Decarbonylation of Unprotected Aldose Sugars by Chlorotris(triphenylphosphine)rhodium(I). A New Descent of Series Approach to Alditols, Deoxyalditols, and Glycosylalditols

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Unprotected C_n aldose sugars are cleanly decarbonylated by 1 equiv of chlorotris(triphenylphosphine)rhodium(I) in 1–24 h at 130 °C in *N*-methyl-2-pyrrolidinone solution to give the corresponding C_{n-1} alditol in about 75–95% yields. This technique represents a useful variation on traditional carbohydrate "descent of series" reactions. The procedure is quite general and also works on a number of aldose derivatives, such as deoxy sugars, N-acetylated amino sugars, and disaccharides, providing convenient small-scale syntheses of deoxyalditols, (acetylamino)-deoxyalditols, and glycosylalditols, respectively. The reactions proceed with complete retention of stereochemistry, the only side products observed being a few percent of the C_n lactones and the C_{n-2} alditol. Attempts to make the reactions catalytic have not yet been very successful.

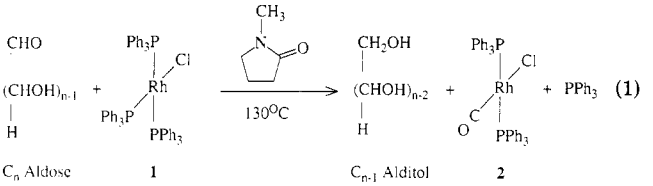
Introduction

Carbohydrate "ascent and descent of series" reactions[1] are among the most fundamental tools of carbohydrate synthesis. Ascent of series reactions have become quite sophisticated,[2] reflecting the challenges involved in stereoselective C–C bond formation. In contrast, descent of series techniques have not advanced much beyond traditional approaches. Another facet of modern carbohydrate synthesis is its increasing reliance on temporary protecting groups to facilitate specific, high-yield transformations of these functionally rich substrates.[3]

Our recent consideration of potential strategies for metal-catalyzed biomass conversion[4,5] has led us to an investigation which simultaneously addresses both carbohydrate descent of series and the inconvenience of protecting groups. Although there are well-known metal-based systems for effecting the stoichiometric[6,7] and catalytic[8] decarbonylation of aldehydes, we were not able to find any documented examples of the application of this reaction to unprotected aldose sugars.[9,10] The present study reports the full details of our success in achieving the one-step, high-yield conversion of C_n aldoses into their corresponding C_{n-1} alditols.[11] The synthetic utility of this new descent of series reaction is demonstrated by its application to improved preparations of deoxyalditols and glycosylalditols. The results also illustrate how the high selectivity characteristics of homogeneous transition-metal reagents can be used to reduce the need for temporary protecting groups.

Results

Every simple C_n aldose sugar investigated is readily decarbonylated by chlorotris(triphenylphosphine)rhodium(I) (**1**) at 110–130 °C in *N*-methyl-2-pyrrolidinone (NMP) solution. The products of the reaction are the C_{n-1} alditol and carbonylchlorobis(triphenylphosphine)rhodium(I) (**2**) (eq 1, Table IA). The progress of the reaction



C_n Aldose **1** C_{n-1} Alditol **2** (1)

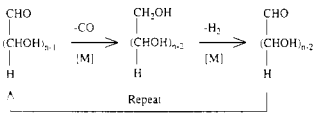
is usually readily monitored by visual observation. The deep red starting color due to **1**[12] gradually lightens, then becomes orange, and in a final titration-like step turns to the bright yellow characteristic of **2**. In some cases the progression of color changes stops slightly short of completion, in which case the reaction may be followed by GC analysis of the sugars (after derivatization[13]) or by infrared analysis of the product rhodium carbonyl. The reactions are remarkably clean, especially considering the thermal sensitivity of unprotected sugars, and the product alditols are formed in about 75–95% GC yield. The only side products observed are a few percent of the C_n lactones corresponding to the starting aldose and about 1% of the

(1) Hough, L.; Robinson, A. C. *The Carbohydrates: Chemistry and Biochemistry*, 2nd ed.; Pigman, W. W., Horton, D., Eds.; Academic Press: New York, 1972; Vol IA, pp 118–138.

(2) For a recent compilation of references, see: Dondoni, A.; Fantin, G.; Fogagnolo, M.; Medici, A.; Pedrini, P. *J. Org. Chem.* **1989**, *54*, 693.

(3) Binkley, R. W. *Modern Carbohydrate Chemistry*; Marcel Dekker: New York, 1988; pp 76, 113–165.

(4) Carbohydrates were originally thought of as carbon hydrates, $(C{\cdot}H_2O)_n$, but they can also be viewed as syn-gas polymers, $(CO{\cdot}H_2)_n$. This suggested to us a possible approach to a novel metal-catalyzed biomass conversion scheme based on the repeated decarbonylation and dehydrogenation of sugars:



(5) Andrews, M. A.; Klaeren, S. A. *J. Am. Chem. Soc.* **1989**, *111*, 4131.

(6) (a) Baird, M. C.; Nyman, C. J.; Wilkinson, G. *J. Chem. Soc. A* **1968**, 348. (b) Ohno, K.; Tsuji, J. *J. Am. Chem. Soc.* **1968**, *90*, 99.

(7) Tsuji, J.; Ohno, K. *Synthesis* **1969**, *1*, 157.

(8) (a) Doughty, D. H.; Pignolet, L. H. *J. Am. Chem. Soc.* **1978**, *100*, 7083. (b) Doughty, D. H.; Anderson, M. P.; Casalnuovo, A. L.; McGuiggan, M. F.; Tso, C. C.; Wang, H. H.; Pignolet, L. H. *Adv. Chem. Ser.* **1982**, *196*, 65. (c) Belani, R. M.; James, B. R.; Dolphin, D.; Rettig, S. J. *Can. J. Chem.* **1988**, *66*, 2072. (d) Domazetis, G.; James, B. R.; Tarpey, B.; Dolphin, D. *ACS Symp. Ser.* **1981**, *152*, 243.

(9) There are several reports that allude to the decarbonylation of glucose by transition metal complexes. These claims are based solely on the formation of metal carbonyl complexes; the sugar product(s) were not identified: (a) Kruse, W. M.; Wright, L. W. *Carbohydr. Res.* **1978**, *64*, 293. (b) Rajagopal, S.; Vancheesan, S.; Rajaram, J.; Kuriacose, J. C. *J. Molec. Catal.* **1983**, *22*, 131.

(10) The decarbonylation of protected sugars has previously been effected with rhodium complexes [(a) Ward, D. J.; Szarek, W. A.; Jones, J. K. N. *Chem. Ind. (London)* **1976**, 162. (b) Iley, D. E.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1975**, *97*, 2563. (c) MacCoss, M.; Chen, A.; Tolman, R. L. *Tetrahedron Lett.* **1985**, *26*, 4287] and by photochemical means [(d) Whistler, R. L.; Ong, K.-S. *J. Org. Chem.* **1971**, *36*, 2575].

(11) For a preliminary account of part of this work, see: Andrews, M. A.; Klaeren, S. A. *J. Chem. Soc., Chem. Commun.* **1988**, 1266–1267.

(12) In NMP solution, **1** probably exists as the solvent complex $RhCl(NMP)(PPh_3)_2$, cf. Halpern, J. *Organotransition-Met. Chem., Proc. Jpn.-Am. Semin., 1st* 1974 (Pub, **1975**), 109; *Chem. Abstr.* **1977**, *86*, 42838*k*.

(13) (*a*) *Analysis of Carbohydrates by GLC and MS*; Biermann, C. J., McGinnis, G. D., Eds.; CRC Press: Boca Raton, FL, 1988. (b) Andrews, M. A. *Carbohydr. Res.*, in press.

