oxidation of carbene complexes **2** and **8** also leads to iron-*N*-alkylporphyrins, the formation of **12** from **8** giving a first example of passage from a carbene to a Fe—O—C—C—N metallacyclic complex. These reactions could occur via high-valent intermediates, formally Fe(V)=CRR′ complexes, such as **9**. A priori there are two possible evolutions of these complexes. The first one (a) could be a reductive elimination leading to ferric bridged carbene complexes such as **5** or **10** followed by a heterolytic cleavage of their Fe–C bonds. The derived enolate anion (such as **11**) should be more stable in the case of **11**[16] and more prone to form a Fe–O bond to give **12**. In that regard, it is noteworthy that the Zn(II) complex of **4** exists as a nonmetallacyclic β-keto-*N*-alkylporphyrin.[9] The second possible evolution (b) could be an isomerization leading to four-membered metallacyclic intermediates analogous to A followed by migration of the σ ligand to a pyrrole nitrogen giving eventually five-membered metallacyclic complexes such as C or **12**. Mechanism (b) should have led from **2** to a metallacyclic complex analogous to **12** but not to **6** as it was found. However, it is still difficult to conclude between paths (a) and (b) as we do not know the relative stabilities, under the reaction conditions, of **12** and of the corresponding metallacyclic complex which could be derived from **2**.

Finally, formation of **2** from a diazocompound and its transformation into a *N*-alkylporphyrin are first evidences for reactions recently postulated for *N*-vinylheme formation upon cytochrome P-450-dependent oxidation of a sydnone.[15]

(14) A recent result[11c] describing the passage from the vinylidene complex Fe[TPP][C=C(pClC$_6$H$_4$)$_2$] to N—CH=C(pClC$_6$H$_4$)$_2$TPPH by acidic treatment could be also interpreted by a similar mechanism involving a Fe(IV) intermediate.

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The Use of Alkoxy-Substituted Anomeric Radicals for the Construction of β-Glycosides

Daniel Kahne,* Dan Yang, Jung Jin Lim, Raymond Miller, and Eduardo Paguaga

Department of Chemistry, Princeton University
Princeton, New Jersey 08544

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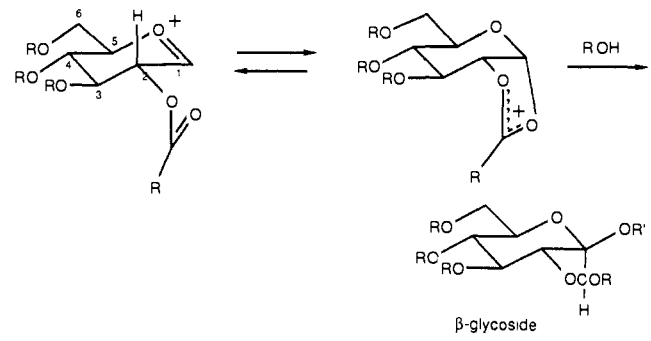
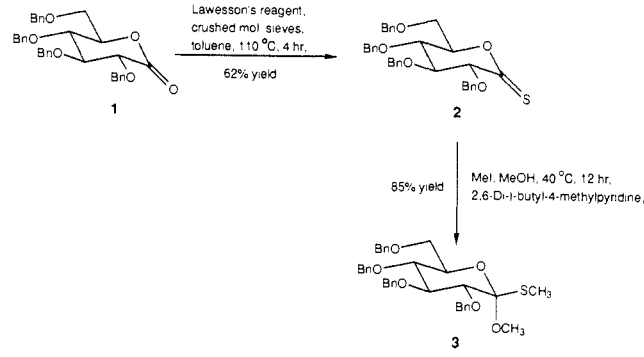
The construction of β-glycosides has been a long standing problem in oligosaccharide synthesis.[1] Most of the methods developed to date rely on S_N2 displacement of glycosyl halides at the anomeric carbon and apply only to a limited set of substrates. For instance, while β-linkages to sugar derivatives containing an equatorial C-2 acetoxy (or benzoyloxy) group can be made relatively easily (Scheme I),[2] it is extremely difficult to form β-linkages to many other sugars, including mannose and rhamnose derivatives (where the C-2 hydroxyl is axial) and all 2-deoxy sugars.[3] Because many biologically important oligosaccharides contain β-linkages to these sugars,[4] more general strategies are necessary. Preliminary results on a radically new method for constructing β-glycosides are presented below.

