The Stereochemical Properties of the 'Schwartz's Reagent' $(\eta_5\text{-}C_5H_5)_2Zr(H)Cl$ in the Reduction of Cyclic Ketones to Alcohols

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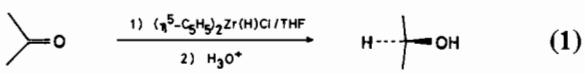
The hydrido complex bis(cyclopentadienyl)zirconiumhydridochloride **1** has been shown by Schwartz to be a versatile reducing agent of different unsaturated compounds [1]. The reduction proceeds *via* stable organozirconium intermediates which react with electrophilic reagents, such as HCl, under mild conditions to give a variety of linear saturated organic products in usually high yields. In the meantime the bis(cyclopentadienyl)zirconiumdichloride, which is formed almost quantitatively, can be easily reduced again to **1** with $LiAlH(t\text{-}BuO)_3$ in THF [2]. Such a relatively easy recycle of the reducing complex hydride makes the 'Schwartz's reagent' more attractive for stoichiometric organic reductions than the classical boron or aluminum complex hydrides [3].

Unfortunately the major amount of the reported experimental work deals with the reduction of C=C or C≡C bonds; the reduction of the C=O bond (such as in ketones or aldehydes) to the corresponding alcohols has been only briefly cited [1] but never reported. Only the reduction of acetone by the related bis(cyclopentadienyl)zirconiumdihydride, $(\eta^5\text{-}C_5H_5)ZrH_2$ was briefly reported [4]. Very few data are available which describe the use of a derivative of complex **1** obtained by condensation of one mol of borane-methyl sulphide with complex **1** to give the bis (cyclopentadienyl) zirconiumchlorotetrahydroborate [5], for the stereoselective reduction of 4-tert-butylcyclohexanone. As the stereochemical aspects of the reductions by complex **1** were never investigated, we wish to report here our investigations concerning the possible use of bis(cyclopentadienyl)zirconiumhydridochloride **1** for the stereoselective reduction of ketones to alcohols.



(1)

Initially, owing to the bulkyness of the hydrido complex **1**, it should be expected that the reduction of cyclic ketones could proceed with relatively high stereoselectivity, as observed with boron hydrides of different bulkyness [6]. We have found that cyclic ketones are reduced in THF or benzene solutions to the corresponding alcohols in rather low yields at room temperature, but by increasing the reaction temperature to 60 °C yields can be improved to acceptable values (Table I).

TABLE I. Catalytic Data.

Ketone[a]	Temp. °C	Time hr.	Yield %	Major[b] isomer %
Cyclohexanone	20	2	100	–
Acetophenone	20	12	3	–
Acetophenone	60	12	3	–
3-Methylcyclohexanone	20	4	47	68 *cis*
4-tert-Butylcyclohexanone	20	4	58	62 *cis*
Menthone	20	6	13	68 neomenthol
Menthone	50	6	64	72 neomenthol
Camphor	20	6	13	75 isoborneol
Camphor	60	6	44	76 isoborneol
3-Cholestanone	20	6	13	80 3-α-cholestanol[c]

[a]Ratio of hydrido complex 1 to ketone of 1.2. [b]Isomers distribution was determined by GLC. [c]3-α- and 3-β-Cholestanol were identified by GLC/MS.

In a standard procedure 1.2 mmol of the hydrido complex **1** are suspended in 5 ml THF under nitrogen; 1 mmol of the appropriate substrate is added by a syringe through a serum cap. The stirred suspension slowly turns to a pale yellow solution. The solution is quenched with 5 ml HCl 1 *M*; the organic layer is dried over Na_2SO_4 and evaporated to small volume leaving a pale yellow oil. The oil is dissolved in 5 ml ethanol and this solution, on standing in freezer, deposits more than 80% of the original bis(cyclopentadienyl)zirconiumdichloride, (calculated on complex **1**). Yields and isomer distribution is determined on the filtered ethanolic solution by GLC. Distillation bulb to bulb affords the alcohols which are identified by IR, NMR and MS and by comparison with pure samples.

In comparison with $(\eta^5\text{-}C_5H_5)_2ZrClBH_4$ [5] the reduction is not so net as with an aromatic ketone such as acetophenone; in this case the yield of reduction is extremely low even if the addition of the ketone to the suspension of **1** involves the dissolution of the hydride to form an homogeneous solution. After hydrolysis with aqueous HCl, effectively all the starting material is recovered. A possible reaction of the enolic form of the ketone is unlikely, in that the evolution of hydrogen has not been observed.

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When the quenching of the organometallic zirconium intermediate is carried out with saturated THF solutions of gaseous HCl, the yield of the desired product is still low but other products such as styrene and α-chloroethylbenzene are formed in variable amounts. In conclusion the presence in α to the carbonyl group of an aromatic ring makes the cleavage of the organometallic zirconium intermediate rather complex, probably *via* a stable carbocation. With cyclic ketones the stereoselectivity observed usually involves a preferential equatorial attack to give the corresponding axial alcohol. It appears that complex **1** resembles the behaviour of the alkohoxy boron hydrides which prefer the equatorial attack but with highest stereoselectivity [6]. A discrepancy appears in the reduction of the 3-methylcyclohexanone in which the attack is predominantly axial to give 3-methylcyclohexanol with a *cis/trans* ratio of 70/30, a value that reflects the composition of the thermodynamic mixture. However, in the reduction of 3-cholestanone the complex **1** shows again a marked preference for the equatorial attack to give the corresponding 3-α-cholestanol. This is an interesting result since with normal reducing hydrides 3-β-cholestanol is preferentially formed [7]. Interestingly the stereoselectivity appears to be reversed on going from complex **1** to $(\eta^5\text{-}C_5H_5)_2ZrClBH_4$, showing how important is the nature of the reducing active site in defining the stereoselectivity of the attack even in complexes which are structurally related [5].

In conclusion we have found that the hydrido complex **1** is a reasonable good reducing agent of cyclic ketones (and also normal ketones) but it does not work properly with ketones having an aromatic group in the α position.

Strangely enough an increase of temperature, which increases the yields of the reduction, does not affect the stereoselectivity.

Work is in progress to investigate the regio- and stereoselectivity in the reduction of different organic molecules of natural origin.

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