

THE OXIDATIVE ADDITION OF BENZYL HALIDES TO
 TETRAKIS(TRIPHENYLPHOSPHINE)NICKEL(O)

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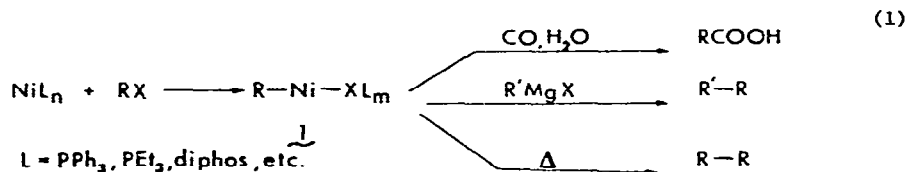
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SUMMARY

The oxidative addition of benzyl chloride or bromide to tetrakis-(triphenylphosphine)nickel(0) followed by carbonylation and the addition of methanol yielded methyl phenylacetate. When (R)- α -D benzyl chloride was subjected to this reaction sequence, racemic ester was obtained, probably as a result of racemization in the oxidative addition step.

INTRODUCTION

Zero valent nickel phosphine complexes readily undergo oxidative addition to a number of organic halides ($R-X$, $X=Cl, Br, I$; $R=aryl, benzyl, vinyl, and alkyl$) (eq. 1)¹⁻¹⁴ to afford a nickel(II) complex (1) containing a nickel-carbon sigma bond. If the nickel(II) complex contains a β -hydrogen, it is in general unisolable because of facile β -hydride elimination.^{2,4} Further reaction of the nickel(II) complex with various reagents leads to products such as carboxylic acids and their derivatives, as well as symmetrical and unsymmetrical coupling products.^{9,19}



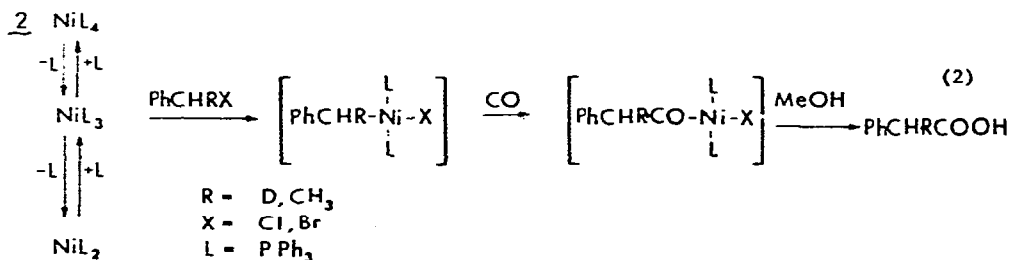
The stereochemistry of the oxidative addition step is of interest for two reasons. First, it may offer information as to the mechanism by which oxidative addition takes place, and second, since transition metals are finding increasingly widespread use in organic syntheses, it may be developed to provide useful synthetic organic reactions.¹⁵⁻¹⁸

Oxidative additions of optically active alkyl halides to other transition metals proceed with retention, racemization, or inversion of configuration at carbon depending on the metal complex and the substrate.¹⁹ In fact, the stereochemical results for any one metal may vary with the ligand and the substrate. In the case of d^{10} phosphine complexes analogous to nickel, the oxidative addition of optically active benzyl halides to palladium(0) has been shown to occur with a high degree of inversion of configuration at carbon,^{20a} and in one case, oxidative addition of an asymmetric benzyl halide to platinum(0) has been shown to proceed with inversion.^{20b}

The stereochemistry of the addition of benzyl halides to nickel(0) has not yet been determined; we wish to report the oxidative addition of benzyl halides to tetrakis(triphenylphosphine)nickel(0) (2).

RESULTS AND DISCUSSION

The following scheme (eq. 2) for the determination of the stereochemistry of the oxidative addition of chiral benzyl halides to tetrakis(triphenylphosphine)nickel(0) has been used previously to investigate the stereochemistry of the oxidative addition of chiral benzyl halides to tetrakis(triphenylphosphine)palladium(0).^{20a}



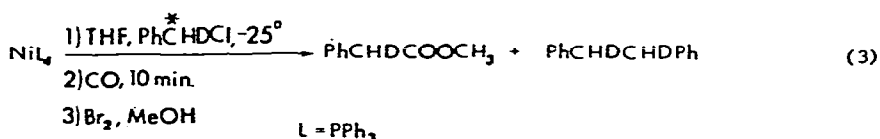
The reaction of the nickel(0) complex with the chiral halide produces

a nickel(II) sigma bonded carbon complex. Insertion of carbon monoxide followed by cleavage of the acyl complex with methanol yields the corresponding methyl esters. Since the absolute rotation of the resulting esters has been determined previously,^{20a} this scheme should allow the determination of the overall stereochemistry of the process. The configuration of the intermediate nickel(II) complex may be deduced from the corresponding ester provided the insertion of carbon monoxide is stereospecific. Insertion of carbon monoxide has been determined to proceed with retention of configuration with all metals examined so far,^{19,20a} including nickel.²¹ Cleavage by methanol does not affect the chiral center, thereby establishing the validity of this approach.

