58. Asymmetric Hydroformylation of α-[^{2}H]-Styrene

Preliminary Communication

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(31. I. 77)

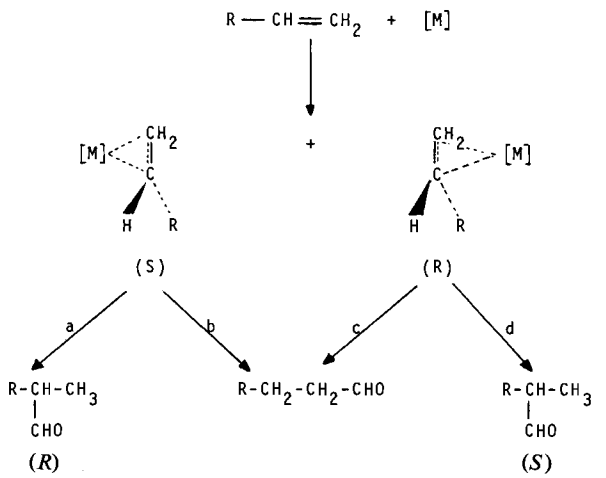
Summary

The hydroformylation of α-[^{2}H]-styrene in the presence of an asymmetric rhodium-catalyst afforded two optically active isomeric aldehydes. The origin of the asymmetric induction is discussed on the basis of the chirality and the optical purity of the two products.

In a preliminary attempt of rational interpretation of the asymmetric induction promoted by optically active catalysts, in the hydroformylation reaction [1], it was assumed that the enantiomeric excess observed for the asymmetric products, arises from the preferential attack of the catalyst at one of the two prochiral faces of the substrate (enantioselectivity). More recently, however [2], the differential regioselectivity of the reaction for the two enantiofaces of a prochiral olefin has been postulated as a possible additional factor controlling the asymmetric induction. *Scheme 1* illustrates both possible ways for the origin of asymmetric induction in the case of an olefin with terminal double bond: when $a+b \neq c+d$, the reaction is enantioselective; when $a/b \neq d/c$, the regioselective factor plays its role in determining the enantiomeric composition of the asymmetric product, and optically active aldehyde will be formed even if $a+b$ equals $c+d$.

According to the above scheme, the asymmetric induction in the hydroformylation of prochiral olefins can in general arise from the independent contribution of both factors. Anyway, their relative importance in the determination of the asymmetric induction can be evaluated only when a new asymmetric centre is originated in both isomeric aldehydes formed by hydroformylation of the double bond. In this case the asymmetric induction arising from the preferential attack at one prochiral face of the substrate ($a+b \neq c+d$) will be identical for both hydroformylation products, and two aldehydes with the same prevalent chirality and enantiomeric excess would be formed in absence of additional factors. On the other hand, the asymmetric induction arising from the different regioselectivity for the two prochiral faces ($a/b \neq d/c$) will

Scheme 1



[M] represents the catalyst.
a, *b*, *c* and *d* represent the molar fractions of the reacting species.

be of opposite sign for the two isomers formed, and have absolute value inversely proportional to their molar fraction.

α-[^{2}H]-Styrene was chosen as a suitable substrate for providing experimental evidence of the hitherto discussed phenomenon. The hydroformylation was carried out in the presence of hydridocarbonyl-tris(triphenylphosphine)rhodium and (−)-DIOP [3], under conditions proved to afford, from styrene, (−)-(*R*)-2-phenylpropanal with substantial asymmetric induction [4]. 2-[^{2}H]-2-Phenylpropanal and 3-[^{2}H]-3-phenylpropanal were obtained in the ratio of 60:40 after 60% conversion. The optical rotation of 2-[^{2}H]-2-phenylpropanal, measured on a mixture containing 30% of this aldehyde, indicated a prevalence of (*R*)-chirality and 15% enantiomeric excess[1]), in agreement with what expected from previous experiments made with unlabeled styrene [4] [6].

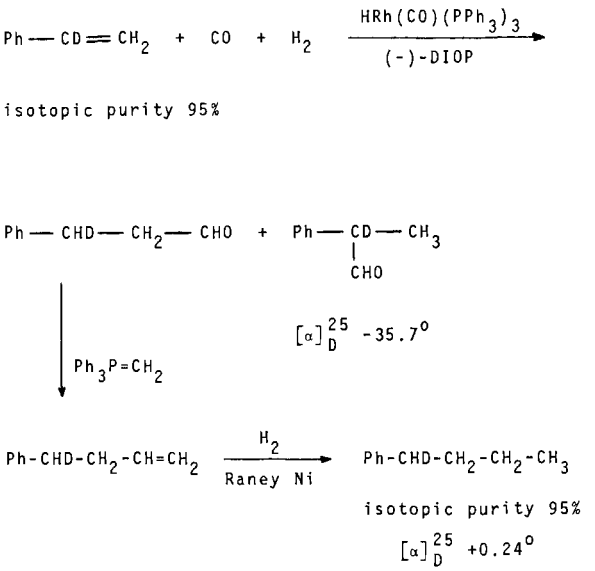
3-[^{2}H]-3-Phenylpropanal was converted into 1-[^{2}H]-1-phenylbutane with complete retention of deuterium in the α-position, according to MS. and NMR. analysis, through the reaction sequence illustrated in *Scheme 2*. The product eventually obtained, purified by VPC., was also optically active: the rotation indicated a prevalence of (*S*)-chirality and 14.2% optical purity[2]), that, corrected for one atom of deuterium per molecule, corresponds to 15% enantiomeric excess.

The prevalence of (*R*)-configuration for 2-[^{2}H]-2-phenylpropanal and (*S*)-configuration for 1-[^{2}H]-1-phenylbutane, corresponds to the preferential attack, in the hydroformylation, at the same face of α-[^{2}H]-styrene, namely the *re-re* face according

[1]) The value extrapolated for the rotation of optically pure (−)-(*R*)-2-phenylpropanal, $[\alpha]_D^{25} = -238°$ [5], has been assumed as maximum value for the optical activity of the corresponding 2-deuterio-compound. In view of the extremely high tendency of optically active 2-phenylpropanal to racemize [5], some racemization during the working up cannot be excluded; the consequent decrease of the optical purity should be contained, in the conditions adopted, within 10% [6].

[2]) $[\alpha]_d = -1.70°$ (neat) has been calculated for optically pure (−)-(*R*)-1-[^{2}H]-1-phenylbutane [7].

Scheme 2



to the *Hanson's* nomenclature [8]. Thus it appears that enantioselectivity is the determinant factor promoting the asymmetric induction observed in the case investigated. Furthermore, the pretty good agreement between the optical purities of the two products obtained, indicates that the regioselective factor does not play, in this case, a significant role.

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