Determination of the Enantiomeric Excess of Horner Phosphines by ^{13}C NMR Spectroscopy. A ^{13}C and ^{31}P NMR Study of the Diastereomeric Complexes Formed with [η^3-(+)(1R,5R)-Pinenyl]nickel Bromide Dimer

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Horner Phosphines, Determination of Optical Purity, ^{31}P NMR Spectra, ^{13}C NMR Spectra

The ^{13}C and ^{31}P NMR data of the Horner phosphines PRR′R″ [R = Me, R′ = *t*-Bu, R″ = Ph (**2**) or *i*-Pr (**4**)] and their diastereomeric 1:1 adducts with [η^3-(+)(1R,5R)-pinenyl]nickel bromide dimer (**3**) and (**5**), respectively, are reported. It is shown that the optical purities of the phosphines can be deduced easily from the NMR spectra. Not only are these values in very good agreement with those obtained from optical rotatory data but they are also obtained much more conveniently.

Introduction

Interest in optically active phosphines, particularly Horner phosphines [1], remains high, especially in view of their application in ligand control in homogeneous catalysis [2]. A precondition for the interpretation of the influence of the phosphine ligand in such experiments is that the enantiomeric purity and absolute configuration of the phosphine employed should be known. Although the absolute configuration can be determined even when the sample is not optically pure by chemical correlation with compounds for which the absolute configuration has been determined by X-ray crystallography, the determination of the optical purity of a phosphine is subject to systematic errors.

In addition to isotopic dilution studies, the following methods could be used to determine the optical purity of chiral phosphines [3]:

(i) chemical correlation by conversion to phosphonium salts or phosphine oxides for which the chiroptical data are known [4],

(ii) determination by NMR using optically active solvents or optically active shift reagents,

(iii) chemical conversion of the phosphines to diastereomers and measurement of the resulting different scalar properties by methods such as NMR or GC.

For example, Duñach and Kagan have reported the use of chiral shift reagents for the measurement of the enantiomeric excesses of phosphine oxides [5], and Kyba and Rines have described the use of ^1H and ^{31}P NMR to determine the optical purity of chiral chelating diphosphines by complexation with a chiral palladium compound [6].

We report here the ^{13}C NMR spectra of diastereomeric complexes of Horner phosphines with (+)(1R,5R)-pinenylnickel bromides (**1**) [7] and show that these spectra provide a convenient and reliable method for determining the enantiomeric purity of the phosphine.

Behrens and Wilke [7] showed that [η^3-(+)(1R,5R)-pinenyl]nickel bromide dimer reacts with Horner phosphines to form 1:1 adducts. Eight different complexes are possible – the phosphine ligand may be *cis* or *trans* to C_1 of the pinenyl residue, the methyl groups of the cyclobutyl ring of the pinenyl group can be *syn* or *anti*, and the phosphorus atoms in the complexes can have either R or S configuration [8]. Only two of these eight complexes, those having the phosphorus atom *cis* to C_1 and with the methyl groups *anti* but differing in the configuration at phosphorus, are actually observed. Thus, in the case of phenyl-*tert*-butylmethylphosphine (**2**) the two diastereomeric complexes **3a** and **3b** are formed.

Frequently one of the diastereomers can be enriched by fractional crystallization; displacement with trimethylphosphine allows the Horner phosphine to be isolated in high optical yield. In the case of **3**, isomer **3b** crystallizes out of diethyl ether preferentially [7a] and has been analysed by X-ray crystallography [9].

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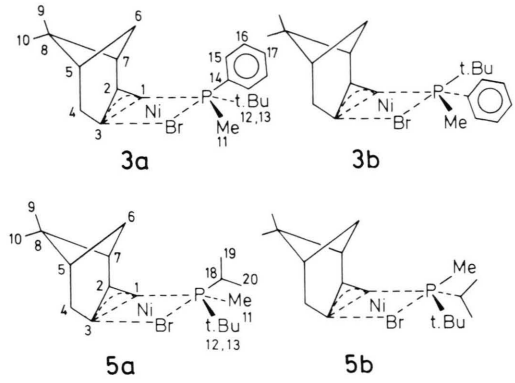

We have taken the complexes formed by phenyl-*tert*-butylmethylphosphine (**2**) and *tert*-butyl-*iso*-propylmethylphosphine (**4**) to illustrate how the enantiomeric excess can be determined by NMR.

NMR Investigation

We have measured the ^{31}P and ^{13}C NMR spectra of recrystallized adducts enriched in one diastereomer and of complexes of racemic phosphines **2** and **4** prepared *in situ*. For the latter it is essential that the phosphine should not be present in excess so that broadening of the NMR signals due to phosphine exchange is avoided.

a) ^{31}P NMR

The ^{31}P NMR data for the phosphines **2** and **4** and the [η^3-(+)(1R,5R)-pinenyl]nickel bromide adducts **3** and **5** are summarized in Table I. As expected, on complexation the ^{31}P resonances of the phosphines are shifted by about 35 ppm to lower field. For each complex two signals are observed, corresponding to the two diastereomers, but at 32.4 MHz their separation is relatively small. Similar observations were made for adducts of other phosphines which are not reported here. Thus, while the relative concentrations of the diastereomers can in principle be determined by ^{31}P NMR, even in favorable cases this requires a high field spectrometer in order to achieve sufficient resolution.

