2, albeit in lower yield. Reaction of the mesylate of tetrabenzylgalactose **4** gave the expected oxyglycal, **5**, in low (15%) yield. Reaction with dppfPd(0) (vide infra) resulted in a slightly better yield of oxyglycal **5** (Table I, entry 3).

Carbon–mesylate bonds possess significant ionic character, so it may be more proper to consider the sugar as consisting of an oxonium ion and a dissociated mesylate prior to oxidative addition.[14] Also, Daves has shown that if the palladium is sufficiently ligated, it is possible to suppress β-hydride elimination entirely and produce a stable palladium complex with a cis β-hydrogen.[15] Thus, the conformation of the oxonium ion and the stability of the palladium intermediate, not the stereochemistry at C-2, appear to be important factors in the effectiveness of this process (entries 1–3).

Treatment of ribose **6** and arabinose **8** under the reaction conditions at room temperature gave essentially the same amount of the corresponding oxyglycal (20%). A brief survey of bases (Ag_2CO_3, Na_2CO_3, NaH, and Proton Sponge) and metal catalysts ($(PPh_3)_2Pd(0)$, $Pd(AsPh_3)_4$, and dppfNi(0)) gave similar or lower yields. Using dppfPd(0), glycal **7** was obtained in 40% yield from ribose **6**, while arabinose **8** gave essentially no reaction. Heating to 50 °C with $Pd(PPh_3)_4$ as the catalyst resulted in dramatically improved yields for both sugars (Table I). Only a few examples of oxyglycals derived from furanoses have been reported.[16,17] Unlike the perbenzoyl analogue,[18] oxyribal **7** is thermally stable and may, therefore, prove to be synthetically useful.

The oxyglycal[20] obtained from 2,3:4,6-bis(isopropylidene)-mannopyranose **9**,[21] represents a new class of acetal-protected oxyglycals, which is unavailable by classic methods. Formation of oxyglycal **10** provides an indication of the gentleness of the oxidative addition, β-hydride elimination process. The properties of oxyglycal **10** have not been fully investigated, but it is stable to brief contact with aqueous acid and silica gel. Attempts to optimize the reaction conditions for acetal-protected carbohydrates are currently underway.

In summary, this work demonstrates the first example of palladium(0) oxidative addition into the anomeric center of carbohydrate electrophiles. Subsequent β-hydride elimination affords a new route to oxyglycals, including examples which cannot currently be prepared by other means. Further studies on the application of these novel electrophiles in other palladium-mediated reactions and on the use of oxyglycals in C-nucleoside synthesis are currently underway.

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Supplementary Material Available: TLC, IR, LCMS, and ^1H and ^{13}C NMR spectral data for compounds **2** and **7** as well as ^1H and ^{13}C NMR spectral data for compound **10** (2 pages). Ordering information is given on any current masthead page.

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Dyotropic (6 + 4)-Hydrogen Migration in a 2,3-Bis(methylene)decahydroanthracene

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The 4*n*-electron homology is firmly established for pericyclic reactions by theory as well as by experiment. However, in one instance, the dyotropic hydrogen migration,[1] the number of reorganizing electrons is still limited to $4\sigma + 2\pi$. We now report on the dyotropic hydrogen migration in 2,3-bis(methylene)-1,2,3,4,4a,5,8,9,9a,10-decahydroanthracene-4a,9a-dicarboxylic anhydride **4**, which involves $4\sigma + 6\pi$ electrons.

The synthesis of the starting material **4** is illustrated in Scheme I: Cycloaddition of 1,2-bis(methylene)cyclobutane[2] to acetylenedicarboxylic acid, accompanied by dehydration, gives anhydride **1**.[3] Diels–Alder addition of **1** to 1,2-bis(methylene)-cyclohex-4-ene (**2**)[4] yields compound **3**,[3] which can be converted to **4**[3] by heating to 117 °C. Thermolysis of **4** at 150 °C yields 2,3-dimethyl-*cis*-1,4,4a,9,9a,10-hexahydroanthracene-4a,9a-dicarboxylic anhydride **5**[3] via dyotropic migration of the anti hydrogens at positions 5 and 8.