Since the carbonylation of benzyl halides via tetrakis(triphenylphosphine)nickel(0) had not previously been reported, preliminary reactions with optically inactive benzyl chloride, benzyl bromide, α -phenethyl chloride and α -phenethyl bromide were carried out. No attempt was made to isolate either the intermediate nickel(II) alkyl complexes or the nickel(II) acyl complexes (both of which are known to be unstable).^{22,23} The results are summarized in Tables I and II.

Benzyl chloride and benzyl bromide were converted to methyl α -phenylacetate in moderate yields, but bibenzyl was always formed as a side product of this reaction. α -Phenethyl chloride and α -phenethyl bromide were converted to methyl α -phenyl propionate in very poor yields (>10%). As a result the reaction was not investigated further.

The reaction of R(-)- α -D-benzyl chloride under the conditions shown in equation 3 yielded methyl α -D-phenylactate which was largely racemic.



The most likely mechanism for loss of optical activity include racemization during the oxidative addition step via a free radical pro-

TABLE I
Reaction of $\text{PhCH}_2\text{-X}$ with $\text{Ni}(\text{PPh}_3)_4$

Run	X	Ni/RX	T°C	t(min)	pCO	$\text{PhCH}_2\text{COOCH}_3$ (%)	$\text{PhCH}_2\text{CH}_2\text{Ph}$ (%)
1	Cl	1	-25	20	1	60 ^{a,c}	8.4
2	Cl	1	-80	4 hr	1	67.5 ^{a,d}	2.14
3	Cl	1	-25	30	1	62.5 ^{a,d,f}	11.8
4	Cl	1	-25	20	1	39.4 ^{b,c}	4.52
5	Cl	2	-25	30	1	8.0 ^{a,c}	10.0
6	Cl	1	-25	20	4	47.5 ^{a,c}	29.6
7	Br	1	-25	30	1	46.5 ^{a,c}	12.8
8	OCOCH_3	1	-10	2 hr	1	no reaction	

^aMeOH cleavage (see experimental section)

^b Br_2 cleavage (see experimental section)

^cproducts analyzed by GC

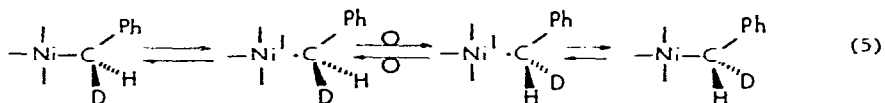
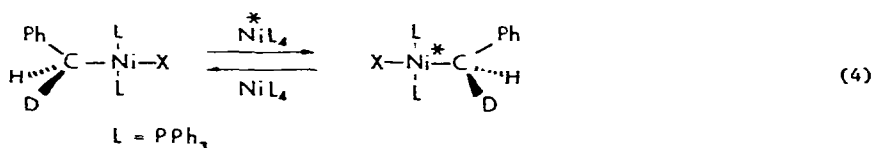
^dproducts analyzed by NMR

TABLE II
Reaction of $\text{Ni}(\text{PPh}_3)_4$ with $\text{PhCH}(\text{CH}_3)\text{X}^a$

Run	Ni/RX	X	T°C	Time	$\text{PhCH}(\text{CH}_3)\text{COOCH}_3$ (%)	$\text{PhCH}(\text{CH}_3)\text{X}$ (% recovered)
1	1	Br	-80	3 hr	7.5	24
2	2	Br	-80	10 min	5	90
3	1.5	Cl	-80	6 hr	7.8	75
4	1.5	Br	-60	-	7.9	38
5	2	Br	-30	4 hr	10	~10
6	1.5	Br	-30	30 min	10	~30
7	1	Cl	-80	30 hr	6.7	19

^aFor all runs, pCO 1 atm., MeOH cleavage (except run 7), reaction analyzed by NMR and GC.

cess, or racemization of the optically active nickel(II) intermediate, either via an exchange process with excess nickel(0) present in solution (eq. 4) or homolytic cleavage of the nickel-carbon bond (eq. 5).



To determine whether a nucleophilic exchange mechanism was operative, the reaction was carried out by slowly adding tetrakis(triphenylphosphine) nickel(0) to a solution of R(-)- α -D-benzyl chloride, thus keeping the concentration of free nickel(0) in solution to a minimum. The methyl α -D-phenylacetate produced in this reaction was also largely racemic. In an effort to convert the alkyl nickel(II) complex to ester, immediately as it was formed, tetrakis(triphenylphosphine)nickel(0) was added to a solution of R(-)- α -D-benzyl chloride in which both carbon monoxide and methanol were present. The ester was not obtained since the formation of nickel phosphine carbonyls, which are inactive under the reaction conditions, occurred much faster than the oxidative addition reaction.² If homolytic cleavage of the nickel carbon bond were the source of racemization, carrying out the reaction at a lower temperature should stabilize the nickel-carbon bond. When the reaction was carried out at -60° (as opposed to -25° used in the other reactions) the resulting ester was again largely racemic. The results of the experiments with R(-)- α -D-benzyl chloride are listed in Table III.

