converted into nonquinonic carbonyl oxygens. The properties of 2 and related systems are currently under study and will be reported in due course.

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Strain-Directed Bridge Cleavage of (Phenylsulfonyl)-7-oxabicyclo[2.2.1]heptane Derivatives: Application to the Total Synthesis of Carba-α-DL-glucopyranose[1]

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Summary: New methodology to prepare highly oxygenated cyclohexenylsulfones by regioselective β-elimination of (phenylsulfonyl)-7-oxabicyclo[2.2.1]heptane derivatives has been developed, and its application to the total synthesis of carba-α-DL-glucopyranose is described.

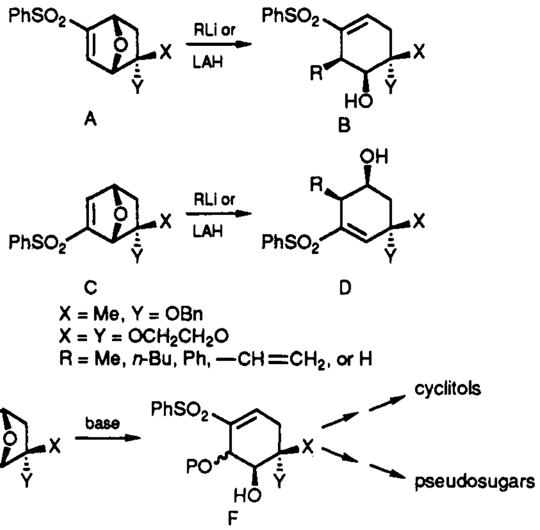
7-Oxanorbornenic derivatives are useful intermediates in syntheses of molecules of biological interest.[2] The key step in many of the efforts in this area is the cleavage of the oxygen bridge under basic,[3] reductive,[4] or acidic[5] conditions. However, most of these methods fail in some cases,[6] and thus this bridge opening step remains a current problem.

A few years ago we reported a regiospecific synthesis of substituted cyclohexenediols from 7-oxanorbornen-2-ols and organolithium reagents.[7] Subsequently, we developed fully regiocontrolled methodology toward either regioisomer via vinyl sulfones A and C (Scheme I) to produce hydroxycyclohexenyl sulfones B and D.[8] While some R groups (—CH=CH$_2$) may be readily transformed into oxygenated functionalities, we sought a more direct route to introduce an oxygen-centered nucleophile in order to increase the scope of the methodology (synthesis of cyclitols, pseudosugars, etc.). Unfortunately, a number of attempts to carry out the direct S$_N$2′ bridge cleavage using oxygen and nitrogen nucleophiles were unsuccessful.

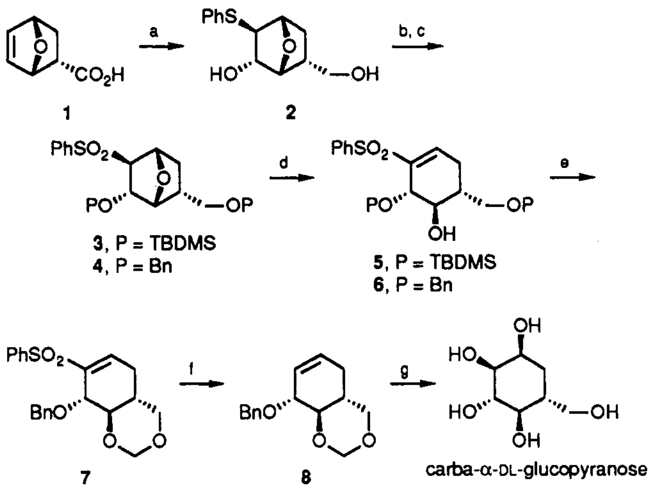
At this stage we envisioned that deprotonation and subsequent β-elimination of a readily available[9] bicyclic sulfone such as E, in which the sulfone functionality is flanked by two ethereal oxygens at the β and β′ positions, could proceed selectively toward F due to the strained character of the oxygen bridge.[10] In this report we disclose our preliminary results in this field and the application of this strain-directed process to the total synthesis of carba-α-DL-glucopyranose.[11]

