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Metal-Catalyzed Cycloetherification Reactions of β,γ- and γ,δ-Allendiols: Chemo-, Regio-, and Stereocontrol in the Synthesis of Oxacycles

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Abstract: Versatile routes that lead to a variety of functionalized enantiopure tetrahydrofurans, dihydropyrans, and tetrahydrooxepines are based on chemo-, regio-, and stereocontrolled metal-catalyzed oxycyclization reactions of β,γ- and γ,δ-allendiols, which were readily prepared from (*R*)-2,3-*O*-isopropylideneglyceraldehyde. The application of Pd^{II}, Pt^{II}, Au^{III}, or La^{III} salts as the catalysts gives controlled access to differently sized oxacycles in enantiopure form. Usually, chemoselective cyclization reactions occurred exclusively by attack of the secondary hydroxy group (except for the oxybromination of phenyl β,γ-allenic diols **3b** and **3d**) to an allenic carbon atom. Regio- and stereocontrol issues are mainly influenced by the nature of the metal catalysts and substituents.

Keywords: allenes · cyclization · gold · palladium · platinum

Introduction

The development of synthetic methods for the preparation of differently sized oxacycles is important because they are present in a wide range of natural products and biologically active molecules.[1] Among the possibilities, the transition-metal-catalyzed intramolecular addition of oxygen nucleophiles across an allene moiety is intriguing from the point of view of regioselectivity and because it is one of the most rapid and convenient methods for the preparation of oxacycles.[2] However, metal-catalyzed heterocyclizations of allenes bearing two contiguous nucleophilic centers have rarely been mentioned because of additional chemoselectivity problems.[3] Namely, the product distribution must depend on the chemo- and regioselectivity of the heterocyclization, but in principle, eight different products are possible.[4] In this context, even if the structure of the substrate suggests numerous possibilities for reactivity, metal-catalyzed processes can lead to specific control of the transition state and result in the controlled formation of products with high selectivity. In continuation of our interest in heterocyclic and allene chemistry,[5] we report herein full details of the chemo- and regioselective palladium-catalyzed cycloetherification of β,γ- and γ,δ-allendiols[6] and the extension of this reaction to precious metals, namely, gold and platinum salts.

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Results and Discussion

Precursors for the oxacycle formation, enantiopure β,γ-allenic diols **3a–d** and γ,δ-allenic diols **4a** and **4b**, were made starting from (*R*)-2,3-*O*-isopropylideneglyceraldehyde (**1**) and (*R*)-2-(benzyloxy)-2-[(*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]acetaldehyde (**2**),[7] respectively, through a regio- and stereocontrolled indium-mediated Barbier-type carbonyl allenylation reaction in aqueous media, followed by protecting-group manipulation (Schemes 1 and 2). Whereas the allenylation of aldehyde **1** with 1-bromobut-2-yne did take place with complete diastereoselectivity, thus forming **5a**, the carbonyl addition reaction of its benzyloxy homologue **2** gave

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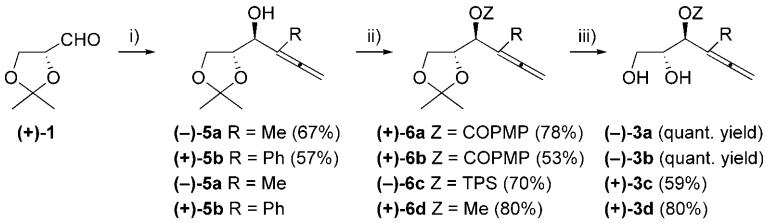
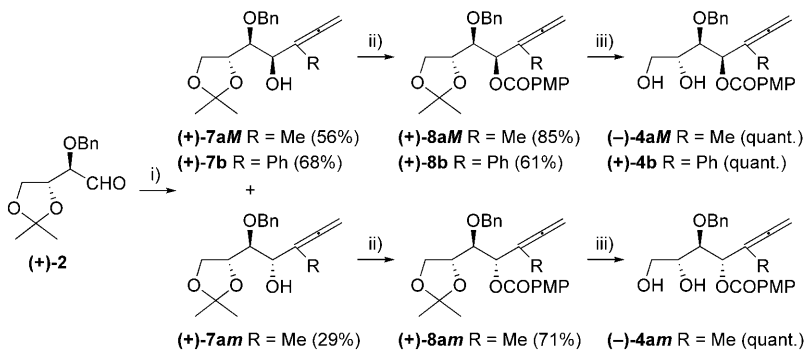


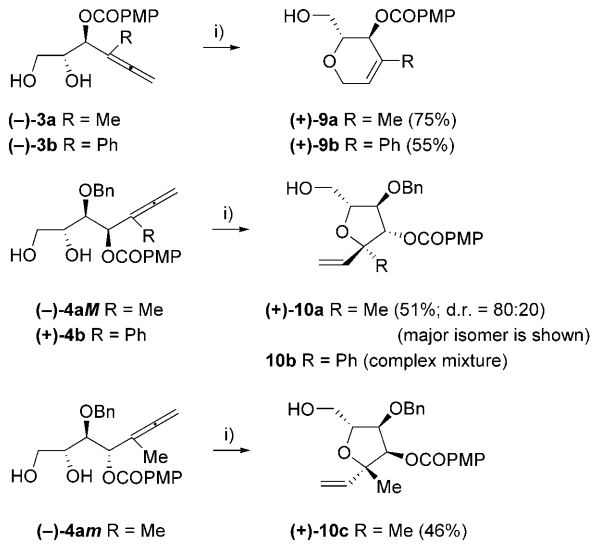
Scheme 1. Preparation of enantiopure β,γ-allenic diols **3a**–**d**. i) 1-Bromobut-2-yne or (3-bromoprop-1-ynyl)benzene, In, THF/NH_4Cl (aq. sat.), RT, 5 h. ii) PMPCOCl, Et_3N, DMAP, CH_2Cl_2, RT, 18 h; TPSCl, imidazole, CH_2Cl_2, reflux, 24 h; or Me_2SO_4, NaOH, TBAI, CH_2Cl_2/H_2O, RT, 12 h; iii) $BiCl_3$ (20 mol%), MeCN/H_2O, RT, 24 h. DMAP = dimethylaminopyridine, PMP = *para*-methoxyphenyl, TBAI = tetrabutylammonium iodide, TPS = *tert*-butyldiphenylsilyl.



Scheme 2. Preparation of enantiopure γ,δ-allenic diols **4**. i) 1-Bromobut-2-yne or (3-bromoprop-1-ynyl)benzene, In, THF/NH_4Cl (aq. sat.), RT, 16 h; ii) PMPCOCl, Et_3N, DMAP, CH_2Cl_2, reflux, **8aM**: 28 h, **8b**: 48 h, **8am**: 24 h; iii) $BiCl_3$ (20 mol%), MeCN/H_2O, RT, **4aM**: 48 h, **4b**: 18 h, **4am**: 48 h. ***M*** = Major isomer; ***m*** = minor isomer.

α-allenols **7a** with poor *syn*/*anti* stereoselectivity (**7aM**/**7am** = 60:40). Fortunately, the diastereomeric α-allenols **7aM** and **7am** were separated by column chromatography. In contrast, coupling reactions of aldehydes **1** and **2** with an organoindium reagent generated in situ from indium and (3-bromoprop-1-ynyl)benzene were totally diastereoselective, thus affording α-allenols **5b** and **7b** as single isomers. The absolute configurations of the new carbinolic stereocenters on α-allenols **5a** and **7aM** were determined according to the empirical model developed by Trost et al. through esterification with (*S*)- and (*R*)-*O*-methylmandelic acids.[8] The calculated differences in the ^1H NMR chemical shifts for the protons of their acetylmandelates allowed us to tentatively attribute the *S* configuration to α-allenol **5a** and the *R* configuration to α-allenol **7aM**.