Table I. ^{31}P Chemical shifts of the free phosphines **2** and **4** and the complexes **3** and **5.**

Compound	δ_P	$\Delta\delta_P$	Complexation shift
2	−11.2	–	–
3	23.16[a] 23.21	0.05	34.4
4	+ 1.5	–	–
5	34.85 34.79[a]	0.04	33.3

[a] The underlined chemical shift is for the complex which crystallizes out preferentially.

b) ^{13}C NMR

^{13}C NMR spectra of both the recrystallized complexes and the racemic mixtures prepared *in situ* were recorded at 25.2 MHz. The signals were assigned with the help of the phosphorus-carbon coupling constants and of multiplicities and $^1J_{CH}$ coupling constants obtained from the proton-coupled spectra. The NMR data are collected in Table II.

For complex **3** all the 17 expected signals were observed and assigned. The signals from the diastereomers **3a** and **3b** are resolved for every carbon atom. For both the complexes **3** and **5,** the signals from C_1, C_4, and C_6 are all triplets in the proton-coupled spectrum but are unambiguously assignable by $^1J_{CH}$ (C_1, $^1J_{CH}$ = 157 Hz, η^3-allyl; C_4, in the cyclohexyl ring, $^1J_{CH}$ = 129 Hz; C_6, in the cyclobutyl ring $^1J_{CH}$ = 138 Hz). $|J_{PC_1}|<|J_{PC_3}|$, consistent with the given stereochemistry. Apart from the η^3-allyl carbons C_1 and C_3, the only carbon nuclei in the pinenyl residue which couple with phosphorus are C_4 and in addition C_8 in **5.** The methyl signal from the pinenyl group at *ca.* 26 ppm has been assigned to C_9 since this atom lies *gauche* to C_6 but *trans* to C_2 and C_4, while the signal at *ca.* 21 ppm is assigned to C_{10}, which lies *gauche* to C_2 and C_4 and *trans* to C_6.

The ^{13}C chemical shift data given in Table II are for the racemic mixtures, in order that the relative chemical shifts of the diastereomers may be compared more accurately. Where possible, the chemical shift difference for each signal pair is given. The splittings of the signals are largest for the phosphine carbons, especially those directly bonded to phosphorus, and C_1 in the pinenyl group. The shift differences do not appear amenable to any simple interpretation. In **5** the *iso*propyl methyl carbons C_{19} and C_{20} are diastereotopic: their chemical shifts differ by 3.59 ppm in **5a** and by 3.10 ppm in **5b,** which is not significantly different from the shift difference in the free ligand (2.87 ppm) [10].

Table II. ^{13}C NMR data for the complexes **3** and **5.**

Carbon	Multiplicity	**3a** δ_c	J_{PC} [Hz]	**3b**[a] δ_c	J_{PC} [Hz]	$\Delta\delta$[b]	Multiplicity	**5a**[a] δ_c	J_{PC}	**5b** δ_c	J_{PC}	$\Delta\delta$[b]
1	t	49.42	5.4	49.69	4.9	−0.27	t	44.55	6.2	44.26	6.5	+0.29
2	s	128.38	–	128.50[c]	–	−0.12		[d]		[d]		
3	d	80.71	20.6	81.06	20.9	−0.34	d	81.03	20.0	80.97	20.3	+0.06
4	t	29.20[e]	~ 2	29.28[e]	~ 2	±0.09	t	29.12	2.2	29.21	2.3	−0.09
5	d	39.90	–	39.98	–	−0.07	d	40.09	–	40.18	–	−0.09
6	t	29.47	–	29.61	–	−0.13	t	29.52	–	(29.52)[f]	–	–
7	d	46.46	–	46.27	–	+0.20	d	46.64	–	46.61	–	+0.03
8	s	39.02	–	39.20	–	−0.18	s	39.27	1.0	(39.27)[f]	(1.0)	–
9	q	26.08	–	26.00	–	+0.08	q	26.06	–	(26.06)[f]	–	–
10	q	21.42[e]	–	21.37[e]	–	±0.05	q	21.42	–	(21.42)[f]	–	–
11	q	9.45	23.5	8.30	23.9	+1.15	q	3.15	20.6	4.74	20.6	−1.59
12	s	30.97	19.6	31.13	19.9	−0.16	s	30.49	19.6	30.95	19.6	−0.46
13	q	27.10	4.9	26.79	4.5	+0.31	q	28.48	5.1	28.62	4.9	−0.14
14	s	133.53	34.1	134.37	33.1	−0.84						
15	d	133.30	10.7	132.95	10.8	−0.35						
16	d	128.25	~ 9	128.17	8.7	+0.07						
17	d	129.96[e]	~ 2	129.92[e]	~ 2	±0.04						
18							d	24.75	19.6	24.41	19.8	+0.34
19							q	21.07	7.1	20.86	6.6	+0.21
20							q	17.48	5.7	17.76	4.6	−0.28

