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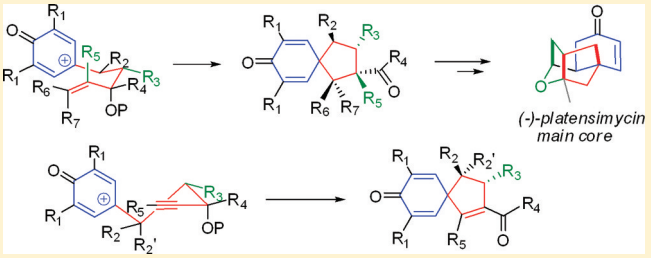
Oxidative Prins-Pinacol Tandem Process Mediated by a Hypervalent Iodine Reagent: Scope, Limitations, and Applications

Marc-André Beaulieu, Kimiaka C. Guérard, Gaëtan Maertens, Cyrille Sabot, and Sylvain Canesi*

Laboratoire de Méthodologie et Synthèse de Produits Naturels, Université du Québec à Montréal, C.P. 8888, Succ. Centre-Ville, Montréal, H3C 3P8 Québec, Canada

Supporting Information

ABSTRACT: An oxidative Prins-pinacol tandem process mediated by a hypervalent iodine reagent has been developed. This oxidative version of the famous tandem process fits within the concept of "aromatic ring umpolung" and allows the stereoselective transformation of simple phenols into highly elaborated spirocyclic dienone cores containing several quaternary carbon centers. The scope and the limitations of this process, including the study of its stereoselectivity, are described in this article. As a direct application of this stereoselective process, we describe the formal synthesis of (−)-platensimycin, an important antibiotic agent.



INTRODUCTION

Cationic molecular transpositions[1] provide an esthetically appealing route to complex molecular structures. A remarkable transformation of this type is the elegant Prins-pinacol tandem process; this method has been used as the key step in several total syntheses of natural products, as demonstrated by Overman and co-workers.[2] An extension of this aliphatic transformation to aromatic systems would open up several opportunities in chemical synthesis. Our interest in oxidative dearomatization of electron-rich aromatics[3] mediated by hypervalent iodine reagents[4−6] led us to question whether an analogous process could be initiated by oxidative activation. While electron-rich aromatic systems normally react as nucleophiles, oxidative activation converts them into highly electrophilic species, which may then be intercepted with appropriate nucleophiles. If one considers the behavior of intermediate **2**, this reversal of reactivity may be thought of as involving "aromatic ring umpolung".[3,4d] Phenol dearomatization processes mediated by hypervalent iodine reagents such as (diacetoxyiodo)benzene (DIB), an environmentally benign reagent, are well-documented in the literature, and this has elicited substantial interest in the synthetic arena.[4−7] An indication of how the formation of the corresponding phenoxonium ion **2** can be efficiently achieved and sufficiently stabilized to be trapped by a nucleophile is well apparent in the work of Kita,[7] who has shown that such processes are best performed in solvents such as hexafluoroisopropanol (HFIP).[8] Extending the aromatic ring umpolung concept[9] to the famous Prins-pinacol transformation would allow the rapid conversion of simple and inexpensive cores, such as phenols, into more complex spirodienone architectures,[3i] while controlling the stereoselective formation of quaternary carbon centers, in a single step.[10] We assumed that during the umpolung activation, mediated by a single-electron transfer (SET), the phenoxonium ion **2** generated would be trapped via an oxidative Prins process by the double bond, possibly through a cyclic chairlike transition state. This would be followed by a stereocontrolled ring contraction that should occur with retention of the configuration of the emerging quaternary carbon center (Figure 1).

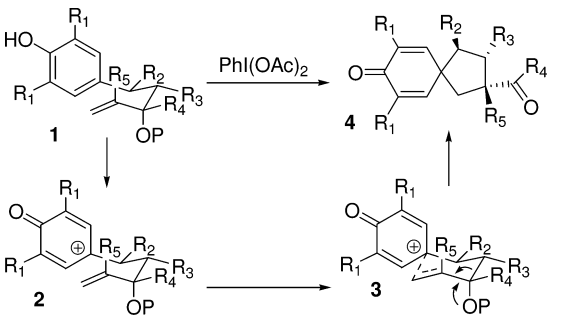


Figure 1. Presumed course of the oxidative Prins-pinacol tandem process.

Such spiro[4,5]decanyl scaffolds **4** are found in several natural products having interesting biological properties such as (+)-anhydro-*β*-rotunol **5**,[11] an antifungal agent, (+)-dehydrosolanascone **6**,[12] an antibacterial product resulting from a potential [2 + 2] cycloaddition process from **5**, (−)-scopadulcic acid A **7**,[13] an antiviral agent against herpes simplex virus type 1, and (+)-magellaninone **8**,[14] a compound belonging to the lycopodium family[15] (Figure 2).

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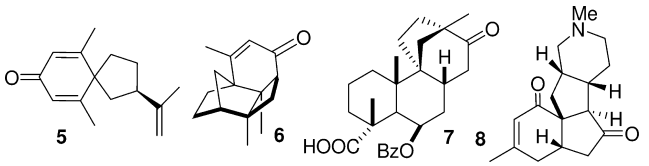


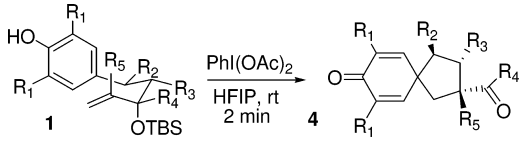
Figure 2. Natural products containing a spiro[4.5]decanyl core.

In this paper, we substantially extend the scope of the oxidative Prins-pinacol process to phenol derivatives containing allylic and propargylic alcohol moieties,[3i] and we present an avenue for the stereoselective formation of tertiary and quaternary carbon centers. Furthermore, as a first application to this process, the synthesis of the known main cage of (−)-platensimycin, a novel important class of antibiotic agent is reported.

RESULTS AND DISCUSSION

We first investigated the scope and limitations of this process on different phenols **1** containing a terminal alkene as an internal nucleophile to trigger the oxidative Prins process followed by a semipinacol-type rearrangement to produce the main spirocyclic system **4**. This reaction could be performed either in HFIP at room temperature or at −15 °C in an equal mixture of DCM/HFIP. To exemplify this transformation, different phenols substituted at any position on the lateral chain or at the *ortho*-positions were oxidized. A TBS moiety was first used as an alcohol protecting group in order to avoid the formation of the cyclic ether compound resulting from a direct attack by the alcohol on the phenoxonium ion **2** generated upon oxidation, as demonstrated by Kita and co-workers.[7] A summary of representative experiments appears in Table 1.

Table 1. Oxidative Prins-Pinacol Tandem Process of Olefinic Substrates



entry	R_1	R_2	R_3	R_4	R_5	yield (%)
a	H	H	H	Me	H	64
b	H	H	H	CH=CH_2	H	60
c	H	H	H	Ph	Me	58
d	H	H	H	Me	Me	68
e	Br	H	H	Me	Me	84
f	H	Me	H	Me	H	50
g	H	H	Me	Me	H	30
h	H	H	allyl	CH=CH_2	H	55

The anticipated ketones **4a**−**h** emerged in good yields (up to 84%) and with very good diastereoselectivity, dictated by allylic strain interactions in the chairlike transition state (entries f−h), and only one other diastereoisomer was detectable by ^{1}H NMR (5−10%). This method produced compact polysubstituted scaffolds containing substituents located at any of the positions on the lateral chain. It should be noted that in the case of R_5 being an alkyl group, the reaction simultaneously produces two quaternary carbon atoms, one of which is also a spiro center. The presence of bromines in *ortho*-positions appears to lead to an increase of the global yield of this transformation. This may be explained by considering that the first intermediate is a highly delocalized carbonium ion, which can be represented by **2** (Figure 1, R_1 = Br) as one of its resonance structures. We believe that, because of the presence of the electron-withdrawing bromine atoms, **2** would be the dominant resonance form rather than the *ortho*-mesomer and thus would be less susceptible to a bimolecular attack by external nucleophiles at the *ortho*-position. As an additional advantage, the bromine atoms provide a handle for the introduction of other substituents, using transition metal chemistry. Compound **4g** was obtained in a low 30% yield, about half of the yield recorded earlier for substrates without substituents in position 2 (R_3 = H). This result could shed light on the stereochemical course of the reaction: a 1:1 epimeric mixture of the tertiary alcohol moiety in **1g** is oxidized, and it is possible that only one diastereoisomer, having minimal $A^{1,3}$ interactions, is a competent substrate for the requisite oxidative Prins-pinacol process. Indeed, the conformation of diastereomer **2g**, which presumably undergoes reaction, is such that the OTBS group is subjected to minimal $A^{1,3}$ interaction with the "inside" vinylic hydrogen.[16] This contrast with diastereomer **2g′**, where the allylic interaction is considerably more severe, due to the presence of a more sterically demanding methyl group in proximity to the same vinylic hydrogen. This interaction could slow the Prins step of diastereoisomer **2g′** and divert the reactive electrophilic species, created upon *umpolung* activation of the phenol, toward other reaction pathways. In either case, the major product of the reaction is *cis*-ketone **4g**[17] (Scheme 1).

To support this hypothesis, compound **1h**, containing an allyl substituent at position 2, was prepared. In this case, both vinyl groups at position 3 (R_4 = vinyl and R_5 = H) were able to trap the phenoxonium ion species, thus automatically placing the OTBS group in an axial position in the transition state **2h**, to generate compound **4h** in a 55% yield, comparable to that obtained with similar substrates.

This transformation is not restricted to the formation of ketones but can be extended to the formation of aldehydes from secondary allylic ethers. In this case, a protecting group more hindered than a TBS group must be used. Indeed, in the absence of a tertiary center, the phenoxonium ion, generated during umpolung activation, is more accessible to the oxygen atom and leads mainly to cycloether **10** via a five-membered ring, and only a small amount of the desired compound **12** was observed. In order to favor the 6-*endo* process, the secondary alcohol moiety was protected with the bulky TIPS protecting group. Moreover, the formation of aldehyde **12** required the use of PIFA (phenyliodine(III)bis(trifluoroacetate) instead of DIB, to prevent the formation of a mixed acetal, such as **15** in 43% yield. The formation of the latter resulted from the nucleophilic attack of an acetate ion, released upon umpolung activation, on intermediate **14**. The presence of the less nucleophilic trifluoroacetate ligands on the hypervalent iodine complex (PIFA) allowed formation of the aldehyde **12** in 61% yield. It should be noted, however, that the mixed acetal function in **15** could be useful if a protected aldehyde is required in the synthesis (Scheme 2).

