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Pt-Catalyzed Rearrangement of Oxaspirohexanes to 3-Methylenetetrahydrofurans: Scope and Mechanism

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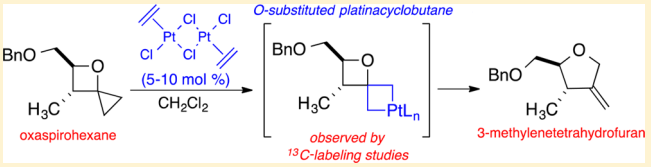
Supporting Information

ABSTRACT: A novel Pt-catalyzed rearrangement of oxaspirohexanes to 3-methylenetetrahydrofurans is reported. Mechanistic studies by ^{13}C-labeling experiments confirm oxidative addition of Pt(II) regioselectively to the least substituted carbon−carbon bond of the cyclopropane to form a platinacyclobutane intermediate. To our knowledge, this is the first alkoxy-substituted platinacyclobutane that has been observed spectroscopically. The scope and a proposed mechanism of this new Pt-catalyzed transformation are described.



INTRODUCTION

In exploring the reactivity of unusual oxetanes, we have shown that oxetane oxocarbenium ions **1**, generated from either 2-methyleneoxetanes[1] or dioxaspirohexanes[2] using electrophiles or Lewis acids (Figure 1), can be converted to a variety of

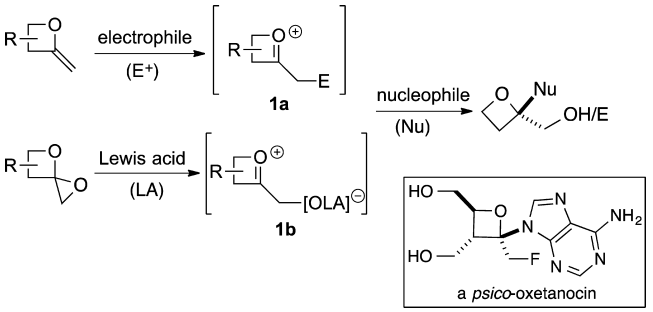


Figure 1. Routes to oxetane intact products from methyleneoxetanes or dioxaspirohexanes through oxocarbenium ions **1a** or **1b**.

oxetane intact species, including *epi*-oxetin[2b] and novel *psico*-nucleosides (e.g., a *psico*-oxetanocin, Figure 1).[1a] We previously reported the preparation of oxaspirohexanes from methyleneoxetanes[3] and were interested in exploring new reactivities of this strained heterocycle. Our attention was captured by reports from Madsen and co-workers that 1,2-cyclopropanated sugars gave C2-substituted glycosides **2** when reacted with alcohols in the presence of Zeise's dimer, $[Pt(C_2H_4)Cl_2]_2$ (**3**) (Figure 2).[4] From these results and prior reports of the reaction of Zeise's dimer with silyloxycyclopropanes[5] and alkoxycyclopropanes,[6] a mechanism involving oxidative addition of platinum into the cyclopropane next to the CO bond to give an oxocarbenium ion[4b] was proposed (Figure 2). On the basis of these Madsen results, we postulated that oxaspirohexanes **4** could be converted to *psico*-nucleosides **5** (Figure 3, for Nu = nucleobase) with Zeise's dimer insertion into the cyclopropane providing an alternative access to oxetane oxocarbenium ions.

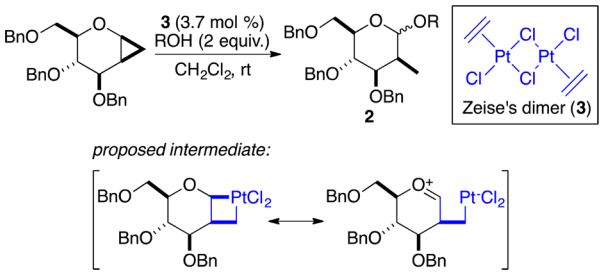


Figure 2. Madsen's Zeise's dimer-catalyzed ring-opening of 1,2-cyclopropanated sugars.[4]

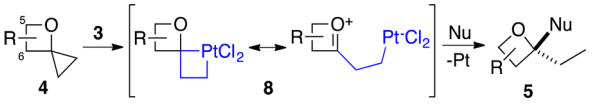


Figure 3. Anticipated transformation of oxaspirohexanes **4** in the presence of **3** to give novel *psico*-nucleosides **5**.

Unexpectedly, under the Madsen conditions,[4] oxaspirohexane **4a** (or **4b**) gave mixtures of two products, 3-methylenetetrahydrofuran **6a** (or **6b**) and allyl ether **7a** (or **7b**) (Table 1). Moreover, in the absence of MeOH, **4a** was converted to just 3-methylenetetrahydrofuran **6a**, while allyl ether **7a** was the sole isolable product in the presence of excess MeOH. Neither outcome could be rationalized by oxocarbenium ions like **8** (Figure 3). Thus, these initial results represented a novel pathway for reactions between oxygen-substituted cyclopropanes and Zeise's dimer.

With the unanticipated rearrangement to synthetically useful 3-methylenetetrahydrofurans,[7] we decided to optimize the reaction and explore the scope of this transformation. Moreover, since it was apparent that oxidative addition of Pt was not occurring in the cyclopropane adjacent to the C−O

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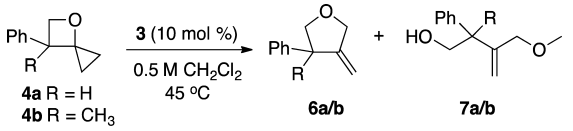
Table 1. Initial Findings on the Reaction of Oxaspirohexanes with Zeise's Dimer[a]



MeOH (equiv)	substrate	ratio[b] (6:7)	% yield 6	% yield 7
2	4a	1:1.5		
	4b	1:2		
excess	4a	7a only	0	50
0	4a	6a only	34	0

[a]Reaction conditions: 0.5−1.0 mmol 4a/b. [b]Ratios are based on ^{1}H NMR of the crude reaction mixture.

bond, mechanistic studies were undertaken. ^{13}C-labeling experiments provided clear evidence of an alternative insertion. These results are described herein.

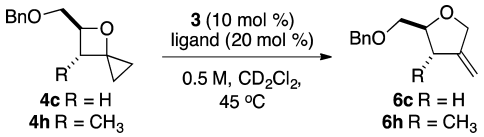
RESULTS AND DISCUSSION

Optimization and Scope. Initial variables examined to optimize the rearrangement of oxaspirohexanes to 3-methylenetetrahydrofurans included solvent, temperature, and concentration (Table 2). Evaluation of solvents for the reaction showed that noncoordinating solvents, such as methylene chloride, chloroform, and toluene, gave clean conversion of oxaspirohexane **4a** to 3-methylenetetrahydrofuran **6a** at concentrations from 0.2 to 1.0 M. Solvents such as diethyl ether, tetrahydrofuran, and ethyl acetate gave poor reaction outcomes. Furthermore, an increase in reaction temperature decreased the time needed for complete conversion (entries 4−7); however, isolated yields decreased slightly at higher temperatures. Subsequent reactions were conducted at 45 °C and with a concentration of 0.5 M in CH_2Cl_2.

On the basis of the literature,[4−6,8] it was initially reasoned that the rearrangement was initiated by oxidative addition of Pt(II); so a variety of Pt catalysts were examined (Table 2, entries 8−13). Oxaspirohexane **4a** did not react with the common Pt catalysts shown. This is consistent with the literature precedent showing that the formation of platinacyclobutanes is achieved almost exclusively using Zeise's dimer as the Pt source.[9,10]

It is well-known that electron-donating ligands stabilize platinacycle complexes;[9] so common nitrogen and phosphorus ligands were examined. In general, phosphine ligands provided improved reactivity and increased isolated yields (Table 3). The use of an electron-withdrawing phosphine (entry 3) blocked conversion, even after 20 h of heating. On the other hand, tricyclohexyl phosphine and triethyl phosphite decreased reaction times to 1 h or less and provided increased isolated yields (up to 70%). In addition, the reaction could be

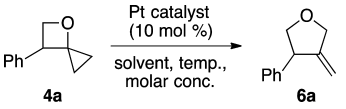
Table 3. Examination of the Effect of Ligands on the Isomerization of Oxaspirohexanes with Zeise's Dimer



entry	substrate	ligand (mol %)	t[a]	isolated yield (%)
1	4h	none	2.5 h	41
2	4c	PPh_3 (20)	20 h	34
3[b]	4c	$P(C_6F_5)_3$ (20)	20 h	0
4	4h	P(*t*-Bu)$_3$ (20)	2 h	60
5	4h	P(*n*-octyl)$_3$ (20)	4.5 h	66
6	4h	bipyridine (10)	2.25 h	61
7	4h	DCPE (10)	30 min	70
8	4c	PCy_3 (20)	45 min	64
9	4h	PCy_3 (20)	40 min	69
10[c]	4h	PCy_3 (20)	6 h	70
11	4h	$P(OEt)_3$ (20)	15 min	68
12[c]	4h	$P(OEt)_3$ (20)	4 h	72
13[c,d]	4h	$P(OEt)_3$ (10)	6 h	73

[a]Reaction time based on complete consumption of starting material as monitored by ^{1}H NMR. [b]After 20 h, no conversion was observed. [c]Reaction run at room temperature. [d]Catalyst loading decreased to 5 mol %.

Table 2. Optimization of Conditions for the Isomerization of Oxaspirohexanes



entry	solvent	Pt catalyst	temp	conc (M)	time[a] (h)	% conv.[b] (yield)
1	CD_2Cl_2	3	rt	0.2	20	65
2	CD_2Cl_2	3	rt	0.5	20	100
3	CD_2Cl_2	3	rt	1.0	20	100
4	CD_2Cl_2	3	45 °C	0.5	1	100
5	CD_2Cl_2	3	45 °C	1.0	1	100 (34%)
6	$CDCl_3$	3	55 °C	1.0	0.75	100 (30%)
7	tol-D_8	3	80 °C	1.0	0.5	100 (25%)
8	CD_2Cl_2	$PtCl_2$	45 °C	1.0	20	0
9	tol-D_8	$PtCl_2$	80 °C	1.0	20	0
10	CD_2Cl_2	$CODPtCl_2$	45 °C	1.0	20	0
11	CD_2Cl_2	C_2H_4-Pt$(PPh_3)_3$	45 °C	1.0	20	0
12	CD_2Cl_2	$(dfmp)_2PtMe_2$[c]	45 °C	1.0	20	0
13	CD_2Cl_2	$(dfepe)_2PtEt_2$[d]	45 °C	1.0	20	0

[a]Time to complete consumption of the starting material or until a reaction time of 20 h. [b]Conversions were monitored by ^{1}H NMR (isolated yields in parentheses). [c]Dfmp = $Me(C_2F_5)_2P$. [d]Dfepe = $(C_2F_5)_2PCH_2CH_2P(C_2F_5)_2$.

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performed at room temperature with no diminution in yield (entries 10, 12, and 13). Also, decreasing the catalyst loading to 5 mol % at room temperature still gave clean conversion with 73% yield (entry 13). Although triethyl phophite provided the highest yield for **4h**, tricyclohexylphosphine gave better results for a broader range of substrates.

A variety of oxaspirohexanes **4a−n** were prepared (Table 4) to explore the scope of the rearrangement. The oxaspirohexanes were synthesized from the corresponding 2-methyleneoxetanes **10a−n** in moderate to high yields by a modified Simmon−Smith cyclopropanation.[3] The methyleneoxetanes were obtained in good yields by methylenation of *β*-lactones **9a−n**.[11]

Monosubstituted oxaspirohexanes rearranged to the corresponding 3-methylenetetrahydrofurans **6c−e** in good yields (Table 5). Similarly, *trans*-3-methylenetetrahydrofurans **6h−j** were obtained in up to 80% yield. Also of note, the reaction tolerated most aromatic groups, but for substrates with aryl groups directly attached to the oxetane ring, such as **4a**, poor conversions and low yields were observed. With substrates containing protected amine substituents at C-6 (**4f** and **4g**), no conversion was observed even with prolonged heating (20 h),

Table 4. . Preparation of 4-Oxaspiro[2.3]hexanes

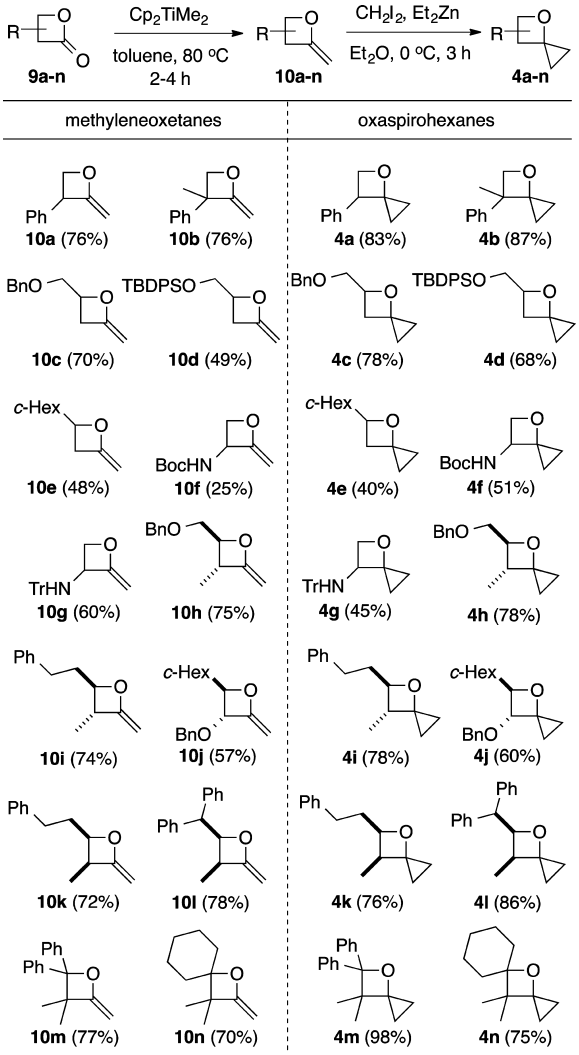
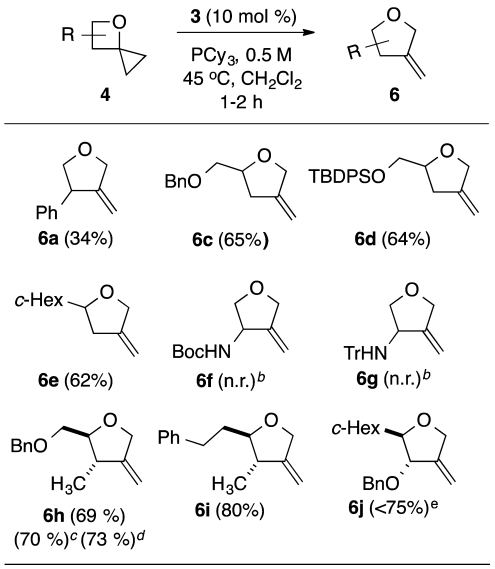