We decided to investigate the distinct reactivity of β,γ- and γ,δ-allenic diols depending on the nature of the metal catalyst that initiates electrophilic activation of the allene moiety. Recently, gold and platinum salts have emerged as powerful catalysts for the formation of C–C and C–heteroatom bonds.[9] Indeed, in an initial screen with β,γ-allendiol substrates **3**, it was found that $AuCl_3$ was a selective catalyst to perform the desired cycloetherification to access functionalized dihydropyrans **9** exclusively in reasonable yields (Scheme 3). These results could be explained through a 6-*endo* cycloisomerization by chemo- and regiospecific attack of the secondary hydroxy group at the terminal allene carbon atom. Worthy of note, in contrast, the $AuCl_3$-catalyzed cycloisomerization of γ,δ-allenic diols **4** represents a selective method to afford tetrahydrofurans **10**



Scheme 3. Gold-catalyzed preparation of dihydropyrans **9** and tetrahydrofurans **10**. i) $AuCl_3$ (5 mol%), CH_2Cl_2, RT, **9a**: 2.5 h, **9b**: 2 h, **10a**: 16 h, **10b**: 16 h, **10c**: 25 h.

Abstract in Spanish: *Se han encontrado rutas versátiles que conducen a tetrahidrooxepinas, dihidropiranos y tetrahidrofuranos funcionalizados enantiopuros, basadas en reacciones de oxiciclación quimio-, regio- y estereocontroladas de β,γ- y γ,δ-alenildioles catalizadas por metales. Los dioles de partida se prepararon fácilmente a partir de (*R*)-2,3-O-isopropilidengliceraldehido. La utilización de sales de Pd^{II}, Pt^{II}, Au^{III} ó La^{III} como catalizadores da lugar a un método de preparación controlada de oxaciclos de diferente tamaño en forma enantiopura. Normalmente, las reacciones de ciclación quimioselectiva ocurren exclusivamente por ataque del grupo hidroxilo secundario (excepto en la oxibromación de los fenil β,γ-alenildioles **3b** y **3d**) a uno de los carbonos alénicos. Tanto el control regio- como el estereoquímico están influídos por la naturaleza del metal y los sustituyentes.*

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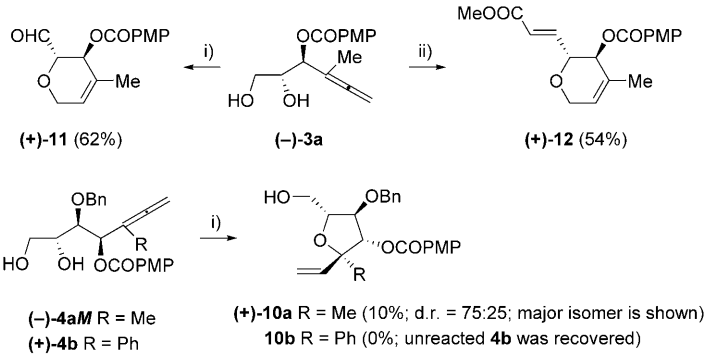
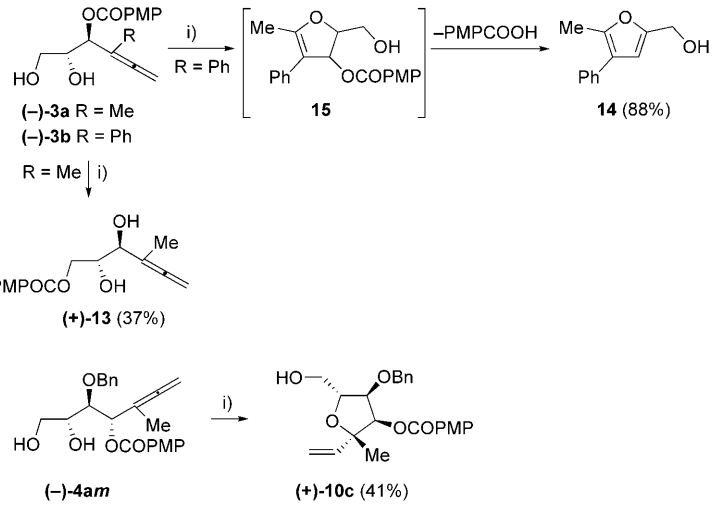
bearing a quaternary stereocenter (Scheme 3).[10,11] Thus, regioselectivity can be completely reversed by using a benzyloxy allendiol homologue, thus favoring the 5-*exo* cyclization of the secondary hydroxy group toward the internal allene carbon atom over the 6-*endo* cyclization toward the terminal allene carbon atom. The reason for the total diastereoselectivity of the 5-*exo* cyclization toward the internal allene carbon atom in methyl allendiol **4a*m***, which gave adduct **10c**, relative to the moderate diastereoselectivity of methyl allendiol **4a*M***, which gave adduct **10a** (Scheme 3), may be related to an increase in ease of access of the incoming oxygen nucleophile to the allene group from the face *trans* to the benzyloxy and *para*-methoxybenzoyloxy groups. Differences in qualitative homonuclear NOE interactions allowed us to assign the stereochemistry at the newly formed stereocenter of tetrahydrofurans **10**. The *para*-methoxybenzoyloxy group comprises a large substituent. Disappointingly, the presence of a large phenyl substituent in the allene moiety (i.e., **4b**) instead of the methyl group (i.e., **4a*M***) did affect the reactivity, thus obtaining oxacycle **10b** within a complex reaction mixture.

The use of gold catalysis in allene chemistry has already witnessed spectacular achievements. In contrast, the platinum-catalyzed reactions with allenols as substrates are an almost unexplored field of noble-metal catalysis.[12] It was nice to observe that upon exposure of the β,γ-allenic diol **3a** to platinum catalysis, carbaldehyde **11**, the result of a chemo- and regiospecific cyclization of the secondary hydroxy group at the distal allene carbon atom with concurrent oxidation,[13] was obtained as the sole product. The fact that the optimum reaction conditions required the addition of an equimolecular amount of phosphine ligand for the platinum center, may suggest that the catalytically active species could be a platinum(II) monophosphine complex. Compound **11** was not particularly stable at room temperature. Thus, the aldehyde must be trapped immediately to avoid decomposition. The trapping/derivatization was accomplished through the use of a stabilized Wittig reagent during the platinum-catalyzed oxycyclization step, thus giving rise to α,β-unsaturated ester **12** (Scheme 4). In contrast, the cyclization of γ,δ-allenic diol **4a*M*** was not as rewarding and tetrahydrofuran **10a** was obtained in low yield (Scheme 4).

The lanthanide-catalyzed hydroalkoxylation of simple allenols has been recently reported.[14] Our investigations began with β,γ-allenic diols **3a** and **3b** as model substrates. Attempts at a cyclization reaction of **3a** with [La{N(SiMe$_3$)$_2$}$_3$] as catalyst failed, thus giving rise to the isomeric α,β-allenic diol **13** instead. However, the reaction of phenyl allenic diol **3b** by using the lanthanide–amide-catalyzed protocol afforded furan **14** in good yield. This outcome could be explained through a selective 5-*exo* cyclization by attack of the secondary hydroxy group at the central allene carbon atom to give the nonisolable dihydrofuran **15**, which under the reaction conditions suffers aromatization to form furan **14** (Scheme 5). Interestingly, the reaction of γ,δ-allenic diol **4a*m*** under identical conditions to those given above could



Scheme 4. Platinum-catalyzed preparation of dihydropyrans **11** and **12** and tetrahydrofurans **10**. i) [{PtCl$_2$(CH$_2$=CH$_2$)}$_2$] (5 mol%), TDMPP (10 mol%), CH_2Cl_2, RT, 2 h; ii) [{PtCl$_2$(CH$_2$=CH$_2$)}$_2$] (5 mol%), TDMPP (10 mol%), methyl(triphenylphosphoranylidene)acetate, CH_2Cl_2, RT, 2 h. TDMPP = tris(2,6-dimethoxyphenyl)phosphine.