In order to broaden the scope and test the limitations of this transformation, we have also substituted the C-1 alkene position with two methyl groups.[9] This result suggests the potential for constructing highly hindered cores containing two contiguous quaternary carbon centers. Indeed, the elaboration of such challenging systems is often prevented by the steric hindrance of the first quaternary carbon center. During the

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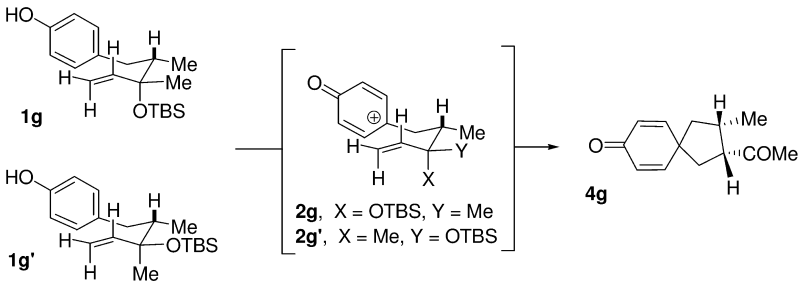
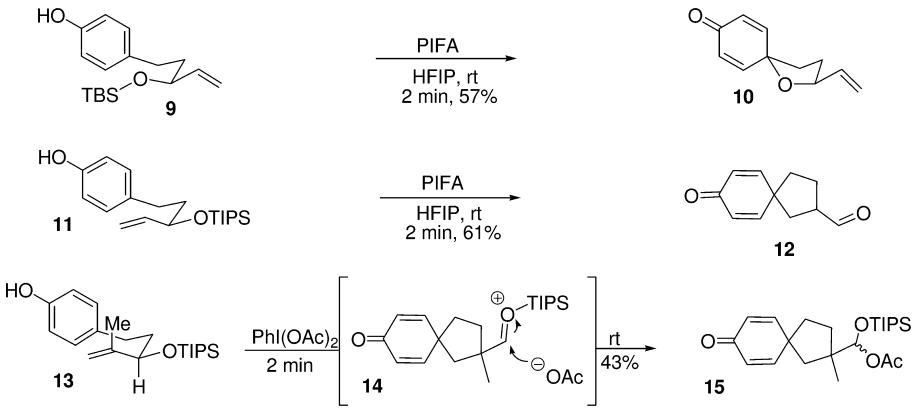
Scheme 1. $A^{1,3}$ Strain Interactions Involved during the Transition State of Compound 1g



Scheme 2. Formation of Aldehyde and Acetal Functionalities



oxidation of compound **16**, the aldehyde **17** formed was not stable and further transformed into the corresponding tricyclic core **18** via a Michael addition on the dienone system mediated by the aldehyde functionality to produce hemiacetal **18** in 40% overall yield. It should be stressed that this is a one-pot multistep, stereoselective transformation producing a functionalized, highly congested tricyclic system **18** (Scheme 3).

Our next stage was to develop an enantioselective pathway enabling the formation of tertiary or quaternary carbon centers from an enantiopure (or an enantioenriched) substrate containing a stereogenic allylic alcohol functionality on the acyclic lateral chain, such as (+)-**13**.[18a] For this to be successful, the conformational equilibrium, involved during the chairlike transition state, had to be easily shifted to one conformer, considering all the possible $A^{1,2}$, $A^{1,3}$, and 1,3-diaxial steric interactions, as well as the stereoelectronic effects involved. Indeed, conformers **19** will lead stereoselectively, after a ring contraction, to the two opposite stereocenters of **20**. In this case, the two conformers **19** and **19′** each have their own steric interactions, resulting in overall low enantioselectivity. Conformer **19′** has to accommodate $A^{1,3}$ and 1,3-diaxial steric interactions, whereas conformer **19** presents more severe $A^{1,2}$ interactions. The balance of these effects results in the formation of both enantiomers of compound **20** in 68% yield with low enantiomeric excess[19] (30%) (Scheme 4). Such a result suggests that, in principle, and depending on the protecting group used, the same enantiopure tertiary alcohol **13** could lead to an excess of either *R* or *S* compound **20**. Indeed, an O-TBS version of (*R*)-**13** that would favor conformer **19′** led to an excess of the opposite enantiomer (*R*)-**20** with a similar ee.[19] To improve this enantioselectivity, we removed the mismatched steric $A^{1,2}$ interaction generated by the allylic methyl group and the smaller TBS protecting group was used. As a result, an enantioenriched form of compound (*R*)-**1a** (70% ee) was synthesized.[18b] During the umpolung activation, the two conformers **21** and **21′** can equilibrate, but the transition state originating from **21′** should be the most stable (Scheme 1). Compound (*R*)-**4a** was obtained with the same optical purity (70% ee)[19] as the starting material used, thus demonstrating the high reaction enantioselectivity in this case (Scheme 4).

In order to develop an efficient stereoselective route to compounds containing a quaternary carbon center, we resorted to a diastereoselective reaction where one transition state would be favored over the other. In the desired conformer **24**, the set stereochemistry of the quaternary methyl group dictates the configuration of the emerging quaternary carbon center, such that chirality transfer takes place with retention of configuration (Scheme 5). Therefore, a *trans*-cycloether **23** was synthesized, and in this case, only the formation the bicyclic transition state **24** was permitted. The required tetrahydrofuran core **23**, involving minimal $A^{1,2}$ interaction between the equatorial oxygen atom and the methyl group, and therefore presumably thermodynamically favored, was obtained by acid treatment of the mixture of triols **22** in 88% yield. The asymmetric version of **22** was assembled using Evans' asymmetric alkylation technology.[20] Umpolung activation of cycloether **23** led to the hemiketal **26** after the ring contraction, ring elongation process in 70% yield. Further treatment of the crude mixture of anomers **26** with Dess–Martin oxidation periodinate[21] led to keto-aldehyde **27** as a single diastereoisomer in 60% yield overall from compound **23**. As anticipated, on the basis of our mechanistic hypothesis, compound **27** displayed a *cis*-relative configuration between the two carbonyl branches. It should be noted that, in this new process, we have efficiently created a pair of contiguous stereocenters, one tertiary and the other quaternary, with complete degree of stereocontrol, thus

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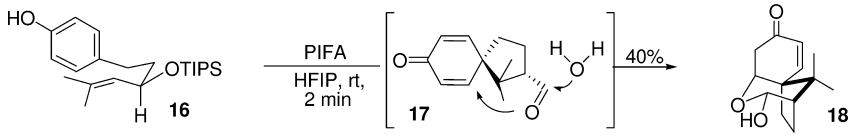
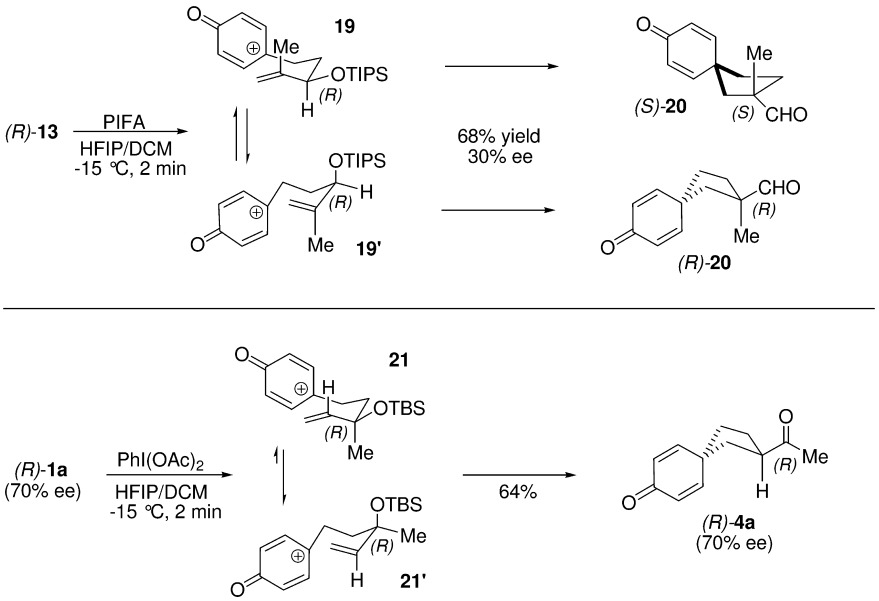
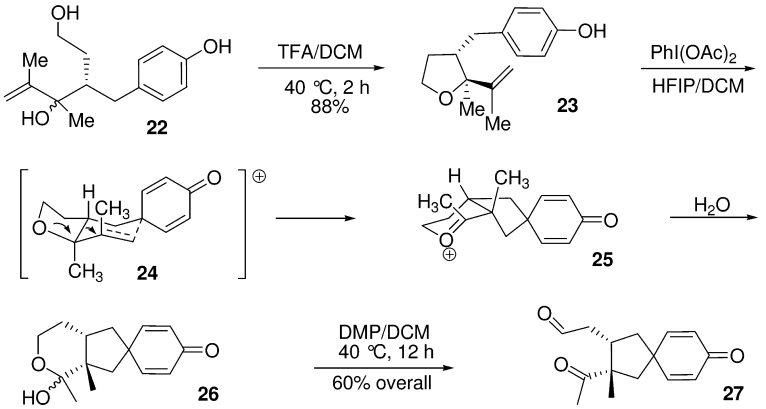
Scheme 3. Formation of Contiguous Quaternary Carbon Centers



Scheme 4. Stereoselectivity Issues Following the Conformational Equilibriums



Scheme 5. Efficient diastereoselective avenue for the formation of a quaternary carbon center



demonstrating the potential practical utility of this oxidative process in a diastereoselective pathway (Scheme 5).

We were also interested in extending this process to acetylenic substrates **28** to readily produce interesting polyfunctionalized and polysubstituted compact spiro[4,5]-decanyl systems **30**. In order to broaden the scope and limitation of this new transformation, different phenols, containing several substituents at any position on the lateral chain, were investigated. The desired compound **30** was obtained in 46−81% yield. A summary of representative experiments appears in Table 2.