Table 5. Reaction of 4-Oxaspirohexanes with Zeise's Dimer[a]

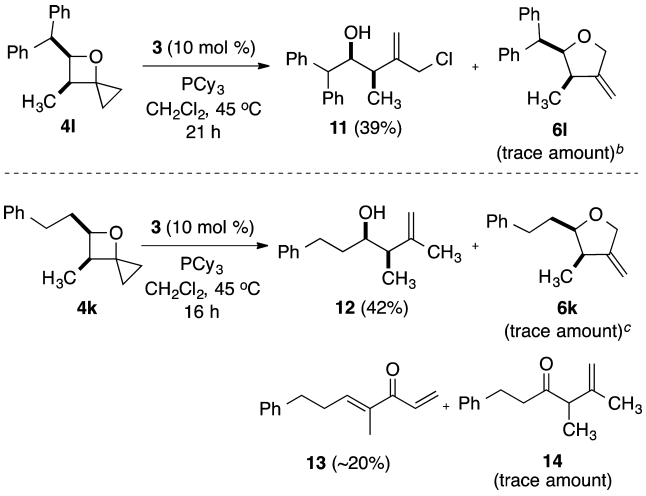


[a]Reaction conditions: 0.5−1.0 mmol scale, 10 mol % $[Pt(C_2H_4)Cl_2]_2$, 20 mol % PCy_3, 0.5 M in CH_2Cl_2. [b]No reaction was observed even after 20 h. [c]Reaction was conducted at room temperature. [d]Reaction was conducted using 5 mol % $Pt(C_2H_4)Cl_2]_2$, 10 mol % $P(OEt)_3$ at room temperature. [e]There was a small amount of an inseparable, unidentified impurity (see spectra in the Supporting Information).

presumably due to the interaction of the catalyst with the nitrogen groups.

Unexpectedly, when 5,6-*cis*-substituted oxaspirohexane **4l** was reacted under the standard conditions, ring-opened allyl chloride **11** was isolated as the major product (Scheme 1). When 5,6-*cis*-substituted oxaspirohexane **4k** was used, ring-opened alcohol **12** was obtained in 42% yield. Analysis of the ^{1}H NMR of the crude reaction mixture and the byproducts isolated from column chromatography showed the formation of additional, inseparable olefinic compounds, which could be the

Scheme 1. Reaction of *cis*-5,6-Oxaspirohexanes with Zeise's Dimer[a]



[a]Reaction conditions: 0.5 mmol scale, 10 mol % **3**, 20 mol % PCy_3, 0.5 M in CH_2Cl_2. [b]*cis*-3-Methylenetetrahydrofuran **6l** was isolated in a trace amount and characterized (see the Experimental Section). [c]*cis*-3-Methylenetetrahydrofuran **6k** was isolated as a mixture with **14**.

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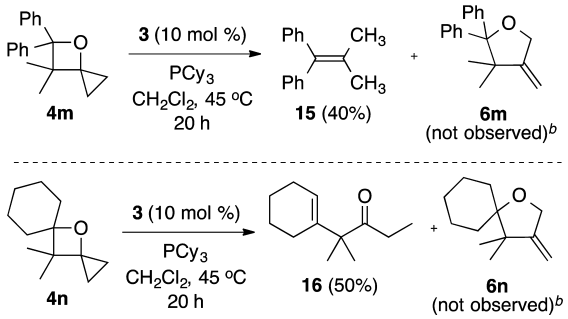
source of the hydrogen needed to form the ring-opened, reduced alcohol product **12**. It is worth noting that consumption of both 5,6-*cis*-substituted oxaspirohexanes took longer than was required for the 5,6-*trans*-substituted compounds. The reactions were also carried out without tricyclohexyl phosphine, and the same products were observed, although the reaction times were even longer. The rearranged products, 3-methylenetetrahydrofurans **6l** and **6k**, were also isolated, but in trace amounts. These alternative outcomes and the longer reaction times will be discussed later.

Completely different results were realized with 5,5,6,6-tetrasubstituted-oxaspirohexanes **4m** and **4n** (Scheme 2).

Scheme 2. Reaction of 5,5-Substituted-Oxaspirohexanes with Zeise's Dimer[a]



[a]Reaction conditions: 1.0 mmol scale, 10 mol % **3**, 20 mol % PCy_3, 0.5 M in CH_2Cl_2. [b]Based on the ^1H NMR analysis of the crude mixture.

When 5,5-diphenylsubstituted oxaspirohexane **4m** was treated with Zeise's dimer, no 3-methylenetetrahydrofuran resulted; instead, tetrasubstituted alkene **15** was isolated in 40% yield. On the other hand, 5,5-dialkyldisubstituted oxaspirohexane **4n** gave *β,γ*-unsaturated ketone **16** in 50% yield as the only isolable product. The different results with **4m** and **4n** and with the oxaspirohexanes with *cis*-substituents on the oxetane ring again led us to question the pathway of these Pt-promoted processes.

Mechanistic Study. It is known that cyclopropanes and the C−O bond of *β*-lactones undergo oxidative addition to Pt(II) to produce stable platinacyclobutane[9,10] and platinalactone[12] complexes, respectively. Likewise, formation of platinaoxetane intermediates has been postulated in the Pt-mediated activation of epoxides.[13] While platinacyclobutanes are known to be stable and isolable, with many being well-characterized, there have been no reports of alkoxy-substituted platinacyclobutanes being isolated or spectroscopically observed. This may be due to favorable formation of oxocarbenium ions, resulting in isomerizations to form ring-opened products.[4−6]

On the basis of the literature precedent related to Pt reactions with strained rings, potential initial oxidative addition of Pt that might be anticipated to occur included (a) into the cyclopropane ring (Figure 4, path *a*) to produce either intermediate **I** or **II** or (b) into the C−O bond of the oxetane ring (path *b*) to give intermediate **III** or **IV**. As previously mentioned, isomerization to the 3-methylenetetrahydrofurans cannot be rationalized from oxocarbenium intermediate **I**. Similarly, intermediate **IV** would not lead to the formation of the observed products, and to date, there have been no reports of oxidative addition of Pt(II) into simple oxetanes.[14]

In order to determine which path was operational, ^{13}C-labeled 4-oxaspirohexane ^{13}C-**4h** was synthesized by cyclopropanation of methyleneoxetane **10h** using ^{13}C-labeled

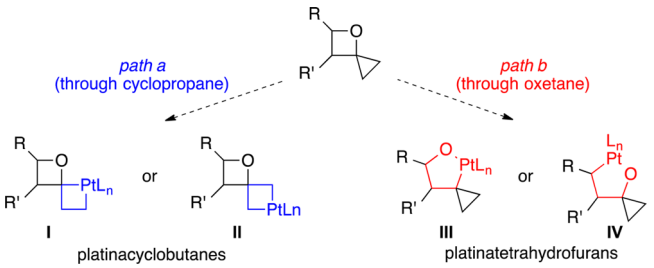
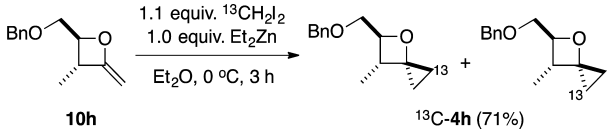


Figure 4. Possible platinacycle intermediates obtained from oxaspirohexanes via the cyclopropane ring (path *a*) or the oxetane ring (path *b*).

diiodomethane (Scheme 3). The labeled compound was obtained in 71% yield as a pair of isotopic stereoisomers.

Scheme 3. Synthesis of ^{13}C-Labeled 4-Oxaspirohexane ^{13}C-4h



^{13}C-labeled **4h** was treated with stoichiometric Zeise's dimer and PCy_3 in CD_2Cl_2 at room temperature, and the reaction was monitored by ^{13}C NMR. Figure 5 provides a summary of the ^{13}C-DEPT NMR analysis of the reaction. Two intermediates with ^{13}C-labeled carbon chemical shifts at 15.04/7.94 ppm (region **A**) and at 49.52/113.70 ppm (regions **B** and **B′**) were observed. These intermediates were present over the course of the reaction (Figure 5b,c) and largely disappeared after complete conversion of ^{13}C-**4h** (Figure 5d). Specifically, they were observed for a span of 3 h when the reaction was monitored at room temperature or could persist for up to 15 h at 0 °C.

The peaks with ^{13}C-labeled carbons at 15.04 and 7.94 ppm (region **A**), correspond to the expected chemical shifts of carbon bonded to Pt in platinacyclobutanes (Figure 6).[9] These ^{13}C-labeled carbons show large Pt-^{13}C coupling constants of 556.6 and 622.4 Hz, respectively, which fall in the range of usual $^1J_{Pt\text{-}^{13}C}$ values in platinacyclobutanes[9] or Pt−C *σ*-bonds in general.[15] This key intermediate was rationalized to be platinacyclobutane ^{13}C-**18** (as a pair of ^{13}C-labeled isotopic stereoisomers).

The additional intermediate peaks observed in regions **B** and **B′** were rationalized to be from Pt-allyl complexes, which can be obtained from the facile ring-puckering[16] of the oxy-platinacyclobutane ^{13}C-**18**. The large differences in ^{13}C chemical shifts (49.5 and 113.70 ppm) and the $J_{P\text{-}^{13}C}$ values (19.1 and 2.5 Hz, respectively) suggest that the intermediate observed is an η^1 Pt-allyl complex[15,17] as a pair of isotopomers. Specifically, the Pt-η^1-allyl intermediate observed in region **B′** corresponds to ^{13}C-**19B′** as indicated by the small $^3J_{Pt\text{-}^{13}C}$ (22.7 Hz), while the intermediate at region **B** corresponds to the other isotopomer, Pt-η^1-allyl ^{13}C-**19B**. Given that the observed $^1J_{Pt\text{-}^{13}C}$ in region **B** (30.6 Hz) is relatively small compared to that of usual Pt−C *σ*-bonds,[15] the Pt−^{13}C bond must be rather weak.[17] The stability of η^1 and η^3 Pt-allyl complexes is highly dependent on the counterion.[16] It would seem that the Pt allyl intermediate prefers a *σ*-coordination mode[17] due to the propensity of intramolecular coordination of the negatively

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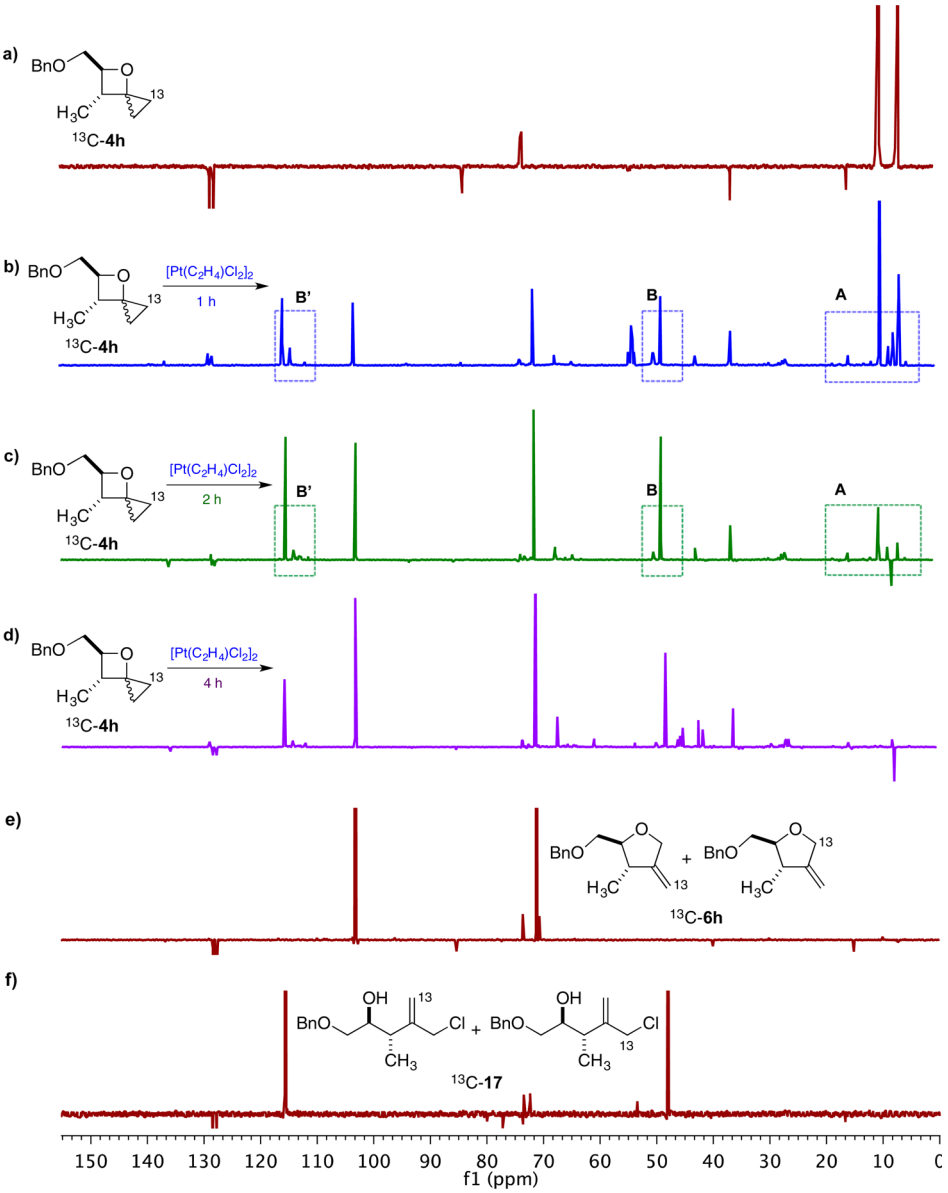

Figure 5. ^{13}C DEPT NMR monitoring of the reaction of ^{13}C-**4h** (0.1 mmol) with a stoichiometric amount of Zeise's dimer and PCy_3 and with 0.2 M ^{13}C-**4h** in CD_2Cl_2 at RT. (a) ^{13}C DEPT NMR spectra of oxaspirohexanes ^{13}C-**4h**. (b) ^{13}C NMR spectrum after 1 h. (c) ^{13}C DEPT after 2 h. (d) ^{13}C DEPT NMR after 4 h. (e) ^{13}C DEPT of methylenetetrahydrofuran products ^{13}C-**6h**. (f) ^{13}C DEPT of allyl chloride byproducts ^{13}C-**17**.

charged oxygen atom to the positively charged Pt to form a six-membered Pt-η^1-allyl complex. Sakaki and co-workers reported that a hydride coordinated Pt-η^1-allyl complex is 8 kcal/mol more stable that its corresponding η^3-allyl complex.[18] Likewise, Pregosin and co-workers have demonstrated that methoxy-modified MOP Pt allyl complexes prefer a σ-coordination mode, albeit with a weak σ-bond.[17] Although the Pt-allyl intermediates observed here appear to be of an η^1 character, the occurrence of Pt-η^3-allyl intermediates is not ruled out. In fact, unresolved peaks were also seen at around 64 and 73 ppm, which may correspond to Pt-η^3-allyl intermediates[15,17] as a pair of isotopomers.

