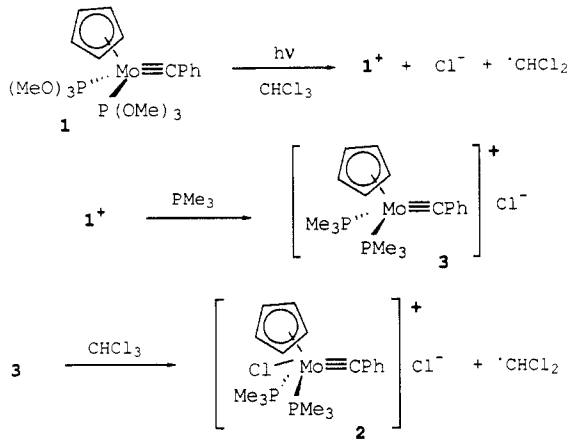
Scheme I



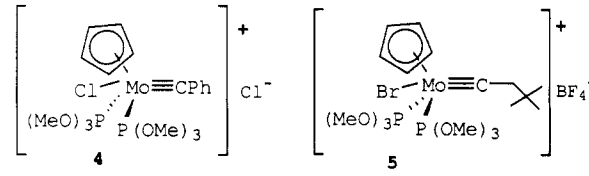
quantitative yield. Irradiation of **1** in $CHCl_3$ in the absence of phosphine does not lead to identifiable products even upon subsequent addition of PMe_3 to the reaction mixture. Cyclic voltammetry of **1** in the absence of additional ligands shows an irreversible oxidation at 0.35 V versus Ag/Ag^+. No evidence of a return wave could be seen at scan rates up to 1 V/s, consistent with decomposition of the cation. Attempts at electrochemistry in the presence of PMe_3 resulted only in phosphine oxidation.

The mechanism shown in Scheme I is consistent with these observations. Electron transfer from excited state **1** to chloroform gives the 17-electron cationic complex $\mathbf{1}^+$, chloride ion, and $^{\bullet}CHCl_2$.[12] The organic radical is then scavenged by the excess phosphine.[13] Ligand exchange of phosphines for phosphites occurs from the 17-electron species $\mathbf{1}^+$ to give **3**. Abstraction of a chlorine atom from the solvent yields the final product **2** and another $^{\bullet}CHCl_2$ radical. The overall reaction sequence thus produces 2 equiv of $^{\bullet}CHCl_2$ radical for each equivalent of **1** consumed, consistent with the assignment of the unidentified phosphine-containing product as the result of radical trapping.

Electron transfer from the MLCT states of metal complexes to halocarbons has previously been observed in the photooxidation of $M(CNPh)_6$ (M = Mo, W) in $CHCl_3$ to give the seven-coordinate product $[M(CNPh)_6Cl]^+Cl^-$.[14] Photochemical reduction of halocarbons by metal complexes has also been observed upon excitation of charge transfer to solvent (CTTS) transitions.[15] However, comparison of the UV-vis spectra of **1** in $CHCl_3$, CH_2Cl_2, and THF reveals no transition in the region 300-550 nm that could be attributed to CTTS. Involvement of CTTS states can thus be ruled out in the photooxidation of **1**. In addition, reaction occurs upon irradiation of the lowest energy transition of **1** ($\lambda > 520$ nm), an absorption that is unchanged in solvents such as THF which are poor electron acceptors.

The irreversibility of the electrochemical oxidation of **1** suggests that $\mathbf{1}^+$ undergoes rapid chemical reaction. In addition, the substitutional lability of organometallic complexes is known to be greatly increased upon oxidation to 17-electron cationic species.[16] Given the π-acidity of the phosphite ligands, it is reasonable that dissociation of $P(OMe)_3$ from $\mathbf{1}^+$ should be facile and exchange for phosphines should be favorable. Conversion from the resulting metal radical **3** to the final product **2** requires abstraction of $Cl^{\bullet}$ from solvent. Such halogen abstractions are well known for metal radicals.[17,18]

Reversing the order of the ligand exchange and atom abstraction steps would result in intermediacy of the 18-electron cationic complex **4**, which would then exchange its $P(OMe)_3$ ligands for



phosphines. We believe this to be less likely as the analogous complex **5** and its hydride analogue have been described as stable.[19] As we see no intermediates in the conversion of **1** to **2**, the ligand exchange process must be fairly rapid. Although no information on the reactivity of **5** with phosphines is available, its reported properties do not suggest that the phosphites are labile enough for the conversion of **4** to **2** to occur without detectable intermediates.