Regio- and stereospecific sulfenolactonization of 7-oxabicyclo[2.2.1]hept-5-ene-2-*endo*-carboxylic acid 1[9,12] followed by reduction with LAH afforded diol 2 in excellent yield[13] (Scheme II). Protection as a bis-(*tert*-butyldimethylsilyl) ether followed by oxidation with magnesium monoperoxyphthalate (MMPP) yielded the desired model bicyclic sulfone 3. Strain-directed β-elimination was then achieved by deprotonation with 1.5 equiv of *n*-BuLi in toluene, using freshly distilled TMEDA (20%) as a cosolvent, at −78 °C to give 5. It should be pointed out that the use of the toluene–TMEDA system is crucial for the success of the reaction.[14] The challenging desulfonylation[15] of highly oxygenated vinyl sulfone 5 was then addressed, and a number of procedures were examined; however, the analysis of the reaction mixtures was com-

Scheme I



Scheme II[a]



[a] Key: (a) (1) PhSCl, CHCl$_3$, 0 °C to rt, 48 h, 82%; (2) LAH, THF, 0 °C, 1 h, 90%; (b) TBDMSCl, imidazole, DMF, rt, 48 h, 95% (for 3) or BnCl, KOH, dioxane, Δ, 3 h, 90% (for 4); (c) MMPP, MeOH, 0 °C, overnight, (95% for 3, 97% for 4); (d) 1.5 equiv *n*-BuLi, Tol/TMEDA, −78 °C, 2 h, 80% (for 5) or 3 equiv of *n*-BuLi, Tol/TMEDA/CH$_2$Cl$_2$, −78 °C, 15 min, 90% (for 6); (e) (MeO)$_2$CH$_2$, *p*-TsOH, CH$_2$Cl$_2$, 3A MS, Δ, 36 h, 88%; (f) Na(Hg), MeOH, Na$_2$HPO$_4$, −20 °C to rt, 4 h, 75%; (g) (1) OsO$_4$, Me$_3$NO, acetone/H$_2$O, rt, overnight, 95%; (2) BF$_3$·OEt$_2$, EtSH, rt, overnight, 90%.

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plicated by undesired silyl migrations and desilylations.[16] Consequently, a different protecting group was required and dibenzyl ether 4 was prepared by conventional methods. It should be mentioned that benzylation and silylation of the secondary alcohol of 2 were unexpectedly slow; therefore, these hydroxyls should be amenable to straightforward differentiation.

Treatment of 4 with *n*-BuLi (3 equiv) in a mixed solvent system (toluene/TMEDA/CH_2Cl_2, 60:20:20),[17] followed by hydrolysis (AcOH, −78 °C) afforded vinyl sulfone 6 in good yield. It was considered that protection of the free alcohol function in 6 under acidic conditions[18] would facilitate evaluation of different desulfonylation protocols. Thus, the reaction of 6 with dimethoxymethane and *p*-TsOH[19] was examined and a surprisingly facile debenzylation of the primary alcohol, and intramolecular acetalation to produce bicyclic vinyl sulfone 7 was observed. After considerable experimentation[20] we found that the use of an excess of freshly prepared Na(Hg) in buffered MeOH, under strictly anhydrous conditions,[21] produced the desired alkene 8 in good yield, without significant amounts of allylic deoxygenation, double-bond migration, or overreduction.[22]

The synthesis of carba-α-DL-glucopyranose was then completed by stereospecific bis-hydroxylation of 8[23,11b] and debenzylation and concurrent acetal cleavage ($BF_3{\cdot}OEt_2$, EtSH).[24] Our synthetic carba-α-DL-glucopyranose, as well as the corresponding pentaacetate, had spectral features identical to those in the literature.[25]

In summary, these results demonstrate that highly functionalized vinyl sulfones F are efficiently prepared via strain-directed β-elimination of oxanorbornanic sulfones. This methodology has been utilized in a total synthesis of carba-α-DL-glucopyranose. Further applications of these cyclohexenyl sulfones[26] in synthesis will be disclosed in due course.