This novel tandem process allows the production, in useful to good yield (up to 81%), of the scaffold **30**, a compact polysubstituted and functionalized subunit present in several natural products. This key functionalized core was easily obtained from simple and inexpensive phenols. It should be stressed that this process occurs even in presence of hindered alkynes with yields similar to those of unhindered alkynes and allows the generation of a contiguous quaternary carbon center and a tetrasubstituted alkene moiety. In addition, the geometry provided by the half-chair transition state **29** appears to tolerate a wide range of bulky substituents on the lateral chain. Indeed, the absence of 1,3-allylic strain interactions allows the presence of substituents in position 2 and leads to good yields of the desired system (up to 81%, **28f** and **28h**), by contrast with compound **4h** (Scheme 1). As already observed in Table 1, the presence of bromines in the *ortho*-position increased considerably the global yield of this transformation (**30e** versus **30f** and **30g** versus **30h**). This reaction can also generate a conjugated aldehyde functionality (**30m**) in 47% yield from compound **28m**. The presence of a more hindered TIPS as an oxygen protecting group was still required with a secondary alcohol moiety to efficiently produce the aldehyde functionality. As a demonstration of the potential of this new process,

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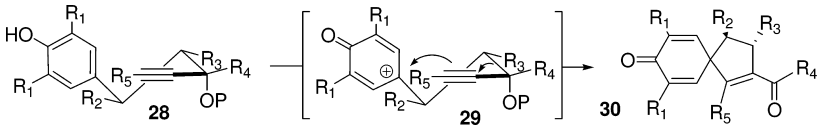
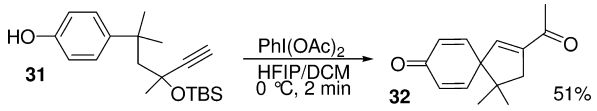
Table 2. Oxidative Prins-Pinacol Tandem Reaction with Alkynes



entry	P	R_1	R_2	R_3	R_4	R_5	yield (%)
a	TBS	H	H	H	Me	H	**51**
b	TBS	H	H	H	Me	*n*-Bu	**48**
c	TBS	H	H	H	Me	*n*-Dec	**55**
d	TBS	H	H	Me	Me	H	**46**
e	TBS	H	H	Me	≡—H	H	**57**
f	TBS	Br	H	Me	≡—H	H	**78**
g	TBS	H	H	Me	≡—*n*-Bu	*n*-Bu	**60**
h	TBS	Br	H	Me	≡—*n*-Bu	*n*-Bu	**81**
i	TBS	H	H	H	≡—*n*-Dec	*n*-Dec	**50**
j	TBS	H	H	Allyl	≡—*n*-Bu	*n*-Bu	**53**
k	TBS	H	Me	H	≡—*n*-Bu	*n*-Bu	**56**
l	TBS	H	Me	H	≡—H	H	**53**
m	TIPS	H	H	H	H	H	**47**

compound **31**, containing a *gem*-dimethyl benzylic functionality, was prepared and the subsequent "umpolung activation" of this polysubstituted phenol resulted in compound **32** in 51% yield. In this case, the compact polyfunctionalized system contains two contiguous quaternary carbon centers and a trisubstituted alkene moiety. Such a hindered structure represents a difficult scaffold to synthesize. This new process represents an expeditious access to such challenging structures (Scheme 6).

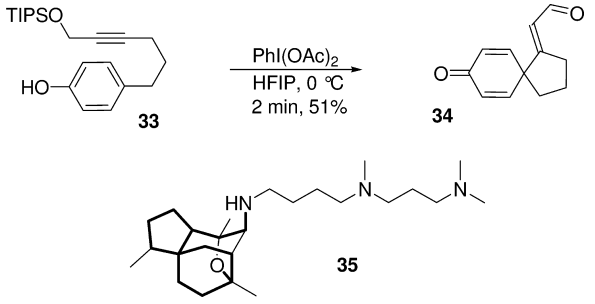
Scheme 6. Formation of Contiguous Quaternary Carbon Centers and a Trisubstituted Alkene Moiety



The process was also extended to compounds containing a propargylic ether in position 6 such as **33**, producing the aldehyde **34** in 51% yield via an exocyclic Prins-pinacol process. In this case, a 5-*exo*-dig cyclization was observed instead of the standard 6-*endo*-dig mode normally observed with substrates such as **28** (Table 2), prompted by the sterically demanding ether moiety generated in position 3. In the case of an unsubstituted position 3, however, with an alkyne segment substituted in position 5, the process now proceeds via a 5-*exo*-dig mode cyclization, leading to the spiro[5.5]undecanyl structure **34** with good selectivity (9/1) in favor of the *E*-isomer, as observed by NMR. This new reaction course of compounds containing an alkyne functionality, which hinges on the position of the ether moiety during the oxidative Prins transformation, opens the door to novel opportunities such as the facilitated construction of the subunit present in the natural product (−)-hispidospermidin **35**[22] (Scheme 7).

It should be noted that the oxidative Prins-pinacol reaction proceeded sometimes with formation of byproducts such as **37** (Scheme 8; in 5−10% yield). The formation of such spiro[5.5]undecanyl systems was rationalized by invoking an alkyl migration from intermediate **36**, occurring in competition with ring contraction, albeit to a minor extent. While the ring contraction was the major pathway, migration of the acyclic moiety could occasionally be observed (Scheme 8).

Scheme 7. 5-*exo*-dig Cyclization of Substrate with Propargylic Ether at Position 7



As an initial application of the oxidative Prins-pinacol tandem sequence, we describe now a formal synthesis of (−)-platensimycin **53**.[23] This substance is an exciting experimental antibiotic that is believed to act as a FabF inhibitor.[23a] Its unusual structure and potent bioactivity have elicited enormous interest in the synthetic community.[23] Our strategic approach to (−)-platensimycin targeted compound **52**, an advanced intermediate in Nicolaou's total synthesis[24] (Figure 3).

The availability of a straightforward route to compounds such as **4** or **30** presents new opportunities for the formation of the main core of natural products such as (−)-platensimycin, **53**. To that effect, the enantioenriched cycloether compound **23** was obtained using Evans's asymmetric alkylation technology from compound **38** (Scheme 5).[3i] At this stage, we had assumed that a Baeyer−Villiger reaction or a similar transformation on the hemiketal **26** would produce the required tertiary alcohol functionality in a compound (**43**) which contains the carbon framework of the desired target. Unfortunately, direct treatment of compound **26** in presence of mCPBA failed to produce **43**, and instead, an epoxide was recovered resulting from mCPBA over oxidation of alkene **42** (Scheme 9). Consequently, we proceeded to investigate alternatives to the Baeyer−Villiger process, such as the useful methodologies developed by Schreiber and co-workers.[25,26] Indeed, during the phenolic activation of cycloether **23** with the hypervalent iodine reagent, the resulting oxonium species **25** (Scheme 5) can be trapped in the same pot with hydrogen peroxide, affording a 3:2 mixture of unassigned diastereoisomers of hydroperoxyketal **39** in 64% yield from **23**

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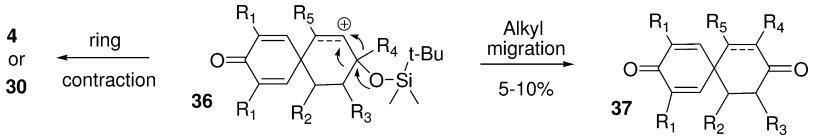
Scheme 8. Formation of Spiro[5.5]undecanyl Byproducts



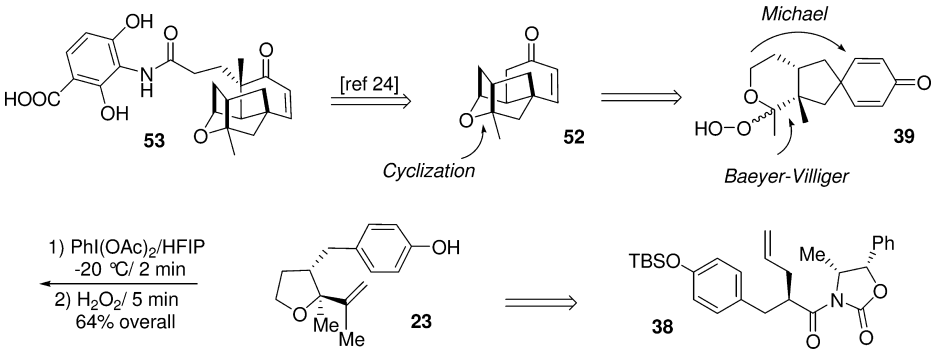
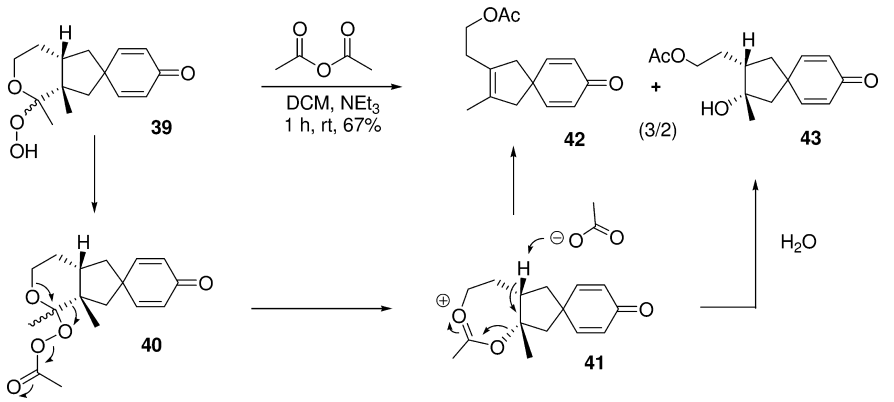


Figure 3. Structure of (−)-platensimycin and retrosynthetic logic.

Scheme 9. Schreiber Fragmentation Process on the Hydroperoxyketal 39

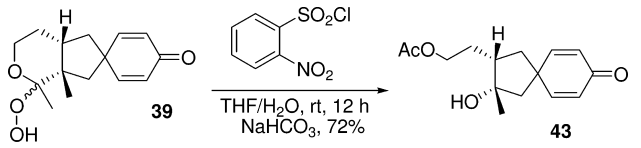


(Figure 3). Further treatment of this hydroperoxyketal in presence of acetic anhydride[25] furnished a mixture of the desired alcohol **43** and the unwanted tetrasubstituted alkene **42** in 67% yield in a 3:2 ratio in favor of the alkene. This alkene functionality presumably results from an elimination promoted by the released acetate ion on the anti-periplanar hydrogen on intermediate **41**; the desired compound **43** would result from the hydrolysis of the oxonium species **41** (Scheme 9).

To optimize the formation of alcohol **43**, we decided to perform this transformation in a biphasic medium using a Schotten−Baumann-type procedure on hydroperoxides **39**. Indeed, in such conditions, the presence of water favored the nucleophilic attack on the oxonium **41**, leading almost exclusively to the formation of the desired alcohol **43** with the required configuration, thereby demonstrating the stereoselectivity of the oxidative process (Scheme 5). This transformation could be performed with acetic anhydride; however, 2-nosyl chloride proved to be more convenient as a peroxide activator, affording **43** in 72% yield. During this transformation, the ketal function of **39** has been replaced by the desired alcohol functionality (**43**) with retention of configuration in good yield (Scheme 10).

