

ADDITION OF TETRACHLOROMETHANE TO STYRENE CATALYZED BY COPPER-CHIRAL AMINE COMPLEXES

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Dedicated to Dr Miloš Kraus on the occasion of his 65th birthday.

Copper(I)-chiral amine complexes were found to be very efficient catalysts for addition reaction of tetrachloro- and bromotrichloromethane with styrene (yields over 90%). However, both monodentate and bidentate chiral amine ligands (I - VIII) gave a low asymmetric induction (up to 2.3% ee).

In recent years a great attention has been paid to the asymmetric reactions such as hydrogenation, hydrosilylation, hydroformylation etc. catalyzed by transition metal complexes with chiral ligands¹. Up to now, the addition reactions of polyhalogenated compounds with alkenes have been the sparsely studied field of asymmetric synthesis. Only a few attempts at the addition by employing chiral catalysts have been reported²⁻⁶. Complexes of ruthenium and rhodium with optically active phosphine ligands (DIOP, refs²⁻⁶) have been used as the catalysts in the addition reactions of sulfonyl chlorides, tetrachloromethane and bromotrichloromethane with substituted styrenes and 1-phenylpropene. The optical yields of 1 : 1 adducts varied in the range 0 - 32%. The Ru complex containing the binaphthyl chiral ligand BINAP provided the addition products of very low specific rotation and the BPPM ligand was completely inactive⁴. Recently, a number of other transition metal catalysts were examined⁷ (no data). However, none of the catalysts produced any significant enantioselectivity.

In recent years our research effort in the field of catalysis of addition reactions have been focused mainly towards synthetic and mechanistic aspects⁸⁻¹³. Copper(I) complexes with nitrogen ligands have been found as very efficient catalysts, affording 1 : 1 adducts in high yield under mild conditions. These results have prompted us to examine asymmetric additions of polyhalomethanes to alkenes employing Cu(I)-complexes with chiral nitrogen ligands. We have expected that the presence of chiral ligand in the coordination sphere of the metal will induce asymmetry in the coordinated species. The

attention paid to the above ligands has originated also from the fact that chiral nitrogen ligands are more chemically resistant than optically active phosphines¹⁴. Moreover, they are usually cheaper, easier to prepare and to recover and can be profitably employed in many asymmetric processes¹⁵⁻¹⁷.

EXPERIMENTAL

Materials. Tetrachloromethane, (Lachema, Brno), *S*-(+)- and *R*-(-)-cyclohexylethylamine, (*S*)-(-)- and (*R*)-(+)-phenylethylamine (Fluka, Buchs), (-)-spartein and (-)-nicotine (Merck). (-)-Ephedrine was kindly submitted by VÚAB (Rožtoky near Prague), (-)-2-*exo*-hydroxy-3-*endo*-methylaminonorbornane VIII was prepared according to known procedure¹⁸. GC analysis was performed on Hewlett-Packard HP 5590 gas chromatograph and optical activity was measured on Polamat polarimetr (Zeiss, Jena) at 20 °C with accuracy of measurement $\pm 0.05^\circ$.

General Procedure for Addition of Tetrachloromethane to Styrene

A 10 ml ampoule equipped with magnetic stirrer and septum was charged with 0.050 g of CuCl or 0.16 g of $\text{Cu}(\text{CH}_3\text{CN})_4\text{ClO}_4$ (0.0005 mol), 1.0 g of styrene (0.01 mol) and with solution of 0.002 mol of an amine (*I*, *III* - *VIII*) in 5 ml of dry solvent (e.g. benzene). The contents were heated to 80 °C, and 3 g of tetrachloromethane (0.02 mol) were added through the septum. After completion of the reaction, the reaction mixture was washed with 7 ml of 10% hydrochloric acid, the organic phase was separated and the aqueous phase was washed twice with 5 ml of tetrachloromethane. Organic phases were collected, dried with anhydrous CaCl_2 . The product, 1,1,1,3-tetrachloro-3-phenylpropane, was isolated by distillation under reduced pressure (b.p. 100 °C/133 Pa). Then, the optical activity of the 1 : 1 adduct was measured in benzene solution (concentration 0.25 g/ml). The same procedure was also used for addition of bromotrichloromethane and in the experiments with stoichiometric amount of the chiral catalysts.