[a] Complex which crystallizes out preferentially; [b] $\Delta\delta = \delta_n(\mathbf{a}) - \delta_n(\mathbf{b})$; [c] identification not certain, partially obscured by solvent; [d] obscured by solvent; [e] the assignment to the **a** or **b** complex was not made; [f] not resolved, chemical shift same as for complex **5a.**

Determination of the Diastereomeric Excess of Complexed Horner Phosphines

Although ^{31}P MNR spectra are more easily measured than ^{13}C NMR and thus might be expected to be more favourable for determining the ratios of the diastereomers, we found that the ^{13}C NMR spectra were more suitable for the following reasons:

(i) the ^{13}C resonances were generally much better resolved than the ^{31}P signals,

(ii) the ^{13}C NMR spectrum provides a reliable check of the structure of the complex and, in contrast to the ^{31}P NMR spectrum, guarantees that the pairs of signals do indeed come from the diastereomers and not from two unrelated compounds, and

(iii) in the ^{31}P NMR spectrum just one signal pair is observed, while in the ^{13}C NMR spectrum several sets of signals can be used to determine the ratio of the diastereomers.

The integrals of the best resolved signals were measured and the intensity ratio for each carbon signal relative to that of the same carbon in the other diastereomer was calculated. This avoids errors due to differences in T_1 or in NOE which affect comparisons between the intensities of signals due to different types of carbon atom. The diastereomeric excess was calculated from the averages of this ratio for a number of signal pairs; the error is estimated to be ±3%. Since these diastereomeric complexes differ only in the configuration at phosphorus, their diastereomeric excess should correspond to the enantiomeric excess for the Horner phosphine itself.

For complex **3** the diastereomeric excess was determined from the carbon signals of C_1, C_3, C_6, C_7 and C_{13}. The average was 74.8%. This is in excellent agreement with the enantiomeric excess of 73.7%, obtained from the specific rotation of the free (S)(−)-phosphine **2** $\{[\alpha]_D^{20} = -37.7°$ (6.0, benzene)$\}$. For this measurement the phosphine had been liberated quantitatively by treatment of complex **3** with an excess of trimethylphosphine. The diastereomeric purity of complex **5** can be obtained from the signals of C_1, C_{11}, C_{12} and C_{14}. The average d.e. was calculated to be 75%, compared with 77.2% e.e. determined from the optical rotation of the free (R)(+)-phosphine **4** $\{[\alpha]_D^{20} = 7.7°$ (5.0, benzene)$\}$.

The advantage of the NMR determination is that it is easy to carry out and interpret. By contrast, not only is the measurement of the specific optical rota-

tion of air-sensitive liquids such as tertiary phosphines experimentally tedious and unpleasant but a chemical correlation with a known reference compound, which is not always at hand, is also required.

Experimental

The ^{13}C NMR spectra were recorded at 25.2 MHz on a Varian XL-100 15A FT spectrometer in deuterobenzene at 35°. Chemical shifts are given relative to internal TMS. Proton decoupled spectra were recorded with an acquisition time of 2 s in order to obtain sufficient resolution. Proton coupled ("gated") spectra were measured to determine the multiplicities. Identification of signals from carbons not bearing protons was confirmed by their selective measurement using low power broad band decoupling.

^{31}P NMR spectra were measured at 32.4 MHz on a Bruker WP-80 FT spectrometer in deuterobenzene and the signals referenced to external 85% aqueous phosphoric acid.

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[10] ^{13}C NMR data for the free phosphines (D_6-benzene, 38°, δ_c relative to internal TMS): **2:** 137.43 (phenyl, C-*ispo*, $^1J_{PC}$ = 20.2); 133.42 (phenyl, C-*o*, $^2J_{PC}$ = 19.5); 128.55 (phenyl, C-*p*); 127.75 (phenyl, C-*m*, $^3J_{PC}$ = 6.8); 28.20 (*tert*-butyl, $^1J_{PC}$ = 13.1); 26.92 (methyl in *tert*-butyl, $^2J_{PC}$ = 14.2); 5.01 (P-methyl, $^1J_{PC}$ = 19.4): **4:** 27.95 (methyl in *tert*-butyl, $^2J_{PC}$ = 13.2); 27.69 (*tert*-butyl, $^1J_{PC}$ = 15.5); 23.95 (CH in *iso*propyl, $^1J_{PC}$ = 17.2); 22.92 and 20.15 (methyl in *iso*propyl, $^1J_{PC}$ = 24.5 and 9.9); 5.38 (P-methyl, $^1J_{PC}$ = 23.6).