commercially available furfural in ether and THF, respectively, as shown in Scheme 1. The enantiomeric resolution of (±)-**1** and **2** catalyzed by PS-C Amano II[13] using vinyl acetate as an acyl donor and THF as solvent afforded (*S*)-(−)-**1** (99% ee) and (*S*)-(+)-**2** (93% ee) after the reaction was stopped at 55% and 52% conversions, respectively. To obtain alcohols (*R*)-(+)-**1** and (*R*)-(−)-**2**, acetates (*R*)-(+)-**3** and (*R*)-(+)-**4** were hydrolyzed quantitatively with NaOH in methanol. Moreover, the enzymatic hydrolysis of (±)-**3** catalyzed by PLE also afforded alcohol (*R*)-(+)-**1** (93% ee) in a pH = 7 phosphate buffer system.[14] All the results are summarized in Table 1. The enyne systems were built on enantiomerically enriched homoallylic and homopropargylic alcohol skeletons by O-propargylation and O-allylation using TMS–propargyl bromide and allyl bromide with NaH in THF, respectively.

To study the applicability of the intramolecular PKR of enynes tethered to chiral 2-furylcarbinols and to explore the control of remote stereochemistry in the synthesis of cyclopentenone–pyran ring skeletons, we submitted compounds (*S*)-**5** and (*S*)-**6** to the most common conditions for PKR.

In this protocol, cobalt alkyne complexes were prepared using enyne–dicobalt octacarbonyl in a molar ratio of 1.0:1.3 in DCM, and then *N*-methylmorpholine *N*-oxide monohydrate was added as a promoter.

The reaction was monitored by thin layer chromatography (TLC). In both cases, single diastereomers of cyclopentenone–pyran products (+)-**7**:*cis* and (+)-**8**:*trans* were obtained (Scheme 2).[15]

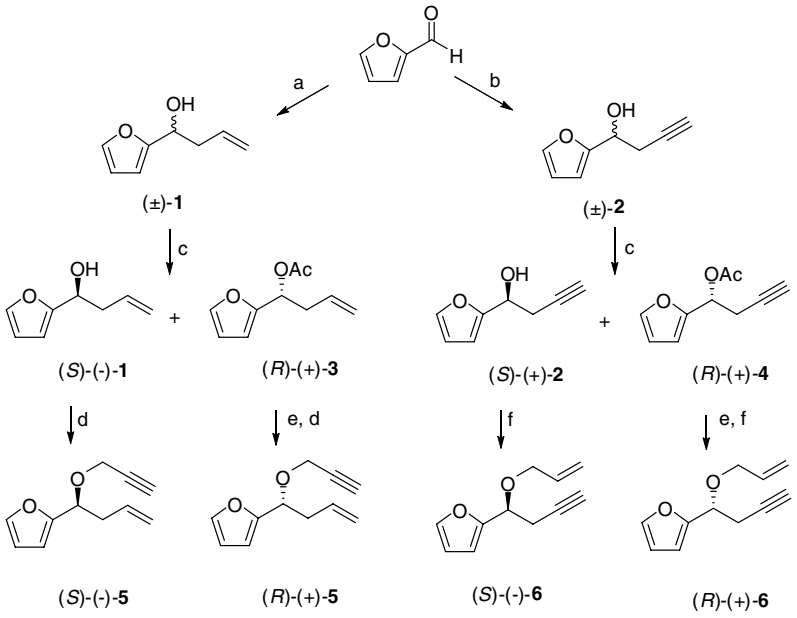
X-ray structures of the cyclopentenone–pyran products *cis*-(+)-**7** and *trans*-(+)-**8** provided an explanation as to why enynes (*S*)-(+)-**5** and (*S*)-(−)-**6**, respectively, afforded single diastereomers (Fig. 1). In compound (+)-**7**, C1–H and C3–H are *cis*, whereas C1–H and C4–H are *trans* in compound (+)-**8**. In both cases, the pyran rings are in the most favored chair conformation and the furyl substituents are in equatorial orientation, as expected.