Addition of *R*-(-)-Cyclohexylethylamine to Methylacrylate

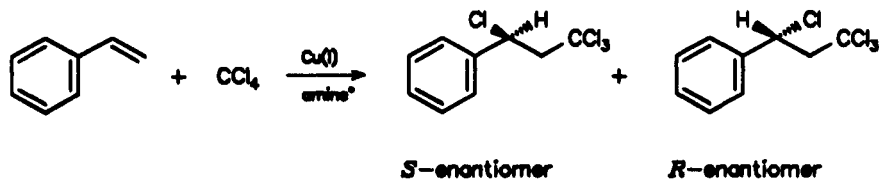
A 25 ml flask equipped with a condenser, a septum, a magnetic stirrer and a drying tube (with KOH) was charged with 4.3 g (0.05 mol) of methyl acrylate in 7 ml anhydrous ethanol. Then, 6.4 g (0.05 mol) of *R*-(-)-cyclohexylethylamine were added dropwise under stirring during 30 min, and the reaction mixture was stirred at room temperature for another 18 h. Then, ethanol was evaporated and the crude material was distilled under reduced pressure. A total of 9.3 g of methyl 3-((1*R*)-1-cyclohexyl)ethylamino)propanoate (87%) were obtained (b.p. 100 - 105 °C/266 Pa).

Reduction of Methyl 3-((1*R*)-1-Cyclohexyl)ethylamino)propanoate

A 100 flask equipped with a condenser, a magnetic stirrer, a septum and a drying tube (with anhydrous calcium chloride) was charged with 1.6 g (0.043 mol) of lithium aluminium hydride and 50 ml of anhydrous diethyl ether. Then 9.3 g (0.043 mol) of methyl 3-((1*R*)-1-cyclohexyl)ethylamino)propanoate in 10 ml of diethyl ether were added dropwise under stirring during 1 h. After addition of the last amount of the amino ester, the reaction mixture was refluxed for another 1 h. The unreacted lithium aluminium hydride was decomposed by water, the organic layer was separated, and the aqueous layer was washed twice with 20 ml of diethyl ether. The organic phases were collected and dried over magnesium sulfate and the solvent was evaporated. The product, 3-((1*R*)-1-cyclohexyl)ethylamino)propanol was obtained as viscous liquid, $[\alpha]_D = -12.7^\circ$ (*c* 17.5, benzene).

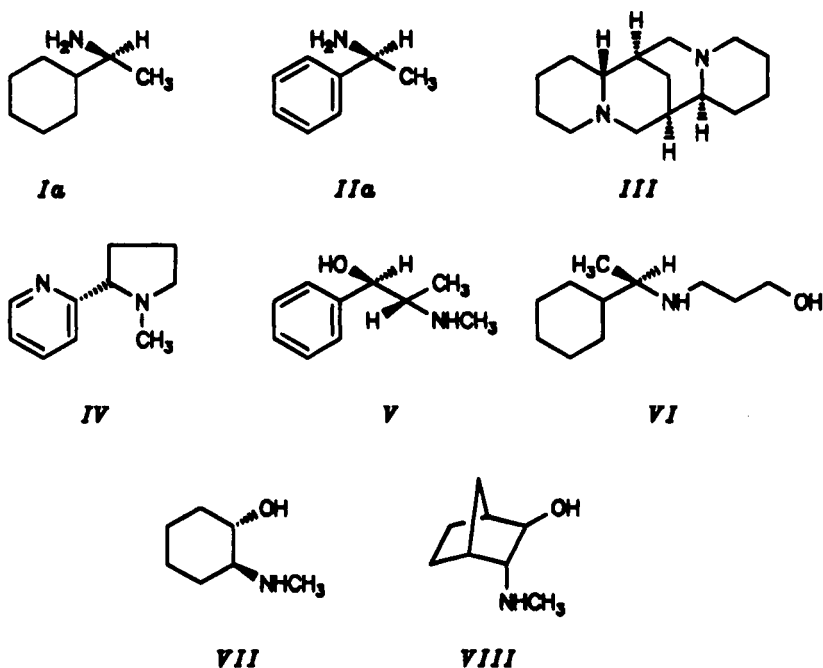
RESULTS AND DISCUSSION

The addition reaction of tetrachloromethane with styrene was chosen as a model reaction (Scheme 1), due to the easy determination of enantiomeric excess (ee)⁵.