After purification, ^{13}C-labeled 3-methylenetetrahydrofurans ^{13}C-**6h** (with ^{13}C peaks at 103.32 and 71.36 ppm, Figure 5e) were isolated in 55% yield as an isotopomeric mixture (Scheme 4). In addition, isotopomeric byproducts ^{13}C-**17** (with ^{13}C peaks at 115.69 and 48.06 ppm, Figure 5f) were also observed and isolated in 20% yield. The formation of the allyl chloride was not observed when a catalytic amount (5−10 mol %) of Zeise's dimer was used.

The evidence delineated above is suggestive of the mechanistic interpretation shown in Figure 7. First, regioselective oxidative addition of Pt(II) into the least substituted C−C bond in the cyclopropane provides platinacyclobutane **20**. Due to the reactivity of oxygen-substituted platinacyclobutanes and perhaps also to the ring strain associated with oxetanes,[19] ring-opening to Pt-allyl complexes results. Cyclization gives 3-methylenetetrahydrofurans **6**. This mechanism is consistent with the formation of allyl ethers/chlorides by intermolecular reactions of the Pt-allyl complexes with methanol or chloride ion when the reaction is conducted in the presence of methanol or a stoichiometric amount of Zeise's dimer. The observed regioselective oxidative addition of Pt(II) into the cyclopropane is remarkable because this has not been the case for all examples of Pt-catalyzed transformations of oxygen-substituted

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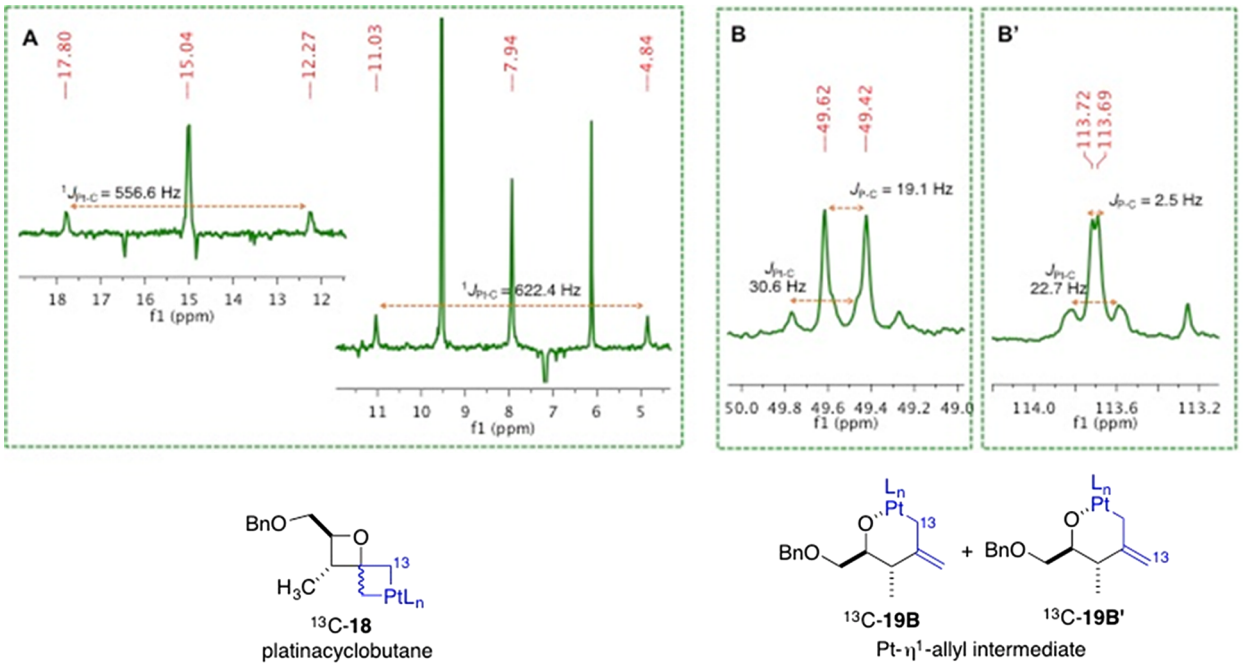
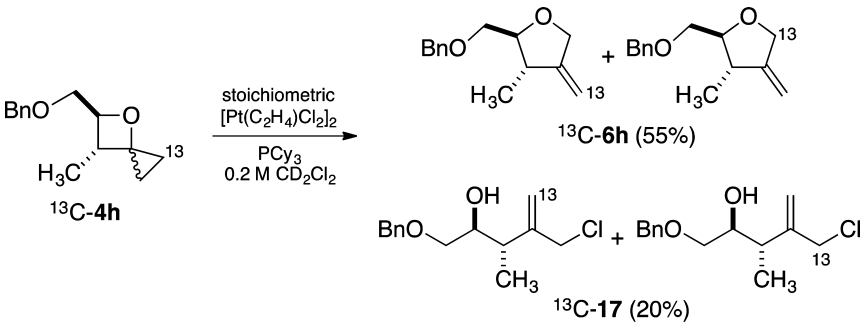


Figure 6. Regions in ^{13}C DEPT NMR monitoring showing the ^{13}C-labeled carbon peaks observed as intermediates from the reaction of ^{13}C-**4h** with Zeise's dimer: (**A**) ^{13}C peaks for platinacyclobutane intermediate ^{13}C-**18** (as a pair of ^{13}C-labeled isotopic stereoisomers) and (**B**/**B′**) ^{13}C peaks for Pt-η^1-allyl intermediate ^{13}C-**19** as a pair of ^{13}C-labeled isotopic stereoisomers.

Scheme 4. Reaction of ^{13}C-Labeled Oxaspirohexane ^{13}C-4h with a Stoichiometric Amount of Zeise's Dimer



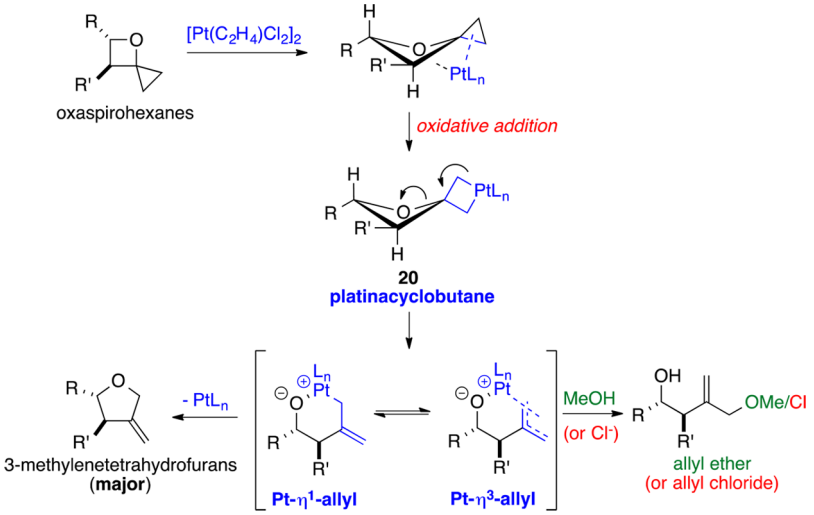


Figure 7. Proposed mechanism for Zeise's dimer-catalyzed rearrangement of oxaspirohexanes to 3-methylenetetrahydrofurans.

cyclopropanes, where C−C bond cleavage has always occurred adjacent to the oxygen.[4−6]

Attempts to isolate the observed platinacyclobutane by adding ligands (e.g., pyridine, bipyridine) used previously in the

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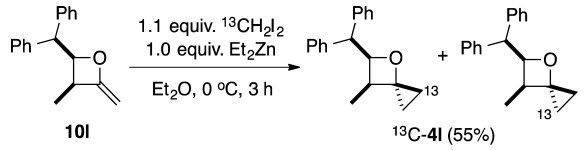
crystallization of platinacyclobutanes[9a] were not successful. In most cases, rearrangement to the 3-methylenetetrahydrofuran was still the outcome.

To understand the unexpected outcome of oxaspirohexanes with *cis*-substituents on the oxetane, ^{13}C-labeling experiments were again conducted. ^{13}C-labeled *cis*-oxaspirohexane ^{13}C-**4l** was obtained as a pair of isotopic stereoisomers from the

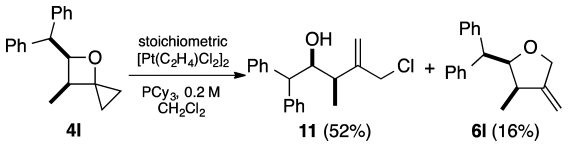
Scheme 5. Synthesis of ^{13}C-Labeled 4-Oxaspirohexane ^{13}C-4l



cyclopropanation of *cis*-methyleneoxetane **10l** (Scheme 5). The ^{13}C-labeled *cis*-oxaspirohexane was treated with a stoichiometric amount of Zeise's dimer under the same conditions as those used for the *trans*-isomer ^{13}C-**4h**, and the reaction was monitored by ^{13}C DEPT NMR (see the Supporting Information).

Somewhat unexpectedly, intermediate peaks analogous to those observed from ^{13}C-**4h** were also witnessed for a span of 3 h. Specifically, peaks at 8.60 and 12.98 ppm (region **A**, Figure 8) correspond to platinacyclobutanes ^{13}C-**21** with Pt satellites ($^1J_{Pt\text{-}^{13}C}$ values of 622.4 and 556.3 Hz, respectively). Likewise, similar to results with ^{13}C-**4h**, isotopomer peaks were observed at 49.4 ppm (region **B**) with a $^1J_{Pt\text{-}^{13}C}$ value of 30.9 ($J_{P\text{-}^{13}C}$ = 33.9 Hz) and at 113.6 ppm (region **B′**) with a $^1J_{Pt\text{-}^{13}C}$ value of 32.4. These shifts correspond to Pt-η^1-allyl intermediates ^{13}C-**22B** and ^{13}C-**22B′**, respectively. As with the unresolved intermediate peaks observed in the reaction of *trans*-oxaspirohexane ^{13}C-**4h**, peaks at around 66 and 68 ppm, which could correspond to Pt-η^3-allyl intermediates,[15,17] were also observed. In contrast to the reaction outcome from ^{13}C-**4h**, *cis*-oxaspirohexane ^{13}C-**4l** gave allyl chloride ^{13}C-**11** and 3-methylenetetrahydrofuran ^{13}C-**6l** as the major and minor products, respectively. As a reference, unlabeled *cis*-oxaspirohexane **4l** was also treated with a stoichiometric amount of Ziese's dimer. Allyl chloride **11** was obtained as the major product in 52% yield, and 3-methylenetetrahydrofuran **6l** was obtained in 16% yield (Scheme 6).