0022-3263/89/1954-5257$01.50/0

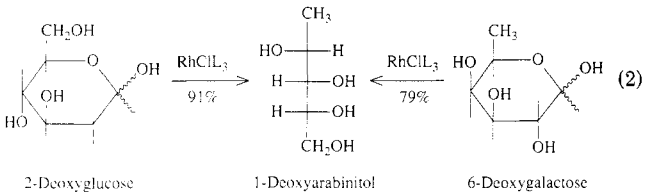
Table I. Decarbonylation of C_n Aldoses to C_{n-1} Alditols by Chlorotris(triphenylphosphine)rhodium(I)[a]

aldose[b]	n	time, h	alditol[b]	yield,[c] %
		A. Simple Aldoses		
glucoheptose	7	<3.5	glucitol	88
glucose	6	8	arabinitol	88
allose	6	<4.5	ribitol	68 (50)
arabinose	5	3	erythritol	86 (87)
xylose	5	<7	threitol	81 (76)
erythrose	4	2.5	glycerol	95
glyceraldehyde	3	0.5	ethylene glycol	95
glycolaldehyde	2	0.3	methanol	85
		B. Deoxyaldoses		
2-deoxyglucose	6	2	1-deoxyarabinitol	91 (83)
6-deoxygalactose	6	6	1-deoxyarabinitol	79
2-deoxygalactose	6	2	5-deoxyarabinitol	89 (69)
6-deoxyglucose	6	7	5-deoxyarabinitol	76
6-deoxymannose	6	4	5-deoxyarabinitol	81
2-deoxyallose	6	<1.5	1-deoxyribitol	91 (81)
2-deoxyribose	5	0.3	1-deoxyerythritol	99 (70)
		C. Functionalized Aldoses		
N-acetylglucosamine	6	12	1-(acetylamino)-1-deoxyarabinitol	56
N-acetylmannosamine	6	15	1-(acetylamino)-1-deoxyarabinitol	47 (37)
N-acetylgalactosamine	6	5	5-(acetylamino)-5-deoxyarabinitol	56
2-deoxy-2-fluoroglucose	6	49	1-deoxy-1-fluoroarabinitol	~40[d]
		D. Disaccharides		
melibiose	12	24	5-*O*-α-galactopyranosylarabinitol	91 (72)
gentiobiose	12	18	5-*O*-β-glucopyranosylarabinitol	82 (50)
lactose	12	24	3-*O*-β-galactopyranosylarabinitol	56 (47)
maltose	12	13	3-*O*-α-glucopyranosylarabinitol	64
cellobiose	12	18	3-*O*-β-glucopyranosylarabinitol	61
3-*O*-β-galactopyranosylarabinose	11	22	2-*O*-β-galactopyranosylerythritol	40

[a] See the Experimental Section for conditions. [b] Trivial names, see the Experimental Section and supplementary material for Chemical Abstracts names. [c] GC yields (see the Experimental Section), isolated yields given in parentheses. [d] Tentatively identified by GC–MS, ca. 20% unreacted aldose still present.

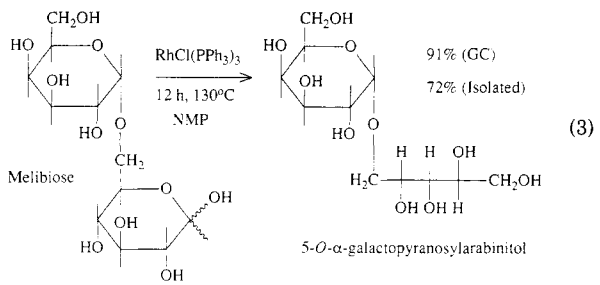
C_{n-2} alditol. Both aqueous and nonaqueous workups have been developed which permit the facile isolation of the product alditol in good yield, even on 25-mg scale reactions.

The reaction is quite general and has been applied to a number of aldose derivatives. Deoxyaldoses are readily decarbonylated, especially those lacking a hydroxyl substituent in the 2-position, to give the expected deoxyalditols (Table IB, eq 2). Functionalized sugars lacking



(2)

strong donor atoms, such as N-acetylated amino sugars, are also decarbonylated (Table IC). In this case, however, thermal decomposition reactions appear to be somewhat more significant. The most striking demonstration of the potential utility of the reaction is provided by the decarbonylation of a number of common disaccharides (Table ID, eq 3). The product glycosylalditols, formed in good



(3)

yield in a single step, would otherwise constitute multistep synthetic challenges. The only aldoses examined that could not be readily decarbonylated are glucosamine hydrochloride and 2-deoxy-2-fluoroglucose. The former led to intractable black solutions. The latter does appear to undergo decarbonylation to 1-deoxy-1-fluoroarabinitol, but the reaction rate is very slow (Table IC).

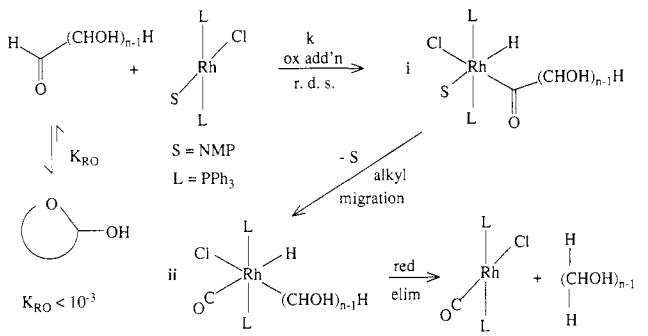
Discussion

Experimental Considerations. Two factors appear to have inhibited the development of metal-mediated aldose decarbonylations in the past. The first problem is the general one of finding a suitable solvent, i.e. one that will dissolve both the sugar and the metal complex but not inhibit the action of the metal by strong coordination. The second, specific to decarbonylations, is that solutions of aldoses typically contain only a few hundredths of a percent free aldehyde due to hemiacetal formation.[14] All previous aldose decarbonylations, both metal-mediated[10a-c] and photolytic,[10d] have therefore employed protected sugars which are soluble in nonpolar organic solvents and have full-fledged aldehyde groups. Our present studies show that neither of these limitations is compelling.

Prior studies of organotransition metal catalyzed reactions of unprotected sugars, though limited, have typically utilized amide solvents.[9,15] Our studies suggest that amides are in fact almost uniquely suited for this purpose. They are about the only good solvents for both sugars and metal complexes that can also function as *weak* donor ligands toward late, low-valent transition metals such as Rh(I).[16-19] An additional constraint in the present case

(14) Angyal, S. J. *Adv. Carbohydr. Chem. Biochem.* **1984**, *42*, 15.
(15) Massoui, M.; Beaupere, D.; Goethals, G.; Uzan, R. *J. Molec. Catal.* **1985**, *29*, 7.
(16) For a review of weak donor ligand complexes of the platinum group metals, see: Davies, J. A.; Hartley, F. R. *Chem. Rev.* **1981**, *81*, 79.

Scheme I. Aldose Decarbonylation Reaction



is that the solvent cannot be a formamide since these contain a pseudo-aldehyde group which can be decarbonylated by 1.[20] We have found *N*-methyl-2-pyrrolidinone (NMP) to be particularly convenient.[21]

The problem of low reaction rates due to extensive masking of the aldehyde carbonyl as a hemiacetal is met by using the excellent aldehyde decarbonylation reagent 1[6,22] at higher than normal temperatures, i.e. ca. 130 °C.[23] For comparison, decarbonylation of 5-(hydroxymethyl)-furfural, a hydroxyaldehyde not subject to hemiacetal formation, occurs at only 70 °C in the same solvent.[24,25] Unfortunately, the resulting carbonyl complex **2** is highly resistant to carbon monoxide dissociation.[26] This prevents the system from becoming catalytic, a nontrivial consideration in the case of a rhodium reagent. The use of efficient, but moderately expensive, reagents such as 1 can nevertheless be very justifiable, especially in light of the increasing trend toward smaller scale reactions. Complex 1 is commercially available[27] or readily prepared in good yield from $RhCl_3 \cdot (H_2O)_n$[28] and is easy to handle,[29] and carbonyl complex **2** can be recycled to 1 if desired.[26]

Attempts to find replacements for 1 that would permit the reaction to become catalytic have not yet proven successful. Cationic complexes $[Rh(Ph_2P(CH_2)_nPPh_2)_2]_2^+$ (n = 2, 3) related to 1 are reported to be long-lived catalysts for the decarbonylation of simple aldehydes,[8a,b] but they are only effective in nondonor solvents at temperatures above 120 °C.[30] As expected, they therefore proved unsatisfactory in the present situation which involves masked aldehydes in polar solvents. Multiple products were observed in the cases examined (glyceraldehyde, glucose, and 2-deoxyribose), including lactones and alditols resulting from net disproportionation of the starting sugar. While other catalytic decarbonylation reagents are known,[8c,d] these metalloporphyrin systems are complex and exhibit undesirable free-radical characteristics. Attempts to use cheaper ruthenium complexes such as $RuCl_2(PPh_3)_3$ as stoichiometric decarbonylation reagents[31] also led to complex product mixtures.

Mechanistic Considerations. The mechanism of aldehyde decarbonylation by 1 has been thoroughly investigated,[12,32] and we have no reason to believe that the aldose decarbonylations proceed any differently, aside from the operation of a hemiacetal–aldehyde preequilibrium (K_{RO}, Scheme I). While mutarotation of sugars can be extremely slow in nonaqueous solvents,[15,33] ring opening of the hemiacetal is not kinetically rate limiting since mutarotation was experimentally found to be much faster than decarbonylation for both glucose and arabinose.[34,35] The rate-determining step of the reaction should therefore be the oxidative addition step ($k_{ox.addn}$),[12] making the overall reaction rate dependent upon the product of K_{RO} and $k_{ox.addn}$. Since $k_{ox.addn}$ should be roughly equal for a series of related sugars, the decarbonylation rates should reflect the percentage of aldehydo sugar present under the reaction conditions. While data for the aldehydo composition of sugars in nonaqueous solvents are almost nonexistent,[14] the relative decarbonylation rates of the sugars in Table I are qualitatively consistent with the aldehyde content of these sugars in aqueous solution.[14,36] We hope to carry out more quantitative studies of this point in future work using circular dichroism[37] and competitive reaction techniques.