Scheme 5. Lanthanide–amide-catalyzed preparation of furan **14**. Reagents and conditions: i) [La{N(SiMe$_3$)$_2$}$_3$] (5 mol%), toluene, reflux, **13**: 4 h, **14**: 24 h, **10c**: 3 h.

proceed smoothly with complete product selectivity to give tetrahydrofuran **10c** through 5-*exo* cycloisomerization of the secondary hydroxy group toward the internal allene carbon atom. It should be noted that the lanthanum-catalyzed oxycyclization of simple γ-allenols afforded six-membered cyclic ethers.[14]

To screen the reactivity of the allenic diol moiety with different palladium-based catalysts, heterocyclization was initially explored by the exposure of β,γ-allendiol **3a** to palladium(0) catalysis. Substrate 2*H*-pyran **16**, which arises from a totally chemo- and regioselective 6-*exo* oxycyclization of the primary hydroxy group at the central allene carbon atom with concurrent dehydration, was obtained in modest yield together with a complicated mixture of byproducts (Scheme 6). Next, **3a** was treated with allyl bromide in the presence of a palladium(II) catalyst. It was nice to observe that the functionalized dihydropyran **17a** was isolated as the

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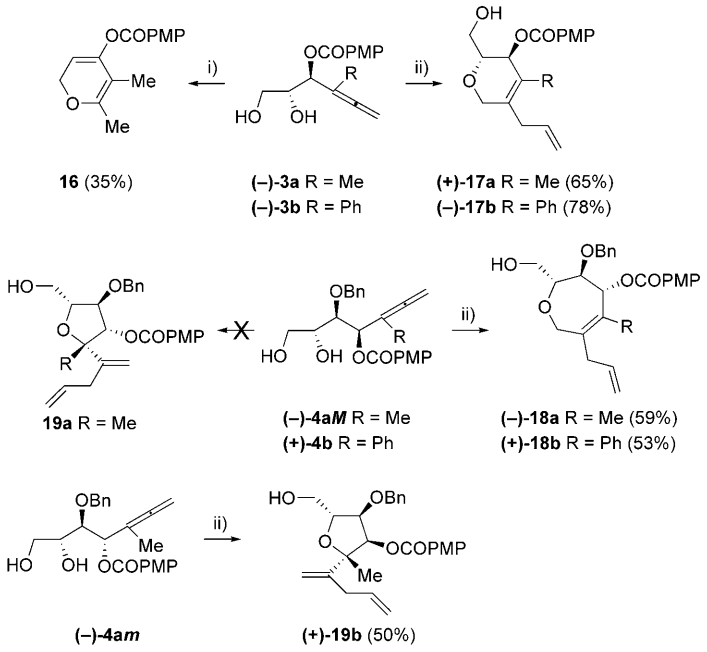
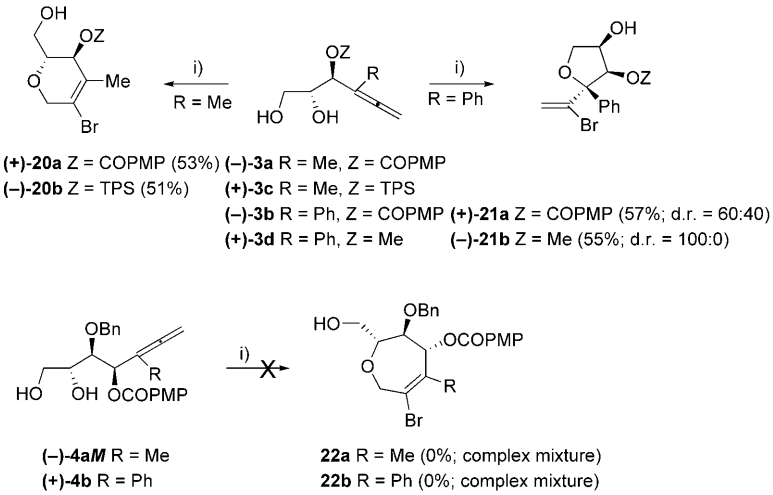


Scheme 6. Palladium-catalyzed preparation of dihydropyrans **17**, tetrahydrooxepines **18**, and tetrahydrofuran **19b**. i) $[Pd(PPh_3)_4]$ (5 mol%), PhI, K_2CO_3, toluene, 80°C, 24 h; ii) allyl bromide, $PdCl_2$ (5 mol%), DMF, RT, **17a**: 3 h, **17b**: 2 h, **18a**: 16 h, **18b**: 16 h, **19b**: 24 h.

sole isomer in a reasonable yield of 65%. Similar behavior was observed for phenyl derivative **3b** (Scheme 6). This result could be explained through a 6-*endo* cyclization by chemo- and regiospecific attack of the secondary hydroxy group at the terminal allene carbon atom. The stage was thus set for the metal-catalyzed cycloetherification reaction of γ,δ-allenic diols **4**. Conversion into the corresponding oxacycle could not be satisfied with palladium(0) promoters. Interestingly, under the reactions conditions used with allyl bromide, $PdCl_2$ could be an excellent catalyst for this purpose. The cycloetherification/coupling sequence of γ,δ-allenic diols **4** was attained; surprisingly, the regioselectivity was changed by inverting the configuration of the stereocenter near to the allene framework (Scheme 6). Thus, we were pleased that γ,δ-allenic diols **4a*M*** and **4b** suffered a 7-*endo* oxycyclization at the distal allene carbon atom to give tetrahydrooxepines **18**, whereas γ,δ-allenic diol **4a*m*** followed a 5-*exo* heterocyclization pathway at the proximal allene carbon atom to afford tetrahydrofuran **19b**. Therefore, an interesting reversal of regioselectivity can be achieved by introducing the epimeric configuration at the allenic contiguous stereocenter. Probably, this outcome is due to steric effects in the transition state. Thus, for β,γ-allendiol **4a*M*** the reaction should take place more unfavorably for the palladium–tetrahydrofuran complex than for the palladium–tetrahydrooxepine intermediate as a result of destabilizing steric interactions around the reactive centers in the former. Differences in the qualitative homonuclear NOE interactions allowed us to assign the stereochemistry at the newly formed stereocenter of tetrahydrofuryl derivative **19b**.

It was interesting at this point to test the reactivity of the allendiol moiety under the conditions for a palladium-catalyzed oxybromination reaction.[15] The treatment of β,γ-allenic diols **3a** and **3c** (bearing a methyl group on the allene group) with lithium bromide by using a Pd–Cu bimetallic catalytic system selectively led to bromoetherification products **20** in reasonable yields of the isolated products that ensued from 6-*endo-trig* cyclization. We also tested the reactivity of β,γ-allendiols **3b** and **3d** bearing a phenyl rather than a methyl allene substituent. To our delight, in contrast to the oxybromination reaction of methyl allendiols **3a** and **3c**, which led to a bromodihydropyran compound, the reaction of phenyl allendiols **3b** and **3d** under identical conditions afforded 2-(1-bromovinyl)tetrahydrofurans **21** bearing a quaternary stereocenter (Scheme 7).[10] Thus, both the chemo- and the regioselectivity can be completely reversed by a subtle variation in the substitution pattern of the β,γ-allendiol (Ph versus Me). This apparently unusual result can be explained by the electron-withdrawing capacities of the phenyl substituent relative to the electron-donating methyl group. Probably, the presence of a Ph substituent in the allene moiety strengthened the electrophilicity of the benzylic carbon atom, thus favoring the 5-*exo* cyclization of the primary hydroxy group over the 6-*endo* cyclization of the secondary hydroxy group. The *para*-methoxybenzoyloxy group comprises a large substituent; however, the *cis* attack, which would be disfavored with a larger ZO group, increas-



Scheme 7. Palladium-catalyzed preparation of dihydropyrans **20** and tetrahydrofurans **21**. i) $Pd(OAc)_2$ (7 mol%), LiBr, $Cu(OAc)_2$, K_2CO_3, MeCN, O_2, RT, 2 h.

