Catalytic hydroformylation of (1S,5S)-(−)- and (1R,5R)-(+)-β-pinene: stereoselective synthesis and spectroscopic characterization of (1S,2R,5S)-, (1S,2S,5S)-, (1R,2R,5R)- and (1R,2S,5R)-10-formylpinane

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Abstract

(1S,5S)-(−)- and (1R,5R)-(+)-β-pinene have been hydroformylated in toluene to give (1S,2R,5S)- and (1R,2S,5R)-10-formylpinane with up to 95% diastereoselectivity using bimetallic CoRh(CO)$_7$ as a catalyst; the latter was generated in situ from preformed Co$_2$Rh$_2$(CO)$_{12}$ or a stoichiometric mixture of either [Rh$_4$(CO)$_{12}$] or [Rh$_6$(CO)$_{16}$] and [Co$_2$(CO)$_8$]. At 70–125°C and under 60 atm of syngas, the yields of hydroformylated products do not exceed 30% because of the concomitant isomerization of β- to α-pinene. In all cases the catalyst is recovered as a mixture of soluble cobalt carbonyl derivatives and a crystalline precipitate that contains most of the rhodium, mainly as [Rh$_6$(CO)$_{16}$]. Comparable yields and diastereoselectivities were obtained from reactions in tetrahydrofuran with a mixture of [Rh$_4$(CO)$_{12}$] and [N(PPh$_3$)$_2$]Cl as the catalyst precursor.

The corresponding (1S,2S,5S)- and (1R,2R,5R)-10-formylpinanes, along with the corresponding alcohols, were obtained diastereoselectively by use of bimetallic Co–Rh or homometallic Rh carbonyl catalysts modified with bis(diphenylphosphine)ethane (dppe). When unidentate phosphines such as triphenylphosphine were used in place of dppe, as the ligand/metal (L/M) ratio was raised the diastereoselectivity of both the hetero- and the homo-metallic catalytic system fell progressively, and was completely lost for L/M ≥ 4. However, a further increase in L/M to ca. 70–100 allows chemio- and diastereo-selective synthesis of both the (1S,2S,5S)- and (1R,2R,5R)-10-formylpinane.

The (1S,2R,5S)-, (1S,2S,5S)-, (1R,2R,5R)- and (1R,2S,5R)-10-formylpinane diastereomers were isolated by distillation under reduced pressure and fully characterized by IR, UV, ^{1}H and ^{13}C NMR and circular dicroism (CD) spectroscopy, and mass spectrometry.

The possible factors favouring the diastereoselective hydroformylation of β-pinenes under the conditions used are discussed.

Keywords: Pinene; Hydroformylation; Cobalt; Carbonyl; Rhodium; Stereoselectivity

1. Introduction

Naturally occurring terpenes are a source of inexpensive olefins that upon hydroformylation give aldehydes of relevance to the perfume industries, and some show antimicrobial activity [1–5]. Stereoselective hydroformylation of chirally pure terpenes could be of value for the industrial production of optically active intermediates that could be employed for optical resolution or asymmetric synthesis [6,7]. Enantiomerically pure (+) and (−) 3-formyl pinanes and 2-formylbornane were obtained several years ago by catalytic hydroformyla-

tion of α-pinenes, and spectroscopically characterized [8,9]. The hydroformylation of β-pinene has been investigated with several Co and Rh homometallic catalysts in the 60–140°C temperature range and under 35–300 atm of syngas [1,8,10–12]. However, owing to the isomerization of β-pinene during catalysis to the thermodynamic mixture of β- and α-pinene (β/α ≈ 4 : 96) and to a less pronounced difference in the steric hindrance of the two enantiotopic faces of the olefin, a complex mixture of several regio-isomeric and diastereomeric aldehydes was often obtained.