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Supplementary Material Available: Experimental and spectroscopic data for all new compounds (8 pages). This material is contained in many 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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(1) Presented in part at the Sixth IUPAC Symposium on Organometallic Chemistry directed toward Organic Synthesis, Aug 25–29, 1991, Utrecht, The Netherlands.

(2) (a) Vogel, P. *Bull. Soc. Chim. Belg.* **1990**, *99*, 395–439. (b) Vogel, P.; Fattori, D.; Gasparini, F.; Le Drian, C. *Synlett* **1990**, 173–185. (c) Bloch, R.; Brillet, C. *Tetrahedron: Asymmetry* **1991**, *2*, 797–800. (d) Wagner, J.; Vogel, P. *Tetrahedron Lett.* **1991**, *32*, 3169–3170. (e) Reymond, J.-L.; Pinkerton, A. A.; Vogel, P. *J. Org. Chem.* **1991**, *56*, 2128–2135. (f) Jeganathan, S.; Vogel, P. *J. Org. Chem.* **1991**, *56*, 1133–1142.

(3) (a) Guildford, A. J.; Turner, R. W. *J. Chem. Soc. Chem. Commun.* **1983**, 466–467. (b) Takahashi, T.; Iyobe, A.; Arai, Y.; Koizumi, T. *Synthesis* **1989**, 189–191 and references cited therein. (c) Le Drian, C.; Vieira, E.; Vogel, P. *Helv. Chim. Acta* **1989**, *72*, 338–347.

(4) Jung, M. E.; Street, L. J. *J. Am. Chem. Soc.* **1984**, *106*, 8327–8329. (b) Mirsadeghi, S.; Rickborn, B. *J. Org. Chem.* **1985**, *50*, 4340–4345.

(5) (a) For a review, see: Suami, T. *Pure Appl. Chem.* **1987**, *59*, 1509–1520. (b) Reynard, E.; Reymond, J.-L.; Vogel, P. *Synlett* **1991**, 469–471.

(6) Jung, M. E.; Truc, V. C. *Tetrahedron Lett.* **1988**, *29*, 6059–6062.

(7) Arjona, O.; Fernández de la Pradilla, R.; García, E.; Martín-Domenech, A.; Plumet, J. *Tetrahedron Lett.* **1989**, *30*, 6437–6440. For related chemistry, see: Lautens, M.; Chiu, P. *Tetrahedron Lett.* **1991**, *32*, 4827–4830 and previous papers by this group.

(8) Arjona, O.; Fernández de la Pradilla, R.; Mallo, A.; Plumet, J.; Viso, A. *Tetrahedron Lett.* **1990**, *31*, 1475–1478. Vinyl sulfones are synthetically useful intermediates. For reviews, see: (a) Simpkins, N. S. *Tetrahedron* **1990**, *46*, 6951–6984. (b) *The Chemistry of Sulphones and Sulphoxides*; Patai, S., Rappoport, Z., Stirling, C. J. M., Eds.; John Wiley & Sons: New York, 1988. (c) De Lucchi, O.; Pasquato, L. *Tetrahedron* **1988**, *44*, 6755–6794. (d) Fuchs, P. L.; Braish, T. F. *Chem. Rev.* **1986**, *86*, 903–917.

(9) It was considered that both E and its regioisomer should be readily available via intra- or intermolecular sulfenoetherification procedures, respectively. For related chemistry see: Arjona, O.; Fernández de la Pradilla, R.; Plumet, J.; Viso, A. *J. Org. Chem.* **1991**, *56*, 6227–6229 and references cited therein.

(10) Concurrent with the research described herein was the application of this concept to prepare oxanorbornenic vinyl sulfides from (phenylsulfenyl)-4,7-dioxatricyclo[3.2.1.0^{3,6}]octane derivatives by selective cleavage of the highly strained oxetane functionality. See: Arjona, O.; Fernández de la Pradilla, R.; Plumet, J.; Viso, A. *J. Org. Chem.* **1992**, *57*, 772–774.