Scheme I



Scheme II



The method relies on generating an alkoxy-substituted radical at the anomeric carbon of a sugar. Previous work has shown that hydrogen atoms delivered to unsubstituted anomeric sugar radicals end up axial in the products, suggesting the anomeric radicals prefer to be axial in order to maximize overlap with the lone pair of the ring ether oxygen.[5] However, the corresponding alkoxy-substituted sugar radicals have never been studied.[6] We recognized that if the hydrogen still ended up axial when an alkoxy substituent was present, the product would be a β-glycoside.

A priori it is difficult to predict the stereochemical outcome in such a case because anomeric alkoxy substituents also prefer to be axial.[7] However, the question is not simply whether the radical or the alkoxy group is more stabilized by orbital overlap with the ring oxygen, because the exocyclic alkoxy group may also help stabilize the radical. Moreover, it is not clear to what extent hydrogen atom delivery to such a system is affected by steric interactions. To complicate matters further, recent ESR studies show that anomeric radicals in sugars can exist in either a boat, chair, or half chair conformation depending on the structure of the parent carbohydrate.[8] It is not known what effect, if any,

(1) See: Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155.

(2) (a) Koenigs, W.; Knorr, E. *Ber.* **1901**, *34*, 957. (b) Pougny, J. R.; Nassr, M. A. M.; Naulet, N.; Sinay, P. *Nouv. J. Chim.* **1978**, *2*, 389. (c) Hanessian, S.; Banoub, J. *Carbohydr. Res.* **1977**, *53*, C13. (d) Mukaiyama, T.; Murai, Y.; Shoda, S. *Chem. Lett.* **1981**, 431; **1983**, 935. (e) Schmidt, R. R.; Grundler, G. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 776. (f) Nicolaou, K. C.; Dolle, R. E.; Papahatjis, D. P.; Randall, J. L. *J. Am. Chem. Soc.* **1984**, *106*, 4189. (g) Dolle, R. E.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1985**, *107*, 1695. (h) Nicolaou, K. C.; Randall, J. L.; Furst, G. T. *J. Am. Chem. Soc.* **1986**, *108*, 5556.

(3) (a) Srivastava, V. K.; Schuerch, C. *Carbohydr. Res.* **1980**, *79*, C13. (b) Warren, C. D.; Auge, C.; Laver, M. L.; Suzuki, S.; Power, D.; Jeanloz, R. W. *Carbohydr. Res.* **1980**, *82*, 71. (c) Paulsen, H.; Lockhoff, O. *Chem. Ber.* **1981**, *114*, 3102. (d) Paulsen, H.; Lorentzen, J. P. *Carbohydr. Res.* **1984**, *133*, C1.

(4) E.g. calicheamicin and esperamicin. See: (a) Golik, J.; Clardy, J.; Dubay, G.; Groenewold, G.; Kawaguchi, H.; Konishi, M.; Krishnan, B.; Ohkuma, H,; Saitoh, K.; Doyle, T. *J. Am. Chem. Soc.* **1987**, *109*, 3461. (b) Golik, J.; Dubay, G.; Groenewold, G.; Kawaguchi, H.; Konishi, M.; Krishnan, B.; Ohkuma, H.; Saitoh, K.; Doyle, T. *J. Am. Chem. Soc.* **1987**, *109*, 3462. (c) Lee, M. D.; Dunne, T. S.; Siegel, M. M.; Chang, C. C.; Morton, G. O.; Borders, D. B. *J. Am. Chem. Soc.* **1987**, *109*, 3464. (d) Lee, M. D.; Dunne, T. S.; Chang, C. C.; Ellestad, G. A.; Siegel, M. M.; Morton, G. O.; McGahren, W. J.; Borders, D. B. *J. Am. Chem. Soc.* **1987**, *109*, 3466.

(5) Descotes, G. *J. Carbohydr. Chem.* **1988**, *7*, 1.

