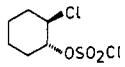
Table I. Addition Products of Chlorine Chlorosulfate 1 to Olefins

olefin	addition product (no.)	% yield	bp (mm), °C	^{1}H NMR, δ
ethylene	$ClCH_2CH_2OSO_2Cl$ (**4**)	85	58–59 (1)[a]	3.80 t (2 H, J = 5.8 Hz, CH_2Cl), 4.67 t (2 H, CH_2O)
trichloroethylene	$Cl_3CCH(Cl)OSO_2Cl$ (**5**) $Cl_2CHCCl_2OSO_2Cl$ (**6**)	56 (**5**:**6** = 1:1)[b]	71–72 (2)	6.10 s
1-hexene	$C_4H_9CH(Cl)CH_2OSO_2Cl$ (**7**) $C_4H_9CH(OSO_2Cl)CH_2Cl$ (**8**)	24 (**7**:**8** = 4:1)	62–63 (0.5)[c]	0.90–2.10 m (C_4H_9), 3.85 d (CH_2Cl of **8**), 4.15 m (CHCl of **7**), 4.55 d (CH_2O of **7**), 5.25 m (CHO of **8**)
methyl methacrylate	$CH_2(OSO_2Cl)C(Cl)(CH_3)COOCH_3$ (**9**) $CH_2(Cl)C(OSO_2Cl)(CH_3)COOCH_3$ (**10**)	88 (**9**:**10** = 3:1)[b]	80–82 (1)	**9**: 1.84 s (CH_3), 3.84 s (OCH), 4.50 and 4.80 (AB system, J = 10.0 Hz, CH_2O) **10**: 1.91 s (CH_3), 3.84 s (OCH_3) and 3.91 m (CH_2Cl)
cyclohexene	 (**11**)	35	65–67 (0.5)[c]	1.30–2.50 m (8 H, CH_2), 4.05 m (1 H, W = 26 Hz, CHCl), 4.80 m (1 H, CHO)

[a] See ref 13. [b] Satisfactory elemental analyses were obtained. [c] Partially decomposed upon distillation in vacuo.

to cyclohexene proceeds stereospecifically to give the trans adduct **11**. The data of Table I show that **1** can react with olefins which are different in character. While such reagents as $ClOSO_2F$[5] and $ClOSO_2CF_3$[6] give only unidentified tars with typical olefins,[7] the chlorine chlorosulfate **1** gives the corresponding adducts in these cases. On the other hand, it is sufficiently reactive to give the adducts **5** and **6** with less reactive electron-deficient olefins, such as trichloroethylene even at room temperature. Chlorine chlorosulfate **1** is a versatile and inexpensive reagent,[14] and its addition to olefins is a novel reaction of general character and of potential synthetic utility, especially taking into account that the $ClSO_3$ group is highly nucleofugic.[17,18]

In conclusion we should like to point to the generalization and ramification of the studied processes. The ability of sulfur trioxide to insert itself into some particular bonds, e.g., Si–Hal,[20] Cl–F,[21] Ac–F,[22] R_2N–Cl,[23] RS–Cl,[24] etc., is known. This communication demonstrates that the "insertion" product **1** can be used as a reactive electrophile. We hope to exploit this approach for the SO_3-mediated additions of weak electrophiles to olefins[25] as well as for other electrophilic processes.

Registry No. **1**, 91948-94-6; **4**, 13891-58-2; **5**, 91948-95-7; **6**, 91948-96-8; **7**, 91948-97-9; **8**, 91948-98-0; **9**, 91948-99-1; **10**, 91949-00-7; **11**, 91949-01-8; ethylene, 74-85-1; trichloroethylene, 79-01-6; 1-hexene, 592-41-6; methyl methacrylate, 80-62-6; cyclohexene, 110-83-8.

(14) Reagent **1** can be used for an oxidative deiodination reaction.[15] For instance, the treatment of methyl iodide with **1** proceeds to give methyl chlorosulfate (cf. ref 16).

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(18) We have found that the adduct **11** reacts with diethylamine with elimination of the chlorosulfate group as a whole. It is worthy to emphasize also that participation of nucleofugic anions in the final step of electrophilic additions is well documented.[19]

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(25) We have successfully used this strategy for SO_3-mediated addition reactions in the case of R_2NCl[23] (formation of 2-chloroethyl sulfamates), of RSCl–CH_3CN and RSSR–CH_3CN[24] (formation of compounds with the 1-RS-2-acetylaminoethane framework, cf. ref 26), of EtONO[27] (formation of chlorosulfates of 2-hydroxy ketones), and of acyl fluorides (cf. ref 22) (formation of β-substituted ketones).