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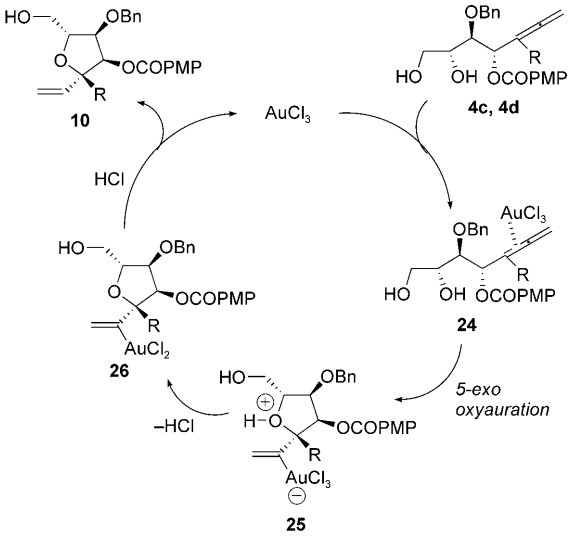
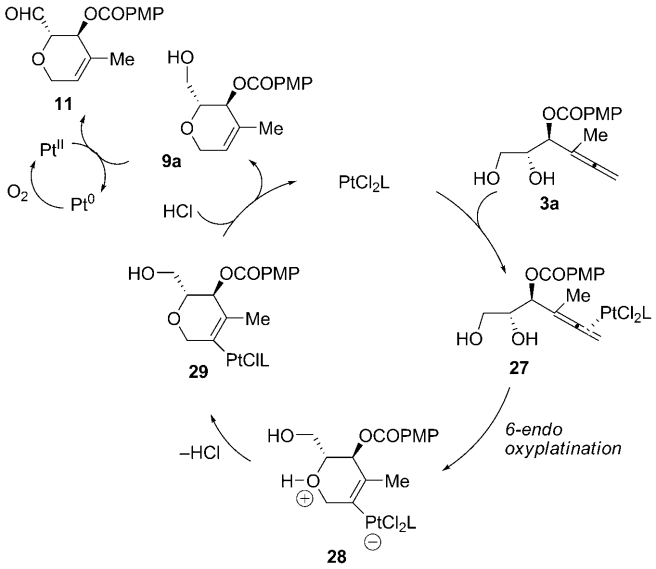
es with **3b** (Z = COPMP) relative to **3d** (Z = Me). The reason for the total diastereoselectivity for 5-*exo* cyclization toward the internal allene carbon atom on phenyl allendiol **3d**, which gave adduct **21b**, relative to the moderate diastereoselectivity of phenyl allendiol **3b**, which gave adduct **21a**, in the examples given in Scheme 7 may be related to unfavorable steric interactions between the ZO group and Pd center in the π-allyl–palladium intermediate derived from **3b**, thus hampering the required conformation for the *trans* attack. Unfortunately, the Pd–Cu bimetallic system could not induce a clean bromoheterocyclization reaction of γ,δ-allenic diols **4** because a complex mixture of products was formed under the conditions for palladium(II) catalysis.

A possible pathway for the gold-catalyzed preparation of tetrahydrofurans **10** may initially involve the formation of a complex **24** through coordination of gold trichloride to the proximal allenic double bond of γ,δ-allenic diols **4**. Next, chemo- and regiospecific 5-*exo* oxyauration forms zwitterionic intermediates **25**, which generate neutral species **26** after loss of HCl. Protonolysis of the carbon–gold bond of **26** liberates adduct **10** with concurrent regeneration of the gold(III) catalytic species (Scheme 8).



Scheme 8. Mechanistic explanation for the gold-catalyzed oxycyclization of γ,δ-allenic diols **4**.

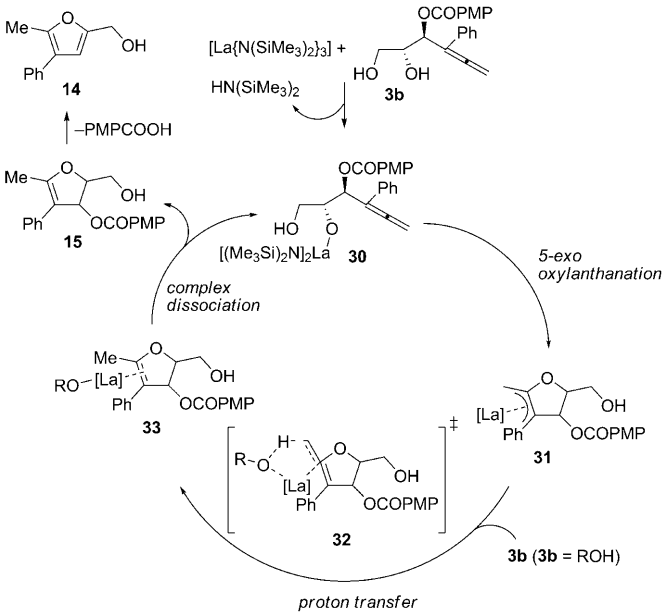
A conceivable mechanism for the formation of dihydropyran **11** may initially involve the formation of π-complex **27** through coordination of the platinum catalyst to the 1,2-diene moiety of β,γ-allenic diol **3a**. Next, chemo- and regioselective 6-*endo* oxyplatination to form species **28** followed by loss of HCl, demetalation, and proton transfer affords the nonisolable (dihydropyranyl)methanol **9a** and regenerates the platinum catalyst (Scheme 9). Intermediate **9a** is transformed by aerobic oxidation into (dihydropyranyl)carbaldehyde **11**. To support the proposition that adduct **9a** is an intermediate, we performed the reaction of **9a**, which is the final product from the gold-catalyzed cycloisomerization



Scheme 9. Mechanistic explanation for the platinum-catalyzed tandem oxycyclization/oxidation of β,γ-allenic diol **3a**. L = ligand.

of allenic diol **3a** (Scheme 4) in the presence of [{Pt(CH_2=CH_2)Cl_2}$_2$] and TDMPP in an oxygen atmosphere, thus affording aldehyde **11** in 70% yield.

Scheme 10 comprises a mechanistic rationale for the [La{N($SiMe_3$)$_2$}$_3$]-promoted conversion of β,γ-allenic diol **3b** into furan **14**. First, a lanthanum precatalyst formed the alkoxide–La complex **30** through protonolysis at the La–{N($SiMe_3$)$_2$}$_3$ bond by allendiol **3b**. Subsequently, one π bond of the oxallene–La complex chemo- and regiospecifically adds across the La–O functionality of **30** to afford oxacyclic



Scheme 10. Mechanistic explanation for the lanthanum-catalyzed oxycyclization of β,γ-allenic diol **3b**.

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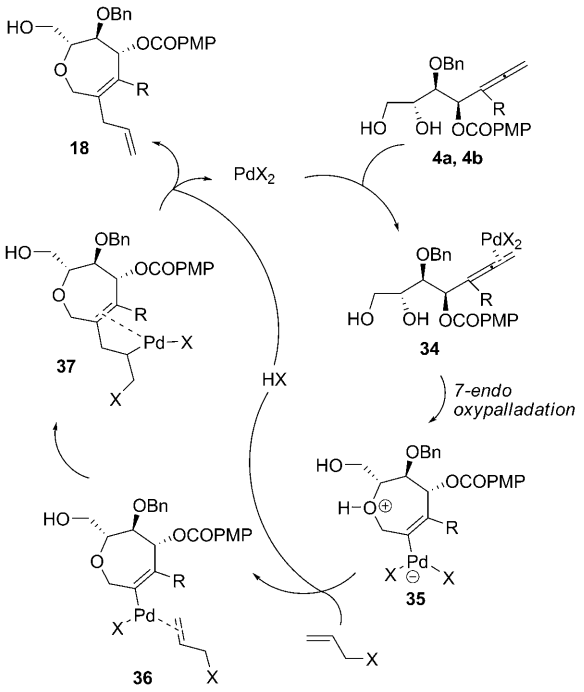
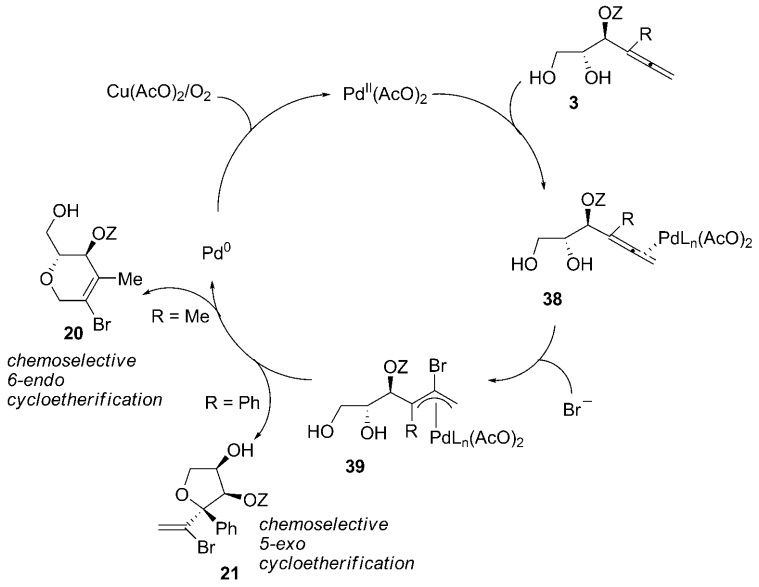
intermediate **31** by 5-*exo* cyclization at the central allene carbon atom. The intervention of a second molecule of allendiol **3b** facilitates the proton-transfer step to afford species **33** via transition state **32**. Species **33** after complex dissociation delivers dihydrofuran **15**, which undergoes aromatization under the reaction conditions to form furan **14**, thus reinitiating the catalytic cycle.