Photooxidation of metal carbyne **1** adds electron transfer to the photoprocesses that have been observed for these complexes. The resulting odd electron species undergoes ligand exchange and halogen abstraction. However, no reaction occurs at the metal-carbon triple bond despite the presence of both metal and organic radicals. Further studies on this reaction are in progress.

Acknowledgment. Funding was provided by the Petroleum Research Fund and the Research Corporation. We thank Dr. Gordon Miskelly for assistance with the electrochemical measurements.

(11) This unstable PMe_3-containing product has a single ^1H NMR signal at 1.87 ppm (d, J_{CP} = 12 Hz). The proton-phosphorus coupling constant suggests that the phosphine is not metal bound, but its lability prevented isolation and further characterization. We believe this compound to result from trapping of radicals by excess phosphine.

(12) One-electron reduction of $CHCl_3$ is known to give the fragmentation products Cl^- and $^{\bullet}CHCl_2$. Buehler, R. E. In *The Chemistry of the Carbon-Halogen Bond*; Patai, S., Ed.; Wiley: London, 1973; pp 795-864.

(13) Krusic, P. J.; Mahler, W.; Kochi, J. K. *J. Am. Chem. Soc.* **1972**, *94*, 6033-6041.

(14) Mann, K. R.; Gray, H. B.; Hammond, G. S. *J. Am. Chem. Soc.* **1977**, *99*, 306-307.

(15) (a) Bock, C. R.; Wrighton, M. S. *Inorg. Chem.* **1977**, *16*, 1309-1313. (b) Miessler, G. L.; Zoebisch, E.; Pignolet, L. H. *Inorg. Chem.* **1978**, *17*, 3636-3644. (c) Vogler, A.; Kunkely, H. *Inorg. Chem.* **1982**, *21*, 1172-1175.

(16) Hershberger, J. W.; Klingler, R. J.; Kochi, J. K. *J. Am. Chem. Soc.* **1982**, *104*, 3034-3043.

(17) Wrighton, M. S.; Ginley, D. S. *J. Am. Chem. Soc.* **1975**, *97*, 2065-2072.

(18) Tyler, D. R.; Schmidt, M. A.; Gray, H. B. *J. Am. Chem. Soc.* **1983**, *105*, 6016-6021.

(19) Beevor, R. G.; Green, M.; Orpen, A. G.; Williams, I. D. *J. Chem. Soc., Dalton Trans.* **1987**, 1319-1328.

Atom-Transfer Annulations in Heterocycle Synthesis. An Efficient Synthesis of (-)-Trachelanthamidine and Related Ring Systems

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Annulation sequences which involve free-radical intermediates have achieved increasing importance for the synthesis of bioactive substances. Among the various methods for effecting radical annulations, those which involve an atom-transfer propagation step would appear optimum for cases in which premature chain termination via hydrogen atom transfer is problematic.[1,2] In this communication we will describe the first examples of γ-butyrolactam-forming atom-transfer annulations of allylic α-iodoacetamides as well as the application of this new method in an en-

(1) (a) Curran, D. P.; Chen, M.-H. *J. Am. Chem. Soc.* **1987**, *109*, 6558. (b) Curran, D. P.; Chang, C.-T. *Tetrahedron Lett.* **1987**, 2477. (c) Curran, D. P.; Chen, M.-H.; Kim, D. *J. Am. Chem. Soc.* **1986**, *108*, 2489. (d) Curran, D. P.; Kim, D. *Tetrahedron Lett.* **1986**, *27*, 5821. (e) Curran, D. P. *Synthesis* **1988**, 417.

(2) (a) Kraus, G. A.; Landgrebe, K. *Tetrahedron* **1985**, *41*, 4039. (b) Kraus, G. A.; Landgrebe, K. *Tetrahedron Lett.* **1984**, *25*, 3939. Degueil-Castaing, M.; DeJeso, B.; Kraus, G. A.; Landgrebe, K.; Maillard, B. *Tetrahedron Lett.* **1986**, 5927.

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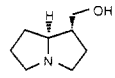
antioselective synthesis of (−)-trachelanthamidine (**1**).



