Catalytic Decarbonylation of Epoxyaldehydes: Applications to the Preparation of Terminal Epoxides

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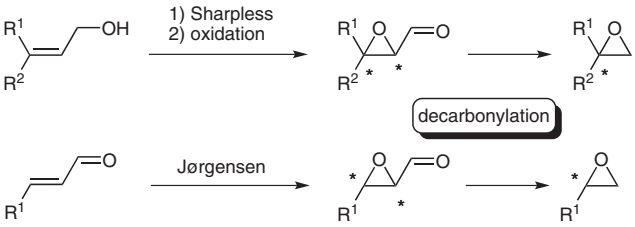
Abstract: A catalytic decarbonylation reaction for epoxyaldehydes is reported. This reaction may be sequentially used with known asymmetric methods to access optically active mono- and disubstituted terminal epoxides, as illustrated for a key example.

Key words: asymmetric synthesis, decarbonylation, epoxides, homogenous catalysis, rhodium

The catalytic decarbonylation of aldehydes has become a well-known reaction since its discovery by Tsuji and Ohno.[1] We previously used this reaction in a new strategy to access chiral building blocks in high optical purity, using the aldehyde as a removable steering group.[2] More recently, Madsen has used the catalytic decarbonylation of unprotected aldoses to generate polyols.[3] Herein we describe a procedure for the decarbonylation of epoxyaldehydes that permits preparation of a range of terminal epoxides. Moreover, this method, coupled with known asymmetric procedures for the preparation of optically active epoxyaldehydes, allows access to optically active terminal epoxides, which can otherwise be difficult to prepare.

Several approaches have been described for the enantioselective synthesis of epoxides. Sharpless pioneered the field with a titanium-mediated epoxidation of allylic alcohols, which still remains one of the most useful reactions in organic synthesis.[4] Jacobsen has described the selective kinetic resolution of terminal epoxides with a cobalt–salen complex.[5] Important additional advances for the enantioselective preparation of epoxides have also appeared.[6] Among these, Jørgensen has described an enantioselective epoxidation reaction of unsaturated aldehydes with hydrogen peroxide and a proline-derived catalyst.[7] Shi has used a sugar-derived organocatalyst in combination with oxone to epoxidize unfunctionalized olefins in high ee's.[8] More recently, List has disclosed a complementary strategy for the enantioselective epoxidation of unsaturated aldehydes.[9] Shibasaki has documented a catalytic, enantioselective approach to 2,2-disubstituted terminal epoxides through the addition of dimethylsulfonium methylide to ketones.[10]

Despite the number of available methods for enantioselective epoxidation, the asymmetric synthesis of terminal epoxides, and mainly disubstituted terminal epoxides, remains a challenge for organic chemistry.[11] Consequently, we sought a complementary strategy for the preparation of optically active epoxides by combining existing methods for the preparation of optically active epoxyaldehydes and catalytic decarbonylation processes (Scheme 1). Herein we document for the first time the decarbonylation reaction of epoxides, a reaction lacking in precedence. The work extends the approach we have previously reported involving the use of removable groups as a strategy for the preparation of optically active building blocks.[2]



Scheme 1 Decarbonylation strategy for the preparation of optically active terminal epoxides

The implementation of the decarbonylation approach with epoxyaldehydes is not without potential pitfalls. Thus, for example, epoxides themselves are known to form rhodaoxetanes with certain rhodium complexes.[12] Of additional concern, it was not clear if it would be possible to decarbonylate epoxyaldehydes without having the product oxirane suffer ring opening.

We initiated the project by identifying optimal conditions for the decarbonylation of racemic citral oxide (Table 1, entry 1), which is easily accessible by aqueous epoxidation of the commercially available citral. Screening of a variety of solvents, reaction temperatures, and ligands with Rh(I) catalysts, afforded an optimal yield of 73% for this substrate. The major side-product of the reaction could be identified as 6-methyl-5-hepten-2-one, which is likely to form via a rhodaoxetane intermediate derived from the oxidative addition of the Rh-catalyst to the product epoxide that subsequently undergoes fragmentation to give the ketone and a rhodium–methylene complex.[12] Nonetheless, encouraged by this result, we investigated the scope of the reaction (Table 1).[13]

The various substrates undergo decarbonylation in 40–73% yield. In all cases, the corresponding rearrangement product, the methylketone or corresponding aldehyde, was isolated as a by-product. The reaction shown in Table 1, entry 5 was problematic and represents a limitation to the method because, under the standard conditions

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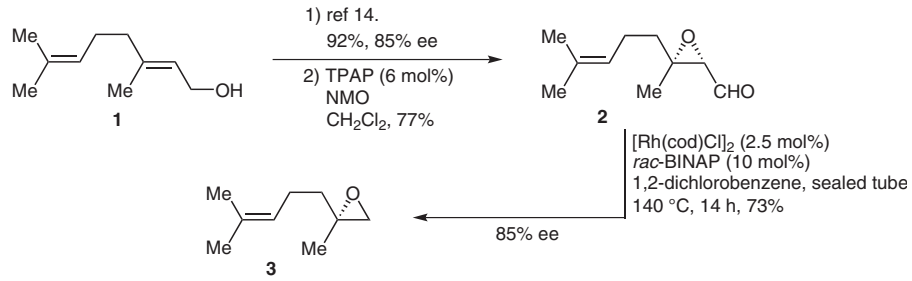
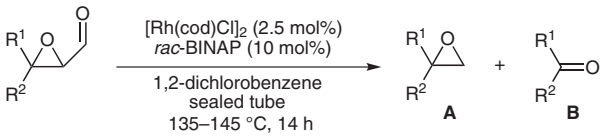
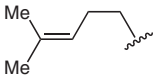
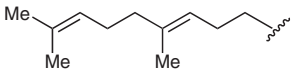
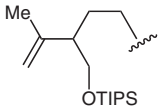