Scheme 11 outlines a mechanistic proposal for the achievement of tetrahydrooxepines **18**. Initial coordination of the palladium(II) center to the 1,2-diene moiety gave allene–palladium complex **34**, which undergoes a chemo- and regioselective 7-*endo* oxycyclization reaction to give the intermediate palladium–tetrahydrooxepine **35**. Treatment of **35** with allyl bromide led, via **36**, to the formation of intermediate **37**, which after a *trans* β-heteroatom elimination generated oxacycles **18** with concurrent regeneration of the palladium(II) catalyst (Scheme 11).

A likely mechanism for the generation of bromodihydropyrans **20** and tetrahydrofurans **21** should involve the initial formation of a π-allyl—palladium species. The allene—palladium complex **38** is formed initially and undergoes nucleophilic attack by the bromide ion to produce an σ-allyl–palladium species, which rapidly equilibrates to the corresponding π-allyl–palladium intermediate **39**. A chemo- and regiospecific intramolecular cycloetherification reaction by attack by either the secondary hydroxy group at the terminal allene carbon atom or by the primary hydroxy group at the internal allene carbon atom onto the π-allyl–palladium complex must account for the formation of dihydropyrans **20** or tetrahydrofurans **21** (Scheme 12). Finally, oxidation of palladium(0) to palladium(II) in situ by $Cu(OAc)_2$ completes the catalytic cycle.



Scheme 11. Mechanistic explanation for the palladium-catalyzed oxycyclization of γ,δ-allenic diols **4**. X = Cl, Br.



Scheme 12. Mechanistic explanation for the oxybromination reaction of β,γ-allendiols **3** under Pd–Cu bimetallic catalysis.

Conclusion

In conclusion, the chemo-, regio-, and stereocontrolled cycloetherification of allenic diols bearing different substituents into differently sized oxacycles has been realized by using various metal-based catalysts, such as Pd^{II}, Pt^{II}, Au^{III}, or La^{III} salts. The scope of these protocols has been investigated and clearly demonstrates their utility for the selective preparation of several enantiopure cyclic ethers from structurally related substrates. At the present time, the application of this methodology into the selective preparation of other types of heterocyclic compounds is ongoing in our group.

Experimental Section

General methods: ^1H and ^{13}C NMR spectra were recorded on Bruker AMX-500, Bruker Avance-300, Varian VRX-300S, or Bruker AC-200 spectrometers. NMR spectra were recorded in $CDCl_3$, unless otherwise stated. Chemical shifts are given in ppm relative to trimethylsilane (TMS; ^1H NMR: $\delta = 0.0$ ppm) or $CDCl_3$ (^{13}C NMR: $\delta = 76.9$ ppm). Low- and high-resolution mass spectra were taken on a HP5989A spectrometer by using electronic impact (EI) or electrospray modes (ES), unless other-

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wise stated. Specific rotation $[\alpha]_D$ is given in 10^{-1} deg cm^2 g^{-1} at 20 °C, and the concentration c is expressed in grams per 100 mL. All commercially available compounds were used without further purification.

General procedure for the Au-catalyzed cyclization of allenic diols 3 and 4: Preparation of dihydropyrans **9** and tetrahydrofurans **10**: $AuCl_3$ (0.05 mmol) was added to a stirred solution of the corresponding allenic diol **3** and **4** (1.0 mmol) in dichloromethane (1.0 mL) under argon. The resulting mixture was stirred at room temperature until disappearance of the starting material (TLC). The reaction was quenched with brine (1.0 mL), the mixture was extracted with ethyl acetate (3×5 mL), and the combined extracts were washed twice with brine. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue eluted with ethyl acetate/hexane gave analytically pure adducts **9** and **10**.[16]

Dihydropyran (+)-9a: Prepared from β,γ-allendiol (−)-**3a** (75 mg, 0.27 mmol), and after chromatography of the residue with hexane/ethyl acetate (3:1) as the eluent (+)-**9a** was obtained as a colorless oil (49 mg, 75%). $[\alpha]_D = +75.1$ ($c = 1.8$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 6.94$ and 8.02 (d, each 2H, $J = 9.0$ Hz, Ar), 5.70 (m, 1H), 5.61 (m, 1H), 4.26 (m, 2H), 3.88 (s, 3H), 3.70 (m, 3H), 1.73 ppm (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 166.5$, 163.8, 132.3, 131.7, 124.4, 121.8, 113.8, 77.6, 67.6, 65.4, 62.4, 55.5, 18.4 ppm; IR ($CHCl_3$): $\tilde{\nu} = 3432$, 1724 cm^{-1}; HRMS (ES): m/z: calcd for $C_{14}H_{16}O_4$: 248.1049 $[M+H]^+$; found: 248.1045.

Dihydropyran (+)-9b: Prepared from β,γ-allendiol (−)-**3b** (50 mg, 0.14 mmol), and after chromatography of the residue with hexane/ethyl acetate (2:1) as the eluent (+)-**9b** was obtained as a colorless oil (21 mg, 55%). $[\alpha]_D = +32.7$ ($c = 1.3$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 7.72$ and 6.80 (d, each 2H, $J = 9.0$ Hz), 7.26 (m, 5H), 6.24 (m, 2H), 4.48 (t, 2H, $J = 2.7$ Hz), 3.82 (m, 3H), 3.81 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 163.6$, 161.0, 137.2, 136.0, 132.3, 131.8, 128.4, 127.5, 126.9, 125.8, 113.6, 77.1, 65.4, 65.2, 62.1, 55.4 ppm; IR ($CHCl_3$): $\tilde{\nu} =$ 3428, 1722 cm^{-1}; HRMS (ES): m/z: calcd for $C_{19}H_{18}O_4$: 310.1205 $[M+H]^+$; found: 310.1210.