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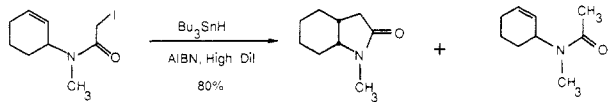
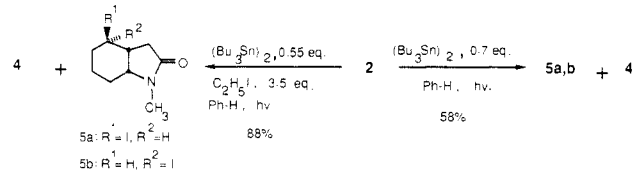
We initiated our investigation by examining the behavior of the *N*-(cyclohex-2-en-1-yl)-*N*-methyliodoacetamide (**2**)[3] under

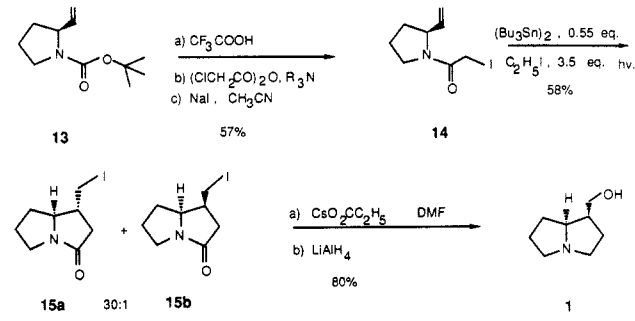


established reaction conditions for reductive and atom-transfer radical cyclizations. Homolytic reduction of **2** with $(n\text{-Bu})_3SnH$ (1.1 equiv) under high dilution conditions (0.02 M in benzene) led to inefficient cyclization with the production of the perhydroindolone **3** and the acetamide **4** (**3**/**4** = 0.5) in 80% isolated yield. By way of contrast, efforts to bring about the cyclization of **2** under typical atom-transfer conditions [$(Bu_3Sn)_2$ 10 mol%, PhH, sunlamp] afforded the anticipated iodoindolones **5a,b** together with **4** (**5a,b**/**4** = 0.5) in <10% yield. In addition, about 90% of the starting iodoacetamide **2** could be recovered from this reaction.[4] Efforts to force the consumption of **2** did little to

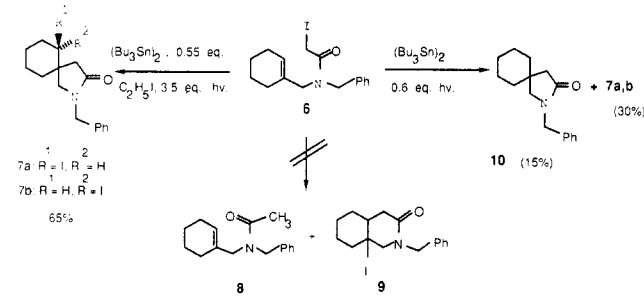


improve the cyclization efficiency of the intermediate radical. Accordingly, treatment of **2** with $(Bu_3Sn)_2$ (0.7 equiv, 0.1 molar in Ph-H, sunlamp) furnished **5a,b** and **4** (**5a,b**/**4** = 0.45) in 58% yield.[5] We speculated that the inefficiency observed for these cyclizations was attributable to the predisposition of α-acylamide radicals to undergo hydrogen atom abstraction as well as to an intrinsically short chain length for this reaction. Moreover, the increased barrier for s-cis/s-trans conformational interconversion of the amide C–N bond relative to that for esters was expected to be strongly expressed in these annulations.[6] In light of the foregoing considerations, the cyclization of **2** was executed with $(Bu_3Sn)_2$ (0.55 equiv) in the presence of C_2H_5I (3.5 equiv, Ph-H, sunlamp) which was expected to serve the dual role of an *S-trans*-acetamide radical sink and an iodine atom source. Under these conditions the desired indolones **5a,b** (**5a**/**5b** = 5.5) were isolated in 68% chromatographed yield together with 20% of the reduction product **4**.[7,8]

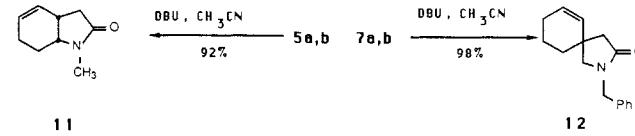
Scheme I



A series of experiments was then conducted with the intent of clarifying the generality and regiochemical course of radical lactam annulations. Atom-transfer cyclization of the iodoacetamide **6**[9] via the action of $(Bu_3Sn)_2$ (0.55 equiv) in the presence of C_2H_5I



