

ASYMMETRIC HYDROSILYLATION OF KETONES*

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A series of eleven dialkyl and alkyl aryl ketones was hydrosilylated by diphenylsilane in the presence of rhodium(I) complexes prepared *in situ* from $[\{\text{RhCl}(\eta\text{-C}_2\text{H}_4)_2\}_2]$ and a chiral tertiary phosphine ligand derived from (R)-tartaric acid. Variations in the structure of the ligand rendered it possible to prepare the alcohols $\text{RCH}(\text{OH})\text{C}_6\text{H}_5$ in 40–56% optical purity and the alcohols $\text{CH}_3\text{CH}(\text{OH})\text{R}$ with an optical purity of 23–35%. Changes in the optical purity of products with the structure of ketones and ligands are confronted with the model proposed for [(2,2-dimethyl-1,3-dioxolane-4,5-diyl)bismethylene]bis(diphenylphosphino)rhodium(I) complexes.

In the previous work¹ we have reported on the efficiency of a series of tertiary phosphines derived from tartaric and malic acids, camphor and galactose as ligands in asymmetric hydrosilylation of ketones catalysed by rhodium(I) complexes of different types. The present work extends this study to a series of dialkyl and alkyl aryl ketones with the aim to ascertain how variations in the structure of the substrates affect the optical purity of products. For this purpose phosphines *I–III*, analogues of the well-known [(2,2-dimethyl-1,3-dioxolane-4,5-diyl)bismethylene]bis(diphenylphosphine)², were employed as ligands, in order to confront the results with the model proposed recently by Glasser³ for prediction of chirality of the major product of asymmetric hydrosilylation catalysed by [(2,2-dimethyl-1,3-dioxolane-4,5-diyl)bismethylene]bis(diphenylphosphino)rhodium(I) complex.

EXPERIMENTAL

Chemicals. The ketones (Fluka A.-G., Buchs) were purified by distillation and stored in an argon atmosphere over a molecular sieve. The alcohols used as gas chromatographic standards were obtained by the reduction of the corresponding ketones by lithium aluminium hydride and were stored similarly as the ketones. The organosilicon hydrides were prepared by reported procedures⁴. The purity of all the compounds was verified by gas chromatography and by n_D^{20} measurements. $[\{\text{RhCl}(\eta\text{-C}_2\text{H}_4)_2\}_2]$ was obtained by the reaction of $\text{RhCl}_3 \cdot 3 \text{H}_2\text{O}$ with ethylene⁵, which was carried out in a sealed vessel under pressure of the gas (1.5 atm), in 90%

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yield. For C_4H_8ClRh (389.0) calculated: 24.70% C, 4.15% H; found: 24.51% C, 4.23% H. Hydrosilylations were performed under argon at 20°C by the procedure reported earlier¹. The experiments were made on millimole scale (20 mmol of dialkyl ketones and 10 mmol of alkyl aryl ketones, except 1-phenyl-2-methyl-1-propanone which was used in 5 mmol amounts). The progress of the reaction was estimated from the consumption of the starting ketone determined by gas chromatography. After disappearance of the ketone or after its concentration attained a constant value, the unreacted ketone, silicon hydride and the solvent were removed by distillation under reduced pressure (0.1 Torr, bath temperature 100°C) and the residue was hydrolysed by 0.5M-KOH in 80% aqueous methanol. It was verified (Table I) that the solvolysis procedure did not affect the optical purity of the product. After shaking for two hours at room temperature, the mixture was filtered, diluted with twofold volume of water and extracted with diethyl ether. The organic layer was separated, washed with water and dried over potassium carbonate. After solvent removal, the residue was distilled under reduced pressure.

Analysis of the reaction mixture. The distillate, which contained in all experiments only alcohol and ketone, was analysed by gas chromatography. Relative amounts of these compounds were calculated from the areas of the corresponding chromatographic peaks using calibration curve determined for each ketone-alcohol pair.