Tetrahydrofuran (+)-10a: Prepared from γ,δ-allendiol (−)-**4a*M*** (66 mg, 0.16 mmol), and after chromatography of the residue with hexane/ethyl acetate (3:1) as the eluent (+)-**10a**, which contained approximately 20% of its epimer, was obtained as a colorless oil (34 mg, 51%). The diastereoisomers of **10a** are inseparable by column chromatography (^{1}H and ^{13}C NMR data were obtained by analyzing the NMR spectra of the mixtures; however, IR and MS spectroscopic data could not be assigned individually for them). $[\alpha]_D = +2.0$ ($c = 2.1$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 8.00$ and 6.95 (d, each 0.4H, $J = 9.0$ Hz), 7.94 and 6.92 (d, each 1.6H, $J = 9.0$ Hz), 7. 13 (m, 5H), 6.07 (dd, 0.2H, $J = 17.3$, 10.7 Hz), 5.90 (dd, 0.8H, $J = 17.3$, 10.7 Hz), 5.47 (d, 0.2H, $J = 2.2$ Hz), 5.41 (m, 0.2H), 5.34 (d, 0.8H, $J = 2.0$ Hz), 5.35 (dd, 0.8H, $J = 17.3$, 1.5 Hz), 5.23 (dd, 0.2H, $J = 10.7$, 1.2 Hz), 5.12 (dd, 0.8H, $J = 11.0$, 1.5 Hz), 4.76 and 4.56 (d, each 0.2H, $J = 17.9$ Hz), 4.82 and 4.59 (d, each 0.8H, $J =$ 17.6 Hz), 4.19 (m, 1H), 4.10 (dd, 0.8H, $J = 5.0$, 1.8 Hz), 4.08 (m, 0.2H), 3.88 (s, 0.6H), 3.87 (s, 2.4H), 3.86 (m, 1H), 3.69 (dd, 0.8H, $J = 11.8$, 4.3 Hz), 3.65 (dd, 0.2H, $J = 12.4$, 3.9 Hz), 1.56 (s, 2.4H), 1.55 ppm (s, 0.6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 165.3$ (m), 165.1 (M), 163.7 (m), 163.6 (M), 138.1 (M+ m), 137.6 (M), 137.5 (m), 131.8 (m), 131.7 (M), 128.5 (M), 128.4 (m), 127.8 (M), 127.7 (m), 127.6 (M+m), 122.0 (M), 121.8 (m), 114.8 (M), 114.2 (m), 113.8 (m), 113.7 (M), 84.9 (m), 84.8 (M), 84.7 (M), 84.6 (m), 81.9 (M), 81.3 (m), 77.2 (M +m), 72.3 (M), 72.2 (m), 62.8 (M), 62.7 (m), 55.5 (m), 55.4 (M), 22.9 (M), 22.1 ppm (m); IR (CHCl): $\tilde{\nu} = 3432$, 1722 cm^{-1}; HRMS (ES): m/z: calcd for $C_{23}H_{27}O_6$: 399.1808 $[M+H]^+$; found: 399.1803.

Tetrahydrofuran (+)-10c: Prepared from γ,δ-allendiol (−)-**4a*m*** (48 mg, 0.12 mmol), and after chromatography of the residue with hexane/ethyl acetate (2:1) as the eluent (+)-**10c** was obtained as a colorless oil (22 mg, 46%). $[\alpha]_D = +2.4$ (c 1.3 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 8.07$ and 6.94 (d, each 2H, $J = 9.0$ Hz), 7.23 (m, 5H), 5.98 (dd, 1H, $J =$ 17.3, 10.5 Hz), 5.47 (d, 1H, $J = 4.2$ Hz), 5.36 (d, 1H, $J = 17.3$ Hz), 5.16 (d, 1H, $J = 10.5$ Hz), 4.62 and 4.42 (d, each 1H, $J = 11.5$ Hz), 4.16 (m, 2H), 3.88 (s, 3H), 3.85 (m, 1H), 3.64 (dd, 1H, $J = 12.0$, 3.9 Hz), 1.40 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 165.6$, 163.7, 142.1, 137.5, 131.9, 128.4, 127.9, 127.8, 122.1, 114.1, 113.8, 84.1, 80.5, 77.2, 75.6, 73.0, 62.5, 55.5, 21.8 ppm; IR ($CHCl_3$): $\tilde{\nu} = 3434$, 1724 cm^{-1}; HRMS (ES): m/z: calcd for $C_{23}H_{27}O_6$: 399.1808 $[M+H]^+$; found: 399.1804.

General procedure for the Pt-catalyzed cyclization of allenic diols 3 and 4: Preparation of tetrahydrofuran **10a** and dihydropyrans **11** and **12**: [{Pt-(CH_2=CH_2)Cl_2}$_2$] (0.01 mmol) and tris(2,6-dimethoxyphenyl)phosphine (0.02 mmol) were added sequentially (methyl(triphenylphosphoranylidene)acetate (1.1 mmol) was also added for the preparation of adduct **12**) to a stirred solution of the corresponding allenic diol **3** and **4** (1.0 mmol) in dichloromethane (1.0 mL) under argon. The resulting mixture was stirred at room temperature until disappearance of the starting material (TLC). The reaction was quenched with brine (1.0 mL), the mixture was extracted with ethyl acetate (3×5 mL), and the combined extracts were washed twice with brine. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue eluting with ethyl acetate/hexane mixtures gave analytically pure adducts **10**–**12**.

Dihydropyran (+)-11: Prepared from β,γ-allendiol (−)-**3a** (50 mg, 0.18 mmol), and after chromatography of the residue with hexane/ethyl acetate (3:2) as the eluent (+)-**11** was obtained as a colorless oil (36 mg, 62%). $[\alpha]_D = +3.2$ ($c = 0.6$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 10.2$ (d, 1H, $J = 8.1$ Hz), 8.06 and 6.95 (d, each 2H, $J = 9.0$ Hz), 6.33 (m, 2H), 5.89 (d, 1H, $J = 8.1$ Hz), 4.38 (m, 2H), 3.88 (s, 3H), 2.09 ppm (d, 3H, $J = 1.2$ Hz); IR ($CHCl_3$): $\tilde{\nu} = 1732$, 1725 cm^{-1}.

Dihydropyran (+)-12: Prepared from β,γ-allendiol (−)-**3a** (50 mg, 0.18 mmol), and after chromatography of the residue with hexane/ethyl acetate (3:1) as the eluent (+)-**12** was obtained as a colorless oil (32 mg, 54%). $[\alpha]_D = +3.4$ ($c = 0.8$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 8.07$ and 6.96 (d, each 2H, $J = 9.0$ Hz, Ar), 7.81 (dd, 1H, $J = 15.1$, 12.0 Hz), 6.94 (m, 1H), 6.07 (m, 2H), 5.85 (d, 1H, $J = 15.1$ Hz), 4.34 (dd, 2H, $J = 5.6$, 1.6 Hz), 3.89 (s, 3H), 3.77 (s, 3H), 2.00 ppm (s ancho, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 163.6$, 163.2, 163.0, 141.9, 139.2, 132.6, 132.3, 126.7, 120.0, 113.7, 63.6, 55.5, 53.4, 51.5, 40.9, 21.0 ppm; IR ($CHCl_3$): $\tilde{\nu} = 1724$, 1720 cm^{-1}; HRMS (ES): m/z: calcd for $C_{19}H_{23}O_6$: 347.1495 $[M+H]^+$; found: 347.1499.

General procedure for the La-catalyzed cyclization of allenic diols 3 and 4: Preparation of tetrahydrofuran **10c**, diol **13**, and furan **14**. [La{N-($SiMe_3$)$_2$}$_3$] (0.05 mmol) was added to a stirred solution of the corresponding allenic diol **3** and **4** (1.0 mmol) in toluene (10.0 mL) under argon. The resulting mixture was stirred at reflux until disappearance of the starting material (TLC). The reaction was filtered through a celite plug before being concentrated under reduced pressure. Chromatography of the residue with ethyl acetate/hexane as the elutent gave analytically pure adducts **10**, **13**, and **14**.

Diol (+)-13: Prepared from β,γ-allendiol (−)-**3a** (50 mg, 0.18 mmol), and after chromatography of the residue with hexane/ethyl acetate (3:1) as the eluent (+)-**13** was obtained as a colorless oil (19 mg, 37%). $[\alpha]_D = +$ 2.6 ($c = 1.6$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 8.02$ and 6.93 (d, each 2H, $J = 9.0$ Hz, Ar), 4.86 (m, 2H), 4.52 (d, 2H, $J = 4.6$ Hz), 4.17 (m, 1H), 4.03 (dd, 1H, $J = 10.2$, 4.6 Hz), 2.58 (brs, 2H), 1.80 ppm (t, 3H, $J = 3.3$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 205.5$, 167.0, 163.6, 131.8, 122.1, 113.7, 98.9, 77.5, 72.9, 71.8, 65.7, 55.4, 15.0 ppm; IR ($CHCl_3$): $\tilde{\nu} = 3440$, 2990, 1942, 1724 cm^{-1}; ES-MS : m/z (%): 279 (100) $[M+H]^+$, 278 (6) $[M]^+$.