3. Conclusion

New enantiomerically enriched 2-furyl substituted enynes tethered to homoallyl and homopropargyl backbones have been synthesized. Their intramolecular PKR showed a high conformational control on the remote stereocenter formed on the cyclopentenone–pyran ring system. We are currently studying the role of conformational control of similar homoallyl and homopropargyl enynes having diverse substituents. This work may be applicable to other easily prepared chiral homoallyl and homopropargyl type compounds.

4. Experimental

All experiments were carried out in pre-dried glassware (1 h, 150 °C) under an inert atmosphere of argon. The following reaction solvents were distilled from the indicated drying agents: dichloromethane (P_2O_5), tetrahydrofuran (sodium, benzophenone). ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker Spectrospin Avance DPX-400 spectrometer and the chemical shift as were expressed in ppm relative to $CDCl_3$ (δ 7.26 and 77.0 for ^{1}H

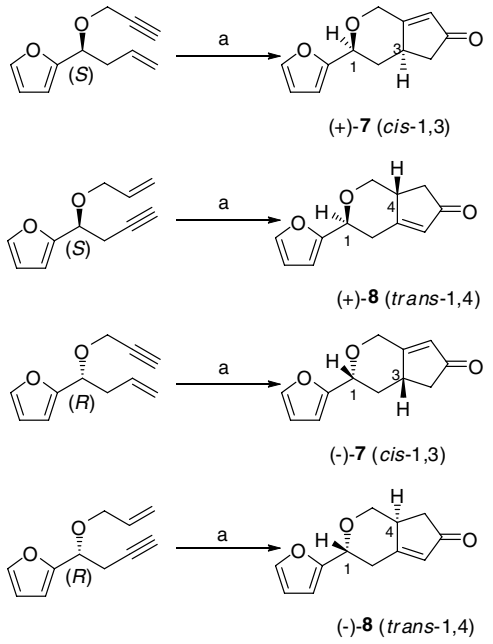


Scheme 1. Reagents and conditions: (a) allylbromide, Mg, dry ether; (b) Zn, Cu, propargylbromide, THF; (c) PS-C Amano II, vinylacetate, THF; (d) NaH, TMS–propargylbromide, THF; (e) NaOH, MeOH; (f) NaH, allylbromide, THF.

Table 1. Enzymatic hydrolysis of **1**–**3**[a,e]

Entry	Substrate	Enzyme	Temperature (°C)	Time (h)	Conv. (%)	ee[b] (%)	$[\alpha]_D^{29}$ (*c*, solvent)	Absolute conf.[c]
1	(±)-**1**	PS-C Amano II	24	4	55	99	−40.0 (*c* 5.0, CH_2Cl_2)	*S*
2	(±)-**2**	PS-C Amano II	24	1.5	52	93	+6.7 (*c* 3.1, MeOH)	*S*
3[d]	(±)-**3**	PLE	15	4.5	47	93	+37.1 (*c* 0.76, $CHCl_3$)	*R*

[a] All data given for the alcohols isolated as a result of enzymatic resolution.
[b] Determined by HPLC analysis employing a Daicel Chiralcel OD–H and OJ–H column.
[c] The absolute configurations of (*S*)-(−)-**1**,[7a] (*S*)-(+)-**2**,[4t] (*R*)-(+)-**1**,[6] (*R*)-(−)-**2**[4t] were found to be (*S*) or (*R*) according to the specific rotations reported in Refs. 6, 7a and 4t.
[d] Compound (±)-**3** was resolved by PLE.[14]
[e] Compound (*R*)-(+)-**4** was chemically hydrolyzed to obtain (*R*)-(−)-**2**.



