

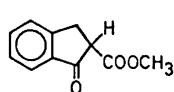
Short Communications

Asymmetric Induction in a Michael-type Reaction

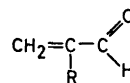
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This paper briefly reports some preliminary results which demonstrate asymmetric induction in a base-catalyzed Michael-reaction. Previous studies on asymmetric Michael additions have involved the use of chiral reagents.¹ Walborsky and co-workers,² for example, studied the addition of (-)-menthyl chloroacetate to ethyl acrylate using achiral alkoxides as catalysts. Similarly, the addition of Grignard reagents to chiral α,β -unsaturated esters has been extensively studied.³ Except for some enzymatic reactions, however, the addition of achiral nucleophiles to the carbon-carbon double bond of an achiral substrate under the influence of a chiral catalyst has been little studied.⁴ Thus, the present paper is the first report of the use of a chiral catalyst in a Michael addition. Recently, a similar asymmetric induction in an aldol-type reaction⁵ was described.

The present investigation deals with the addition of methyl 2-carboxy-1-indanone (I) to acrolein (IIa) or α -isopropylacrolein (IIb) using optically active 2-(hydroxy-methyl)-quinuclidine (III) as catalyst in benzene solution at room temperature. The course of the reactions were followed by PMR, with which it was shown that the addition products (IV) are formed quantitatively. The optical rotations of the reaction mixtures were also followed as a function of time and found to change continuously towards a limiting value different from zero, thus indicating the formation of optically active products. The addition products (IVa) and (IVb),

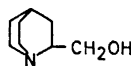


I

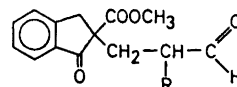


II

- a) R = H
b) R = CH₃-CH-CH₃



III



IV

- a) R = H
b) R = CH₃-CH-CH₃

respectively, were isolated and found to be optically active. As an additional test for the optical activity of the products, the semicarbazone derivatives were prepared, purified and tested for optical activity.

The Michael addition reaction involves at least three steps. Firstly, the catalyzing base removes the acidic proton in I with the generation of the nucleophilic stabilized carbanion. Secondly, this nucleophile adds to the activated carbon-carbon double bond in II, and finally the intermediate addition product is protonated at the carbon atom in the α -position to the aldehyde group with the formation of the end product IV. When acrolein (IIa) is used as a reactant, only one asymmetric centre is created in the product IVa. The fact that this product is optically active proves that the catalyzing base, or more precisely its corresponding acid, is present in the second step of the reaction. The most plausible interpretation is that an ion pair between the enolate ion of I and the protonated form of III constitutes the nucleophilic species which adds to the activated double bond in IIa.

When α -isopropylacrolein (IIb) is used as a substrate, the optical activity found

in the product IVb does not prove that the catalyzing base is present in the addition step, since optical activity would also be created in the final protonation step if this is accomplished by the protonated form of III. By analogy with the reaction involving IIa it seems probable, however, that the asymmetric induction also occurs in the addition step for IIb. Product IVb is, of course, a mixture of two diastereomers, as demonstrated by the PMR-spectrum. Preliminary experiments have shown that the initially observed diastereomeric ratio is kinetically controlled.

As yet it is not possible to say anything regarding the degree of asymmetric induction in these reactions.

Experimental. The PMR-spectra were recorded with a Varian A60-D instrument at 34°C. Optical rotations were measured with a Perkin-Elmer 141 M apparatus at 546 nm. The microanalyses were performed at the Department of Analytical Chemistry, University of Uppsala.

Methyl 2-(2-formylethyl)indan-1-on-2-carboxylate (IVa). In a 100 ml volumetric flask 0.82 g (0.147 mol) of freshly distilled acrolein, 2.76 g (0.146 mol) of 2-carbomethoxy-1-indanone⁶ and 0.0058 g (0.00004 mol) of a freshly sublimed and partially resolved (*R*)-(+)-2-(hydroxymethyl)-quinuclidine (III)⁷ ($[\alpha]_{546}^{25.0} = +77.0^\circ$, 57% enantiomeric excess¹) were dissolved in benzene and diluted to 100 ml. The reaction temperature was $22.00 \pm 0.02^\circ\text{C}$. After 20 h, the reaction was complete as determined by PMR and polarimetry. The reaction mixture was washed with 5×100 ml of water and 150 ml of a saturated sodium chloride solution. The benzene layer was then dried, evaporated and the residue distilled; b.p. $150-152^\circ\text{C}/0.1$ mmHg. PMR chemical shifts (δ ppm. relative TMS) methylene 2.00–2.75, methylene in the ring 2.85–3.85, methyl ester 3.67, aldehyde 9.65, and aromatic protons 7.30–7.80. The specific rotation of IVa was $[\alpha]_{546}^{21.0} = +8.83^\circ$ (*c* 6.53, CCl_4). (Found: C 68.70; H 5.75. Calc. for $\text{C}_{14}\text{H}_{14}\text{O}_4$ (246): C 68.29; H 5.69.)

The semicarbazone derivative⁸ of IVa had m.p. $133-135^\circ\text{C}$ and a specific rotation $[\alpha]_{546}^{20.0} = +3.75^\circ$ (*c* 0.96, ethanol). (Found: C 59.44; H 5.66; N 13.82. Calc. for $\text{C}_{15}\text{H}_{12}\text{N}_3\text{O}_4$ (303): C 59.40; H 5.61; N 13.86.)

Methyl 2-(2-formyl-3-methylbutyl)indan-1-on-2-carboxylate (IVb). As above 2.76 g (0.028

mol) of freshly distilled α -isopropylacrolein⁹ and 4.77 g (0.025 mol) 2-carbomethoxy-1-indanone⁶ were dissolved in benzene and 0.2376 g (0.0017 mol) of freshly sublimed and partially resolved (*R*)-(+)-III ($[\alpha]_{546}^{25.0} = +77.0^\circ$)⁷ was added. The mixture was diluted to 100 ml with benzene and kept at $44.00 \pm 0.1^\circ\text{C}$. After 30 days, the reaction was complete according to PMR analysis. The mixture was washed with 5×100 ml of water and 150 ml of a saturated sodium chloride solution. The organic layer was dried and evaporated. The residue was not sufficiently stable to be distilled but the raw product of IVb had a specific rotation $[\alpha]_{546}^{44.0} = +28.8^\circ$ (*c* 5.22, benzene). PMR chemical shifts (δ ppm. relative TMS) methylene and methine 1.60–2.60, methylene in the ring 2.75–3.75, methyl 0.80–1.10, methyl ester 3.60, aldehyde 9.40–9.58 and aromatic protons 7.30–7.80.

The semicarbazone derivative of IVb⁸ had m.p. $196.0-197.5^\circ\text{C}$ and a specific rotation $[\alpha]_{546}^{20.0} = -3.2^\circ$ (*c* 0.25, dimethyl sulphoxide). (Found: C 62.34; H 6.69; N 12.10. Calc. for $\text{C}_{18}\text{H}_{23}\text{N}_3\text{O}_4$ (345): C 62.60; H 6.66; N 12.17.)

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