Biomass Conversion

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Expanding the Scope of Biomass-Derived Chemicals through Tandem Reactions Based on Oxorhenium-Catalyzed Deoxydehydration**

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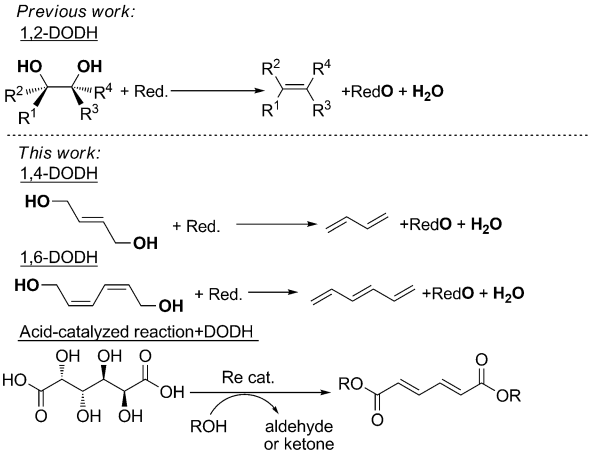
With the growing demand for sustainability, cellulosic biomass has attracted much attention as a renewable, carbon-neutral and inexpensive feedstock for chemicals and fuels. However, the conversion of biomass faces the fundamental challenge that saccharides and their polyol derivatives, the most basic platform chemicals accessible from cellulose, are too oxygen-rich to be compatible with the current petroleum-based infrastructure. The search for efficient deoxygenation methods has resulted in rapidly growing interest in the catalytic deoxydehydration (DODH) reaction to remove two adjacent hydroxyl groups from vicinal diols to afford alkenes.[1] Although preliminary studies on ruthenium,[2] vanadium,[3] molybdenum,[4] and rhenium carbonyl catalysts ($Re_2(CO)_{10}$ or $BrRe(CO)_5$)[5] have been reported, most precedents of DODH employ high-valent oxorhenium catalysts in conjunction with various reductants, such as phosphines,[6] H_2,[7] and $NaSO_3$.[8] In 2012, we reported the methyltrioxorhenium (MTO)-catalyzed DODH reaction using a sacrificial alcohol (3-pentanol, 3-octanol, 1-butanol) as reductant/solvent.[9] This system smoothly converted sugar alcohols and sugars into linear alkene products and aromatics with remarkable selectivity. Oxorhenium-catalyzed DODH of diols using glycerol[10] or benzyl alcohol[11] as reductants were also independently reported by the Abu-Omar and Nicholas groups.

Although the significant potential of the DODH reaction in the context of biomass conversion has been well recognized, the method development is still in the early stages. As previously noted, one particular feature of the DODH reaction is the need for a vicinal *cis*-diol structure (1,2-DODH): For example, whereas *cis*-1,2-cyclohexanediol is reactive, *trans*-1,2-cyclohexanediol is not. This observation has been explained by the required formation of a metal *cis*-diolate intermediate,[12] which undergoes the equivalent of the reverse reaction of the OsO_4-catalyzed *cis*-dihydroxylation of olefins.[13] However, we have found that oxorhenium complexes catalyze not only the DODH reaction, but also the [1,3]-OH shift of allylic alcohols[14] in a tandem manner, and we herein report novel modes of DODH (1,4-DODH and 1,6-DODH, respectively) from 2-ene-1,4-diols and 2,4-diene-1,6-diols (Scheme 1). To the best of our knowledge, these are the first examples of formal 1,4-DODH and 1,6-DODH, thus opening new possibilities for DODH reaction development.



Scheme 1. The general DODH reaction. Red. = reductant.