(6) Relative rates of hydrogen atom abstraction from cyclic and acyclic acetals and orthoformates have been measured by using an ESR technique. (a) Brunton, G.; Ingold, K. U.; Roberts, B. P.; Beckwith, A. L. J.; Krusic, P. J. *J. Am. Chem. Soc.* **1977**, *99*, 3177. (b) Malatesta, V.; Ingold, K. V. *J. Am. Chem. Soc.* **1981**, *103*, 609. (c) Beckwith, A. L. J.; Easton, C. J. *J. Am. Chem. Soc.* **1981**, *103*, 615. (d) Griller, D.; Howard, J. A.; Marriot, P. R.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 619. (e) Athelstan, L.; Beckwith, J.; Brumby, S. *J. Chem. Soc., Perkin Trans. 2* **1987**, 1801.

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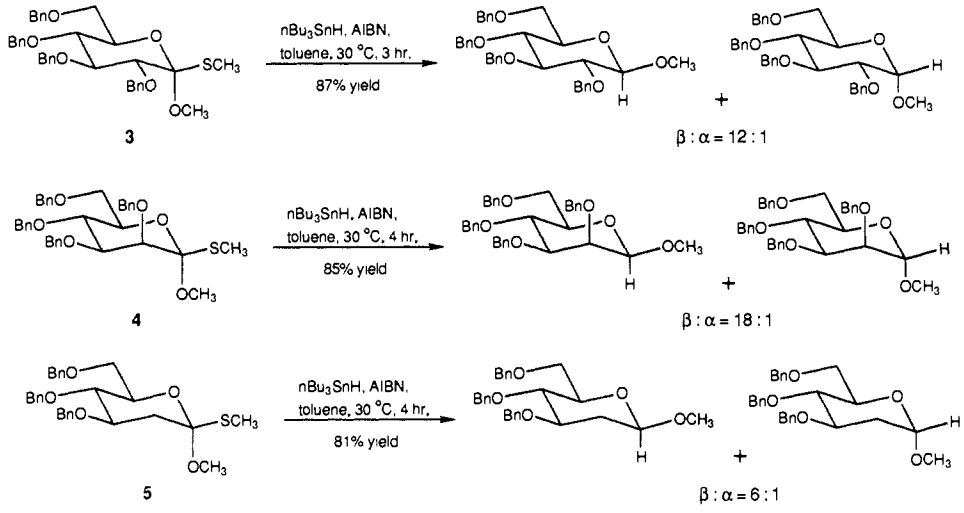
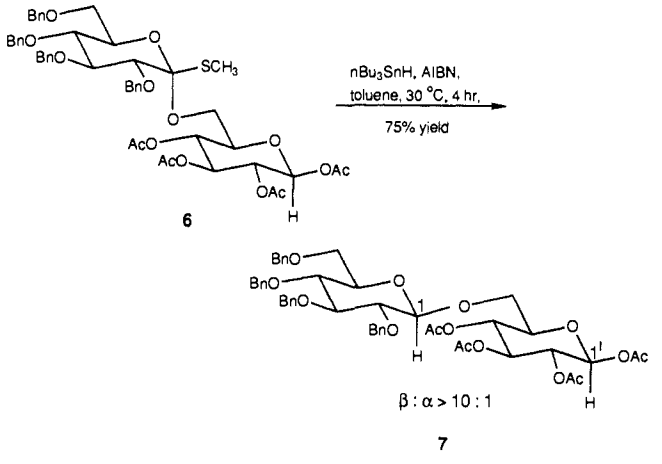
Scheme III



Scheme IV



an exocyclic alkoxy group would have on the conformation of a given anomeric radical.

To determine the stereochemical outcome of hydrogen atom transfer to an alkoxy substituted anomeric radical, hemithio ortho ester **3** was synthesized in two steps from the known lactone **1** (Scheme II).[9] Treatment of lactone **1** (0.05 M) with Lawesson's reagent (4 mol equiv) and crushed molecular sieves (3 A, 1:1 by wt with Lawesson's reagent) in toluene at 110 °C for 4 h gave thionolactone **2** (62%),[10] which was converted to the desired hemithio ortho ester **3**[11] by refluxing in methyl iodide containing 10 equiv of MeOH (0.23 M) and 2 equiv of 2,6-di-*tert*-butyl-4-methylpyridine (0.047 M) for 12 h (85%). Treatment of a 0.02 M solution of **3** in degassed (argon) toluene with 5 equiv of tributyltin hydride and 2 equiv of AIBN at room temperature (30 °C) under photolytic conditions (4 h at 350 nm in a Rayonet reactor with a Pyrex filter) produced two compounds (87%) which were found to be identical with authentic samples of the β- and α-methyl glucosides (Scheme III).[12] The product ratio was determined to be β:α = 12:1 by HPLC analysis of the crude reaction mixture (resolve silica 5μ, 8 mm × 10 cm, flow rate 1.8 mL/min, hexane–ethyl acetate 95:5, UV 254 nm, retention time: β = 21.3 min, α = 41.8 min). The selectivity for the β-anomer decreased to 9:1 at 80 °C (thermal initiation, 5 equiv, 0.01 M *n*-Bu_3SnH, 2 equiv of AIBN) and 7:1 at 110 °C. As a control experiment, the pure β- and α-methyl glucosides were submitted separately to the reaction conditions (*n*-Bu_3SnH–AIBN in toluene at 110 °C) and found to be configurationally stable.[13]