Very few side products are observed in these reactions. Traces of the C_{n-2} alditols are formed. Presumably alkyl hydride intermediate ii (Scheme I), which 99% of the time

(17) The successful functioning of many homogeneous catalysts depends on the use of a solvent or ligand that can stabilize reactive intermediates by weak coordination. For example, decarbonylations using 1 often employ a nitrile solvent to prevent precipitation of the rhodium dimer $[RhCl(PPh_3)_2]_2$,[6b] presumably by formation of a $RhCl(RCN)(PPh_3)_2$ solvate. Sulfoxides might also be usable in certain cases but they are somewhat stronger ligands and can lead to carbohydrate oxidation reactions.

(18) Early transition-metal complexes would probably be too oxophilic to effect catalytic transformations of carbohydrates but could make very effective stoichiometric reagents.

(19) Water-soluble analogues of 1 containing sulfonated phosphine ligands are known, but they are not readily available. For comprehensive compilations of references related to water soluble phosphine ligands, see: (a) Joo, F.; Toth, Z. *J. Molec. Catal.* **1980**, *8*, 369. (b) Amrani, Y.; Lecomte, L.; Sinou, D.; Bakos, J.; Toth, I.; Heil, B. *Organometallics* **1989**, *8*, 542.

(20) Rusina, A.; Vlcek, A. A. *Nature* **1965**, *206*, 295.

(21) NMP has a relatively low order of toxicity [*M-Pyrol Summary of Toxicity Information*; GAF Chemical Corporation: 1361 Alps Road, Wayne, NJ 07470], represents a minimal storage and fire hazard, is readily available in good purity at a price comparable to other common solvents, and is ideal for use as a solvent in the GC analysis of sugars.[13b] Its 200 °C boiling point is sometimes inconvenient but not troublesomely so and contributes to its safe handling.

(22) Slightly faster reaction rates are observed in the decarbonylation of sugars with the dimer derived from 1, $[RhCl(PPh_3)_2]_2$, but the dimer did not appear to offer any other significant advantages in this case. In the decarbonylation of simple organic aldehydes, use of the dimer in place of 1 can simplify the workup by eliminating the formation of a mole of triphenylphosphine.[6b] The methyldiphenylphosphine analogue of 1 has been reported to be a more effective decarbonylation agent than 1 in at least one case.[10a]

(23) While sugars are not particularly stable at these temperatures in NMP (M. Andrews, unpublished observation), the rhodium apparently effectively traps the reactive intermediate aldehydo form of the sugar before it can undergo undesirable degradation reactions.

(24) Andrews, M. *Organometallics*, in press.

(25) The decarbonylation of simple aliphatic aldehydes in noncoordinating solvents can be effected at room temperature.[6]

(26) Geoffroy, G. L.; Denton, D. A.; Keeney, M. E.; Bucks, R. R. *Inorg. Chem.* **1976**, *15*, 2382.

(27) Aldrich Chemical Co., ca. $25.00/g corresponding to about $6.00/100 mg of a C_6 sugar.

(28) Osborn, J. A.; Wilkinson, G. *Inorg. Synth.* **1967**, *10*, 67.

(29) 1 is air-stable in the solid state for weeks to months but is air-sensitive in solution.

(30) Cf. our studies related to ketose decarbonylations, ref 24.

(31) Cf. the findings cited in ref 9.

(32) (a) Kampmeier, J. A.; Harris, S. H.; Mergelsberg, I. *J. Org. Chem.* **1984**, *49*, 621. (b) Milstein, D. *Organometallics* **1982**, *1*, 1549. (c) Suggs, J. W. *J. Am. Chem. Soc.* **1978**, *100*, 640. (d) Walborsky, H. M.; Allen, L. E. *J. Am. Chem. Soc.* **1971**, *93*, 5465.

(33) Kuhn, R.; Grassner, H. *Ann.* **1957**, *610*, 122.

(34) The rate of hemiacetal ring opening to the aldehydo form of the sugar should be at least as fast as mutarotation since the aldehydo sugar is generally believed to be an intermediate in mutarotation, see: Goux, W. J. *J. Am. Chem. Soc.* **1985**, *107*, 4320. Snyder, J. R.; Johnston, E. R.; Serianni, A. S. *J. Am. Chem. Soc.* **1989**, *111*, 2681 for recent articles with leading references.

(35) It should be noted that this could be critically dependent on the purity of the solvent, however, since mutarotation is strongly catalyzed by both acids and bases.[34]

(36) The very slow rate of decarbonylation of 2-deoxy-2-fluoroglucose suggests that solutions of this aldose probably contain an even lower percentage of aldehydo sugar than glucose (0.001% in water at 25 °C: Maple, S. R.; Allerhand, A. *J. Am. Chem. Soc.* **1987**, *109*, 3168). This would not be unexpected since the greater electron-withdrawing power of a fluorine over a hydroxyl group should enhance hemiacetal formation.

(37) Cf. Hayward, L. D.; Angyal, S. J. *Carbohydr. Res.* **1977**, *53*, 13.

undergoes reductive elimination to give the C_{n-1} alditol, undergoes a β-hydrogen elimination 1% of the time to give the C_{n-1} aldose. This aldose would in turn undergo decarbonylation to the observed C_{n-2} alditol. The only other side products observed are C_n lactones in low yields.[38] In particular, as predicted by the proposed mechanism, there is no evidence for products due to stereochemical isomerization.

Utility of the Reaction. The present reaction constitutes an interesting variation on traditional carbohydrate "descent of series" reactions.[1] Instead of converting a C_n aldose into the C_{n-1} aldose, in what is typically a multistep, moderate yield reaction at best, it gives the C_{n-1} alditol in a very convenient and clean fashion. Most notably, no hydroxyl protecting groups are required. While the decarbonylation of simple monosaccharide aldoses is not likely to be of much synthetic utility, it might prove useful in the structural analysis of higher sugars (vide infra). The technique holds particular promise, however, as a highly predictable means of synthesizing uncommon mono- and disaccharide pentitols and tetritols for GC, NMR, and MS reference purposes from the often more readily available hexose and pentose precursors.

A. Structural Determinations. Descent of series reactions have traditionally been used to help determine the structures of higher sugars. In any one carbon degradative structural probe, information concerning the stereochemistry at the α-carbon is lost. There is an additional ambiguity in the present degradative scheme if the product alditol lacks a symmetry element, because there is then no way to determine which end of the alditol corresponds to C_n in the original aldose. These drawbacks are partially compensated for by the ease with which the analysis can be carried out on a micro scale. For example, 0.5 mg of D-*glycero*-D-*gulo*-heptose was treated with 5 mg of 1 in 100 μL of NMP in a GC derivatization vial under argon for 4 h at 130 °C. The reaction mixture was then derivatized in situ with MBTFA[39] in pyridine and injected onto a DB-1701 capillary GC column for identification of the resulting glucitol trifluoroacetate.[13,40] The decarbonylation reaction could also be used in place of borohydride to label the reducing end(s) of an oligosaccharide by converting them to alditols prior to hydrolysis and subsequent component analysis.

B. Synthesis of Deoxyalditols. 1-Deoxyalditols were thought to be rare in nature,[41] but have recently been found to be a normal component (of yet unknown origin) in human urine.[42] They are most conveniently synthesized by borohydride reduction of the corresponding ω-deoxyaldose, but only two of these, 6-deoxymannose (rhamnose) and 6-deoxygalactose (fucose), are commercially available. The existing preparations of 1-deoxyalditols, therefore, normally involve multistep syntheses of the appropriate deoxyaldose[43] or other precursors,[41] or the use of noxious reagents such as ethanethiol[44] or hydrazine.[45] All of the 1-deoxytetritols[46,47] and -pentitols[44,45,46c,d,48] are known, but modern spectral data are rather scarce. The aldose decarbonylation technique reported here now offers a very convenient one-step synthesis of most of these compounds from either 2- or ω-deoxyaldoses (Table IB). The use of a 2-deoxyaldose precursor, if available, is preferred over the ω-deoxyaldose precursor because the reaction is faster and cleaner, presumably due to the higher percentage of aldehydo sugar present in the former case.[14] The reaction should also be applicable to other deoxy sugars to give nonterminal and multideoxyalditols.