SCHEME 1

The following chiral amines were used as ligands: (*S*)-(+)- and (*R*)-(-)-cyclohexylamine (*Ia*, *Ib*); (*S*)-(-)- and (*R*)-(+)-phenylethylamine (*IIa*, *IIb*); natural alkaloids: (-)-sparteine (*III*), (*S*)-(-)-nicotine (*IV*). Moreover, some amino alcohols such as (-)-ephedrine (*V*), the synthesized 3-((1*R*)-1-cyclohexyl)ethylamino)propanol (*VI*), (+)-*trans*-2-methylaminocyclohexan-1-ol (*VII*) and (-)-2-*exo*-hydroxy-3-*endo*-methylaminonorbornane (*VIII*) were also used as chiral ligands, because it is known that the addition reaction of polyhalogenated compounds with olefins can be catalyzed by copper–amino alcohol complexes (e.g. ethanolamine)^{19,20}.



In all cases, the yields of 1 : 1 adducts exceeded 90% under mild reaction conditions (80 °C) and moderate reaction times (30 – 270 min), indicating the high catalytic activity of copper(I)–amine complexes. These were prepared in situ by adding chiral amine to copper(I) salt (CuCl or Cu[CH₃CN]₄ClO₄). No difference in the catalytic activity or enantioselectivity of both copper(I) salts was observed.

A copper(I) complex with *S*-cyclohexylethylamine *Ia* provided an 1 : 1 adduct with *R*-configuration. With *R*-cyclohexylethylamine *Ib* an 1 : 1 adduct with *S*-configuration was obtained in 0.4% enantiomeric excess (Table I). The low ee did not depend on Cu : amine ratio (1 : 8 – 32) and on reaction temperature (20 – 80 °C). The experiments performed with bromotrichloromethane gave similar results. The 1 : 1 adducts were obtained in only 0.3% ee and this value was also independent on the reaction conditions.

The copper complexes with *S*-(-)-nicotine *IV* (bidentate ligand) afforded (Table II) only 0.1% ee of enantiomer with *R*-configuration. Somewhat better results were obtained with (-)-spartein *III* giving 1.2% ee of enantiomer with the same configuration (Table II). These results indicate that bidentate ligands with rigid structure give better

TABLE I
Addition of tetrachloromethane and bromotrichloromethane to styrene catalyzed by copper(I)-complexes with ligands *Ia* and *Ib*

XCCl ₃	Amine	Amine : Cu mol. ratio	Temp. °C	Cat. conc. mole %	[α] _D	ee % (config.)
CCl ₄	<i>Ia</i>	8 : 1	80	1	+0.4	0.4(<i>R</i>)
	<i>Ib</i>	8 : 1	80	1	-0.4	0.4(<i>S</i>)
CCl ₃ Br	<i>Ia</i>	6.7 : 1	20	1	+0.2	0.3(<i>R</i>)
	<i>Ia</i>	8 : 1	80	1	+0.3	0.4(<i>R</i>)
	<i>Ib</i>	6.7 : 1	20	1	-0.2	0.3(<i>S</i>)

TABLE II
Addition of tetrachloromethane to styrene catalyzed by copper(I)-complexes with ligands *III* and *IV*

Amine	Solvent	Amine : Cu mol. ratio	[α] _D	ee % (config.)
<i>III</i>	benzene	4 : 1	+1.2	1.2(<i>R</i>)
<i>III</i>	1,2-dichloroethane	4 : 1	+0.3	0.3(<i>R</i>)
<i>IV</i>	benzene	4 : 1	+0.1	0.1(<i>R</i>)
<i>IV</i>	benzene	4 : 1	+0.1	0.1(<i>R</i>)

results. In the case of a copper(I)-spartein complex a small solvent effect on asymmetric induction was observed. It was found that the addition reaction in benzene gives a somewhat higher ee (1.2%) than that carried out in 1,2-dichloroethane (0.3%) (Table II).