Scheme 6. Reaction of Oxaspirohexane 4l with a Stoichiometric Amount of Zeise's Dimer



Results from the ^{13}C-labeling studies with *cis*-isomer ^{13}C-**4l** demonstrate that the initial intermediates involved in the reactions of *cis*-oxaspirohexanes with Zeise's dimer are identical to those observed with the *trans*-oxaspirohexanes, even though the product distribution is different. Initial oxidative addition of cyclopropane to Pt to form platinacyclobutanes is followed by ring-opening to Pt-allyl intermediates (Figure 9). However, rather than cyclization, the allyl intermediate reacts with a chloride ion to form allyl chloride **11**. For **4k**, the Pt-allyl intermediate undergoes reductive elimination to give homoallyl alcohol **12** (Scheme 1). The contrasting outcome (reduction vs substitution) between *cis*-oxaspirohexanes **4k** and **4l** requires that the allyl intermediates undergo different reactions. For the reaction of **4k**, the isolation of a significant amount of dienone **13** (which must arise from **4k**, rather than a Pt-allyl intermediate) suggests a hydride source. Steric encumbrance could prevent **4l** from providing a hydride. We propose that the low reactivity of the *cis*-isomers is due to steric effects that

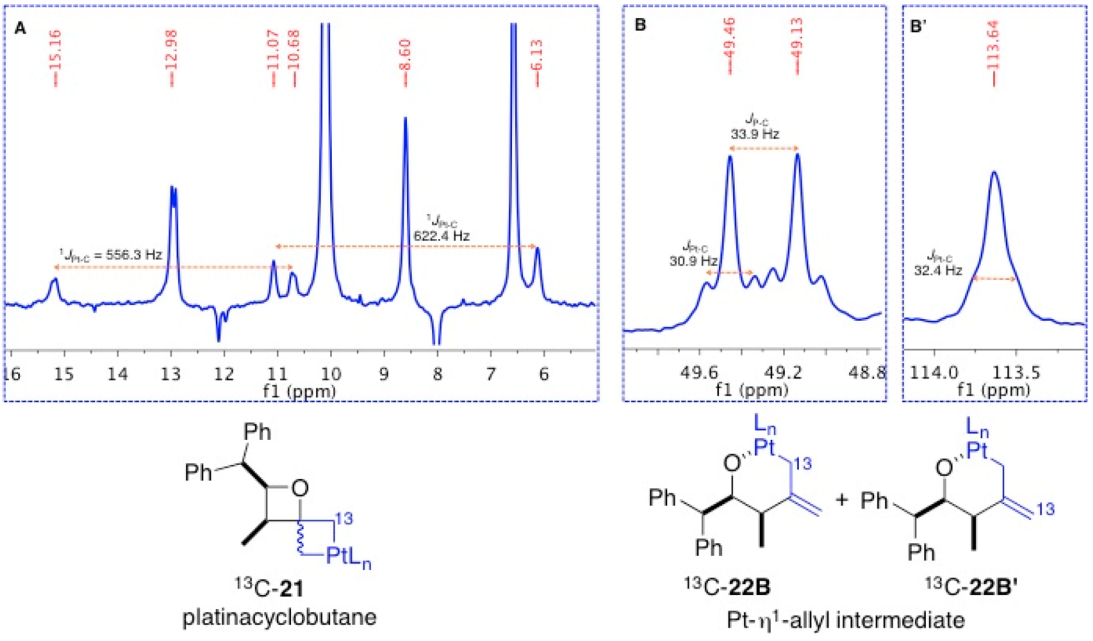


Figure 8. Regions in ^{13}C DEPT NMR monitoring showing the ^{13}C-labeled carbon peaks observed as intermediates from the reaction of ^{13}C-**4l** with Zeise's dimer: (**A**) ^{13}C peaks for platinacyclobutane intermediate ^{13}C-**21** (as a pair of ^{13}C-labeled isotopic stereoisomers) and (**B**/**B′**) ^{13}C peaks for Pt-η^1-allyl intermediate ^{13}C-**22** as an isotopomeric mixture.

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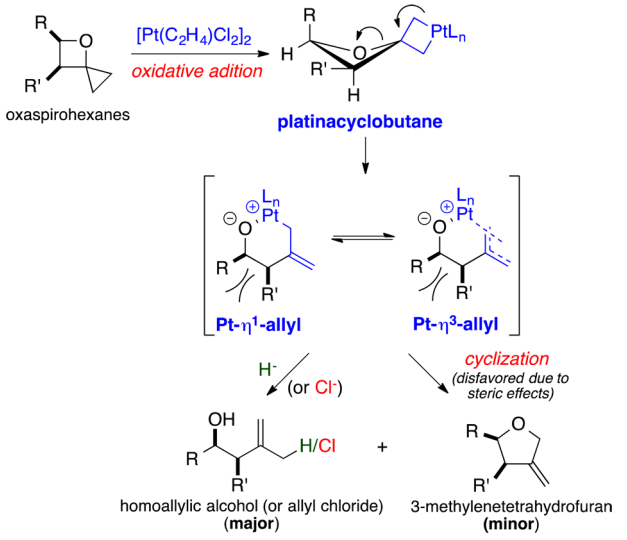


Figure 9. Proposed explanation for alternative pathway for the Zeise's dimer-catalyzed rearrangement of *cis*-oxaspirohexanes.

disfavor the conformation required for the formation of 3-methylenetetrahydrofurans, which leaves the door open for alternative pathways.

For the case of 5,5-disubstituted oxaspirohexanes, we postulate a rearrangement where Pt-mediated bond breaking of the C−O bond in the oxetane ring occurs before cleavage of the cyclopropane (Figure 10). This is presumably due to the

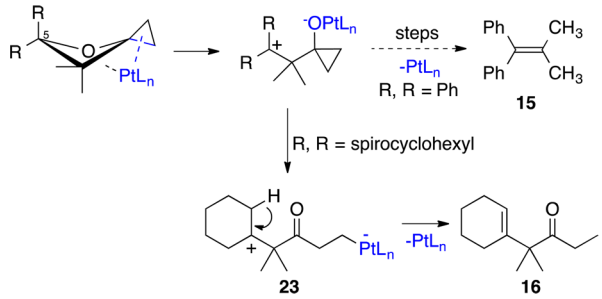
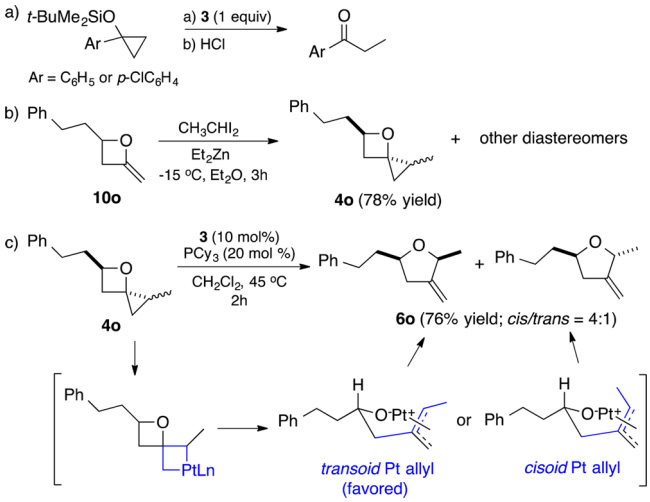


Figure 10. Rationalization of the different outcomes of 5,5-disubstituted oxaspirohexanes.

formation of a tertiary carbocation that ultimately leads to **15** or **16**. The zwitterionic β-platinum(II) ketone intermediate **23** is analogous to the intermediates proposed[5] and the platinum complex[20] isolated by Ryu and Sonoda during their mechanistic investigation of the Pt-catalyzed isomerization of silyloxycyclopropane to allyl silylethers.

It could be argued that the regioselective formation of a platinacyclobutane between the methylenes of the cyclopropane is governed by steric effects. Indeed, most reports of the reaction of Zeise's dimer with 1,1-disubstituted cyclopropanes give products consistent with initial substitution into this less-hindered C−C bond.[9a] However, earlier reports of the reaction of Zeise's dimer with silyloxycyclopropanes had included 1,1-disubstituted compounds. For example, arylsiloxycyclopropanes were converted to aryl ketones in the presence of Zeise's dimer (Scheme 7a).[20] Formation of the ketone requires cleavage of the oxygen-substituted cyclopropane C−C bond. Thus, our initial expectation of platinacyclobutane formation through the C−C bond adjacent to the oxetane

Scheme 7. (a) Reaction of a 1,1-Disubstituted Cyclopropane with Zeise's Dimer.[20] (b) Preparation of Cyclopropane-Substituted Oxaspirohexane 4o. (c) Reaction of Oxaspirohexane 4o with Zeise's Dimer[a]



[a]Reaction conditions: 1.0 mmol scale, 10 mol % **3**, 20 mol % PCy_3, 0.5 M in CH_2Cl_2. *Cis*/*trans* ratio was based on ^1H NMR analysis of the crude mixture.

was warranted. Nevertheless, it seemed worthwhile to examine the effect of placing additional substitution on the cyclopropane. An oxaspirohexane bearing a substituent at the cyclopropyl moiety was prepared by the cyclopropanation of **10o** using diodoethane (Scheme 7b). This provided **4o** in 78% yield (isolated as a single enantiomeric pair, but with the relative stereochemistries unknown). Other diastereomeric products were also obtained as an inseparable mixture in trace amounts. 1-Methyl-substituted oxaspirohexane **4o** was treated with Zeise's dimer, and 3-methylenetetrahydrofuran, isolated in 76% yield (4:1 *cis*/*trans*), resulted (Figure 7c). The observed complete regioselectivity and formation of the *cis*-isomer as the major product further supports the intermediacy of a Pt-allyl intermediate that undergoes a 5-*exo* cyclization mode via the more stable *transoid* Pt-allyl intermediate. Such outcomes were observed in cyclizations of related Pd-allyl systems with O-nucleophiles.[21] These results demonstrate that an additional alkyl substituent on the cyclopropane did not alter the outcome of the reaction, confirming that the regioselectivity cannot be entirely explained by steric effects.

CONCLUSION

A novel Zeise's dimer-catalyzed rearrangement of oxygen-substituted cyclopropanes that provides functionalized tetrahydrofurans has been discovered. This work highlights the first detection of alkoxy-substituted platinacyclobutane intermediates. In contrast to previous reactions with oxygen-substituted cyclopropanes, where oxidative addition to Pt occurred adjacent to the C−O bond, regioselective platinacyclobutane formation through the distal methylene carbons of the cyclopropane ring resulted. The key platinacyclobutane and Pt-allyl intermediates were observed by ^{13}C NMR studies using ^{13}C-labeled oxaspirohexanes. In particular, these studies clarified that, although outcomes with *cis*-5,6-disubstituted oxaspirohexanes were different than those with *trans*-5,6-disubstituted (or 5- or 6-substituted) oxaspirohexanes, the intermediates were identical. An oxaspirohexane bearing a

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substituent on the cyclopropane ring was also efficiently converted to a 3-methylenetetrahydrofuran with complete regioselectivity.

EXPERIMENTAL SECTION

Preparation of β-Lactones. Known β-lactones **9a**,[22] **b**,[11] **c**,[23a] **d**,[23b] **f**,[2b] **g**,[24] **i**,[25] **m**,[26] and **n**[26] were prepared by literature procedures. Spectral data are in accordance with the literature references.

*4-Cyclohexyloxetan-2-one (**9e**).*[27] A solution of $Ag(SbF_6)_3$ (9.10 g, 26.6 mmol) in dry CH_2Cl_2 (60 mL) was added to a solution of $AlCl_3$ (1.18 g, 8.88 mmol) and *i*-Pr_2EtN (4.60 mL, 26.6 mmol) in CH_2Cl_2 (60 mL) at −25 °C under N_2 to form a heterogeneous mixture. *i*-Pr_2EtN (7.70 mL, 44.4 mmol), acetyl chloride (4.70 mL, 66.5 mmol), and a solution of cyclohexylcarboxaldehyde (5.00 g, 44.3 mmol) in CH_2Cl_2 (13 mL) were added, and the resulting mixture was stirred at −25 °C for 4 h. The reaction mixture was then filtered through a pad of Celite, and the Celite was washed with CH_2Cl_2 (3 × 5 mL). The filtrate was then concentrated to give a pale yellow oil. Purification by flash chromatography on silica gel (petroleum ether/EtOAc, 90:10) afforded **9e** as a colorless oil (4.9 g, 72%):[28] ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.20 (m, 1H), 3.43 (dd, J = 16.3, 5.8 Hz, 1H), 3.11 (dd, J = 16.3, 4.4 Hz, 1H), 1.97−1.52 (m, 6H), 1.39−0.90 (m, 5H).

*trans-4-Benzyloxymethyl-3-methyloxetan-2-one (**9h**).*[29] Anhydrous $ZnCl_2$ (5.45 g, 39.9 mmol) was freshly fused at ∼0.5 mmHg. After cooling to ambient temperature, CH_2Cl_2 (140 mL) was added, and the $ZnCl_2$ was broken up into small pieces with a spatula. 2-Benzyloxyacetaldehyde[30] (4.00 g, 26.6 mmol) dissolved in dry CH_2Cl_2 (20 mL) was then added, resulting in a cloudy solution. After 15 min of stirring, TBS-thiopyridylketene acetal[29] (8.25 g, 29.3 mmol) in dry CH_2Cl_2 (20 mL) was added, and the reaction mixture was stirred for 45 h at rt. After completion of the reaction, freshly made phosphate buffer (pH = 7, 25 mL) was added, and the resulting mixture was stirred vigorously for 15 min. It was then filtered through Celite, and the Celite was washed with CH_2Cl_2 (3 × 10 mL). The aqueous and organic layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were dried ($MgSO_4$), and $CuBr_2$ (8.50 g, 38.1 mmol) was added. The reaction mixture was stirred for 1.5 h at rt. It was then filtered through a pad of Celite, and the Celite was washed with CH_2Cl_2 (3 × 10 mL). The filtrate was washed with saturated aqueous K_2CO_3 (15 mL) and then brine (15 mL). The organic layer was dried ($MgSO_4$) and concentrated to give a sticky oil. Purification by flash chromatography on silica gel (petroleum ether/EtOAc, 90:10) yielded **9h** as a colorless oil (3.85 g, 70%): IR (neat) 3064, 3031, 2975, 1936, 2875, 1822, 1454, 1120, 839 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.26 (m, 5H), 4.61 (d, J = 12.6 Hz, 1H), 4.58 (d, J = 12.6 Hz, 1H), 4.31 (ddd, J = 4.0, 4.0, 4.0 Hz, 1H), 3.79 (dd, J = 11.8, 3.7 Hz, 1H), 3.72 (d, J = 11.1, 4.7 Hz, 1H), 3.58 (dq, J = 7.7, 4.4 Hz, 1H), 1.39 (d, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 137.6, 128.7, 128.1, 127.9, 77.5, 73.9, 69.3, 47.6, 12.4; HRMS (ESI) calcd for $C_{12}H_{15}O_3$ $(M + H)^+$ m/z 207.1021, found 207.1011.

(2R,3R*)-2-Benzyloxy-3-cyclohexyl-3-hydroxy-1-S-tert-butyl-thiopropiolate (**24**).*[31] 2-Benzyloxy-*S*-*tert*-butyl-1-thioacetate[32] (4.25 g, 17.8 mmol) was dissolved in dry CH_2Cl_2 (60 mL) under nitrogen and cooled to −78 °C. A solution of $TiCl_4$ (1 M in CH_2Cl_2, 17.8 mL, 17.8 mmol) was added to the flask dropwise over 10 min. After 5 min, Et_3N (5.00 mL, 35.7 mmol) was added. The solution was stirred at −78 °C for 30 min, and then a solution of cyclohexylcarboxylaldehyde (2.00 g, 17.8 mmol) in CH_2Cl_2 (18 mL) was added dropwise. The reaction was stirred at −78 °C for 4 h. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (30 mL), and the resulting slurry was filtered through Celite. The Celite was washed with CH_2Cl_2 (3 × 5 mL). The organic and aqueous layers were then separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Purification by flash chromatography on silica gel (petroleum ether/EtOAc, 85:15) afforded **24** as a colorless oil (3.18 g, 51%): IR (neat) 3031, 2912, 2853, 1826, 1728, 1452, 1115, 892 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.30 (m, 5H), 4.81 (d, J = 11.4 Hz, 1H), 4.45 (d, J = 11.4 Hz, 1H), 3.85 (d, J = 6.4 Hz, 1H), 3.63 (ddd, J = 4.8, 4.8, 4.8 Hz, 1H) 2.33 (d, J = 4.9 Hz, 1H), 1.70 (m, 2H), 1.63 (m, 4H), 1.51 (s, 9H), 1.30−1.03 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.4, 137.1, 128.6, 128.3, 128.2, 85.5, 76.6, 73.5, 47.6, 39.2, 29.8, 26.7, 26.5, 26.4, 26.1; HRMS (ESI) calcd for $C_{20}H_{31}O_3S$ $(M + H)^+$ m/z 351.1994, found 351.1998.

