Tetrahedron 70 (2014) 1336–1347

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Stereoselective synthesis of side chain-functionalized tetrahydropyrans from 5-hexenols

Patrick Fries, Melanie Kim Müller, Jens Hartung *

Fachbereich Chemie, Organische Chemie, Technische Universität Kaiserslautern, Erwin-Schrödinger-Straße, D-67663 Kaiserslautern, Germany

ARTICLE INFO

Article history:
Received 17 July 2013
Received in revised form 3 December 2013
Accepted 7 December 2013
Available online 13 December 2013

Keywords:
Addition
Aerobic oxidation
Alkenol
Alkene
Bromocyclization
Catalysis
Dioxygen
Cobalt(II) complexes
Michael acceptor
Radical
Stereoselective synthesis
Tetrahydropyran

ABSTRACT

Molecular oxygen stereoselectively converts 5-hexenols into 2,6-trans-, 2,5-trans-, and 2,4-cis-derivatives of 2-methyltetrahydropyran via oxidative cyclization/radical functionalization cascades, when activated by fluoro-substituted cobalt(II) bis-(β-diketonate) complexes in solutions of cyclohexa-1,4-diene (CHD). Aerobic 5-hexenol oxidations in solutions of bromotrichloromethane and CHD furnish products of 6-*exo*-bromocyclization, as exemplified by synthesis of diastereomerically pure 2,4,6-substituted tetrahydropyrans. The cobalt method extends to intermolecular alkene/alkanol cross-coupling and to multi-component reactions between dimethyl fumarate, CHD, a 5-hexenol, and dioxygen, providing α-tetrahydropyranyl-2-methyl succinates in synthetically useful yields.

1. Introduction

Constitutionally dissymmetric tetrahydropyrans are secondary metabolites, biosynthetically formed from terpenols,[1,2] acetogenins,[3] polyketides, and oxidative enzymes.[4,5] Terminal oxidants to bring about the alkenol ring closure in biosynthesis are dioxygen and hydrogen peroxide, being activated by metalloproteins.[6,7] The protein coordinating the metal co-factor controls electronic properties of the oxidant and folding of the alkenol chain at the active site for attaining stereospecific oxidative tetrahydropyran ring closure.[8,9]

In organic synthesis, as in biosynthesis, the important method for constructing constitutionally dissymmetric tetrahydropyrans (cf. Fig. 1) is the 5-hexenol ring closure.[10,11] Since the oxygen and the carbon–carbon double bond in non-Michael-type alkenols are nucleophiles, one of the functional groups has to be converted into an electrophile for accomplishing the alkenol cyclization.

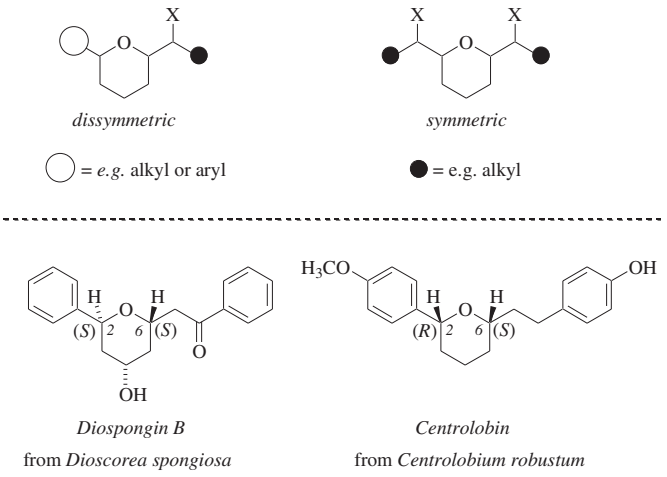


Fig. 1. General structure formulas for constitutionally dissymmetric and symmetric 2,6-substituted tetrahydropyran nuclei (X=e.g., OH), and examples for tetrahydropyran natural products showing (2*S*,6*S*)- (i.e. 2,6-*like*)[27]-configuration (cf. diospongin B)[28] and (2*R*,6*S*)- (i.e. 2,6-*unlike*)[27]-configuration (cf. centrolobin).[29]

* Corresponding author. Tel.: +49 631 205 2431; fax: +49 631 205 3921; e-mail address: hartung@chemie.uni-kl.de (J. Hartung).

0040-4020/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2013.12.019

Changing polarity at the alkenol oxygen is feasible by abstracting the hydroxyl hydrogen, to give an alkenoxyl radical.[12] 5-Hexenoxyl radicals add 6-*exo*-selectively to non-activated carbon–carbon double bonds with rate constants of 10^7 s^{-1} and above, to furnish 2,4-cis, 2,5-trans-, and 2,6-cis-isomers of sidechain-functionalized tetrahydropyrans as major products, when trapped by a suitable heteroatom donor.[13]

Changing polarity at the alkenol π-bond is feasible by activating the alkene subunit using soft Lewis acids, such as gold(III)- or mercury (II) compounds,[14] or alternatively by oxidants such as bromine,[15–17] high-valent transition metal oxo compounds,[18,19] or transition metal peroxido complexes.[20] Electrophile-induced 5-hexenol cyclizations furnish in most instances ~70:30 mixtures of stereoisomers, containing the 2,3-trans-, 2,4-cis-, 2,5-trans-, and 2,6-cis-stereoisomer in excess. This stereochemical sequence and the degree of diastereoselection reflect conformational preferences associated with transition structures of C,O-cyclization, hereafter referred to as substrate control.[21]

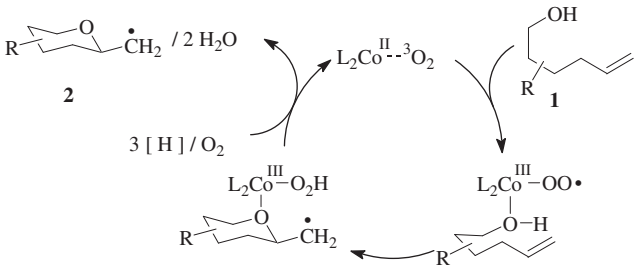
Successful concepts for improving stereoselectivity in substrate-controlled alkenol cyclizations use specially designed auxiliaries for sterically blocking the unwanted mode of cyclization, for example, in transition metal-catalyzed oxidations.[20] Approaches for reversing stereoselectivity in substrate-controlled 5-hexenol ring closures commonly change the mechanism for intramolecular carbon–oxygen bond formation, as successfully put into practice by dichloroacetylperrhenate/dichloroacetic anhydride-mediated cyclizations,[22] and oxidations of 1,6-dienes[23,24] or hept-6-ene-1,2-diols by high-valent transition metal oxo compounds.[25,26] 1,6-Dienes and hept-6-ene-1,2-diols under such conditions furnish derivatives of *trans*-2,6-bis(hydroxymethyl)-tetrahydropyran in notable diastereomeric excess. Both methods are for structural reasons not the method of choice for finalizing synthesis of constitutionally dissymmetric 2,6-substituted tetrahydropyrans, such as diospongin B or centrolobin (Fig. 1).

For stereoselectively preparing constitutionally dissymmetric tetrahydropyrans by a new approach (Scheme 1), we chose to oxidize 5-hexenols by molecular oxygen in cobalt(II)-catalyzed reactions. The method extends the Mukaiyama oxidation of 4-pentenols, which uses dioxygen and *tert*-butyl hydroperoxide as terminal oxidants.[30] Shi[31] and Pagenkopf[32,33] and their collaborators applied the Mukaiyama method for landmark contributions on stereoselective synthesis of tetrahydrofuran natural products. Changing the original Mukaiyama-auxiliary to fluorinated diketones allowed us to use air as exclusive terminal oxidant without the need to add *tert*-butyl hydroperoxide.[34] The true potential of the cobalt method for synthesis of cyclic ethers became apparent from mechanistic studies,[35,36] uncovering that the aerobic 4-pentenol oxidation furnishes (tetrahydrofuran-2-yl)-methyl radicals, which enable to prepare a variety of new, side chain-functionalized tetrahydrofurans by heteroatom-trapping or addition to Michael-type alkenes (for a related mechanism devised as concept for the present study on tetrahydropyran synthesis, see Scheme 1).

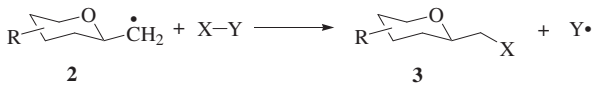
In a project on alkenol methylsulfanyl cyclization, we discovered that a 1,2-disubstituted 5-hexenol furnishes a diastereomerically pure 2,3,6-substituted tetrahydropyran, when oxidized by air in the presence of a cobalt(II)-diketonate complex.[37] In the present study we systematically investigated stereodirecting effects exerted by one substituent in position 1 or 2, and by two substituents in 5-hexenol positions 1,2 or 1,3. We furthermore explored (tetrahydropyran-2-yl)-methyl radical trapping by heteroatom donors and alkenes, for diversifying the methods used for carbon radical functionalization.

The major results from the study show that 5-hexenols yield 2,6-trans-, 2,5-trans-, and 2,4-cis-substituted tetrahydropyrans as major products, when exposed at elevated temperatures to air and cyclohexa-1,4-diene in solutions of toluene, containing a fluorinated cobalt bis-(β-diketonate) complex. Oxidizing 5-hexenols in solutions of bromotrichloromethane chemoselectively gives 6-*exo*-bromocyclized products in up to 89% yield, as exemplified by synthesis of diastereomerically pure 2,4,6-substituted tetrahydropyrans. Multi-component reactions between 5-hexenols, dioxygen, dimethyl fumarate, and cyclohexa-1,4-diene (CHD), catalyzed by cobalt complexes furnish α-tetrahydropyranyl-2-methyl succinates in synthetically useful yields.

(i) *aerobic 5-hexenol oxidation*



(ii) *(tetrahydropyran-2-yl)methyl radical functionalization*



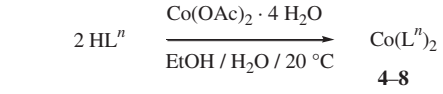
Scheme 1. Concept for tetrahydropyran formation from aerobic 5-hexenol oxidation (step i) and radical trapping (step ii); [H]=hydrogen atom from, e.g., cyclohexa-1,4-diene (CHD); R=aryl or alkyl; L^-=1-arylbutane-1,3-dione monoanion (Table 1); X–Y=e.g. CHD or $BrCCl_3$; the dashed line indicates triplet-dioxygen ($^3O_2$)-binding to cobalt(II) bis-(β-diketonate) complex CoL_2 (for structure formula of CoL_2, refer to Section 2.1).

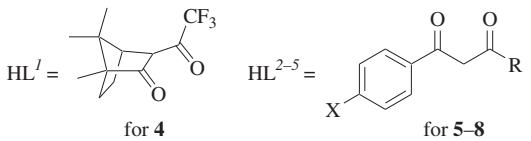
2. Results and discussion

2.1. Cobalt complexes

From a screening of catalysts, we selected fluoro-substituted cobalt(II) bis(β-diketonate)-complexes of the general formula

Table 1
Preparation and spectroscopic characteristics of fluorinated bis-[butane-1,3-dionato(−1)]-cobalt(II) complexes





Entry	HL^n	X	R	**4**–**8**[a]/%	λ_{max} (log $\varepsilon/\varepsilon^*$)[b]/nm	$\nu_{C=O}$[c]/cm^{-1}
1	HL^1	—	—	**4**: 89	309 (3.25)	1560, 1654
2	HL^2	H	CF_3	**5**: 99	319 (3.55)	1576, 1609
3	HL^3	F	CH_3	**6**: 84	316 (3.01)	1575, 1603
4	HL^4	F	CF_3	**7**: 89	319 (3.04)	1586, 1616
5	HL^5	F	C_7F_{15}	**8**: 96	323 (2.93)	1593, 1617

[a] Dihydrate.
[b] ε in m^2 mol^{-1}; ε^*=1 m^2 mol^{-1}.
[c] From samples pelletized in potassium bromide.

$Co(L^n)_2$ (Table 1) for catalyzing aerobic 5-hexenol cyclization. Compounds **4**, **5**, and **6** were available from a previous study.[34,35] *p*-Fluorophenylbutane-1,3-dione-derived cobalt(II) complexes **7** and **8** were newly prepared by mixing two aliquots of diketones[38] HL^{4-5} and one equiv of cobalt(II)-acetate tetrahydrate in aqueous ethanol (Table 1, entries 3 and 5). All cobalt compounds were characterized by infrared spectroscopy, electron spectroscopy (UV/vis), combustion analysis, ESI-mass spectrometry, and fluorine-19 NMR spectroscopy (Table 1 and Supplementary data).

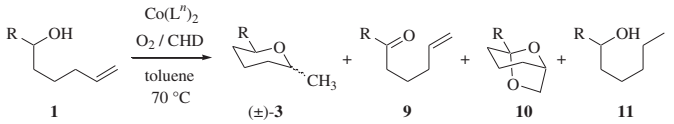
Cobalt complexes **7** and **8** precipitate as yellow (**7**) and orange (**8**) dihydrates, which were used for activating dioxygen. Co-crystallized ethanol and water can be removed by drying at 90 °C and a pressure of 0.2 mbar, as experimentally verified by disappearance of the OH-stretching mode at ~3400 reciprocal wavenumbers for the dihydrate of complex **6**. The anhydrous formulation of **6** is a brown powder, which is similarly active in catalyzing oxidative 5-hexenol cyclization as the hydrated material.

Fluorinated bis-[butane-1,3-dionato(−1)]cobalt(II) complexes **4**–**8** dissolve sparingly at room temperature in cyclohexa-1,4-diene/toluene mixtures. At temperatures of ~40 °C and above the solutions turn yellow, indicating that the cobalt complexes dissolve under conditions used for conducting aerobic oxidations. The yellow color changes to green upon contact with air at elevated temperatures. The green color prevails until the reaction is terminated by filtering the solution through a short pad of sodium thiosulfate and magnesium sulfate, for removing cobalt residues and water, prior to analyzing product mixtures by gas chromatography in combination with mass spectrometry.