The inspiration of DODH on non-vicinal diols arose from our efforts to clarify the polyol DODH mechanism. In our previous study on the MTO-catalyzed DODH of sugar alcohols,[9] we generally observed only complete DODH products. For example, the DODH of erythritol (**21**) gave butadiene (**2**) as a major product and the partial DODH product (*Z*)-but-2-ene-1,4-diol (**1**) was not observed. Likewise, D-*chiro*-inositol, *muco*-inositol, and *allo*-inositol all gave high benzene yields (> 45 %), without forming cyclohexa-2,5-diene-1,4-diol and cyclohexa-3,5-diene-1,2-diol. This led us to speculate that, in addition to *cis*-vicinal diols, 1,4- and 1,6-allylic diols might be reactive toward DODH through the oxorhenium-catalyzed [1,3]-OH shift of an allylic alcohol.[14] To examine this hypothesis and gain insights into the origin of the observed exquisite selectivity in polyol DODH reactions, we tested a series of 2-ene-1,4-diol and 2,4-diene-1,6-diol substrates and indeed observed the unprecedented 1,4-DODH and 1,6-DODH reactions (Table 1).[15] Both *cis*- and *trans*- 2-butene-1,4-diol (**1** and **4**, respectively) were reactive, excluding the possibility of the direct coordination of 1,4-diols to Re forming a 7-membered ring Re diolate (entries 1 and 2). The observation that no **2** was produced from (*Z*)-4-methoxy 2-buten-1-ol (**5**) under the same conditions supports the requirement for two OH groups (entry 3). Trisubstituted alkene **6** gave more dehydration product[16] than DODH product, possibly because the electron-donating alkyl group stabilizes the allylic carbocation intermediate (entry 4). No significant reactivity difference was observed between *cis*- and *trans*- cyclic diols, which suggests that [1,3]-OH shift is in

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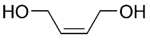
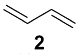
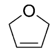
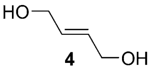
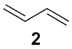
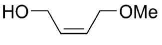
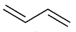
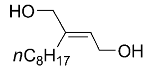
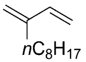
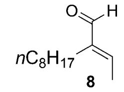
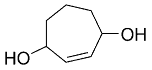
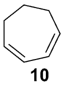
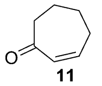
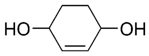
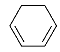
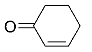
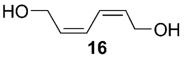
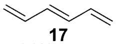
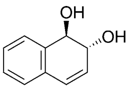
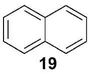
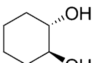
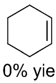
Table 1: The DODH of 2-ene-1,4-diol and 2,4-diene-1,6-diol moieties.

diol $\xrightarrow[\text{3-pentanol, 170 °C, N}_2\text{, 0.5 h}]{\text{CH}_3\text{ReO}_3\text{ (2.5 mol\%)}}$ deoxygenated product

Entry	Diol	DODH product	Dehydration product
1[a]	 **1**	 **2** 70% yield	 **3** 6% yield
2[a]	 **4**	 **2** 70% yield	
3[a]	 **5**	 **2** 0% yield decomposition	
4	 **6**	 **7** 18% yield	 **8** 45% yield
5[b]	 **9a**: *cis*-diol **9b**: *trans*-diol (racemic)	 **10** **9a:** 36% yield **9b:** 58% yield	 **11** 17% yield 14% yield
6[c]	 **12a**: *cis* diol **12b**: *trans* diol (racemic)	 **13** **12a**: 35% yield **12b**: 23% yield	 **14** 5% yield 12% yield  **15** trace 12% yield
7[d,e]	 **16**	 **17** 31% yield	
8[e]	 **18**	 **19** 9% yield	1-naphthol 73% yield + 2-naphthol 10% yield
9[e]	 **20**	 0% yield no reaction	

[a] 3-octanol was used instead of 3-pentanol. [b] 5 mol% catalyst loading. [c] It was not determined whether benzene was formed by dehydration of the substrate or by oxidation of 1,3-cyclohexadiene.[7b] [d] Reaction temperature was 200 °C. [e] Reaction time was 1 h.