The first complete ^1H and ^{13}C NMR data for several of the 1-deoxyalditols are reported in the Experimental Section.[49] The spectra were recorded in DMSO-d_6, rather than D_2O as is common in the literature. This permits (in the absence of traces of water and acid) observation of characteristic, well-resolved signals due to the hydroxyl protons,[50] thereby providing unique "fingerprint" information for future identification. The ^1H NMR spectrum of 1-deoxyarabinitol was sufficiently well-resolved to permit a complete spectral assignment with the aid of selective decoupling experiments. The derived vicinal H–H coupling constants agree within 0.1–0.8 Hz with those found for aqueous solutions,[48d] indicating that the average conformation of this deoxyalditol is nearly the same in dimethyl sulfoxide as in water. This is somewhat surprising in view of the marked differences in hydrogen-bonding characteristics of the two solvents.

C. Synthesis of 1-(Acetylamino)-1-deoxyalditols. Amino sugars and their derivatives are among the most common functionalized sugars known. Since an amide solvent is used in the present studies, it seemed likely that complex 1 could be used to decarbonylate *N*-acetylaldosamines. This proved to be the case, 2-(acetylamino)-2-deoxyhexoses giving the corresponding 1-(acetylamino)-1-deoxypentitol (Table IC), although the yields are only moderate, probably due to thermolysis of these more labile sugars.[51] Aminoalditols and their *N*-acetyl

(38) Lactone formation could be due to metal-catalyzed dehydrogenation (via transfer hydrogenation of a solvent impurity) and/or adventitious air oxidation. Both of these find some experimental support. Purification of the NMP by distillation from barium oxide resulted in less lactone formation, whereas the intentional addition of air led to enhanced quantities of lactone (though less than would be expected for a stoichiometric oxidation).

(39) MBTFA = *N*-methylbis(trifluoromethyl)acetamide, see: Englmaier, P. *Carbohydr. Res.* **1985**, *144*, 177.

(40) The GC signal-to-noise on this 100:1 split injection was high enough that the analysis could have easily been performed on less than 0.1 mg of aldose.

(41) Brimacombe, J. S.; Webber, J. M. *The Carbohydrates: Chemistry and Biochemistry*, 2nd ed.; Pigman, W. W., Horton, D., Eds.; Academic Press: New York, 1972; Vol IA, p 511.

(42) Niwa, T.; Yamada, K., Ohki, T.; Saito, A.; Mori, M. *J. Chromatogr.* **1984**, *336*, 345 and references therein.

(43) (a) Williams, N. R.; Wander, J. D. *The Carbohydrates: Chemistry and Biochemistry*, 2nd ed.; Pigman, W. W., Horton, D., Eds.; Academic Press: New York, 1980; Vol IB, p 761. (b) Hanessian, S. *Adv. Carbohydr. Chem.* **1966**, *21*, 143. (c) Snyder, J. R.; Serianni, A. S. *Carbohydr. Res.* **1987**, *163*, 169.

(44) Jones, J. K. N.; Mitchell, D. L. *Can. J. Chem.* **1958**, *36*, 206 and references therein.

(45) Williams, J. M. *Carbohydr. Res.* **1984**, *128*, 73.

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derivatives have been known for a long time,[52] although the 1-amino-1-deoxypentitols[53] and 1-(acetylamino)-1-deoxypentitols[54] have not been well-characterized by modern methods. NMR data for two of these compounds are given in the Experimental Section.

D. Synthesis of Glycosylalditols. Glycosylalditols are a significant specialized class of disaccharides. They are common components of tissue extracts from lower plants (algae, fungi, lichen)[55] and are a fundamental constituent of the teichoic acids found in the cell walls and membranes of Gram-positive bacteria.[56] They are also the key terminal identification products of several traditional degradative disaccharide structural analysis schemes.[57] It is therefore somewhat surprising that most of these compounds have not been thoroughly characterized, particularly with respect to NMR. Glycosylhexitols are simply prepared by borohydride reduction of the corresponding disaccharide, a technique not normally readily applicable to the preparation of glycosylpentitols due to the relative inaccessibility of the disaccharide precursors. Glycosyltetritols and -glycerols, on the other hand, are usually prepared by lead tetraacetate cleavage of disaccharides followed by borohydride reduction.[57]

The aldose decarbonylation reaction reported here provides an extremely attractive approach to the synthesis of glycosylpentitols. Representative examples of the facile one-step preparation of a number of these compounds from common sugars are given in Table ID. The identity of the products was established by elemental analysis, spectroscopic data, hydrolysis to their component aldose and alditol, and in one case by independent synthesis via borohydride reduction of the only commercially available hexosylpentose. The early literature contains a number of references to 3-*O*-β-D-galactopyranosyl-D-arabinitol (**3**), but the lichen extract in question, umbilicin, was later shown to be 2-*O*-β-D-galactofuranosyl-D-arabinitol.[58] In that study, authentic **3** was prepared but only minimally characterized. It has since been mentioned as a substrate for galactosidase.[59] None of the other hexopyranosylarabinitols prepared here have been definitively characterized before.[60] 2-*O*-β-D-Galactopyranosyl-D-erythritol is a well-known product of the oxidative/reductive degradation of lactose,[61] but no NMR spectral data seem to have been reported.

Summary

Chlorotris(triphenylphosphine)rhodium(I) is the first effective aldose decarbonylation reagent. While its bulk synthetic utility is limited by cost, its use provides an extremely convenient and general procedure for the small-scale preparation of a large number of alditol derivatives. This new descent of series technique is especially suited to the preparation of pentitols, since the corresponding hexose precursors are usually readily available. As such, it complements the long-established borohydride reduction of aldoses to alditols which provides ready access to hexitols. Since the reagent exhibits excellent specificity for the aldehyde functionality, it can be directly applied to unprotected aldoses, including those with additional functional groups.

Experimental Section

Materials. Aldoses and commercially available reference alditols were used as received from Pfanstiehl, Sigma, Aldrich, Research Plus, and Calbiochem. The complexes $RhCl(PPh_3)_3$,[28] $[RhCl(PPh_3)_2]_2$,[28] $[Rh(Ph_2PCH_2CH_2CH_2PPh_2)_2]^+[BF_4]^-$,[62] and $[Rh(Ph_2PCH_2CH_2PPh_2)_2]^+[BF_4]^-$[62] were prepared according to the cited methods. GC internal standards (Aldrich: bibenzyl, 1,2-diphenoxyethane, *p*-terphenyl. Phillips: tetradecane) were used as received except bibenzyl, which was recrystallized from ethanol. *N*-Methyl-2-pyrrolidinone (NMP, Aldrich HPLC grade) was dried over activated 4-Å molecular sieves. Tetraethylene glycol dimethyl ether (tetraglyme, Aldrich Gold Label) and *N*,*N*-dimethylacetamide (DMA, Aldrich HPLC grade) were used as received. [Note: Solvents employed in the decarbonylation reactions do not need to be rigorously dried but must be free of oxygen and potential carbon monoxide donors. All NMP used in the present studies gave less than 1 μmol of carbonyl complex **2** per milliliter of solvent when a 25 mM solution of **1** was heated at 130 °C for 24 h. Toward the end of our studies it was found that distillation of the NMP from BaO led to a reduction in the amount of byproduct lactones formed.]

Reaction Analyses. Capillary GC analyses were performed employing trimethylsilylation (TMS) and trifluoroacetylation (TFA) techniques, normally in conjunction with O-methyloximation or O-benzyloximation, as described elsewhere,[13] except that TMS disaccharide analyses were carried out isothermally at 300 °C on the 0.25 mm × 30 m, 1.0 μm film DB-5 column.[13b] GC yields quoted are for alditol TMS derivatives and should be accurate to better than 5%, except when it was necessary to use estimated response factors (ERF) determined by interpolation from comparable compounds. In these latter cases GC yields should be accurate to within 10%. $Rh(CO)Cl(PPh_3)_2$ was identified by comparison with an authentic sample[63] and quantitated by measuring the absorbance of its characteristic infrared CO stretch at 1977 cm^{-1} (NMP solution) using a Nicolet MX-1 or Mattson Polaris FT-IR spectrometer at 1-cm^{-1} resolution (absorption extinction coefficient ~1650 M^{-1} cm^{-1}, integrated absorption extinction coefficient ~34 500 M^{-1} cm^{-2}, quantitation error estimated to be less than 5%).

Standard Aldose Decarbonylation Procedure. Aldose (ca. 150–200 μmol), $RhCl(PPh_3)_3$ (0.95–1.05 equiv), and bibenzyl (ca. 65 mg, GC internal standard) were weighed together in a tared 25-mL screw-cap Erlenmeyer flask in an argon-filled glovebox. [Note: Most reactions also included 1,2-diphenoxyethane (ca. 100 mg) as a secondary internal GC standard. Disaccharide reactions used *p*-terphenyl (ca. 90 mg) in place of bibenzyl. In some cases alternative standards were used as noted.] NMP (4–5 mL, amount

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generally determined by weight, $d = 1.033$) was then added, and the flask was sealed with an open-top screw cap fitted with a Teflon-faced silicone rubber septum. The reaction flask was removed from the glovebox and heated at 130 °C, generally by immersion above the solvent level in a Haake F3 constant-temperature bath. The progress of the reaction was monitored by both color change and GC analysis. [Note: Experiments show that the reaction is not overly sensitive to small amounts of air (vide infra), hence any standard inert atmosphere technique[64] should suffice.]

