Synthesis and Reactivity of Optically Active Spiroketals by Ring-Expansion of Chromium Carbene Complex-Derived Cyclobutanones

Ana B. Bueno and Louis S. Hegedus*

Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523

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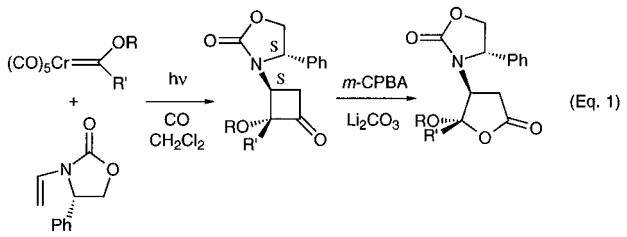
Photolysis of cyclic chromium alkoxycarbene complexes with an optically active ene−carbamate gave spirofused, optically active cyclobutanones. Baeyer−Villiger ring expansion followed by further functionalization gave optically active spiroketals. Photochemical ring expansion of these spirofused cyclobutanones in the presence of acetic acid or thiophenol gave 2-acetoxy- or 2-(thiophenoxy)-4-spirofused tetrahydrofurans. Elimination of the thiophenoxy group gave a 3,4-dihydrofuran that underwent Heck arylation and photochemical cycloaddition with chromium carbene complexes to give cyclobutanones.

The spiroketal unit is a widespread substructure in many natural products with biological activity, such as avermectins, milbemycins, steroidal saponins, insect pheromones, polyether ionophores, and toxic metabolites from algae and fungi. As a consequence, much effort has been focused on the development of general methods for the synthesis of spiroketals.[1] Most of the chemistry in this area is focused on the [4,4], [4,5], and [5,5] ring systems, because most natural products fall into one of these structural categories. Despite the variety of general methods existing for the construction of the spiroketal moiety, the control of the stereochemistry at the anomeric center is, almost exclusively, based on the thermodynamically favored isomer in the acid-catalyzed spiroketalization.[1b] When all factors that control the spirocyclization (maximum anomeric effect, minimum steric interactions, possible hydrogen bonding) are reinforcing, a major isomer is produced.[1c] The stereoselectivity is lower when some of these preferences must be compromised.[1d] In general, high stereoselectivity is observed in the acid-catalyzed spirocyclization of [5,5]-spiroketals mainly controlled by the anomeric effect,[1c] but mixtures are usually observed in the spirocyclization of [4,5]-spiroketals[1e] and especially [4,4]-spiroketals,[1f] where the anomeric effect is almost nonexistant. Only a few examples of enantioselective syntheses of [4,4]-spiroketals have been described.[2]

An efficient synthesis of chiral 2-alkyl-2-alkoxycyclobutanones by photochemical reaction of chromium alkoxycarbene complexes with optically active ene−carbamates derived from phenylglycine as well as their transformation into butyrolactones were recently reported by these laboratories (eq 1).[3,4]



The photochemical reaction was general for a variety of R and R′ groups, including R = R′ = $(CH_2)_4$. The reaction was very stereoselective, resulting in the syn disposition of large groups in the major isomer and having a predictable configuration at the two new centers, depending on the configuration of the starting ene−carbamate.

Despite the existence of a large number of five- and six-membered oxacyclic carbene complexes of the Fisher-type in the literature, only a few synthetic applications of them have been described.[5] The easy accessibility of cyclic chromium carbene complexes and the high stereoselectivity of the reaction of chromium carbene complexes with olefins prompted the study of a new approach to the synthesis of [4,4]- and [4,5]-spiroketals consisting of the ring-expansion of spirocyclobutanones with a preestablished configuration at the spirocyclic center.

The viability of this strategy was assesed by the synthesis of simple spiroketals such as A (basic structure units of spiroketal enol ether polyacetylenes[1] and intermediate in the synthesis of more functionalized spiroketals[6]) and B, pheromones of insects (eq 2).[1a] In addition, unsaturated spiroketal C was generated and its reaction chemistry briefly examined.

(1) For a review see: (a) Perron, F.; Albizati, K. F. *Chem. Rev. (Washington, D.C.)* **1989**, *89*, 1617. (b) Pothier, N.; Goldstein, S.; Deslongchamps, P. *Helv. Chim. Acta* **1992**, *75*, 604 and references therein. (c) Iwata, C.; Masahire, F.; Moritani, Y.; Hattori, K.; Imanishi, T. *Tetrahedron Lett.* **1987**, *28*, 3135. (d) Ireland, R. E.; Thaisrvongs, S.; Dussault, P. H. *J. Am. Chem. Soc.* **1988**, *110*, 5768. (e) Mori, K.; Watanabe, H. *Tetrahedron Lett.* **1984**, *25*, 6025. (f) Rosini, G.; Ballini, R.; Petrini, M.; Marotta, E. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 941.

(2) Solladié, G.; Huser, N.; Fischer, J.; Decian, A. *J. Org. Chem.* **1995**, *60*, 4988 and references therein.

(3) Hegedus, L. S.; Bates, R. W.; Soderberg, B. C. *J. Am. Chem. Soc.* **1991**, *113*, 923.

(4) Miller, M.; Hegedus, L. S. *J. Org. Chem.* **1993**, *58*, 6779.

(5) Schmidt, B.; Kocienski, P.; Reid, G. *Tetrahedron* **1996**, *52*, 1617.

(6) Kocienski, P.; Fall, Y.; Whitby, R. *J. Chem. Soc., Perkin Trans. 1* **1989**, 841.

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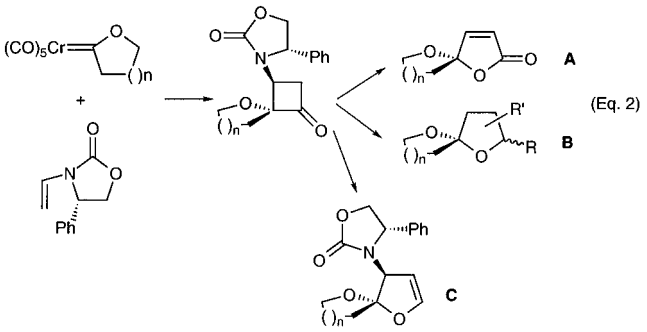
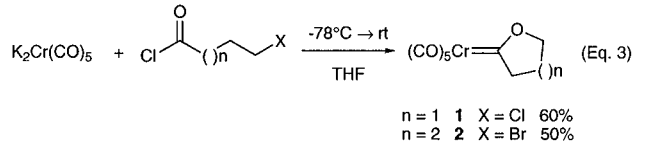


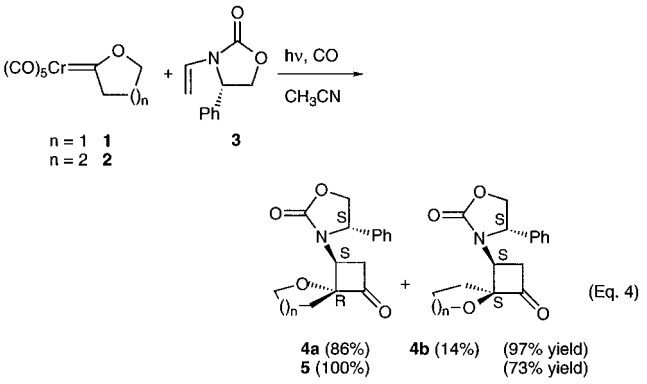
Results and Discussion

Carbene complexes **1**[7,8] and **2** were obtained in a single step by allowing $K_2Cr(CO)_5$ to react with commercially available 4-chlorobutyryl chloride and 5-bromovaleryl chloride, respectively (eq 3).



n = 1 **1** X = Cl 60%
n = 2 **2** X = Br 50%

Both the five-membered and the six-membered complexes underwent the photochemical reaction with the ene−carbamate under the described reaction conditions,[3] in CH_3CN under 90 psi of CO pressure after 48 h of irradiation (eq 4).



n = 1 **1**
n = 2 **2**

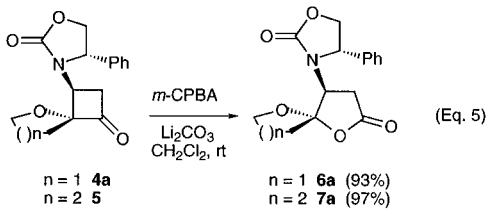
3

4a (86%) **4b** (14%) (97% yield)
5 (100%) (73% yield)

Complete stereoselectivity was observed by ^1H NMR spectroscopy for the reaction of **2**, whereas a 86:14 mixture of isomers was obtained for the [3,4]-spiro compound. These two isomers were easily separated by flash chromatography, **4a** being obtained in an 83% isolated yield. The absolute configuration for **4** and **5** was assigned on the basis of the previous work (see eq 1).

