1185 (w), 1155 (w), 1140 (w), 1073, 1033, 967 (w), 861 (w), 849 (w) cm^{-1}.

Reaction of 7 with KOH. Into a 5-mL round-bottomed flask were weighed 0.41 g of **7** (1.9 mmol) and 0.10 g of KOH (1.8 mmol). The flask was equipped with magnetic stirrer and a reflux condenser, and the mixture was heated over a 180 °C oil bath for 1 h. The mixture was cooled to room temperature, and then 1 mL of $CDCl_3$ was used to wash down the inside of the reflux condenser into the reaction vessel. The reaction mixture was washed three times with 2-mL portions of water and then dried over anhydrous calcium sulfate. ^1H NMR analysis showed a 3.7:1 ratio of **11** to unreacted **7**.

Reaction of 8 with KOH. Into a 5-mL screw-top tube were weighed 0.15 g of **8** (1.2 mmol), 0.18 g of KOH (3.2 mmol), and 0.07 g of deionized water. The mixture was magnetically stirred and heated over an oil bath at 184–210 °C for 3.5 h. The mixture was cooled to 0 °C, taken up in 0.75 g of $CDCl_3$, washed with three 2-mL portions of 3 M HCl and two 3-mL portions of water, and then dried over anhydrous $CaSO_4$. The resulting solution was analyzed by ^1H and ^{13}C NMR and found to contain predominantly **11** along with a small amount of some unidentified high molecular weight side products.

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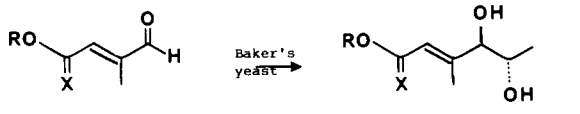
Registry No. **4**, 117711-58-7; **5**, 117711-59-8; **7**, 117711-60-1; **8**, 117711-61-2; **10**, 117711-62-3; **11**, 636-82-8; CF_2Br_2, 75-61-6; cyclohexene, 110-83-8.

Communications

Conversion of 4-Oxy-Substituted Crotonaldehyde into 1-Protected (2*R*)-1,2,4-Butanetriol: A New Synthetic Capacity of Bakers' Yeast

Summary: The bakers' yeast mediated conversion of 4-oxy-substituted crotonaldehydes **3** and **4** into 1-protected (2*R*)-1,2,4-butanetriols **7a** and **8a**, in ca. 25% yield, is reported.

Sir: The ability of bakers' yeast to reduce the carbonyl group and to saturate the double bond of α,β-unsaturated aldehydes is well known.[1] When an aromatic substituent is present in the γ-position of the substrate (e.g., in cinnamaldehyde), the above transformations compete with the decarboxylative incorporation of pyruvate. The resulting (3*R*)-$C_6H_5CH{=}CHCH(OH)COCH_3$ is subsequently reduced to the 2*S*,3*R* diol $C_6H_5CH{=}CHCH(OH)CH(OH)CH_3$.[2] Crotonaldehyde and tiglic aldehyde do not undergo the latter acyloin-type condensation. However, current studies[3] indicate that, under suitable experimental conditions, γ-oxy-substituted tiglic aldehydes like **1** and **2** afford the corresponding diols **5** and **6**, the ultimate products of the acyloin-type condensation, in 35% and 10% yield, respectively.