Standard Alditol Isolation Procedures. [Note: Workup can be performed in air.] NMP was removed from the crude reaction mixture by bulb-to-bulb distillation at reduced pressure (ca. 1 mmHg) with the aid of a warm (ca. 50 °C) water bath until a nearly dry residue was obtained. Isolation of the sugar can then be achieved by either an aqueous or nonaqueous procedure. Unless otherwise noted, the reactions conducted here used the nonaqueous method since this facilitates the high-yield isolation of water-free solids suitable for NMR characterization of the hydroxyl protons in DMSO-d_6. The water workup might be preferable for larger scale syntheses.

A. Nonaqueous Workup. Rhodium complexes, PPh_3, and any $OPPh_3$ were removed by repeatedly stirring the residue with 3-mL aliquots of chloroform until the extracts were colorless. [Note: Because of solubility constraints, we have not been able to find a suitable substitute for chloroform for this purpose.[65] Up to one volume of toluene can be added to the chloroform to facilitate settling of the insoluble sugar products, followed by centrifuging if necessary. It is convenient to conduct the workup in a heavy-walled conical centrifuge tube equipped with a standard taper joint.] The remaining solids were dried under vacuum to give the product alditol, whose purity was usually greater than 95% (NMR), the primary impurities being traces of PPh_3 and the starting sugar and its lactone(s). If desired, further purification can be effected by recrystallization, typically from methanol/ether.

B. Aqueous Workup. Chloroform (15 mL) was added to the residue and stirred to dissolve most of the phosphine and rhodium complexes. Water (5 mL) was then added to the mixture to complete the dissolution of the solids. The layers were separated, and the chloroform layer was extracted with another aliquot of water. The combined water extracts were filtered, if necessary, and evaporated. The resulting syrupy sugar could then be purified by standard techniques such as recrystallization from alcohol, etc.

Decarbonylation of D-Glucose to D-Arabinitol. The standard procedure was used with D-glucose (37.0 mg, 205 μmol), **1** (190 mg, 206 μmol), and NMP (4.4 g). After 6 h only 8% of the glucose was left. GC (15 h): D-arabinitol (163 μmol, 80%), D-glucose (8 μmol, 4%), 1,5-D-gluconolactone (8 μmol, 4%), 1,4-D-gluconolactone (8 μmol, 4%), erythritol (2 μmol, 1%). The primary sugar product was confirmed to be D-arabinitol by evaporation of NMP from a similar reaction, dissolution in DMSO-d_6 and comparison of the ^1H NMR spectrum with that of authentic sample (see the supplementary material).

Similar reactions gave up to 88% GC yield of arabinitol and IR yields of **2** of 96%. A solution of β-D-glucopyranose in NMP allowed to stand at 24 °C mutarotated to an equilibrium composition (α-D-glucopyranose:β-D-glucopyranose = 44:56) within about 24 h. A solution of α-D-glucopyranose mutarotated to the same composition. With **1** present, the α-glucose (α:β = 96:4) reached a near equilibrium composition of 51:49 α:β (vs 54:46 final) in less than 50 min at 110 °C, at which point less than 25% decarbonylation had occurred.

Decarbonylation of D-Arabinose to Erythritol. The standard procedure was used with D-arabinose (27.0 mg, 180 μmol), **1** (167 mg, 180 μmol), and NMP (3.9 g). GC (3 h): erythritol (155 μmol, 86%), arabinonolactone (ca. 10 μmol, 6%). Workup of a similar reaction gave erythritol (87%), identical by ^1H NMR with an authentic sample (see the supplementary material).

In similar experiments, GC yields of erythritol were 77%, 81%, and 84%, and IR yields of **2** were 94%. Similar results were obtained with use of $[RhCl(PPh_3)_2]_2$ in place of **1** except that the rate of reaction was about 2–5 times faster. A solution of β-D-arabinopyranose in NMP allowed to stand at room temperature mutarotated to an equilibrium composition within about 4 h as judged by quenching the reaction by trimethylsilylation and analyzing by GC. With **1** present, the arabinose reached an equilibrium composition in less than 10 min at 110 °C, at which point less than 15% decarbonylation had occurred.

Decarbonylation of 2-Deoxy-D-*arabino*-hexose (2-Deoxy-D-glucose) to 1-Deoxy-D-arabinitol. The standard procedure was used with 2-deoxy-D-glucose (33.5 mg, 204 μmol), **1** (185 mg, 200 μmol), and NMP (4.0 g). The reaction mixture turned yellow within 2 h. GC: 1-deoxy-D-arabinitol (182 μmol, 91% (ERF)). IR: **1** (184 μmol, 92%). Workup gave a white solid (23 mg, 83%), identified as 1-deoxy-D-arabinitol by ^1H[48d] and ^{13}C NMR (data given below).

Decarbonylation of 2-(Acetylamino)-2-deoxy-D-glucose (*N*-Acetyl-D-glucosamine) to 1-(Acetylamino)-1-deoxy-D-arabinitol. The standard procedure was used with *N*-acetyl-D-glucosamine (40.1 mg, 181 μmol), **1** (167 mg, 181 μmol), NMP (5 mL). The reaction was run for 10 h at 125 °C followed by 12 h at 110 °C. GC: 1-(acetylamino)-1-deoxy-D-arabinitol (102 μmol, 56% (ERF)), *N*-acetyl-D-glucosamine (15 μmol, 8%), furfuryl alcohol (9 μmol, 5%). IR (similar reaction): **2** (87%). Workup gave 20 mg of crude solid (mp 135 °C), which was recrystallized from methanol/ether to give the product as white crystals, mp 144 °C (lit.[54b] mp 146.5–147.5 °C). NMR spectral data (given below) were consistent with those expected for 1-(acetylamino)-1-deoxy-D-arabinitol.

Decarbonylation of 6-*O*-α-D-Galactopyranosyl-D-glucopyranose (D-Melibiose) to 5-*O*-α-D-Galactopyranosyl-D-arabinitol. The standard procedure was used with D-melibiose monohydrate (60.5 mg, 168 μmol), **1** (157 mg, 169 μmol), NMP (4.0 g). GC (24 h): 5-*O*-α-D-galactosyl-D-arabinitol (153 μmol, 91%), unknown (ca. 12 μmol, 7%). IR: **2** (155 μmol, 92%). Workup and recrystallization from methanol/ether gave 5-*O*-α-D-galactopyranosyl-D-arabinitol as a white solid (38 mg, 72%) (characterization data given below). Hydrolysis (vide infra) gave a 1:1 mixture of arabinitol and galactose.

Standard Procedure for Disaccharide Hydrolysis. Disaccharide (ca. 5 mg) was dissolved in aqueous HCl (200 μL, 1 M) under argon in a GC derivatization vial and heated for about 2 h at 100 °C. The solution was then neutralized with 1 M sodium bicarbonate, and the water was removed at 60 °C under an argon purge or with a rotary evaporator at 45 °C. The resulting monosaccharides were extracted from the inorganic salts with NMP (300 μL) and a 25-μL aliquot derivatized with *O*-methylhydroxylamine and *N*-(trimethylsilyl)imidazole for analysis by GC.

NOTE: Detailed descriptions of all of the other decarbonylation reactions included in Table I are available as supplementary material.

Decarbonylation of D-Glucose in the Presence of Air. The standard procedure was used (D-glucose, 35.1 mg, 195 μmol; **1**, 183 mg, 198 μmol; NMP, 4.1 mL) except that air (10 mL, ca 90 μmol O_2) was slowly bubbled through the solution with a gas syringe prior to heating. GC (time, glucose, arabinitol, 1,4- plus 1,5-gluconolactones): 10 min, 68%, 16%, 9%; 45 min, 20%, 54%, 13%; 2.3 h, 6%, 69%, 13%; 10 h, 0.5%, 78%, 14%. A similar reaction was stirred open to the air at room temperature for 1.5 h. GC: glucose (86%), gluconolactones (5%). The flask was then closed and heated at 130 °C for 7 h. GC: glucose (4%), gluconolactones (16%), 5-(hydroxymethyl)furfural (3%), unknowns (ca. 25%, possibly anhydroglucoses[66]), arabinitol (ca. 0%).

Attempted Decarbonylation of D-Glucose by $RuCl_2(PPh_3)_3$. The standard procedure was used (D-glucose (37 mg, 205 μmol), NMP (4.4 g)), except that $RuCl_2(PPh_3)_3$ (212 mg, 221 μmol) was used in place of **1**. GC (1 h): glucose (11 μmol, 5%), glucitol (2 μmol, 1%), 1,5-gluconolactone (14 μmol, 7%), 1,4-gluconolactone (9 μmol, 4%), fructose (18 μmol, 9%), erythritol (2 μmol, 1%), threitol (2 μmol, 1%), 2,5-furandimethanol (19 μmol, 9%), glycerol (13 μmol, 3%), 1,3-dihydroxyacetone (3 μmol, 1%), ethylene glycol (4 μmol, 1%).