The kinetic parameters of this process were determined by monitoring the UV spectra of degassed, sealed samples of **4** in isooctane ($0.9\ 10^{-3}$ M) at six temperatures from 160 to 185 °C. The first-order rate constant k changes with temperature according to the Arrhenius equation

$$\log k = (11.1 \pm 1.1) - (31500 \pm 2100)/2.3RT \qquad (R = 1.98\ \text{cal/K·mol}) \quad (1)$$

The transition state for the conversion **4** → **5** requires a folded conformation in which the migrating hydrogens are near the termini of the diene. Force field calculations[5] show that **4f** (Scheme II) possesses a 2.9 kcal/mol higher enthalpy of formation than the preferred open form **4o**. When this preequilibrium is considered, the activation energy for the (6 + 4)-dyotropic hydrogen migration is 28.6 kcal/mol, close to the values reported (25.1–28.2 kcal/mol) for the (4 + 2)-dyotropic shift in conformationally rigid isodrin systems.[6]

In order to investigate the mechanism of this reaction, tetra- and dideuterated **4** were prepared from appropriately labeled **2**: **2**-d_4 was obtained by cycloaddition of 1,1,4,4-tetradeuteriobutadiene[7] to dimethyl acetylenedicarboxylate and transformation of the ester groups into methylene groups via reduction to the diol ($LiAlH_4$), formation of the dibromide (PBr_3), and debromination (Zn-Cu).

The electrochemical reduction of benzocyclobutene in THF–D_2O[8] yielded a 1:1 mixture of *cis*- and *trans*-2,5-dideuterio-

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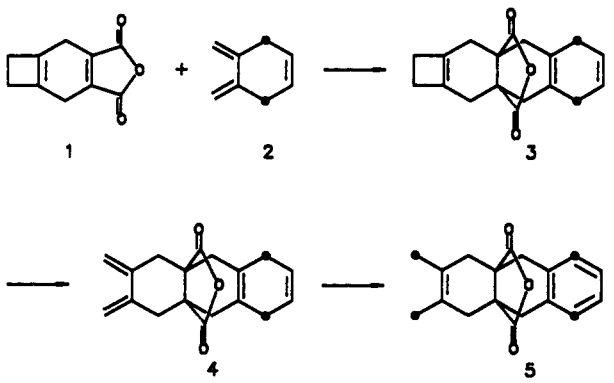
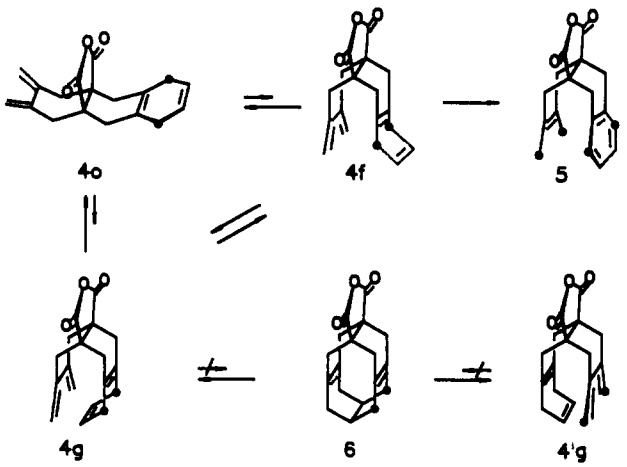
Scheme I[a]



[a] **2**-d_2–**4**-d_2: Each of the marked positions is substituted by one deuterium. **5**-d_2: Any two of the marked positions, separated by σ_v, are substituted by one deuterium. **2**-d_4–**4**-d_4: Each of the marked positions is substituted by two deuteriums. **5**-d_4: Each of the marked positions is substituted by one deuterium.

Scheme II[a]



[a] **4**-d_4, **6**-d_4: Each of the marked positions is substituted by two deuteriums. **5**-d_4: Each of the marked positions is substituted by one deuterium.

bicyclo[4.2.0]octa-1(6),3-diene, which after flash vacuum pyrolysis led to both stereoisomers of **2**-d_2.