Subsequently, the acetate group was removed and the primary alcohol obtained was selectively oxidized to the hemiketal **44** in presence of IBX in 80% yield. Further

Scheme 10. Stereoselective Formation of the Tertiary Alcohol Moiety



treatment of **44** with thiophenol and TFA produced thio-acetal **45** in 70% yield. Unfortunately, all radical or anionic attempts to produce the main cage core **52** from **45** failed, and only traces of the desired compound **52** was observed during the treatment of **45** with lithium naphthalenide (LN) (Scheme 11).

As first demonstrated by Nicolaou,[24] it appears that the formation of the main cage was not so straightforward, most probably due to the presence of the quaternary carbon center. Indeed, in the literature, few reactions allowing the formation of such a system by a Michael addition have been reported;[24] as an example, the Stetter transformation did not proceed.[24] To be able to produce a formal synthesis of (−)-platensimycin, we decided to sacrifice the second quaternary carbon center generated with total stereocontrol during the "umpolung activation" to obtain a flat and less hindered cyclopentene moiety, in order to favor the Michael addition required. In the

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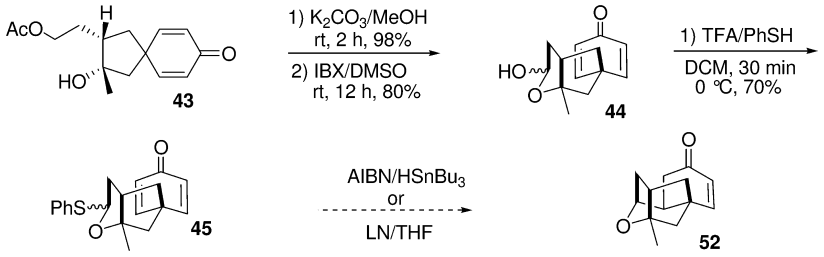
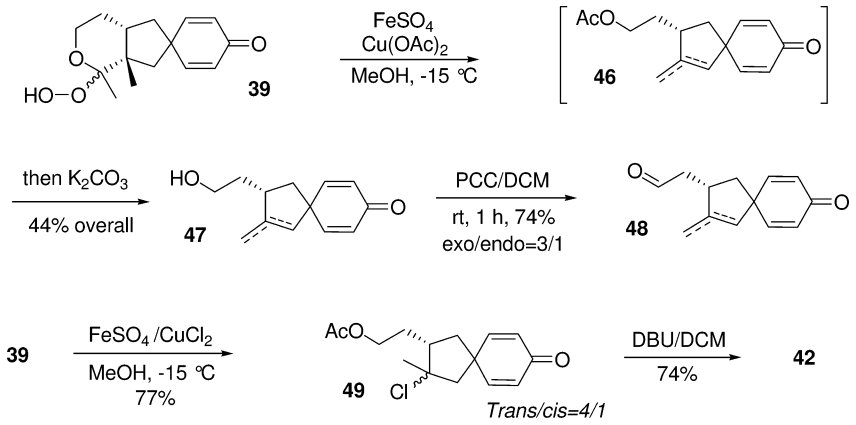
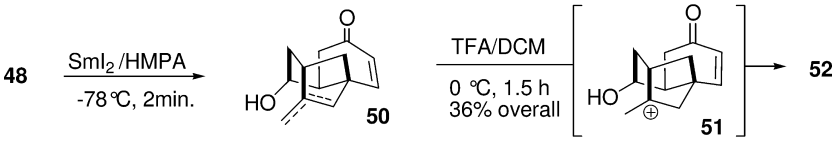
Scheme 11. First Unsuccessful Pathway to the Main Core



Scheme 12. Schreiber–Fenton Fragmentation Process



Scheme 13. Formal Synthesis of (−)-Platensimycin



event, hydroperoxide **39** was treated with a mixture of the Fenton reagent ($FeSO_4$) and $Cu(OAc)_2$ in MeOH to produce the intermediate **46**, and a subsequent addition of K_2CO_3 to the reaction mixture induced conversion to **47** in 44% overall yield from **29**. Compound **47** was obtained as a 3:1 mixture of exocyclic (major) and endocyclic alkenes. The substitution of $Cu(OAc)_2$ by $CuCl_2$ during the Schreiber fragmentation[26] led exclusively to the chloro compound **49** in good yield (74%) with 4:1 selectivity in favor of the *trans* isomer but, as presumed, subsequent treatment with DBU led mainly to the undesired tetrasubstituted alkene **42**. As demonstrated first by Nicolaou et al.,[24] both isomers of compound **48** converge to the tetracyclic main core of platensimycin **52**. Accordingly to this hypothesis, no separation was required at this stage. The alcohol mixture **47** was thus advanced to a mixture of the corresponding aldehydes **48** in 74% yield by PCC oxidation (Scheme 12).

Both compounds in the mixture **48** are known synthetic precursors[24] for (−)-platensimycin. Accordingly, they were treated by Kagan's reagent (SmI_2),[27] whereupon stereoselective cyclization to alcohols **50** occurred via a regular aliphatic umpolung transformation (Scheme 13).[28] Finally, the alkene mixture **50** was transformed to the known cage compound **52** upon treatment with TFA via the formation of a common tertiary carbocation **51**. The final elaboration of **52** to (−)-platensimycin is well-known in the literature.[24] Therefore, the synthesis of **52** represents a formal synthesis of (−)-platensimycin (Scheme 13).

■ CONCLUSION

In summary, an oxidative Prins-pinacol tandem process has been developed. This version represents an extension to aromatic systems of this important transformation and allows the generation of compact polyfunctionalized and polysubstituted spiro[4.5]decanyl systems containing several quaternary carbon centers from inexpensive phenol derivatives. In addition, we have devised an enantioselective and a diastereoselective pathway to compounds containing tertiary and quaternary carbon centers; these scaffolds are present in numerous natural products that bear important biological activities. As the first application of this novel process, a formal synthesis of (−)-platensimycin has been achieved. This demonstrates the synthetic potential of this novel oxidative extension of the Prins-pinacol process, as well as the utility of the "aromatic ring umpolung" concept.

■ EXPERIMENTAL SECTION

Unless otherwise indicated, ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, in $CDCl_3$ solutions. Chemical shifts are reported in parts per million on the δ scale. Multiplicities are described as s (singlet), d (doublet), dd, ddd, etc. (doublet of doublets, doublet of doublets of doublets, etc.), t (triplet), q (quartet), quin (quintuplet), m (multiplet), and further qualified as app (apparent), br (broad). Coupling constants, J, are reported in hertz. IR spectra (cm^{-1}) were

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recorded from thin films. Mass spectra (m/e) were measured in the electrospray (ESI) mode.

General Procedure for the Oxidative Prins-Pinacol Process. A solution of $PhI(OAc)_2$ ("DIB", 38 mg, 0.11 mmol, 1.1 equiv) in $(CF_3)_2CHOH$ ("HFIP", 0.25 mL) was added over 5 s to a vigorously stirred solution of phenol (0.1 mmol, 1 equiv) in 0.75 mL of a solution of CH_2Cl_2/HFIP (2/1) cooled to −15 °C for a few seconds (to avoid precipitation of HFIP) or in 0.75 mL of HFIP at room temperature. After addition of DIB, the solution was stirred for 2 min, quenched with 0.1 mL of acetone, filtered directly over silica gel (*n*-hexane/EtOAc, 1:1), and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography with a mixture of ethyl acetate/hexane to afford the corresponding dienone.

2-Acetylspiro[4.5]deca-6,9-dien-8-one (***4a***): Pale yellow oil, 0.064 mmol, 12.2 mg, 64% yield; IR ν (cm^{-1}) 2957, 1707, 1660, 1623; ^1H NMR (600 MHz, $CDCl_3$) δ 6.87 (dd, J = 10.2, 3.0 Hz, 1H), 6.86 (dd, J = 10.2, 3.0 Hz, 1H), 6.21 (d, J = 10.8 Hz, 2H), 3.31 (quin, J = 7.8 Hz, 1H), 2.22 (s, 3H), 2.21−2.10 (m, 3H), 1.95−1.78 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.7, 185.9, 154.1, 152.9, 127.7, 127.6, 51.3, 48.5, 38.9, 37.5, 29.2, 28.0; HRMS (ESI) calcd for $C_{12}H_{15}O_2$ $(M + H)^+$ 191.1067, found 191.1065.

2-Acryloylspiro[4.5]deca-6,9-dien-8-one (***4b***): Pale yellow oil, 0.060 mmol, 12.0 mg, 60% yield; IR ν (cm^{-1}) 2935, 1661, 1615, 1404; ^1H (600 MHz, $CDCl_3$) δ 6.91 (d, J = 9.6 Hz, 2H), 6.43 (dd, J = 17.4, 9.6 Hz, 1H), 6.40 (d, J = 17.4 Hz, 1H), 6.23 (d, J = 9.6 Hz, 2H), 5.89 (d, J = 9.6 Hz, 1H), 3.58 (quin, J = 8.4 Hz, 1H), 2.21−2.17 (m, 3H), 1.99−1.82 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 200.6, 186.0, 154.2, 152.9, 135.4, 129.1, 127.7, 127.7, 48.7, 47.6, 39.1, 37.7, 28.5; HRMS (ESI) calcd for $C_{13}H_{15}O_2$ $(M + H)^+$ 203.1067, found 203.1063.

2-Benzoyl-2-methylspiro[4.5]deca-6,9-dien-8-one (***4c***): Pale yellow oil, 0.058 mmol, 15.5 mg, 58% yield; IR ν (cm^{-1}) 2935, 1667, 1622, 1445, 1260; ^1H (300 MHz, $CDCl_3$) δ 7.88 (d, J = 7.6 Hz, 2H), 7.54 (d, J = 7.6 Hz, 1H), 7.45 (d, J = 7.6 Hz, 2H), 6.93 (dd, J = 10.0, 2.9 Hz, 2H), 6.80 (dd, J = 10.0, 2.9 Hz, 1H), 6.23 (dd, J = 10.0, 1.7 Hz, 1H), 6.15 (dd, J = 10.0, 1.7 Hz, 1H), 2.81 (dt, J = 12.9, 7.0 Hz, 1H), 2.78 (d, J = 14.0 Hz, 1H), 2.06 (dt, J = 12.9, 7.0 Hz, 1H), 2.00 (dt, J = 12.9, 7.0 Hz, 1H), 1.93 (d, J = 14.0 Hz, 1H), 1.84 (dt, J = 12.9, 7.0 Hz, 1H), 1.64 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 204.1, 185.9, 154.5, 153.6, 135.1, 132.3, 129.2, 128.3, 127.6, 127.0, 55.5, 48.7, 47.8, 37.5, 37.3, 28.6; HRMS (ESI) calcd for $C_{18}H_{19}O_2$ $(M + H)^+$ 267.1380, found 267.1381.

