good reproducibility for experiments with different catalysts samples.

Activation energies E_a were obtained from plots of $1/T$ vs. log k_ϕ. For benzylic hydrogen exchange, E_a = 0.9 kcal/mol, and for aromatic hydrogen exchange, E_a = 8 kcal/mol.[16-18] These results clearly explain why such selective benzylic deuteration is possible. As would be expected, the ratios k_ϕ(toluene)/k_ϕ(benzene) increase dramatically as temperature is lowered. For example at 25 °C this ratio is 2570, at 100 °C, 234, at 200 °C, 31, and at 300 °C it is 8.5 (see Table I). Also, such a low E_a for benzylic exchange predicts that exchange could occur at very low temperature; indeed we have observed such exchange at below −100 °C, and these results will be reported fully later.

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(16) We believe these E_a values are correct and not influenced by restricted internal diffusion of the hydrocarbons through the MgO particles. First of all, the particles are extremely porous, crumbling to a fine powder upon being touched lightly. Furthermore, these MgO samples have large surface areas (130–170 m^2/g) and large pore diameters (25–75 Å).[3]

(17) Note that a high excess of D_2 was employed to minimize complications due to approach to isotopic equilibrium. Although conversions were often carried to >50% good straight line plots of log $(\phi_\infty - \phi)$ vs. time were always obtained.

(18) Although only small amounts of toluene were converted while collecting these kinetic data, deuteration of large amounts was possible by continued operation. In other words, the MgO definitely behaves as a catalyst and, as an example, in one large-scale, long-term experiment >50 turnovers took place. We have also used the same catalyst sample over and over again on occasion. We have not yet determined the maximum number of turnovers possible.

Serial Radical Cyclization via a Vinyl Group Immobilized by a Pyranoside. A Route to Bis-Annulated Pyranosides[1]

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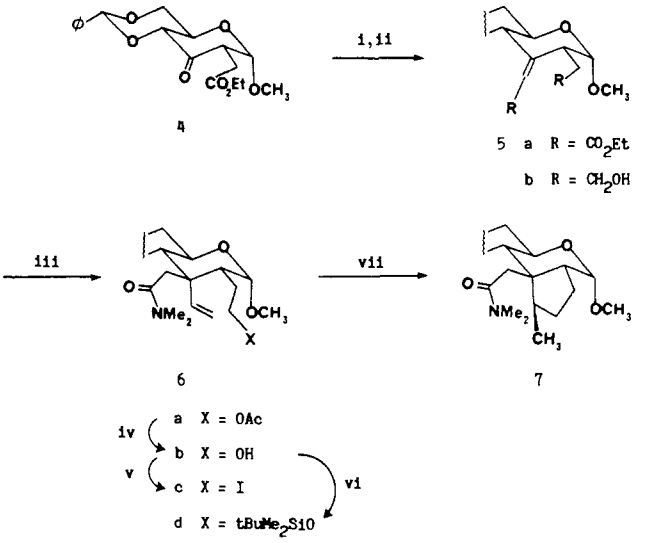
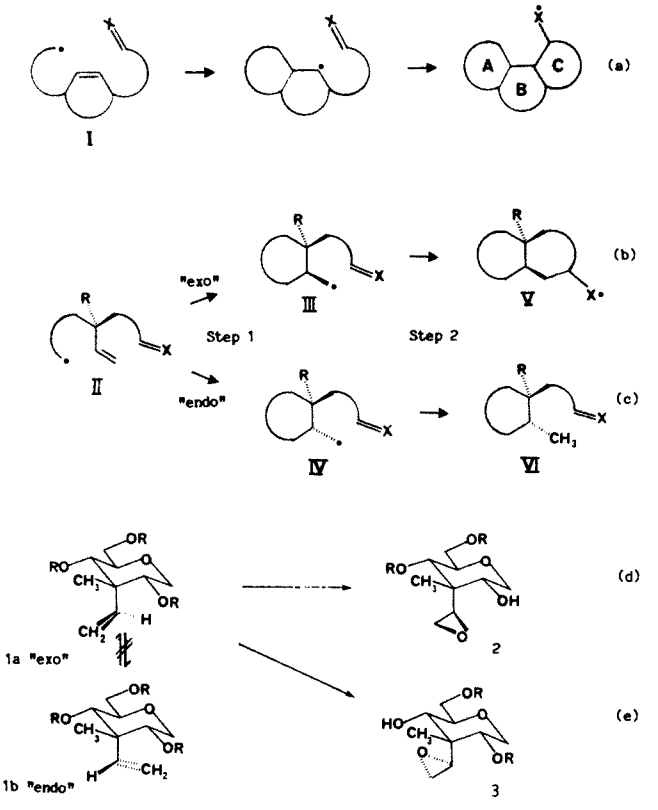
Three vibrant areas of chemical research are currently (i) the synthetic potential of free radical reactions,[2-7] (ii) the synthesis of polyquinanes,[8-10] and (iii) the utility of carbohydrates in organic synthesis.[11-14] The combination of (i) and (ii) has been cleverly explored by Curran[8] and Beckwith[9] in the context of the linearly fused triquinanes, and a combination of (i) and (iii) has received evaluation by Giese,[4] Vasella,[14] and Wilcox.[15] The surprising suitability of carbohydrates as substrates for free radical reactions had been noted previously in this laboratory in connection with