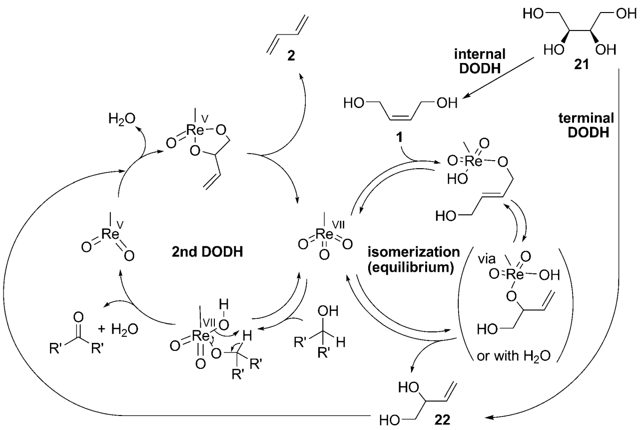


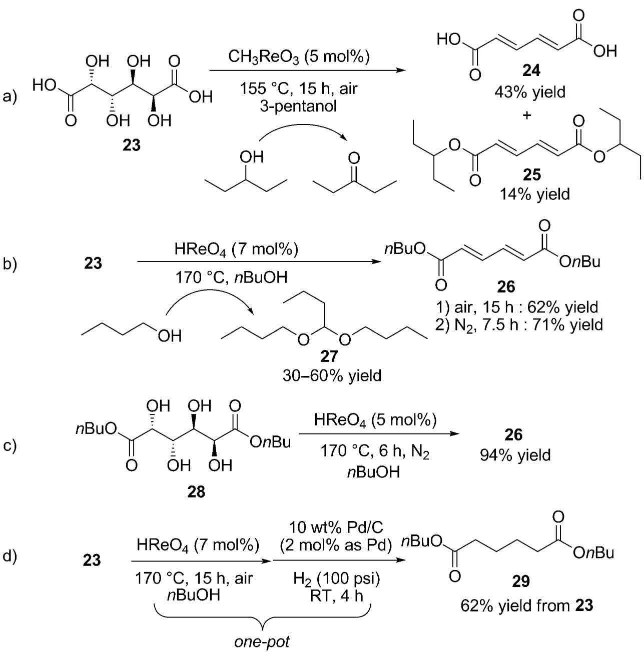
Figure 1. Proposed catalytic cycle for the oxorhenium-catalyzed DODH reaction.

a fast equilibrium (entries 5 and 6). Furthermore, the DODH reaction was also applicable to *cis,cis*-muconic alcohol **16**, affording (*E*)-hexatriene **17** (entry 7). Although aromatization to naphthols was inevitable, a small amount of naphthalene was also obtained from **18** (entry 8), in marked contrast to the non-conjugated *trans*-diol **20** that produced no trace of cyclohexene (entry 9).

On the basis of these observations, a plausible catalytic cycle[9,17] is shown in Figure 1, depicting erythritol (**21**) as a representative substrate. We propose that the 1,4- and 1,6-DODH reactions proceed through a five-membered ring reduced rhenium–diolate intermediate before the olefin extrusion, which is identical to the last step of 1,2-DODH from vicinal *cis*-diols. This hypothesis suggests that the DODH reaction is particularly useful for the total deoxygenation of polyols by merging different intermediates into one product and thereby increasing product selectivity. Therefore, the solvent-alcohol-driven DODH system may be exceptionally well suited for polyol DODH compared to other reductant systems not merely because the substrates have better solubility, but also because the enhanced proton transfer[12a] maximizes the benefit of auto-selectivity increase.