*trans-3-Benzyloxy-4-cyclohexyloxetan-2-one (**9j**).* (2R*,3R*)-2-Benzyloxy-*S*-*tert*-butyl-3-cyclohexyl-3-hydroxy-1-thiopropiolate (**24**) (2.00 g, 5.71 mmol) was dissolved in dry CH_3CN (200 mL) under nitrogen at rt. $Hg(OTFA)_2$ (2.74 g, 6.41 mmol) was added to this solution at once. The resulting reaction mixture was quickly immersed into a preheated oil bath (50 °C). After 5 min, the mixture was filtered through a pad of Celite, which was washed with CH_2Cl_2 (3 × 5 mL). The filtrate was then concentrated to give a pale brown oil. Purification by flash chromatography on silica gel (petroleum ether/EtOAc, 92:8) afforded **9j** as a colorless oil (0.68 g, 46%): IR (neat) 3064, 3032, 2928, 2854, 1833, 1451, 1146, 865, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.32 (m, 5H), 4.81 (d, J = 11.6 Hz, 1H) 4.66 (d, J = 11.5 Hz, 1H), 4.64 (d, J = 3.6 Hz, 1H), 4.22 (dd, J = 8.5, 3.6 Hz, 1H), 1.87 (m, 1H) 1.79−1.50 (m, 5H), 1.28−1.13 (m, 3H), 1.08−0.96 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 136.4, 128.7, 128.4, 128.1, 83.8, 83.6, 72.5, 40.1, 28.4, 27.1, 25.9, 25.3, 25.1; HRMS (ESI) calcd for $C_{16}H_{21}O_3$ $(M + H)^+$ m/z 261.1491, found 261.1465.

*cis-3-Methyl-4-(2-phenylethyl)oxetan-2-one (**9k**).* 3-Methylene-4-(2-phenylethyl)oxetan-2-one[35] (1.88 g, 10 mmol) and 10% Pd on carbon (0.30 mmol, 0.32 g) were mixed in dry THF (10 mL) under a N_2 atmosphere. The reaction vessel was purged with H_2 for 10 min. The reaction mixture was stirred at rt for 2 h under a balloon filled with H_2. The crude mixture was filtered through a pad of Celite. The Celite was washed with CH_2Cl_2 (3 × 10 mL), and the filtrate was concentrated to give a pale yellow oil. ^{1}H NMR analysis of the crude product showed a diastereomer ratio of 10:1 (*cis*:*trans*). Purification by flash chromatography on silica gel (petroleum ether/EtOAc, 92:8) afforded **9k** as a pale yellow oil (1.67 g, 88%):[34] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.24 (m, 5H), 4.57 (ddd, J = 4.5, 4.5, 4.5 Hz, 1H), 3.74 (dq, J = 14.6, 7.4 Hz, 1H), 2.90 (ddd, J = 14.2, 5.3, 5.3 Hz, 1H), 2.73 (m, 1H), 2.06 (m, 2H), 1.28 (d, J = 7.7 Hz, 3H).

*cis-4-Benzhydryl-3-methyloxetan-2-one (**9l**).* 4-Benzhydryl-3-methyleneoxetan-2-one[33] (4.0 mmol, 1.0 g) and 10% Pd on carbon (0.12 mmol, 0.12 g) were mixed in dry THF (4 mL) under a N_2 atmosphere. The reaction vessel was purged with H_2 for 10 min. The reaction mixture was stirred at rt for 2 h under a balloon filled with H_2. The crude mixture was filtered through a pad of Celite. The Celite was washed with CH_2Cl_2 (3 × 10 mL), and the filtrate was concentrated to give a pale yellow oil. ^{1}H NMR analysis of the crude product showed a diastereomer ratio of 20:1.7 (*cis*:*trans*). Purification by flash chromatography on silica gel (petroleum ether/EtOAc, 92:8) afforded **9l** as a pale yellow oil (0.91g, 88%): IR (neat) 3054, 3035, 2950, 1820, 1450, 1144 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.21 (m, 10H), 5.28 (dd, J = 11.2, 6.1, 1H), 4.28 (d, J = 11.2, 1H), 3.86 (m, 1H), 1.12 (d, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 140.8, 139.6, 129.2, 128.8, 128.4, 128.0 127.5, 127.3, 76.9, 51.5, 48.0, 9.1; HRMS (ESI) calcd for $C_{17}H_{17}O_2$ $(M + H)^+$ m/z 253.1229, found 253.1233.

General Procedure for the Preparation of 2-Methyleneoxetanes. A solution of dimethyltitanocene[11] (0.5 M in toluene, 1.5−2.5 equiv) and β-lactone (1 equiv) was stirred in the dark at 80 °C under N_2. The progress of the reaction was monitored over a period of 2−4 h by TLC until the disappearance of the starting material. The cooled reaction mixture was added to petroleum ether (10 volumes) and stirred overnight. The resulting mixture was filtered through a pad of Celite, washing with petroleum ether until the filtrate was colorless. The filtrate was concentrated to about one-third of the original volume of toluene, and the residue was purified by flash column chromatography on silica gel (deactivated by 4% Et_3N in petroleum ether).

Spectral data for known methyleneoxetanes **10a**,[1b] **b**,[1b] **e**,[35] **f**,[2b] **g**,[2b] **i**,[1b] and **m**[3] are in accordance with the literature references.

*4-tert-Butyldiphenylsilyloxymethyl-2-methyleneoxetane (**10d**).* 4-*tert*-Butyl-diphenylsilyloxymethyl-2-methyleneoxetane (**10d**) was pre-

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pared from **9d** (1.2 g, 3.6 mmol) using 2.0 equiv of dimethyltitanocene. Purification by flash column chromatography on silica gel (petroleum ether/Et_3N 98:2) gave **10d** as a yellow oil (0.6 g, 49%): IR (neat) 3047, 2935, 2858, 1471, 802, 743 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (m, 4H), 7.44 (m, 6H), 4.84 (m, 1H), 4.18 (m, 1H), 3.90 (dd, J = 11.8, 3.5 Hz, 1H), 3.85 (dd, J = 11.8, 4.4 Hz, 1H), 3.78 (m, 1H), 3.15 (m, 2H), 1.10 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 135.9, 135.8, 133.4, 130.0, 127.9, 127.9, 79.9, 78.7, 65.6, 30.5, 27.0, 19.5; HRMS (ESI) m/z calcd for $C_{21}H_{26}O_2Si$ $(M + Na)^+$ 361.1594, found 361.1597.

*trans-4-Benzyloxymethyl-3-methyl-2-methyleneoxetane (**10h**).* *trans*-4-Benzyloxymethyl-3-methyl-2-methyleneoxetane (**10h**) was prepared from **9h** (0.50 g, 2.4 mmol) using 2.5 equiv of dimethyltitanocene. Purification by flash chromatography on silica gel (petroleum ether/EtOAc/Et_3N, 95.5:4:0.5) afforded **10h** as a pale yellow oil (0.38 g, 75%): IR (neat) 3031, 2934, 2878, 1715, 1496, 1454, 1359, 1275, 1114, 740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37−7.28 (m, 5H), 4.62 (m, 2H), 4.57 (ddd, J = 4.7, 4.7, 4.7 Hz, 1H), 4.13 (dd, J = 3.6, 2.3 Hz, 1H), 3.79 (dd, J = 3.6, 1.7 Hz, 1H), 3.75−3.65 (m, 2H), 3.30 (m, 1H), 1.30 (d, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.4, 138.1, 128.5, 127.8, 112.1, 85.5, 78.4, 73.7, 71.4, 38.6, 16.5; HRMS (ESI) calcd for $C_{13}H_{17}O_2$ $(M + H)^+$ m/z 205.1229, found: 205.1220.

*trans-3-Benzyloxy-4-cyclohexyl-2-methyleneoxetane (**10j**).* *trans*-4-Benzyloxy-3-cyclohexyl-2-methyleneoxetane (**10j**) was prepared from **9j** (0.42 g, 1.6 mmol) using 1.5 equiv of dimethyltitanocene. Purification by flash chromatography on silica gel (petroleum ether/Et_2O/Et_3N, 95.5:4:0.5) afforded **10j** as a clear oil (0.23 g, 57%): IR (neat) 2927, 2853, 1726, 1451, 1119, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ7.35 (4H), 7.32−7.25 (m, 1H), 4.61 (s, 2H), 4.57 (dd, J = 1.7, 1.7 Hz, 1H), 4.42 (dd, J = 8.2, 3.8 Hz, 1H), 4.25 (dd, J = 3.3, 1.6 Hz, 1H), 4.01 (dd, J = 3.5, 1.0 Hz, 1H), 1.86 (m, 1H), 1.78−1.74 (m, 2H), 1.70−1.63 (m, 2H), 1.60−1.53 (m, 1H), 1.25−1.12 (m, 3H), 1.03−0.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ164.2, 137.7, 128.7, 128.2, 128.0, 91.2, 81.7, 77.7, 71.1, 41.1, 28.1, 26.9, 26.4, 25.7, 25.4; HRMS (ESI) calcd for $C_{17}H_{23}O_2$ $(M + H)^+$ m/z 259.1698, found 259.1674.

*cis-3-Methyl-2-methylene-4-(2-phenylethyl)oxetane (**10k**).* *cis*-3-Methyl-2-methylene-4-(2-phenylethyl)oxetane (**10k**) was prepared from **9k** (0.5 g, 2.7 mmol) using 2 equiv of dimethyltitanocene. Purification by flash chromatography on silica gel (petroleum ether/Et_2O/Et_3N, 97.5:2:0.5) afforded **10k** as a pale yellow oil (0.36 g, 72%): IR (neat) 3026, 2924, 2854, 1706, 1603, 1496, 1454, 1180, 1082, 1030 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33−7.26 (m, 2H), 7.22−7.18 (m, 3H), 4.80 (ddd, J = 9.6, 7.0, 3.9 Hz, 1H), 4.09 (dd, J = 3.4, 2.4 Hz, 1H), 3.73 (dd, J = 3.4, 1.7 Hz, 1H), 3.55 (m, 1H), 2.81 (ddd, J = 14.1, 9.9, 5.1 Hz, 1H), 2.60 (m, 1H), 2.16 (dddd, J = 19.1, 14.4, 9.5, 5.2 Hz, 1H), 1.88 (dddd, J = 20.8, 10.8, 6.9, 4.0 Hz, 1H), 1.18 (d, J = 7.3 Hz, 3H); ^{13}C NMR (75 Hz, $CDCl_3$) δ 169.8, 141.5, 128.7, 126.3, 82.4, 78.0, 38.3, 32.8, 31.5, 12.4; HRMS (ESI) calcd for $C_{13}H_{17}O$ (M^+) m/z 189.1279, found 189.1268.

*cis-4-Benzhydryl-3-methyl-2-methyleneoxetane (**10l**).* *cis*-4-Benzhydryl-3-methyl-2-methyleneoxetane (**10l**) was prepared from **9l** (0.15 g, 0.60 mmol) using 2 equiv of dimethyltitanocene. Purification by flash chromatography on silica gel (petroleum ether/Et_2O/Et_3N, 97.5:2:0.5) afforded **10l** as a pale yellow oil (0.12 g, 78%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.05−6.99 (m, 6H), 6.96−6.89 (m, 4H), 5.27 (dd, J = 11.2, 6.8 Hz, 1H), 4.14 (d, J = 11.2 Hz, 1H), 3.86 (dd, J = 3.6, 2.2 Hz, 1H), 3.50 (dd, J = 3.6, 1.7 Hz, 1H), 3.37 (m, 1H), 0.78 (d, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.8, 141.6, 140.7, 129.0, 128.8, 128.5, 128.2, 127.0, 127.0, 83.9, 78.4, 51.9, 39.0, 13.4; HRMS (ESI) calcd for $C_{18}H_{18}O$ $(M + H)^+$ m/z 251.1435, found 251.1422.

*3,3-Dimethyl-2-methylene-1-oxaspiro[3.5]nonane (**10n**).* 3,3-Dimethyl-2-methylene-1-oxaspiro[3.5]nonane (**10n**) was prepared from **9n** (1.5 g, 8.9 mmol) using 2 equiv of dimethyltitanocene. Purification by flash chromatography on silica gel (petroleum ether/Et_3N, 99.5:0.5) afforded **10n** as a pale yellow oil (1.1 g, 70%): IR (neat) 2925, 2859, 1693, 1469, 1368, 1123 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.93 (d, J = 3.3 Hz, 1H), 3.62 (d, J = 3.3 Hz, 1H), 1.97−1.92 (m, 2H), 1.64−1.52 (m, 8H), 1.22 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.1, 90.1, 75.2, 46.4, 33.0, 25.3, 22.7, 22.1; HRMS (ESI) calcd for $C_{11}H_{19}O$ $(M + H)^+$ m/z 167.1436, found 167.1424.