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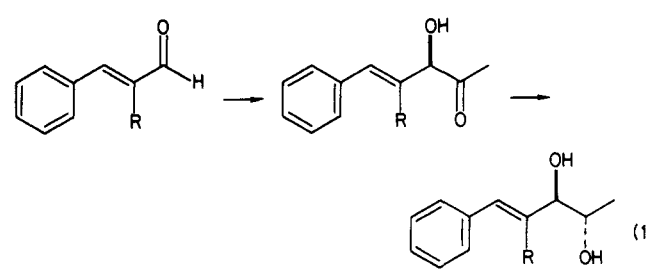
On the Steric Course of Baker's Yeast Reduction of α-Hydroxy Ketones

Summary: The baker's yeast mediated conversion of the α-hydroxy ketones **1**–**6** into the diols **8**–**14** is reported.

Sir: The baker's yeast mediated conversion of aromatic α,β-unsaturated aldehydes into the 2*S*,3*R* diols of eq 1 can



(1)

be viewed as the overall consequence of two distinct chemical operations.[1] (i) Addition of a C_2 unit equivalent of acetaldehyde onto the *si* face of the carbonyl carbon of the α-position unsaturated aldehydes forms (*R*)-α-hydroxy ketones, in an acyloin-type condensation, and (ii) reduction of the latter intermediates on the *re* face of the carbonyl gives rise to the diols actually isolated. Under suitable experimental conditions[2] (*R*)-hydroxy ketones can be ob-

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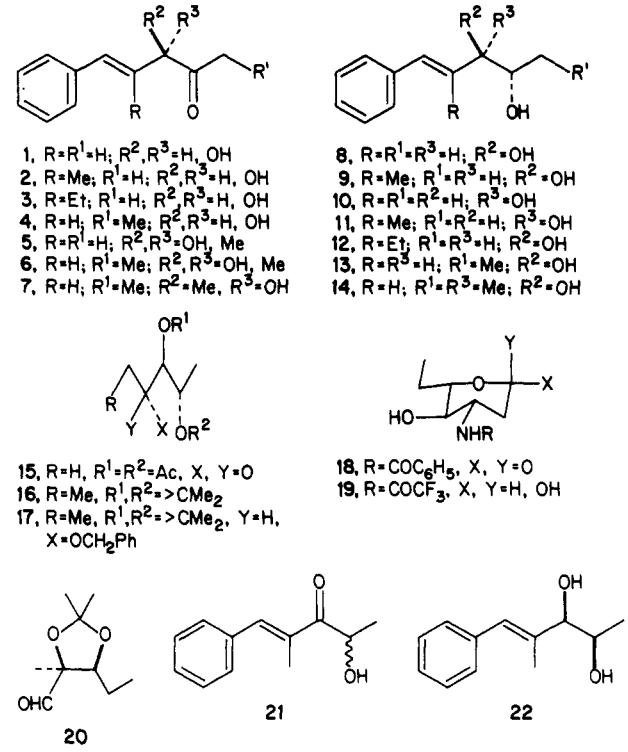
tained as sole transformation products of the aldehydes by the actively fermenting yeast. Exploratory experiments[3] indicated that there is some tolerance by the enzymic system(s) involved in the reaction of eq 1 as far as the structure of the aromatic aldehydes and the substituents in α-position are concerned. However, α-ethyl- and α-*n*-propylcinnamaldehydes are not converted into the corresponding methyl diols. Furthermore, acetaldehyde is the only aldehyde accepted as second terminus of the reaction, since, when cinnamaldehyde was incubated with yeast in the presence of propionaldehyde or butyraldehyde, (2*S*,3*R*)-8 was isolated as the sole transformation material. Finally, when [formyl-^{2}H]cinnamaldehyde was incubated with baker's yeast [3-^{2}H]-8 with complete deuterium retention was obtained. This result indicates that if the enediol form of the α-hydroxy ketone participates to the reaction sequence of eq 1, hydrogen removal and hydrogen addition takes place with retention of the label.