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(65) Complex **2** dissolves readily in dichloromethane but precipitates back out within a few minutes, apparently as a dichloromethane solvate.

(66) The same two products are observed when glucose is treated with a catalytic amount of concentrated aqueous HCl in NMP. One of these has the same GC retention time as 1,6-anhydroglucose.

Attempted Catalytic Decarbonylations. A. Glyceraldehyde. Glyceraldehyde (101 mg, 1.13 mmol), $[Rh(Ph_2PCH_2CH_2CH_2PPh_2)_2]^+[BF_4]^-$ (53.2 mg, 52 μmol, 0.05 equiv), bibenzyl (65 mg), and tetraglyme (3 mL) were placed in a 5-mL Kontes Airless-ware micro reaction flask equipped with a septum port, magnetic stirbar, and a water-cooled 14/20 West condenser connected via a U-shaped vacuum distillation adapter to a 25-mL round-bottom flask immersed in ice water. A steady stream of argon was bubbled through the reaction solution by inserting an 20-gauge needle through the septum port, the exit gases flowing out the vacuum distillation take-off adapter to a mercury bubbler. The reaction was heated at 150 °C for 2 h, during which time the solution turned dark. GC analysis of the reaction mixture at that time showed glyceraldehyde (40 μmol, 3%), 1,3-dihydroxyacetone (340 μmol, 30%), ethylene glycol (15 μmol, 1%), glycerol (15 μmol, 1%), and a large number of other small unidentified products. GC analysis of the trap showed that it contained only a small amount of ethylene glycol.

B. Glucose. D-Glucose (178 mg, 1.00 mmol), $[Rh(Ph_2PCH_2CH_2PPh_2)_2]^+[BF_4]^-$ (71.2 mg, 72 μmol, 0.07 equiv), and NMP (4 mL) were placed in the same reaction set-up as described above and heated at 140 °C under an argon purge for 21 h, during which time the reaction turned dark. GC analysis of the reaction showed that essentially all of the glucose had been consumed. Products included 1,4-D-gluconolactone (250 μmol, 25%), 1,5-D-gluconolactone (25 μmol, 3%), D-arabinitol (1 μmol, 0.1%), 5-(hydroxymethyl)furfural (200 μmol, 20%), furfuryl alcohol (20 μmol, 2%), glucitol (5 μmol, 0.5%), and two unknowns (ca. 100 μmol, 10% possibly anhydroglucoses[66]).

C. 2-Deoxy-D-ribose. 2-Deoxy-D-ribose (82.6 mg, 503 μmol), $[Rh(Ph_2PCH_2CH_2CH_2PPh_2)_2]^+BF_4^-$ (38.1 mg, 38 μmol, 0.074 equiv), and tetraglyme (3 mL) were placed in the same reaction set-up as described above and heated at 150 °C under an argon purge for 2 h, during which time the reaction mixture darkened slightly. GC: 1-deoxyerythritol (99 μmol (ERF), 20%, 3 turnovers), 2-deoxyribonolactone (ca. 225 μmol, 45%, 6 turnovers), 2-deoxyribitol (130 μmol, 25% (ERF), 3.5 turnovers). Product identities were established by GC–MS analysis of their TFA and TMS derivatives and by comparisons with samples prepared by other routes.

Compound Characterization Techniques and Data. NMR spectra were obtained on a Bruker AM-300 in DMSO-d_6 (dried over activated 4-Å molecular sieves) using residual solvent resonances (^{1}H DMSO at δ 2.49, ^{13}C DMSO δ 39.5) as internal reference. ^{13}C spectra were recorded with both CPD broad band and gated proton decoupling at 0.5-Hz digital resolution. Mass spectra were obtained on trimethylsilyl ether (TMS) and/or trifluoroacetate (TFA) derivatives on a Finnigan MAT 5100 GC–MS in EI mode at 70 eV (upper mass limit ~800 amu). Elemental analyses were performed by Galbraith Laboratories.

1-Deoxy-D-erythritol.[46,47] ^{1}H NMR (DMSO-d_6): δ 4.40 (d, J = 5.1 Hz, 1 H, CHO*H*), 4.37 (d, J = 5.4 Hz, 1 H, CHO*H*), 4.33 (t, J = 5.7 Hz, 1 H, CH_2O*H*), 3.50–3.40 (m, 2 H, CH_2OH), 3.33–3.25 (m, 1 H, CHOH), 3.22–3.14 (m, 1 H, CHOH), 1.03 (d, J = 6.3 Hz, 3 H, CH_3). ^{13}C NMR (DMSO-d_6): δ 75.70 (d, J = 137 Hz), 67.38 (d, J = 141.5 Hz), 63.38 (t, J = 139 Hz), 19.29 (q, J = 125 Hz). Mass spectrum of tris(trifluoroacetate): m/z (relative intensity) 379 $[M - CH_3]^+$ (0.5), 281 $[M - CF_3CO_2]^+$ (14), 267 $[M - CH_2O_2CCF_3]^+$ (1.5), 265 $[M - CH_3 - CF_3CO_2H]^+$ (2), 253 $[M - CH_3 - CHO_2CCF_3]^+$ (5), 183 $[M - CF_3CO - CF_3CO_2H]^+$ (2), 167 $[M - CF_3CO_2 - CF_3CO_2H]^+$ (50), 141 $[M - CH_2O_2CCF_3 - CHO_2CCF_3]^+$ (100), 140 (57), 113 $[CF_3CO_2]^+$ (35), 97 $[CF_3CO]^+$ (44), 69 $[CF_3]^+$ (saturated).

1-Deoxy-D-arabinitol.[44,45,46c,d,48] ^{1}H NMR (DMSO-d_6): δ 4.47 (d, $J_{4,OH}$ = 5.2 Hz, 1 H, C(4)HO*H*), 4.32 (t, $J_{5,OH}$ = 5.6 Hz, 1 H, C(5)H_2O*H*), 4.25 (d, $J_{3,OH}$ = 7.0 Hz, 1 H, C(3)HO*H*), 4.15 (d, $J_{2,OH}$ = 6.1 Hz, 1 H, C(2)HO*H*), 3.81 (quint of d, $J_{1,2} \sim J_{2,OH}$ = 6.3 Hz, $J_{2,3}$ = 2.4 Hz, 1 H, C(2)*H*OH), 3.55 (ddd, $J_{5B,5A}$ = 10.6 Hz, $J_{5B,OH}$ = 5.6 Hz, $J_{5B,4}$ = 2.9 Hz, 1 H, C(5)H_AH_BOH), 3.42 (m, 1 H, C(4)*H*OH), 3.35 (ddd, $J_{5A,5B}$ = 10.7 Hz, $J_{5A,4}$ = 6.0 Hz, $J_{5A,OH}$ = 5.6 Hz, 1 H, C(5)H_AH_BOH), 3.05 (t of d, $J_{3,4} \sim J_{3,OH}$ = 7.1 Hz, $J_{2,3}$ = 2.4 Hz, 1 H, C(3)*H*OH), 1.05 (d, $J_{1,2}$ = 6.5 Hz, 3 H, CH_3) [lit.[48d] (D_2O): $J_{1,2}$ = 6.6 Hz, $J_{2,3}$ = 3.0 Hz, $J_{3,4}$ = 7.5 Hz, $J_{4,5A}$ = 6.5 Hz, $J_{4,5B}$ = 3.0 Hz, $J_{5A,5B}$ = −11.5 Hz]. ^{13}C NMR (DMSO-d_6): δ 74.34 (d, J = 138.5 Hz), 71.85 (d, J = 140.5 Hz), 65.68 (d, J = 141.5 Hz), 63.63 (t, J = 140 Hz), 19.87 (q, J = 125 Hz). Mass spectrum of tetrakis(trifluoroacetate): m/z (relative intensity) 505 $[M - CH_3]^+$ (0.04), 407 $[M - CF_3CO_2]^+$ (2), 393 $[M - CH_2O_2CCF_3]^+$ (0.3), 379 $[M - CH_3 - CHO_2CCF_3]^+$ (0.4), 293 $[M - CF_3CO_2 - CF_3CO_2H]^+$ (4), 267 $[M - CH_2O_2CCF_3 - CHO_2CCF_3]^+$ (2), 266 (5), 265 $[M - CH_3 - CHO_2CCF_3 - CF_3CO_2H]^+$ (1), 253 $[M - CH_3 - CHO_2CCF_3 - CHOCCF_3]^+$ (3), 248 (3), 179 $[M - CF_3CO_2 - 2CF_3CO_2H]^+$ (19), 141 $[M - CH_2O_2CF_3 - 2CHO_2CF_3]^+$ (100), 113 $[CF_3CO_2]^+$ (29), 97 $[CF_3CO]^+$ (25), 83 (31), 69 $[CF_3]^+$ (saturated).