Scheme 2. Reagents and conditions: (a) Co_2CO_8, DCM, NMO.

and ^{13}C NMR, respectively) as the internal standard. Standard COSY, HETCOR, and DEPT experiments were performed to establish NMR assignments. Infrared spectra were recorded on a Varian 1000 FT-IR spectrophotometer. High-resolution mass spectral data were obtained with a Varian MAT 212. Optical rotations were measured employing a Rudolph research analytical, Autopol III automatic polarimeter. Melting points were determined on an Electrothermal (Mel-Temp) apparatus (Model No: 1002D) on are uncorrected. High performance liquid chromatography (HPLC) was done with a Thermo Separation Products, Inc., P1500-SN-4000-UV2000 instrument using Daicel Chiralcel OD-H, OJ-H and Regis technologies Inc., Whelk O1 chiral columns.

Flash column chromatography was performed by using thick-walled glass columns with a flash grade (Merc Silica Gel 60). The reactions were monitored by thin layer chromatography using pre-coated silica gel plates (Merc Silica Gel PF-254), visualized by UV-light and polymolybden phosphoric acid in ethanol as appropriate. All extracts were dried over anhydrous magnesium sulfate and solutions were concentrated under vacuum by using rotary evaporator.

4.1. Synthesis of homopropargyl alcohol (±)-2

A Zn–Cu couple preparation was formed in an oxygen-free environment. Zinc dust (6.5 g, 100 mmol) was suspended in distilled water (10 mL). Acidic cupric chloride solution (0.15 M in 5% hydrochloric acid, 22 mL) was then added with vigorous magnetic stirring. When the evolution of gas ceased the suspension was filtered and the black solid was washed with water until the wash gave a negative test with 6% silver nitrate solution. The Zn–Cu was then washed twice with acetone.[12,18]

To a stirred mixture of 2-furaldehyde (6.90 g, 72 mmol) and freshly prepared Zn–Cu couple (1.03 g, 79.6 mmol) in THF (20 mL), propargyl bromide (0.21 g, 79.6 mmol, 80% solution in toluene) was added dropwise at 0 °C. The mixture was then refluxed for 6 h (TLC monitoring). The resultant mixture was hydrolyzed with 1 M HCl (8 mL) and extracted with ether (3 × 30 mL), dried over $MgSO_4$, and evaporated in vacuo. The crude product was purified by flash column chromatography (EtOAc–hexane, 1:10), (7.83 g, 80% yield). All spectroscopic data are in accordance with that in the literature.[4t]

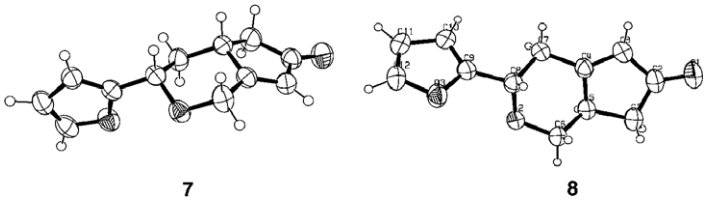


Figure 1. X-ray structure of compounds *cis*-(+)-**7** and *trans*-(+)-**8**.

4.2. General procedure for enzymatic resolution

To a solution of (±)-**1**–**2** (1 mmol) in anhydrous THF (1 mL) and vinyl acetate (0.9 mL, 10 mmol) in a 25 mL round-bottomed flask, was added lipase (1 equiv w/w). The reaction mixture was stirred at constant temperature (24 ± 1 °C) and monitored by TLC and recorded on HPLC. On achieving the desired conversion the reaction was stopped by filtering the enzyme on a sintered glass funnel. The filtrate was concentrated and purified by column chromatography on silica gel using mixtures of hexane and ethyl acetate as eluents to afford (*R*)-acetates and (*S*)-alcohols.

4.2.1. (*S*)-(−)-1-(2-Furyl)but-3-en-1-ol, (*S*)-(−)-1. This is a yellow oil; $[\alpha]_D^{29} = -40.0$ (*c* 5.0, CH_2Cl_2) for 99% ee. The absolute configuration and enantiomeric purity of the product were determined by HPLC analysis (Daicel Chiralcel OJ-H, hexane/*i*-PrOH 96:4, flow rate = 1 mL min^{-1}, $\lambda = 230$ nm, $t_R = 11.20$ min [(*R*)-isomer], $t_R = 12.64$ min [(*S*)-isomer] in comparison with the racemic sample).