These are shown in Fig. 1, with the adopted numbering scheme. For instance, [Rh$_6$(CO)$_{16}$] catalyzes the hydroformylation of β-pinene to the cis-10-for-

mylpinane with a good diastereoselectivity, but the activity was very low and β-pinene was found to isomerize to α-pinene [12]. When [Co$_2$(CO)$_8$] was used as catalyst, it displayed even lower hydroformylation TF values, and the rate of isomerization of β- to α-pinene was increased, the thermodynamic ratio being reached within 3 h starting from pure β-pinene. Furthermore, probably as a consequence of the greater ability of cobalt to catalyze the hydroformylation of cyclic olefins [1], trans-3-formylpinane became the major product [12]. Low activity and ready isomerization of β- to α-pinene was also observed with the dinuclear [{Rh(μ-S^{t}Bu)(CO)P(OPh)$_3$}$_2$], which afforded a ca. 1:1 mixture of cis-10- and trans-3-formylpinane [10]. In contrast, both [RhCl(CO)(PPh$_3$)$_2$] and [HRh(CO)(PPh$_3$)$_3$], in the presence of free phosphine, are very active [1,11]. At a low phosphine/rhodium ratio (PPh$_3$/Rh = 11), [HRh(CO)(PPh$_3$)$_3$] shows very little stereoselectivity, and the cis- and trans-10-formylpinanes are obtained in comparable amounts. However, at higher PPh$_3$/Rh ratios (78–79), whereas [RhCl(CO)(PPh$_3$)$_2$] remained only weakly stereoselective, [HRh(CO)(PPh$_3$)$_3$] catalyzed the synthesis of cis-10-formylpinane with good selectivity [1]. Replacement of triphenylphosphine by tris(2-t-butylphenyl)phosphite as the ancillary ligand on rhodium caused a significant drop in the activity but allowed the trans-10-formylpinane, which is usually

obtained only in minor amounts, to be produced with a very high selectivity [1].

Since only a very few spectroscopic data for these 10-formylpinanes were available and the selectivity displayed by some catalysts appeared puzzling, we decided to undertake an investigation of the hydroformylation of (1S,5S)-(−)- and (1R,5R)-(+)-β-pinene, with the aim of gaining a better understanding of the factors favouring diastereospecific hydroformylation. An outcome of the work was that we obtained in high optical purity (> 90%) the (1S,2R,5S)-(−)-, (1S,2S,5S)-(−)-, (1R,2S,5R)-(+)- and (1R,2R,5R)-(+)-10-formylpinane diastereomers, which were characterized spectroscopically by IR, UV, and ^{1}H and ^{13}C NMR spectroscopic studies, and by mass spectrometry and circular dichroism (CD) investigations.

2. Results

2.1. Hydroformylation of (1S,5S)-(−)- and (1R,5R)-(+)-β-pinene

The high diastereoselectivity observed in the hydroformylation of α-pinene [6,10,11], and more recently of a t-butyl-oxazoline derivative [13], was attributed to the difference in steric hindrance between the two enan-
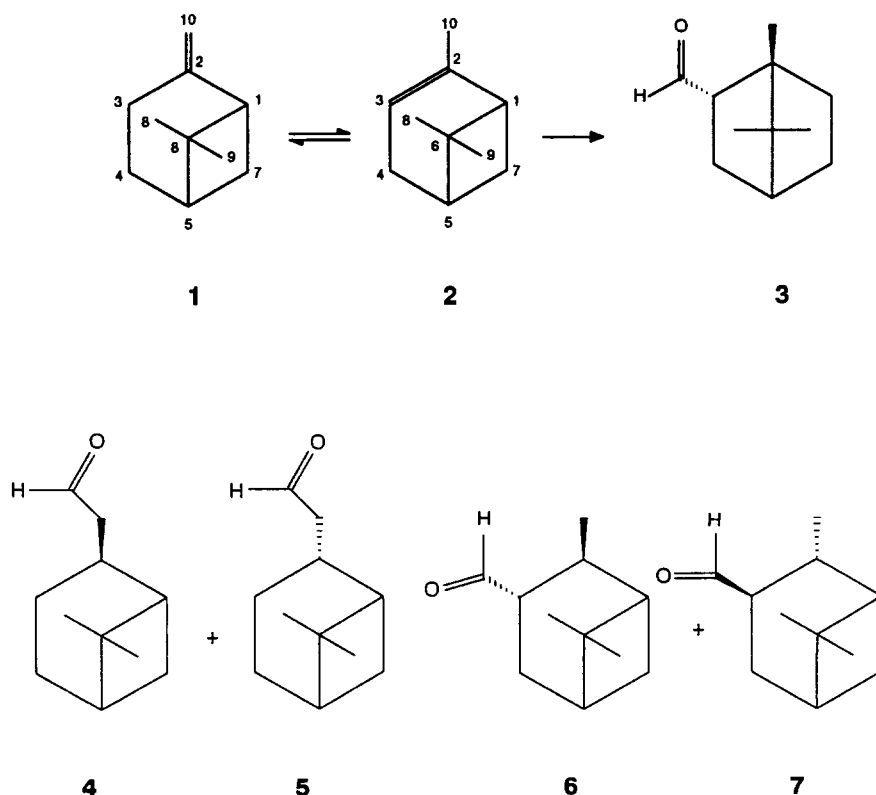