The optical purity of the alcohols was determined by two different procedures, depending on the structure of the alcohol. Aliphatic alcohols were measured *in substantia* after the distillate had been worked-up in the following way. The mixture of alcohol and ketone was added to a suspension of lithium aluminium hydride (1.5 molar excess) in diethyl ether and kept under reflux for several minutes. The excess hydride was decomposed by 2M-NaOH, the precipitate was filtered-off and the ether distilled-off through a Vigreux column. The residue was distilled under reduced pressure. The optical purity of the alcohols was calculated according to refs⁶⁻¹⁰. This procedure was verified with the distillate resulting from hydrosilylation of 4-methyl-2-pentanone. The distillate containing 17% of the ketone was dissolved in 7 ml of methanol and water was added dropwise until the liquid turned turbid. After the addition of 1.8 g of sodium acetate

TABLE I

The Effect of the Solvolytic Medium on the Optical Purity of the Product of Hydrosilylation of Acetophenone by Diphenylsilane

Medium	<i>(R)</i> - $C_6H_5CH(OH)CH_3$	
	alcohol, % ^a	optical purity, %
0.3M-HCl, CH_3OH	71.5	22.3
0.2M-KOH, 80% CH_3OH	74	22.4
0.5M-KOH, 80% CH_3OH	72	22.2
1.5M-KOH, 80% CH_3OH	74	22.1
0.5M-KOH, CH_3OH	79.5	22.6
0.3M- CH_3ONa , CH_3OH	81	22.7

^a The content of the alcohol in the reaction mixture worked-up by the procedure described in Experimental.

and 1.2 g of thiosemicarbazide hydrochloride, the mixture was refluxed for 0.5 h, allowed to stand overnight at 2°C, the precipitate filtered-off and the filtrate introduced into 50 ml of water. The product was extracted with diethyl ether. After the work-up of the organic layer, the alcohol was obtained by distillation under reduced pressure. Both procedures afforded the product of the same optical purity.

The optical purity of aryl-substituted alcohols was measured without isolation of alcohols from the distillate. In this case, the mixture of alcohol and ketone was weighed into a 10 ml-volumetric flask such that the concentration of the alcohol (determined by gas chromatography) was similar to the concentrations with which the optical rotation of pure alcohols was measured in refs¹¹⁻¹³ and the volume of the flask was made up with the solvent. This procedure was verified in the case of 1-phenylethanol in the following way. The reaction mixture containing the optically active alcohol and acetophenone was reduced by lithium aluminium hydride similarly as described above for 4-methyl-2-pentanone and the optical rotation of the sample was measured *in substantia*. This sample was then diluted with acetophenone to the original alcohol concentration and its optical rotation was measured in the solution. Both procedures gave similar results.

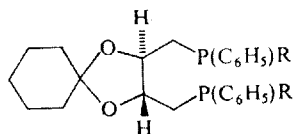
RESULTS AND DISCUSSION

Before entering into a discussion of the results obtained with series of dialkyl and alkyl aryl ketones, several comments should be made concerning the catalyst system. The rhodium-ethylene complex used as a precursor also catalyses the reaction of organosilicon hydrides with ketones. In this case, however, dehydrogenating condensation (reaction (A)), leading after solvolysis of the formed silyl enol ether to the ketone reformation (reaction (B)), is the main reaction. Thus, for example, 62% of the ketone reappeared in the solvolyzed reaction mixture after hydrosilylation of acetophenone by diphenylsilane catalyzed by this complex. This side reaction is efficiently suppressed when the phosphine ligand is used in the 2 : 1 molar ratio with respect to the rhodium complex. On the basis of preliminary experiments described earlier¹, the Rh: ketone molar ratio $4 \cdot 10^{-3}$ and the silicon hydride to ketone molar ratio 1 were used as optimum conditions. At the catalyst to ketone molar ratio lower than 10^{-3} the reaction was characterized by long and irreproducible induction period. Since the efficiency of the catalyst decreased even under storing its solution in an argon atmosphere, freshly prepared catalyst solutions were used in further experiments. It is worthy of note that in contact with air oxygen, the dissolved catalyst is rapidly oxidized to the less active and selective species even at room temperature. Under the conditions described above, the reaction of all the ketones with diphenylsilane proceeded as a fast exothermic reaction (no ketone was found after 30 min even in the case of 1-phenyl-2,2-dimethyl-1-propanol).