4.2.2. (*R*)-(+)-1-(2-Furyl)but-3-en-1-yl acetate, (*R*)-(+)-3. This is a yellow oil; $[\alpha]_D^{29} = +22.2$ (*c* 1.02, CH_2Cl_2) for 96% ee. The absolute configuration and enantiomeric purity of the product were determined by HPLC analysis (Whelk, hexane/*i*-PrOH 96:4, flow rate = 1 mL min^{-1}, $\lambda = 230$ nm, $t_R = 5.49$ min, $t_R = 6.25$ in comparison with the racemic sample).

4.2.3. (*R*)-(+)-1-(2-Furyl)but-3-en-1-ol, (*R*)-(+)-1. To a stirred solution of (±)-**3** (500 mg, 2.7 mmol) in 0.1 M phosphate buffer (pH 7.00, 75 mL), was added PLE (100 μL) at one portion and the reaction mixture was stirred at 15 °C for 4.5 h. The reaction mixture was extracted with ethyl acetate (3 × 50 mL), dried over $MgSO_4$ and then evaporated under vacuum. The crude product was separated by flash column chromatography (EtOAc/hexane, 1:4) (0.24 g, 47% yield).[6]

4.2.4. (*S*)-(+)-1-(Furan-2-yl)but-3-yn-1-ol, (*S*)-(+)-2. This is a yellow oil; $[\alpha]_D^{29} = +6.7$ (*c* 3.1, MeOH) for 93% ee. The absolute configuration and enantiomeric purity of the product were determined by HPLC analysis (Daicel Chiralcel OD-H, hexane/*i*-PrOH 96:4, flow rate = 1 mL min^{-1}, $\lambda = 230$ nm), $t_R = 16.842$ min, $t_R = 23.15$ in comparison with an authentic sample).

4.2.5. (*R*)-(+)-1-(Furan-2-yl)but-3-ynyl acetate, (*R*)-(+)-4. This is a yellow oil; $[\alpha]_D^{29} = +54.6$ (*c* 4.0, MeOH) for 90% ee. The absolute configuration and enantiomeric purity of the product were determined by HPLC analysis (Whelk, hexane/*i*-PrOH 96:4, flow rate = 1 mL min^{-1}, $\lambda = 230$ nm), $t_R = 5.89$ min, $t_R = 6.11$ in comparison with the authentic sample. ^{1}H NMR ($CDCl_3$): δ 7.32 (s, 1H), 6.34 (d, $J = 3.2$ Hz, 1H), 6.27 (d, $J = 1.79$ Hz, 1H), 5.89 (t, $J = 6.9$, 1H), 2.73 (dd, $J = 7.69$ and 7.67 Hz, 2H), 2.00 (s, 3H), 1.91 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 169.9, 151.2, 142.8, 110.3, 109.1, 78.9, 70.6, 66.5, 23.0, 20.9. Anal. Calcd: C, 67.41; H, 5.66. Found: C, 67.13; H, 5.46.

4.2.6. (*R*)-(−)-1-(Furan-2-yl)but-3-yn-1-ol, (*R*)-(−)-2. To a solution of (*R*)-(+)-**4** (500 mg, 2.7 mmol) in methanol (30 mL) and water (10 mL), 1 M solution of NaOH (2.7 mL) was added and stirred at room temperature until the hydrolysis was complete (TLC). The solution was extracted with chloroform (3 × 25 mL), dried over $MgSO_4$, and evaporated under vacuum (495 mg, 99% yield).