2-Acetyl-2-methylspiro[4.5]deca-6,9-dien-8-one (***4d***): Pale yellow oil, 0.059 mmol, 12.1 mg, 59% yield; IR ν (cm^{-1}) 2928, 1701, 1662, 1623; ^1H NMR (600 MHz, $CDCl_3$) δ 6.86 (d, J = 10.2 Hz, 2H), 6.17 (d, J = 10.2 Hz, 1H), 6.15 (d, J = 10.2 Hz, 1H), 2.48 (d, J = 14.4 Hz, 1H), 2.41−2.37 (m, 1H), 2.21 (s, 3H), 1.92−1.73 (m, 3H), 1.59 (d, J = 14.4 Hz), 1.41 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 211.1, 185.9, 154.4, 154.1, 127.2, 126.9, 56.7, 48.4, 45.3, 37.2, 36.1, 25.8, 25.2; HRMS (ESI) calcd for $C_{13}H_{17}O_2$ $(M + H)^+$ 205.1223, found 205.1222.

2-Acetyl-7,9-dibromo-2-methylspiro[4.5]deca-6,9-dien-8-one (***4e***): Pale yellow oil, 0.084 mmol, 30.2 mg, 84% yield; ^1H NMR (600 MHz, $CDCl_3$) δ 7.38 (d, J = 2.9 Hz, 1H), 7.33 (d, J = 2.9 Hz, 1H), 2.64 (d, J = 14.1 Hz, 1H), 2.37 (m, 1H), 2.24 (s, 3H), 2.41−2.37 (m, 1H), 2.21 (s, 3H), 1.97 (m, 1H), 1.91−1.82 (m, 2H), 1.65 (d, J = 14.1 Hz), 1.44 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 210.7, 172.5, 154.4, 120.4, 120.2, 56.8, 53.9, 44.2, 36.7, 36.3, 25.4, 25.1; HRMS (ESI) calcd for $C_{13}H_{15}Br_2O_2$ $(M + H)^+$ 362.9412, found 362.9416.

trans-3-Acetyl-1-methylspiro[4.5]deca-6,9-dien-8-one (***4f***): Pale yellow oil, 0.050 mmol, 10.1 mg, 50% yield; IR ν (cm^{-1}) 2924, 1711, 1663, 1624; ^1H NMR (300 MHz, $CDCl_3$) δ 6.86 (dd, J = 10.4, 2.2 Hz, 1H), 6.74 (dd, J = 10.4, 2.2 Hz, 1H), 6.36 (d, J = 10.4 Hz, 1H), 6.33 (d, J = 10.2 Hz, 1H), 3.34 (m, 1H), 2.40−2.10 (m, 3H), 2.23 (s, 3H), 1.94 (dd, J = 13.2, 8.2 Hz, 1H), 1.85 (d, J = 13.2, 8.2 Hz), 0.77 (d, J = 7.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.8, 186.4, 154.5, 149.4, 129.9, 129.8, 53.0, 49.0, 44.4, 39.3, 34.9, 29.1, 14.1; HRMS (ESI) calcd for $C_{13}H_{17}O_2$ $(M + H)^+$ 205.1223, found 205.1218.

cis-2-Acetyl-3-methylspiro[4.5]deca-6,9-dien-8-one (***4g***): Pale yellow oil, 0.030 mmol, 6.0 mg, 30% yield; IR ν (cm^{-1}) 2958, 2930, 1707, 1661, 1620; ^1H (300 MHz, $CDCl_3$) δ 7.20 (dd, J = 9.9, 2.7 Hz, 1H), 6.93 (dd, J = 9.9, 2.7 Hz, 1H), 6.20 (d, J = 9.9 Hz, 1H), 6.16 (d, J = 9.9 Hz, 1H), 3.39 (q, J = 8.1 Hz, 1H), 2.81−2.70 (m, 1H), 2.32 (dd, J = 14.4, 7.8 Hz, 1H), 2.22 (s, 3H), 1.92−1.72 (m, 3H), 1.30 (d, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 209.8, 186.0, 155.8, 153.6, 127.5, 126.5, 54.7, 46.9, 44.8, 38.3, 36.9, 31.8, 16.5; HRMS (ESI) calcd for $C_{13}H_{17}O_2$ $(M + H)^+$ 205.1223, found 205.1226.

cis-2-Acryloyl-3-allylspiro[4.5]deca-6,9-dien-8-one (***4h***): Pale yellow oil, 0.055 mmol, 11.2 mg, 55% yield; IR ν (cm^{-1}) 2928, 1701, 1662, 1623; ^1H NMR (600 MHz, $CDCl_3$) δ 6.82 (d, J = 10.0 Hz, 1H), 6.74 (d, J = 10.0 Hz, 1H), 6.38 (d, J = 10.0 Hz, 1H), 6.35 (d, J = 10.0 Hz, 1H), 5.68 (m, 2H), 5.09 (d, J = 17 Hz, 1H), 5.07 (d, J = 10 Hz, 1H), 4.94 (d, J = 16.4 Hz, 1H), 4.91 (d, J = 10 Hz, 1H), 2.57 (m, 2H), 2.45 (m, 1H), 2.39 (t, J = 7.6 Hz, 1H), 2.26 (m, 1H), 2.09 (dd, J = 13.5, 8.8 Hz, 1H), 1.91 (t, J = 11.7 Hz), 1.83 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.2, 185.8, 154.1, 148.2, 135.1, 134.3, 130.8, 130.4, 118.1, 117.3, 58.8, 48.2, 45.5, 38.4, 35.3, 30.6; HRMS (ESI) calcd for $C_{16}H_{19}O_2$ $(M + H)^+$ 243.1380, found 243.1377.

8-Oxospiro[4.5]deca-6,9-diene-2-carbaldehyde (***12***): Pale yellow oil, 0.061 mmol, 10.7 mg, 61% yield; ^1H NMR (300 MHz, $CDCl_3$) δ 9.74 (s, 1H), 6.87 (d, J = 9.8 Hz, 1H), 6.77 (d, J = 9.8 Hz, 1H), 6.17 (d, J = 10.2 Hz, 1H), 6.22 (d, J = 9.8 Hz, 2H), 3.18 (m, 1H), 2.29−2.14 (m, 3H), 1.99 (dd, J = 13.7, 9.4 Hz, 1H), 1.83 (t, J = 7.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.4, 185.8, 153.4, 152.5, 128.0, 127.8, 51.0, 48.3, 37.4, 36.7, 25.5; HRMS (ESI) calcd for $C_{11}H_{13}O_2$ $(M + H)^+$ 177.0910, found 177.0908.

2-Hydroxy-10,10-dimethyl-4,5,9,9a-tetrahydro-2H-3,5a-methanobenzo-oxepin-8(3H)-one (***18***): Pale yellow oil, 40% yield; ^1H NMR (600 MHz, $CDCl_3$) δ 6.52 (dd, J = 10.2, 2.3 Hz, 2H), 6.17 (d, J = 10.4 Hz, 1H), 5.35 (m, 1H), 4.09 (m, 1H), 2.77 (dd, J = 7.8, 3.4 Hz, 1H), 2.20 (dd, J = 7.8, 3.4 Hz, 1H), 1.94 (s, 1H), 1.94 (dd, J = 7.8, 3.4 Hz, 1H), 1.33 (s, 3H), 1.30 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.8, 152.3, 126.8, 82.8, 80.7, 68.5, 56.2, 38.3, 33.0, 31.4, 31.1, 29.6, 23.2; HRMS (ESI) calcd for $C_{13}H_{19}O_3$ $(M + H)^+$ 223.1329, found 223.1327.

2-Methyl-8-oxospiro[4.5]deca-6,9-diene-2-carbaldehyde (***20***): Pale yellow oil, 68% yield; IR ν (cm^{-1}) 2930, 1718, 1663, 1623; ^1H NMR (600 MHz, $CDCl_3$) δ 9.57 (s, 1H), 6.92 (dd, J = 10.2, 3.2 Hz, 1H), 6.87 (dd, J = 10.2, 3.2 Hz, 1H), 6.21 (dd, J = 10.2, 3.2 Hz, 1H), 6.20 (dd, J = 10.2, 3.2 Hz, 1H), 2.40 (d, J = 14.4 Hz, 1H), 1.92−1.77 (m, 3H), 1.62 (d, J = 14.4 Hz, 1H), 1.92−1.73 (m, 3H), 1.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.9, 185.7, 153.8, 153.6, 127.3, 127.3, 54.8, 48.5, 43.3, 37.2, 34.2, 22.4; HRMS (ESI) calcd for $C_{12}H_{15}O_2$ $(M + H)^+$ 191.1067, found 191.1066.

2-Acetylspiro[4.5]deca-1,6,9-trien-8-one (***30a***): Pale yellow oil, 0.05 mmol, 9.7 mg, 51% yield; IR ν (cm^{-1}) 2923, 1667, 1621, 1367; ^1H (300 MHz, $CDCl_3$) δ 6.80 (d, J = 9.6 Hz, 2H), 6.29 (d, J = 9.6 Hz, 2H), 6.11 (s, 1H), 2.82 (t, J = 7.5 Hz, 2H), 2.35 (s, 3H), 2.17 (t, J = 7.5 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.0, 185.2, 150.3, 148.7, 141.9, 128.7, 54.8, 34.6, 30.5, 26.9; HRMS (ESI) calcd for $C_{12}H_{13}O_2$ $(M + H)^+$ 189.0910, found 189.0907.

2-Acetyl-1-butylspiro[4.5]deca-1,6,9-trien-8-one (***30b***): Pale yellow oil, 0.045 mmol, 10.9 mg, 45% yield; IR ν (cm^{-1}) 2925, 1665, 1615, 1370; ^1H (600 MHz, $CDCl_3$) δ 6.74 (d, J = 9.9 Hz, 2H), 6.24 (d, J = 9.9 Hz, 2H), 2.43 (t, J = 7.2 Hz, 2H), 2.15 (t, J = 7.2 Hz, 2H), 2.11 (s, 3H), 2.10 (t, J = 7.2 Hz, 2H), 1.46−1.22 (m, 4H), 0.87 (t, J = 6.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 206.7, 185.0, 150.9, 149.9, 129.4, 128.3, 84.7, 76.1, 38.8, 38.2, 33.6, 30.5, 30.1, 21.8, 18.3, 13.5; HRMS (ESI) calcd for $C_{16}H_{21}O_2$ $(M + H)^+$ 245.1536, found 245.1539.