Ensured of the efficiency of the polyol DODH reaction, we then turned to applying our system to the production of commodity chemicals from biomass. In this regard, sugar acids, particularly C6 aldaric acids, caught our attention because the expected product muconic acid[18] has wide utility in the chemical industry as a precursor to adipic acid,[19] terephthalic acid,[20] and 1,6-hexanediol.[21] Moreover, although C6 aldaric acids have four internal hydroxyl groups, our findings in the 1,4-DODH reaction suggested that, regardless of whether the first DODH takes place at the α,β-position or on β,γ-position, the second DODH would furnish muconic acid. We therefore tested mucic acid (**23**), the oxidized form of galactose, because the product bearing the stable *trans,trans*-stereochemistry (**24**) was expected both from β,γ-/α,δ- DODH (sterics) and from α,β-/γ,δ- DODH (*cis*-diol stereospecificity).[22]

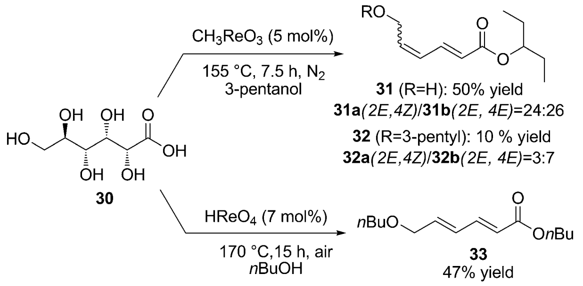
In the initial experiment using MTO and 3-pentanol (reductant/solvent), we obtained **24** in 43% yield,[23] exclusively with *trans,trans*-stereochemistry, accompanied by diester **25** (14% yield; Scheme 2a). As **25** was easier to manipulate and purify than **24**, we sought to shift the selectivity towards the ester product. We thus envisioned replacing MTO with perrhenic acid ($HReO_4$), which earlier studies identified as a promising DODH catalyst.[9] While the Brønsted acidity of perrhenic acid had previously caused decomposition of sugar substrates, we anticipated that $HReO_4$ may conveniently catalyze both DODH and the in situ acid-catalyzed esterification reaction of sugar acids in a tandem manner. Gratifyingly, by using a slightly higher temperature and the sterically accessible primary alcohol 1-butanol instead of a secondary alcohol, we obtained *trans,trans*-dibutyl muconate **26** in 62% yield under air and in 71% yield under an inert atmosphere (Scheme 2b).[24] The majority of 1-butanal was trapped as acetal **27** with this system. When mucic acid was pre-esterified in refluxing 1-butanol/HCl, mucic acid dibutyl ester **28** was converted into **26** in near-quantitative yield, thus confirming the efficiency of the



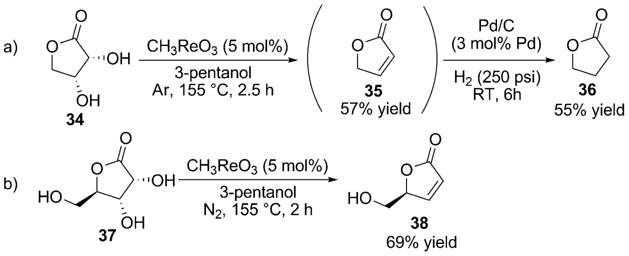
Scheme 2. DODH of mucic acid and mucic acid dibutyl ester.

DODH step (Scheme 2c). To emphasize the utility of muconic acid and its ester (**24**–**26**) in commodity chemical synthesis, we also demonstrated the one-pot two-step conversion of **23** into dibutyl adipate **29** (Scheme 2d). There was no interference from the Re catalyst during the Pd/C-catalyzed hydrogenation step.[25]

Encouraged by the efficient DODH of mucic acid to muconic acid, a potential feedstock for nylon 6-6, we sought to obtain ε-caprolactone from C6 aldonic acid for the production of nylon 6. As shown in Scheme 3, when D-gluconic acid **30** was examined, the attempt to preserve the terminal OH group by using the secondary alcohol–CH_3ReO_3 conditions afforded **31a**/**31b** in 50% total yield, with ethers **32a**/**32b** being the minor products. In contrast, by using the acidic $HReO_4$ catalyst, the products converged to the (2*E*,4*E*)-ether **33**. While our efforts on the downstream conversion of these unsaturated products to nylon 6 are underway, we also demonstrated the one-pot two-step conversion of D-erythronolactone (**34**) to γ-butyrolactone (**36**) through γ-crotonolactone (**35**) (Scheme 4a). Upon treatment with NH_3,[26] **36** furnishes 2-pyrrolidone, which can be converted into nylon 4[27] or used as a precursor to *N*-methylpyrrolidone (NMP), polyvinylpyrrolidone (PVP), and polyvinylpolypyrrolidone (PVPP).[28] Additionally, D-(+)-ribono-1,4-lactone (**37**), a C5 aldonic acid lactone derivative, was smoothly converted into **38** without optimization (Scheme 4b).