Samples of **3**, **3**-d_2, and **3**-d_4 were heated in degassed 0.023 M benzene solution at 160.7 °C for 17.5 h and analyzed by ^{1}H NMR spectroscopy. From the conversion of **4** (84%) and **4**-d_4 (44%), the primary kinetic isotope effect for the dyotropic migration of two deuterium atoms, $k_{2H}/k_{2D} = 3.16$ (±0.16), is obtained directly. **4**-d_2, however, resulting from **2**-d_2 via **3**-d_2, is a 1:2:1 mixture of three stereoisomers with respect to the orientation of the deuterium atoms. Only in the main isomer with trans deuteriums do H and D migrate, whereas the other two isomers behave as **4** or **4**-d_4, neglecting secondary isotope effects. The measured conversion of **4**-d_2 (67%) had to be corrected for this reason as well as for partial deuteration (82% d_2) to obtain the actual conversion of *trans*-**4**-d_2 (66.4%). From the latter is derived the isotope effect for the dyotropic migration of H and D, $k_{2H}/k_{HD} = 1.68$ (±0.08).

In a synchronous migration, the lower zero point energies of two breaking C–D bonds add in raising the activation energy, i.e., the isotope effects are squares: $k_{2H}/k_{HD} = (k_{2H}/k_{2D})^{1/2} = 1.78$ (±0.05). In a stepwise process, on the other hand, the two isotope effects are related by eq 2,[9] which links $k_{2H}/k_{2D} = 3.16$ (±0.16) with $k_{2H}/k_{HD} = 1.52$ (±0.08).

$$k_{2H}/k_{HD} = 2k_{2H}/(k_{2H} + k_{2D}) \quad (2)$$

A distinction between the two mechanisms using the double-labeling experiment is not possible because of the error involved in measuring the small isotope effect. An argument for a concerted process is the enthalpy of formation of the diradical intermediate, obtained by addition of increments,[10] which lies 35.5 kcal/mol above that of the reactant **4f** and 7 kcal/mol above that of the transition state. Acid catalysis of the reaction is ruled out by the observation that a 3-fold increase in the surface of the reaction vessel by the addition of glass chips did not affect the rate.

Another possible fate of **4** in the folded conformation **4g** would be closure to the tetrahydro[4]beltene **6**.[11] Although this compound was shown by force field calculations[5] to be 10 kcal/mol more stable than **4g**, it is not produced in the thermolysis reaction. The use of **4**-d_4 allows one to decide whether the failure to observe **6** has a thermodynamic or kinetic origin: Due to the C_{2v} symmetry of **6**, its occurrence even as a minor equilibrium component would transfer the label into the methylene groups of **4'g**-d_4. Since no deuterium could be detected by ^{1}H NMR spectroscopy in the methylene groups of recovered **4**-d_4, the closure of **4** to **6** must be foiled for kinetic reasons.

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Registry No. 1, 138090-41-2; **2**, 54290-41-4; *cis*-**2**-d_2, 138090-46-7; *trans*-**2**-d_2, 138090-47-8; **2**-d_4, 138090-45-6; **3**, 138090-42-3; **3**-d_2, 138090-48-9; **3**-d_4, 138090-49-0; **4**, 138090-43-4; **4**-d_2, 138090-51-4; **4**-d_4, 138090-50-3; **5**, 138090-44-5; D_2, 7782-39-0.

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Preassociating α-Nucleophiles[1]

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Research on cyclodextrin (CD) transacylase mimics has been among the most fruitful in the artificial enzyme field. While most proteases function efficiently at pH 7.4, βCD itself is well-known to be inert at this pH; rather, it reacts rapidly with esters only when its secondary hydroxyl groups (pK_a 12.1) have begun to deprotonate.[4] Thus, the synthesis of synthetic transacylases with reactivity at neutral pH presents itself as an important goal of practical significance. Toward this end, CDs have been prepared bearing imidazole as a group with reactivity at pH 7;[5] pendant coordination complexes have likewise been employed.[6] However,

(1) This paper is dedicated to Professor Ronald C. D. Breslow on the occasion of his 60th birthday.
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