4.3. General procedure for O-allylation and O-propargylation

To a solution of (*S*)-(−)-**1** or (*S*)-(+)-**2** (1.4 mmol) in dry THF (10 mL) was added NaH (0.62 g, 60% dispersion in oil, 1.54 mmol) under argon. Allylbromide or TMS–propargylbromide (1.54 mmol) was then added dropwise. The mixture was refluxed for 1 h and hydrolyzed by the cautious addition of water (15 mL). The aqueous layer was extracted with ether (3 × 20 mL). The combined organic phase was dried over $MgSO_4$ and evaporated in vacuo. The crude product mixture was separated by flash column chromatography using ethylacetate/hexane (1:9) as the eluent to afford the product.

4.3.1. (*S*)-(−)-2-(1-(Prop-2-ynyloxy)but-3-enyl)furan, (*S*)-(−)-5. This is a yellow oil (0.20 g, 83% yield). $[\alpha]_D^{29} = -67.5$ (*c* 2.7, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 7.24 (d, $J = 0.8$ Hz, 1H), 6.32–6.38 (m, 2H), 5.70–5.83 (m, 1H), 4.93 (dd, $J = 1.2$ and 17.1 Hz, 1H), 4.88 (d, $J = 1.2$ and 10.2 Hz, 1H), 4.42 (t, $J = 7.0$ Hz, 1H), 3.98 (dd, $J = 2.2$ and $J = 15.8$ Hz, 1H), 3.78 (dd, $J = 2.2$ and 15.8 Hz, 1H), 2.36–2.56 (m, 2H), 2.23 (t, $J = 2.2$ Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 152.4, 142.1, 133.3, 116.8, 109.5, 108.5, 79.2, 73.8, 72.5, 55.0, 37.8. Anal. Calcd: C, 74.98; H, 6.86. Found: C, 74.36; H, 6.81.

4.3.2. (*R*)-(+)-2-(1-(Prop-2-ynyloxy)but-3-enyl)furan. (*R*)-(+)-**5**: $[\alpha]_D^{29} = +66.4$ (*c* 2.6, CH_2Cl_2).

4.3.3. (*S*)-(−)-2-(1-Allyloxy)but-3-ynyl)furan, (*S*)-(−)-6. This is a yellow oil (0.19 g, 80% yield). $[\alpha]_D^{29} = -8.5$ (*c* 0.5, MeOH). ^{1}H NMR ($CDCl_3$): δ 7.34 (br s, 1H), 6.28–6.29 (overlapped br s, 2H), 5.77–5.86 (m, 1H), 5.20 (dd, $J = 1.2$ and 17.2 Hz, 1H), 5.11 (dd, $J = 1.2$ and 10.4 Hz, 1H), 4.48 (t, $J = 6.9$ Hz, 1H), 3.96 (dd, $J = 5.1$ and 12.8 Hz, 1H), 3.86 (dd, $J = 5.1$ and 12.8 Hz, 1H), 2.65–2.77 (m, 2H), 1.90 (t, $J = 2.6$ Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 153.3, 143.0, 134.7, 117.8, 110.4, 108.9, 80.6, 72.8, 70.3, 70.2, 24.9. Anal. Calcd: C, 74.98; H, 6.86. Found: C, 74.52; H, 6.74.

4.3.4. (*R*)-(+)-2-(1-(Allyloxy)but-3-ynyl)furan. (*R*)-(+)-**6**: $[\alpha]_D^{29} = +8.2$ (*c* 0.5, MeOH).

4.4. General procedure for the Pauson–Khand reaction

To a solution of (*S*)-(−)-**5** (0.204 g, 1.16 mmol) or (*S*)-(−)-**6** (0.197 g, 1.12 mmol) in CH_2Cl_2 (10 mL) was added $Co_2(CO)_8$ (0.683 g, 2.0 mmol), and stirred for 2 h (TLC monitoring). Then, NMO (1.56 g, 11.6 mmol) was added and stirred for 24 h. The crude product was purified by flash column chromatography (EtOAc–hexane, 2:1).