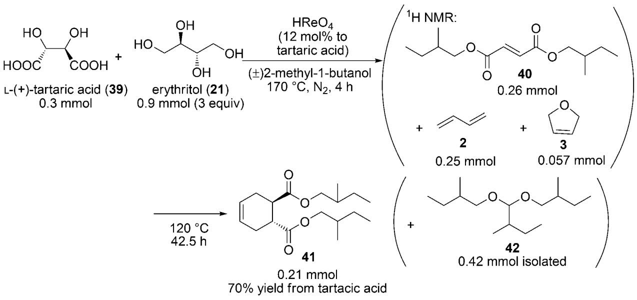


Scheme 3. DODH of gluconic acid.



Scheme 4. Conversion of D-erythronolactone and D-(+)-ribono-1,4-lactone.

Finally, we sought to further exploit the unique capability of $HReO_4$ to serve as a DODH/acid dual-catalyst by combining DODH with other reactions. To this end, we obtained the 4-cyclohexene-1,2-dicarboxylic acid ester **41**, a plausible plasticizer precursor, from L-(+)-tartaric acid (**39**) and erythritol (**21**) by a sequence of tandem DODH, esterification, and Diels–Alder reaction in a simple one-pot two-step procedure (70% yield, Scheme 5).[29] The alkene functional group of **41** would serve as a good manipulation handle to either oxidize/disproportionate to phthalates,[30] or to hydrogenate to cyclohexane-1,2-dicarboxylic acid esters,[31] which are both common plasticizer skeletons. This reaction combines the total deoxygenation of the sugar alcohol into unsaturated hydrocarbons and the selective deoxygenation of the sugar acid while preserving the ester group, and exemplifies the capability of the DODH reaction to construct structures with very specific functionality from biomass-derived polyols. It also underscores the advantage of the DODH reaction over conventional biomass deoxygenation methods such as hydrogenation and hydrogenolysis, in that the product alkenes are deoxygenated but still synthetically versatile.



Scheme 5. One-pot conversion of L-(+)-tartaric acid and erythritol into plasticizer precursor **41**.

In summary, we have found that the oxorhenium-catalyzed DODH reaction using a sacrificial alcohol as a reductant/solvent is viable not only for vicinal diols (1,2-DODH) but also for 2-ene-1,4-diols (1,4-DODH) and 2,4-diene-1,6-diols (1,6-DODH) through a tandem [1,3]-OH shift-DODH process. These unprecedented reactivity modes substantially expand the future directions of DODH reaction development and shed light on the polyol DODH mechanism. The strategy of using oxorhenium for tandem DODH/acid-catalyzed reactions was further applied to the conversion of sugar acids into unsaturated esters. In this context, $HReO_4$ was identified as a particularly interesting catalyst because it well mediates not only DODH and the above-mentioned [1,3]-OH shift, but also other Brønsted acid catalyzed reactions, such as esterification. The power of this approach was best exemplified in the one-pot synthesis of plasticizer precursors from tartaric acid and erythritol. We believe that this work demonstrates the high potential of DODH as a unique and selective key transformation in the context of biomass-derived chemicals synthesis.

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[1] a) S. Dutta, *ChemSusChem* **2012**, *5*, 2125 – 2127; b) J. O. Metzger, *ChemCatChem* **2013**, *5*, 680 – 682.

[2] a) S. Stanowski, K. M. Nicholas, R. S. Srivastava, *Organometallics* **2012**, *31*, 515 – 518; b) S. Murru, K. M. Nicholas, R. S. Srivastava, *J. Mol. Catal. A* **2012**, *363 – 364*, 460 – 464.