2-Acetyl-1-decylspiro[4.5]deca-1,6,9-trien-8-one (***30c***): Pale yellow oil, 0.055 mmol, 18.0 mg, 55% yield; IR ν (cm^{-1}) 2925, 2854, 1720, 1673, 1628; ^1H (600 MHz, $CDCl_3$) δ 6.75 (d, J = 9.8 Hz, 2H), 6.25 (d, J = 9.8 Hz, 2H), 2.43 (t, J = 7.8 Hz, 2H), 2.15 (t, J = 7.8 Hz, 2H), 2.11 (s, 3H), 2.10 (t, J = 7.8 Hz, 2H), 1.46 (quin, J = 7.8 Hz, 1H), 1.47 (quin, J = 7.8 Hz, 2H), 1.36−1.21 (m, 16H), 0.87 (t, J = 7.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 206.7, 185.0, 150.9, 150.0, 129.4, 128.3, 84.8, 38.8, 38.2, 33.6, 31.8, 30.1, 29.5, 29.4, 29.2, 29.0,

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28.7, 28.7, 28.5, 22.6, 18.6, 14.0; HRMS (ESI) calcd for $C_{22}H_{32}NaO_2$ $(M + Na)^+$ 351.2295, found 351.2297.

2-Acetyl-3-methylspiro[4.5]deca-1,6,9-trien-8-one (**30d**): Pale yellow oil, 0.046 mmol, 9.3 mg, 46% yield; IR ν (cm^{-1}) 3482, 2959, 1663, 1622, 1666; ^1H (600 MHz, $CDCl_3$) δ 6.84 (dd, J = 10.0, 2.3 Hz, 1H), 6.72 (dd, J = 10.0, 2.3 Hz, 1H), 6.3 (d, J = 10.0 Hz, 1H), 6.28 (d, J = 10.0 Hz, 1H), 6.07 (s, 1H), 3.34 (hex, J = 7.0 Hz, 1H), 2.40 (ddd, J = 13.5, 8.2, 1.1 Hz, 1H), 2.34 (s, 3H), 1.79 (ddd, J = 13.5, 5.9, 1.1 Hz, 1H), 1.28 (d, J = 8.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.3, 185.1, 152.3, 151.6, 151.0, 141.5, 128.6, 128.5, 53.7, 42.8, 39.2, 27.5, 20.6; HRMS (ESI) calcd for $C_{13}H_{15}O_2$ $(M + H)^+$ 203.1067, found 203.1064.

3-Methyl-2-propioloylspiro[4.5]deca-1,6,9-trien-8-one (**30e**): Pale yellow oil, 0.057 mmol, 12 mg, 57% yield; IR ν (cm^{-1}) 2092, 1662, 1636, 857; ^1H (300 MHz, $CDCl_3$) δ 6.84 (dd, J = 10.4, 3.3 Hz, 1H), 6.73 (dd, J = 10.4, 3.3 Hz, 1H), 6.52 (d, J = 9.6 Hz, 1H), 6.34 (dd, J = 10.4, 3.3 Hz, 1H), 6.31 (dd, J = 10.4, 3.3 Hz, 1H), 3.37 (m, 1H), 3.25 (s, 1H), 2.47 (dd, J = 13.7, 8.8 Hz, 1H), 1.87 (dd, J = 13.7, 8.8 Hz, 1H), 1.33 (d, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.0, 174.3, 152.3, 150.9, 150.1, 148.2, 129.0, 128.9, 80.1, 78.6, 53.5, 43.3, 38.5, 20.3; HRMS (ESI) calcd for $C_{14}H_{13}O_2$ $(M + H)^+$ 213.0910, found 213.0905.

7,9-Dibromo-3-methyl-2-propioloylspiro[4.5]deca-1,6,9-trien-8-one (**30f**): Pale yellow oil, 78% yield; IR ν (cm^{-1}) 2092, 1733, 1677, 1641, 1072; ^1H (300 MHz, $CDCl_3$) δ 7.31 (d, J = 2.7 Hz, 1H), 7.20 (d, J = 2.7 Hz, 1H), 6.52 (d, J = 1.6 Hz, 1H), 3.37 (m, 1H), 3.30 (s, 1H), 2.56 (dd, J = 13.7, 8.8 Hz, 1H), 1.97 (dd, J = 13.7, 8.8 Hz, 1H), 1.33 (d, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.7, 172.0, 153.0, 150.9, 150.2, 144.9, 129.3, 122.5, 122.3, 80.0, 79.2, 58.5, 42.7, 38.7, 25.5, 20.0; HRMS (ESI) calcd for $C_{14}H_{11}Br_2O_2$ $(M + H)^+$ 370.9100, found 370.9094.

1-Butyl-2-(hept-2-ynoyl)-3-methylspiro[4.5]deca-1,6,9-trien-8-one (**30g**): Pale yellow oil, 60% yield; IR ν (cm^{-1}) 2933, 2205, 1667, 1626; ^1H (600 MHz, $CDCl_3$) δ 6.78 (d, J = 9.9 Hz, 1H), 6.76 (d, J = 9.9 Hz, 1H), 6.28 (d, J = 9.9 Hz, 1H), 6.22 (d, J = 9.9 Hz, 1H), 2.67 (dd, J = 14.0, 8.2 Hz, 1H), 2.60 (qd, J = 8.2, 2.9 Hz, 1H), 2.37 (t, J = 7.0 Hz, 2H), 2.17 (t, J = 7.0 Hz, 2H), 1.70 (dd, J = 13.4, 2.9 Hz, 1H), 1.60−1.56 (m, 4H), 1.50−1.37 (m, 5H), 1.20 (d, J = 7.0 Hz, 3H), 0.94 (t, J = 7.0 Hz, 3H), 0.92 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.3, 185.0, 150.1, 149.9, 128.4, 128.2, 96.4, 84.9, 80.0, 76.1, 44.8, 42.4, 39.2, 30.5, 29.6, 21.9, 21.8, 18.8, 18.6, 18.3, 13.5, 13.4; HRMS (ESI) calcd for $C_{22}H_{29}O_2$ $(M + H)^+$ 325.2162, found 325.2156.

7,9-Dibromo-1-butyl-2-(hept-2-ynoyl)-3-methylspiro[4.5]deca-1,6,9-trien-8-one (**30h**): Pale yellow oil, 81% yield; IR ν (cm^{-1}) 2923, 2205, 1733, 1677; ^1H (600 MHz, $CDCl_3$) δ 7.21 (d, J = 2.7 Hz, 1H), 7.19 (d, J = 2.7 Hz, 1H), 2.67 (dd, J = 14.3, 9.3 Hz, 1H), 2.59 (m, 1H), 2.39 (t, J = 7.0 Hz, 2H), 2.18 (t, J = 7.0 Hz, 2H), 1.79 (dd, J = 13.7, 2.7 Hz, 1H), 1.63−1.27 (m, 8H), 1.20 (d, J = 7.0 Hz, 3H), 0.94 (t, J = 7.0 Hz, 3H), 0.91 (t, J = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.7, 171.9, 150.3, 149.8, 121.8, 97.2, 86.8, 80.0, 73.4, 44.7, 44.5, 42.8, 30.3, 29.6, 21.9, 21.9, 18.7, 18.4, 13.5, 13.4; HRMS (ESI) calcd for $C_{22}H_{27}Br_2O_2$ $(M + H)^+$ 483.0353, found 483.0343.

1-Decyl-2-(tridec-2-ynoyl)spiro[4.5]deca-1,6,9-trien-8-one (**30i**): Pale yellow oil, 0.05 mmol, 23.9 mg, 50% yield; IR ν (cm^{-1}) 2925, 2854, 1674, 1627; ^1H (600 MHz, $CDCl_3$) δ 6.76 (d, J = 9.8 Hz, 2H), 6.26 (d, J = 9.6 Hz, 2H), 2.57 (t, J = 7.8 Hz, 2H), 2.16 (t, J = 7.2 Hz, 4H), 1.56 (quin, J = 7.8 Hz, 1H), 1.47 (quin, J = 7.8 Hz, 2H), 1.40−1.21 (m, 28H), 0.87 (t, J = 7.8 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 185.9, 185.0, 149.7, 132.9, 128.4, 115.2, 95.5, 85.1, 80.5, 80.5, 75.8, 40.4, 38.7, 33.9, 31.8, 29.5, 29.5, 29.4, 29.2, 28.9, 29.2, 29.0, 28.9, 28.8, 28.8, 28.5, 27.6, 22.6, 18.9, 18.6, 14.0; HRMS (ESI) calcd for $C_{33}H_{50}NaO_2$ $(M + Na)^+$ 501.3703, found 501.3700.

3-Allyl-1-butyl-2-(hept-2-ynoyl)spiro[4.5]deca-1,6,9-trien-8-one (**30j**): Pale yellow oil, 53% yield; IR ν (cm^{-1}) 2923, 2205, 1667, 1625, 1461; ^1H (300 MHz, $CDCl_3$) δ 6.75 (dd, J = 9.8, 2.7 Hz, 1H), 6.71 (dd, J = 9.8, 2.7 Hz, 1H), 6.28 (d, J = 9.8, 1.7 Hz, 1H), 6.21 (d, J = 9.8, 1.7 Hz, 1H), 5.65 (m, 1H), 5.11 (d, 17.0 Hz, 1H), 5.08 (d, J = 8.0, 1H), 2.59 (m, 2H), 2.45 (m, 1H), 2.37 (t, J = 7.0 Hz, 2H), 2.22 (m, 1H), 2.17 (t, J = 7.0 Hz, 2H), 1.80 (dt, J = 12.1, 7.1 Hz, 1H), 1.60−1.31 (m, 6H), 1.25 (d, J = 9.2 Hz, 1H), 0.93 (t, J = 7.8 Hz, 3H). 0.90 (t, J = 7.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.3, 185.0, 150.1, 149.8, 133.9, 128.5, 128.2, 118.3, 96.6, 85.0, 80.4, 49.7, 39.5, 39.1, 37.2, 30.5, 29.6, 21.9, 18.7, 18.4, 13.5; HRMS (ESI) calcd for $C_{24}H_{31}O_2$ $(M + H)^+$ 351.2319, found 351.2305.