Furan 14: Prepared from β,γ-allendiol (−)-**3b** (50 mg, 0.14 mmol), and after chromatography of the residue with hexane/ethyl acetate (5:1) as the eluent **14** was obtained as a colorless oil (24 mg, 88%). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 7.38$ (m, 5H, Ar), 6.44 (s, 1H), 4.62 (s, 2H), 3.88 (br s, 1H), 2.46 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta =$ 151.6, 148.0, 133.9, 128.6, 127.4, 126.4, 121.6, 109.5, 57.5, 13.1 ppm; IR ($CHCl_3$): $\tilde{\nu} = 3432$ cm^{-1}; ES-MS: m/z (%): 189 (100) $[M+H]^+$, 188 (19) $[M]^+$.

Procedure for the Pd^0-catalyzed preparation of dihydropyran 16: [Pd-(PPh_3)$_4$] (11 mg, 0.0093 mmol) was added to a mixture of β,γ-allendiol (−)-**1a** (50 mg, 0.18 mmol), iodobenzene (22 μL, 0.19 mmol), and silver carbonate (99 mg, 0.36 mmol) in DMF (1.5 mL) under argon, and the resulting mixture was heated at 80 °C until disappearance of the starting material (TLC, 24 h). The reaction was quenched with brine (1.8 mL) and the mixture was extracted with ethyl acetate (3×3 mL). The organic

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extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue with ethyl acetate/hexane (1:3) as the eluent gave **16** as a colorless oil (16 mg, 35%).

Dihydropyran 2: ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ = 8.02 and 6.90 (d, each 2H, J = 9.0 Hz), 6.26 (s, 1H), 5.18 (s, 2H), 3.86 (s, 3H), 2.22 (br s, 3H), 1.94 ppm (br s, 3H); IR ($CHCl_3$): $\tilde{\nu}$ = 1725 cm^{-1}; ES-MS: m/z (%): 275 (100) $[M+H]^+$, 274 (11) $[M]^+$.

General procedure for the Pd^{II}-catalyzed cyclization of allenic diols 3 and 4 in the presence of allyl bromide: Preparation of dihydropyrans **17**, tetrahydrooxepines **18**, and tetrahydrofuran (+)-**19b**. Palladium(II) chloride (0.005 mmol) was added to a stirred solution of the corresponding allenic diol **3** and **4** (0.10 mmol) and allyl bromide (0.50 mmol) in DMF (0.6 mL). The reaction was stirred in an argon atmosphere until disappearance of the starting material (TLC). Water (0.5 mL) was added to the reaction mixture, which was extracted with ethyl acetate (3×4 mL). The organic phase was washed with water (2×2 mL), dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue with hexane/ethyl acetate as the eluent gave analytically pure adducts **17**–**19**.

Dihydropyran (+)-17a: Prepared from β,γ-allendiol (−)-**3a** (75 mg, 0.27 mmol), and after chromatography of the residue with hexane/ethyl acetate (4:1) as the eluent (+)-**17a** was obtained as a colorless oil (76 mg, 65%). $[\alpha]_D$ = +21.9 (c = 1.1 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ = 8.02 and 6.94 (d, each 2H, J = 9.0 Hz), 5.74 (m, 1H), 5.61 (d, 1H, J = 7.8 Hz), 5.11 (dd, 1H, J = 9.3, 1.7 Hz), 5.04 (t, 1H, J = 1.8 Hz), 4.16 (m, 2H), 3.88 (s, 3H), 3.68 (m, 3H), 2.87 and 2.68 (dd, each 1H, J = 15.5, 6.0 Hz), 1.67 ppm (br s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ = 166.7, 163.2, 134.0, 132.0, 131.9, 125.6, 121.9, 116.0, 113.7, 77.2, 68.3, 67.8, 62.4, 55.5, 33.2, 13.4 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3420, 1720 cm^{-1}; HRMS (ES): m/z: calcd for $C_{18}H_{22}O_5$: 318.1467 $[M^+]$; found: 318.1459.

Dihydropyran (−)-17b: Prepared from β,γ-allendiol (−)-**3b** (50 mg, 0.14 mmol), and after chromatography of the residue with hexane/ethyl acetate (3:1) as the eluent (−)-**17b** was obtained as a colorless oil (42 mg, 78%). $[\alpha]_D$ = −15.2 (c = 1.4 in $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ = 7.69 and 6.80 (d, each 2H, J = 9.0 Hz), 7.22 (m, 5H), 5.93 (br s, 1H), 5.69 (m, 1H), 5.05 (m, 2H), 4.41 and 4.28 (dd, each 1H, J = 16.0, 2.0 Hz), 3.82 (s, 3H), 3.76 (m, 3H), 2.72 ppm (d, 2H, J = 6.3 Hz); ^{13}C NMR ($CDCl_3$): δ = 166.3, 163.5, 136.8, 134.9, 132.0, 131.6, 128.7, 128.3, 128.1, 127.2, 121.8, 116.6, 113.5, 77.4, 67.7, 67.4, 62.3, 55.4, 34.5 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3424, 1715 cm^{-1}; ES-MS : m/z (%): 380 (17) $[M^+]$, 379 (100) $[M^+-1]$.

Tetrahydrooxepine (−)-18a: Prepared from γ,δ-allendiol (−)-**4a*M*** (76 mg, 0.19 mmol), and after chromatography of the residue with hexane/ethyl acetate (1:1) as the eluent (−)-**18a** was obtained as a colorless oil (49 mg, 59%). $[\alpha]_D$ = −1.5 (c = 0.1 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ = 8.05 and 6.90 (d, each 2H, J = 9.0 Hz), 7.35 (s, 5H), 5.76 (m, 1H), 5.68 (d, 1H, J = 3.6 Hz), 5.06 (m, 1H), 4.81 and 4.57 (d, each 1H, J = 11.6 Hz), 4.49 (dd, 1H, J = 16.3, 1.9 Hz), 4.19 (dd, 1H, J = 16.3, 1.7 Hz), 3.87 (s, 3H), 3.84 (m, 1H), 3.66 (m, 2H), 3.51 (m, 1H), 2.78 (dd, 1H, J = 15.6, 5.6 Hz), 2.62 (dd, 1H, J = 15.6, 6.3 Hz), 1.93 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ = 165.8, 163.4, 137.7, 134.5, 134.2, 131.7, 128.4, 128.1, 127.9, 122.8, 115.9, 113.7, 80.7, 79.3, 74.9, 73.5, 72.7, 63.9, 55.4, 35.3, 20.6 ppm; IR ($CHCl_3$: $\tilde{\nu}$ = 3431, 1728 cm^{-1}; HRMS (ES): m/z: calcd for $C_{26}H_{31}O_6$: 439.2121 $[M+H]^+$; found: 439.2124.

Tetrahydrooxepine (+)-18b: Prepared from γ,δ-allendiol (+)-**4b** (28 mg, 0.06 mmol), and after chromatography of the residue with hexane/ethyl acetate (3:1) as the eluent (+)-**18b** was obtained as a colorless oil (16 mg, 53%). $[\alpha]_D$ = +2.0 (c = 0.3 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ = 7.99 and 6.93 (d, each 2H, J = 9.0 Hz), 7.26 (m, 10H), 5.95 (d, 1H, J = 2.1 Hz), 5.69 (m, 1H), 5.03 (m, 2H), 4.73 and 4.52 (d, each 1H, J = 11.3 Hz), 4.71 and 4.41 (d, each 1H, J = 16.6 Hz), 3.88 (s, 3H), 3.82 (m, 2H), 3.71 and 3.56 (d, each 1H, J = 11.9 Hz), 2.69 (dd, 1H, J = 15.0, 6.2 Hz), 2.59 ppm (dd, 1H, J = 15.7, 6.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ = 165.4, 163.4, 142.3, 138.5, 137.5, 135.4, 134.0, 131.8, 128.5, 128.4, 128.3, 128.2, 127.4, 126.9, 116.6, 113.7, 81.0, 79.4, 74.5, 73.3, 72.6, 64.0, 55.5, 36.7 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3430, 1725 cm^{-1}; HRMS (ES): m/z: calcd for $C_{31}H_{32}NaO_6$: 523.2097 $[M+Na]^+$; found: 523.2095.