Scheme I[a]



[a] (i) Ph_3PCHCO_2Et (86%); (ii) DIBALH (76%); (iii) $CH_3C(OMe)_2NMe_2$ (98%); (ii) NaOMe/MeOH (100%); (v) Ph_3P, I_2 (94%); (vi) t-$BuMe_2SiCl$ (100%); (vii) $(n\text{-}Bu)_3SnH$ (98%).

photochemical induced alkylation reactions.[16,17] In this paper we describe a novel combination of (i)–(iii), which has implications



(1) We are grateful to NIH for support of this work (GM 32569).

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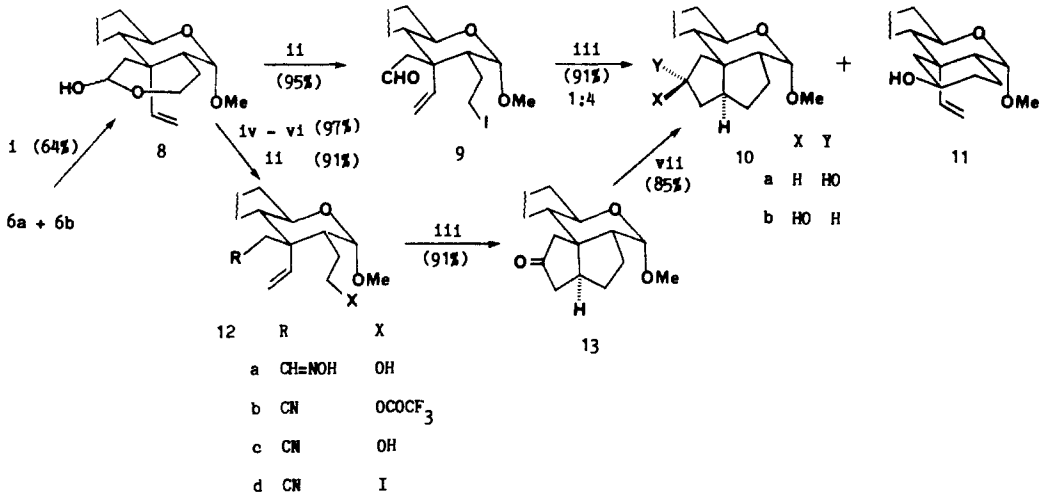
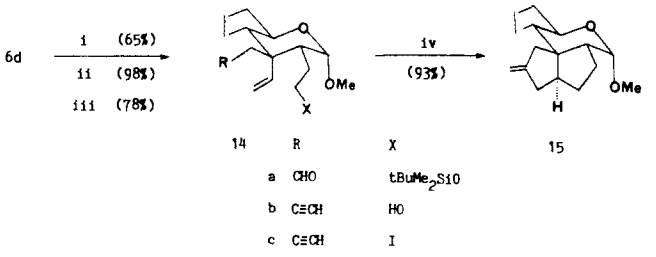
Scheme II[a]



[a] (i) $HAl[N(CH_2CH_2)_2NMe]_2$; (ii) Ph_3P, I_2; (iii) $(n\text{-}Bu)_3SnH$; (iv) $NH_2OH{\cdot}HCl$; (v) $(CF_3CO)_2O$, py; (vi) NaOMe, MeOH; (vii) $NaBH_4$.