(11) Pseudosugars and their derivatives may act as enzyme inhibitors, sweeteners, antibiotics, etc. (a) For a recent review, see: Suami, T.; Ogawa, S. The Chemistry of Carba-sugars and their derivatives. *Adv. Carbohydr. Chem. Biochem.* **1990**, *48*, 21–90. For recent syntheses, see: (b) Shing, T. K. M.; Cui, Y.-X.; Tang, Y. *J. Chem. Soc., Chem. Commun.* **1991**, 756–757. (c) Shing, T. K. M.; Tang, Y. *Tetrahedron* **1991**, *47*, 4571–4578. (d) Takahashi, T.; Kotsubo, H.; Iyobe, A.; Namiki, T.; Koizumi, T. *J. Chem. Soc., Perkin Trans. 1* **1990**, 3065–3072.

(12) Acid 1 is readily available by copper(II) tetrafluoroborate catalyzed Diels–Alder cycloaddition between furan and acrylic acid and recrystallization. See: (a) Moore, J. A.; Partain, E. M., III; *J. Org. Chem.* **1983**, *48*, 1105–1106. (b) Suami, T.; Ogawa, S.; Nakamoto, K.; Kasahara, I. *Carbohydr. Res.* **1977**, *58*, 240–244. For the optical resolution of 1, see: Ogawa, S.; Iwasawa, Y.; Nose, T.; Suami, T.; Ohba, S.; Ito, M.; Saito, Y. *J. Chem. Soc., Perkin Trans. 1* **1985**, 903–906.

(13) All new compounds gave satisfactory elemental analyses and possessed spectral properties consistent with the assigned structures (see supplementary material).

(14) A number of different experimental conditions, including different bases, solvents, reaction temperatures and substrates (sulfides, sulfoxides, and sulfones), had to be tested to find the appropriate conditions.

(15) Treatment of a related acyclic vinyl sulfone with Na(Hg) resulted exclusively in allylic deoxygenation. See: Simpkins, N. S. *Tetrahedron Lett.* **1987**, *28*, 989–992.

(16) Further application of 5, including its smooth isomerization to a single isomer of an allylic sulfone will be reported in a full account of this work. For synthetic applications of allyl sulfones, see: Trost, B. M. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 107–124.

(17) The use of CH_2Cl_2 in this case results in higher yields and ensures reproducibility, presumably due to 6 being sparingly soluble in toluene/TMEDA at − 78 °C.

(18) Basic conditions resulted in quantitative double bond migration to afford allylic sulfones. These observations will be described in detail in a full account of this research.

(19) Dieter, R. K.; Datar, R. *Org. Prep. Proced. Int.* **1990**, *22*, 63–70.

(20) The procedures tested include: $Na_2S_2O_4$, $Ni(acac)_2/n\text{-}BuMgCl$, SmI_2, lithium naphthalenide, etc. The desired cyclohexenol 8 was not obtained in a synthetically useful yield in any case.

(21) Padwa, A.; Bullock, W. H.; Dyszlewski, A. D.; McCombie, S. W.; Shankar, B. B.; Ganguly, A. K. *J. Org. Chem.* **1991**, *56*, 3556–3564.

(22) After completion of the synthesis we found that alcohol 6 could be desulfonylated with Na(Hg) albeit in lower yield (65%) than acetal 7. Subsequent hydroxylation and removal of the benzyl groups proceeded smoothly as described for 8.

(23) (a) Evans, D. A.; Kaldor, S. W. *J. Org. Chem.* **1990**, *55*, 1698–1700. (b) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron* **1984**, *40*, 2247–2255.

(24) Fuji, K.; Ichikawa, K.; Node, M.; Fujita, E. *J. Org. Chem.* **1979**, *44*, 1661–1664.

(25) Paulsen, H.; von Deyn, W. *Liebigs Ann. Chem.* **1987**, 125–131.

(26) For leading references on the rich chemistry of vinyl sulfones, see: Trost, B. M.; Grese, T. A.; Chan, D. M. T. *J. Am. Chem. Soc.* **1991**, *113*, 7350–7362. (b) Trost, B. M.; Grese, T. A. *Ibid.* **1991**, *113*, 7363–7372. (c) Weichert, A.; Hoffmann, H. M. R. *J. Org. Chem.* **1991**, *56*, 4098–4112. (d) For reviews, see ref 8.