4.4.1. (3*S*,4a*R*)-(+)-3-(Furan-2-yl)-3,4,4a,5-tetrahydrocyclopenta[*c*]pyran-6(1*H*)-one, (+)-7. This is a white solid (0.18 g, 75% yield); mp 89 °C. $[\alpha]_D^{29} = +35.5$ (*c* 1.7, CH_2Cl_2); ^1H NMR ($CDCl_3$): δ 7.33 (d, $J = 1.0$ Hz, 1H), 6.29 (m, 1H), 6.24 (d, $J = 3.2$ Hz, 1H) 5.94 (s, 1H), 4.74 (d, $J = 13.5$ Hz, 1H), 4.63 (dd, $J = 1.3$ and 11.5 Hz, 1H), 4.35 (d, $J = 13.5$ Hz, 1H), 2.97–3.00 (m, 1H), 2.62 (dd, $J = 6.5$ and 18.8 Hz, 1H), 2.36 (dd, $J = 5.8$ and 13.0 Hz, 1H), 2.08 (dd, $J = 2.8$ and 18.6 Hz, 1H), 1.80 (dd, $J = 12.2$ and 24.4 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 207.4, 174.2, 153.0, 142.6, 127.8, 110.3, 107.1, 72.2, 67.0, 41.8, 39.0, 37.9. IR (KBr): 1702, 1622, 1403 cm^{-1}. Anal. Calcd: C, 70.57; H, 5.92. Found: C, 70.36; H, 5.78.

4.4.2. (3*R*,4a*S*)-(−)-3-(Furan-2-yl)-3,4,4a,5-tetrahydrocyclopenta[*c*]pyran-6(1*H*)-one, (−)-7. $[\alpha]_D^{29} = -34.4$ (*c* 1.8, CH_2Cl_2).

4.4.3. (3*S*,7a*R*)-(+)-3-(Furan-2-yl)-3,4,7,7a-tetrahydrocyclopenta[*c*]pyran-6(1*H*)-one, (+)-8. This is a white solid (0.19 g, 81% yield); mp 81–82 °C. $[\alpha]_D^{29} = +99.1$ (*c* 3.6, MeOH). ^1H NMR ($CDCl_3$): δ 7.37 (br s, 1H), 6.31 (br s, 2H), 5.95 (s, 1H), 4.32–4.39 (m, 3H), 3.21 (t, $J = 11.0$ Hz, 1H), 2.98 (d, $J = 13.3$ Hz, 1H), 2.86 (t, $J = 12.4$ Hz, 1H), 2.45 (dd, J= 6.6 and 18.8 Hz, 1H), 1.89 (d, $J = 18.8$ Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 207.5, 178.4, 152.7, 142.9, 128.1, 110.4, 107.6, 73.3, 73.2, 40.9, 37.0, 35.3. IR (KBr): 1704, 1618, 1381 cm^{-1}. Ion mode; FAB+ MS (*m*/*z*) exact mass; 205.0786 (M+1); observed; 205.0802 (M+1).

4.4.4. (3*R*,7a*S*)-(+)-3-(Furan-2-yl)-3,4,7,7a-tetrahydrocyclopenta[*c*]pyran-6(1*H*)-one, (−)-8. $[\alpha]_D^{29} = -95.7$ (*c* 3.6, MeOH).

4.5. General procedure for the chemical hydrolysis of (*R*)-acetates

To a solution of acetates (*R*)-**3**–**4** (0.2 mmol) in methanol (4 mL) and water (1 mL), a 1 M solution of NaOH (0.2 mL, 0.2 mmol) was added. The mixture was stirred at room temperature until the hydrolysis was completed (TLC). The solution was extracted with chloroform, dried with anhydrous Na_2SO_4, and evaporated to give respective (*R*)-alcohols, which were purified with column chromatography eluting with a hexane–ethyl acetate mixture and the specific rotation of these alcohols was determined.