1-Butyl-2-(hept-2-ynoyl)-4-methylspiro[4.5]deca-1,6,9-trien-8-one (**30k**): Pale yellow oil, 56% yield; IR ν (cm^{-1}) 2929, 2854, 2210, 1670; ^1H (300 MHz, $CDCl_3$) δ 6.80 (dd, J = 9.8, 2.7 Hz, 1H), 6.72 (dd, J = 9.8, 2.7 Hz, 1H), 6.32 (d, J = 9.8 Hz, 2H), 2.88 (dd, J = 16.4, 2.2 Hz, 1H), 2.61 (m, 1H), 2.59 (m, 2H), 2.45 (m, 1H), 2.38 (t, J = 7.0 Hz, 2H), 2.34 (dd, J = 16.4, 9.8 Hz, 1H), 2.20 (t, J = 7.0 Hz, 2H), 1.60−1.31 (m, 6H), 1.03 (d, J = 7.0 Hz, 3H), 0.98 (t, J = 7.8 Hz, 3H). 0.91 (t, J = 7.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.0, 185.2, 167.1, 148.7, 148.6, 133.0, 129.4, 129.2, 115.2, 95.2, 85.7, 80.8, 75.7, 48.0, 43.2, 37.9, 30.5, 29.6, 21.9, 21.9, 18.6, 18.4, 15.3, 13.5, 13.4; HRMS (ESI) calcd for $C_{22}H_{29}O_2$ $(M + H)^+$ 325.2162, found 325.2164.

4-Methyl-2-propioloylspiro[4.5]deca-1,6,9-trien-8-one (**30l**): Pale yellow oil, 54% yield; IR ν (cm^{-1}) 2925, 2854, 1674, 1627; ^1H (300 MHz, $CDCl_3$) δ 6.79 (dd, J = 10.4, 3.3 Hz, 1H), 6.71 (dd, J = 10.4, 3.3 Hz, 1H), 6.61 (s, 1H), 6.41 (dd, J = 8.8, 3.3 Hz, 2H), 3.27 (s, 1H), 3.03 (dd, J = 16.5, 8.2 Hz, 1H), 3.03 (dd, J = 16.5, 8.2 Hz, 1H), 2.69 (m, 1H), 2.46 (ddd, J = 16.4, 10.4, 2.2 Hz, 1H), 0.99 (t, J = 7.1 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 185.4, 174.1, 167.1, 150.3, 148.6, 146.3, 130.8, 130.6, 79.7, 79.2, 57.6, 44.6, 36.8, 14.4; HRMS (ESI) calcd for $C_{14}H_{13}O_2$ $(M + H)^+$ 213.0910, found 213.0907.

8-Oxospiro[4.5]deca-1,6,9-triene-2-carbaldehyde (**30m**): Pale yellow oil, 45% yield; IR ν (cm^{-1}) 2928, 1701, 1662, 1623; ^1H NMR (600 MHz, $CDCl_3$) δ 9.86 (s, 1H), 6.79 (d, J = 10.0 Hz, 2H), 6.33 (d, J = 10.0 Hz, 2H), 6.30 (s, 1H), 2.83 (d, J = 7.6 Hz, 2H), 2.25 (d, J = 7.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ189.2, 185.3, 149.9, 149.8, 149.7, 129.3, 54.6, 35.1, 28.7; HRMS (ESI) calcd for $C_{11}H_{11}O_2$ $(M + H)^+$ 175.0754, found 175.0751.

2-Acetyl-4,4-dimethylspiro[4.5]deca-1,6,9-trien-8-one (**32**): Pale yellow oil, 51% yield; IR ν (cm^{-1}) 1667, 1621; ^1H NMR (600 MHz, $CDCl_3$) δ 6.85 (d, J = 10.2 Hz, 2H), 6.37 (d, J = 10.2 Hz, 1H), 6.16 (t, J = 1.6 Hz, 1H), 2.64 (d, J = 1.6 Hz, 1H), 2.34 (s, 3H), 1.10 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.3, 184.9, 148.5, 148.0, 142.0, 130.4, 59.8, 49.7, 44.9, 26.4, 25.8; HRMS (ESI) calcd for $C_{14}H_{17}O_2$ $(M + H)^+$ 217.1223, found 217.1232.

(E)-2-(8-Oxospiro[4.5]deca-6,9-dien-1-ylidene)acetaldehyde (**34**): 9.6 mg, 0.051 mmol, 51%, as an oil; IR ν (cm^{-1}) 2923, 2858, 1667, 1622, 1403, 1253, 1154, 863; ^1H NMR (300 MHz, $CDCl_3$) δ 9.84 (d, 1H, J = 7.0 Hz), 6.76 (d, 2H, J = 10.1 Hz), 6.31 (d, 2H, J = 10.1 Hz), 5.77 (dt, 1H, J = 7.0, 2.5 Hz), 3.11 (td, 2H, J = 7.0, 2.5 Hz), 2.14 (m, 2H), 2.06 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 190.7, 185.5, 168.4, 149.7, 128.1, 125.1, 53.9, 37.2, 30.7, 24.0; HRMS (ESI) calcd for $C_{12}H_{13}O_2$ $(M + H)^+$ 189.0910, found 189.0910.

4-(((2S,3S)-2-methyl-2-(prop-1-en-2-yl)tetrahydrofuran-3-yl)-methyl)phenol (**23**). To a solution of the triols **22**[3i] (50 mg, 0.2 mmol) in dry CH_2Cl_2 (2 mL) was added TFA (45 mg, 0.4 mmol, 2 equiv) and the solution was stirred for 90 min at 40 °C. The crude mixture is purified directly on silica gel (*n*-hexane/EtOAc, 7:3) to afford **23** compound 35 mg, 0.15 mmol) in 75% yield as an oil: IR ν (cm^{-1}) 3312, 1610, 1221, 1164; ^1H NMR (300 MHz, $CDCl_3$) δ 7.04 (d, J = 8.2 Hz, 2H), 6.77 (d, J = 8.2 Hz, 2H), 4.99 (s, 1H), 4.85 (s, 1H), 3.74 (q, J = 8.2 Hz, 1H), 2.78 (d, J = 10.4 Hz, 1H), 2.31 (m, 2H), 1.89 (m, 1H), 1.82 (s, 3H), 1.71 (m, 1H), 1.30 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.9, 149.7, 133.1, 129.7, 115.2, 109.8, 86.1, 65.9, 47.4, 35.4, 31.4, 20.8, 18.8; HRMS (ESI) calcd for $C_{15}H_{21}O_2$ $(M + H)^+$ 233.1536, found 233.1536.

3-Acetyl-3-methyl-8-oxospiro[4.5]deca-6,9-dien-2-yl)-acetaldehyde (**27**). The crude mixture **26** resulting from the direct oxidation of compound **23** (0.1 mmol, 25 mg) was quickly filtrated by chromatography (EtOAc), concentrated under reduced pressure, and dissolved in dry CH_2Cl_2 (0.75 mL). Dess−Martin periodinane (85 mg, 0.2 mmol) was added. The solution was stirred overnight (and verified by TLC) at 40 °C. Then a solution of 2 mL of saturated aqueous $NaHCO_3$ and 2 mL of saturated aqueous sodium thiosulfate were added. The mixture was diluted with 4 mL of ethyl acetate, the organic

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layer removed, and the aqueous phase extracted with EtOAc (2 × 4 mL), and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude was purified by chromatography (*n*-hexane/EtOAc, 1:1) to afford 263 mg (60% over two steps) of compound **27** as a colorless oil: IR ν (cm^{-1}) 2932, 1723, 1692, 1656; ^1H NMR (300 MHz, $CDCl_3$) δ 9.77 (s, 1H), 6.98 (d, J = 9.8 Hz, 2H), 6.16 (d, J = 9.8 Hz, 2H), 2.73−2.48 (m, 3H), 2.36 (d, J = 14.3 Hz, 1H), 2.19 (s, 3H), 1.99 (d, J = 9.8 Hz, 2H), 1.71 (d, J = 14.3 Hz, 1H), 1.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.2, 185.7, 155.0, 154.6, 127.0, 126.1, 57.9, 47.5, 45.7, 44.2, 43.9, 42.0, 28.2, 24.1; HRMS (ESI) calcd for $C_{15}H_{18}O_3Na$ $(M + Na)^+$ 269.1148, found 269.1147.

*2-(3-Methyl-8-oxospiro[4.5]deca-2,6,9-trien-2-yl)ethyl acetate (**42**).* A solution of $PhI(OAc)_2$ ("DIB", 80 mg, 0.25 mmol) in $(CF_3)_2CHOH$ ("HFIP", 0.75 mL) was added over 10 s to a vigorously stirred solution of phenol **23**[3i] (0.2 mmol, 1 equiv) in 2 mL of a solution of CH_2Cl_2/HFIP (3/2) cooled to −17 °C for a few seconds (to avoid precipitation of HFIP). After addition of DIB, the solution was stirred for 1 min, and H_2O_2 (35%, 0.75 mL) was added to the medium. The reaction was stirred for 5 min and filtered directly over silica gel (*n*-hexane/EtOAc, 1:1), and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (ethyl acetate/hexane, 3:1) to afford a mixture (37 mg, 64%) of two diastereoisomers **39** as an oil.[3i] The epimeric mixture of compound **39** was rapidly used (17 mg, 0.064 mmol) in dry DCM (0.6 mL); NEt_3 (30 μL, 0.200 mmol, 3.1 equiv) was added followed by Ac_2O (20 μL, 0.200 mmol, 3.1), and the solution was stirred for 1 h under argon and filtered directly over silica gel (*n*-hexane/EtOAc, 1:1). The crude product was purified by chromatography (*n*-hexane/EtOAc, 1:1) to afford 6.0 mg (38%) of compound **42** as well as 4.0 mg (24%) of compound **43** (oils): IR ν (cm^{-1}) 1738, 1664, 1233; ^1H NMR (300 MHz, $CDCl_3$) δ 6.97 (d, J = 10.0 Hz, 2H), 6.21 (d, J = 10.0 Hz, 2H), 4.12 (t, J = 7.5 Hz, 2H), 2.53 (s, 2H), 2.50 (s, 2H), 2.43 (t, J = 7.5 Hz, 2H), 2.06 (s, 3H), 1.69 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.3, 170.9, 154.9, 132.5, 129.3, 127.1, 62.4, 47.8, 45.8, 27.5, 20.9, 13.6; HRMS (ESI) calcd for $C_{15}H_{19}O_3$ $(M + H)^+$ 247.1329, found 247.1336.

*2-((2S,3S)-3-Hydroxy-3-methyl-8-oxospiro[4.5]deca-6,9-dien-2-yl)ethyl acetate (**43**).* To a solution of compound **39** (see formation of compound **42**, 63 mg, 0.239 mmol) in THF (2.5 mL) was added a solution (2.5 mL) of saturated aqueous $NaHCO_3$ followed by *ortho*-NsCl (320 mg, 1.448 mmol, 6.0 equiv), then the solution was stirred for 12 h and H_2O (10.0 mL) was added. The aqueous phase was extracted with EtOAc (3 × 5 mL), and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by chromatography (*n*-hexane/EtOAc, 1:1) to afford 45.5 mg (72%) of the desired alcohol as an oil: IR ν (cm^{-1}) 2921, 1732, 1660, 1557; ^1H NMR (300 MHz, $CDCl_3$) δ 7.16 (dd, J = 10.0, 2.7 Hz, 1H), 6.86 (dd, J = 10.0, 2.7 Hz, 1H), 6.16 (dd, J = 10.0, 2.7 Hz, 1H), 6.13 (dd, J = 10.0, 2.7 Hz, 1H), 4.12 (m, 2H), 2.06 (s, 3H), 2.01−1.89 (m, 7H), 1.68 (m, 2H), 1.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.1, 171.0, 157.0, 155.4, 126.1, 125.8, 81.1, 63.3, 51.4, 46.4, 44.8, 41.3, 27.2, 25.9, 20.9; HRMS (ESI) calcd for $C_{15}H_{20}NaO_4$ $(M + Na)^+$ 287.1254, found 287.1267.