1 R= Et; X= O
2 R= COC_6H_5; X= H_2
5 R= Et; X= O
6 R= COC_6H_5; X= H_2

We now report a new synthetic capacity of bakers' yeast toward α,β-unsaturated aldehydes that emerges when 4-(benzoyloxy)- and 4-(benzyloxy)crotonaldehyde (**3** and **4**) are incubated with bakers' yeast under the conditions in which **1** and **2** are converted to **5** and **6**. In a typical experiment, a mixture of aldehyde **3** (8 g) and D-glucose (100 g) in tap water (1.5 L) at pH 5–5.2 and 35 °C is stirred as commercial bakers' yeast (200 g) is added in portions during 3 h. After that time, extractive workup (AcOEt) affords in 60–70% yield a mixture, separated by column chromatography, composed of unreacted aldehyde **3** (15%), a mixture of alcohols **9** and **10** in variable ratios (60%), and diol **7a** (25%). The last product, an oil showing a moderate negative rotation, was characterized as the diacetate (**7b**), $[\alpha]^D_{20}$ +17° (*c* 1, MeOH). Acidic hydrolysis of **7a** and acetylation afforded the triacetate **7c**, $[\alpha]^D_{20}$ +10.3° (*c* 1, MeOH). ^1H NMR spectra of **7c** in the presence of tris[3-(trifluoromethyl)hydroxymethylene]-[(+)-camphorato]europium(III) and comparison with racemic material, showed the presence of a single enantiomer (95%). This was assigned the 2*R* absolute configuration depicted in **7c** because the triacetyl derivative of (2*S*)-1,2,4-butanetriol, prepared by hydrolysis of the 2-THP derivative,[4] obtained in turn from (*S*)-malic acid, showed $[\alpha]^D_{20}$ −10.8° (*c* 1, MeOH). Similar results were obtained by using (4-(benzyloxy)crotonaldehyde (**4**) as substrate: together with the expected reduction products, diol **8a** was obtained in ca. 25% yield. Acetylation of the latter afforded the diacetate **8b**, $[\alpha]^D_{20}$ +14° (*c* 1, MeOH), which after hydrogenolysis (H_2/Pd–C/AcOEt) gave **8c**, which was then acetylated to **7c**, $[\alpha]^D_{20}$ +9.85° (C 1, MeOH). As above, ^1H NMR studies indicated predominance of the 2*R* enantiomer (90–95%). Alcohol **9** is apparently not converted into the diol **7a** under the above conditions.

The formation of diols **7a** and **8a** from **3** and **4** is expected to be the consequence of two chemical changes involving water addition across the double bond of **3** and **4**, followed by reduction of the intermediate 3-hydroxy aldehydes. The steric course of the water addition is identical with that observed recently[5] in the microbiological conversion of the 4-nitrogen-substituted α,β-unsaturated crotonobetaine $Me_3N^+CH_2CH{=}CHCOO^-$ and in the enoyl-CoA hydratase (EC 4.2.1.17)-catalyzed conversion of crotonoyl-CoA to (3*R*)-3-hydroxybutyryl-CoA.[6]

In order to determine the steric course of the water addition, we prepared [2,3-$^2H_2$]-4-(benzoyloxy)croton-

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(2) Fuganti, C.; Grasselli, P.; Servi, S.; Spreafico, F.; Zirotti, C.; Casati, P. *J. Org. chem.* **1984**, *49*, 4087.
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(5) Eur. Pat. Appl. 122,794 (to Ajinomoto); *Chem. Abstr.* **1985**, *102*, 60778u.
(6) Stern, J. R. *The Enzymes* **1961**, *5*, 511.

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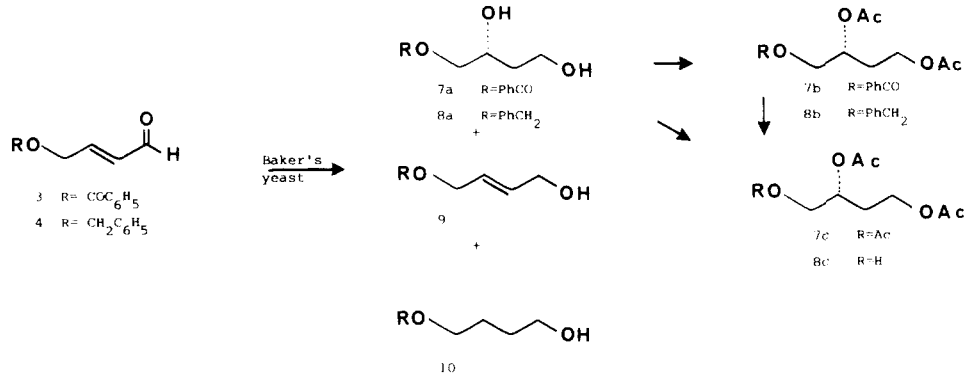
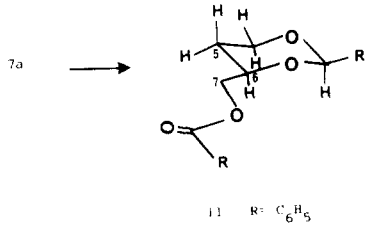
Scheme I