2.2. Synthesis of tetrahydropyrans

2.2.1. From monosubstituted 5-hexenols. From systematic parameter variation we found that 1-phenyl-5-hexen-1-ol (**1a**) is chemoselectively converted into 2-phenyl-6-methyltetrahydropyran **3a**, when heated for 22 h in a solution of toluene and CHD containing 5 mol % of a cobalt(II) bis-(β-diketonate)-complex (Table 2, entries 1–8). For attaining effective substrate turnover air is allowed to diffuse into the reaction mixture from the top of a flask equipped with a reflux condenser. No tetrahydropyran **3a** forms, when air is replaced by an atmosphere of nitrogen, or when no fluorinated cobalt(II) diketonate complex is added.

Table 2
Products of aerobic oxidation from 1-substituted 5-hexenols **1a**–**c**



1 (±)-**3** **9** **10** **11**

Entry	R/**1**[a]	$Co(L^n)_2$	Conv.[b] **1**/%	**3**/% (cis/trans)	**9**/%	**10**/%	**11**/%
1	Ph/**a**	**4** (*n*=1)	64	23 (7:93)	14	2	—[c]
2	Ph/**a**	**5** (*n*=2)	>99	66 (11:89)	4	8	11
3	Ph/**a**	**6** (*n*=3)	37	7 (8:92)	20	—[c]	—[c]
4	Ph/**a**	**7** (*n*=4)	98	59 (12:88)	6	6	11
5	Ph/**a**	**8** (*n*=5)	96	69 (16:84)	6	6	9
6	CH_3/**b**	**5** (*n*=2)	>99	60 (17:83)	—[c]	—[c]	—[c]
7	*c*-C_6H_{11}/**c**	**5** (*n*=2)	87	40 (7:93)	1	5	—[c]

[a] For compounds **1**, **3**, **9**–**11**; $c_1^0 = 0.5$ M, $c_{CHD}^0 = 5.0$ M.
[b] Refers to 22 h reaction time and 5 mol % $Co(L^n)_2$ (c^0=25 mM).
[c] Not detected.

The degree of oxidative alkenol conversion within 22 h differs from moderate to quantitative, depending on the nature of the cobalt catalyst. The structure of the cobalt catalyst has no significant effect on cis/trans-selectivity of the oxidative 5-hexenol ring closure (Table 2, entries 1–5). The dihydrate of cobalt(II) compound **6**, showing excellent catalytic properties in aerobic methylsulfanyl cyclization of 4-pentenols, did not convincingly catalyze oxidative 5-hexenol cyclization. Perfluoroheptyl-substituted cobalt derivative **8** was not able to mediate quantitative alkenol turnover within 24 h at 70 °C in a solution having half the volume of toluene replaced by bromoperfluoroheptane. Since fluorinated solvents dissolve higher concentration of dioxygen than non-fluorinated hydrocarbons,[39] we assumed from this experiment that the rate of dioxygen diffusion into toluene/CHD mixtures is not rate limiting for oxidizing 5-hexenols in cobalt-catalyzed reactions. 1,1,1-Trifluoro-4-phenylbutane-1,3-dione-derived cobalt complex **5** was the only catalyst in the screening leading to quantitative oxidative turnover of alkenol **1a** under the chosen conditions. This finding caused us to use cobalt reagent **5** in all succeeding oxidation experiments as catalyst.

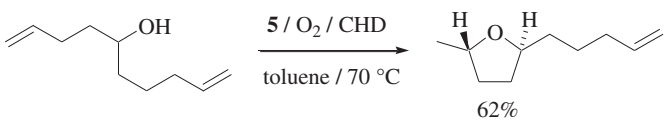
Further products obtained from substrate **1a** and dioxygen are hexenophenone **9a**, bicyclic acetal **10a**, and phenylhexanol **11a**, supplementing the mass balance of 5-hexenol-derived products to ~90% (Table 2, entry 2). Ketones are familiar by-products from aerobic cobalt-catalyzed oxidation of secondary alcohols. Ketone formation, however, is not observed in aerobic 1-phenyl-4-pentenol oxidation conducted in solutions of CHD, which we interpret in terms of a slower rate of the aerobic 5-hexenol cyclization compared to 4-pentenol cyclization (vide infra).[34]

Reductions of alkenes are common side reactions in cobalt-catalyzed oxidations conducted in an environment having comparatively weak carbon–hydrogen bonds available, such as in isopropanol or in acetals as solvent. Alkene reduction catalyzed by cobalt complexes under such conditions is related to in situ-generation of hydridocobalt complexes, adding across carbon–carbon double bonds to yield alkanes after reducing intermediate organocobalt compounds.[40,41] In a similar manner, we associate hydrogenation of alkenol **1a** in solutions containing cobalt complex **5** and CHD with hydridocobalt complex formation.

Bicyclic acetals, such as **10a**, are without precedent in cobalt-catalyzed aerobic oxidation, but are likely to arise from hydroxylative or hydroperoxylative trapping of an underlying 2,6-*trans*-configured (tetrahydropyran-2-yl)methyl radical, followed by benzylic oxidation and subsequent ring closure to form the bicyclic acetal core.

Substituting phenyl in 5-hexenol **1a** by methyl (in **1b**) or cyclohexyl (**1c**) provides substrates, which are selectively oxidized by dioxygen in cobalt-catalyzed reactions to furnish 2,6-*trans*-substituted tetrahydropyrans **3b** and **3c** (Table 2, entries 6 and 7). The observed diastereoselectivity improves from 17:83 for methyl to 7:93 for cyclohexyl. 1-Cyclohexyl-5-hexenol **1c** affords ketone **9c** (1%) and bicyclic acetal **10c** (5%) as by-products (Table 2, entry 7). No by-products were isolated from aerobic oxidation of 1-methyl-5-hexenol **1b**.

For comparing relative rates of aerobic 6-*exo*- and 5-*exo*-cyclization, we subjected dienol **1d** to standard conditions developed for the 5-hexenol ring closure (Scheme 1). The experiment furnishes exclusively 2,5-*trans*-disubstituted tetrahydrofuran *trans*-**12** (Scheme 2). Considering detection limits of routine NMR-analysis, we estimate that aerobic 5-*exo*-cyclization in dienol **1d** is by a factor of at least 24 faster than the 6-*exo*-ring closure.



1d 62% (±)-*trans*-**12**

Scheme 2. Experiment for comparing relative rate of aerobic 5-*exo*- to 6-*exo*-alkenol cyclization.

For assigning configuration of stereoisomers of tetrahydropyrans **3a**–**c** we used NMR spectroscopy. Fine structures of proton-NMR resonances provide information on axial and equatorial positioning of carbon–hydrogen bonds. Cross signals in NOESY-spectra were observed for 1,3-diaxially arranged substituents in tetrahydropyran (for **3a** see Fig. 2). Axially bound substituents are apparent from upfield shifts of resonances of carbons for α- and γ-positions (Scheme 2).[42]

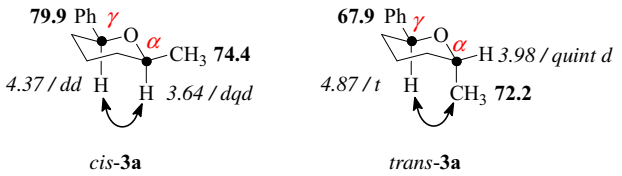
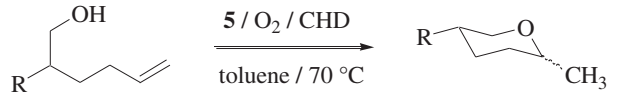


Fig. 2. NMR-spectroscopic information relevant for stereochemical analysis of 2-phenyl-6-methyltetrahydropyran (**3a**) (double headed arrows symbolize NOESY-interactions; numbers in bold refer to carbon-13 chemical shifts in deuterochloroform of endocyclic positions marked by black bullets; information printed in italics refers to proton-NMR shifts and fine structures in deuterochloroform; α and γ are locators for carbon-13 NMR spectroscopy, describing relative positions of substituents).

To determine effects exerted by substituents in position 2, we dissolved 2-phenyl- and 2-isopropyl-substituted 5-hexenol **1e** or **1f**, CHD, and catalytic amounts of cobalt complex in toluene and exposed such solutions at 70 °C to air. Both alkenols are quantitatively consumed within 22 h, to afford tetrahydropyrans **3e**–**f** as ~12:88 mixtures of 2,5-cis/trans-stereoisomers (Table 3).

Table 3
Formation of 2,5-disubstituted tetrahydropyrans from 2-substituted 5-hexenols

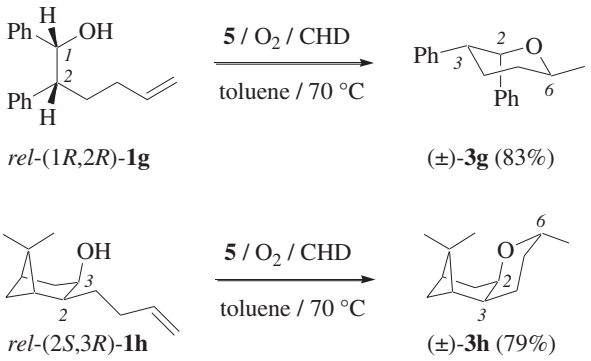


1 (±)-**3**

Entry	1	R	**3**/% (cis/trans)
1	**e**	Ph	**3e**: 66 (12:88)
2	**f**	$CH(CH_3)_2$	**3f**: 57 (11:89)

2.2.2. From disubstituted 5-hexenols. 5-Hexenols having substituents bound to asymmetrically substituted carbons 1 and 2, or 1 and 3 exist as pair of diastereomers. The nomenclature recommended by IUPAC for naming such diastereomers is *like* in case of identical configuration (*R*,*R* or *S*,*S*) and *unlike* for opposite configuration (*R*,*S* or *R*,*S*). For elucidating stereodirecting effects of two substituents in aerobic 6-*exo*-cyclization, we used *like*- and *unlike*-stereoisomers of 1,2- and 1,3-disubstituted 5-hexenols.[27]

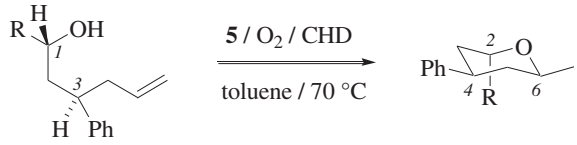
rel-(1*R*,2*R*)-1,2-Diphenyl-5-hexenol **1g** furnishes diastereomerically pure 2,3,6-substituted tetrahydropyran **3g**, when oxidized by air in a solution of toluene/CHD containing 5 mol percent of cobalt(II) complex **5** (Scheme 3, top). Subjecting *cis*-2-butenyl-6,6-dimethylbicyclo[3.1.1]heptan-3-ol **1h** to similar conditions affords bicylohexyl-fused tetrahydropyran **3h** as single diastereomer (Scheme 3, bottom). The time required for attaining quantitative oxidative alkenol conversion in both instances is by a factor ~2 shorter than for oxidation of monosubstituted congeners **1a**–**c** (cf. Table 2). From NOESY-spectra, vicinal coupling constants, and the Karplus-relationship for correlating dihedral angles between vicinal protons to $^3J_{H,H}$-coupling constants we assigned trans-configuration to the newly formed stereocenter at carbon 6 with respect to substituents at carbons 2 and 3 in tetrahydropyrans **3g** and **3h**.



Scheme 3. Stereoselective tetrahydropyran formation from *rel*-(1*R*,2*R*)-1,2-diphenylhexenol **1g** and *rel*-(1*S*,2*S*,3*R*,5*R*)-2-(buten-4-yl)-6,6-dimethylbicyclo[3.1.1]heptan-3-ol (**1h**).

1,3-*like*-Disubstituted 5-hexenols *rel*-(1*R*,3*R*)-**1i**–**k** provide tetrahydropyrans **3i**–**k** as single diastereomers in yields of ~80%, when oxidized by air under standard conditions (Table 4, entries 1–3). From a triplet coupling of $^3J_{H,H}$=13 Hz in the doublet of triplet fine structure of the resonance for the proton bound to carbon 5, a high-field shift of ~2.9 ppm for the proton attached to carbon 4, and a ~5 Hz-doublet splitting of the resonance of 2-H, we assigned 2,4-trans–2,6-trans-configuration to tetrahydropyrans obtained from 5-hexenols *like*-**1i**–**k** (Table 4).

Table 4
Synthesis of 2,4,6-trisubstituted tetrahydropyrans from 1,3-*like*-configured 5-hexenols *rel*-(1*R*,3*R*)-**1**[a]



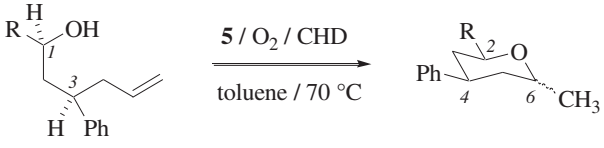
1 **3**

Entry	*rel*-(1*R*,3*R*)-**1**	R	*rel*-(2*R*,4*R*,6*S*)-**3**/%
1	**i**	Ph	**3i**: 80
2	**j**	2-Thienyl	**3j**: 79
3	**k**	2,4-Difluorophenyl	**3k**: 79

[a] For all entries: quantitative substrate conversion.

Oxidizing 1,3-*unlike*-diastereomers of 5-hexenols **1i**–**k** affords ~50:50 mixtures of cis/trans-stereoisomers with respect to the newly formed stereocenter at tetrahydropyran carbon 6 (Table 5, entries 1–3).

Table 5
Stereoselective synthesis of 2,4,6-trisubstituted tetrahydropyrans from 1,3-*unlike*-configured 5-hexenols *rel*-(1*S*,3*R*)-**1**[a]



1 **3**

Entry	*rel*-(1*S*,3*R*)-**1**	R	*rel*-(2*S*,4*R*)-**3**[b]/% (cis/trans)
1	**i**	Ph	68 (50:50)
2	**j**	2-Thienyl	74 (43:57)
3	**k**	2,4-Difluorophenyl	70 (51:49)

[a] For all entries: quantitative substrate conversion.
[b] Relative configuration of substituents at C2 and C6.