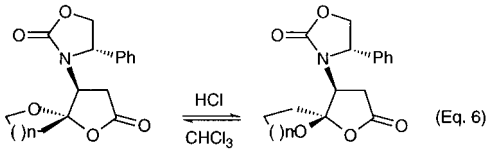
The first ring-expansion attempted was the Baeyer−Villiger oxidation since it had been successfully used in related systems for the synthesis of butenolides.[3] Thus, the treatment of **4a** or **5** with *m*-CPBA gave the corresponding [4,4]- and [4,5]-spiroketals in excellent yield (eq 5).

Treatment of spiroketals **6a** or **7a** with acid produced equilibration at the spiranic center (eq 6). Spiroketal **6b** was identical with that obtained by Baeyer−Villiger oxidation of **4b**, confirming that the two [3,4]-spirocyclobutanones **4a** and **4b** obtained by photoreaction (eq 4) were epimers at that center.



n = 1 **4a**
n = 2 **5**

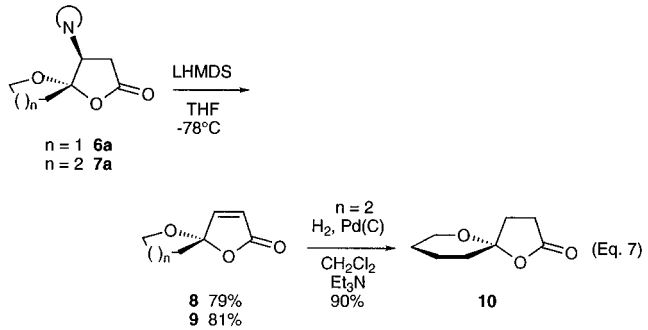
n = 1 **6a** (93%)
n = 2 **7a** (97%)



n = 1 **6a** (20%)
n = 2 **7a** (16%)

6b (80%)
7b (84%)

The elimination of the carbamate moiety with LHMDS provided the butenolides **8** and **9** in good yield. The enantiomeric purity of these systems was determined by the use of chiral shift lanthanide reagents to be >96%. Spiroketals **8** and **9** can be versatile starting materials for the synthesis of other spiroketals since 4-alkoxy-4-alkyl-disubstituted butenolides display a very rich chemistry.[9] Hydrogenation of **9** in the presence of a catalytic amount of Et_3N gave rise to compound **10** in 90% yield. In the absence of base, complete racemization was observed. Compound **10** has been previously used in its racemic form as an intermediate in the synthesis of pheromones of the common wasp and the olive fruit fly.[10] The enantiomers of **8**−**10** could be easily synthesized by using **6b** and **7b** as starting materials in eq 7.



n = 1 **6a**
n = 2 **7a**

8 79%
9 81%

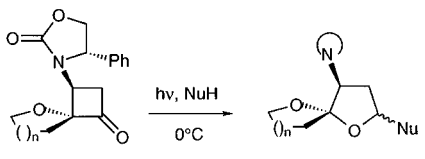
90%

10

A different ring-expansion of the spirocyclobutanones was also explored. The irradiation of a cyclobutanone in the presence of a nucleophile and a source of protons affords 2-substituted tetrahydrofurans.[11] When a solution of **4a** or **5** in degassed solvent was irradiated in the presence of a nucleophile (AcOH, PhSH, or H_2O), the corresponding spiroketals were obtained as inseparable mixtures of epimers at C-2 (eq 8).

Transformation of spiroketals **12** and **13** was accomplished by oxidation of the thioether moiety. The use of 1 equiv of *m*-CPBA provided the corresponding sulfoxides, whose pyrolysis in benzene at reflux[12] afforded the allylic carbamates **15** and **16** in good yield. Reaction

(7) Semmelhack, M. F.; Lee, G. R. *Organometallics* **1987**, *6*, 1839.
(8) Betschart, C.; Hegedus, L. S. *J. Am. Chem. Soc.* **1992**, *114*, 5010.
(9) Reed, A.; Hegedus, L. S. *J. Org. Chem.* **1995**, *60*, 3787.
(10) DeShong, P.; Rybczynski, P. J. *J. Org. Chem.* **1991**, *56*, 3207.
(11) Lee-Ruff, E.; Wan, W.-Q.; Jiang, J.-L. *J. Org. Chem.* **1994**, *59*, 2114.
(12) Danishefsky, S. J.; Armistead, D. M.; Wincott, F. E.; Selnick, H. G.; Hungate, R. *J. Am. Chem. Soc.* **1989**, *111*, 2967.

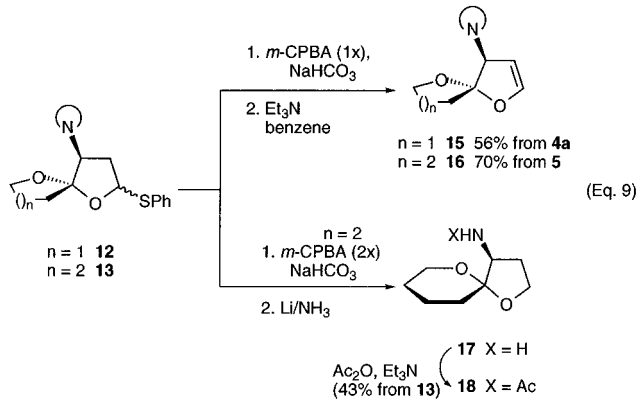


(Eq. 8)

NuH	n = 1	n = 2 (yield)
AcOH		**11** (84)
PhSH	**12** (65)	**13** (95)
H_2O		**14** (-)[a]

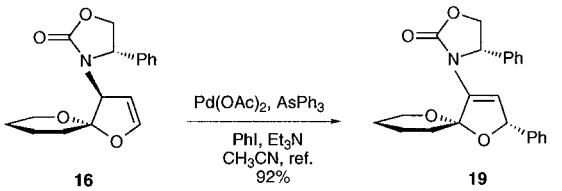
a. not determined

of spirothioether **13** with 2 equiv of *m*-CPBA gave rise to the corresponding sulfone as a mixture of epimers. Reductive cleavage with Li/NH_3 removed the sulfone and cleaved the carbamate in one step to the free amine **17**, which was characterized as its acetyl derivative **18** (eq 9).



(Eq. 9)

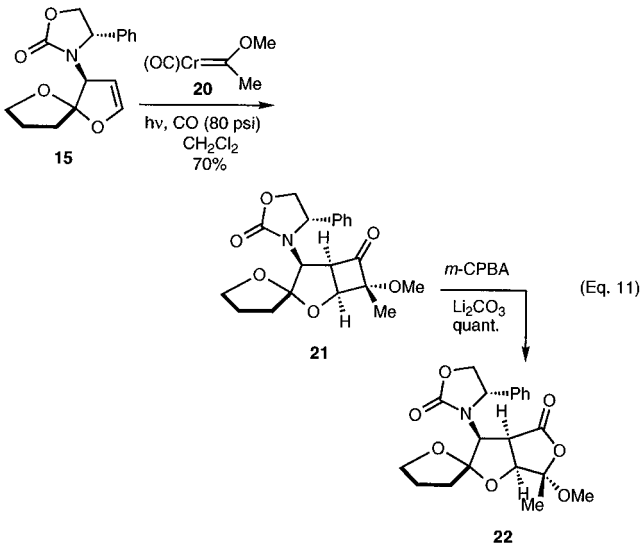
Compounds **15** and **16** were further functionalized. The Heck reaction of the olefin **16** was attempted. When **16** was treated with iodobenzene in the presence of $Pd(OAc)_2$ in CH_3CN under reflux,[13] the product of coupling **19** was obtained as a single isomer tentatively assigned as depicted in eq 10. Under the same reaction conditions 1-iodohexene failed to react with **16**.