5-Deoxy-D-arabinitol.[44,45,46c,d,48] ^{1}H NMR (DMSO-d_6) [peaks slightly broadened due to incipient OH exchange]: δ 4.43 (t, J ~ 6.5 Hz, 1 H, CH_2O*H*), 4.42 (d, J ~ 5.5 Hz, 1 H, CHO*H*), 4.14 (d, J = 6.0 Hz, CHO*H*), 4.10 (d, J = 7.4 Hz, 1 H, CHO*H*), 3.65 (~q, J ~ 5 Hz, 1 H), 3.55 (~sextet, J ~ 6.5 Hz, 1 H), 3.35 (m, 2 H), 3.07 (t of d, J = 7.5, 1.8 Hz, 1 H), 1.07 (d, J = 6.2 Hz, 3 H, CH_3). ^{13}C NMR (DMSO-d_6): δ 74.44 (d, J = 139 Hz), 70.24 (d, J = 139.5 Hz), 66.52 (d, J = 140 Hz), 63.1 (t, J = 138.5 Hz), 20.49 (q, J = 125 Hz). Mass spectrum of the tetrakis(trifluoroacetate) was essentially identical with that of 1-deoxyarabinitol trifluoroacetate.

1-Deoxy-D-ribitol.[44,45,46c,d,48] ^{1}H NMR (DMSO-d_6) [peaks slightly broadened due to incipient OH exchange]: δ 4.56 (d, J ~ 4.5 Hz, 1 H, CHO*H*), 4.41 (d, J ~ 5.1 Hz, 2 H, CHO*H*), 4.33 (t, J ~ 5.3 Hz, 1 H, CH_2O*H*), 3.69 (~sextet, J ~ 5.8 Hz, 1 H), 3.56 (~quintet, J ~ 5.8 Hz, 1 H), 3.34 (m, 2 H), 3.21 (~q, J ~ 5.5 Hz, 1 H), 1.01 (d, J = 6.3 Hz, 3 H, CH_3). ^{13}C NMR (DMSO-d_6): δ 75.01 (d, J ~ 140 Hz), 72.99 (d, J ~ 143 Hz), 67.44 (d, J = 140.5 Hz), 63.43 (t, J = 140 Hz), 18.16 (q, J = 125 Hz). Mass spectrum of the tetrakis(trifluoroacetate) was essentially identical with that of 1-deoxyarabinitol trifluoroacetate.

1-(Acetylamino)-1-deoxy-D-arabinitol.[54] ^{1}H NMR (DMSO-d_6): δ 7.83 (br t, J ~ 5.5 Hz, 1 H, NHOAc), 4.46 (d, J = 5.5 Hz, 1 H, CHO*H*), 4.35 (d, J = 6.6 Hz, 1 H, CHO*H*), 4.33 (t, J = 5.6 Hz, 1 H, CHO*H*), 4.28 (d, J = 7.3 Hz, 1 H, CHO*H*), 3.69 (~q, J ~ 6.3 Hz, 1 H), 3.58 (ddd, J = 10.4, 5.5, 3.1 Hz, 1 H), 3.43 (m, 1 H), 3.37 (m, 1 H), 3.18–2.9 (m, 3 H), 1.79 (s, 3 H, NHCOCH_3). ^{13}C NMR (DMSO-d_6): δ 169.54 (s, NHCOCH$_3$), 71.18 (d, J = 139.5 Hz, 2 C (coincidental overlap), CHOH), 68.31 (d, J = 142 Hz, CHOH), 63.64 (t, J = 140.5 Hz, CH_2OH), 42.20 (t, J = 137.5 Hz, CH_2NHCOCH$_3$), 22.53 (q, J = 127 Hz, NHCOCH$_3$). Mass spectrum of tetrakis(trimethylsilyl ether): m/z (relative intensity) 466 $[M - CH_3]^+$ (0.2), 376 $[M - CH_3 - Me_3SiOH]^+$ (0.3), 319 (2.7), 288 $[M - CH_2OSiMe_3 - Me_3SiOH]^+$ (8.4), 276 $[M - CH_2OSiMe_3 - CHOSiMe_3]^+$ (10.8), 259 (4.5), 247 (7.4), 217 $[Me_3SiOCH{=}CHCH{=}OSiMe_3]^+$ (25.3), 205 $[CHOSiMe_3CH_2OSiMe_3]^+$ (11.1), 186 $[M - CH_2OSiMe_3 - CHOSiMe_3 - Me_3SiOH]^+$ (25.5), 174 $[M - CH_2OSiMe_3 - 2(CHOSiMe_3)]^+$ (81.3), 147 $[Me_3SiO{=}SiMe_2]^+$ (33.5), 73 $[Me_3Si]^+$ (100).

5-(Acetylamino)-5-deoxy-D-arabinitol.[54] ^{1}H NMR (DMSO-d_6) [peaks broadened due to partial OH exchange]: δ 7.81 (~t, NHOAc), 4.77 (br s, CH_xO*H*), 4.45 (br s, CH_xO*H*), 4.36 (d, J ~ 5.5 Hz, –CHO*H*), 4.15 (br d, J ~ 5.3 Hz, CHO*H*), 3.7–3.0 (multiplets), 1.82 (s, NHCOCH_3). ^{13}C NMR (DMSO-d_6): δ 170.12 (s, NHCOCH$_3$), 71.08 (d, J = 139.5 Hz, CHOH), 69.94 (d, J = 140 Hz, CHOH), 69.75 (d, J = 140 Hz, CHOH), 62.90 (t, J = 139 Hz, CH_2OH), 42.91 (t, J = 137.5 Hz, CH_2NHCOCH$_3$), 22.52 (q, J = 127 Hz, NHCOCH$_3$). Mass spectrum of tetrakis(trimethylsilyl ether) was essentially identical with that of the above 1-deoxy isomer.

3-O-α-D-Glucopyranosyl-D-arabinitol. ^{1}H NMR (DMSO-d_6) [peaks slightly broadened due to incipient OH exchange]: δ 5.02 (d, J ~ 7.5 Hz, 1 H), 4.89 (d, J ~ 4.8 Hz, 1 H), 4.85 (d, J ~ 3.8 Hz, 1 H), 4.78 (d, J ~ 3.1 Hz, 1 H), 4.65–4.4 (m, 5 H), 3.7–3.3 (m, ~10 H), 3.2–3.0 (m, 3 H). ^{13}C NMR (DMSO-d_6): δ 100.41 (d, J = 168 Hz, anomeric C(1')), 80.58 (d, J = 143 Hz, glycosidic C(3)), 73.36 (d, J ~ 146.5 Hz), 73.09 (d, J = 145.5 Hz), 72.34 (d, J ~ 142.5 Hz), 72.26 (d, J ~ 142.5 Hz), 71.42 (d, J ~ 142.5 Hz), 69.99 (d, J = 140.5 Hz), 62.85 (t, J = 140.5 Hz), 62.13 (t, J = 140 Hz), 60.70 (t, J = 141 Hz). Mass spectrum of octakis(trifluoroacetate): m/z (relative intensity) 547 $[M - OR]^+$ (1.8) where OR = $OCH(CHOAc^dCH_2OAc^f)_2$, 519 (5.5), 413 (1.2), 405 (2.4), 404 (3.0), 319 $[M - OR - 2CF_3CO_2H]^+$ (69.9), 265 (20.4), 252 (8.8), 22.1 (11.8), 193 (14.2), 177 (73.1), 69 (100). Anal. Calcd for $C_{11}H_{22}O_{10}$: C, 42.04; H, 7.06. Found: C, 42.00; H, 7.06.

3-O-β-D-Glucopyranosyl-D-arabinitol. ^{1}H NMR (DMSO-d_6) [peaks slightly broadened due to incipient OH exchange]: δ 5.19

(d, J = 4.3 Hz, 1 H), 4.95 (m, 2 H), 4.75 (br t, 1 H), 4.56 (d, J = 5.2 Hz, 1 H), 4.42 (m, 2 H), 4.21 (d, J = 7.7 Hz, 1 H), 4.17 (d, J = 5.8 Hz, 1 H), 3.75–3.5 (m, ~6 H), 3.35–3.2 (m, ~3 H), 3.2–3.05 (m, 2 H), 3.05–2.9 (m, 2 H). ^{13}C NMR (DMSO-d_6): δ 103.21 (d, J = 159 Hz, anomeric C(1')), 78.50 (d, J = 139 Hz, glycosidic C(3)), 76.80 (d, J = 141.5), 76.49 (d, J = 142 Hz), 73.63 (d, J = 145 Hz), 70.85 (d, J = 143 Hz), 70.66 (d, J = 144 Hz), 69.82 (d, J = 142.5 Hz), 62.44 (t, J = 139 Hz), 61.86 (t, J = 140.5 Hz), 61.50 (t, J = 141.5 Hz). Anal. Calcd for $C_{11}H_{22}O_{10}\cdot H_2O$: C, 39.76; H, 7.29. Found: C, 39.50; H, 7.03.