2.2.3. On the mechanism of aerobic oxidative 5-hexenol cyclization. For explaining the origin of stereoinduction in cobalt-catalyzed oxidative 5-hexenol ring closure we extended the mechanistic model developed for the aerobic 4-pentenol cyclization.

Theory predicts that dioxygen binds in cis-position to water in bis-[trifluoroacetylacetonato(−1)](aquo)cobalt(II), leading to a low-spin cobalt(III) superoxo complex, being stabilized by an intramolecular hydrogen bond (cf. Fig. 3).[43] Cobalt(III) complexes bearing fluorinated O-donor ligands, such as carboxylates or β-diketonates are strong Lewis acids, able to bind alkenols and alkenes.[34,44] π-Bonding of the alkenol to cobalt(III) in combination with σ-bonding via a non-bonding electron pair at oxygen provides a mechanism for explaining the proposed electron transfer from the alkene subunit to the superoxo ligand. Transferring a π-electron converts the double bond into a radical cation, able to attract the hydroxyl oxygen for closing the tetrahydropyran ring. Proton transfer to the superoxide ligand follows to give a neutral (tetrahydropyran-2-yl)-methyl radical, which is trapped by CHD or other suitable reagents (cf. Scheme 1). Cyclohexa-1,4-diene reduces the superoxide ligand to water[36] and cobalt(III) to cobalt(II) for propagating the catalytic cycle.

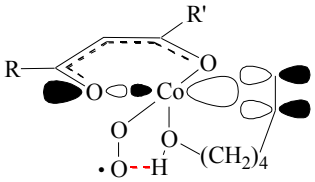


Fig. 3. Model for visualizing hydrogen bonding between the alkenol- and the superoxo ligand (dashed red line), π-bonding between the carbon–carbon double bond and a virtual molecular orbital associated with a cobalt–oxygen bond (R, R′=CF_3, CH_3, or aryl; cf. Table 1; for the sake of clarity, the second diketonate auxiliary is omitted).

The 5-hexenol cyclization, according to our model, proceeds via transition structures similar to C,O-stretched chair conformers of tetrahydropyran (Fig. 4). Substituents in a chair conformer favor equatorial positions and disfavor axial sites, explaining the experimentally observed preference for 2,4-cis- and 2,5-trans-6-*exo*-ring closures. According to the model, a substituent at carbon 4 gives rise 2,3-trans-selective aerobic 5-hexenol cyclizations, which has yet to be experimentally verified.

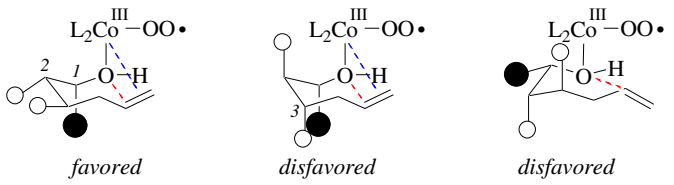


Fig. 4. Model for predicting stereoselectivity in aerobic cobalt-catalyzed 5-hexenol cyclization (black circles mark the stereochemical leading substituent in position 1 of the alkenol; dashed red lines represent trajectories for C,O-bond formation, blue dashed lines mark proposed π-bonding between cobalt and the alkenol).

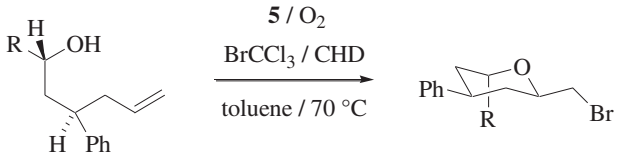
For explaining the origin of 2,6-trans-selective 6-*exo*-cyclization via a chair-like transition structure, the substituent at carbon 1 in this picture has to be situated axially. Positioning a 2-phenyl-substituent in tetrahydropyran at room temperature axially requires a Gibbs free energy of 15 kJ mol^{-1}, as approximated by the *A*-value using density functional theory (Supplementary data).[45] For the moment we think that steric repulsion between the cobalt catalyst and the substituent bound to carbon 1 of the 5-hexenol is responsible for the observed 2,6-trans-selectivity in aerobic oxidative 5-hexenol cyclization (Fig. 4).[46,47]

2.3. Functionalized tetrahydropyrans

To broaden the synthetic scope of the cobalt-method, we developed methods for brominative trapping of (tetrahydropyran-2-yl)methyl radicals and radical addition to dimethyl fumarate, serving as an archetype of a Michael-type alkene.[48]

2.3.1. Bromocyclization. When oxidized by air in solutions of toluene containing bromotrichloromethane, CHD, and cobalt(II) complex **5**, 1,3-substituted 5-hexenols **1i–j** furnish 2,4-substituted 6-bromomethyltetrahydropyrans **13i–j** in up to 89% yield (Tables 6 and 7). For attaining reasonable time/yield-factors, three portions of cobalt(II) reagent **5** in quantities of 5 mol percent were successively added to solutions of the reactants. 1,3-*like*-Stereoisomers of 5-hexenols **1i–j** furnish diastereomerically pure bromomethyltetrahydropyrans *rel*-(2*R*,4*R*,6*R*)-**13i–j** (Table 6), while 1,3-*unlike*-isomers afford 50:50 mixtures of 2,6-cis/trans-stereoisomers of bromocyclized products *rel*-(2*S*,4*R*)-**13i–j** (Table 7). Cobalt β-diketonate complex **5** gradually breaks down under turnover conditions to afford cobalt(II) bromide. The cobalt salt is not able to catalyze aerobic 5-hexenol bromocyclization, explaining the need to apply larger quantity of cobalt(II) catalyst **5** in such experiments than in cyclizations conducted in the absence of bromotrichloromethane.

Table 6
Stereoselective 6-*exo*-bromocyclization of 1,3-*like*-configured 5-hexenols *rel*-(1*R*,3*R*)-**1i–j**[a]

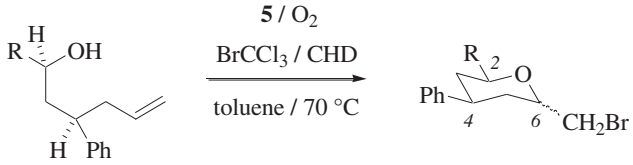


1 **13**

Entry	*rel*-(1*R*,3*R*)-**1**	R	*rel*-(2*R*,4*R*,6*R*)-**13i**/%
1	**i**	Ph	**13i**: 76
2	**j**	2-Thienyl	**13j**: 89

[a] Quantitative substrate conversion.

Table 7
Synthesis of bromomethyltetrahydropyrans from 1,3-*like*-configured 5-hexenols *rel*-(1*S*,3*R*)-**1i–j**[a]



1 **13**

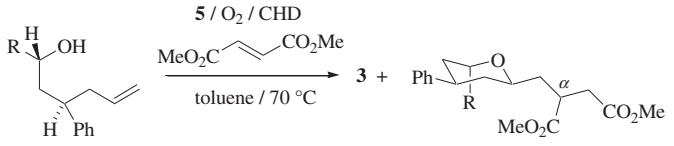
Entry	*rel*-(1*S*,3*R*)-**1**	R	*rel*-(2*S*,4*R*)-**13**[b]/% (cis/trans)
1	**i**	Ph	**13i**: 77 (50:50)
2	**j**	2-Thienyl	**13j**: 75 (41:59)

[a] For entries 1 and 2: quantitative substrate conversion.
[b] Relative configuration of substituents at C2 and C6.

2.3.2. α-(Tetrahydropyranyl-2-methyl) succinates from three-component reactions. α-(Tetrahydropyran-2-yl)-methyl succinates **14i–j**, are available in 57–58% yield from three-component reactions starting from dimethyl fumarate, CHD, 5-hexenols *like*-**1i–j**,

dioxygen, and cobalt catalyst **5** in solutions of toluene (Table 8). Under such conditions, methyltetrahydropyrans **3i–j** form as by-products in yields between 19 and 21%.

Table 8
Products of aerobic oxidation/alkene-trapping cascades

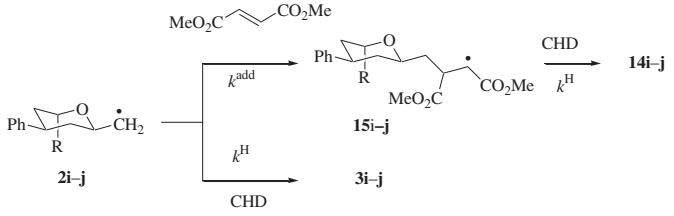


1 14

Entry	R	*rel*-(1*R*,3*R*)-**1**	*rel*-(2*R*,4*R*,6*S*)-**3**/%	*rel*-(2*R*,4*R*,6*R*)-**14**[a]/%
1	Ph	**i**	21	57
2	2-Thienyl	**j**	19	58

[a] 50:50 Ratio of stereoisomers at C_α.

The experimental tetrahydropyranyl-2-methyl succinate/2-methyltetrahydropyran-ratio reflects differences in rate constants of tetrahydropyranyl-2-methyl radical trapping by CHD and dimethyl fumarate (Scheme 4). Improving the yield of **14** requires to raise concentration of the alkene or to lower concentration of CHD. Dimethyl fumarate is a solid, used in synthesis of succinates **14i–j** as saturated solution in toluene/CHD. Lowering CHD concentration slows rates of hydrogen transfer to carbon radicals **2i–j**, cobalt(III)-reduction, and hydrogen atom trapping by adduct radicals **15i–j**. The yields of succinates **14i–j** compare to values obtained from tributyltinhydride-mediated carbon radical addition to dimethyl fumarate.[48] In view of the benefits of the cobalt method for catalytic carbon radical generation we think that this result will stimulate further research for finding one day a more chemoselective hydrogen atom donor.

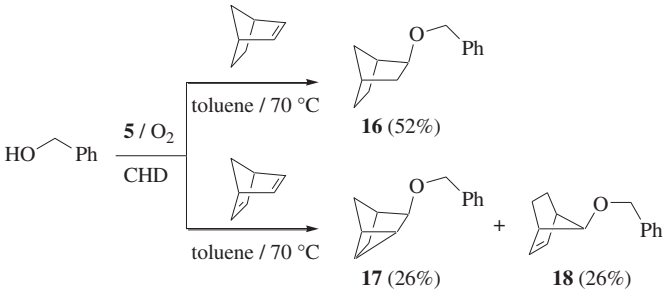


Scheme 4. Elementary steps in (tetrahydropyran-2-yl)methyl radical trapping by CHD and dimethyl fumarate (k^H=rate constant for H-atom transfer; k^{add}=rate constant for addition).

2.4. Alkanol/alkene cross-coupling

The reaction model outlined in Fig. 3 implies that alkenol binding to bis-(β-diketonate)(superoxo)cobalt(III) complexes occurs via π- and σ-bonding. From this model we predicted that catalyst **5** should be able to mediate intermolecular cross-coupling between an alkanol and an alkene. A method for cross-coupling nucleophiles under pH-neutral conditions in cascades affording carbon radicals for trapping under reductive conditions supplements existing procedures for ether synthesis, and motivated us to explore feasibility of this approach.

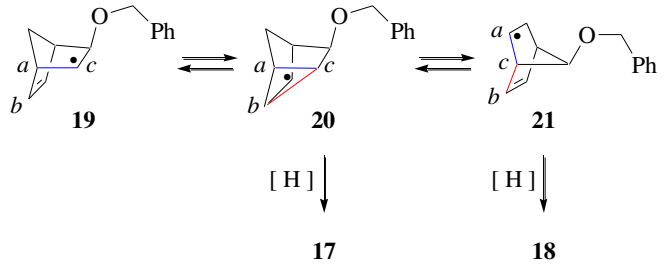
Benzyl alcohol, a 2.5-fold excess of norbornene, CHD, and 2.5-mol percent of cobalt catalyst **5** furnish 2-*exo*-benzyloxynorbornane **16** in 52% yield (Scheme 5), when oxidized by air in a solution of toluene. In an atmosphere of nitrogen or in the absence of cobalt catalyst **5**, no alkanol/alkene cross-coupling occurs. A second experiment starting from benzyl alcohol and



Scheme 5. Products of intermolecular carbon–oxygen bond formation from aerobic cobalt-catalyzed oxidation.

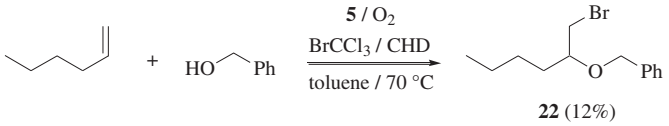
norbornadiene afforded a ~50:50 mixture of *O*-benzyl ethers **17** and **18** in 52% total yield (Scheme 5).

From proton-NMR shifts, fine structures of resonances, NOESY-spectra, and carbon-13 NMR shifts we deduced that the benzyloxy group adds to the e*xo*-face of norbornene, to afford bicyclic ether **16** and tricyclic derivative **17**. Formation of norbornene derivative **18**, having the benzyloxy group attached to the methylene bridge, can be explained according to the general model by adding benzyl alcohol to the *exo*-face of norbornene,[36,35] leading to α-benzyloxynorbornenyl radical **19** (Scheme 6).[49] Norbornenyl radicals similar to **19** are known to cyclize to cyclopropylmethyl radicals, such as **20**, which ring-open by breaking the β-carbon–carbon bond to afford carbon radical **21**.[50] Trapping of rearranged radicals **20** and **21** by CHD furnishes *O*-benzyl ethers **17** and **18**, explaining structures of major products by the model that also describes selectivity in 5-hexenol cyclization.



Scheme 6. Proposed pathway for product formation from aerobic benzyl alcohol/norbornadiene cross-coupling (cf. Scheme 5; [H]=CHD).