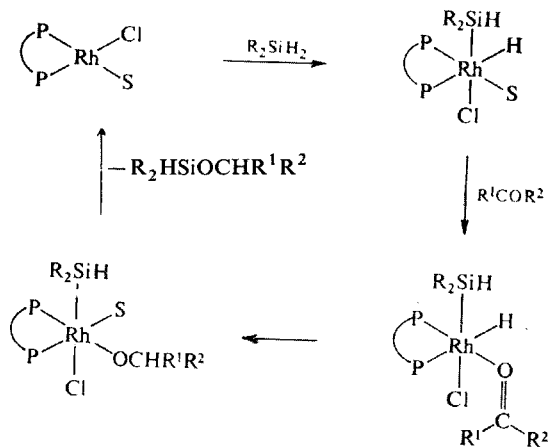
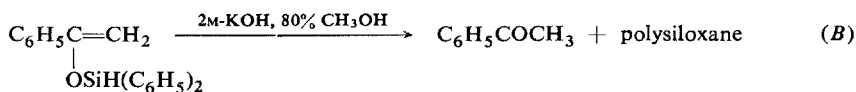
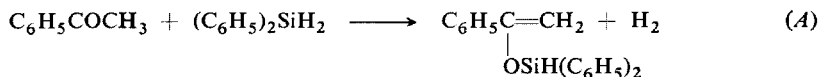
Several further facts are of interest in connection with the mechanism of the hydrosilylation reaction. It has been proposed¹⁴ that hydrosilylation of ketones proceeds *via* catalytic cycle analogous to that generally accepted for hydrosilylation of alkenes (Scheme 1). Some of the reaction steps which are important from stereochemical point of view are not, however, quite clear. The coordination of ketone may proceed

in the two ways: through π -orbitals of the carbonyl group or through the unshared electron pairs of the oxygen. Although the latter possibility is preferred by several authors^{14,15}, experimental evidence in favour of this assumption is lacking. It is not also known, whether formation of C—H and Si—O bonds takes place in two steps or as a four-center process.

We have already reported¹ that the selectivity of the reaction decreases with decreasing catalyst to ketone or silicone hydride to ketone molar ratios. This fact can be accounted for by formation of the less selective catalytic species at higher catalyst concentrations and to the more selective transfer of the second hydrogen of the



- I, R = C₆H₅
 II, R = cyclo-C₆H₁₁
 III, R = CH₂C₆H₅



S = solvent

SCHEME 1

dihydrosilane in the more sterically hindered system. Since the alkoxyasilanes $R^1R^2Si(OR^3)H$ do not react with ketones under the conditions used, the second hydrogen must be transferred by a process which does not involve the activation of the silicon hydride of this type. From the observed dependence of the extent of asymmetric synthesis upon the L: Rh molar ratio (Table II) it can be concluded that the rhodium-alkene complex and the species containing phosphine ligand catalyse hydrosilylation of ketones at comparable rates. The increase in the optical purity of the product is proportional to the added ligand up to 1 : 1 molar ratio, then it slowly increases to a maximum at the 2 : 1 molar ratio. It is of interest that the system exhibits catalytic activity even at 10 : 1 ligand to rhodium molar ratio. This observation contradicts the assumption¹⁶ that at the molar ratio higher than 2 : 1, the inactive cationic complex $(L_2Rh)^+ Cl^-$ is formed. These facts make

TABLE II

The Effect of the Rh to Ligand Molar Ratio (A) on the Yield and Optical Purity of Alcohols Obtained by Hydrosilylation Catalysed by $[\{RhCl(\eta-C_2H_4)_2\}_2] +$ Phosphine I