We now report on studies on the yeast transformation of a series of synthetic racemic α-hydroxy ketones, suggesting that the lack of incorporation of α-ethylcinnamaldehyde and -propionaldehyde into the type of diols of eq 1 is likely to be due to the inability of these materials to be accepted as substrates by the condensing enzyme(s) (first part of eq 1), since the synthetic α-hydroxy ketones derived from the above aldehydes, as well as those from other carbonyl compounds, are stereospecifically reduced by yeast. To this end, the hydroxy ketones **1**–**6** were prepared[4] and submitted to the yeast transformation under standard conditions, at pH 7.5–6.5.[5] There is a dramatic difference in the yield of conversion and in the type of products between the methyl ketones **1** and **2** and the higher homologues **3** and **4** (Chart I). Whereas **1** and **2** afforded ca. 70–80% of a ca. 6:4 mixture of (2*S*,3*R*)-**8** and **9** and (2*S*,3*S*)-**10** and -**11**, respectively, α-hydroxy ketones **3** and **4** gave rise in 15–20% yield to the erythro diols **12** and **13**, contaminated by ca. 10% of the isomeric threo materials. Product **8** was isolated from the crude diol fraction by chromatography. The minor component which accompanies **8** was assiged the 2*S*,3*S* absolute configuration depicted in **10** because the crude diol fraction, once converted into the isopropylidene derivative, afforded, on ozonolysis and $(C_6H_5)_3P$ treatment, a ca. 6:4 mixture of erythro and threo C_4 aldehydes, as shown by GLC analysis and comparison with authentic samples. The crude aldehyde fraction, on treatment with methanolic K_2CO_3, a process which causes α-epimerization of the erythro to the threo aldehyde, gave, following known procedures, optically pure *N*-benzoyl-L-daunosamine.[6] Product **9** separated as crystals, mp 107 °C, α^{20}_D +31°.[7,8] From the mother liquors, on SiO_2 column chromatography, oily **11**, α^{20}_D −76° was obtained. The 2*S*,3*S* absolute configuration was assigned to the latter compound because, once converted into the diacetate, oil, α^{20}_D +2.4°, it yielded, on ozonolysis, (3*R*,4*S*)-3,4-diacetoxypentan-2-one (**15**), α^{20}_D −41.5° (*c* 1, $CHCl_3$) (lit.[9] for the enantiomer, +42°).

Chart I



The major product of the ca. 9:1 mixture of diols obtained from **3** separated as crystals from ethyl acetate–hexane, mp 67–69 °C, α^{20}_D +41.6°. This was assigned the 2*S*,3*R* stereochemistry depicted in **12** because of its conversion through the ketone **16**, obtained by ozonolysis of the isopropylidene derivative, $LiAlH_4$ reduction, *O*-benzylation, and acid hydrolysis, into (2*S*,3*S*,4*R*)-4-(benzyloxy)hexane-2,3-diol (**17**), α^{20}_D −20° (*c* 1, $CHCl_3$), well in agreement with the literature value.[10] Similarly, the crude diol fraction from **4** separated crystalline **13**, mp 65 °C, α^{20}_D +9.4°. The erythro stereochemistry of **13** was demonstrated on the basis of its conversion[11] into the arabino δ-lactone (**18**), mp 186 °C, α^{20}_D −5.6°.[12] The preparation of **18** from **13** involved as key intermediate ethyl (4*R*,5*S*)-4,5-(isopropylidenedioxy)hept-2-enoate. Addition of ammonia onto the α,β-unsaturated ester takes place stereoselectively to give an adduct yielding on acid hydrolysis and N-benzoylation lactone **18**. In the *N*-trifluoroacetyl series, diisobutylaluminum hydride reduction of the C_7 lactone afforded the 3-aminoheptose derivative **19**, mp 195–197 °C, α^{20}_D −56° → −46° (*c* 1.3, EtOH). The negative sign of the optical rotation of **18** and **19** would suggest the L absolute configuration for these compounds and the 3*S*,4*R* stereochemistry depicted in **13** for the major product obtained from **4**, in analogy with the observed behavior of similar compounds from (2*S*,3*R*)-**8**.[11]

The α-hydroxy-α-methyl ketones **5** and **6** behave toward yeast reduction as the sets **1**–**2** and **3**–**4**, respectively. Whereas compound **5**, a methyl ketone similar to **1** and **2** affords in 80% yield a ca. 1:1 mixture of diastereoiso-

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(12) ^{1}H NMR (Me_2SO-d_6) δ 2.45 (H-2, J(2,2′) = 17.1 Hz), 3.07 (H-2′, J(2,3) = 6.4 Hz), 4.22 (H-3, J(2′,3) = 7.6 Hz), 3.66 (H-4, J(3,4) = 8 Hz), 4.09 (H-5, J(4,5) = 9.4 Hz), 1.58 (H-6, J(5,6) = 7.7 Hz), 1.89 (H-6′, J(5,6′) = 3.1 Hz, J(6,6′) = 14.4 Hz), 0.96 (CH_3, J(CH_3,6) = 7.2 Hz, J(CH_3,6′) = 6.4 Hz), 5.53 (OH, J(4,OH) = 6.1 Hz), 8.54 (NH, J(3,NH) = 7.8 Hz).