Attempts to prepare vicinal bromohydrin ethers from norbornene, benzyl alcohol, and bromotrichloromethane afforded mixtures of 2-trichloromethyl-3-bromobicyclo[2.2.1]-heptane, unidentified products, and traces of 2-benzyloxy-3-bromobicyclo[2.2.1]heptane. We repeated the experiment and replaced 1-hexene for norbornene (Scheme 7). From this reaction, we isolated 12% of bromohydrin ether **22** along with benzaldehyde (9%), dibenzyl ether (12%), and benzyl benzoate (26%). The major product obtained from the experiment is 1,1,1-trichloro-2-bromoheptane, the addition product of bromotrichloromethane across the double bond of 1-hexene. Since the final step leading to β-bromohydrin ether **22** occurs via homolytic substitution, we concluded that the concept of aerobic oxidation/radical-trapping cascades also applies to intermolecular cross-coupling.



Scheme 7. β-Bromohydrin formation from a three-component reaction.

3. Concluding remarks

Molecular oxygen, when activated by 1,1,1-trifluoro-4-phenylbutane-1,3-dione-derived cobalt complex **5**, is a surprisingly chemoselective reagent for stereoselectively converting 5-hexenols into derivatives of 2-methyltetrahydropyran. The reaction is a two-step cascade, proceeding via intermediate (tetrahydropyran-2-yl)-methyl radicals, which are trapped by the reductant cyclohexa-1,4-diene, or alternatively by bromotrichloromethane, or by dimethyl fumarate in combination with cyclohexa-1,4-diene.

The cross-over in reactivity from oxidative for generating carbon radicals to reductive for chemoselectively trapping carbon radicals without providing alkyl hydroperoxides and typical successor products,[51] such as carbonyl compounds or alcohols, probably is the most important benefit from the cobalt method for synthesis of cyclic ethers. Carbon radical trapping offers more perspectives for diversifying syntheses than polar reactions.[52] Selectivity in radical substitutions and additions is marginally affected by solvents or additives such as Lewis acids or other polar components. In radical chemistry, selectivity arises to significant extent from kinetic parameters, being influenced predominantly by orbital effects, temperature, and reactant concentration. Changing the chemical nature of the trapping reagent by replacing a heteroatom donor by an alkene often leaves the underlying chemistry unaffected. Polar transformations often experience considerable selectivity changes upon such modifications.

The second noteworthy characteristic of aerobic cobalt-catalyzed 5-hexenol cyclization is the unusual 2,6-trans-selectivity. The procedure therefore is a valuable supplement to existing 2,6-cis-selective electrophile-induced 5-hexenol cyclizations. The cobalt-method has the potential to provide answers to standing questions, for example, in syntheses of other heterocycles than tetrahydrofurans or tetrahydropyrans. We furthermore think that cobalt chemistry is able to contribute to develop new approaches to intermolecular cross-coupling of nucleophiles, once the key question on the chemical nature of the intermediate that guides selectivity in oxidative carbon–oxygen bond formation is answered.

4. Experimental

4.1. General remarks

Standard instrumentation and general remarks have been disclosed previously (see also the Supplementary data). All solvents and reagents were purified following recommended standard procedures.[53]

4.2. Reductive termination

*4.2.1. Oxidation of 1-phenylhex-5-en-1-ol (**1a**).* A solution of alcohol **1a** (712 mg, 4.04 mmol) and cobalt complex **5** (108 mg, 206 μmol) in toluene (4.0 mL) and CHD (4.0 mL) was stirred at 70 °C for 14.5 h while being exposed to laboratory atmosphere. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. *cis-6-Methyl-2-phenyl tetrahydropyran cis-(**3a**).*[54] Yield: 47.7 mg (271 μmol, 7%), R_f 0.88 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (600 MHz, $CDCl_3$) 1.26 (3H, d, *J* 6.2), 1.28–1.36 (1H, m), 1.44–1.58 (1H, m), 1.61–1.75 (2H, m), 1.77–1.86 (1H, m), 1.88–1.98 (1H, m), 3.64 (1H, dqd, J_d 11.2, J_q 6.5, J_d 2.4), 4.37 (1H, dd, *J* 11.2, 2.0), 7.21–7.42 (5H, m). δ_C (150 MHz, $CDCl_3$) 22.3, 24.1, 33.1, 33.5, 74.4, 79.9, 126.0, 127.2, 128.3, 143.5. NOESY (cross-peaks) 2-H↔6-H. MS (EI) *m*/*z* 176 (56) [M^+], 158 (5), 147 (2), 132 (9), 129 (8), 117 (14), 105 (98), 104 (100), 98 (5), 91 (27), 79 (34), 77 (48), 70 (9), 65 (9), 55 (17), 51 (17). *trans-6-Methyl-2-phenyltetrahydropyran trans-(**3a**).*[55] Yield: 417 mg (2.36 mmol, 59%), R_f 0.80 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (600 MHz, $CDCl_3$) 1.27 (3H, d, *J* 6.2), 1.39–1.46 (1H, m), 1.62–1.82 (3H, m), 1.92 (2H, q, *J* 5.5), 3.98 (1H, quind, J_{quin} 6.5, J_d 3.8), 4.87 (1H, t, *J* 5.3), 7.21–7.27 (1H, m), 7.32–7.37 (2H, m), 7.37–7.42 (2H, m). δ_C (150 MHz, $CDCl_3$) 18.8, 19.4, 30.3, 31.3, 67.9, 72.2, 126.4, 126.8, 128.3, 142.4. MS (EI) *m*/*z* 176 (40) [M^+], 158 (5), 147 (2), 132 (8), 117 (16), 107 (84), 105 (84), 104 (100), 91 (30), 79 (31), 77 (39), 70 (8), 65 (7), 55 (16), 51 (15). *1-Phenylhex-5-en-1-one (**9a**).*[56] Yield: 31.4 mg (180 μmol, 4%), R_f 0.80 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (600 MHz, $CDCl_3$) 1.61–1.82 (2H, m), 2.17 (2H, q, *J* 7.3), 2.96–3.01 (2H, m), 4.99–5.05 (2H, m), 5.83 (1H, ddt, J_d 17.0, 10.2, J_t 6.7), 7.37–7.42 (1H, m), 7.43–7.50 (2H, m), 7.52–7.60 (1H, m), 7.92–7.99 (2H, m). MS (EI) *m*/*z* 174 (7) [M^+], 145 (1), 133 (1), 120 (55), 105 (100), 91 (4), 77 (55). *5-Phenyl-6,8-dioxabicyclo[3.2.1]octane (**10a**).* Yield: 58.5 mg (309 μmol, 8%), R_f 0.60 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (600 MHz, $CDCl_3$) 1.20–1.35 (1H, m), 1.54–1.63 (1H, m), 1.74–1.82 (1H, m), 1.88–2.11 (3H, m), 4.00 (1H, ddd, *J* 6.7, 5.3, 1.2), 4.10 (1H, d, *J* 6.4), 4.71 (1H, s). δ_C (150 MHz, $CDCl_3$) 17.3, 28.1, 36.1, 69.2, 75.4, 108.0, 125.1, 128.1, 128.2, 141.3. MS (EI) *m*/*z* 190 (4) [M^+], 160 (1), 133 (1), 117 (4), 105 (100), 91 (5) 77 (25). ν_{max} (KBr)/cm^{-1} 3058, 3029, 2937, 2888, 1718 (CO), 1684 (CO), 1598 (CO), 1492, 1449, 1348, 1286, 1119, 1024, 1011. *1-Phenylhexan-1-ol (**11a**).*[57] Yield: 79.5 mg (446 μmol, 11%), R_f 0.53 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (600 MHz, $CDCl_3$) 0.78–0.92 (3H, m), 1.20–1.50 (6H, m), 1.66–1.88 (3H, m), 4.66 (1H, t, *J* 6.6), 7.26–7.31 (1H, m), 7.32–7.37 (4H, m). δ_C (150 MHz, $CDCl_3$) 14.0, 22.6, 25.5, 31.7, 39.1, 74.7, 125.9, 127.5, 128.4, 144.9. MS (EI) *m*/*z* 178 (4) [M^+], 160 (15), 128 (3), 117 (50), 107 (100), 91 (20), 79 (40). Analytic data agree with published values.

*4.2.2. Oxidation of hept-6-en-2-ol (**1b**).* A solution of alcohol **1b** (108 mg, 946 μmol) and cobalt complex **5** (28.7 mg, 54.6 μmol) in toluene (1.0 mL) and CHD (1.0 mL) was stirred at 70 °C for 16 h while being exposed to laboratory atmosphere. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. *cis-2,6-Dimethyltetrahydropyran cis-(**3b**).*[58] Yield: 10.5 mg (93.2 μmol, 10%), R_f 0.88 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 1.17 (6H, d, *J* 6.1), 1.07–1.38 (6H, m), 3.82–3.97 (2H, m). δ_C (100 MHz, $CDCl_3$) 18.2, 21.8, 33.1, 73.7. MS (EI) *m*/*z* 114 (13) [M^+], 99 (100), 81 (51), 70 (36), 55 (62). *trans-2,6-Dimethyltetrahydropyran trans-(**3b**).*[58] Yield: 52.9 mg (463 μmol, 50%), R_f 0.78 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 1.18 (6H, d, *J* 6.6), 1.20–1.36 (6H, m), 3.95–4.01 (2H, m). δ_C (100 MHz, $CDCl_3$) 18.2, 19.6, 31.5, 66.8. MS (70 eV, EI): *m*/*z* (%)=114 (13, M^+), 99 (100), 81 (51), 70 (36), 55 (62).

*4.2.3. Oxidation of 1-cyclohexylhex-5-en-1-ol (**1c**).* A solution of alcohol **1c** (182 mg, 1.00 mmol) and cobalt complex **5** (28.7 mg, 54.6 μmol) in toluene (1.0 mL) and CHD (1.0 mL) was stirred at 70 °C for 18 h while being exposed to laboratory atmosphere. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. Starting material **1c** was recovered in 13% (23.6 mg, 129 μmol). *Cyclohexyl-6-methyltetrahydropyran (**3c**).* Yield: 71.3 mg (392 μmol, 40%) as 7:93 mixture of cis/trans-isomers, R_f 0.83 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. *cis-2-Cyclohexyl-6-methyltetrahydropyran cis-(**3c**).* δ_H (400 MHz, $CDCl_3$) 0.81–0.96 (2H, m), 1.15 (3H, d, *J* 6.4), 1.17–1.33 (3H, m), 1.39–1.51 (1H, m), 1.51–1.68 (7H, m), 1.69–1.79 (2H, m), 1.86–1.95 (2H, m), 3.61 (1H, td, J_t 7.9, J_d 6.2), 3.79–3.84 (1H, m). MS (EI) *m*/*z* 135 (18), 99 (100), 81 (80), 67 (17), 55 (46). *trans-2-Cyclohexyl-6-methyltetrahydropyran trans-(**3c**).* δ_H (400 MHz, $CDCl_3$) 0.81–0.96 (2H, m), 1.15 (3H, d, *J* 6.4), 1.17–1.33 (3H, m), 1.39–1.51 (1H, m), 1.51–1.68 (7H, m), 1.69–1.79 (2H, m), 1.86–1.95 (2H, m), 3.30–3.37 (1H, m), 3.85 (1H, quind, J_{quin} 6.5, J_d 3.5). δ_C (100 MHz, $CDCl_3$) 18.6, 19.7, 26.1, 26.2, 26.6, 26.8, 29.3, 31.7, 38.9, 66.9, 75.6. MS

(EI) *m/z* 181 (1), 149 (1), 135 (1), 99 (100), 83 (12), 81 (73), 67 (13), 55 (36). *1-Cyclohexylhex-5-en-1-one (**9c**)*.[59] Yield: 2.00 mg (10.9 μmol, 1%), R_f 0.71 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 1.18–1.40 (5H, m), 1.51–1.85 (7H, m), 1.98–2.10 (2H, m), 2.43 (2H, t, *J* 7.4), 4.92–5.05 (2H, m), 5.76 (1H, ddt, J_d 17.1, 10.2, J_t 6.7). *5-Cyclohexyl-6,8-dioxabicyclo[3.2.1]octane (**10c**)*. Yield: 10.2 mg (52.0 μmol, 5%), R_f 0.61 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 1.02–1.31 (6H, m), 1.39–1.94 (11H, m), 3.77 (1H, ddd, *J* 6.7, 5.3, 1.2), 3.91 (1H, d, *J* 6.8), 4.49 (1H, m). δ_C (100 MHz, $CDCl_3$) 16.9, 26.29, 26.32, 26.4, 27.0, 27.1, 28.7, 30.8, 45.2, 68.9, 74.8, 110.5. MS (EI) *m/z* 196 (6) [M^+], 168 (1), 127 (2), 122 (2), 111 (55), 95 (3), 83 (100), 67 (14).

*4.2.4. Oxidation of deca-1,9-dien-5-ol (**1d**).* A solution of alcohol **1d** (137 mg, 890 μmol) and cobalt complex **5** (26.7 mg, 50.8 μmol) in toluene (1.0 mL) and CHD (1.0 mL) was stirred at 70 °C for 13.5 h while being exposed to laboratory atmosphere. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. *trans-5-Methyl-2-(pent-4-enyl)-tetrahydrofuran (**12**)*. Yield: 85.0 mg (55.1 mmol, 62%), R_f 0.74 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 1.21 (3H, d, *J* 6.0), 1.32–1.66 (6H, m), 1.96–2.12 (4H, m), 3.92–4.02 (1H, m), 4.03–4.16 (1H, m), 4.89–5.04 (2H, m), 5.80 (1H, ddt, J_d 17.0, 10.3, J_t 6.6). δ_C (100 MHz, $CDCl_3$) 21.4, 25.5, 32.3, 33.8, 34.0, 35.7, 74.4, 78.6, 114.4, 138.8. NOESY (cross-peaks) 2-H↔CH_3, 5-H↔1′-H. MS (EI) *m/z* 136 (1), 125 (3), 111 (15), 98 (10), 95 (4), 85 (100), 81 (5), 67 (29), 57 (16), 55 (18). HRMS (EI^+) *m/z* 154.1343 [M^+] calculated mass for $C_{10}H_{18}O^+$: 154.1358.