A	Conversion, % ^a	(R)-C ₆ H ₅ CH(OH)R	
		yield, % ^b	purity, %
C ₆ H ₅ COCH ₃			
3 : 1	97	52	9
2 : 1	100	62	14
1 : 1	100	80	23
1 : 2	98	89	30
1 : 5	85	88	29
1 : 10	86	92	28
C ₆ H ₅ COCH(CH ₃) ₂			
1 : 1	92	95	32
1 : 2	92	90	40
1 : 5	93	92	38
C ₆ H ₅ COC(CH ₃) ₃			
1 : 1	89	100	36
1 : 2	92	100	43
1 : 5	92	100	42

^a Overall conversion of the ketone by reaction with the silicon hydride determined by gas-liquid chromatography of the reaction mixture before solvolysis (*i.e.* conversion to both silyl ether and silyl enolether). ^b The relative amount of ketone converted into the silyl ether; determined as the content of the alcohol in the reaction mixture worked-up as described in Experimental.

mechanistic explanation of the absolute configurations of the alcohols obtained as well as the observed variations in their optical purity with the ligand difficult (Tables III and IV).

Glasser have recently proposed³ a model for the correlation of the absolute configuration of the product with the configuration of [(2,2-dimethyl-1,3-dioxolane-4,5-diyl)bismethylene]bis(diphenylphosphine). Although the absolute configurations of products of several different reactions have been correctly predicted, this model is not of general validity. As nearly all the correlations employed in the asymmetric synthesis¹⁷, also this model is based on the concept of the small, medium and large groups. According to this, the optical purity of the product would increase with increasing difference in the size of substituents on the carbonyl group. While in the case of phosphine *I* and aliphatic ketones (Table III) the results obtained can be accounted for by this model, variations in the optical purity of the products of hydrosilylation of aryl alkyl ketones have opposite trend: the asymmetric yield increases from the methyl to tert-butyl derivative, although the bulk of the substituent approaches that of the phenyl group. The effective van der Waals radius of the tert-butyl group is greater than that of the phenyl group¹⁸. In such a case, the product should even be of the opposite configuration when compared to the other members of the series. Such dependences of the configuration of the product and the extent

TABLE III

Hydrosilylation of Ketones by Diphenylsilane Catalysed by $[\{\text{RhCl}(\eta\text{-C}_2\text{H}_4)_2\}_2]$ and Phosphine *I*

Ketone	Conversion, % ^a	(R)-Alcohol	
		yield, % ^b	Optical purity, %
CH ₃ COC ₂ H ₅	92	85	23
CH ₃ COC ₃ H _{7-n}	90	90	25
CH ₃ COC ₃ H _{7-i}	86	89	28
CH ₃ COC ₄ H _{9-i}	97	90	24
CH ₃ COC ₄ H _{9-t}	92	94	30
CH ₃ COCH ₂ C ₆ H ₅	97	93	14
CH ₃ COCH ₂ CH ₂ C ₆ H ₅	91	96	18
CH ₃ COC ₆ H ₅	100	87	24
C ₂ H ₅ COC ₆ H ₅	97	82	25
i-C ₃ H ₇ COC ₆ H ₅	93	97	32
t-C ₄ H ₉ COC ₆ H ₅	92	100	36

^{a,b} See Table II.

of the asymmetric synthesis were observed with phosphine *II* (Table IV). On the other hand, phosphine *III* gave the products with opposite configuration compared to phosphines *I* and *II*.

These discrepancies cannot be explained by a simple model based solely on the consideration of the size of substituents. According to the Curtin–Hammett postulate¹⁹, the ratio of the formed enantiomers depends only on the difference between the enthalpies of the transition states leading to individual optical enantiomers and not on the difference in the enthalpy of the initial states. The results obtained with phosphine *I* indicate that coordination of the ketone is not the rate-determining step of the reaction. This should be sought for in either hydrogen or silyl group transfer. Any correlation of the absolute configuration of the product based on the preferred coordination of a prochiral ketone by pro-re or pro-si face of the double bond is then unwarranted.