[3]General Procedure for the Preparation of 4-Oxaspiro[2.3]-hexanes. A flame-dried three-neck reaction flask with a stir bar was charged with dry Et_2O (3/4 total volume) under N_2. After the solvent was cooled to −15 °C, neat Et_2Zn (2.0 equiv) was added dropwise. The cloudy solution was stirred until clear (approximately 5 min), and CH_2I_2 (4.0 equiv) was then added while maintaining the internal temperature below −15 °C. After the addition was complete, the reaction was allowed to warm to −5 °C (over 10 min). The solution was cooled to −15 °C again, and a solution of 2-methyleneoxetane (1 equiv, 1.0 to 1.5 M) in dry Et_2O (1/4 total volume) was then added. The solution was stirred at −15 °C for 5 min and was then transferred to an ice bath (0 °C). The reaction was stirred at 0 °C until complete consumption of 2-methyleneoxetane was observed by TLC (3−4 h). The reaction was quenched with saturated aqueous NH_4Cl (5 mL) by dropwise addition at 0 °C with stirring for 5 min. The aqueous and organic layers were then separated, and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. Spectral data for known 4-oxaspiro[2.3]hexanes **4a**, **4b**, and **4m** are in accordance with the literature.[3]

*5-Benzyloxymethyl-4-oxaspiro[2.3]hexane (**4c**).* 5-Benzyloxymethyl-4-oxaspiro[2.3]hexane (**4c**) was prepared using **10c** (0.14 g, 0.75 mmol). Purification by flash chromatography on silica gel (petroleum ether/Et_2O, 94:6) afforded **4c** as a colorless oil (0.12 g, 78%): IR (neat) 2922, 1558, 1457, 1103 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 (m, 5H), 4.94 (m, 1H), 4.68 (d, J = 12.1 Hz, 1H), 4.65 (d, J = 12.1 Hz, 1H), 3.80 (dd, J = 10.9, 5.8 Hz, 1H), 3.71 (dd, J = 10.9, 3.8 Hz, 1H), 2.88 (dd, J = 10.8, 7.9 Hz, 1H), 2.70 (dd, J = 10.8, 6.2 Hz, 1H), 0.84 (m, 2H), 0.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 128.6, 127.9, 127.8, 75.8, 73.7, 73.6, 66.2, 31.3, 10.6, 10.5; HRMS (ESI) calcd for $C_{13}H_{16}O_2$ $(M + Na)^+$ m/z 227.1043, found 227.1066.

*5-tert-Butyldiphenylsilyloxymethyl-4-oxaspiro[2.3]hexane (**4d**).* 5-*tert*-Butyldiphenylsilyloxymethyl-4-oxaspiro[2.3]hexane (**4d**) was prepared using **10d** (0.32 g, 0.95 mmol). Purification by flash chromatography on silica gel (petroleum ether/EtOAc 98:2) afforded **4d** as a colorless oil (0.23 g, 68%): IR (neat) 3072, 2958, 1428, 1113, 824, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (m, 4H), 7.42 (m, 6H), 4.83 (m, 1H), 3.87 (d, J = 4.2 Hz, 2H), 2.84 (dd, J = 10.5, 7.7 Hz, 1H), 2.76 (dd, J = 10.7, 6.0 Hz, 1H), 0.95 (s, 9H), 0.83 (m, 2H), 0.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.9, 135.9, 133.8, 133.7, 129.8, 127.9, 76.9, 67.0, 66.0, 30.5, 27.0, 19.5, 10.8, 10.6; HRMS (ESI) calcd for $C_{22}H_{28}O_2SiNa$ $(M + Na)^+$ m/z 375.1751, found 375.1740.

*5-Cyclohexyl-4-oxaspiro[2.3]hexane (**4e**).* 5-Cyclohexyl-4-oxaspiro[2.3]hexane (**4e**) was prepared using **10e** (0.27 g, 1.8 mmol). Purification by flash chromatography on silica gel (petroleum ether/Et_2O, 99:1) afforded **4e** as a pale yellow oil (0.12 g, 40%): IR (neat) 1966, 1925, 1738, 1570, 1076 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.42 (ddd, J = 7.2, 7.2, 7.2 Hz, 1H), 2.75 (dd, J = 10.7, 7.6 Hz, 1H), 2.54 (dd, J = 11.2, 6.4 Hz, 1H), 1.90 (m, 1H), 1.78−1.74 (m, 2H), 1.70−1.61 (m, 4H), 1.32−1.14 (m, 2H), 0.98 (m, 2H), 0.83−0.70 (m, 2H), 0.53 (ddd, J = 11.8, 5.9, 5.9 Hz, 1H), 0.43 (ddd, J = 10.4, 5.4, 5.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ81.2, 65.2, 44.3, 32.6, 27.9, 26.7, 26.6, 25.9, 25.7, 10.7, 10.6.; HRMS (ESI) calcd for $C_{11}H_{19}O$ $(M + H)^+$ m/z 167.1436, found 167.1417.

*(S)-6-tert-Butoxycarbonylamino-4-oxaspiro[2.3]hexane (**4f**).* (*S*)-6-*tert*-Butoxycarbonylamino-4-oxaspiro[2.3]hexane (**4f**) was prepared using **10f** (0.22 g, 1.2 mmol). Purification by flash chromatography on silica gel (petroleum ether/EtOAc 90:10) afforded **4f** as a white solid (0.12 g, 51%): mp 97−99 °C; $[\alpha]_D^{25}$ 22.3 (c 0.52, CH_2Cl_2); IR (KBr) 3339, 2970, 1687, 1538, 1368, 1255, 1165 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 4.96 (m, 2H), 4.82 (dd, J = 6.6, 6.6 Hz, 1H), 4.33 (dd, J = 6.0, 6.0 Hz, 1H), 1.39 (s, 9H), 0.92 (m, 1H), 0.64 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0, 80.2, 75.1, 74.6, 50.5, 28.5, 10.2, 6.7; HRMS (FAB) calcd for $C_{10}H_{17}NO_3Na$ $(M + Na)^+$ m/z 222.1101, found 222.1123.

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*(S)-6-Tritylamino-4-oxaspiro[2.3]hexane (**4g**).* (*S*)-6-Tritylamino-4-oxaspiro[2.3]hexane (**4g**) was prepared using **10g** (0.18 g, 0.59 mmol). Purification by flash chromatography on silica gel (petroleum ether/EtOAc 95:5) afforded **4g** as a white solid (0.09 g, 45%): mp 177−179 °C; $[\alpha]_D^{25}$ 13.0 (*c* 0.26, CH_2Cl_2); IR (KBr) 3055, 2885, 1490, 1450, 1191, 946, 741, 712 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 7.45 (m, 6H), 7.32−7.21 (m, 9H), 4.22 (ddd, *J* = 12.6, 6.7, 6,7 Hz, 1H), 3.99 (dd, *J* = 6.5, 6.5 Hz, 1H), 3.66 (dd, *J* = 6.3, 6.3 Hz, 1H), 2.34 (d, *J* = 11.6 Hz, 1H), 0.96 (ddd, *J* = 12.8, 6.8, 6.8 Hz, 1H), 0.82 (ddd, *J* = 11.7, 7.0, 7.0 Hz, 1H), 0.66 (ddd, *J* = 13.0, 6.9, 6.9 Hz, 1H), 0.40 (ddd, *J* = 11.4, 7.0, 7.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.5, 128.5, 128.3, 126.8, 78.9, 75.4, 70.2, 53.5, 9.0, 6.4; HRMS (ESI) calcd for $C_{24}H_{23}NONa$ $(M + Na)^+$ *m*/*z* 364.1672, found 364.1695.

*trans-5-Benzyloxymethyl-6-methyl-4-oxaspiro[2.3]hexane (**4h**).* *trans*-5-Benzyloxymethyl-6-methyl-4-oxaspiro[2.3]hexane (**4h**) was prepared using **10h** (0.57 g, 2.8 mmol). Purification by flash chromatography on slica gel (petroleum ether/EtOAc 95:5) afforded **4h** as a colorless oil (0.49 g, 78%): IR (neat) 3065, 3031, 2961, 2926, 2871, 1722, 1455, 1116 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ7.34−7.28 (m, 4H), 7.25−7.20 (m, 1H), 4.61 (d, *J* = 12.4 Hz, 1H), 4.57 (d, *J* = 12.2 Hz, 1H), 4.46 (ddd, *J* = 5.7, 5.7, 3.9 Hz, 1H), 3.72 (dd, *J* = 10.9, 5.7 Hz, 1H), 3.64 (dd, *J* = 10.9, 3.8 Hz, 1H), 2.90 (dq, *J* = 6.7, 6.7 Hz, 1H), 1.10 (d, *J* = 6.9 Hz, 3H), 0.81 (m, 1H), 0.58 (m, 2H), 0.40 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 128.4, 127.7, 127.7, 83.8, 73.5, 72.9, 71.3, 36.4, 15.6, 9.9, 6.5; HRMS (ESI) calcd for $C_{14}H_{19}O_2$ $(M + H)^+$ *m*/*z* 219.1385, found 219.1388.

*trans-6-Methyl-5-(2-phenylethyl)-4-oxaspiro[2.3]hexane (**4i**).* *trans*-6-Methyl-5-(2-phenylethyl)-4-oxaspiro[2.3]hexane (**4i**) was prepared using **10i** (0.34 g, 1.8 mmol). Flash chromatography on silica gel (petroleum ether/Et_2O, 97:3) afforded **4i** as a colorless oil (0.28 g, 78%): IR (neat) 3027, 2927, 1604, 1454, 1194, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32−7.17 (m, 5H), 4.35 (ddd, *J* = 7.2, 5.8, 5.8 Hz, 1H), 2.80−2.72 (m, 2H), 2.69−2.61 (m, 1H), 2.23−2.13 (m, 1H), 2.11−2.01 (m, 1H), 1.10 (d, *J* = 6.9 Hz, 3H), 0.84 (ddd, *J* = 11.8, 7.5, 6.5 Hz, 1H), 0.66−0.56 (m, 2H), 0.44 (ddd, *J* = 10.6, 7.7, 6.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.8, 128.6, 126.0, 84.9, 70.4, 39.8, 38.6, 30.9, 15.7, 10.0, 6.5; HRMS (ESI) calcd for $C_{14}H_{19}O$ $(M + H)^+$ *m*/*z* 203.1436, found 203.1419.

*trans-6-Benzyloxy-5-cyclohexyl-4-oxaspiro[2.3]hexane (**4j**).* *trans*-6-Benzyloxy-5-cyclohexyl-4-oxaspiro[2.3]hexane (**4j**) using **10j** (0.19 g, 0.75 mmol). Purification by flash chromatography on silica gel (petroleum ether/Et_2O, 99:1) afforded **4j** as pale yellow oil (0.12 g, 60%): IR (neat) 3067, 3034, 2865, 1729, 1451, 1274, 1112, 1026 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36−7.27 (m, 5H), 4.51 (d, *J* = 11.8 Hz, 1H), 4.39 (d, *J* = 2.9 Hz, 1H), 4.36 (dd, *J* = 3.8, 3.8 Hz, 1H), 4.33 (d, *J* = 4.6 Hz, 1H), 1.87 (m, 1H), 1.80−1.67 (m, 4H), 1.65−1.58 (m, 1H), 1.31−1.13 (m, 3H), 1.03 (dd, *J* = 11.8, 3.6 Hz, 1H), 0.97 (dd, *J* = 11.8, 3.4 Hz, 1H), 0.87 (m, 2H), 0.74 (m, 1H), 0.50−0.43 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.1, 128.6, 128.0, 127.8, 89.9, 79.8, 71.5, 70.6, 42.0, 28.3, 27.2, 26.5, 25.9, 25.7, 9.8, 6.9; HRMS (ESI) calcd for $C_{18}H_{23}O_2$ $(M - H)^+$ *m*/*z* 271.1698, found 271.1694.

*cis-6-Methyl-5-(2-phenylethyl)-4-oxaspiro[2.3]hexane (**4k**).* *cis*-6-Methyl-5-(2-phenylethyl)-4-oxaspiro[2.3]hexane (**4k**) was prepared using **10k** (0.50 g, 2.6 mmol). Purification by flash chromatography on silica gel (petroleum ether/Et_2O, 97:3) afforded **4k** as a colorless oil (0.41 g, 76%): IR (neat) 3078, 3063, 2933, 2238, 1641, 1497, 1173, 798 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35−7.21 (m, 5H), 4.83 (ddd, *J* = 9.7, 8.3, 4.5 Hz, 1H), 3.17 (dq, *J* = 7.1, 7.1 Hz, 1H), 2.78 (ddd, *J* = 13.9, 10.0, 5.1 Hz, 1H), 2.58 (ddd, *J* = 13.9, 9.7, 6.6 Hz, 1H), 2.18 (dddd, *J* = 14.2, 9.9, 9.9, 5.4 Hz, 1H), 1.89 (dddd, *J* = 10.6, 10.6, 6.6, 4.2 Hz, 1H) 1.04 (d, *J* = 7.0 Hz, 3H), 0.89−0.83 (m, 1H), 0.63−0.58 (m, 1H), 0.56−0.51 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.9, 128.6, 128.5, 126.0, 80.1, 71.2, 36.1, 33.7, 31.4, 11.1, 9.7, 6.7; HRMS (ESI) calcd for $C_{14}H_{19}O$ $(M + H)^+$ *m*/*z* 203.1436, found 203.1418.

*cis-5-Benzhydryl-6-methyl-4-oxaspiro[2.3]hexane (**4l**).* *cis*-5-Benzhydryl-6-methyl-4-oxaspiro[2.3]hexane (**4l**) was prepared using **10l** (0.12 g, 0.48 mmol). Purification by flash chromatography on silica gel (petroleum ether/Et_2O, 96:4) afforded **4l** as a colorless oil (0.11 g, 86%): IR (neat) 3082, 2925, 1495, 1451, 970, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33−7.13 (m, 10H), 5.63 (dd, *J* = 11.0, 7.4 Hz, 1H), 4.47 (d, *J* = 11.0 Hz, 1H), 3.20 (dq, *J* = 7.2, 7.2 Hz, 1H), 0.96 (d, *J* = 7.2 Hz, 3H), 0.92−0.87 (m, 1H), 0.67−0.62 (m, 1H) 0.60−0.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1, 141.5, 128.9, 128.7, 128.5, 128.3, 126.8, 126.7, 81.8, 70.9, 52.7, 37.0, 12.0, 10.0, 6.4; HRMS (ESI) calcd for $C_{19}H_{21}O$ $(M + H)^+$ *m*/*z*, 265.1592, found 265.1599.