*4.2.5. Oxidation of 2-phenylhex-5-en-1-ol (**1e**).* A solution of alcohol **1e** (177 mg, 1.00 mmol) and cobalt complex **5** (27.1 mg, 51.6 μmol) in toluene (1.0 mL) and CHD (1.0 mL) was stirred at 70 °C for 15 h while being exposed to laboratory atmosphere. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. *3-Phenyl-6-methyltetrahydropyran (**3e**)*. Yield: 117 mg (664 μmol, 66%) as 12:88 mixture of cis/trans-isomers, R_f 0.80 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. *cis-3-Phenyl-6-methyltetrahydropyran cis-(**3e**)*. δ_H (400 MHz, $CDCl_3$) 1.28 (3H, d, *J* 6.2), 1.34–2.10 (4H, m), 2.72–2.87 (1H, m), 3.67 (1H, dqd, J_d 9.2, J_q 6.2, J_d 3.1), 3.89 (1H, dd, *J* 11.7, 3.5), 4.19 (1H, dq, J_d 12.1, J_q 1.8), 7.15–7.25 (3H, m), 7.42–7.49 (2H, m). δ_C (100 MHz, $CDCl_3$) 20.9, 28.8, 29.2, 38.9, 69.6, 72.7, 125.9, 128.1, 128.3, 144.8. MS (EI) *m/z* 176 (18) [M^+], 161 (2), 154 (3), 117 (14), 104 (100), 91 (16), 78 (8). HRMS (EI^+) *m/z* 176.1197 [M^+]; calculated mass for $C_{12}H_{16}O^+$: 176.1201. *trans-3-Phenyl-6-methyltetrahydropyran trans-(**3e**)*. δ_H (400 MHz, $CDCl_3$) 1.28 (3H, d, *J* 6.2), 1.46 (1H, qd, J_q 12.4, J_d 5.2), 1.80 (1H, qd, J_q 12.8, J_d 4.0), 1.77–1.87 (1H, m), 2.04–2.11 (1H), 2.86 (1H, tt, *J* 11.6, 4.0), 3.43 (1H, t, *J* 11.3), 3.50 (1H, dqd, J_d 11.7, J_q 6.0, J_d 3.0), 4.01 (1H, dq, J_d 11.2, J_q 2.2), 7.18–7.25 (3H, m), 7.28–7.34 (2H, m). δ_C (100 MHz, $CDCl_3$) 21.9, 30.6, 33.6, 42.6, 73.7, 73.8, 126.6, 127.3, 128.5, 142.4. MS (EI) *m/z* 176 (4) [M^+], 161 (1), 143 (1), 129 (4), 117 (16), 104 (100), 98 (7), 91 (22), 85 (29), 78 (10). HRMS (EI^+) *m/z* 176.1208 [M^+]; calculated mass for $C_{12}H_{16}O^+$: 176.1201.

*4.2.6. Oxidation of 2-isopropylhex-5-en-1-ol (**1f**).* A solution of alcohol **1f** (125 mg, 881 μmol) and cobalt complex **5** (27.0 mg, 51.4 μmol) in toluene (1.0 mL) and CHD (1.0 mL) was stirred at 70 °C for 23 h while being exposed to laboratory atmosphere. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. *3-Isopropyl-6-methyl tetrahydropyran (**3f**)*. Yield: 70.8 mg (498 μmol, 57%) as 11:89 mixture of cis/trans-isomers, R_f 0.85 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. *cis-3-Isopropyl-6-methyltetrahydropyran cis-(**3f**)*. δ_H (400 MHz, $CDCl_3$) 0.87 (6H, dd, *J* 6.5, 2.6), 0.90–0.98 (1H, m), 1.16 (3H, d, *J* 6.1), 1.17–1.38 (3H, m), 1.53–1.60 (1H, m), 1.88–1.96 (1H, m), 3.47–3.55 (2H, m), 3.93 (1H, dt, J_d 11.7, J_t 2.6) δ_C (100 MHz, $CDCl_3$) 20.8, 21.2, 21.3, 25.2, 25.7, 29.3, 40.8, 69.0, 73.4. MS (EI) *m/z* 142 (9) [M^+], 128 (8), 127 (100), 109 (40), 83 (27), 70 (47), 55 (51). HRMS (EI^+) *m/z* 142.1359 [M^+]; calculated mass for $C_9H_{18}O^+$: 142.1358. *trans-3-Isopropyl-6-methyltetrahydropyran trans-(**3f**)*. δ_H (400 MHz, $CDCl_3$), 0.87 (6H, dd, *J* 6.5, 2.6), 0.90–0.98 (1H, m), 1.16 (3H, d, *J* 6.1), 1.17–1.38 (3H, m), 1.60–1.67 (1H, m), 1.82–1.89 (1H, m), 3.13 (1H, t, *J* 10.9), 3.31 (1H, dqd, J_d 11.2, J_q 6.0, J_d 2.4), 3.98 (1H, dq, J_d 11.3, J_q 2.1). δ_C (100 MHz, $CDCl_3$) 19.8, 20.2, 21.9, 27.4, 29.9, 33.7, 41.9, 71.9, 73.7. MS (EI) *m/z* 142 (19) [M^+], 128 (10), 127 (1), 129 (100), 109 (54), 99 (3), 97 (4), 95 (6), 83 (23), 70 (41), 55 (59). HRMS (EI^+) *m/z* 142.1362 [M^+]; calculated mass for $C_9H_{18}O^+$: 142.1358.

*4.2.7. Oxidation of like-1,2-diphenylhex-5-en-1-ol (**1g**).* A solution of alcohol **1g** (127 mg, 504 μmol) and cobalt complex **5** (11.2 mg, 24.7 μmol) in toluene (2.0 mL) and CHD (1.0 mL) was stirred at 70 °C for 5 h while being exposed to laboratory atmosphere. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. *rel-(2R,3R,6S)-6-Methyl-2,3-diphenyltetrahydropyran (**3g**)*. Yield: 106 mg (419 μmol, 83%), R_f 0.56 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 1.21 (3H, d, *J* 6.1), 1.39–1.49 (1H, m), 1.58–1.68 (1H, m), 1.85–2.00 (1H, m), 3.92 (1H, d, *J* 8.4), 4.09 (1H, quind, J_{quin} 7.9, J_d 6.1), 4.76 (1H, dt, J_d 8.4, J_t 6.2), 7.14–7.19 (2H, m), 7.23–7.29 (6H, m), 7.33–7.37 (1H, m). δ_C (100 MHz, $CDCl_3$) 21.4, 31.6, 33.6, 57.0, 75.3, 80.4, 126.1, 126.3, 128.2, 128.4, 128.6, 128.7, 142.8, 143.1. MS (EI) *m/z* 252 (1) [M^+], 178 (3), 165 (17), 152 (7), 115 (5), 85 (100), 77 (3). Anal. Calcd for $C_{18}H_{20}O$ (252.35): C 85.67; H 7.99. Found: C 85.46; H 7.73.

*4.2.8. Oxidation of (1S,2S,3R,5R)-2-(but-3-enyl)-6,6-dimethylbicyclo[3.1.1]-heptan-3-ol (**1h**).* A solution of alcohol **1h** (98.0 mg, 504 μmol) and cobalt complex **5** (13.2 mg, 25.1 μmol) in toluene (2.0 mL) and CHD (1.0 mL) was stirred at 70 °C for 2 h while being exposed to laboratory atmosphere. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. *(1R,3R,5R,8S,9S)-5,10,10-Trimethyl-4-oxatricyclo[7.1.0^{3,8}]undecane (**3h**)*. Yield: 77.5 mg (399 μmol, 79%), R_f 0.76 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 0.89 (1H, d, *J* 9.7), 1.04 (1H, tdd, J_t 13.5, J_d 10.1, 2.9), 1.16 (3H, s), 1.18 (3H, s), 1.18 (3H, d, *J* 6.2), 1.37 (1H, ddt, J_d 12.7, 6.4, J_t 3.2), 1.62 (1H, qd, J_q 13.2, J_d 3.0), 1.79 (1H, q, *J* 2.4), 1.81–1.91 (4H, m), 2.08 (1H, dddd, *J* 13.0, 9.0, 6.2, 2.4), 2.28–2.41 (2H, m), 4.02 (1H, dquin, J_d 9.8, J_{quin} 6.7), 4.14 (1H, td, J_t 9.3, J_d 3.1). δ_C (100 MHz, $CDCl_3$) 20.3, 21.8, 24.3, 28.1, 31.7, 32.6, 35.7, 38.5, 40.9, 45.9, 46.0, 61.8, 69.0. MS (EI) *m/z* 194 (1) [M^+], 176 (2), 153 (9), 136 (7), 125 (100), 107 (9), 91 (23), 82 (46), 69 (44). HRMS (EI^+) *m/z* 194.1675 [M^+]; calculated mass for $C_{13}H_{22}O^+$: 194.1671.

*4.2.9. Oxidation of like-1,3-diphenylhex-5-en-1-ol rel-(1R,3R)-(**1i**).* A solution of alcohol *rel*-(1*R*,3*R*)-**1i** (126 mg, 501 μmol) and cobalt complex **5** (13.4 mg, 25.5 μmol) in toluene (2.0 mL) and CHD (0.5 mL) was stirred at 70 °C for 5 h while being exposed to laboratory atmosphere. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. *rel-(2R,4R,6S)-6-Methyl-2,4-diphenyltetrahydropyran rel-(2R,4R,6S)-(**3i**)*. Yield: 102 mg (403 μmol, 80%), R_f 0.60 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (600 MHz, $CDCl_3$) 1.24 (3H, d, *J* 6.2), 1.54 (1H, td, J_t 12.8, J_d 11.1), 1.73 (1H, dddd, *J* 12.8, 3.4, 2.1), 2.18 (1H, ddd, *J* 13.9, 12.8, 5.6), 2.52 (1H, dddd, *J* 13.9, 3.4, 1.6), 2.88 (1H, tt, *J* 12.5, 3.5), 3.71 (1H, dqd, J_d 11.1, J_q 6.2, J_d 2.1), 5.25 (1H, d, *J* 5.3), 7.20–7.25 (3H, m), 7.26–7.30 (1H, m), 7.30–7.34 (2H, m), 7.41 (2H, t, *J* 7.8), 7.48 (2H, d, *J* 8.2). δ_C (150 MHz, $CDCl_3$) 21.9, 33.7, 36.5, 41.2, 66.5, 73.5, 126.3, 126.6, 126.7, 128.6, 140.7, 145.8. MS (EI) *m/z* 252 (13) [M^+], 209 (6), 174 (46), 147 (6), 131 (13), 117 (18), 104 (100), 91 (21), 77 (18).

HRMS (EI$^+$) m/z 252.1505 [M$^+$]; calculated mass for $C_{18}H_{20}O^+$: 252.1514.

*4.2.10. Oxidation of unlike-1,3-diphenylhex-5-en-1-ol rel-(1S,3R)-(**1i**).* A solution of alcohol *rel*-(1*S*,3*R*)-**1i** (137 mg, 544 μmol) and cobalt complex **5** (28.5 mg, 54.3 μmol) in toluene (1.2 mL) and CHD (0.5 mL) was stirred at 70 °C for 15 h while being exposed to laboratory atmosphere. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. *rel-(2S,4R,6S)-6-Methyl-2,4-diphenyltetrahydropyran rel-(2S,4R,6S)-(**3i**).* Yield: 47.6 mg (189 μmol, 35%), R_f 0.57 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 1.33 (3H, d, *J* 6.2), 1.51 (1H, td, J_t 12.7, J_d 11.1), 1.69 (1H, td, J_t 12.7, J_d 11.3), 1.89 (1H, ddt, J_d 13.2, 3.8, J_t 2.0), 2.05 (1H, ddt, J_d 13.2, 3.7, J_t 2.0), 2.97 (1H, tt, *J* 12.3, 3.7), 3.80 (1H, dqd, J_d 11.0, J_q 6.2, J_d 2.0), 4.53 (1H, dd, *J* 11.2, 2.0), 7.17–7.26 (4H, m), 7.27–7.35 (4H, m), 7.38–7.42 (2H, m). δ_C (150 MHz, $CDCl_3$) 22.1, 40.7, 40.9, 42.1, 74.1, 79.5, 125.9, 126.3, 126.7, 127.3, 128.3, 128.5, 142.9, 145.5. MS (EI) m/z 252 (8) [M$^+$], 209 (8), 174 (27), 147 (3), 131 (8), 117 (17), 104 (100), 91 (22), 77 (21). HRMS (EI$^+$) m/z 252.1509 [M$^+$]; calculated mass for $C_{18}H_{20}O^+$: 252.1514. *rel-(2S,4R,6R)-6-Methyl-2,4-diphenyltetrahydropyran rel-(2S,4R,6R)-(**3i**).* Yield: 46.0 mg (182 μmol, 34%), R_f 0.55 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 1.48 (3H, d, *J* 6.8), 1.69–1.78 (2H, m), 2.00–2.10 (2H, m), 3.19 (1H, tt, *J* 12.6, 3.7), 4.54 (1H, quin, *J* 6.5), 4.82 (1H, dd, *J* 11.5, 2.1), 7.17–7.35 (8H, m), 7.37–7.42 (2H, m). δ_C (150 MHz, $CDCl_3$) 17.2, 36.2, 37.1, 41.5, 69.7, 71.4, 125.9, 126.3, 126.8, 127.3, 128.3, 128.5, 143.1, 145.6. MS (EI) m/z 252 (3) [M$^+$], 234 (3), 194 (10), 174 (19), 147 (15), 131 (10), 117 (18), 104 (100), 91 (24), 77 (24). HRMS (EI$^+$) m/z 252.1512 [M$^+$]; calculated mass for $C_{18}H_{20}O^+$: 252.1514.