Scheme 2 Preparation of an optically active epoxide

Table 1 Decarbonylation of Racemic Epoxyaldehydes



Entry	R^1	R^2	Yield A (%)[a]	Yield B (%)[a]
1		Me	73	23
2		Me	45	40
3	Ph	H	63	26
4	*n*-Heptyl	H	64	23[b]
5[c]	Ph	Me	40	20[b,d]
6		Me	64	30
7		Me	54	34

[a] Isolated yield.
[b] NMR yields.
[c] Reaction performed in *p*-cymene with (*S*)-BINAP as ligand.
[d] 35% of 2-phenylpropanal was isolated.

described above, this reaction gave 2-phenylpropanal as the major product without any traces of α-methylstyrene oxide. The formation of 2-phenylpropanal might be rationalized by a Pinacol-type rearrangement of the corresponding decarbonylated epoxide. However, the use of a less polar solvent, *p*-cymene, provided moderate yields of the desired product epoxide. (*S*)-BINAP was used in this case since precipitation was observed to occur with the *rac*-BINAP in *p*-cymene, whereas the complex formed with (*S*)-BINAP produced a homogenous solution throughout the reaction course. To our knowledge, this difference in behavior between the racemic and the enantiopure BINAP has not been previously noted.

The reaction conditions are compatible with trisubstituted double bonds (Entries 1 and 6). This last result is of relevance, since known asymmetric epoxidation methods of unfunctionalized olefins are based on electrophilic reagents and are, thus, unable to selectively epoxidize electron-poor double-bonds in the corresponding precursors.

After having explored the scope of the reaction on racemic substrates, we prepared an optically active epoxyaldehyde in order to test whether the decarbonylation of chiral epoxyaldehydes would afford optically active epoxides. Sharpless asymmetric epoxidation[14] of **1**, followed by TPAP/NMO oxidation, furnished **2** in 71% yield and 85% ee (Scheme 2). Subjecting this epoxyaldehyde to decarbonylation conditions provided **3** in 73% yield and 85% ee. Thus, no significant loss of optical purity was observed in the course of the decarbonylation reaction.

In conclusion, we have developed a new catalytic decarbonylation reaction, which was not previously known for epoxyaldehydes. When coupled with known asymmetric transformations that yield optically active epoxyaldehydes, decarbonylation provides access to optically active terminal epoxides **3** in good ee without any observable racemization, as determined for a test substrate.

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(13) **General procedure for the decarbonylation reaction:** $[Rh(cod)Cl]_2$ (3.8 mg, 0.0077 mmol) and *rac*-BINAP (18.5 mg, 0.03 mmol) were dissolved in *o*-dichlorobenzene (3 mL) in a 25 mL sealed tube under an argon atmosphere. After 15 min of stirring at r.t., a homogenous dark-red solution formed. The corresponding α,β-epoxyaldehyde (0.3 mmol) was then added to the stirring mixture, the tube was evacuated and filled with argon three times and finally sealed under vacuum. The reaction mixture was then immerged in a pre-heated oil bath at the corresponding temperature (140 °C). After 14 h, the mixture was cooled to r.t. and directly loaded onto a column packed with silica gel. Prior elution with pure pentane to remove the *o*-dichlorobenzene, followed by elution with the corresponding solvent mixture (pentane–Et_2O) afforded the pure compound as an oil. **Caution: careful work-up is necessary since some of the products are highly volatile!**

Triisopropyl{3-methyl-2-[2-(2-methyloxiran-2-yl)ethyl]but-3-enyloxy}silane (Table 1, entry 7, A): ^{1}H NMR (300 MHz, $CDCl_3$): δ (mixture of isomers) = 4.81 (br s, 1 H), 4.70 (br s, 1 H), 3.62–3.58 (m, 2 H), 2.60–2.57 (m, 2 H), 2.19 (m, 1 H), 1.63 (s, 3 H), 1.60–1.40 (m, 4 H), 1.30 (s, 3 H), 1.05 (m, 21 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (mixture of isomers) = 145.4, 112.1, 66.4, 57.0, 54.1, 53.8, 49.8, 34.4, 25.0, 21.1, 21.0, 20.3, 20.2, 18.2, 12.1. IR (neat): 2924 (m), 2865 (m), 1462 (m), 1106 (m), 882 (s), 680 (s) cm^{-1}. HRMS (ESI): *m*/*z* calcd for $C_{19}H_{38}O_2SiNa^+$: 349.2534; found: 349.2534.

6-Methyl-5-[(triisopropylsilyloxy)methyl]hept-6-en-2-one (Table 1, entry 7, B): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.81 (s, 1 H), 4.70 (s, 1 H), 3.62–3.58 (m, 2 H), 2.43–2.38 (m, 2 H), 2.19 (m, 1 H), 2.12 (s, 3 H), 1.82 (m, 1 H), 1.66 (s, 3 H) 1.60 (m, 1 H), 1.05 (m, 21 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 209.1, 145.3, 112.3, 66.2, 49.2, 41.5, 29.8, 23.4, 19.8, 17.9, 11.9. IR (neat): 2942 (m), 2865 (m), 1719 (s), 1112 (m), 881 (s), 679 (s) cm^{-1}. HRMS (ESI): *m*/*z* calcd for $C_{18}H_{36}O_2SiNa^+$: 335.2377; found: 335.2376.

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