aldehyde from the monobenzoate of butyne-1,4-diol in two steps: (a) D_2/Lindlar catalyst/AcOEt; (b) pyridinium chlorochromate oxidation. While the intermediate monobenzoate contained over 95% deuterium at positions 2 and 3, the resulting *E* aldehyde (**3**) contained over 95% deuterium at position 3 but only 55–60% deuterium at position 2. Incubation of the latter material at pH 5.2 as above yielded unreacted **3** and products **7a**, **9**, and **10** each containing >95% deuterium at the position corresponding to position 3 of the precursor. In contrast, considerable variation was found in the amount of deuterium label retained at the 2 position: recovered **3** (ca. 5–10% ^2H), **9** and **10** (40%), and **7a** (ca. 20%). Diol **7a** was converted (C_6H_5CHO, TsOH, toluene, reflux) into the 1,3-dioxane (**11**). ^1H NMR analysis allowed the assignment of the



stereochemistry of the ring protons.[7] ^2H NMR spectroscopy indicated that the retained deuterium is equally distributed into the axial (δ 1.59) and equatorial (δ 0.84) positions at C-5. The deuterium labeling experiments thus indicate (i) almost complete loss of ^2H at position 2 of the recovered aldehyde **3**, (ii) consistent retention at the same positions in alcohols **9** and **10**, and (iii) retention of less than 50% of the deuterium (equally in both configurations) in **7a**.

A reasonable interpretation of these results might be the following. A reversible water addition across the double bond gives rise to (3*R*)-3-hydroxy-4-(benzoyloxy)butyraldehyde. The deuterium at position 2 of the latter is subsequently lost by enolization prior to enzymic reduction to **7a**, thus causing scrambling of the remaining deuterium.

Consideration of the mechanism and the nature of the enzyme(s) involved in the above processes is outside the scope of the present paper. However, it is worthwhile to note the dramatic difference in reactivity observed between **2** (acyloin condensation) and **3** (water addition and reduction) as a consequence of the additional methyl group in the former. Also the present process extends the scope of enzymic transformations of nonconventional substrates in organic synthesis.[8] The regioselectively protected 1,2,4-butanetriols **7a** and **8a** are formally derivatives of the unnatural (*R*)-malic acid, a starting material of current interest in the synthesis of enantiomerically pure compounds.[9]

Supplementary Material Available: Experimental procedures for **4**, **7a**, **8a**, **7b**, **8b**, **7c**, and **11** (2 pages). Ordering information is given on any current masthead page.

(7) ^1H NMR (C_6D_6): 5.31 (s, 1 H, H-2), 4.31 (dd, 1 H, H-7a, *J*(7a,7b) = 11.1, *J*(7a,6) = 5.7 Hz), 4.25 (dd, 1 H, H-7b, *J*(7b,6) = 4.0 Hz), 3.88 (ddd, 1 H, H-4e, *J*(4e,5a) = 5.0, *J*(4e,5e) = 1.5, *J*(4e,4a) = 11.5 Hz), 3.75 (m, 1 H-6a, *J*(6a,7a) = 11.5, *J*(6a,7e) = 2.5 Hz), 3.40 (ddd, 1H, H-4a, *J*(4a,5a) = 12.5, *J*(4a,5e) = 2.5 Hz), 1.59 (m, 1 H, H-5a, *J*(5a,5e) = 13.0 Hz), 0.84 (m, 1 H, H-5e).

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(9) Tanner, D.; Somfai, P. *Tetrahedron Lett.* **1988**, *29*, 2373.

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Intramolecular 4 + 3 Cycloadditions of 2-Alkoxyallylic Cations Derived from 2-Alkoxyallylic Sulfones

Summary: Certain 2-alkoxyallylic sulfones lead to 2-alkoxyallylic cations, which can be intramolecularly trapped by a furan ring via a 4 + 3 cycloaddition.

Sir: Notwithstanding the many advances made in the synthesis of carbocyclic compounds, there is a continuing need to develop new synthetic methodology for the purposes of versatility, expediency, and practicality. Seven-membered rings fall into that class of substructures particularly significant because of their occurrence in a wide variety of structurally intriguing or biologically active natural products. Specific examples include tumor-promoting diterpenes such as phorbol,[1] antiviral agents such as reiswigin A,[2] the fenestrane laurenene,[3] and the myriad of guiane and pseudoguiane sesquiterpenes.[4] In ap-

(1) For the first synthesis of the phorbol skeleton and leading references, see: Wender, P. A.; Keenan, R. M.; Lee, H. Y. *J. Am. Chem. Soc.* **1987**, *109*, 4390.
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