(3.50 equiv) (Ph-H, sunlamp) provided the γ-iodolactams **7a** and **b** (**7a**/**7b** = 1.3) via the corresponding secondary cyclohex-2-yl radical in 65% chromatographed yield. It is worthy of note that none of the uncyclized amide **8** nor the isomeric δ-lactam **9** (which would have arisen from a tertiary cyclohex-1-yl radical) were detected as byproducts from this reaction. In consequence with our previous experience, the utilization of C_2H_5I was mandatory for the enhancement of cyclization efficiency. Accordingly, exposure of **6** to $(Bu_3Sn)_2$ (0.60 equiv) in the absence of C_2H_5I (Ph-H, sunlamp) furnished **7a** and **b** in only 30% yield admixed with 15% of the hydrogen atom abstraction product **10**.[10] In principle, the iodo moieties of the γ-lactams **5a,b** and **7a,b** could be transformed into other useful functionality. To this end the lactams **5a,b** and **7a,b** were cleanly and in the former case regiospecifically dehydrohalogenated to the corresponding cyclohexene derivatives **11** (92%) and **12** (98%) via treatment with DBU in CH_3CN.



We envisaged an enantioselective approach to the azabicyclic skeleton of (−)-trachelanthamidine (**1**) from L-proline which was destined to rely on an atom-transfer γ-lactamization. The prospective key cyclization was also expected to provide the first example of diastereoface selection in an atom-transfer annulation.

(*S*)-2-Vinyl-*N*-(*tert*-butoxycarbonyl)pyrrolidine (**13**)[11] was transformed into the iodoacetamide **14** in 57% overall yield as illustrated in Scheme I. Cyclization of **14** as before secured the pyrrolizidone **15a** along with the stereoisomer **15b** (**15a**/**15b** = 30) in 58% isolated yield.[12,13] Treatment of this mixture with

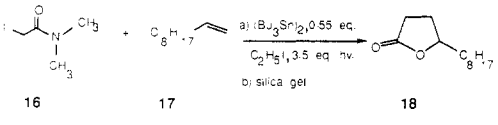
(3) Iodoamide **2** was prepared by the acylation of the corresponding amine [$(ClCH_2CO)_2O$, $(i\text{-Pr})_2NEt$, CH_2Cl_2, 0 °C] followed by halide exchange (NaI–CH_3CN, 25 °C, 12 h).

(4) In contrast to this finding, the corresponding cyclohex-2-en-1-yl iodoacetate has been successfully cyclized under standard atom-transfer conditions.[1b]

(5) All new compounds have been fully characterized by 300 MHz NMR, ^{13}C NMR, and IR spectrometry and possess satisfactory (C, H) analyses or exact mass.

(6) The barrier to rotation about an amide C–N bond is ca. 11 kcal/mol higher in energy than the corresponding barrier to rotation about an ester C–O bond.

(7) It is significant that corresponding *intermolecular* additions of α-iodoacetamides to alkenes (e.g., **16** → **18**) also proceed inefficiently under standard atom-transfer conditions. The facility of intermolecular addition is readily restored in the presence of $(Bu_3Sn)_2$ (0.5 equiv) and C_2H_5I (3.5 equiv, sunlamp) to afford **18** in 65% isolated yield.



(8) The use of alternative alkyl iodides (e.g., 2-iodopropane or iodemethane) led to comparable yields of iodolactams in these reactions.

(9) The iodoamide **6** was prepared in a manner analogous to **2**.

(10) For comparative purposes, the iodo-γ-butyrolactams **5a,b** and **7a,b** were *quantitatively* reduced to γ-butyrolactams (e.g., **10**) via the action of $(n\text{-Bu})_3Sn$-H in Ph-H.

(11) Parker, K. A.; O'Fee, R. *J. Am. Chem. Soc.* **1983**, *105*, 654.

(12) Pyrrolizidone **15b** was detectable by HPLC and GCMS.

$CsO_2CC_2H_5$ (DMF, 60 °C)[14,15] followed by reduction ($LiAlH_4$, THF, reflux) afforded (−)-trachelanthamidine (**1**) ($[\alpha]^{25}_D$ −14.1° (*c* 3.6, C_2H_5OH), lit.[16] −13.5° (*c* 2, C_2H_5OH)] in 80% yield after chromatography.

Acknowledgment. Support for this research by a grant from the National Institutes of Health is gratefully acknowleged.