(Eq. 10)

Reaction of **15** with methoxymethylchromium carbene complex **20** in the presence of light and under CO pressure provided the spirocyclobutanone **21** as a single isomer. The configuration of **21** was assigned on the basis of previous work[14] and was confirmed by NOE studies. Ring expansion of **21** under Baeyer−Villiger reaction conditions provided the highly functionalized lactone **22** having five adjacent chiral centers (eq 11).

The presence of a carbamate, a relatively good leaving group, in an allylic position in **15** and **16** suggested the



(Eq. 11)

possibility of allylic substitution[15] catalyzed by Pd(0). Although a vast range of allylic groups can be used for this chemistry, to our knowledge urethanes have not been utilized as leaving groups. However, other functionalities based on nitrogen, such as ammonium salts,[16] disubstituted aliphatic amines,[17] indolines,[18] aziridines,[19] and sulfonamides[20] have been shown to be active for this reaction. A study on a model system **23**[21] was first undertaken.

Allyloxazolidinone **23** did not react with Pd(0) under a variety of conditions (different sources of Pd, ligands, solvents, and temperatures), although it could be easily transformed in the trimethylammonium salt **25**, the tosylamine **28**, or the triflamide **29**, which were substituted by malonate in the presence of Pd(0) (Scheme 1, eq 12).

With these results in hand, direct coupling of **16** with Pd(0) was first attempted, although, as for the model system, reaction did not occur under a variety on conditions. The reaction of **16** with LiOH at 100 °C[22] did not produce amino alcohol after 48 h. When the temperature was raised to 115 °C, only decomposition was observed. Variations in these conditions (use of LiOOH or Cs_2CO_3) were undertaken but in no case was the product of opening of the oxazolidinone observed. Ring opening was tried with a thiolate.[23] Unfortunately, opening of the carbamate moiety of **16** with ethylthiolate provided the amino thioether in only a 30% yield.

(13) Chen, J. J.; Walker, J. A., II; Liu, W.; Wise, D. S.; Townsend, L. B. *Tetrahedron Lett.* **1995**, *36*, 8363.

(14) Soderberg, B. C.; Hegedus, L. S.; Sierra, M. A. *J. Am. Chem. Soc.* **1990**, *112*, 4364.

(15) Lewis acid assisted allylic substitution on **15** with allyl trimethylsilane in the presence of TMSOTf (see: Haraguchi, K.; Tanaka, H.; Itoh, Y.; Yamaguchi, K.; Miyasaka, T. *J. Org. Chem.* **1996**, *61*, 851) generated a mixture of at least three different isomers of allylated compound identified by NMR spectroscopy. Only ring opening and reclosure of the spiroketal can explain the presence of more than two isomers in the reaction.

(16) Hirao, T.; Yamada, N.; Ohshiro, Y.; Agawa, T. *J. Organomet. Chem.* **1982**, *236*, 409.

(17) Atkins, K. E.; Walker, W. E.; Manyik, R. M. *Tetrahedron Lett.* **1970**, 3821.

(18) Zhang, D.; Liebeskind, L. S. *J. Org. Chem.* **1996**, *61*, 2594. Bailey, W. F.; Jiang, X.-L. *J. Org. Chem.* **1996**, *61*, 2596.

(19) Satake, A.; Shimizu, I.; Yamamoto, A. *Synlett* **1995**, 64. Matano, Y.; Yoshimune, M.; Suzuki, H. *J. Org. Chem.* **1995**, *60*, 4663.

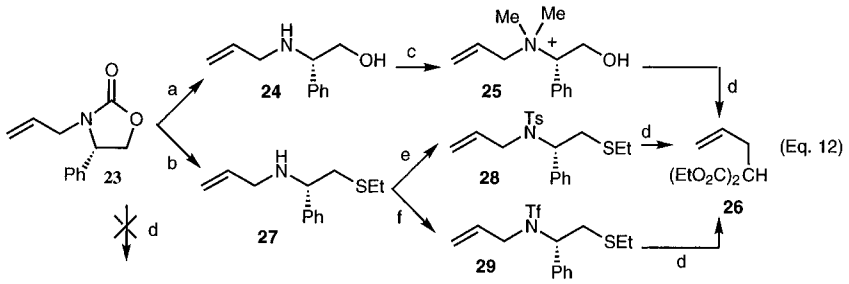
(20) Jung, M. E.; Rhee, H. *J. Org. Chem.* **1994**, *59*, 4719.

(21) Le Coz, S.; Mann, A. *Synth. Commun.* **1993**, *23*, 165.

(22) Dyen, M. E.; Swern, D. *Chem. Rev. (Washington, D.C.)* **1967**, *67*, 197.

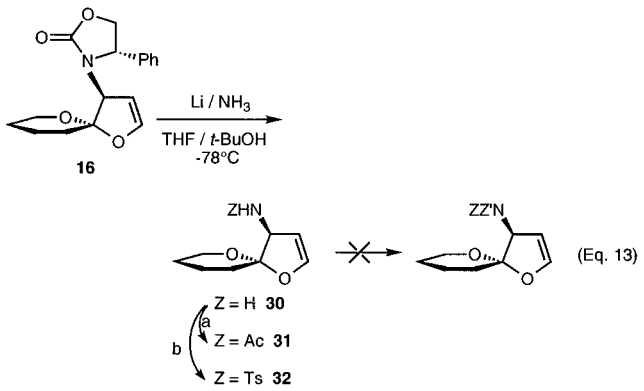
(23) Corey, E. J.; Weigel, L. O.; Floyd, D.; Bock, M. G. *J. Am. Chem. Soc.* **1978**, *100*, 2916.

Scheme 1[a]



[a] Key: (a) LiOH, EtOH, 100 °C; (b) EtSLi, HMPA, rt; (c) MeI, $KHCO_3$, MeOH, 30 °C; (d) $Pd(PPh_3)_4$, $CH_2(CO_2Et)_2$, NaH, THF, ref; (e) TsCl, Et_3N, CH_2Cl_2, rt; (f) Tf_2O, CH_2Cl_2, −78 °C.

Scheme 2[a]



[a] Key: (a) Ac_2O, Et_3N, CH_2Cl_2, rt, 83% from **16**; (b) TsCl, Et_3N, rt, 60% from **16**.

Reductive cleavage of the oxazolidinone **16** with Li in liquid ammonia[24] provided the free amine **30**. When the crude reaction was treated with an excess of Ac_2O, the acetamide **31** was formed in good yield. Treatment of the amine **30** with excess TsCl gave rise to the tosylamine **32**. Neither the tosyl derivative **32** nor the acetamide **31** were reactive toward Pd(0). All attempts to introduce a second withdrawing group in the amine (a tosyl or a acetyl group) led to formation of mixtures of many unidentified compounds. Attempts to synthesize a triflamide or a quaternary ammonium salt from **30** were also unfruitful (Scheme 2, eq 13).

In conclusion, enantiomerically pure [4,4]- and [4,5]-spiroketals have been synthesized for the first time by two stereoselective ring expasions of spirocyclobutanones. These reactions provide a lactone or a thioketal moiety that has been used for further functionalization of the spiroketals.

Experimental Section

Silica gel was neutralized by passing through it the corresponding eluent with 5% of Et_3N followed by washing several times with the eluent before loading the product.