3-*O*-β-D-Galactopyranosyl-D-arabinitol. ^{1}H NMR (DMSO-d_6) [peaks broadened due to partial OH exchange]: δ 5.06 (br s, 1 H), ~4.65 (br m, 3 H), ~4.35 (br m, 3 H), 4.16 (d, J = 6.8 Hz, 1 H, anomeric CH), ~4.15 (br s, 1 H), 3.75–3.4 (m, ~9 H), 3.4–3.2 (m, ~4 H). ^{13}C NMR (DMSO-d_6): δ 104.04 (d, J = 159 Hz, anomeric C(1')), 79.30 (d, J = 140.5 Hz, glycosidic C(3)), 75.22 (d, J = 134 Hz), 73.45 (d, J = 136 Hz), 70.89 (d, J ~ 144.5 Hz, 2 C (coincidental overlap)), 70.17 (d, J = 140 Hz), 68.25 (d, J = 142 Hz), 62.50 (t, J = 139 Hz), 61.80 (t, J = 142.5 Hz), 60.75 (t, J ~ 140 Hz). Anal. Calcd for $C_{11}H_{22}O_{10}\cdot 0.5H_2O$: C, 40.86; H, 7.18. Found: C, 40.66; H, 6.92.

5-*O*-α-D-Galactopyranosyl-D-arabinitol. ^{1}H NMR (DMSO-d_6) [peaks slightly broadened due to incipient OH exchange]: δ 4.63 (d, J ~ 2.2 Hz, 1 H), 4.56–4.44 (m, 4 H), 4.38–4.33 (m, 2 H), 4.20 (d, J = 6.3 Hz, 1 H), 4.13–4.06 (m, ~1 H), 3.75–3.3 (m, ~12 H), 3.15 (d, J = 4.8 Hz, 1 H). ^{13}C NMR (DMSO-d_6): δ 99.06 (d, J = 167.1 Hz, anomeric C), 70.95 (d, J ~ 140 Hz), 70.28 (d, J = 136.5 Hz), 69.8 (d, J ~ 141 Hz, 2 C (coincidental overlap)), 69.8 (t, J ~ 142 Hz, glycosidic C(5)), 69.13 (d, J ~ 138 Hz), 68.9 (d, J ~ 143 Hz), 68.8 (d, J ~ 143 Hz), 62.88 (t, J = 139 Hz), 60.48 (t, J = 139.5 Hz). Anal. Calcd for $C_{11}H_{22}O_{10}\cdot 0.5H_2O$: C, 40.86; H, 7.18. Found: C, 40.84; H, 7.26.

5-*O*-β-D-Glucopyranosyl-D-arabinitol. ^{1}H NMR (DMSO-d_6) [peaks slightly broadened due to incipient OH exchange]: δ 5.1–4.9 (m, 3 H), 4.6–4.4 (m, 3 H), 4.3–4.1 (m, 3 H), 4.03 (d, J = 9.7 Hz, 1 H), 3.75–3.55 (m, 3 H), 3.5–3.25 (m, 5 H), 3.2–2.9 (m, 5 H). ^{13}C NMR (DMSO-d_6): δ 103.74 (d, J = 161 Hz, anomeric C), 76.84 (d, J = 140 Hz), 76.33 (d, J = 139.5 Hz), 73.70 (d, J ~ 144 Hz), 72.68 (t, J ~ 144 Hz, glycosidic C(5)), 70.43 (d, J = 138 Hz), 70.01 (d, J ~ 140 Hz, 69.91 (d, J = 138 Hz), 62.89 (t, J ~ 142 Hz), 60.96 (t, J ~ 142 Hz). Anal. Calcd for $C_{11}H_{22}O_{10}\cdot 0.5H_2O$: C, 40.86; H, 7.18. Found: C, 40.89; H, 7.31.

2-*O*-β-D-Galactopyranosylerythritol.[61] ^{1}H NMR (DMSO-d_6) [peaks broadened due to partial OH exchange]: δ 5.00 (br d, 1 H), 4.73 (br d, 1 H), 4.60 (br s, 1 H), 4.58 (d, J = 6 Hz, 1 H), 4.41 (d, J = 4 Hz, 2 H), 4.20–4.14 (br m, 2 H), 3.7–3.2 (m, ~12 H). ^{13}C NMR (DMSO-d_6): δ 104.10 (d, J = 156 Hz, anomeric C(1')), 83.06 (d, J = 141 Hz, glycosidic C(2)), 75.27 (d, J = 138 Hz), 73.26 (d, J = 137 Hz), 71.19 (d, J = 140 Hz, 70.84 (d, J ~ 147 Hz), 68.13 (d, J = 142 Hz), 62.84 (t, J = 140 Hz), 61.91 (t, J = 142 Hz), 60.40 (t, J = 143 Hz).

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Registry No. 1, 14694-95-2; 3, 53716-93-1; $RuCl_2(PPh_3)_3$, 15529-49-4; $[Rh(Ph_2PCH_2CH_2CH_2PPh_2)_2]^+(BF_4)^-$, 70196-21-3; D-glucose, 50-99-7; D-arabinitol, 488-82-4; D-arabinose, 10323-20-3; erythritol, 149-32-6; 2-deoxy-D-*arabino*-hexose, 154-17-6; 1-deoxy-D-arabinitol, 13942-77-3; *N*-acetyl-D-glucosamine, 7512-17-6; 1-(acetylamino)-1-deoxy-D-arabinitol, 92283-19-7; D-melibiose, 585-99-9; 5-*o*-α-D-galactopyranosyl-D-arabinitol, 122741-76-8; glyceraldehyde, 367-47-5; 2-deoxy-D-ribose, 533-67-5; D-glucoheptose, 3146-50-7; D-glucitol, 50-70-4; ribitol, 488-81-3; D-allose, 2595-97-3; D-xylose, 58-86-6; D-threitol, 2418-52-2; D-erythrose, 583-50-6; glycerol, 56-81-5; DL-glyceraldehyde, 56-82-6; ethylene glycol, 107-21-1; glycolaldehyde, 141-46-8; methanol, 67-56-1; D-fucose, 3615-37-0; 2-deoxy-D-allose, 6605-21-6; 1-deoxy-D-ribitol, 13046-76-9; 2-deoxy-D-galactose, 1949-89-9; 5-deoxy-D-arabinitol, 67968-44-9; L-rhamnose, 3615-41-6; 5-deoxy-L-arabinitol, 97466-38-1; 6-deoxy-D-glucose, 7658-08-4; 1-deoxy-D-erythritol, 4144-94-9; *N*-acetyl-D-mannosamine, 3615-17-6; *N*-acetyl-D-galactosamine, 1811-31-0; 5-(acetylamino)-5-deoxy-D-arabinitol, 122741-77-9; 2-(acetylamino)-2-deoxy-D-galactonolactone, 24960-16-5; 2-deoxy-2-fluoro-D-glucose, 29702-43-0; 1-deoxy-1-fluoro-D-arabinitol, 122741-78-0; D-maltose, 69-79-4; 3-*O*-α-D-glucopyranosyl-D-arabinitol, 122795-46-4; cellobiose, 528-50-7; 3-*O*-β-D-glucopyranosyl-D-arabinitol, 122795-47-5; D-lactose, 63-42-3; gentiobiose, 554-91-6; 5-*O*-β-D-glucopyranosyl-D-arabinitol, 122741-79-1; 3-*O*-β-D-galactopyranosyl-D-arabinose, 6057-48-3; 2-*O*-β-D-galactopyranosylerythritol, 14955-25-0.

Supplementary Material Available: Additional experimental details and spectroscopic data (10 pages). Ordering information is given on any current masthead page.

Stereochemistry of the Diels–Alder Reaction of Butadiene with Cyclopropene

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1(*E*)-Deuteriobutadiene and cyclopropene react at 0 °C to give 2-*endo*-deuteriobicyclo[4.1.0]hept-3-ene; 1-(*Z*)-deuteriobutadiene leads to the 2-*exo*-deuterio bicyclic product. Analysis of these products through ^{2}H NMR spectroscopy reveals complete stereospecificity, indicating that the transition structure having an endo orientation of diene and cyclopropene is strongly favored over the alternative exo geometry.

Introduction

The [2 + 4] cycloaddition of butadiene with ethylene is the prototypical Diels–Alder reaction, the one most readily studied through calculational methods.[1-3] The reaction of butadiene with cyclopropene[4] is the simplest Diels–Alder combination of hydrocarbons for which an

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