*(3a′S,6a′S)-2′-Hydroxy-6a′-methyl-2′,3′,3a′,4′,6′,6a′-hexahydrospiro[cyclohexa[2,5]diene-1,5′-cyclopenta[b]furan]-4-one (**44**).* To a solution of compound **43** (23 mg, 0.85 mmol) in methanol (2.0 mL) was added finely powdered potassium carbonate (12.0 mg, 0.9 mmol, 1.05 equiv). The reaction mixture was stirred for 25 min, and the methanol was partly removed by evaporation under reduced pressure. The crude product was directly purified by chromatography (DCM/MeOH, from 9:1 to 8:2) to afford 18.5 mg (97%) of the desired compound. The corresponding diol (15.5 mg, 0.07 mmol) was disolved in a (1/1) DMSO/EtOAc mixture (2 mL), and then was added IBX (30 mg, 0.11 mmol, 1.5 equiv). The reaction mixture was stirred for 2 h, and H_2O (5.0 mL) was added. The aqueous phase was extracted with EtOAc (4 × 5 mL), and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure to afford 24.0 mg (80%) of the desired mixture of hemiketals: HRMS (ESI) calcd for $C_{13}H_{15}O_2$ $(M + H - H_2O)^+$ 203.1067, found 203.1074.

*(3a′S,6a′S)-6a′-Methyl-2′-(phenylthio)-2′,3′,3a′,4′,6′,6a′-hexahydrospiro[cyclohexa[2,5]diene-1,5′-cyclopenta[b]furan]-4-one (**45**).* To a solution of the compound **44** (8.0 mg, 0.036 mmol) in DCM (1.0 mL) were added PhSH (5 μL, 0.048 mmol, 1.4 equiv) and TFA (5 μL, 0.068 mmol, 1.9 equiv). The reaction mixture was stirred for 1 h. The crude product was directly purified by chromatography (*n*-hexane/EtOAc, 80:20) to afford 7.0 mg (62%) of the desired diastereomeric mixture as an oil: HRMS (ESI) for $C_{19}H_{20}NaO_2S$ $(M + Na)^+$ 335.1076, found 335.1073.

*(S)-2-(2-Hydroxyethyl)-3-methylenespiro[4.5]deca-6,9-dien-8-one (**47**).* To a solution of compounds **39** (see formation of compound **42**, 18 mg, 0.068 mmol) in degassed MeOH at −15 °C was dissolved $Cu(OAc)_2$ (27 mg, 2 equiv), and the solution was stirred 5 min until the salt was soluble, then $FeSO_4$ (12.5 mg, 1.2 equiv) was added at −20 °C . The reaction was stirred until the starting material disappeared by TLC (ethyl acetate/hexane 1:1), then the solution was filtrated on silica gel chromatography and concentrated under vacuum. The residue was dissolved in methanol (2 mL); K_2CO_3 solid (14 mg, 0.1 mmol) was added, and the solution was stirred until the starting material disappeared by TLC, affording a mixture of alkenes **47** (6 mg, 44%) in a ratio ∼3/1 in favor of the exo isomer: colorless oil; ^1H NMR (exo isomer, 300 MHz, $CDCl_3$) δ 6.98 (dd, J = 9.8, 3.3 Hz, 1H), 6.81 (dd, J = 9.8, 2.3 Hz, 1H), 6.16 (t, J = 9.8, 1.6 Hz, 2H), 5.08 (s, 1H), 5.02 (s, 1H), 3.74 (m, 2H), 2.92, (m,1H), 2.67 (dq, J = 15.9, 2.2 Hz, 1H), 2.43 (dd, J = 15.9, 1.6 Hz, 1H), 2.06 (m, 2H), 1.75 (m, 2H); LRMS (ESI) for $C_{13}H_{16}O_2Na$ $(M + Na)^+$ 227, identical to the literature.[24]

*(S)-2-(3-Methylene-8-oxospiro[4.5]deca-6,9-dien-2-yl)-acetaldehyde (**48**).* The alkene mixture **47** (11 mg, 0.054 mmol) was dissolved in 2 mL of DCM, and PCC (24 mg, 0.11 mmol) was added; the reaction was stirred until the starting material disappeared by TLC (ethyl acetate/hexane 3:1) and filtered directly over silica gel (*n*-hexane/EtOAc, 1:3). The filtrate was concentrated under reduced pressure and purified by silica gel chromatography with a mixture of ethyl acetate/hexane (3:1) to afford a mixture of aldehydes **48** (8.1 mg, 74%) as a colorless oil: ^1H NMR (exo isomer, 300 MHz, $CDCl_3$) δ 9.83 (s, 1H), 6.98−6.95 (m, 1H), 6.79−6.76 (m, 1H), 6.27−6.23 (m, 2H), 5.10 (s, 1H), 4.98 (s, 1H), 3.30 (m, 1H), 2.90 (dd, J = 18.1, 5.5 Hz, 1H), 2.66 (m, 2H), 2.47 (m, 1H), 2.15 (ddd, J = 13.0, 8.0, 1.6 Hz, 1 H), 1.69 (m, J = 13.0, 10.3 Hz, 1H); LRMS (ESI) $C_{13}H_{14}O_2Na$ $(M + Na)^+$ 225, identical to the literature.[24]

*2-(3-Chloro-3-methyl-8-oxospiro[4.5]deca-6,9-dien-2-yl)ethyl acetate (**49**).* To a solution of compounds **39** (see formation of compound **42**, 26.5 mg, 0.1 mmol) in degassed MeOH (2 mL) at rt was dissolved $Cu(Cl)_2$ (27 mg, 0.2 mmol, 2 equiv), and the solution was stirred 5 min until the salt was soluble. The mixture was cooled at −30 °C, and $FeSO_4$ (41 mg, 0.15 mmol, 1.5 equiv) was added. The reaction was stirred 10 min at −30 °C, and the crude product was directly purified by chromatography (*n*-hexane/EtOAc, 1:1), affording a mixture of alkenes **47** (20.4 mg, 74%) in a ratio ∼4/1 in favor of the *trans* isomer as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.25 (dd, J = 9.8, 3.8 Hz, 1H), 6.86 (dd, J = 9.8, 3.8 Hz, 1H), 6.20 (dd, J = 9.8, 3.8 Hz, 1H), 6.17 (t, J = 9.8, 3.8 Hz, 1H), 4.14 (m, 2H), 2.50 (d, J = 15.4 Hz, 1H), 2.20 (d, J = 15.4 Hz, 1H), 2.17−1.98 (m, 2H), 2.08 (s, 3H), 1.79 (m, 1H), 1.71 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 185.6, 171.1, 154.3, 154.3, 127.8, 126.6, 74.6, 63.1, 53.4, 49.9, 44.9, 41.3, 28.5, 27.2, 21.2; HRMS (ESI) calcd for $C_{15}H_{19}ClNaO_3$ $(M + Na)^+$ 305.0915, found 305.0919.

*(4aS,5S,7R,8S,9aS)-8-Methyl-4a,5,6,7,8,9-hexahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-3(4H)-one (Cage Compound **52**).* To a vigorously stirred solution of compound **48** (8 mg, 0.04 mmol), HMPA (73 mg, 0.4 mmol), and HFIP (10 mg, 0.06 mmol) in THF (1.2 mL) at −78 °C was rapidly added SmI_2 (0.09 mmol, 0.53 mL, 0.17 M in THF). The resulting mixture was stirred at that temperature for 20 s before it was quenched with saturated aqueous NH_4Cl solution (4 mL). After extraction with EtOAc (3 × 5 mL), the combined organic phase was dried over Na_2SO_4 and filtered. The solvent was removed under vacuum, and the residue was dissolved in

CH_2Cl_2 (0.1 mL). To the resulting solution at 0 °C was added TFA (0.25 mL), and the resulting mixture was stirred at that temperature for 1.5 h. The solvent was then removed by a stream of argon, and the residue was dissolved in EtOAc (5 mL). The resulting organic phase was washed with saturated aqueous $NaHCO_3$ solution (4 mL) and brine (4 mL) and dried over Na_2SO_4. After filtration and removal of the solvent under vacuum, the residue was purified by flash column chromatography with EtOAc/hexanes (2/3) as eluent to give cage compound **31** (2.8 mg, 36%): $[\alpha]_D^{20} = -21$ (c = 0.5 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.62 (d, J = 10.0 Hz, 1H), 5.94 (d, J = 10.0 Hz, 1H), 4.17 (t, J = 3.4 Hz, 1H), 2.43−2.29 (m, 4H), 1.97−1.94 (m, 2H), 1.90 (d, J = 11.6 Hz, 1H), 1.79−1.74 (m, 2H), 1.66 (d, J = 11.2 Hz, 1H), 1.45 (s, 3H); LRMS (ESI) $C_{13}H_{16}O_2Na$ $(M + Na)^+$ found 227, identical to the literature.[24]

■ ASSOCIATED CONTENT

Supporting Information

Complete experimental procedures and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: canesi.sylvain@uqam.ca.

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(18) (a) The enantiopure alcohol **9** has been obtained via optical resolution using enantiopure (*R*)-*O*-acetyl-L-mandelic acid. (b) Enantioenriched compound (*S*)-**1a** was obtained using a Sharpless dihydroxylation process, and the ee was calculated on the (*R*)-*O*-acetyl-L-mandelic ester by NMR; see Supporting Information: Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K. S.; Kwong, H. L.; Morikawa, K.; Wang, Z. M.; Xu, D.; Zhang, X. L. *J. Org. Chem.* **1992**, *57*, 2768.

(19) The enantiomeric excess was calculated by NMR using a Mosher strategy: the aldehyde functionality of compound **18** was selectively reduced to the corresponding alcohol at 0 °C in THF, in presence of 1.1 equiv of lithium tri-*tert*-butoxyaluminum hydride, and this alcohol was coupled with the (*R*)-Mosher acid in presence of EDC in CH_2Cl_2; see Supporting Information.

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