*9,9-Dimethyl-3-oxadispiro[2.2.5.0]undecane (**4n**).* 9,9-Dimethyl-3-oxadispiro[2.2.5.0]undecane (**4n**) was prepared using **10n** (0.70 g, 4.2 mmol). Flash chromatography on silica gel (petroleum ether/Et_2O, 99.5:0.5) afforded **4n** as a colorless oil (0.56 g, 75%): ^1H NMR (400 MHz, $CDCl_3$) δ 2.00 (m, 2H), 1.59−1.50 (br m, 8H), 1.05 (s, 6H), 0.58 (m, 2H), 0.44 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 86.9, 72.9, 41.3, 33.8, 25.6, 22.7, 20.7, 7.0; HRMS (ESI) calcd for $C_{12}H_{21}O$ $(M + H)^+$ *m*/*z* 181.1592, found 181.1587.

*1-Methyl-6-(2-phenylethyl)-4-oxaspiro[2.3]hexane (**4o**).* 1-Methyl-6-(2-phenylethyl)-4-oxaspiro[2.3]hexane (**4o**) was prepared using 2-methylene-4-(2-phenylethyl)oxetane[11] (**10o**) (0.17 g, 1.0 mmol) and diiodoethane (3 equiv). Purification by flash chromatography on silica gel (petroleum ether/Et_2O, 99:1) afforded **4o** as colorless oil (0.15 g, 78%): IR (neat) 3061, 3025, 2926, 2867, 1453, 1440, 1279, 1016 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31−7.17 (m, 5H), 4.74 (dddd, *J* = 6.4, 6.4, 6.4, 6.4 Hz, 1H), 2.81−2.63 (m, 2H), 2.68 (dd, *J* = 9.7, 6.3 Hz, 1H), 2.47 (dd, *J* = 10.6, 6.3 Hz, 1H), 2.21 (dddd, *J* = 13.4, 10.3, 6.1, 6.1 Hz, 1H), 2.06 (dddd, *J* = 12.4, 10.1, 6.1, 6.1 Hz, 1H), 1.11 (d, *J* = 6.2 Hz, 3H), 0.76−0.71 (m, 1H), 0.60 (dd, *J* = 9.8, 6.6 Hz, 1H), 0.32 (dd, *J* = 6.6, 6.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.9, 128.6, 128.6, 126.1, 77.3, 68.4, 39.5, 35.0, 30.9, 17.4, 15.6, 12.6; HRMS (ESI) calcd for $C_{14}H_{19}O$ $(M + H)^+$ *m*/*z* 203.1436, found 203.1441.

*^{13}C-Labeled trans-5-Benzyloxymethyl-6-methyl-4-oxaspiro[2.3]-hexane (**^{13}C-4h**).* Compound ^{13}C-**4h** was prepared using **10h** (0.1 g, 0.5 mmol) and $^{13}CH_2I_2$ (1.1 equiv). Purification by column chromatography on silica gel (petroleum ether/EtOAc 95:5) afforded ^{13}C-labeled *trans*-5-benzyloxymethyl-6-methyl-4-oxaspiro[2.3]hexane (^{13}C-**4h**) as a pair of ^{13}C-labeled isotopic stereoisomers (colorless oil) (0.08 g, 71%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.42−7.25 (m, 5H), 4.65 (d, *J* = 12.2 Hz, 1H), 4.62 (d, *J* = 12.2 Hz, 1H), 4.50 (ddd, *J* = 5.7, 5.7, 3.8 Hz, 1H), 3.76 (dd, *J* = 11.0, 5.8 Hz, 1H), 3.76 (dd, *J* = 11.0, 3.8 Hz, 1H), 2.94 (m, 1H), 1.14 (d, *J* = 6.9 Hz, 3H), 1.10−0.14 (m,[36a] 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 128.6, 127.8, 127.8, 83.9, 73.7, 73.0, 71.5 (71.3 for the other isotopic stereoisomer), 36.5, 15.7, <u>10.0</u> (^{13}C-labeled), <u>6.6</u> (^{13}C-labeled); HRMS (ESI) calcd for $C_{13}{}^{13}CH_{17}O_2$ $(M + H)^+$ *m*/*z* 220.1385, found 220.1375.

*^{13}C-Labeled cis-5-Benzhydryl-6-methyl-4-oxaspiro[2.3]hexane (**^{13}C-4l**).* Compound ^{13}C-**4l** was prepared using **10l** (120 mg, 0.48 mmol) and $^{13}CH_2I_2$ (1.1 equiv). Purification by column chromatography on silica gel (petroleum ether/EtOAc 95:5) afforded ^{13}C-labeled *cis*-5-benzhydryl-6-methyl-4-oxaspiro[2.3]hexane (^{13}C-**4l**) as a pair of ^{13}C-labeled isotopic stereoisomers (colorless oil) (69 mg, 55%): IR (neat) 3082, 2925, 1495, 1451, 970, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32−7.11 (m, 10 H), 5.62 (dd, *J* = 11.1, 7.3 Hz, 1H), 4.46 (d, *J* = 11.1 Hz, 1H), 3.20 (m, 1H), 0.95 (d, *J* = 7.2 Hz, 3H), 1.26−0.53 (m,[36a] 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.1, 141.5, 128.9, 128.7, 128.6, 128.3, 126.8, 126.7, 81.8, 71.0 (70.8 for the other isotopic stereoisomer), 52.7, 37.0, <u>10.0</u> (^{13}C-labeled carbon), <u>6.4</u> (^{13}C-labeled carbon); HRMS (ESI) calcd for $C_{18}{}^{13}CH_{21}O$ $(M + H)^+$ *m*/*z* 266.1592, found 266.1605.

General Procedure for the Pt-Catalyzed Rearrangement of Oxaspirohexanes (4a−n). Dry CH_2Cl_2 (0.5 mL) was added to a nitrogen purged flask containing Zeise's dimer (0.1 mmol). PCy_3 (0.2 mmol) was added to the solution all at once at rt. 4-Oxaspiro[2.3]-hexane (1 mmol) dissolved in dry CH_2Cl_2 (1.5 mL) was then added, and the reaction was heated at 45 °C. The reaction was monitored by ^1H NMR/TLC for the disappearance of the 4-oxaspiro[2.3]hexane. Products were isolated by column chromatography on neutral alumina or silica gel.

*3-Methylene-4-phenyltetrahydrofuran (**6a**).* The general procedure was followed using **4a** (0.10 g, 0.63 mmol). The reaction was stirred for 3.5 h. Purification by flash chromatography on neutral alumina (petroleum ether/EtOAc, 96:4) afforded **6a** as a colorless oil

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(34 mg, 34%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (m, 2H), 7.24 (m, 3H), 5.05 (m, 1H), 4.77 (dd, J = 4.6, 2.2 Hz, 1H), 4.51 (m, 2H), 4.29 (dd, J = 6.2, 6.2 Hz, 1H), 3.85 (m, 1H), 3.81 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.6, 141.3, 128.8, 128.5, 127.0, 106.2, 76.2, 72.3, 50.8. HRMS (ESI) calcd for $C_{11}H_{11}O$ $(M - H)^+$ m/z 159.0810, found 159.0795.

*3-Methoxymethyl-2-phenylbut-3-en-1-ol (**7a**).* The general procedure was followed using **4a** (60 mg, 0.37 mmol) in the presence of MeOH (20 equiv). The reaction was stirred for 2 h. Purification by flash chromatography on neutral alumina (petroleum ether/EtOAc, 95:5) afforded **7a** as a yellow oil (44 mg, 50%): IR (neat) 3060, 2924, 2853, 1715, 1453, 1111 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ7.34−7.22 (m, 5H), 5.30 (s, 1H), 5.15 (s, 1H), 4.02 (dd, J = 18.1, 10.7 Hz, 1H), 3.91 (dd, J = 17.6, 6.8 Hz, 1H), 3.77 (d, J = 12.8 Hz, 1H), 3.75 (d, J = 12.6 Hz, 1H), 3.61 (dd, J = 7.0, 7.0 Hz, 1H), 3.27 (s, 3H), 2.01 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7, 140.2, 128.8, 128.4, 127.2, 114.2, 75.2, 65.2, 58.2, 51.3; HRMS (FAB) calcd for $C_{12}H_{17}O_2$ $(M + H)^+$ m/z 193.1229, found 193.1236.

*2-Benzyloxymethyl-4-methylenetetrahydrofuran (**6c**).* The general procedure was followed using **4c** (39 mg, 0.19 mmol). The reaction mixture was stirred for 40 min. Purification by flash chromatography on neutral alumina (petroleum ether/EtOAc 96:4) afforded **6c** as a colorless oil (25 mg, 65%):[37] IR (neat) 2919, 2857, 1497, 1101, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ7.30 (m, 5H), 4.96 (ddd, J = 4.4, 2.2, 2.2 Hz, 1H), 4.90 (ddd, J = 4.3, 2.1, 2.1 Hz, 1H), 4.59 (d, J = 12.1 Hz, 1H), 4.54 (d, J = 12.1 Hz, 1H), 4.39 (m, 1H), 4.26 (m, 1H), 4.19 (m, 1H), 3.15 (m, 2H), 2.58 (m, 1H), 2.37 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.5, 138.2, 128.4, 127.7, 127.6, 104.4, 78.5, 73.4, 72.0, 71.2, 35.2; HRMS (ESI) calcd for $C_{13}H_{15}O_2$ $(M - H)^+$ m/z 203.1072, found 203.1046.

*2-tert-Butyldiphenylsilyloxymethyl-4-methylenetetrahydrofuran (**6d**).* The general procedure was followed using **4d** (0.20 g, 0.57 mmol). The reaction was stirred for 2 h. Purification by flash chromatography on neutral alumina (petroleum ether/EtOAc 98:2) afforded **6d** as a colorless oil (128 mg, 64%): IR (neat) 2929, 2856, 1113, 824, 701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (m, 4H), 7.42 (m, 6H), 5.01 (s, 1H), 4.93 (s, 1H), 4.41 (d, J = 12.4 Hz, 1H), 4.31 (d, J = 13.0 Hz, 1H), 4.19 (ddd, J = 11.7, 6.2, 6.2 Hz, 1H), 3.73 (m, 2H), 2.65 (dd, J = 16.0, 6.6 Hz, 1H), 2.53 (dd, J = 15.3, 5.3 Hz, 1H), 1.09 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 135.8, 133.8, 129.8, 127.9, 104.4, 80.1, 71.5, 66.2, 35.1, 27.0, 19.5; HRMS (ESI) m/z calcd for $C_{22}H_{28}NaO_2Si$ $(M + Na)^+$ 375.1751, found 375.1777.

*2-Cyclohexyl-4-methylenetetrahydrofuran (**6e**).* The general procedure was followed using **4e** (35 mg, 0.21 mmol). The reaction was stirred for 1.5 h. Purification by flash chromatography on neutral alumina (petroleum ether/Et_2O, 99:1) afforded **6e** as a colorless oil (21 mg, 62%):[23a] ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.95 (dd, J = 2.2, 2.2 Hz, 1H), 4.87 (dd, J = 2.2, 2.2 Hz, 1H), 4.36 (m, 1H), 4.21 (m, 1H), 3.60 (m, 1H), 2.56 (m, 1H), 2.25 (m, 1H), 1.96 (m, 2H), 1.80−1.59 (m, 4H), 1.44−1.14 (m, 3H), 0.99 (m, 2H).

*trans-2-Benzyloxymethyl-3-methyl-4-methylenetetrahydrofuran (**6h**).* The general procedure was followed using **4h** (50 mg, 0.23 mmol). The reaction mixture was stirred for 45 min. Purification by flash chromatography on neutral alumina (petroleum ether/EtOAc, 96:4) afforded **6h** as a colorless oil (34 mg, 69%): IR (neat) 3064, 2964, 2931, 2872, 1766, 1723, 1453, 1379, 1091, 913 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.25 (m, 5H), 4.92 (m, 1H), 4.88 (ddd, J = 2.5, 2.5, 2.5 Hz, 1H), 4.60 (s, 2H), 4.52−4.48 (m, 1H), 4.35−4.30 (m, 1H), 3.67−3.54 (m, 3H), 2.46 (m, 1H), 1.09 (d, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 138.4, 128.6, 127.9, 127.8, 103.3, 85.4, 73.7, 71.3, 40.1, 15.1; HRMS (ESI) calcd for $C_{14}H_{17}O_2$ $(M + H)^+$ m/z 217.1229, found 217.1198.

*trans-3-Methyl-4-methylene-2-(2-phenylethyl)tetrahydrofuran (**6i**).* The general procedure was followed using **4i** (50 mg, 0.25 mmol). The reaction mixture was stirred for 45 min. Purification by flash chromatography on neutral alumina (petroleum ether/Et_2O, 98:2) afforded **6i** as a colorless oil (40 mg, 80%): IR (neat) 3027, 2917, 2853, 1765, 1496, 1455, 1377, 1030, 909 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23−7.10 (m, 5H), 4.84 (m, 1H), 4.79 (m, 1H), 4.42 (m, 1H), 4.23 (m, 1H), 3.32 (ddd, J = 8.8, 8.8, 3.1 Hz, 1H), 2.82 (ddd, J = 13.9, 10.8, 5.1 Hz, 1H), 2.62 (ddd, J = 13.8, 10.3, 6.4 Hz, 1H), 2.2 (m, 1H), 1.88 (m, 1H), 1.77 (m, 1H), 1.0 (d, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 142.5, 128.6, 128.6, 126.0, 102.9, 85.8, 70.9, 43.7, 36.0, 32.7, 14.9; HRMS (ESI): calcd for $C_{14}H_{17}O$ $(M - H)^+$ m/z 201.1279, found: 201.1278.

