This Week's Citation Classic


April 5, 1989

I became aware of the extensive work of Alexander McKenzie and coworkers only in 1948 by reading a review article of P.D. Ritchie about asymmetric synthesis. Since 1948 they had studied optical activity of α-hydroxy acids obtained by treatment of α-keto acid esters of chiral alcohols with Grignard reagents and saponification of the resulting esters.

On the basis of the assumption that in acyclic cases the stereoselectivity is sterically controlled by conformation, a simple scheme was proposed to predict the steric course of these asymmetric reactions. It gave me great satisfaction that several previous experimental results, which were not in agreement with these predictions, turned out to be erroneous. By repeating McKenzie’s experimental work we could show that those results, which contradicted the scheme, were due to partial asymmetric saponification of the α-hydroxy acid esters of the chiral alcohols. When saponification was complete, the results were in agreement with our predictions.

By this discovery I became so confident about the predictive power of the scheme that I started to use, successfully as it turned out, the asymmetric synthesis of α-lactone acid, from phenylglyoxylic acid esters of chiral natural alcohols, to determine the unknown absolute configuration of these α-esters.5,6 Applying the same ideas to the steric control of "asymmetric syntheses," we also designed and prepared auxiliary alcohols, leading to increased optical yields of α-hydroxy acids.6,7

I lectured about this work in the summer of 1951 to the XIth International Congress of Pure and Applied Chemistry in New York City.8 On a trip after the congress I met Don Cram for the first time. He told me that he developed ideas similar to ours to explain the stereoselectivity of reactions studied by his group. His seminal paper about this topic appeared in 1952.9 Our common early efforts to predict and control stereoselectivity, which today plays such an enormous role in organic chemistry [see, for example, reference 8], stimulated experimental work as well as criticism from many chemists. This is probably the reason my paper is also often cited.