[3] K. M. Nicholas, G. Chapman, Jr., *Chem. Commun.* **2013**, *49*, 8199 – 8201.

[4] L. Hills, R. Moyano, F. Montilla, A. Pastor, A. Galindo, E. Álvarez, F. Marchetti, C. Pettinari, *Eur. J. Inorg. Chem.* **2013**, 3352 – 3361.

[5] E. Arceo, J. A. Ellman, R. G. Bergman, *J. Am. Chem. Soc.* **2010**, *132*, 11408 – 11409.

[6] a) G. K. Cook, M. A. Andrews, *J. Am. Chem. Soc.* **1996**, *118*, 9448 – 9449; b) S. Raju, J. T. B. H. Jastrzebski, M. Lutz, R. J. M. Klein Gebbink, *ChemSusChem* **2013**, *6*, 1673 – 1680.

[7] a) J. E. Ziegler, M. J. Zdilla, A. J. Evans, M. M. Abu-Omar, *Inorg. Chem.* **2009**, *48*, 9998 – 10000; b) A. L. Denning, H. Dang, Z. Liu, K. M. Nicholas, F. C. Jentoft, *ChemCatChem* **2013**, DOI: 10.1002/cctc.201300545.

[8] a) P. Liu, K. M. Nicholas, *Organometallics* **2013**, *32*, 1821 – 1831; b) I. Ahmad, G. Chapman, K. M. Nicholas, *Organometallics* **2011**, *30*, 2810 – 2818; c) S. Vkuturi, G. Chapman, I. Ahmad, K. M. Nicholas, *Inorg. Chem.* **2010**, *49*, 4744 – 4746.

[9] M. Shiramizu, F. D. Toste, *Angew. Chem.* **2012**, *124*, 8206 – 8210; *Angew. Chem. Int. Ed.* **2012**, *51*, 8082 – 8086.

[10] J. Yi, S. Liu, M. M. Abu-Omar, *ChemSusChem* **2012**, *5*, 1401 – 1404.

[11] C. Boucher-Jacobs, K. M. Nicholas, *ChemSusChem* **2013**, *6*, 597 – 599.

[12] a) S. Qu, Y. Dang, M. Wen, Z.-X. Wang, *Chem. Eur. J.* **2013**, *19*, 3827 – 3832; b) S. Liu, A. Senocak, J. L. Smeltz, L. Yang, B. Wegenhart, J. Yi, H. I. Kenttämaa, E. A. Ison, M. M. Abu-Omar, *Organometallics* **2013**, *32*, 3210 – 3219.

[13] T. Strassner in *Computational Modeling of Homogeneous Catalysis*, *Vol. 25* (Eds.: F. Maseras, A. Lledós), Springer, New York, **2002**, pp. 253 – 268.

[14] A. T. Herrmann, T. Saito, C. E. Stivala, J. Tom, A. Zakarian, *J. Am. Chem. Soc.* **2010**, *132*, 5962 – 5963.

[15] Conversion was complete in all cases except entry 9. Yields were determined by ^{1}H NMR spectroscopy using mesitylene as an internal standard. The ^{1}H NMR spectra and the GCMS spectra/retention time matched those of authentic samples. Compounds **7** and **8** were also isolated (see the Supporting Information).

[16] a) T. J. Korstanje, E. F. de Waard, J. T. B. H. Jastrzebski, R. J. M. Klein Gebbink, *ACS Catal.* **2012**, *2*, 2173 – 2181; b) T. J. Korstanje, J. T. B. H. Jastrzebski, R. J. M. Klein Gebbink, *ChemSusChem* **2010**, *3*, 695 – 697; c) T. J. Korstanje, J. T. B. H. Jastrzebski, R. J. M. Klein Gebbink, *Chem. Eur. J.* **2013**, *19*, 13224 – 13234.