*trans-3-Benzyloxy-2-cyclohexyl-4-methylenetetrahydrofuran (**6j**).* The general procedure was followed using **4j** (60 mg, 0.22 mmol). The reaction mixture was stirred for 2 h. Purification by flash chromatography on neutral alumina (petroleum ether/Et_2O, 95:5) afforded **6j** as a colorless oil (45 mg, 75%): IR (neat) 2925, 2853, 1731, 1573, 1451, 1260, 1065 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35−7.34 (m, 4H), 7.30−7.27 (m, 1H), 5.24 (m, 1H), 5.19 (m, 1H), 4.66 (d, J = 11.7 Hz, 1H), 4.51 (d, J = 11.7 Hz, 1H), 4.46−4.43 (m, 1H), 4.32−4.27 (m, 1H), 4.09 (m, 1H), 3.76 (dd, J = 7.4, 3.0 Hz, 1H), 1.82 (m, 1H), 1.74−1.72 (m, 2H), 1.65−1.61 (m, 2H), 1.39−1.32 (m, 1H), 1.25−1.13 (m, 3H), 1.10−0.97 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 138.4, 128.6, 128.0, 127.8, 109.8, 88.6, 81.9, 70.2, 70.0, 40.6, 29.6, 28.8, 26.6, 26.3, 26.1; HRMS (ESI): calcd for $C_{18}H_{25}O_2$ $(M + H)^+$ m/z 273.1855, found 273.1837.

*Reaction of cis-6-Methyl-5-(2-phenylethyl)-4-oxaspiro[2.3]-hexane (**4k**).* The general procedure was followed using **4k** (110 mg, 0.54 mmol). The reaction mixture was stirred for 16 h. Purification by flash chromatography on neutral alumina (petroleum ether/EtOAc 99.5:0.5 to 95:5) afforded **12**, **13**, and **6k**. **(3*R**,4*R**)-4,5-Dimethyl-1-phenylhex-5-en-3-ol (12)** was obtained as the major product in the above reaction as a clear oil (46 mg, 42%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.26 (m, 2H), 7.22−7.16 (m, 3H), 4.85 (s, 1H), 4.78 (s, 1H), 3.59 (m, 1H), 2.85 (ddd, J = 14.0, 9.3, 6.0 Hz, 1H), 2.66 (ddd, J = 16.4, 9.0, 7.0 Hz, 1H), 2.20 (dq, J = 6.8, 6.8 Hz, 1H), 1.76 (m, 2H), 1.69 (s, 3H), 1.06 (d, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 142.4, 128.6, 128.6, 126.0, 111.7, 72.0, 46.6, 36.7, 32.8, 21.4, 13.6; HRMS (ESI) calcd for $C_{14}H_{21}O$ $(M + H)^+$ m/z 205.1592, found 205.1583. **(*E*)-4-Methyl-7-phenylhepta-1,4-diene-3-one (13)** was obtained as the minor product from the above reaction as a colorless oil (21 mg, 20%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.28 (m, 2H), 7.22−7.18 (m, 3H), 6.87 (dd, J = 17.0, 10.6 Hz, 1H), 6.65 (m, 1H), 6.19 (dd, J = 17.0, 1.8 Hz, 1H), 5.68 (dd, J = 10.6, 1.8 Hz, 1H), 2.79 (dd, J = 7.4, 7.4 Hz, 1H), 2.59 (ddd, J = 7.4, 7.4, 7.4 Hz, 1H), 1.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.7, 142.7, 141.2, 138.3, 132.1, 128.7, 128.5, 128.1, 126.4, 34.9, 31.1, 11.8; HRMS (ESI): calcd for $C_{14}H_{17}O$ $(M + H^+)$ m/z 201.1279, found 201.1249. ***cis*-3-Methyl-4-methylene-2-(2-phenylethyl)tetrahydrofuran (6k)** was also observed and obtained as a colorless oil in a trace amount with an unknown impurity: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22−7.16 (m, 5H), 4.89 (m, 1H), 4.84 (m, 1H), 4.41 (d, J = 13.3 Hz, 1H), 4.30 (d, J = 14.0 Hz, 1H), 3.95 (ddd, J = 8.9, 6.0, 4.6 Hz, 1H), 2.85 (m, 2H), 2.69 (m, 2H), 1.01 (d, J = 7.1 Hz, 3H).

*Reaction of cis-5-Benzhydryl-6-methyl-4-oxaspiro[2.3]hexane (**4l**).* The general procedure was followed using **4l** (27 mg, 0.1 mmol). The reaction mixture was stirred for 21 h. The reaction was monitored by NMR/TLC for disappearance of *cis*-5-benzhydryl-6-methyl-4-oxaspiro[2.3]hexane. The crude product was purified by flash chromatography on neutral alumina (petroleum ether/EtOAc 99:1 to 95:5). **(2S*,3R*)-4-Chloromethyl-3-methyl-1,1-diphenylpent-4-ene-2-ol (11)** was obtained as a clear oil (13 mg, 39%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.19 (m, 10H), 5.30 (s, 1H), 5.12 (s, 1H), 4.53 (ddd, J = 9.4, 3.1, 3.1 Hz, 1H), 4.14 (d, J = 3.1 Hz, 1H), 4.04 (d, J = 11.8 Hz, 1H), 4.04 (d, J = 9.5 Hz, 1H), 2.51 (m, 3H), 1.56 (d, J = 3.1 Hz, 1H), 1.13 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.4, 142.1, 141.9, 129.1, 128.8, 128.4, 127.1 127.0, 116.2, 74.5, 56.1, 47.9, 38.8, 12.0; HRMS (ESI) calcd for $C_{19}H_{25}NClO$ $(M + NH_4)^+$ m/z 318.1625, found 318.1632. ***cis*-2-Benzhydryl-3-methyl-4-methylene-tetrahydrofuran (6l)** was obtained from the reaction of *cis*-5-benzhydryl-6-methyl-4-oxaspiro[2.3]hexane (**4l**) in a trace amount as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81−7.14 (m, 10H), 4.91 (m, 1H), 4.84 (m, 1H), 4.68 (dd, J = 10.9, 4.7 Hz, 1H), 4.48 (m, 1H), 4.23 (m, 1H), 4.03 (d, J = 10.9 Hz, 1H), 2.66 (m, 1H), 0.98 (d, J = 7.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 143.4, 142.3, 128.9, 128.7, 128.3, 128.1, 126.8, 126.6, 103.7, 84.3, 70.7, 52.6, 41.5,

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15.5; HRMS (ESI) calcd for $C_{19}H_{21}O$ $(M + H)^+$ m/z 263.1436, found 263.1439.

*1,1-Diphenyl-2-methylpropene (**15**).* The general procedure for the reaction of 4-oxaspirohexane with Zeise's dimer was followed using **4m** (20 mg, 0.075 mmol). The reaction was stirred for 20 h. Purification by flash chromatography on neutral alumina (petroleum ether/EtOAc, 99:1) afforded **15** (6 mg, 40%):[38] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, J = 7.4 Hz, 4H), 7.21 (t, J = 7.3 Hz, 2H), 7.17 (d, J = 7.3 Hz, 4H), 1.83 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.3, 138.8, 130.9, 129.7, 127.8, 125.9, 22.4.

*2-(1-Cyclohexenyl)-2-methylpentan-3-one (**16**).* The general procedure for the reaction of 4-oxaspirohexane with Zeise's dimer was followed using **4n** (20 mg, 0.11 mmol). Purification by flash chromatography on neutral alumina (petroleum ether/EtOAc, 99:1) afforded **16** as clear oil (10 mg, 50%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.62 (m, 1H), 2.35 (q, J = 7.3 Hz, 2H), 2.05 (m, 2H), 1.75 (m, 2H), 1.54 (m, 4H), 1.15 (s, 6H), 0.99 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 215.6, 140.4, 122.1, 53.6, 29.7, 26.1, 25.7, 23.3, 23.3, 22.4, 8.7; HRMS (ESI) calcd for $(M + H)^+$ $C_{12}H_{21}O$ m/z 181.1592, found 181.1562.

*^{13}C-Labeled trans-5-Benzyloxymethyl-4-methyl-3-methylene-tetrahydrofuran (^{13}C-**6h**).* The general procedure was followed using ^{13}C-**4h** (22 mg, 0.1 mmol). The reaction mixture was concentrated *in vacuo*. Purification by column chromatography using petroleum ether/Et_2O (95:5) afforded an isotopomeric mixture of ^{13}C-labeled *trans*-5-benzyloxymethyl-4-methyl-3-methylenetetrahydrofuran (^{13}C-**6h**) as a colorless oil (12 mg, 55%): ^{1}H NMR (400 MHz, $CDCl_3$) for isotopomer **A**: δ 7.35−7.25 (m, 5H), 4.96 (dm, ^{36b} $^1J_{^{13}C\text{-}H}$ = 156.9 Hz, 1H), 4.91 (dm, ^{36b} $^1J_{^{13}C\text{-}H}$ = 157.7 Hz, 1H), 4.63 (s, 2H), 4.53−4.49 (m, 1H), 4.39−4.31 (m, 1H), 3.70−3.57 (m, 3H), 2.49 (m, 1H), 1.12 (d, J = 6.7 Hz, 3H); for isotopomer **B**: δ 7.35−7.25 (m, 5H), 4.96 (m, 1H), 4.91 (m, 1H), 4.63 (s, 2H), 4.53−4.49 (dm, ^{36b} $^1J_{^{13}C\text{-}H}$ = 146.4 Hz, 1H), 4.35−4.30 (dm, ^{36b} $^1J_{^{13}C\text{-}H}$ = 143.0 Hz, 1H), 3.70−3.57 (m, 3H), 2.49 (m, 1H), 1.12 (d, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 138.4, 128.6, 127.9, 127.8, 103.3 (^{13}C-labeled carbon in isotopomer **A**), 85.4, 73.7, 71.3, (^{13}C-labeled carbon in isotopomer **B**), 70.8, 40.0, 15.1 (match with compound **6h**); HRMS (ESI) calcd for $C_{13}{}^{13}CH_{19}O_2$ $(M + H)^+$ m/z 220.1385, found 220.1379; $(M + NH_4)^+$, calc. 237.1651, found 237.1629, $(M - OH)^+$, 202.1279, found 202.1298 and $(M - H)^+$, 218.1229, found 218.1224.

^{13}C-Labeled (2R, 3S*)-1-Benzyloxy-4-chloromethyl-3-methyl-pent-4-ene-2-ol (^{13}C-**17**).* The title compound was obtained as the minor product (colorless oil, 5 mg, 20%): ^{1}H NMR (400 MHz, $CDCl_3$) for isotopomer **A**: δ 7.38−7.30 (m, 5H), 5.31 (d, $^1J_{^{13}C\text{-}H}$ = 157.8 Hz, 1H), 5.11 (d, $^1J_{^{13}C\text{-}H}$ = 156.8 Hz, 1H), 4.59 (d, J = 11.2 Hz), 4.54 (d, J = 11.9 Hz), 4.14 {dd, J = 5.9 Hz ($^3J_{^{13}C\text{-}H}$), 5.9 Hz, 2H}, 3.79 (m, 1H), 3.59 (dd, J = 9.6, 3.1 Hz, 1H), 3.43 (dd, J = 9.6, 7.2 Hz, 1H), 2.54 (m, 1H), 2.35 (d, J = 3.7 Hz, 1H), 1.09 (d, J = 7.1 Hz, 3H); for isotopomer **B**: δ 7.38−7.30 (m, 5H), 5.31 (d, $^3J_{^{13}C\text{-}H}$ = 8.0 Hz, 1H), 5.11 (d, $^3J_{^{13}C\text{-}H}$ = 13.6 Hz, 1H), 4.59 (d, J = 11.2 Hz), 4.54 (d, J = 11.9 Hz), 4.14 {dd, J = 151.0 Hz ($^1J_{^{13}C\text{-}H}$), 7.0 Hz, 2H}, 3.79 (m, 1H), 3.59 (dd, J = 9.6, 3.1 Hz, 1H), 3.43 (dd, J = 9.6, 7.2 Hz, 1H), 2.54 (m, 1H), 2.35 (d, J = 3.7 Hz, 1H), 1.09 (d, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.4 138.1, 128.7, 128.1, 128.0, 115.9 (^{13}C-labeled carbon in isotopomer **A**), 77.4, 73.7, 72.6, 53.6, 48.3 (^{13}C-labeled carbon in isotopomer **B**), 16.9; HRMS (ESI) calcd for $C_{13}{}^{13}CH_{20}ClO_2$ $(M + H)^+$ m/z 256.1152, found 256.1168.

*2-Methyl-3-methylene-5-(2-phenylethyl)tetrahydrofuran (Cis/Trans Mixture) (**6o**).* The general procedure was followed using **4o** (0.1 g, 0.5 mmol). The reaction mixture was stirred for 45 min. Purification by flash chromatography on silica gel (petroleum ether/Et_2O, 98:2) afforded **6o** (4:1 *cis*/*trans* mixture) as a colorless oil (76 mg, 76%): IR (neat) 3026, 2973, 2928, 2857, 1665, 1603, 1495, 1453, 1052, 1030, 882 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) of major isomer (*cis*-**6o**) δ 7.30−7.16 (m, 5H), 4.92 (dd, J = 4.3, 2.2 Hz, 1H), 4.80 (dd, J = 4.6, 2.1 Hz, 1H), 4.33 (m, 1H), 3.85 (dq, J = 9.4, 5.9 Hz, 1H), 2.76 (m, 2H), 2.68 (m, 2H), 1.99 (m, 1H), 1.85 (m, 1H), 1.33 (d, J = 6.3 Hz, 3H); for the minor isomer (*trans*-**6o**) δ 7.30−7.16 (m, 5H), 4.96 (dd, J = 4.2, 2.1 Hz, 1H), 4.83 (dd, J = 4.2, 2.1 Hz, 1H), 4.54 (m, 1H), 4.07 (m, 1H), 2.29 (m, 2H), 2.24 (m, 2H), 1.97−1.88 (m, 1H), 1.78−1.70 (m, 1H), 1.28 (d, J = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) of major isomer (*cis*) δ 153.5, 142.2, 128.6, 128.6, 126.0, 104.1, 76.5, 75.9, 39.1, 37.2, 32.5, 20.6; for the minor isomer (*trans*-**6o**) δ 153.4, 142.2, 128.6, 128.6, 126.0, 104.6, 76.5, 75.9, 38.9, 37.1, 32.5, 21.1. HRMS (ESI): calcd for $C_{14}H_{19}O$ $(M + H)^+$ m/z 203.1436, found 203.1444.

■ ASSOCIATED CONTENT

Supporting Information

^{13}C-labeling studies and ^{1}H and ^{13}C NMR spectra for all new compounds. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00604.

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Notes

The authors declare no competing financial interest.

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