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DIASTEREOSELECTIVE ALDOLIZATION TO TETROSES AND PYRANOSES MEDIATED BY RHODIUM

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SUMMARY: Rhodium ions bind to oxygen and unsaturated sites in ethane-1,2-diol derivatives to orient and catalyze these molecules for participation in diastereogenic carbon-carbon, carbon-oxygen, and carbon-hydrogen bond formation.

Aldol condensation is a powerful synthetic methodology for stereoselective carbon-carbon coupling and build-up of organic structures. With rhodium as the promoter, enolsilanes and aldehydes couple to form aldols.^{1,2} These aldols have a 5-12% enantiomeric excess when the rhodium bears a chiral ligand. For those aldol products with greater than one optically active center, however, stereoselection remains undetermined² or very limited.¹ We now report a rhodium-mediated aldol condensation in which the two-carbon chain from an ethylene glycol derivative and diether [1,2-diethoxyethane (1)] is diastereoselectively EtOCH₂CH₂OEt

(1)CH > 0E t 0:CHCH20Et Ft0 нο three O:CHCH(OEt)CH(OH)CH2OEt

joined [following its conversion in situ to ethoxyacetaldehyde (3)] to give aldol and dialdol products³ that are the tetrose and pyranose derivatives 4 and 5.⁴ In series with the well-known⁵ production of ethylene glycol and its derivatives from carbon monoxide and hydrogen (i.e., synthesis gas) in rhodium-mediated reactions (albeit quite different ones), this constitutes a two-step chemical route that is mediated by rhodium compounds in both steps and that leads from carbon monoxide and hydrogen to sugar derivatives.

Conversion of diethoxyethane 1 to two key reaction intermediates, ethoxyacetaldehyde (3) and ethenyl ethyl ether (9) is catalyzed by rhodium. Although equimolar quantities of the two starting materials are used, 45% of 1 is reacted but only 10% of rhodium compound 2 is consumed after two days in deuterochloroform (based on quantitation of 1 H and 31 P NMR spectra). Rhodium initially attacks diether 1 at a C-H bond of a $-CH_2OCH_2$ - moiety to give rhodium species such as 6 and 7, which collapse to release alkenes (8 and 9), aldehydes (3 and 10), and hydrogen (eq 2). Mixtures of rhodium(I) compounds and dihydrogen⁷ or hydrogen donors⁸ hydrogenate alkenes and aldehydes, and these systems are in equilibrium between the pairs of hydrogen acceptors and donors. Incomplete reaction makes formation of the unsaturated products 3, 8, and 9 possible. Aldehyde 10 has not been isolated from this system; it forms an aldol.⁹ Alkene 9 is isolated as such and, also gives 2-chloroethyl ethyl ether (cf. Table I).



Table I. Organic Products from EtOCH2CH2OEt and Rh(I)^a

product (by GC-MS)	% (product distribution, by $^1\mathrm{H}$ NMR)
ethoxyacetaldehyde (3)	<2 ^b
2,4-di- <u>O</u> -ethylthreose (4)	10
2,4,6-tri- <u>O</u> -ethyl-ß-galacto-	
(or gluco-) pyranose (5)	30
1,2-diethoxyethene (8)	<2 ^b
ethenyl ethyl ether (9)	<2 ^b
chloroethyl ethyl ether	18

^aReaction over 3 d under N₂ at \leq 30 ^oC in CDCl₃, 0.14 M in 1 and 2. ^bBased on GC-MS analysis; below limit of NMR detection.

Aldehydes do not decarbonylate in this system. Although no excess of carbon monoxide is present to suppress its loss, 10 no evidence exists for decarbonylation products such as ethyl methyl ether from aldehyde 3. Aldehyde 3 probably is stabilized (against decarbonylation) in part as an internally chelated rhodium enolate (11). 11 Condensation of 11 with an orthogonally coordinated aldehyde (See 12a) preferentially leads to the three aldel, 2,4-di-Q-ethylthreese, which constitutes >76% of the self dimer from 3 and Rh(I). 12 An analogously complexed enolate (12b) leads from aldel 4 to dialdel 5.

Complexes of the dialdol, a 2,4,6-tri-<u>O</u>-ethylpyranose,¹⁴ with rhodium ions exhibit chemically induced dynamic nuclear polarization (CIDNP)¹⁶ in the ¹H NMR spectrum at -50 °C. Negative net and multiple effects, the participating NMR lines (eq 3) and an overall



lifetime (of 10^{-5} to 10^{-3} s) for the associated chemical equilibration are all consistent with an interchange that involves 13 (a pyranose form of dialdol 5), an unimolecular diradical, and acyclic species 14 (See eq 3, where partners in the CIDNP are indicated). This is a sigmatropic hydrogen transfer between C-2 of 13 and rhodium of 14. Compound 14 is a derivatized form of an acyclic hexose of the type that participates in pyranose-furanose interconversion¹⁷ of monosaccharides.¹⁸



References and Notes

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