[17] Alhough the Re diolate may exist in equilibrium with its dinuclear form, only the monomer is shown for simplicity. The order of diol isomerization, Re diolate formation, and the reduction of Re has not been clarified, and the catalytic cycle might be based on Re^{III}–Re^{V} instead of Re^{V}–Re^{VII} as suggested by Abu-Omar et al. (Ref. [12b]).

[18] For biocatalytic routes to *cis,cis*-muconic acid from glucose, see: a) W. Niu, K. M. Draths, J. W. Frost, *Biotechnol. Prog.* **2002**, *12*, 201 – 211; b) K. M. Draths, J. W. Frost, *J. Am. Chem. Soc.* **1994**, *116*, 399 – 400.

[19] The concept of synthesizing adipic acid from glucose through DODH was touched on by Metzger in his minireview on biomass deoxygenation (Ref. [1b]) while we were preparing this manuscript, but no specific pathway for such a reaction has been reported.

[20] a) D. Schweitzer (Amyris, Inc.), WO2012/82725A1, **2012**; b) J. W. Frost, A. Miermont, D. Schweitzer, V. Bui (Amyris, Inc.), US 20100314243A1, **2010**.

[21] V. Bui, J. W. Frost (Amyris, Inc.), WO2012/141993A1, **2012**.

[22] Glucaric acid (aldaric acid derived from glucose) is commercially available in salt form only (Na, Ca, K). These salts were themselves unreactive toward DODH, possibly because of the basicity. Glucosaminic acid and *N,N′*-dibenzyl-D-glucaramide also did not give any appreciable products. When monopotassium glucarate was preacidifed with cation exchange resin and subjected to DODH conditions in 1-butanoldibutyl muconate was obtained in 25 % yield (*trans,trans*/*cis,trans* = 7:18). See the Supporting Information for details.

[23] In Schemes 2–5, isolated yields are reported. Although conversion could not be rigorously determined because of the low solubility of polyol substrates in organic solvents, the disappearance of the solid starting materials suggested complete conversion. Product **24** was also insoluble in organic solvent, but ^{1}H NMR analysis of the islated compound in [D$_6$]DMSO confirmed the complete consumption of **23**. See the Supporting Information.

[24] **23** was not produced in an isolable amount. The monoester was not observable by TLC.

[25] We were not able to convert **28** into **29** or **26** using H_2 as the sole reductant in the absence of alcohol; see Ref. [7a].

[26] a) Dairen Chemical Corporation; S.-C. Chen, J.-M. Lin, C.-L. Tsai, F.-S. Lin, L.-A. Hsu, US6350883 B1, **2002**; b) F. B. Minnock, P. D. Taylor (ISP Investments Inc.), US5393888, **1995**; c) M. Rudloff, P. Stops, E. Henkes, H. Schmidtke, R.-H. Fischer, M. Julius, R. Lebkuecher, K.-H. Ross (BASF Aktiengesellschaft), WO 2003022811, **2003**.

[27] C. E. Barnes, *Lenzinger Ber.* **1987**, *62*, 62 – 66.

[28] A. L. Harreus, R. Backes, J. O. Eichler, R. Feuerhake, C. Jäkel, U. Mahn, R. Pinkos, R. Vogelsang, *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH, Weinheim, **2000**.

[29] Higher yields were obtained using either butadiene instead of erythritol, or a two-pot two-step procedure to separately convert **39** into **40** and **21** into **2** before combining the two streams for the Diels–Alder reaction. See the Supporting Information.

[30] a) C. M. Buchan, J. I. G. Cadogan, I. Gosney, B. J. Hamill, S. F. Newlands, D. A. Whan, *J. Chem. Soc. Chem. Commun.* **1983**, 725–726; b) X. Zhang, L. Xu, X. Wang, N. Ma, F. Sun, *Chin. J. Chem.* **2012**, *30*, 1525–1530.

[31] M. Brunner, A. Bottcher, B. Breitscheidel, K. Halbritter, J. Henkelmann, L. Thil, R. Pinkos (BASF Aktiengesellschaft), US6284917 B1, **2001**.