Pentacarbonyl[tetrahydropyranyl-1-carbene]chromium(0) (2). A solution of $K_2Cr(CO)_5$ (37.80 mmol) in 350 mL of THF was prepared by standard methods[7] and cooled at −78 °C under argon. A solution of 5-bromobutyryl chloride (2.50 mL, 18.90 mmol) in 50 mL of THF was added by cannula to the dianion. After 10 min, the reaction was allowed to warm to rt and stirred for 1 h. The crude reaction was filtered through Celite eluting with ether. Celite was added to the liquid layer, and solvents were evaporated. The residue was purified by SiO_2 chromatography, eluting with 4:1 hexane/ethyl acetate to give 2.53 g (48% yield) of **2** as an orange solid. The product was stored in the freezer under argon to minimize decomposition. Its spectroscopic data are consistent with those described in the literature.[25]

General Procedure for the Preparation of Spirocyclobutanones. In an Ace pressure tube were placed under an argon atmosphere the ene−carbamate **3** (1 equiv) and the carbene complex (1.5 equiv) in dry degassed acetonitrile. The vessel was saturated with CO (three cycles to 90−100 psi of CO) and irradiated at 25 °C for 48 h under 90 psi of CO. The solvent was removed, and the residue was purified by flash chromatography (SiO_2). The first yellow band was concentrated, placed in a Ace tube dissolved in methanol, and stirred under 90 psi of CO for 24 h. It was filtered through Celite to recover the $Cr(CO)_6$.

(3*S*,4*R*,5′*S*)-1-Oxo-3-(4-phenyl-1,3-oxazolidin-3-yl)-5-oxaspiro[3.4]octane (4). Carbene complex **1** (1.90 g, 7.20 mmol) and ene−carbamate **3** (0.91 g, 4.82 mmol) were photolyzed in 24 mL of CH_3CN according to the general procedure. Flash chromatography of the crude reaction (eluent hexane/ethyl acetate 1.5:1) gave 1.16 g of **4a** and 0.18 g of **4b** as white solids (97% yield in cyclobutanones, 83% yield of the major isomer). Data for **4a**: mp 115−117 °C; ^{1}H NMR ($CDCl_3$) δ 7.42−7.24 (m, 5H), 4.81 (dd, 1H, J = 5.3, 8.7 Hz), 4.68 (t, 1H, J = 8.7 Hz), 4.26 (dd, 1H, J = 5.3, 8.7 Hz), 3.96 (t, 1H, J = 9.7 Hz), 3.77 (dt, 1H, J = 4.5, 7.5 Hz), 3.59 (dd, 1H, J = 8.4, 17.9 Hz), 3.38 (q, 1H, J = 8.0 Hz), 2.69 (dd, 1H, J = 10.2, 17.9 Hz), 2.15−1.75 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 207.9, 156.7, 138.2, 128.6 (2C), 128.5, 126.2 (2C), 98.8, 69.4, 69.0, 61.1, 50.8, 41.9, 27.9, 25.1; IR ($CHCl_3$) 1791, 1750 cm^{-1}; $[\alpha]^{25}_D$ = +62° (c = 1, CH_2Cl_2). Anal. Calcd for $C_{16}H_{17}NO_4$: C, 66.89, H, 5.96, N, 4.87. Found: C, 66.90, H, 6.14, N, 4.86. Spectroscopic data for **4b**: mp 137−139 °C; ^{1}H NMR ($CDCl_3$) δ 7.41−7.25 (m, 5H), 4.99 (dd, 1H, J = 5.8, 9.1 Hz), 4.67 (t, 1H, J = 9.1 Hz), 4.36 (X part of ABX system, 1H), 4.10 (dd, 1H, J = 5.8, 9.1 Hz), 3.99 (m, 2H), 2.90 and 2.51 (AB part of ABX system, 2H), 2.20−1.70 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 209.1, 159.4, 140.2, 129.4 (2C), 128.9, 126.4 (2C), 97.7, 71.6, 70.8, 58.9, 52.3, 44.8, 34.1, 25.4; IR ($CHCl_3$) 1786, 1746 cm^{-1}; $[\alpha]^{25}_D$ = +82° (c = 1, $CHCl_3$).

(3*S*,4*R*,5′*S*)-1-Oxo-3-(4-phenyl-1,3-oxazolidin-3-yl)-5-oxaspiro[3.5]nonane (5). Carbene complex **2** (1.07 g, 3.90 mmol) and ene−carbamate (0.49 g, 2.60 mmol) were photolyzed in 26 mL of CH_3CN according to the general procedure. Purification via flash chromatography (eluent hexanes/EtOAc 2:1) gave 0.50 g (76% yield) of **5** as a white solid. Its data were consistent with those reported previously in the literature.[3]

General Procedure for the Baeyer−Villiger Oxidation of the Cyclobutanones. The cyclobutanone (1.0 equiv), *m*-CPBA (50−60% in water) (1.50 equiv), and Li_2CO_3 (0.30 equiv) in CH_2Cl_2 were stirred at 25 °C overnight. The crude reaction was poured in a separatory funnel, washed with Na_2SO_3 (satd) (10 mL) and with $NaHCO_3$ (3 × 10 mL), and dried

(24) Evans, D. A.; Sjogren, B. E. *Tetrahedron Lett.* **1985**, *26*, 3783.

(25) Landtrada, L.; Licandro, E.; Maiorana, S.; Papagri, A. In *Advances in Metal Carbene Chemistry*; Schubert, U., Ed.; Kluver Academic: Dordrecht, The Netherlands, 1989; pp 149−151.

over $MgSO_4$. Trituration of the residue with hexanes/EtOAc 3:1 followed by filtration gave most of the butyrolactones. Concentration of the mother liquor and flash chromatography gave the rest of the pure lactone.

(4*S*,5*S*,5′*S*)-2-Oxo-4-(4-phenyl-1,3-oxazolidin-3-yl)-1,6-dioxaspiro[4.4]nonane (6a). Cyclobutanone **4a** (1.49 g, 5.20 mmol), *m*-CPBA (2.20 g, 7.80 mmol), and Li_2CO_3 (0.12 g, 1.50 mmol) in 50 mL of CH_2Cl_2 were subjected to the Baeyer−Villiger reaction. Trituration of the crude reaction with hexanes/EtOAc gave 1.46 g (93% yield) of **6a** as a white solid: mp 129−130 °C; ^{1}H NMR ($CDCl_3$) δ 7.44−7.27 (m, 5H), 4.72−4.58 (m, 3H), 4.22 (dd, 1H, J = 4.2, 8.0 Hz), 4.05 (dt, 1H, J = 4.5, 7.9 Hz), 3.91 (c, 1H, J = 7.6 Hz), 2.82 (dd, 1H, J = 8.5, 18.2 Hz), 2.34−2.0 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 173.3, 157.9, 138.8, 129.6, 129.5, 126.7, 117.3, 70.8, 69.4, 59.2, 57.4, 32.5, 31.8, 23.4; IR ($CHCl_3$) ν 1780, 1753 cm^{-1}; $[\alpha]^{25}_D$ = +87° (c = 1, $CHCl_3$). Anal. Calcd for $C_{16}H_{17}NO_5$: C, 63.36; H, 5.65, N, 4.62. Found: C, 63.26, H, 5.69, N, 4.61.