4.6. X-ray structure analysis

For the crystal structure determination, the single-crystal of compounds *cis*-(+)-**7** ($C_{12}H_{12}O_3$) and $C_{12}H_{12}O_3$ *trans*-(+)-**8** was used for data collection on a four-circle Rigaku R-AXIS RAPID-S diffractometer equipped with a two-dimensional area IP detector. The graphite-monochromatized Mo K_α radiation ($\lambda = 0.71073$ Å) and oscillation scans technique with $\Delta\omega = 5°$ for one image were used for data collection. The images for *cis*-(+)-**7** and *trans*-(+)-**8** were taken successfully by varying ω with three sets of different χ and φ values. For each compound the 108 images for six different runs covering about 99.8% of the Ewald spheres were performed. The lattice parameters were determined by the least-squares methods on the basis of all reflections with $F^2 > 2\sigma(F^2)$. Integration of the intensities, correction for Lorentz and polarization effects and cell refinement were performed using CrystalClear software.[16] The structures were solved by direct methods (SHELXS-97) and non-H atoms were refined by full-matrix least-squares method with anisotropic temperature factors (SHELXL-97).[17]

4.6.1. Crystal data for compound *cis*-(+)-7. $C_{12}H_{12}O_3$, crystal system, space group: monoclinic, $P21/c$; (no:14); unit cell dimensions: $a = 5.5093(3)$, $b = 18.8250(6)$, $c = 10.2240(5)$ Å, $\beta = 105.466(2)°$; volume: 1021.96(6) Å^3; $Z = 4$; calculated density: 1.33 mg/m^3; absorption coefficient: 0.095 mm^{-1}; $F(000)$: 432; crystal size: $0.031 \times 0.025 \times 0.012$ mm^3; θ range for data collection 2.2–30.5°; completeness to θ: 30.5°, 99.8%; refinement method: full-matrix least-square on F^2; data/restraints/parameters: 3117/0/160; goodness-of-fit on F^2: 1.386; final R indices $[I > 2\sigma(I)]$: $R_1 = 0.073$, $wR_2 = 0.183$; R indices (all data): $R_1 = 0.074$, $wR_2 = 0.183$; extinction coefficient: 0.00; largest diff. peak and hole: 0.226 and −0.239 e Å^{-3}.

4.6.2. Crystal data for compound *trans*-(+)-8. $C_{12}H_{12}O_3$, crystal system, space group: orthorhombic, $P212121$; (no: 14); unit cell dimensions: $a = 7.8398(8)$, $b = 11.4097(8)$, $c = 11.9476(9)$ Å, $\beta = 90°$; volume: 1068.71(2) Å^3; $Z = 4$; calculated density: 1.27 mg/m^3; absorption coefficient: 0.091 mm^{-1}; $F(000)$: 432; crystal size: $0.021 \times 0.015 \times 0.012$ mm^3; θ range for data collection 2.5–30.6°; completeness to θ: 30.6°, 99.7%; refinement method: full-matrix least-square on F^2; data/restraints/parameters: 3275/0/138; goodness-of-fit on F^2: 1.139; final R indices $[I > 2\sigma(I)]$: $R_1 = 0.076$, $wR_2 = 0.150$; R indices (all data): $R_1 = 0.130$, $wR_2 = 0.171$; extinction coefficient: 0.0090; largest diff. peak and hole: 0.132 and −0.123 e Å^{-3}.

Crystallographic data (excluding structure factors) for the structures of *cis*-(+)-**7**: and *trans*-(+)-**8**: in this paper have been deposited with the Cambridge Crystallographic Data center as supplementary publication numbers CCDC 622252 and 622253, respectively. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

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13. Enzymatic resolution of compound (±)-**1** was carried out by using the procedure given in Ref. 7a. The same conditions were applied to substrate (±)-**2**. The absolute configurations of (−)-**1** and (+)-**2** were found to be (*S*) as reported.[7a,4t]
14. We applied the conditions given in Ref. 6.
15. Final compounds were identified and characterized by ^{1}H NMR, ^{13}C NMR, FTIR, COSY, HMBC, HMQC and HRMS, and/or elemental analysis. The new chiral center on the final products can be discerned in the X-ray structure relative to homoallylic and homopropargylic alcohols.
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