*4.2.11. Oxidation of like-1-(thien-2-yl)-3-phenyl-hex-5-en-1-ol rel-(1R,3R)-(**1j**).* A solution of alcohol *rel*-(1*R*,3*R*)-**1j** (158 mg, 610 μmol) and cobalt complex **5** (14.8 mg, 28.2 μmol) in toluene (2.0 mL) and CHD (1.0 mL) was stirred at 70 °C for 4 h while being exposed to laboratory atmosphere. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. *rel-(2R,4R,6S)-6-Methyl-4-phenyl-2-(thien-2-yl)-tetrahydropyran rel-(2R,4R,6S)-(**3j**).* Yield: 124 mg (479 μmol, 79%), R_f 0.58 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 1.14 (3H, d, *J* 6.1), 1.44 (1H, td, *J* 12.5, 11.5), 1.67 (1H, ddt, J_d 12.9, 3.5, J_t 1.8), 2.09 (1H, ddd, *J* 14.2, 12.5, 5.7), 2.28 (1H, ddt, J_d 13.9, 3.5, J_t 1.7), 2.98 (1H, tt, *J* 12.5, 3.5), 3.82 (1H, dqd, J_d 11.5, J_q 6.1, J_d 1.7), 5.32 (1H, d, *J* 5.5), 6.88–6.91 (1H, m), 6.94 (dd, *J* 4.9, 3.5), 7.11–7.18 (3H, m), 7.21–7.27 (3H, m). δ_C (100 MHz, $CDCl_3$) 21.8, 35.5, 36.8, 40.7, 67.0, 71.8, 124.5, 125.1, 126.4, 126.8, 127.0, 128.6, 145.5, 146.2. MS (EI) m/z 258 (55) (M$^+$), 215 (4), 200 (4), 180 (21), 131 (22), 118 (25), 111 (32), 104 (100), 91 (28), 77 (23). Anal. Calcd for $C_{16}H_{18}OS$ (258.38): C 74.38; H 7.02; S 12.41. Found: C 74.31; H 7.02; S 12.19. HRMS (EI$^+$) m/z 258.1086 [M$^+$]; calculated mass for $C_{16}H_{18}OS^+$: 258.1078.

*4.2.12. Oxidation of unlike-1-(thien-2-yl)-3-phenyl-hex-5-en-1-ol rel-(1S,3R)-(**1j**).* A solution of alcohol *rel*-(1*S*,3*R*)-**1j** (145 mg, 560 μmol) and cobalt complex **5** (14.7 mg, 28.0 μmol) in toluene (2.0 mL) and CHD (1.0 mL) was stirred at 70 °C for 15 h while being exposed to laboratory atmosphere. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. *rel-(2S,4R,6S)-6-Methyl-4-phenyl-2-(thien-2-yl)-tetrahydropyran rel-(2S,4R,6S)-(**3j**).* Yield: 61.4 mg (238 μmol, 42%), R_f 0.58 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 1.32 (3H, d, *J* 6.1), 1.53 (1H, td, J_t 12.7, J_d 11.1), 1.79–1.92 (2H, m), 2.19 (1H, ddt, J_d 13.1, 3.8, J_t 1.9), 2.96 (1H, tt, *J* 12.3, 3.7), 3.82 (1H, dqd, J_d 11.2, J_q 6.1, J_d 1.7), 4.79 (1H, dd, *J* 11.1, 1.7), 6.94–6.97 (1H, m), 7.00 (1H, dd, *J* 3.4, 1.0), 7.20–7.27 (4H, m), 7.30–7.35 (2H, m). δ_C (100 MHz, $CDCl_3$) 22.0, 40.4, 40.6, 41.9, 74.3, 75.4, 123.4, 124.4, 126.4, 126.8, 128.6, 145.2, 146.0. MS (EI) m/z 258 (26) [M$^+$], 215 (3), 200 (5), 180 (19), 131 (19), 118 (24), 111 (30), 104 (100), 91 (27), 77 (20). Anal. Calcd for $C_{16}H_{18}OS$ (258.38): C 74.38; H 7.02; S 12.41. Found: C 74.33; H 7.01; S 12.19. HRMS (EI$^+$) m/z 258.1077 (M$^+$); calculated mass for $C_{16}H_{18}OS^+$: 258.1078. *rel-(2S,4R,6R)-6-Methyl-4-phenyl-2-(thien-2-yl)-tetrahydropyran rel-(2S,4R,6R)-(**3j**).* Yield: 46.4 mg (180 μmol, 32%), R_f 0.56 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 1.47 (3H, d, *J* 6.8), 1.72 (1H, ddt, J_d 13.2, 3.7, J_t 1.7), 1.85 (1H, td, J_t 12.6, J_d 11.5), 2.07 (1H, td, J_t 13.1, J_d 5.7), 2.17 (1H, dt, J_d 12.6, J_t 3.7), 3.16 (1H, tt, *J* 12.6, 3.7), 4.54 (1H, quin, *J* 6.5), 5.08 (1H, dd, *J* 11.5, 2.2), 6.93–6.98 (2H, m), 7.19–7.27 (4H, m), 7.29–7.34 (4H, m). δ_C (100 MHz, $CDCl_3$) 17.2, 36.0, 36.8, 41.6, 67.7, 70.0, 123.2, 124.3, 126.4, 126.8, 128.6, 145.2, 146.7. MS (EI) m/z 258 (44) [M$^+$], 215 (3), 200 (3), 180 (13), 131 (17), 118 (22), 111 (24), 104 (100), 91 (25), 77 (12). Anal. Calcd for $C_{16}H_{18}OS$ (258.38): C 74.38; H 7.02; S 12.41. Found: C 74.12; H 6.85; S 12.46. HRMS (EI$^+$) m/z 258.1077 [M$^+$]; calculated mass for $C_{16}H_{18}OS^+$: 258.1078.

*4.2.13. Oxidation of like-1-(2,4-difluorophenyl)-3-phenylhex-5-en-1-ol rel-(1R,3R)-(**1k**).* A solution of alcohol *rel*-(1*R*,3*R*)-**1k** (146 mg, 507 μmol) and cobalt complex **5** (13.0 mg, 24.7 μmol) in toluene (2.0 mL) and CHD (1.0 mL) was stirred at 70 °C for 4 h while being exposed to laboratory atmosphere. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. *rel-(2R,4R,6S)-6-Methyl-4-phenyl-2-(2,4-difluorophenyl)tetrahydropyran rel-(2R,4R,6S)-(**3k**).* Yield: 116 mg (402 μmol, 79%), R_f 0.60 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 1.25 (3H, d, *J* 6.2), 1.59 (1H, td, J_t 13.0, J_d 10.7), 1.80–1.87 (1H, m), 2.17 (1H, td, J_t 13.3, J_d 6.0), 2.50–2.57 (1H, m), 2.94 (1H, tt, *J* 12.4, 3.6), 3.76 (1H, dqd, J_d 11.0, J_q 6.2, J_d 1.9), 5.32 (1H, d, *J* 5.9), 6.83 (1H, ddd, *J* 11.3, 8.8, 2.5), 6.92 (1H, td, J_t 8.3, J_d 2.6), 7.22–7.27 (3H, m), 7.52 (1H, td, J_t 8.9, J_d 6.4). δ_C (100 MHz, $CDCl_3$) 22.0, 34.9, 37.2 (d, *J* 4.5), 37.2, 40.6, 67.4, 70.4, 104.5 (dd, *J* 27.2, 25.3), 110.9 (dd, *J* 20.7, 3.6), 123.9 (dd, *J* 12.7, 3.6), 126.4, 126.7, 130.1 (dd, *J* 9.1, 6.4), 145.5, 160.3 (dd, *J* 134, 11.8), 162.7 (dd, 131, 12.7). MS (EI) m/z 288 (2) [M$^+$], 270 (2), 210 (41), 141 (19), 127 (10), 117 (18), 104 (100), 91 (19), 78 (15). HRMS (EI$^+$) m/z 288.1328 [M$^+$]; calculated mass for $C_{18}H_{18}OF_2^+$: 288.1328.

*4.2.14. Oxidation of unlike-1-(2,4-difluorophenyl)-3-phenylhex-5-en-1-ol rel-(1S,3R)-(**1k**).* A solution of alcohol *rel*-(1*S*,3*R*)-**1k** (147 mg, 509 μmol) and cobalt complex **5** (13.1 mg, 24.9 μmol) in toluene (2.0 mL) and CHD (1.0 mL) was stirred at 70 °C for 15 h while being exposed to laboratory atmosphere. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. *rel-(2S,4R,6S)-6-Methyl-4-phenyl-2-(2,4-difluorophenyl)-tetrahydropyran rel-(2S,4R,6S)-(**3k**).* Yield: 50.2 mg (174 μmol, 34%), R_f 0.58 [SiO_2, acetone/pentane=1:5 (v/v)], colorless crystalline solid. δ_H (400 MHz, $CDCl_3$) 1.35 (3H, d, *J* 6.2), 1.54 (1H, td, J_t 12.7, J_d 11.1), 1.93 (1H, ddt, J_d 13.1, 3.8, J_t 1.9), 2.06–2.10 (1H, m), 3.02 (1H, tt, *J* 12.3, 3.7), 3.84 (1H, dqd, J_d 10.9, J_q 6.2, J_d 2.0), 4.84 (1H, dd, *J* 11.1, 1.3), 6.78 (1H, ddd, *J* 10.5, 9.0, 2.5), 6.90 (1H, tdd, J_t 8.4, J_d 2.5, 1.2), 7.20–7.27 (3H, m), 7.30–7.36 (2H, m), 7.57 (1H, td, J_t 8.6, J_d 6.4). δ_C (100 MHz, $CDCl_3$) 22.0, 40.0, 40.5, 41.9, 72.8, 74.3, 103.4 (t, *J* 25.4), 111.3 (dd, *J* 19.7, 3.6), 126.2 (dd, *J* 13.6, 3.6), 126.4, 126.7, 128.3 (dd, *J* 9.2, 6.4), 128.5, 145.2, 159.4 (dd, *J* 248, 11.8), 162.0 (dd, *J* 248, 11.8). MS (EI) m/z 288 (5) [M$^+$], 270 (2), 210 (20), 140 (14), 127 (9), 117 (16), 104 (100), 91 (16), 78 (13). HRMS (EI$^+$) m/z 288.1333 [M$^+$]; calculated mass for $C_{18}H_{18}OF_2^+$: 288.1326. *rel-(2S,4R,6R)-6-Methyl-4-phenyl-2-(2,4-difluorophenyl)-tetrahydropyran rel-(2S,4R,6R)-(**3k**).* Yield: 52.7 mg (183 μmol, 36%), R_f 0.56 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 1.50 (3H, d, *J* 6.8), 1.64 (1H, td, J_t 12.7, J_d 11.4), 1.76 (1H, ddt, J_d 13.2, 3.6, J_t 1.8), 2.02–2.12 (2H, m), 3.22 (1H, tt, *J* 12.6, 3.6), 4.55 (1H, quin, *J* 6.5), 5.13 (1H, dd, *J* 11.3, 1.9), 6.77 (1H, ddd, *J* 10.5, 8.8, 2.5), 6.89 (1H, tdd, J_t 8.4, J_d 2.6, 1.3), 7.21–7.28 (3H, m), 7.29–7.35 (2H, m), 7.54 (1H, td, J_t 8.5, J_d 6.5). δ_C (100 MHz,

$CDCl_3$) 17.0, 36.0, 37.0, 40.6, 64.7, 69.9, 103.4 (t, *J* 25.4), 111.3 (dd, *J* 21.1, 3.6), 126.4, 126.8, 128.2 (dd, *J* 9.9, 6.5), 128.5, 145.3, 159.2 (dd, *J* 248, 11.8), 162.0 (dd, *J* 248, 11.8). MS (EI) *m/z* 288 (1) [M^+], 270 (3), 210 (21), 147 (16), 140 (10), 127 (8), 117 (19), 104 (100), 91 (20), 78 (14). HRMS (EI^+) *m/z* 288.1316 [M^+]; calculated mass for $C_{18}H_{18}OF_2^+$: 288.1326.

*4.2.15. Oxidation of norbornene and benzyl alcohol (**15**).* A solution of benzyl alcohol (**15**) (221 mg, 2.02 mmol) and cobalt complex **5** (26.2 mg, 50.6 μmol) in toluene (2.0 mL), CHD (1.0 mL) and norbornene (487 mg, 5.12 mmol) was stirred at 70 °C for 19 h while being exposed to laboratory atmosphere. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/pentane=1:10 (v/v)]. *2-exo-Benzyloxynorbornane (**16**).*[60] Yield: 213 mg (1.05 mmol, 52%), colorless oil.

*4.2.16. Oxidation of norbornadiene and benzyl alcohol (**15**).* A solution of benzyl alcohol (**15**) (113 mg, 1.04 mmol) and cobalt complex **5** (13.3 mg, 25.3 μmol) in toluene (2.0 mL), CHD (0.5 mL) and norbornadiene (235 mg, 2.53 mmol) was stirred at 70 °C for 24 h while being exposed to laboratory atmosphere. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/pentane=1:10 (v/v)]. *7-anti-Benzyloxy-bicylo[2.2.1]hept-2-ene (**18**).* Yield: 53.1 mg (265 μmol, 26%), R_f 0.59 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (600 MHz, $CDCl_3$) 0.98–1.02 (2H, m), 1.83–1.87 (2H, m), 2.70 (2H, dq, J_d 3.7, J_q 2.1), 3.33 (1H, s), 4.44 (2H, s), 5.98 (2H, t, *J* 2.1), 4.49 (2H, dd, *J* 24.5, 11.7), 7.27–7.38 (5H, m). δ_C (100 MHz, $CDCl_3$) 21.9, 43.4, 70.2, 88.9, 127.4, 127.5, 128.3, 134.2, 138.5. MS (EI) *m/z* 200 (1) [M^+], 120 (9), 91 (100), 79 (33). HRMS (EI^+) *m/z* 200.1204 [M^+] calculated mass for $C_{14}H_{16}O^+$: 200.1201. *3-exo-Benzyloxynortricyclene (**17**)* Yield: 52.3 mg (261 μmol, 26%), R_f 0.55 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (600 MHz, $CDCl_3$) 1.15–1.20 (2H, m), 1.23–1.29 (3H, m), 1.35 (1H, d, *J* 10.6), 1.89 (1H, d, *J* 9.7), 2.02 (1H, s), 3.63 (1H, t, *J* 1.2), 4.49 (2H, dd, *J* 24.5, 11.7), 7.26–7.29 (1H, m), 7.32–7.37 (4H, m). δ_C (100 MHz, $CDCl_3$) 11.0, 12.8, 14.1, 29.7, 30.4, 32.5, 71.0, 84.3, 127.4, 127.7, 128.3, 138.8. MS (EI) *m/z* 200 (1) [M^+], 109 (29), 91 (100), 79 (43). HRMS (EI^+) *m/z* 200.1213 [M^+]; calculated mass for $C_{14}H_{16}O^+$: 200.1201.