(13) Representative experimental procedure is as follows: An oven-dried 100-mL, three-necked, round-bottomed flask, equipped with a magnetic stirring bar, nitrogen inlet, serum cap, and reflux condensor, was thoroughly flushed with nitrogen. To the flask was added **14** (1.325 g, 5 mmol), benzene (50 mL), iodoethane (2.73 g, 17.5 mmol), and Bu_3Sn_2 (1.595 g, 2.75 mmol). The resulting solution was stirred and irradiated with a 275-W sunlamp for 20 min whereupon GC and TLC indicated the consumption of **14**. The benzene was evaporated under reduced pressure, and the residue was subjected to column chromatography on silica gel to provide **15a** and **b** (**15a**/**15b** = 30) (0.77 g, 58%), mp 48–49 °C; $[\alpha]^{25}_D$ −23.9 (*c* 1.13, C_2H_5OH).

(14) Dijkstra, G.; Kruizinga, W. H.; Kellogg, R. M. *J. Org. Chem.* **1987**, *52*, 4230.

(15) In addition, ca. 5% of the corresponding alkene was formed by a competing elimination reaction.

(16) Robins, D. J.; Sakdarat, S. *J. Chem. Soc., Perkin Trans. 1* **1981**, 909.

Vicinal Diol Cyclic Sulfates: Like Epoxides Only More Reactive

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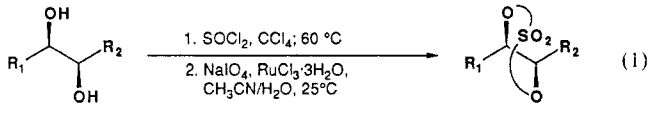
Received August 3, 1988

Epoxides play a unique role in organic synthesis: they simultaneously activate and protect adjacent functionalized carbon atoms for nucleophilic attack, and they are usually superior to equivalent acyclic synthons because their cyclic nature renders competing elimination processes stereoelectronically unfavorable.[1] The same fortunate properties are shared by another class of vicinally substituted electrophiles—the 1,2-cyclic sulfates.[2]



1 2 (1)

However, these diol cyclic sulfates **2** are not found in the repertoire of main line organic synthesis. This deficit is apparently due to lack of a good method for their preparation. Our recent discovery of a catalytic process for the asymmetric dihydroxylation of olefins provided incentive to find uses for the chiral diol products.[3] We report here on a facile process for conversion of diols **1** to cyclic sulfates **2** and on the versatile electrophilic behavior of this overlooked functional group.

(1) Having the crucial insight that stereoelectronic factors would disfavor eliminations in small rings has enabled Seebach to develop ingenious synthetic methods which depend on such eliminations not occurring, see: Seebach, D.; Aebi, J. D.; Gander-Coquoz, M.; Naef, R. *Helv. Chim. Acta* **1987**, *70*, 1194 and references cited therein.

(2) For reviews, see: (a) Breslow, D. S.; Skolnik, H. *Multi-Sulfur and Sulfur and Oxygen Five- and Six-Membered Heterocycles, Part One*; Wiley-Interscience: New York, 1966; p 17. (b) Fisher, G. W.; Zimmermann, T. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, 1984; Vol. 6, p 851. (c) Tillett, J. G. *Phosphorus and Sulfur* **1976**, *1*, 341.

(3) (a) Jacobsen, E. N.; Markó, I.; Mungall, W. S.; Schröder, G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 1968. (b) For additional examples of substrate scope see the Aldrich advertisement on the back of *J. Org. Chem.* **1988**, *53*(*12*), June 10 issue.

Table I. One-Pot Synthesis of Cyclic Sulfates **2**[a]

entry	cyclic sulfate **2**	R_1	R_2	yield[b] (%)	mp (°C)
1	**2a**	CO_2i-pr	CO_2i-Pr	90–93[c]	
2	**2b**	CO_2Et	CO_2Et	69[c]	75–76
3	**2c**	CO_2Me	CO_2Me	63[c]	70–71
4	**2d**	n-C_8H_{17}	H	92	
5	**2e**	c-C_6H_{11}	H	97[d]	75–76
6	**2f**	n-C_4H_9	n-C_4H_9	89	
7	**2g**	n-$C_{15}H_{31}$	CO_2Me	90–95	45–46
8	**2h**	c-C_6H_{11}	CO_2Et	95–97	
9	**2i**	H	CO_2c-C_6H_{11}	88	55–57
10	**2j**	H	$CONHCH_2Ph$	64	95–97

[a] Reactions were performed as described in ref 8. [b] Isolated yields. [c] (2*R*,3*R*)-(+)-Tartrates were used. [d] Prepared by Dr. B. B. Lohray.