The copper(I)-complex with ephedrine (V) ligand afforded 2.3% ee of an enantiomer with *S*-configuration (Table III). The other amino alcohols VI, VII and VIII exhibited much lower enantioselectivity < 0.1%, 0.1% and 1.2% ee (Table III), giving in all cases an enantiomer with *S*-configuration in excess.

In the case Cu(I)-ephedrine (ligand V) complexes, the influence of solvent was investigated. It was found (Table IV) that asymmetric induction is influenced by solvent (as in the case of (-)-spartein III). The enantiomeric excess in the addition reaction catalyzed by copper(I)-ephedrine complex increased in the following order: acetonitrile < tert-butanol < 1,2-dichloroethane < benzene = tetrachloromethane (Table IV), following increasing nonpolarity of the solvent.

In order to examine a possible influence of catalyst concentration on ee, the stoichiometric reactions were performed. The additions of tetrachloromethane with styrene mediated by stoichiometric amount of copper(I)-chiral amine complex were studied

TABLE III
Additions of tetrachloromethane to styrene catalyzed by copper(I)-complexes with ligands V – VIII

Amine	Solvent	Amine : Cu mol. ratio	$[\alpha]_D$	ee % (config.)
V	benzene	4 : 1	-2.3	2.3(<i>S</i>)
VI	benzene	4 : 1	< -0.1	< 0.1(<i>S</i>)
VII	benzene	4 : 1	-0.1	0.1(<i>S</i>)
VIII	benzene	4 : 1	-1.2	1.2(<i>S</i>)

TABLE IV
Solvent effect in the addition reaction of tetrachloromethane with styrene catalyzed by copper(I)-ligand V complex

Solvent	Amine : Cu mol. ratio	$[\alpha]_D$	ee % (config.)
Acetonitrile	4 : 1	-0.3	0.3(<i>S</i>)
tert-Butanol	4 : 1	-1.2	1.2(<i>S</i>)
1,2-Dichloroethane	4 : 1	-1.4	1.4(<i>S</i>)
Tetrachloromethane	4 : 1	-2.3	2.3(<i>S</i>)
Benzene	4 : 1	-2.3	2.3(<i>S</i>)

both with monodentate and bidentate complexes, giving almost the same results as those obtained in catalytic reactions (Table V).

Summarizing, copper(I)-chiral amine complexes, although exhibiting high chemical selectivity in the studied addition reactions, were of rather low enantioselectivity. Regardless to the low enantioselectivity, the results are of mechanistic value, indicating that the addition reaction catalyzed by copper(I)-complexes proceeds in the coordination sphere of the complex.

TABLE V

Addition reaction of tetrachloromethane with styrene in the presence of a stoichiometric amount of copper(I)-complex with ligands *Ia*, *Ib*, *IIa*, *IIb*, *III*, *IV* and *V*

Amine	Solvent	Amine : Cu mol. ratio	$[\alpha]_D$	ee % (config.)
<i>Ia</i>	benzene	2 : 1	+0.9	0.9(<i>R</i>)
<i>Ib</i>	benzene	2 : 1	-0.8	0.8(<i>S</i>)
<i>IIa</i>	benzene	2 : 1	< +0.1	< 0.1(<i>R</i>)
<i>IIb</i>	benzene	2 : 1	-0.4	0.4(<i>S</i>)
<i>III</i>	benzene	1 : 1	+0.6	0.6(<i>R</i>)
<i>IV</i>	1,2-dichloroethane	1 : 1	+0.1	0.1(<i>R</i>)
<i>V</i>	benzene	1 : 1	-2.0	2.0(<i>S</i>)

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