

Intramolecular Induction of Asymmetric Darzen's Condensation of Aldehydes with Chiral α -Chloroacetates

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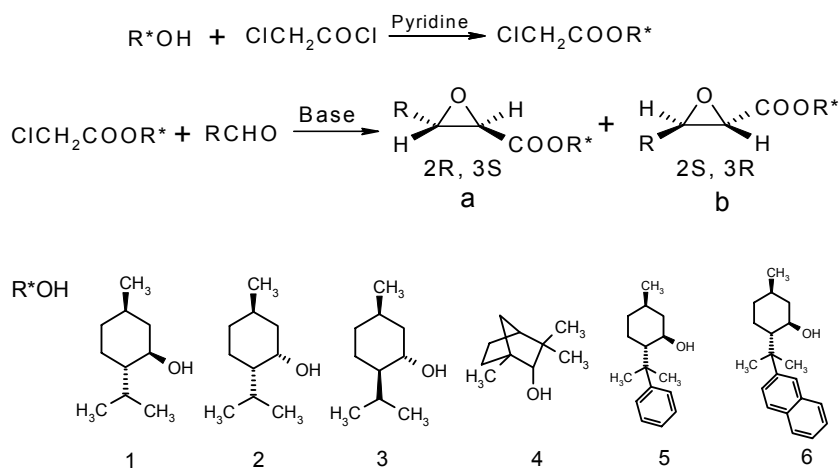
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Abstract: The asymmetric Darzen's condensation of aldehydes with α -chloroacetates of some naturally occurring or synthetic chiral alcohols was described. The de% of products fell over the range of 4.78% to 99%.

Keywords: Asymmetric Darzen's condensation, chiral α -chloroacetates.

In convergent with our interest in the asymmetric synthesis of natural products, intramolecular induction of asymmetric Darzen's condensation¹ of aldehydes with α -chloroacetates of chiral alcohols was studies, as shown in **Scheme 1**.

Scheme 1.



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|---------------------------|---------------------------|--|
| 1. (-)-menthol (45.0%) | 3. (+)-isomenthol (15.6%) | 5. (-)-8-phenylmenthol (74%) |
| 2. (+)-neomenthol (14.7%) | 4. (+)-fenchol (4.78%) | 6. (-)-8- β -naphthylmenthol (99%) |

The numbers in the parenthesis indicated the ee% of the corresponding methyl 3-phenylglycidate obtained by transesterification.

Benzaldehyde reacted with α -chloroacetates of chiral alcohols (**1-4**) on treatment with sodium hydride to afford *trans*-3-phenylglycidic esters (**a+b**) with chemical yields of 66.2~82%. The crude product was transesterified with NaOMe/MeOH directly to give the methyl *trans*-3-phenylglycidate of which the specific rotation was determined and calculated. The values of ee% obtained were in range of 4.78~45.0%, and with the exception of 2 and 3, all the others gave the 2R, 3S configuration. Among them, (-)-menthyl *trans*-3-phenylglycidate with good optical and chemical purity was obtained in 40% yield (mp: 60~62°C, $[\alpha]_{\text{D}}^{20} = -167$, (c 1.2 CHCl₃) after repeated recrystallizations of the crude product. The recrystallized product was transesterified with MeONa/MeOH to give (-)-2R, 3S-methyl 3-phenylglycidate in 85% yield $\{[\alpha]_{\text{D}}^{20} = -171$, c 1.1 CHCl₃; lit²: $[\alpha]_{\text{D}}^{15} = -171.2$, c 1.13 CHCl₃}.}

In order to improve the optical yield, α -chloroacetates of (-)-8-phenylmenthol³ **5** and (-)-8- β -naphthylmenthol⁴ **6** were applied. The enantioselectivity was raised to 74% and 99% respectively in case of benzaldehyde. Benzaldehydes substituted with electron donating groups such as p-methoxybenzaldehydes gave the product (de%=99%) with higher de% than that of benzaldehydes with electron withdrawing groups such as p-nitrobenzaldehyde (de%=33%). While aliphatic aldehydes were used as substrates, the de values (20~50%) of the products were reduced significantly.

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