Scheme III[a]



[a] (i) $HAl[N(CH_2CH_2)_2NMe]_2$ → **14a**; (ii) Ph_3P, CBr_4, Zn; *n*-BuLi; $(n\text{-}Bu)_4NF$ → **14b**; (iv) $(n\text{-}Bu)_3SnH$.

for future developments in all three individual areas.

In the serial cyclizations pioneered by Stork[5b] and Curran[8] as summarized in equation a, the olefinic "relay box" was incorporated in a ring, for example, I. The essential nature of this requirement can be best appreciated by considering the situation in eq b and c where the olefinic entity in the substrate, II, is a vinyl group. Freedom of rotation of the vinyl group means that the first cyclization can lead to III as well as IV. However, further cyclization of III is a comparatively poor process—particulary where 5/5 fused system is concerned.[18] Thus, a likely product in this case would be the methylcycloalkane VI. The problem could be circumvented only if it were possible to freeze the vinyl residue in the desired "exo" orientation.

That this could be achieved was suggested by the results summarized in eq d and e. We have recently[19] described the stereocontrolled formation of geminal dialkyl systems such as **1** (vide infra), and in the course of exploring the utility of these systems, we discovered that the oxiranes **2** and **3** could be obtained *mutually exclusively* from **1**, depending on whether the C2 or C4 hydroxyl group, respectively, was free.[20] The surprising implication of these results was that the vinyl group was reacting entirely via the exo orientation, **1a**, even though Dreiding models show that reaction via the "endo" rotamer, **1b**, is possible. A further implication was that the pyran ring could engender the requirements for serial cyclizations involving a pendant vinyl group, as depicted in eq b.

The recently described keto ester **4**[21] provided us with ready access to the substrates required for testing this novel idea in stereocontrol. Thus, the iodo amide **6c** was prepared via the diester **5a**, diol **5d**, and the alcohol **6b**[22] (Scheme I).

The success of step 2 in eq b requires the presence of a good radical trap (i.e., C=X) and/or that the quenching of the radical be stalled. The amide group proved to be an ineffective trap, since the product from treatment of **6c** with $(n\text{-}Bu)_3SnH$ was the methylcyclopentane **7**.[22]

On the basis of the ranking of radical acceptors developed by Giese,[4b] we decided to evaluate the aldehydo group. Accordingly, reduction of the amides **6a** and **6b** by means of the Mukaiyama procedure[23] afforded the hemiacetal **8**[22] from which the iodo aldehyde **9** was readily obtained. Exposure of **9** to $(n\text{-}Bu)_3SnH$ did effect the desired serial cyclization to give **10a**;[22] but the formation of the cyclohexanol **11**[22] as the principal product made this achievement a muted success (Scheme II).

A nitrile[7] was next examined. The substrate, **12d**[22] was prepared from **8** by standard transformations, and treatment with $(n\text{-}Bu)_3SnH$ for 0.5 h followed by evaporation and silica gel chromatography afforded ketone **13**[22] smoothly in 91% yield. Interestingly, the endo alcohol **10b**[22] was obtained exclusively by reducing **13** with sodium borohydride.

Finally, the alkynyl group[7] was evaluated. Application of the Cory–Fuchs procedure[24] to aldehyde **14a** afforded the alkyne **14b**.[22] The iodide **14c** obtained therefrom afforded **15**[22] in 93% yield (Scheme III).

Recent publications from this[25] and other[26] laboratories have emphasized the merits of "annulated sugars" for stereocontrolled synthesis of optically active carbocycles, and the effectiveness of the pyranoside ring as an agent for controlling stereoselectivity on the carbocyclic annulus has been demonstrated by a recent synthesis of actinobolin.[27] The fact that **10**, **13**, and **15** are bis-annulated sugars is therefore a promising development. *A stereochemical audit is also appropriate, for although stereochemistry is lost at C2 and C3 of the sugar moiety during the formation of* **4**,[28] *there is a complete recovery with the formation of* **6**, *and with the formation of* **10**, *two new centers have been created. Furthermore, the larger part of the pyranoside residue of* **10** *remains available for future synthetic manipulations.*

(18) See, for example, ref 9, where the 5/5 fused system **13b** was formed in 6% yield.
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