TABLE IV
Hydrosilylation of Ketones by Diphenylsilane Catalysed by $[\{\text{RhCl}(\eta\text{-C}_2\text{H}_4)_2\}_2]$ and Phosphine *II* or *III*

Ketone	Conversion, % ^a	Alcohol	
		yield, % ^b	optical purity, % ^c
Phosphine <i>II</i>			
CH ₃ COC ₂ H ₅	92	83	25 (<i>R</i>)
CH ₃ COC ₃ H _{7-n}	86	83	23 (<i>R</i>)
CH ₃ COC ₃ H _{7-i}	95	91	31 (<i>R</i>)
CH ₃ COC ₄ H _{9-i}	91	92	27 (<i>R</i>)
CH ₃ COC ₄ H _{9-t}	94	90	35 (<i>R</i>)
CH ₃ COCH ₂ C ₆ H ₅	95	87	18 (<i>R</i>)
CH ₃ COCH ₂ CH ₂ C ₆ H ₅	100	88	28 (<i>R</i>)
CH ₃ COC ₆ H ₅	84	79	44 (<i>R</i>)
C ₂ H ₅ COC ₆ H ₅	100	89	52 (<i>R</i>)
<i>i</i> -C ₃ H ₇ COC ₆ H ₅	93	97	2 (<i>R</i>)
<i>t</i> -C ₄ H ₉ COC ₆ H ₅	62	100	9 (<i>S</i>)
Phosphine <i>III</i>			
CH ₃ COC ₆ H ₅	94	74	8 (<i>S</i>)
C ₂ H ₅ COC ₆ H ₅	89	78	23 (<i>S</i>)
CH ₃ COCH ₂ C ₆ H ₅	87	69	4 (<i>S</i>)
CH ₃ COCH ₂ CH ₂ C ₆ H ₅	97	72	10 (<i>S</i>)

^{a, b} See Table II; ^c absolute configuration in brackets.

Furthermore, the model should account also for changes in the optical purity of the alcohols with the structure of organosilicon hydrides (Table V). We believe that a relevant model must differentiate between diastereoisomeric transition states leading from a species containing Rh—O or Rh—C σ -bond to the product. Also in this case however, the purely steric model cannot explain the results obtained with phosphine *I* for the series of alkyl aryl ketones, without assuming the forced reversal in the size of substituents (*e.g.* CH₃ > C₆H₅) or without introducing some additional assumptions, such as interactions between phenyl groups of the phosphine and the ketone. While in the case of phosphine *I* these diastereoisomers arise after coordination of a prochiral ketone, with phosphines *II* and *III* they are present already in ligands with (*R,R*)-chiral carbon atoms and chiral phosphorus atom of unknown absolute configuration. It should be noted that 99.9% asymmetric yield corresponds to a difference of about 3 kcal mol⁻¹ in the free enthalpy of the diastereoisomeric transition states. This magnitude corresponds to relatively weak nonbonding interactions. Taking the change in the extent of the asymmetric synthesis observed in our case, this value is even much smaller. This shows that for such a complicated system and without the knowledge of decisive factors (the structure of the catalytic species, the nature of stereoselectivity- and rate-determining steps) any interpretation of the observed results would be very speculative.

TABLE V
Hydrosilylation of Acetophenone by Various Organosilicon Hydrides Catalysed by $\{[\text{RhCl}(\eta\text{-C}_2\text{H}_4)_2\}_2\}$ and Phosphine *II*

Silicon hydride	Conversion, % ^a	<i>(R)</i> -C ₆ H ₅ CH(OH)CH ₃	
		yield, % ^b	optical purity, %
C ₆ H ₅ CH ₂ SiH ₃	100	98	0.4
C ₆ H ₅ SiH ₃	100	89	2.1
(<i>i</i> -C ₃ H ₇)SiH ₂	95	92	6.8
(C ₂ H ₅) ₂ SiH ₂	100	88	7.2
(<i>n</i> -C ₃ H ₇) ₂ SiH ₂	100	93	9.1
CH ₃ (C ₆ H ₅)SiH ₂	90	92	11.2
(C ₆ H ₅) ₂ SiH ₂	100	87	23

^{a,b} See Table II.

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