meric diols, α^{20}_D +14.5°, product **6**, an ethyl ketone like **4**, afforded in 15% yield (3*S*,4*R*)-**14**, oil, α^{20}_D −11.5°. Its absolute configuration is supported by the conversion via isopropylidene derivative and ozonolysis, into the optically pure aldehyde **20**, α^{20}_D +11.9° (lit.[13] −9.8° for the enantiomer). The hydroxy ketone recovered from the production of **14** showed α^{20}_D −22°. The latter material was submitted to the yeast reduction in two subsequent runs to give **14** in ca. 10% and 8% yield, respectively. The unreacted hydroxy ketone recovered at the end of this series of experiments showed α^{20}_D −56° and ^{1}H NMR studies on the material using tris[3-[(trifluoromethyl)-hydroxymethylene)]-(+)-camphorato]europium(III) indicated it to contain ca. 80% of a single enantiomer which we assign the 4*S* configuration depicted in **7**. The significance of the present results is further supported by the fact that the hydroxy ketone **21**, on yeast reduction, afforded ca. 70% yield of the 2*S*,3*R* diol **9** and the threo isomer **22**, α^{20}_D +74°, enantiomer of **11**, in ca. 6:4 ratio and which were separated by SiO_2 chromatography.

In summary, the above results point to the following conclusions. (a) For **1** and **2**, and probably for **5**, hydride addition to the carbonyl occurs on the *re* face regardless of the configuration of the adjacent chiral center. For **3**, **4**, and **6**, however, only the *R* enantiomer is reduced to a significant extent. (b) Hydride addition onto the *si* face of the carbonyl takes place in **21** irrespective of the configuration of the adjacent center. (c) Synthetic hydroxy ketones **1** and **2** are better substrates for the yeast enzymes than **3** and **4**. The first two are intermediates in the conversion of the aldehydes into diols (eq 1), whereas the second two are not formed directly from the corresponding aldehydes by yeast.

From a preparative point of view, the present work provides access to highly functionalized chiral carbonyl compounds like **7**, **15**, **16**, and **20**. Recently,[14] the enantiomer of the aldehyde **20** has been used as starting material in the synthesis of (+)-methynolide. A microbially aided synthesis of the enantiomer of **20** has been reported.[15] Furthermore, via yeast reduction of isomeric materials like **2** and **21**, the two enantiomeric forms **11** and **22** of products of potential synthetic interest for the synthesis of *N*-acyl derivatives of L- and D-vancosamine[16] become available.

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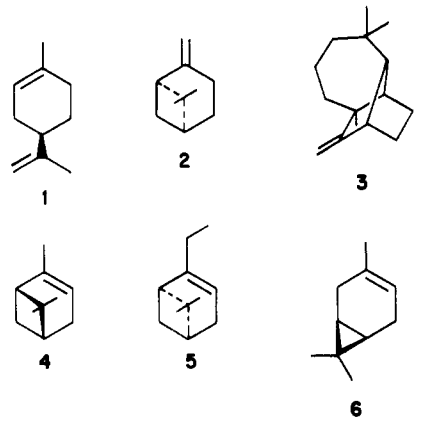
B-Allyldiisocaranylborane: A New, Remarkable Enantioselective Allylborating Agent for Prochiral Aldehydes. Synthesis of Homoallylic Alcohols Approaching 100% Enantiomeric Purities

Summary: *B*-Allyldiisocaranylborane undergoes enantioselective allylboration with a variety of aldehydes to furnish the corresponding homoallylic alcohols in 86–99% enantiomeric purities.

Sir: Several chiral *B*-allyldialkylboranes were prepared from readily available terpene hydrocarbons and treated with acetaldehyde to provide optically active 4-penten-2-ol. Among the various chiral allylboranes studied, *B*-allyldiisocaranylborane proved the most effective chiral allylborating agent. It undergoes condensation with a variety of aldehydes of different steric requirements to furnish secondary homoallylic alcohols with enantiomeric purities approaching 100%.

Homoallylic alcohols are synthetically valuable intermediates that have been used for stereoselective iodocyclization[1] and epoxidation.[2] Recently we reported that homoallylic alcohols with enantiomeric purities in the range of 83–96% are readily prepared by condensation of aldehydes with *B*-allyldiisopinocampheylborane.[3] In order to see if we could improve upon these highly promising results, we undertook exploration of other chiral *B*-allyldialkylboranes and studied the effect of the chiral ligand in this asymmetric allylboration[4] reaction.

B-Allyldialkylboranes were prepared from (+)-limonene (**1**), (−)-β-pinene (**2**), (+)-longifolene (**3**), (+)-α-pinene (**4**), (−)-10-methyl-α-pinene (**5**), and (+)-3-carene (**6**).



The preparation of the *B*-allyldialkylboranes in all these cases, except for (+)-limonene and (−)-β-pinene, is straightforward. Thus the terpene hydrocarbon is hydroborated with borane–methyl sulfide complex (BH_3·SMe_2) to the R_2BH stage, and the resulting dialkylborane is methanolyzed to provide the *B*-methoxydialkylborane. This intermediate, on subsequent treatment with allylmagnesium bromide, provides the desired *B*-allyldialkylborane. In the case of (−)-β-pinene, however, hydroboration with BH_3·SMe_2 cannot be stopped at the di-

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