(4*S*,5*S*,5′*S*)-2-Oxo-4-(4-phenyl-1,3-oxazolidin-3-yl)-1,6-dioxaspiro[4.5]decane (7a). Cyclobutanone **5** (0.59 g, 1.96 mmol), *m*-CPBA (1.0 g, 2.90 mmol), and Li_2CO_3 (0.04 g, 0.60 mmol) in 20 mL of CH_2Cl_2 were subjected to the Baeyer−Villiger reaction. Trituration of the crude reaction with hexane/ethyl acetate gave 0.56 g of pure lactone **7a**. Flash cromatography of the residue obtained by concentration of the mother liquor (hexane/ethyl acetate 1:1) gave 0.04 g of **7a** (97% yield): mp 162−164 °C; ^{1}H NMR ($CDCl_3$) δ 7.50−7.27 (m, 5H), 4.69−4.61 (m, 2H,), 4.41 (d, 1H, J = 8.3 Hz), 4.21 (m, 1H), 3.83 (m, 1H), 3.71 (m, 1H), 2.84 (dd, 1H, J = 8.5, 18.2 Hz), 1.96 (d, 1H, J = 18.2 Hz), 1.93−1.55 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 174.0, 158.0, [139.2, 129.4, 126.5 (6C)], 108.3, 70.7, 63.1, 59.0, 58.3, 31.7, 28.4, 24.0, 18.8; IR ($CHCl_3$) ν 1785, 1751 cm^{-1}; $[\alpha]^{25}_D$ = +79° (c = 1, CH_2Cl_2). Anal. Calcd for $C_{17}H_{19}NO_5$: C, 64.34, H, 6.03, N, 4.41. Found: C, 64.32, H, 5.90, N, 4.41.

General Procedure for the Epimerization of 2-Oxospiroketals. The spiroketal (0.16 mmol) was dissolved in 4 mL of $CHCl_3$, and 5 drops of HCl (concentrated) were added. After 1.5 h, $NaHCO_3$ (satd) was added dropwise. The reaction mixture was poured into 20 mL of CH_2Cl_2 and washed with $NaHCO_3$ (satd) (2 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated.

(4*S*,5*S*,5′*S*)-2-Oxo-4-(4-phenyl-1,3-oxazolidin-3-yl)-1,6-dioxaspiro[4.4]nonane (6b). Compound **6a** (0.04 g) was epimerized under the general conditions to give 0.04 g of a 80:20 mixture of epimers. Column chromatography on neutralized silica gel (eluent 2:1 hexane:ethyl acetate) gave 0.03 g (72% yield in this isomer) of **6b** as a white solid: mp 151−153 °C; ^{1}H NMR ($CDCl_3$) δ 7.45−7.35 (m, 3H), 7.35−7.20 (m, 2H), 5.21 (dd, 1H, J = 3.8, 8.7 Hz), 4.88 (dd, 1H, J = 8.6, 11.2 Hz), 4.64 (t, 1H, J = 8.7 Hz), 4.20 (dt, 1H, J = 4.9, 8.3 Hz), 4.07 (c, 1H, J = 7.6 Hz), 2.40−1.95 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 171.6, 158.6, 140.2, 129.5 (2C), 129.2, 126.0 (2C), 115.9, 71.0, 70.1, 58.2, 53.3, 33.9, 31.6, 23.6; IR ($CHCl_3$) 1785, 1746 cm^{-1}; $[\alpha]^{25}_D$ = +34° (c = 1, $CHCl_3$).

(4*S*,5*S*,5′*S*)-2-Oxo-4-(4-phenyl-1,3-oxazolidin-3-yl)-1,6-dioxaspiro[4.5]decane (7b). 7a (0.07 g) was epimerized to give 0.07 g of a 85:15 mixture of epimers. Column chromatography on neutralized silica gel (eluent 3:1 hexane:ethyl acetate) gave 0.05 g (76% yield in this isomer) of **7b** as a white solid: mp 153−155 °C; ^{1}H NMR ($CDCl_3$) δ 7.45−7.30 (m, 3H), 7.24−7.20 (m, 2H), 5.25 (dd, 1H, J = 3.6, 8.7 Hz), 4.67 (t, 1H, J = 8.6 Hz), 4.54 (X part of ABX system, 1H), 4.13 (dd, 1H, J = 3.6, 8.6 Hz), 3.90 (m, 2H), 2.32 and 2.09 (AB part of ABX system, 2H), 2.04−1.60 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 171.9, 158.4, 140.2, 129.3 (2C), 128.9, 125.4 (2C), 107.6, 70.7, 63.4, 58.3, 55.8, 31.0, 30.4, 24.1, 18.6; IR ($CHCl_3$) 1785, 1746 cm^{-1}; $[\alpha]^{25}_D$ = +47° (c = 1.02, $CHCl_3$).

General Procedure for the Conversion of γ-Lactones to Butenolides. To a solution of γ-lactone in dry THF at −78 °C was added by syringe under Ar atmosphere LHMDS (1.0 equiv, 1 M in THF). T he solution was stirred at the same temperature for 15 min. Most of the solvent was removed under vacuum at 0 °C. Without going to dryness, ether was added, and the mixture was stirred and filtered. The ether filtrate was evaporated at 0 °C, and the residue was purified by chromatography on silica gel. Solvent was removed on a rotatory evaporator at 0 °C.

(*S*)-2-Oxo-1,6-dioxaspiro[4.4]non-3-ene (8). The reaction of compound **6a** (0.06 g, 0.21 mmol) with LHMDS (0.21 mL, 1.0 M in hexanes) in 4 mL of THF under the general reaction conditions gave, after purification by chromatography (eluent ether/pentane 2:1) and removal of the solvents at 0 °C, 0.02 g (79% yield) of **8** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.10 (d, 1H, J = 5.8 Hz), 6.13 (d, 1H, J = 5.8 Hz), 4.28−4.21 (m, 1H), 4.11−4.02 (m, 1H), 2.32−2.05 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 169.8, 151.8, 124.2, 114.4, 70.5, 35.2, 24.1; $[\alpha]^{25}_D$ = +159° (c = 1.11, $CHCl_3$). Its other data were consistent with those reported previously in the literature.[26]

(*S*)-2-Oxo-1,6-dioxaspiro[4.5]dec-3-ene (9). The reaction of compound **7a** (0. 10 g, 0.31 mmol) with LHMDS (0.31 mL, 0.31 mmol) in 6 mL of THF gave, after purification by chromatography (eluent ether/pentane 1:1) and removal of the solvents at 0 °C, 0.04 g (81% yield) of pure butenolide **9**: ^{1}H NMR ($CDCl_3$) δ 7.12 (d, 1H, J = 5.5 Hz), 6.09 (d, 1H, J = 5.5 Hz), 4.05−3.85 (m, 2H, CH_2O), 2.0−1.60 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 170.5, 154.1, 122.8, 106.8, 64.8, 31.9, 23.9, 18.8; $[\alpha]^{25}_D$ = +123° (c = 1.07, $CHCl_3$). Its other data were consistent with those reported previously in the literature.[26]

(*S*)-2-Oxo-1,6-dioxaspiro[4.5]decane (10). Compound **7a** (0.03 g, 0.30 mmol) was dissolved in 3 mL of dry CH_2Cl_2. Pd on carbon (10%, 0.02 g) and Et_3N (0.01 mL, 0.06 mmol) were added, and the mixture was stirred under 1 atm of H_2 for 3 h at room temperature. The crude reaction mixture was filtered through Florisil, washing with ether. The solvent was removed with a rotatory evaporator at 0 °C to give 0.03 g of **10** (90% yield) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 3.88 (dt, 1H, J = 4.0, 11.6 Hz), 3.77 (m, 1H), 2.76 and 2.48 (AB part of ABX system, 2H), 2.20 and 2.02 (AB part of ABX system, 2H), 2.0−1.55 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 176.5, 107.7, 63.3, 34.6, 33.8, 28.2, 24.3, 19.3; IR (neat) 1777 cm^{-1}; $[\alpha]^{25}_D$ = +40° (c = 1.2, $CHCl_3$).

General Procedure for the Photochemical Ring Expansion of Cyclobutanones. The cyclobutanone (1.0 mmol) was dissolved in 20 mL of degassed solvent under argon in a Pyrex test tube. The X−H component (5.0 mmol) was added. The sample was immersed in a bath at 0 °C, and it was irradiated until consumption of the starting material by TLC was complete. The subsequent treatment of the crude reaction is indicated in each case.