The ring strain energy (~5–6 kcal/mol)[4] of 1,2-cyclic sulfates is most often cited as the reason for the very poor yields in attempted direct preparations from the diol and SO_2Cl_2 or related SO_2X_2 species.[5] However, cyclic sulfites form readily from 1,2-diols, and hence permanganate oxidation of the sulfite has been the favored route to cyclic sulfates.[2] Even so, the permanganate approach often gives poor yields and impure products. In 1981 Denmark (1,3-cyclic sulfites) and in 1983 Lowe (1,2-cyclic sulfites) reported that the oxidation step was much cleaner when effected by a stoichiometric quantity of RuO_4,[6] but this procedure is too expensive for preparative work. We now report that our catalytic RuO_4 system[7] is highly active for this same transformation. The oxidations are complete in less than 1 h with as little as 1 part in 1500 of the ruthenium catalyst. A general procedure for the conversion of diols to cyclic sulfates was developed (Table I). The simplicity of this one-pot procedure is exemplified by the details given for the case of diisopropyl tartrate in ref 8. Pure cyclic sulfates are obtained by simple extraction and filtration of the crude product through a pad of silica gel.[9]

Most of the 30 cyclic sulfates we have prepared by this method are new compounds.[10] Many are from complex synthetic intermediates, such as sugar derivatives, and their novelty is not surprising. However, the entries in Table I, all previously unknown, were selected for their simplicity to reveal just how little the chemistry of this functional group has been developed.

Although there are a number of studies of the reactivity of cyclic sulfate compounds,[2b,11] there are only a few reported applications

(4) Kaiser, E. T.; Panar, M.; Westheimer, F. H. *J. Am. Chem. Soc.* **1963**, *85*, 602.

(5) (a) Tewson, T. J. *J. Org. Chem.* **1983**, *48*, 3507 and references cited therein. (b) Tewson, T. J.; Soderlind, M. J. *Carbohydr. Chem.* **1985**, *4*, 529.

(6) Denmark, S. E. *J. Org. Chem.* **1981**, *46*, 3144. Lowe, G.; Salamone, S. J. *J. Chem. Soc., Chem. Commun.* **1983**, 1392.

(7) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.

(8) Preparation of **2a**: A 250-mL, three-necked, round-bottomed flask equipped with a reflux condenser and topped with a $CaCl_2$ drying tube connected to an HCl trap, a stopper, and a rubber septum was charged with (+)-diisopropyl tartrate (11.72 g, 50 mmol) and CCl_4 (50 mL). Thionyl chloride (4.4 mL, 60 mmol) was added via a syringe to the flask, and the resulting solution was refluxed for 30 min. [These intermediate cyclic sulfites, especially if water soluble, can undergo partial hydrolysis during the following oxidation. To suppress this hydrolysis one expels most of the HCl formed in the first step by refluxing, as done here, or by performing the oxidation rapidly (<5 min) by using up to 1 mol % ruthenium catalyst. Refluxing is needed, in most cases, only for acid removal; sulfite formation is rapid even at room temperature. Alternatively, the HCl can be scavenged by Et_3N or pyridine (0 °C, <10 min), but this necessitates isolation of the sulfite before oxidation to the sulfate.] The solution was then cooled with an ice–water bath and diluted with CH_3CN (50 mL). $RuCl_3·3H_2O$ (8 mg, 0.03 mmol) and $NaIO_4$ (16 g, 75 mmol) were added followed by water (75 mL). The resulting orange mixture was stirred at room temperature for 60 min. The mixture was then diluted with ether (400 mL), and the two phases were separated. The organic layer was washed with water (20 mL), saturated aqueous $NaHCO_3$ (2 × 20 mL), and brine (20 mL). After drying over $MgSO_4$, the solution was filtered through a small pad of silica gel to remove the brown color. The filtrate was then concentrated to afford **2a** as an anlytically pure colorless liquid (13.6 g, 92%): $[\alpha]_D^{23}$−71.43° (*c* 4.41, $CHCl_3$).

(9) This filtration removes a brown or dark green ruthenium species.

(10) The cyclic sulfates not included here will be described in the planned full account.

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