We wondered whether the stereochemistry of the radical is influenced by the substituent on C-2.[14] Therefore, we synthesized the hemithio ortho esters of perbenzylated mannose and 2-deoxyglucose and compared the stereochemical outcome of hydrogen atom transfer for the three cases (Scheme III). The mannose derivative **4** was reduced under photolytic conditions as above, and the selectivity for the β-anomer was found to be 18:1 (85% yield) by HPLC (hexane–ethyl acetate 95:5, retention time: α = 35.28 min, β = 101.52). The 2-deoxyglucose derivative **5** was also reduced photolytically and found to give a 6:1 mixture (81% yield) in favor of the β anomer (hexane–ethyl acetate 95:5, retention time: α = 34.61 min; β = 36.42 min). As these results show, the β-anomer is formed selectively in all three cases, but the presence of an alkoxy substituent at C-2 enhances the β-selectivity.

Finally, to determine whether this method could be used to construct β-linked disaccharides, we synthesized compound **6**[15] and photolyzed it as above (Scheme IV). HPLC comparison with authentic samples of the α- and β-linked disaccharides (stepwise gradient, CH_2Cl_2–CH_3CN, 97:3 25 min, 96:4 20 min, 95:5 15 min, 94:6, retention time, α = 41.1 min, β = 61.21 min) indicated that the selectivity for the β-anomer was greater than 10:1.[16]

We have shown that hydrogen atom delivery to alkoxy substituted anomeric radicals produces the corresponding β-pyranosides. When the alkoxy substituent was a sugar, a β-linked disaccharide was formed selectively. We are currently exploring the generality of this method for the construction of oligosaccharides containing β-linkages, especially to mannose, rhamnose, and the 2-deoxy sugars.

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(9) Lewis, M. D.; Cha, J. K.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 4976.

(10) All new compounds were characterized by ^1H and ^{13}C NMR, IR, and high resolution mass spectral analysis. **2**: ^{13}C NMR ($CDCl_3$, 270 MHz) C=S 215.0.

(11) Only one isomer of the hemithio ortho ester is obtained. We have assumed that the methyl sulfide is equatorial based on stereoelectronic arguments. See Chapter 2 in: Deslongschamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon Press: 1983. **3**: ^{13}C NMR ($CDCl_3$, 270 MHz) C-1 108.7, -SCH_3 12.6, -OCH_3 49.7; ^1H NMR ($CDCl_3$, 270 MHz) -SCH_3 2.12 (s, 3 H), -OCH_3 3.38 (s, 3 H).

(12) Authentic β- and α-anomers were synthesized by treating the perbenzylated lactol (0.1 M) with acidic methanol (1% acetyl chloride in refluxing methanol, 12 h). The compounds were separated by flash chromatography on silica gel with 15% ethyl acetate–petroleum ether.

(13) Although the products cannot be equilibrated thermally, it is possible to selectively destroy the β-anomer photolytically, especially at wavelengths below 300 nm. Even with the Pyrex filter, we have observed some selective destruction of the β-anomer.

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(15) **6**: ^{13}C NMR ($CDCl_3$, 270 MHz) C-1 108.1, C-1′ 91.3, -SCH_3 12.9; ^1H NMR ($CDCl_3$, 270 MHz) 2.10 (s, 3 H).

(16) **7**: ^{13}C NMR ($CDCl_3$, 270 MHz) C-1 103.8, C-1′ 91.5.