Tetrahydrofuran (+)-19b: Prepared from γ,δ-allendiol (−)-**4a*m*** (46 mg, 0.12 mmol), and after chromatography of the residue with hexane/ethyl acetate (1:1) as the eluent (+)-**19b** was obtained as a colorless oil (25 mg, 50%). $[\alpha]_D$ = +1.2 (c = 0.8 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ = 8.08 and 6.96 (d, each 2H, J = 9.0 Hz), 7.24 (m, 5H), 5.84 (m, 1H), 5.57 (d, 1H, J = 5.0 Hz), 4.58 and 4.42 (d, each 1H, J = 11.5 Hz), 4.21 (m, 1H), 4.08 (dd, 1H, J = 8.0, 5.0 Hz), 3.89 (s, 3H), 3.87 (dd, 1H, J = 12.2, 3.0 Hz), 3.66 (dd, 1H, J = 11.9, 5.0 Hz), 2.90 (d, 2H, J = 7.0 Hz), 1.44 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ = 165.6, 163.7, 150.8, 137.5, 136.4, 131.8, 128.3, 127.9, 127.8, 122.1, 116.7, 113.8, 111.3, 86.4, 80.3, 77.3, 74.8, 73.0, 62.9, 55.5, 36.2, 22.0 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3436, 1724 cm^{-1}; HRMS (ES): m/z: m/z: calcd for $C_{26}H_{31}O_6$: 439.2121 $[M+H]^+$; found: 439.2118.

General procedure for the Pd^{II}-catalyzed cyclization of allenic diols 3 in the presence of lithium bromide: Preparation of dihydropyrans **20** or tetrahydrofurans **21**: Palladium(II) acetate (0.01 mmol), lithium bromide (0.74 mmol), potassium carbonate (0.18 mmol), and copper(II) acetate (0.32 mmol) were added sequentially to a stirred solution of the corresponding β,γ-allendiol **3** (0.15 mmol) in acetonitrile (5 mL). The resulting suspension was stirred at room temperature in an oxygen atmosphere until the disappearance of the starting material (TLC). The organic phase was diluted with brine (2 mL), extracted with ethyl acetate (3×5 mL), washed with brine (2 mL), dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue with hexane/ethyl acetate as the eluent gave analytically pure adducts **20** and **21**.

Dihydropyran (+)-20a: Prepared from β,γ-allendiol (−)-**3a** (100 mg, 0.36 mmol), and after chromatography of the residue with hexane/ethyl acetate (3:1) as the eluent (+)-**20a** was obtained as a colorless oil (68 mg, 53%). $[\alpha]_D$ = +3.5 (c = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ = 8.07 and 6.95 (d, each 2H, J = 9.0 Hz), 5.71 (m, 1H), 4.34 (m, 2H), 3.89 (s, 3H), 3.72 (m, 3H), 1.84 ppm (d, 3H, J = 1.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ = 163.9, 164.0, 132.3, 132.0, 130.6, 119.7, 113.7, 77.3, 70.3, 68.7, 62.0, 55.5, 17.5 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3425, 1716 cm^{-1}; HRMS (ES): m/z: calcd for $C_{15}H_{17}BrO_5$: 356.0259 $[M]^+$; found: 356.0268.

Dihydropyran (−)-20b: Prepared from β,γ-allendiol (+)-**3c** (75 mg, 0.20 mmol), and after chromatography of the residue with hexane/ethyl acetate (6:1) as the eluent (−)-**20b** was obtained as a colorless oil (47 mg, 51%). $[\alpha]_D$ = −22.8 (c = 0.5 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ = 7.72 (m, 4H), 7.32 (m, 6H), 4.14 (m, 3H), 3.72 (td, 1H, J = 6.8, 3.1 Hz), 3.46 (dd, 1H, J = 7.3, 3.2 Hz), 3.36 (dd, 1H, J = 6.8, 5.1 Hz), 1.80 (br s, 3H), 1.06 ppm (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ = 135.9, 135.8, 134.8, 133.3, 132.6, 130.0, 127.8, 127.7, 119.4, 79.5, 70.4, 68.9, 61.9, 27.1, 26.8, 19.8 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3429 cm^{-1}; EI-MS : m/z (%): 461 (23) $[M^+]$, 443 (100).

Tetrahydrofuran (+)-21a: Prepared from β,γ-allendiol (−)-**3b** (50 mg, 0.14 mmol), and after chromatography of the residue with hexane/ethyl acetate (3:1) as the eluent (+)-**21a** (33 mg, 57%), which contained approximately 40% of its epimer as a colorless oil. The diastereoisomers of **21a** are inseparable by column chromatography (the ^{1}H and ^{13}C NMR data were obtained by analyzing the NMR spectra of the mixtures; however, the IR and MS spectroscopic data could not be assigned individually for them). $[\alpha]_D$ = +5.9 (c = 0.8 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ = 8.11 and 6.98 (d, each 0.8H, J = 9.0 Hz), 7.61 (m, 2H), 7.40 (m, 3H), 6.59 and 5.80 (d, each 0.6H, J = 2.0 Hz), 6.28 and 5.68 (d, each 0.4H, J = 1.7 Hz), 6.12 (d, 0.4H, J = 4.6 Hz), 5.29 (m, 0.6H), 4.67 (dd, 0.6H, J = 12.4, 3.2 Hz,), 4.07 (m, 2H), 3.89 (s, 1.8H), 3.87 (m, 0.4H), 3.77 ppm (s, 1.2H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ = 164.0 (m), 163.9 (M), 163.3 (m), 163.2 (M), 150.4 (M + m), 132.2 (M + m), 128.5 (m), 128.4 (M + m), 128.3 (M + m), 128.2 (M), 127.8 (M + m), 127.6 (M + m), 126.3 (M), 126.2 (m), 113.8 (m), 113.3 (M), 88.1 (M + m), 82.1 (M), 77.5 (m), 71.8 (m), 71.5 (M), 67.1 (m), 63.4 (M), 55.5 (M), 55.2 ppm (m); IR ($CHCl_3$): $\tilde{\nu}$ = 3435, 1718 cm^{-1}; EI-MS : m/z (%): 420 (98) $[M^+ + 2]$, 418 (100) $[M^+]$.

Tetrahydrofuran (−)-21b: Prepared from β,γ-allendiol (+)-**3d** (65 mg, 0.30 mmol), and after chromatography of the residue with hexane/ethyl acetate (3:1) as the eluent (−)-**21b** was obtained as a colorless oil (49 mg, 55%). $[\alpha]_D$ = −26.3 (c = 0.4 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ = 7.52 (m, 2H), 7.37 (m, 3H), 6.26 and 5.70 (d, each 1H, J = 1.7 Hz), 4.30 (m, 2H), 3.99 (dd, 1H, J = 9.5, 6.3 Hz,), 3.85 (dd, 1H, J = 9.5, 4.9 Hz), 3.74 (s, 3H), 3.48 ppm (d, 1H, J = 6.8 Hz); ^{13}C NMR

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(75 MHz, $CDCl_3$, 25 °C): $\delta = 150.7$, 128.5, 128.3, 128.1, 126.3, 118.7, 85.8, 77.2, 72.7, 71.2, 61.3 ppm; IR ($CHCl_3$): $\tilde{\nu} = 3432\ cm^{-1}$; HRMS (ES): m/z: calcd for $C_{13}H_{15}BrO_3$: 298.0205 $[M]^+$; found: 298.0212.

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