4.3. Brominative termination

*4.3.1. Oxidation of like-1,3-diphenylhex-5-en-1-ol rel-(1R,3R)-(**1i**).* A solution of alcohol *rel*-(1*R*,3*R*)-**1i** (127 mg, 504 μmol) and cobalt complex **5** (13.5 mg, 25.7 μmol) in toluene (2.0 mL), bromotrichloromethane (0.5 mL) and CHD (0.5 mL) was stirred at 70 °C for 24 h while being exposed to laboratory atmosphere. A second (13.4 mg) and third (13.2 mg) batch of cobalt catalyst were added after 2 and 5 h. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. *rel-(2R,4R,6R)-6-Bromomethyl-2,4-diphenyltetrahydropyran rel-(2R,4R,6R)-(**13i**).* Yield: 126 mg (381 μmol, 76%), R_f 0.55 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (600 MHz, $CDCl_3$) 1.67 (1H, td, J_t 12.4, J_d 11.3), 1.88 (1H, ddt, J_d 12.7, 3.9, J_t 2.1), 2.26 (1H, ddd, *J* 14.0, 13.0, 5.6), 2.58 (1H, ddt, J_d 13.9, 3.5, J_t 1.8), 2.97 (1H, tt, *J* 12.5, 3.7), 3.43–3.51 (2H, m), 3.87 (1H, dddd, *J* 11.2, 6.6, 4.3, 2.2), 5.39 (1H, d, *J* 5.6), 7.26–7.30 (3H, m), 7.33–7.40 (3H, m), 7.47 (2H, t, *J* 7.8), 7.58 (2H, d, *J* 8.2). δ_C (150 MHz, $CDCl_3$) 33.4, 36.0, 36.1, 37.7, 69.7, 73.9, 126.56, 126.63, 127.0, 128.7, 139.6, 144.9. MS (EI) *m/z* 330/332 (6/6) [M^+], 252/254 (25/25), 193 (24), 173 (13), 145 (9), 131 (36), 115/117 (18/18), 104 (100), 91 (42), 77 (29). Anal. Calcd for $C_{18}H_{19}BrO$ (331.25): C 65.27; H 5.78. Found: C 65.36; H 5.88. HRMS (EI^+) *m/z* 330.0644, 323.0627 [M^+]; calculated mass for $C_{18}H_{19}OBr^+$: 330.0619, 332.0599.

*4.3.2. Oxidation of unlike-1,3-diphenylhex-5-en-1-ol rel-(1S,3R)-(**1i**).* A solution of alcohol *rel*-(1*S*,3*R*)-**1i** (127 mg, 503 μmol) and cobalt complex **5** (13.2 mg, 25.1 μmol) in toluene (2.0 mL), bromotrichloromethane (0.5 mL) and CHD (0.5 mL) was stirred at 70 °C for 24 h while being exposed to laboratory atmosphere. A second (13.4 mg) and third (13.5 mg) batch of cobalt catalyst were added after 2 and 5 h. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. *rel-(2S,4R,6R)-6-Bromomethyl-2,4-diphenyltetrahydropyran rel-(2S,4R,6R)-(13i) and rel-(2S,4R,6S)-6-bromomethyl-2,4-diphenyltetrahydropyran rel-(2S,4R,6S)-(**13i**).* Yield: 129 mg (389 μmol, 77%) as 50:50 mixture of 2,6-cis/trans-isomers, R_f 0.59 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 1.51 (1H, td, J_t 12.8, J_d 10.9), 1.63 (1H, td, J_t 12.5, J_d 11.9), 1.70 (1H, td, J_t 12.8, J_d 11.6), 1.92–2.13 (5H, m), 2.93 (1H, tt, *J* 12.0, 3.4), 2.99 (1H, tt, *J* 12.3, 3.7), 3.39 (1H, dd, *J* 10.4, 5.6), 3.46 (1H, dd, *J* 10.4, 5.4), 3.65 (1H, dd, *J* 10.3, 7.8), 3.77 (1H, dd, *J* 10.4, 7.3), 3.81 (1H, dtd, J_d 10.8, J_t 5.5, J_d 2.1), 4.39 (1H, q, *J* 7.2), 4.51 (1H, dd, *J* 11.3, 2.1), 4.63 (1H, dd, *J* 11.5, 2.5), 7.10–7.34 (20H, m). δ_C (150 MHz, $CDCl_3$) 31.5, 33.2, 35.5, 36.3, 37.0, 40.5, 40.6, 41.6, 72.4, 73.5, 76.96 79.5, 125.7, 125.9, 126.68, 126.71, 127.6, 128.3, 128.4, 128.56, 128.61, 142.1, 142.2, 144.6, 144.7. MS (EI) *m/z* 330/332 (9/9) [M^+], 252/254 (23/23), 193 (24), 173 (10), 145 (8), 131 (27), 117 (15), 104 (100), 91 (38), 77 (25). HRMS (EI^+) *m/z* 330.0622, 330.0604, 332.0608, 332.0594 [M^+]; calculated mass for $C_{18}H_{19}OBr^+$: 330.0619, 332.0599.

*4.3.3. Oxidation of like-1-(thien-2-yl)-3-phenyl-hex-5-en-1-ol rel-(1R,3R)-(**1j**).* A solution of alcohol *rel*-(1*R*,3*R*)-**1j** (107 mg, 416 μmol) and cobalt complex **5** (11.4 mg, 21.7 μmol) in toluene (2.0 mL), bromotrichloromethane (0.5 mL) and CHD (0.5 mL) was stirred at 70 °C for 24 h while being exposed to laboratory atmosphere. A second (11.2 mg) and third (11.5 mg) batch of cobalt catalyst were added after 2 and 5 h. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. *rel-(2R,4R,6R)-6-Bromomethyl-4-phenyl-2-(thien-2-yl)-tetrahydropyran rel-(2R,4R,6R)-(**13j**).* Yield: 125 mg (370 μmol, 89%), R_f 0.54 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 1.64 (1H, td, J_t 12.6, J_d 11.1), 1.89 (1H, ddt, J_d 12.8, 3.9, J_t 2.0), 2.22 (1H, ddd, *J* 13.8, 12.8, 5.9), 2.35–2.41 (1H, m), 3.11 (1H, tt, *J* 12.6, 3.6), 3.43–3.46 (2H, m), 4.02 (1H, dqd, J_d 5.9, J_q 5.4, J_d 2.1), 5.50 (1H, d, *J* 5.7), 7.02–7.06 (2H, m), 7.24–7.37 (6H, m). δ_C (100 MHz, $CDCl_3$) 35.4, 36.0, 36.4, 37.2, 70.1, 72.2, 125.0, 125.4, 126.7, 127.1, 128.7, 144.7, 144.8. MS (EI) *m/z* 336/338 (68/68) [M^+], 258/260 (21/21), 199 (15), 179 (15), 145 (11), 131 (76), 110 (72), 104 (100), 91 (53), 77 (25). HRMS (EI^+) *m/z* 336.0171, 338.0168 [M^+]; calculated mass for $C_{16}H_{17}OSBr^+$: 336.0183, 338.0163.

*4.3.4. Oxidation of unlike-1-(thien-2-yl)-3-phenyl-hex-5-en-1-ol rel-(1S,3R)-(**1j**).* A solution of alcohol *rel*-(1*S*,3*R*)-**1j** (105 mg, 408 μmol) and cobalt complex **5** (11.5 mg, 21.9 μmol) in toluene (2.0 mL), bromotrichloromethane (0.5 mL) and CHD (0.5 mL) was stirred at 70 °C for 24 h while being exposed to laboratory atmosphere. A second (11.5 mg) and third (11.2 mg) batch of cobalt catalyst were added after 2 and 5 h. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. *rel-(2S,4R,6R)-6-Bromomethyl-4-phenyl-2-(thien-2-yl)-tetrahydropyran rel-(2S,4R,6R)-(**13j**) and rel-(2S,4R,6S)-6-bromomethyl-4-phenyl-2-(thien-2-yl)-tetrahydropyran rel-(2S,4R,6S)-(**13j**).* Yield: 103 mg (305 μmol, 75%) as 49:51 mixture of 2,6-cis/trans-isomers, R_f 0.50 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 1.57–1.64 (1H, m), 1.87–1.98 (2H, m), 2.10 (1H, ddd, *J* 14.3, 12.9, 5.7), 2.17 (2H, tdt, J_t 14.4, J_d 3.3, J_t 1.8), 2.24 (1H, d, *J* 12.9), 3.02 (1H, tt, *J* 12.3, 3.7), 3.08 (1H, tt, *J* 12.6, 3.7), 3.45 (1H, dd, *J* 10.3, 5.7), 3.56 (1H, dd, *J* 10.3, 5.6), 3.74 (1H, dd, *J* 10.4, 8.1), 3.87 (1H, dd, *J* 10.4, 7.5), 3.93 (1H, dtd, J_d 10.9, J_t 5.8, J_d 2.1), 4.47 (1H, q, *J* 6.8), 4.86 (1H, dd, *J* 11.2, 1.5), 5.01 (1H, dd, *J* 11.4, 1.8), 6.97–7.01 (2H, m), 7.02–7.05 (2H, m), 7.24–7.39 (12H, m). δ_C (150 MHz, $CDCl_3$) 31.3, 32.9, 35.0, 36.1, 36.8, 40.2, 40.5, 41.3, 68.6, 73.6, 75.7, 77.3, 123.6, 123.8, 124.8, 126.5, 126.71, 126.74, 128.6, 128.7, 144.2, 144.4, 145.1, 145.3. *rel-(2S,4R,6R)-(**13j**).* MS (EI) *m/z*

336/338 (48/48) [M^+], 258/260 (11/11), 199 (11), 131 (57), 111 (53), 104 (100), 91 (49), 69 (25). HRMS (EI^+) *m/z* 336.0190, 338.0173 [M^+]; calculated mass for $C_{16}H_{17}OSBr^+$: 336.0183, 338.0163. *rel-(2S,4R,6S)-(**13j**)*. MS (EI) *m/z* 336/338 (26/26) [M^+], 258/260 (14/14), 199 (21), 131 (63), 111 (68), 104 (100), 91 (51), 69 (30). HRMS (EI^+) *m/z* 336.0189, 338.0177 [M^+]; calculated mass for $C_{16}H_{17}OSBr^+$: 336.0183, 338.0163.

*4.3.5. Oxidation of 1-hexene and benzyl alcohol (**15**).* A solution of benzyl alcohol (**15**) (217 mg, 2.01 mmol) and cobalt complex **5** (26.8 mg, 51.0 μmol) in bromotrichloromethane (1.0 mL), CHD (1.0 mL) and 1-hexene (3.0 mL) was stirred at 70 °C for 72 h while being exposed to laboratory atmosphere. A second (26.7 mg) and third (27.1 mg) batch of cobalt catalyst were added after 24 and 48 h. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/pentane=1:20 (v/v)]. 2-Benzyloxy-1-bromohexane and dibenzyl ether appeared to be inseparable and were obtained as a combined fraction. *2-Benzyloxy-1-bromohexane (**22**)*. Yield: 66.7 mg (246 μmol, 12%), R_f 0.74 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 0.91 (3H, t, *J* 7.0), 1.26–1.50 (4H, m), 1.63–1.71 (2H, m), 3.47 (2H, d, *J* 5.1), 3.59 (1H, ddt, J_d 7.0, 5.9, J_t 5.1), 4.55 (1H, d, *J* 11.5), 4.67 (1H, d, *J* 11.5), 7.28–7.42 (5H, m). δ_C (100 MHz, $CDCl_3$) 14.0, 22.6, 27.3, 32.9, 35.0, 71.7, 78.2, 127.7, 128.4, 129.3, 133.3, 150.6. MS (EI) *m/z* 177 (9), 105 (3), 91 (100), 77 (3). HRMS (EI^+) *m/z* 270.0634, 272.0627 [M^+]; calculated mass for $C_{13}H_{19}OBr^+$: 270.0619, 272.0599.

4.4. Alkylative termination

*4.4.1. Oxidation of like-1,3-diphenylhex-5-en-1-ol rel-(1R,3R)-(**1i**).* A solution of alcohol *rel*-(1*R*,3*R*)-**1i** (107 mg, 423 μmol), dimethyl fumarate (355 mg, 2.46 mmol), and cobalt complex **5** (11.4 mg, 21.7 μmol) in toluene (2.0 mL) and CHD (0.5 mL) was stirred at 70 °C for 24 h while being exposed to laboratory atmosphere. A second (11.6 mg) and third (11.3 mg) batch of cobalt catalyst were added after 2 and 5 h. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. *rel-(2R,4R,6S)-6-Methyl-2,4-diphenyltetrahydropyran rel-(2R,4R,6S)-(**3i**)*. Yield: 22.1 mg (87.6 μmol, 21%), colorless oil. *Dimethyl 2-[rel-(2R,4R,6R)-2,4-diphenyltetrahydropyranyl-6-yl]-methyl succinate rel-(2R,4R,6R)-(**14i**)*. Yield: 95.1 mg (240 μmol, 57%), 50:50 mixture of diastereoisomers with respect to the carbon in α-position to the succinate ester group, R_f 0.34 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 1.39–1.53 (3H, m), 1.58–1.77 (2H, m), 1.97 (1H, ddd, *J* 14.4, 9.2, 5.1), 2.04–2.16 (2H, m), 2.40–2.84 (6H, m), 2.79–2.91 (2H, m), 3.10–3.23 (2H, m), 3.38–3.54 (2H, m), 3.58 (3H, s), 3.61 (3H, s), 3.62 (6H, s), 3.59 (2H, t, *J* 5.0), 7.12–7.27 (12H, m), 7.31 (4H, td, J_t 7.7, J_d 3.7), 7.37–7.43 (4H, m). δ_C (100 MHz, $CDCl_3$) 33.3, 35.3, 36.1, 36.3, 36.9, 37.8, 37.9, 38.0, 38.8, 39.6, 39.8, 51.7, 51.8, 51.9, 67.5, 68.0, 73.3, 73.4, 126.37, 126.41, 126.78, 126.83, 126.9, 128.53, 128.55, 140.1, 140.2, 145.36 145.44, 172.1, 172.2, 175.2, 175.5. MS (EI) *m/z* 396 (1) [M^+], 346 (3), 291 (27), 259 (32), 209 (49), 193 (35), 146 (18), 115 (25), 104 (100), 91 (36), 77 (16). HRMS (EI^+) *m/z* 396.1949 [M^+]; calculated mass for $C_{24}H_{28}O_5^+$: 396.1937.