(2*S*,4*S*,5*S*,5′*S*)- and (2*R*,4*S*,5*S*,5′*S*]-2-Acetoxy-4-(4-phenyl-1,3-oxazolidin-3-yl)-1,6-dioxaspiro[4.5]decane (11). Cyclobutanone **5** (0.17 g, 0.60 mmol) and dry acetic acid (0.18 mL, 3.20 mmol) were irradiated in 12 mL of THF for 24 h. The solvent was removed with a rotary evaporator, and acetic acid was eliminated on the vacuum line. The residue was purified by a rapid chromatography (hexane/ethyl acetate 3:1) using neutralized silica gel, affording 0.17 g (84% yield) of **11** as a 70:30 oily mixture of epimers: ^{1}H NMR (mixture 70:30 of epimers) ($CDCl_3$) δ 7.48−7.22 (m, 5H), 6.11 (dd, 0.3H, J = 2.2, 7.0 Hz), 6.03 (dd, 0.7H, J = 4.6, 6.6 Hz), 5.03 (dd, 0.3H, J = 1.8, 8.1 Hz), 4.76 (dd, 0.7H, J = 3.6, 8.8 Hz), 4.65−4.55 (m, 1.7H), 4.45 (dd, 0.3H, J = 1.6, 9.2 Hz), 4.28−4.02 (m, 1H), 3.90−3.60 (m, 2H), 2.58 (m, 0.3 H), 2.30 (ddd, 0.7H, J = 4.7, 8.3, 13.0 Hz), 2.04 (s, 3H), 1.90−1.50 (m, 7H); ^{13}C NMR ($CDCl_3$) δ [170.3, 169.0] (1C), [158.8, 158.4] (1C), [129.4, 129.1, 128.4, 125.9, 125.5] (5C), [108.4, 108.1] (1C), [97.3, 96.6] (1C), [71.0, 70.7] (1C), [61.7, 61.5] (1C), [61.2, 58.8, 58.1, 57.7] (2C), [33.0, 31.6] (1C), [28.6, 28.3] (1C), [24.5, 19.3] (1C), [21.1, 20.9] (1C); IR (neat) 1751, 1741 cm^{-1}.

(2*S*,4*S*,5*S*,5′*S*)- and (2*R*,4*S*,5*S*,5′*S*)-2-(Phenylsulfenyl)-4-(4-phenyl-1,3-oxazolidin-3-yl)-1,6-dioxaspiro[4.4]-nonane (12). Cyclobutanone **4a** (0.20 g, 0.70 mmol) was reacted with PhSH (0.36 mL, 3.50 mmol) at 0 °C in 14 mL of CH_2Cl_2. After 2 days, the crude reaction was diluted with 20 mL of CH_2Cl_2 and washed with NaOH (10%) (3 × 10 mL). The aqueous layer was extracted with CH_2Cl_2, the combined

(26) Fukuda, H.; Takeda, M.; Sato, Y.; Mitsunobu, O. *Synthesis* **1979**, 368.

organic layers were dried over $MgSO_4$ and filtered, and the solvent was eliminated in vacuo. Purification by a rapid flash chromatography on neutralized SiO_2 (eluent hexane/EtOAc 2:1) provided 0.13 g of **12** as an oil consisting of a 70:30 mixture of epimers (63% yield based on 78% conversion): ^{1}H NMR ($CDCl_3$) δ 7.45−7.15 (m, 10H), 5.28 (t, 0.3H, J = 7.9 Hz), 4.99 (t, 0.7H, J = 7.6 Hz), 4.96 (dd, 0.3H, J = 2.4, 8.3 Hz), 4.77 (dd, 0.7H, J = 4.3, 8.9 Hz), 4.66 (d, 0.7H, J = 7.0 Hz), 4.64−4.52 (m, 1.3H), 4.10−3.85 (m, 3H), 2.50 (ddd, 0.3H, J = 8.0, 8.9, 16.8 Hz), 2.32 (td, 0.7H, J = 7.6, 14.9 Hz), 2.20−1.90 (m, 4.7H), 1.82 (ddd, 0.3H, J = 4.6, 7.9, 14.6 Hz); ^{13}C NMR ($CDCl_3$) δ 158.5 (1C), 140.6, 140.4 (1C), 136.0, 134.9 (1C), 130.5−126.0 (8C), 117.1, 117.0 (1C), 85.6, 81.9 (1C), 71.1, 70.8 (1C), 67.8, 67.5 (1C), 59.9, 58.9 (1C), 58.3, 58.2 (1C), 35.5, 32.8 (1C), 31.3, 30.9 (1C), 23.9, 23.8 (1C); IR (NaCl) 1748 cm^{-1}.

(2*S*,4*S*,5*S*,5′*S*)- and (2*R*,4*S*,5*S*,5′*S*)-2-(Phenylsulfenyl)-4-(4-phenyl-1,3-oxazolidin-3-yl)-1,6-dioxaspiro[4.5]-decane (13). Cyclobutanone **5** (1.0 g, 3.30 mmol) and PhSH (1.70 mL, 16.50 mmol) were reacted 48 h in 64 mL of CH_2Cl_2. The reaction was worked up as for compound **12** and purified by flash chromatography on neutral SiO_2 (eluent hexane/ethyl acetate 4:1) to give 1.06 g (83% yield, 90% based on 91% conversion) of **13** as a solid: ^{1}H NMR (mixture 65:35 of epimers) ($CDCl_3$) δ 7.50−7.20 (m, 10H), 5.31 (t, 0.6H, J = 7.6 Hz), 5.22 (dd, 0.4H, J = 7.0, 7.9 Hz), 5.0 (dd, 0.4H, J = 2.1, 8.3 Hz), 4.76 (dd, 0.6H, J = 3.7, 8.9 Hz), 4.61−4.52 (m, 1.6H), 4.47 (dd, 0.4H, J = 3.4, 9.2 Hz), 4.08−3.99 (m, 1.6H), 3.77−3.61 (m, 1.4H), 2.55 (ddd, 0.4H, J = 5.8, 6.7, 15.0 Hz), 3.22 (dt, 0.6H, J = 6.7, 14.7 Hz), 1.97 (dd, 0.6H, J = 7.3, 14.3 Hz), 1.90−1.40 (m, 6.4H); ^{13}C NMR ($CDCl_3$) δ [158.2, 158.1] (1C), [140.8, 140.7] (1C), [136.4, 134.8] (1C), 129.6−125.4 (11C), [108.0, 107.6] (1C), [86.1, 82.2] (1C), [70.7, 70.3] (1C), [61.3, 60.6, 60.0, 57.6, 57.3] (3C), [33.7, 32.1] (1C), [28.4, 28.3] (1C), [24.5, 24.3] (1C), [19.3, 19.2] (1C); IR ($CHCl_3$) ν 1746, 1413, 1086, 992 cm^{-1}.

(2*S*,4*S*,5*S*,5′*S*)- and (2*R*,4*S*,5*S*,5′*S*)-2-Hydroxy-4-(4-phenyl-1,3-oxazolidin-3-yl)-1,6-dioxaspiro[4.5]decane (14). Cyclobutanone **5** (50 mg, 0.2 mmol) and water (0.09 mL, 0.9 mmol) in 5 mL of THF were reacted 24 h. Solvents were removed, giving the hemiketal **14** as a mixture 71:29 of epimers: ^{1}H NMR (from the crude reaction) ($CDCl_3$ + D_2O) δ 7.50−7.20 (m, 5H), 5.43 (dd, 0.21H, J = 1.8, 6.7 Hz), 5.16 (dd, 0.79H, J = 4.6, 6.1 Hz), 4.91 (dd, 0.21H, J = 6.4, 8.8 Hz), 4.73 (dd, 0.79H, J = 3.7, 8.9 Hz), 4.66 (t, 0.21 H, J = 8.8 Hz), 4.56 (t, 0.79H, J = 8.9 Hz), 4.25 (dd, 0.21H, J = 6.1, 8.9 Hz), 4.07 (dd, 0.79H, J = 3.7, 8.5 Hz), 3.93 (dt, 0.79H, J = 3.3, 11.0 Hz), 3.77 (dt, 0.21H, J = 3.1, 11.6 Hz), 3.64 (m, 0.79H), 3.43 (m, 0.21H), 2.70 (ddd, 0.21H, J = 7.0, 9.7, 16.8 Hz), 2.10−1.20 (m, 7.21H); IR ($CHCl_3$) 3413, 1742 cm^{-1}.

