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ENANTIOSELECTIVITY OF ACYL MIGRATION IN 2,2,4-TRIMETHYLPENTANE-1,3-DIOL MONOESTERS IN THE PRESENCE OF CHIRAL BINOL CATALYST

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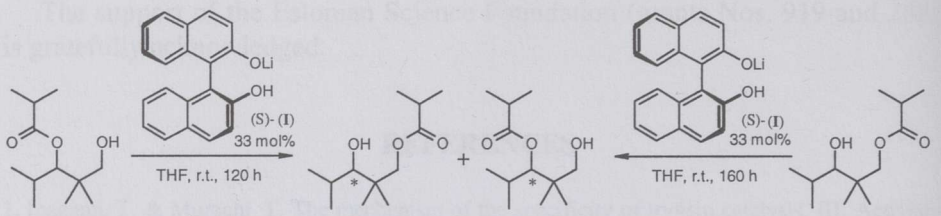
ENANTIOSELEKTIIVSUS 2,2,4-TRIMETÜÜLPENTAAN-1,3-DIOOLI MONOESTRITE ATSÜÜL-MIGRATSIOONIL KIRAALSE BINOL-KATALÜSAATORI MANULUSEL. Olavi LOOG ja Uno MÄEORG

Key words: enantioselectivity, acyl migration, 1,3-diol monoesters, binaphthol catalyst, stereochemistry.

Acyl migration in 1,3-diol monoesters may be treated as the intramolecular transesterification where the acyl donor and acceptor are in the same molecule in the close proximity, limiting the possible reaction paths compared with intermolecular transesterification. In a few cases, the acyl transfer in the regioisomers of 1,3-diol monoesters is mentioned [1–5] and found to be dependent on substrate, reaction conditions and time [1–3], but the chiral aspects of this isomerization have not been studied so far.

Investigating the self-condensation reaction of 2-methylpropanale to 2,2,4-trimethylpentane-1,3-diol monoesters, we have also observed the acyl migration, where the initially formed secondary monoester (**1**) is partially re-esterified to the sterically less crowded primary monoester (**2**) [1]. However, when the reaction was performed in the presence of chiral binaphthol catalysts, the enantiomeric composition of products seemed to be also affected by the acyl migration. Two experiments were performed for further confirmation. In both, a racemic regioisomer of monoester was used as a substrate in the conditions similar to the aldehyde self-condensation reaction. The results of these reactions are given in the Table below.

Re-esterification reactions of diol monoesters with catalyst (S)-(I)[a]



Entry	Sub-strate	Reaction time, h	(1')/(2')[b]	Enantiomeric composition of (1')[c]			Enantiomeric composition of (2')		
				(S)-(1') %	(R)-(1') %	ee %	(S)-(2') %	(R)-(2') %	ee %
1	(1)[d]	120	38/62	43.0	**57.0**	14.0	**55.0**	45.0	10.0
2	(2)	160	28/78	**55.4**	44.6	10.8	47.8	**52.2**	4.4

[a] Reactions were performed by adding substrate to the solution of (S)-(**I**) in THF and quenched with saturated solution of NH_4Cl. Monoesters were separated from catalyst by distillation *in vacuo* and the regioisomers were separated by column chromatography on silica gel. Yield of (**1'**) + (**2'**) was after distillation 88% for entry 1, and 92% for entry 2.

[b] The ratios of primary and secondary monoesters were calculated from the chromatographic data.

[c] Monoesters were hydrolyzed and then derivatized to diacetates before the determination of enantiomeric compositions with GLC on chiral capillary column Chiraldex™ B-PH. The absolute configurations were assigned comparing the retention times of enantiomers in the samples and enantiomers with known configuration ((S)-2,2,4-trimethylpentane-1,3-diol diacetate eluted first from Chiraldex™ B-PH). Pure diol enantiomers with known configurations were prepared by the method described by Harada [6].

[d] Monoester (**1**) contained initially ~15% of monoester (**2**).

The enantiomeric excesses were quite small in those model experiments, but they clearly showed that the acyl migration in both directions is affected by the chiral catalyst (S)-(**I**) so that the monoesters with (S)-configuration will be preferentially re-esterified. The results also indicate that the acyl migration must be intramolecular proceeding in both directions through the similar activated complexes co-ordinated on metal atom in the catalyst. Activated complex may be co-ordinated not only on the added catalyst, but to some extent also on the surface of reaction container walls. For example, we have observed the acyl migration in pure secondary monoester samples if they were kept in glass vials at +4°C for several months. This reasoning is supported by the following observations: only monoesters are present in the reaction mixtures; and the enantiomeric ratios are proportional in secondary and primary monoesters (if one enantiomer in one monoester is in excess, then it is present proportionally in a lesser amount in the other).

The practical value of this kind of re-esterification for preparing enantiopure diols seems to be limited, because even if the selectivity could be enhanced in other conditions or using other catalysts, it would still be the equilibrium reaction (the enantiomeric excesses of both products will gradually decrease as the reaction reaches the equilibrium [7, p. 414]). However, as shown above, the intramolecular acyl migration may affect the stereochemistry of products and should be considered in analogous systems, whenever the chiral selector is present.

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