*4.4.2. Oxidation of like-1-(thien-2-yl)-3-phenyl-hex-5-en-1-ol rel-(1R,3R)-(**1j**).* A solution of alcohol *rel*-(1*R*,3*R*)-**1j** (118 mg, 457 μmol), dimethyl fumarate (398 mg, 2.76 mmol), and cobalt complex **5** (12.1 mg, 23.0 μmol) in toluene (2.0 mL) and CHD (0.5 mL) was stirred at 70 °C for 24 h while being exposed to laboratory atmosphere. A second (11.7 mg) and third (12.2 mg) batch of cobalt catalyst were added after 2 and 5 h. The reaction mixture was cooled to 20 °C and purified by column chromatography [SiO_2, Et_2O/acetone/pentane=1:1:20 (v/v)]. *rel-(2R,4R,6S)-6-Methyl-4-phenyl-2-(thien-2-yl)-tetrahydropyran rel-(2R,4R,6S)-(**3j**)*. Yield: 22.2 mg (85.9 μmol, 19%), colorless oil. *Dimethyl 2-[rel-(2R,4R,6R)-4-phenyl-2-(thien-2-yl)-tetrahydropyr-6-yl]-methyl succinate rel-(2R,4R,6R)-(**14j**)*. Yield: 107 mg (266 μmol, 58%), 50:50 mixture of diastereoisomers with respect to the carbon in α-position to the succinate ester group, R_f 0.28 [SiO_2, acetone/pentane=1:5 (v/v)], colorless oil. δ_H (400 MHz, $CDCl_3$) 1.47–1.78 (6H, m), 1.87 (1H, ddd, *J* 14.3, 8.3, 2.8), 2.05 (1H, ddd, *J* 14.3, 9.4, 4.8), 2.13–2.24 (2H, m), 2.33–2.41 (2H, m), 2.56–2.81 (4H, m), 3.09 (2H, app. tdt, J_t 12.4, J_d 3.3, J_t 3.1), 3.16–3.24 (2H, m), 3.67 (3H, s), 3.691 (3H, s), 3.694 (3H, s), 3.71 (3H, s), 5.40 (2H, t, *J* 5.3), 3.74–3.88 (2H, m), 6.98–7.05 (4H, m), 7.21–7.27 (6H, m), 7.29–7.37 (6H, m). δ_C (100 MHz, $CDCl_3$) 35.3, 35.4, 36.5, 36.6, 36.7, 37.7, 38.0, 39.2, 39.4, 51.7, 51.8, 51.9, 68.1, 68.9, 71.6, 71.7, 124.8, 124.9, 125.1, 125.3, 126.5, 126.7, 126.97, 127.01, 128.6, 145.1, 145.2, 145.4, 145.6, 172.3, 175.2, 175.6. MS (EI) *m/z* (%)=402 (23) [M^+], 257 (13), 215 (87), 200 (27), 146 (22), 110 (56), 104 (100), 91 (30), 77 (12). HRMS (EI^+) *m/z* 402.1510 [M^+]; calculated mass for $C_{22}H_{26}O_5S^+$: 402.1501.

Acknowledgements

This work was supported by the Schering Stiftung (scholarship for P.F.) and the Stiftung Rheinland-Pfalz für Innovation (grant 898). The study is taken from the diploma work of M.K.M and is part of the Ph.D. thesis of P.F.

Supplementary data

Instrumentation, reagent specification, preparation of alkenols, carbon-13 NMR-spectra of selected compounds, and *A*-value analysis of 2-phenyltetrahydropyran. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.12.019.

References and notes

1. Fernández, J. J.; Souto, M. L. *Nat. Prod. Rep.* **2002**, *19*, 235–240.
2. Grayson, D. H. *Nat. Prod. Rep.* **2000**, *17*, 385–419.
3. Bermejo, A.; Figadère; Zafra-Polo, M.-C.; Barrachina, I.; Estornell, E.; Cortes, D. *Nat. Prod. Rep.* **2005**, *22*, 269–303.
4. Faulkner, D. J. *Nat. Prod. Rep.* **1999**, *16*, 155–198.
5. Simpson, T. J. *Nat. Prod. Rep.* **1987**, *4*, 339–376.
6. Hill, A. M. Polyketide Polyethers In *Natural Products in Chemical Biology*; Civjan, N., Ed.; Wiley; Hoboken, New Jersey: 2012; Chapter 8, pp 189–207.
7. Holland, H.; Holland, L. *Organic Synthesis with Oxidative Enzymes*; Wiley-VCH: Weinheim, Germany, 1992; Chapter 1, pp 1–40.
8. Vilotijevic, I.; Jamison, T. F. *Science* **2007**, *317*, 1189–1192.
9. Hartung, J.; Drees, S.; Greb, M.; Schmidt, P.; Murso, A.; Stalke, D.; Svoboda, I.; Fuess, H. *Eur. J. Org. Chem.* **2003**, 2388–2408.
10. Clarke, P. A.; Santos, S. *Eur. J. Org. Chem.* **2006**, 2045–2053.
11. Shindo, M. *Top. Heterocycl. Chem.* **2006**, *5*, 179–254.
12. Kempter, I.; Groß, A.; Hartung, J. *Tetrahedron* **2012**, *68*, 10378–10390.
13. Schneiders, N.; Gottwald, T.; Hartung, J. *Eur. J. Org. Chem.* **2009**, 797–800.
14. (a) Aponick, A.; Li, C.-Y.; Biannic, B. *Org. Lett.* **2008**, *10*, 669–671; (b) Barluenga, J.; Yus, M. *Chem. Rev.* **1988**, *88*, 487–509.
15. Brücher, O.; Bergsträßer, U.; Kelm, H.; Hartung, J.; Greb, M.; Svoboda, I.; Fuess, H. *Tetrahedron* **2012**, *68*, 6968–6980.
16. Singh, P.; Bhardway, A.; Kaur, S.; Kumar, S. *Eur. J. Med. Chem.* **2009**, *44*, 1278–1287.
17. Bartlett, P. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: Orlando, FL, 1984; Vol. 3, pp 411–454.
18. Piccialli, V. *Synthesis* **2007**, *17*, 2585–2607.
19. Tan, H. S.; Espenson, J. H. *J. Mol. Catal. A* **2000**, *152*, 83–89.
20. Hartung, J.; Greb, M. *J. Organomet. Chem.* **2002**, *661*, 67–84.
21. (a) Cardillo, G.; Oreno, M. *Tetrahedron* **1990**, *46*, 3321–3408; (b) Dowle, M. D.; Davies, D. I. *Chem. Soc. Rev.* **1979**, *8*, 171–197.
22. McDonald, F. E.; Singhi, A. D. *Tetrahedron Lett.* **1997**, *38*, 7683–7686.
23. Klein, E.; Rojahn, R. *Tetrahedron* **1965**, *21*, 2353–2358.
24. Roth, S.; Stark, C. B. W. *Angew. Chem.* **2006**, *118*, 6364–6367.
25. Ward, A. F.; Xu, Y.; Wolfe, J. P. *Chem. Commun.* **2012**, 609–611.
26. Davies, S. G.; Donohoe, T. J.; Lister, M. A. *Tetrahedron: Asymmetry* **1991**, *2*, 1089–1092.
27. For IUPAC-recommendation on stereodescriptors for diastereomers with two chirality elements, see: (a) Prelog, V.; Helmchen, G. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 567–583; (b) Moss, G. *Pure Appl. Chem.* **1996**, *68*, 2193–2222.
28. Kumaraswamy, G.; Narish, P.; Jagadoesh, B.; Sridhar, B. *J. Org. Chem.* **2009**, *74*, 8468–8471.
29. Rogano, F.; Rüdi, P. *Helv. Chim. Acta* **2010**, *93*, 1281–1298.

30. For discovery of cobalt(II)-catalyzed aerobic alkenol cyclization, see: Inoki, S.; Mukaiyama, T. *Chem. Lett.* **1990**, 67–70.
31. Wang, Z.-M.; Tian, S.-K.; Shi, M. *Eur. J. Org. Chem.* **2000**, 349–356.
32. Palmer, C.; Morra, N. A.; Stevens, A. C.; Bajtos, B.; Machin, B. P.; Pagenkopf, B. L. *Org. Lett.* **2009**, *11*, 5614–5617.
33. Nicholas, C.; Morra, A.; Pagenkopf, B. L. *Tetrahedron* **2013**, *69*, 8632–8644.
34. Menéndez Pérez, B.; Schuch, D.; Hartung, J. *Org. Biomol. Chem.* **2008**, *6*, 3532–3540.
35. Fries, P.; Halter, D.; Kleinschek, A.; Hartung, J. *J. Am. Chem. Soc.* **2011**, *133*, 3906–3912.
36. Schuch, D.; Fries, P.; Dönges, M.; Menéndez Pérez, B.; Hartung, J. *J. Am. Chem. Soc.* **2009**, *131*, 12918–12920.
37. Fries, P.; Müller, M. K.; Hartung, J. *Org. Biomol. Chem.* **2013**, *11*, 2630–2637.
38. For synthesis of auxiliaries HL^{3-4}, see: (a) Joshi, K. C.; Pathak, V. N.; Bhargava, S. *J. Inorg. Nucl. Chem.* **1977**, *39*, 803–810; (b) Bellamy, L. J.; Branch, R. F. *J. Chem. Soc.* **1954**, 4491–4494.
39. For reviews and applications of oxygen solubility in perfluorocarbons, see: (a) Clark, L. C.; Gollan, F. *Science* **1966**, *152*, 1755–1756; (b) Costa Gomes, M. F.; Deschamps, J.; Menz, D.-H. *J. Fluorine Chem.* **2004**, *125*, 1325–1329; (c) Klement, I.; Lütjens, H.; Knochel, P. *Angew. Chem., Int. Ed.* **1997**, *36*, 1454–1456.
40. Nishinaga, A.; Yamada, T.; Fujisawa, H.; Oshizaki, K.; Ihara, H.; Matsuuka, T. *J. Mol. Catal.* **1988**, *48*, 249–264.
41. Yamada, T.; Mukaiyama, T. *Chem. Lett.* **1989**, *18*, 519–522.
42. Kalinowski, H. O.; Berger, S.; Braun, S. In *^{13}C-NMR-Spektroskopie*; Thieme: Stuttgart, Germany, 1984.
43. Kubas, A.; Hartung, J.; Fink, K. *Dalton Trans.* **2011**, 11289–11295.
44. Sheldon, R. A.; Kochi, J. K. In *Metal-catalyzed Oxidations of Organic Compounds*; Academic: New York, NY, 1981.
45. For calculated *A*-values of 2-alkyl-substituted tetrahydropyrans, see: (a) Freeman, F.; Kasner, J. A.; Kasner, M. L.; Hehre, W. J. *J. Mol. Struct.: Theochem.* **2000**, *496*, 10–39; (b) For calculated *A*-values of 2-alkyl-substituted tetrahydropyrans, see Supplementary data.
46. Wolfe, J. P.; Hay, M. B. *Tetrahedron* **2007**, *63*, 261–290.
47. Jalce, G.; Franck, X.; Figadère, B. *Tetrahedron: Asymmetry* **2009**, *20*, 2537–2581.
48. Giese, B. In *Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds*; Pergamon: Oxford, UK, 1986.
49. Schur, C.; Becker, N.; Bergsträßer, U.; Gottwald, T.; Hartung, J. *Tetrahedron* **2011**, *67*, 2338–2347.
50. Giese, B.; Jay, K. *Chem. Ber.* **1979**, *112*, 304–309.
51. Heydt, H.; Hartung, J. In *Science of Syntheses*; Berkessel, A., Ed.; Thieme: Stuttgart, Germany, 2008; Vol. 38, pp 109–141.
52. For examples of methods for terminating carbon radical chain reactions by heteroatom donors or addition to alkenes and rate constants for key radical elementary, see: In *Radicals in Organic Synthesis*, Renaud, P.; Sibi M. P., Eds., Wiley-VCH: Weinheim, Germany, 2001; Vol. 1 (*Basic Principles*) and Vol. 2 (*Applications*).
53. Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals*, 4th ed.; Butterworth Heinemann: Oxford, UK, 1996.
54. Hartung, J.; Miller, M.; Schmidt, P. *Chem.—Eur. J.* **1996**, *2*, 1014–1023.
55. Brown, D. S.; Bruno, M.; Davenport, R. J.; Ley, S. V. *Tetrahedron* **1989**, *45*, 4293–4308.
56. Hilt, G.; Bolze, P.; Heitbaum, M.; Hasse, K.; Harms, K.; Massa, W. *Adv. Synth. Catal.* **2007**, *349*, 2018–2026.
57. Jana, R.; Tunge, J. A. *J. Org. Chem.* **2011**, *76*, 8376–8385.
58. Eliel, E. L.; Manoharan, M.; Pietrusiewicz, K. M.; Hargrave, K. D. *Org. Magn. Reson.* **1983**, *21*, 94–107.
59. Yanagisawa, A.; Habaue, S.; Yasue, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 6130–6141.
60. Taylor, J. G.; Whittal, N.; Hii, K. K. *Chem. Commun.* **2005**, 5103–5105.