General Procedure for the Conversion of the Thioethers to Olefins. In a flask equipped with a pressure-equalizing addition funnel was dissolved the thioether (1.0 equiv) in CH_2Cl_2. $NaHCO_3$ (4.0 equiv) was added, and the suspension was cooled at −78 °C. The funnel was charged with a solution of *m*-CPBA (50−85%) (1.0 equiv) in CH_2Cl_2, which was added dropwise to the flask. The reaction was monitored by TLC. When all the starting material was consumed, a solution of $Na_2S_2O_3$ (10% in water) was added, and the mixture was allowed to warm to rt. The layers were separated, and the organic layer was washed with $NaHCO_3$, dried over $MgSO_4$, and evaporated to dryness. The crude residue was dissolved in benzene, Et_3N was added, and the mixture was heated at reflux for 30 min. Elimination of the solvent and purification of the residue by chromatography on neutralized SiO_2 gave the pure dihydrofurans.

(4*S*,5*S*,5′*S*)-4-(4-Phenyl-1,3-oxazolidin-3-yl)-1,6-dioxaspiro[4.4]non-2-ene (15). Compound **12** (0.50 g, 1.74 mmol) dissolved in 34 mL of CH_2Cl_2 was subjected to the general reaction conditions. Pyrolysis of the sulfoxide was performed in 20 mL of benzene and 2 mL of Et_3N. Purification of the residue (eluent hexane/ethyl acetate 3:1) gave 0.31 g (86% yield) of **15** as a white solid: mp 137−141 °C; ^{1}H NMR ($CDCl_3$) δ 7.40−7.15 (m, 5H), 6.24 (dd, 1H, J = 1.5, 2.8 Hz), 4.96 (m, 1H), 4.59 (m, 2H), 4.37 (t, 1H, J = 3.1 Hz), 4.11−4.0 (m, 3H), 2.30−2.0 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 158.0, 147.6, 141.4, 129.0 (2C), 128.4, 126.0 (2C), 117.6, 99.8, 70.7, 68.5, 61.6, 58.3, 30.8, 23.8; IR ($CHCl_3$) ν 1743, 1618, 1404, 1040 cm^{-1}; $[\alpha]^{25}_D$ = +368° (c = 1, $CHCl_3$). Anal. Calcd for $C_{16}H_{17}NO_4$: C, 66.87, H, 5.96, N, 4.87. Found: C, 66.70, H, 6.11, N, 4.87.

(4*S*,5*S*,5′*S*)-4-(4-Phenyl-1,3-oxazolidin-3-yl)-1,6-dioxaspiro[4.5]dec-2-ene (16). Thioether **13** (0.67 g, 1.70 mmol) dissolved in 34 mL of CH_2Cl_2 was allowed to react under the general reaction conditions and purified via flash chromatography (eluent hexane/EtOAc 4:1) to provide 0.40 g (77% yield) of **16** as a white solid: mp 123−127 °C; ^{1}H NMR ($CDCl_3$) δ 7.50−7.35 (m, 5H), 4.67 (dd, 1H, J = 2.5, 8.5 Hz), 4.54 (t, 1H, J = 8.5 Hz), 4.43 (d, 1H, J = 7.6 Hz), 4.34 (m, 1H), 4.07 (dd, 1H, J = 2.5, 8.5 Hz), 3.79 (dt, J = 3.3, 11.6 Hz), 3.65 (m, 1H), 3.60 (m, 1H), 2.80 (tdd, 1H, J = 2.5, 8.0, 17.1 Hz), 2.10−1.60 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 158.1, 147.6, 141.9, 129.1 (2C), 128.3, 125.9 (2C), 108.5, 100.1, 70.6, 63.7, 62.9, 58.4, 28.4, 24.5, 19.1; IR ($CHCl_3$) ν 1746, 1618, 1091, 1042 cm^{-1}; $[\alpha]^{25}_D$ = +468° (c = 0.60, $CHCl_3$). Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.76, H, 6.35, N, 4.65. Found: C, 67.49, H, 5.99, N, 4.64.

Opening of the Oxazolidinone with Li/NH_3. In a flame-dried three-neck round-bottom flask provided with a dry ice condenser and cooled at −78 °C was dissolved a shiny piece of Li in liquid NH_3. A solution of the oxazolidinone in a 10:1 mixture of THF/*t*-BuOH was added via cannula. After 2 min, NH_4Cl was added until the blue color disappeared. The reaction was allowed to warm to rt while passing through a flow of Ar to remove the excess NH_3.

(4*S*,5*S*)-4-(*N*-Acetylamino)-1,6-dioxaspiro[4.5]decane (18). A round-bottom flask equipped with an addition funnel was charged with **13** (0.22 g, 0.55 mmol) dissolved in 5 mL of CH_2Cl_2, $NaHCO_3$ (0.41 g, 4.88 mmol) was added, and the mixture was cooled to −78 °C. The addition funnel was charged with 50−86% *m*-CPBA (0.42 g, 50−60% in water) dissolved in 6 mL of CH_2Cl_2 and added dropwise to the first solution. After the addition was complete, the reaction was allowed to warm to 0 °C and stirred for 2 h. The crude reaction was poured into a separatory funnel, washed with Na_2SO_3 (2 × 10 mL) and $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. The corresponding sulfones were obtained (0.23 g, 97% yield) as white solids, which were used for the next reaction without purification.

The crude mixture of sulfones (0.11 g, 0.25 mmol) and Li (0.04 g, 6.3 mmol) was allowed to react according to the general procedure. After quenching of the reaction with NH_4Cl and elimination of the excess of ammonia, the crude reaction mixture was dissolved in CH_2Cl_2, Ac_2O (0.59 mL, 6.50 mmol) and Et_3N (0.87 mL, 6.50 mmol) were added, and the mixture was allowed to react at rt overnight. The reaction was washed with $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by chromatography on neutralized SiO_2 (eluent acetone/CH_2Cl_2 1:6), providing 0.02 g (44% yield) of **18** as a white solid: mp 120−124 °C; ^{1}H NMR ($CDCl_3$) δ 5.60 (bd, 1H, J = 8.6 Hz), 4.39 (ddd, 1H, J = 1.8, 7.3, 9.5 Hz), 3.96 (dt, 1H, J = 6.1, 8.6 Hz), 3.86 (dt, 1H, J = 5.6, 8.9 Hz), 3.74 (dt, 1H, J = 3.3, 11.3 Hz), 3.61 (m, 1H), 2.52 (m, 1H), 1.98 (s, 3H), 1.75−1.45 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 169.3, 106.0, 64.4, 61.4, 56.0, 31.3, 28.3, 25.0, 23.3, 19.7; IR (neat) ν 3421, 1650 cm^{-1}; $[\alpha]^{25}_D$ = +57° (c = 1, $CHCl_3$). Anal. Calcd for $C_{10}H_{17}NO_3$: C, 60.28; H, 8.60; N, 7.03. Found: C, 60.28; H, 8.43; N, 7.15.