During the course of the oxidative addition no CIDNP could be observed. However, while presence of CIDNP is taken as proof for the presence of free radicals, the absence of CIDNP does not disprove them.

CONCLUSION

The mechanism of racemization of chiral benzyl halides could not conclusively be determined, although it probably occurs during the oxidative addition step. No conditions which would allow for the stereochemical control of the reaction could be found. Loss of stereochemistry during oxidative addition coupled with facile β -hydride elimination from substrates which contain a β -hydrogen severely limits the potential of this reaction as a method of ester synthesis.

TABLE III
Reaction of R(-) α -D-benzyl Chloride with
Tetrakis(triphenylphosphine)nickel(O).^{a,b}

Run	T°C	$[\alpha]_D^{25}$	ee
1	-25	0.000 \pm 0.040° (CH ₂ Cl ₂)	0.0 \pm 5.5 %
2	-25	0.040 \pm 0.015° (neat)	5.49 \pm 2.05%
3 ^c	-25	0.021 \pm 0.013° (neat)	2.88 \pm 1.78%
4 ^c	-25	0.083 \pm 0.455° (neat)	11.3 \pm 6.2 %
5	-60	0.024 \pm 0.024° (neat)	3.22 \pm 3.22%

^aFor all runs, oxidative addition was allowed to proceed for four hours, the mixture was stirred under 1 atm CO for 10 min followed by cleavage with bromine and the addition of methanol.

^bThe maximum reported rotation for (S)(+) α -D-phenylacetate was used in the calculations: $[\alpha]_D^{25} = +0.73^\circ$.²⁰

^cNi(PPh₃)₄ was added to a solution of PhCH₂Cl.

EXPERIMENTAL

Reaction of Tetrakis(triphenylphosphine)nickel(O) with Benzyl Halides.

General procedure. Since tetrakis(triphenylphosphine)nickel(O) is extremely oxygen sensitive both in the solid state and in solution, all reactions were run under a nitrogen atmosphere using deoxygenated solvents.

Tetrakis(triphenylphosphine)nickel(O)²⁴ 5.0 g (5.5 mmole) was loaded in a nitrogen filled glove bag into a flask equipped with gas inlet and outlet tubes.

To the flask was added 50 ml of tetrahydrofuran via a syringe and the mixture was cooled (-25 to -80°) with stirring. A solution of the organic halide in 10 ml of tetrahydrofuran was then added via a syringe and the mixture was stirred at the same temperature for 20 min to 30 hr. Carbon monoxide was introduced and after 10 min the acyl complex was cleaved either by the addition of 5 ml of methanol or the addition of 5 mmoles of bromine in carbon tetrachloride at -80° followed by the addition of methanol. The mixture was then allowed to warm to room temperature. The tetrahydrofuran was removed in vacuo and the residue was extracted with hexane and the mixture was then filtered. This removed most of the nickel salts and part of the excess triphenylphosphine. The hexane in the filtrate was removed in vacuo and the residue was distilled in a Kugelrohr apparatus at 70° and 0.1 mm Hg. The distillate was analyzed for content and percent yield either by GC (10' x 1/4" Carbowax 20M on Chromabsorb W 60/80 mesh, 140-180° using a variable temperature program) or by NMR (Varian EM 360 ¹H spectrometer) using acetophenone as an internal standard in both cases. In reactions involving R(-)α-D-benzyl chloride,^{19,25} the distillate was further purified by passage through an 8" silica gel column eluted first with hexane, which removed the R(-)α-D-benzyl chloride, bibenzyl, and any remaining triphenylphosphine, followed by pentane methylene chloride (1:1) which removed the methyl α-D-phenylacetate. The products were identified by comparison of their NMR spectra and GC retention times to those of authentic samples. Optical rotations were determined on a Perkin-Elmer model 141 polarimeter using a 10 cm. cell.

Observation of the Reaction of Tetrakis(triphenylphosphine)nickel(0) With Benzyl Chloride via NMR.

The Proton spectra were run on a Bruker HX 90E Fourier Transform Spectrometer, and spectra were then recorded every 15 seconds for 5 minutes.

ACKNOWLEDGEMENT

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22. $\text{PhCH}_2\text{Ni(X)L}_2$ (X = Cl, Br; L = PPh_3) has only recently been isolated as violet air sensitive crystals.³ It decomposes in solution in the presence of excess triphenylphosphine³. $\text{PhCH}(\text{CH}_3)\text{-NiXL}_2$ (X = Cl, Br; L = PPh_3) has not been isolated. PhCH(X)CH_3 is known to react with $\text{Ni}(\text{PPh}_3)_4$ at room temperature yielding styrene³ (43%) and ethylbenzene (12%)⁴ as the isolable organic products⁴. Nickel aroyl complexes, PhCO-NiXL_2 , have been previously observed to undergo spontaneous decarbonylation in solution yielding the corresponding aryl complexes Ph-NiXL_2 (X = Cl, Br; L = PPh_3)^{4,5,23}

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