(2*R*,5*S*,5′*S*)-4-(4-Phenyl-1,3-oxazolidin-3-yl)-2-phenyl-1,6-dioxaspiro[4.5]dec-3-ene (19). In a flame-dried round-bottom flask provided with a reflux condenser $Pd(OAc)_2$ (0.002 g, 0.01 mmol) and $AsPh_3$ (0.006 g, 0.02 mmol) was stirred in 3 mL of dry CH_3CN for 30 min. Iodobenzene (0.02 mL, 0.16 mmol), Et_3N (0.07 mL, 0.52 mmol), and **16** (0.04 g, 0.13 mmol) were added, and the mixture was stirred at 75 °C for 48 h. Elimination of the solvent and purification of the residue by flash chromatography in neutralized silica gel (eluent hexanes/EtOAc 5:1) provided 0.05 g (92% yield) of **19** as a white solid: mp 159−161 °C; ^{1}H NMR ($CDCl_3$) δ 7.45−7.20 (m, 10H), 6.20 (d, 1H, J = 1.8 Hz), 5.65 (d, 1H, J = 1.8 Hz), 5.34 (dd, 1H, 3.4, 8.3 Hz), 4.66 (t, 1H, J = 8.3 Hz), 4.15 (dd, 1H, J = 3.4, 8.6 Hz), 3.95 (dt, 1H, J = 2.5, 11.3 Hz), 3.71 (m, 1H), 1.90−1.15 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 156.7, 141.0, 140.7, 135.9, 129.2,

128.6, 128.4, 127.9, 126.8, 126.2, 120.0, 107.5, 83.9, 71.0, 62.7, 59.8, 32.9, 24.3, 19.2; IR ($CHCl_3$) 1757 cm^{-1}; $[\alpha]^{25}_D = +229°$ ($c = 0.75$, $CHCl_3$). Anal. Calcd for $C_{23}H_{23}NO_4$: C, 73.19; H, 6.14; H, 3.71. Found: C, 73.24; H, 6.21; N, 3.76.

Compound 21. In a dry Ace pressure tube, spiroketal **15** (0.10 g, 0.35 mmol) was dissolved in 4 mL of CH_2Cl_2 and methylmethoxychromium carbene complex **20**[27] (0.13 g, 0.52 mmol) was added. The mixture was degassed, charged with CO (80 psi), and irradiated with visible light at 35 °C for 36 h. The solvent was removed, and the residue was purified by chromatography on neutralized SiO_2 to give 90 mg (70% yield) of the spiroketal **21** obtained as a white solid: mp 118−121 °C; ^{1}H NMR ($CDCl_3$) δ 7.42−7.28 (m, 5H), 4.70−4.65 (m, 2H), 4.56 (t, 1H, $J = 8.6$ Hz), 4.08 (dd, 1H, 4.3, 8.2 Hz), 3.95−3.80 (m, 3H), 3.48 (d, 1H, $J = 6.4$ Hz), 3.11 (s, 3H), 2.12−1.90 (m, 4H), 1.21 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 201.9, 158.0, 139.6, 129.3 and 126.3 (5C), 119.2, 96.3, 80.0, 70.8, 68.1, 64.4, 60.8, 58.3, 52.3, 31.2, 24.3, 10.5; IR (neat) 1787, 1751 cm^{-1}; $[\alpha]^{25}_D = +88$ ($c = 1$, $CHCl_3$). Anal. Calcd for $C_{20}H_{23}NO_6$: C, 64.33, H, 6.21, N, 3.75. Found: C, 64.50C, H, 6.17, N, 3.75.

Compound 22. Cyclobutanone **21** (0.03 g, 0.09 mmol) was ring-expanded following the general procedure for the Baeyer−Villiger reaction to provide 0.03 g (98% yield) of **22** as a colorless oil. Trituration with ether/hexanes provided 0.01 g of **22** as a white solid: ^{1}H NMR ($CDCl_3$) δ 7.50−7.30 (m, 5H), 4.77 (bs, 1H), 4.76 (dd, 1H, $J = 4.9$, 8.8 Hz), 4.60 (t, 1H, $J = 8.6$ Hz), 4.11 (dd, 1H, $J = 4.9$, 8.6 Hz), 3.96 (d, 1H, $J = 6.4$ Hz), 3.95−3.82 (m, 2H), 3.16 (s, 3H), 2.98 (d, 1H, $J = 6.4$ HZ), 2.15−1.85 (M, 4H), 1.47 (S, 3H); ^{13}C NMR ($CDCl_3$) δ 173.9, 157.9, 139.4, 129.6, 129.5, 126.4, 117.3, 110.3, 84.4, 70.7, 68.5, 63.4, 58.8, 50.0, 48.8, 31.0, 24.3, 16.7; IR (neat) 1774, 1755 cm^{-1}; $[\alpha]^{25}_D = +55°$ ($c = 1$, $CHCl_3$).

(4*S*,5*S*)-4-(*N*-Acetylamino)-1,6-dioxaspiro[4.5]dec-2-ene (31). Reaction of **16** (0.15 g, 0.50 mmol) with Li (0.03 g, 5.0 mmol) in 15 mL of NH_3, 2.5 mL of THF, and 0.5 mL of *t*-BuOH and treatment of the residue obtained with Ac_2O (0.78 mL, 8.25 equiv) and Et_3N (0.91 mL, 6.60 mmol) in 20 mL of CH_2Cl_2 for 4 h provided, after washing the crude reaction with $NaHCO_3$ (3 × 20 mL), drying over $MgSO_4$, filtering, and concentrating, the crude acetamide. Column chromatography on neutralized SiO_2 (eluent EtOAc) provided 0.08 g (83% yield) of the acetamide **31** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.53 (dd, 1H, $J = 1.2$, 2.8 Hz), 5.32 (bs, 1H), 5.00 (t, 1H, $J = 2.7$ Hz), 4.83 (ddd, 1H, $J = 1.5$, 2.7, 8.9 Hz), 3.93 (m, 1H), 3.72 (m, 1H), 2.00 (s, 3H), 1.85−1.50 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 170.0, 147.9, 108.4, 100.9, 62.8, 59.3, 28.1, 24.4, 22.9, 19.0; IR (neat) 3280, 1651 cm^{-1}; $[\alpha]^{25}_D = +179°$ ($c = 1.81$, $CHCl_3$).

(4*S*,5*S*)-4-[*N*-(*p*-Toluenesulfonyl)amino]-1,6-dioxaspiro-[4.5]dec-2-ene (32). Compound **16** (0.15 g, 0.50 mmol) was reacted with Li (0.03 g, 5.0 mmol) in 15 mL of NH_3, 2.50 mL of THF, and 0.50 mL of *t*-BuOH. Treatment of the residue obtained with TsCl (0.48 g, 2.50 mmol) and Et_3N (0.70 mL, 10.0 mmol) overnight followed by washing with $NaHCO_3$ (3 × 10 mL), drying over $MgSO_4$, and concentrating of the solvents provided 88 mg (60% yield) of the tosylamine **32** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.35 and 7.31 (AA′BB′ system, 2H), 6.39 (dd, 1H, $J = 1.5$, 2.5 Hz), 4.59 (t, 1H, $J = 2.6$ Hz), 4.35 (bd, 1H, $J = 9.2$ Hz), 4.08 (ddd, 1H, $J = 1.5$, 2.9, 9.6 Hz), 3.90 (dt, 1H, $J = 3.3$, 11.4 Hz), 3.71 (m, 1H), 2.43 (s, 3H), 1.90−1.50 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 148.3, 143.6, 137.6, 129.8, 127.0, 108.8, 100.6, 63.9, 63.3, 29.2, 24.6, 21.5, 19.4; IR (neat) ν 3267, 1161 cm^{-1}; $[\alpha]^{25}_D = +91°$ ($c = 0.94$, $CHCl_3$).

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Supporting Information Available: ^{1}H NMR spectra for compounds **4b**, **6b**, **7b**, **10**, **11a**,**b**, **12a**,**b**, **13a**,**b**, **14**, **21**, **22**, and **30**−**32** and ^{13}C NMR spectra for compounds **4b**, **6b**, **7b**, **10**, **11a**,**b**, **12a**,**b**, **13a**,**b**, **22**, **31**, and **32** (27 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(27) Bao, J.; Wulff, W. D.; Dominy, J. B.; Fumo, M. J.; Grant, E. B.; Rob, A. C.; Whitcomb, M. C.; Yeung, S.-M.; Ostrander, R. L.; Rheingold, A. L. *J. Am. Chem. Soc.* **1996**, *118*, 3392.