Fig. 1. Possible products of the hydroformylation of β-pinene with Co and Rh catalysts.
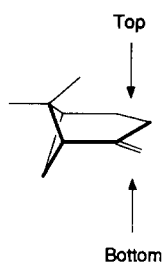
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Fig. 2.

tiotopic faces of the olefin. This difference for the exocyclic double bond of β-pinene is small and so the diastereoselective hydroformylation should be less but not trivial. It seemed puzzling, however, that metal carbonyl centres without substituents [12] and completely substituted metal centres [1,11] could both selectively attack the olefin from the least hindered face (i.e. from the bottom in Fig. 2), whereas increased steric hindrance by the ancillary ligand favoured attack on the most hindered face (i.e. from the top in Fig. 2) [1]. We therefore, undertook a study of the hydroformylation of β-pinene with a series of catalysts which could be expected to be very active and which could be thought to involve either metal carbonyl centres without substituents or those bearing ancillary ligands of a size comparable to CO, viz. the bimetallic Co–Rh carbonyl catalysts [14,15] and the $[Rh_4(CO)_{12}]/Cl^-$ system [16]. Indeed, it is known that bimetallic Co–Rh catalytic systems derived either from preformed $[Co_2Rh_2(CO)_{12}]$

or from stoichiometric mixtures of $[Co_2(CO)_8]$ and $[Rh_4(CO)_{12}]$ or $[Rh_6(CO)_{16}]$ often give hydroformylation rates much higher than those observed for the corresponding homometallic catalysts [14,15]. One possible explanation of this synergetic effect can be derived from the observation that under a carbon monoxide or a syngas atmosphere the bimetallic Co–Rh cluster mentioned above, and also mixtures of Co and Rh homometallic clusters, readily undergo equilibration with $CoRh(CO)_7$ [17]. As can also be inferred from studies carried out on carbonyl-substituted derivatives under syngas, $[CoRh(CO)_{7-x}L_x]$ ($x = 0–2$) [18] probably activate hydrogen by oxidative addition to the M–M bond leading to the formation of $[HCo(CO)_4]$ and $[HRh(CO)_3]$ [19,20] without the requirement of carbon monoxide elimination as for $[Co_2(CO)_8]$ [21], or the breaking of several Rh–Rh bonds as for both $[Rh_4(CO)_{12}]$ and $[Rh_6(CO)_{16}]$. Moreover, it is known that on increasing the temperature and in the absence of sufficient CO soluble $[Rh_4(CO)_{12}]$ is converted into $[Rh_6(CO)_{16}]$ which separates out from catalytic solutions owing to its very low solubility. Therefore, a second reason for this synergetic effect may be the ability of $[Co_2(CO)_8]$ to maintain most of the rhodium in solution through the above equilibrium with $[CoRh(CO)_7]$. Consequently, it appeared conceivable that attainment of a high hydroformylation rate through the generation of the catalyst precursor $[CoRh(CO)_7]$ under experimental conditions in which Rh carbonyls are diastereoselective and the isomerization rate of β- to α-pinene mainly catalyzed

Table 1
Hydroformylation of $(1S,5S)$-$(-)$-β-pinene [a]

Catalyst	Pressure (atm)	Temp. (°C)	Time (h)	Conversion (%)	Selectivity (%) [b]		
					4	5	3 + 6 + 7
$[Co_2Rh_2(CO)_{12}]$	60	100	1	32 [c]	1.6	95	3
$[Rh_4(CO)_{12}] + [Co_2(CO)_8]$	60	70	5	17 [c]	1.9	88	4.5
$[Rh_4(CO)_{12}] + [Co_2(CO)_8]$	60	100	1	31 [c]	1.6	92	4.4
$[Rh_4(CO)_{12}] + [Co_2(CO)_8]$ [d]	60	100	3	30 [c]	2.2	91	4.8
$[Rh_4(CO)_{12}] + [Co_2(CO)_8]$	60	125	0.5	32 [c]	0.6	76	12.5
$[Rh_4(CO)_{12}]/2Cl^-$	60	125	8	30 [c]	7.4	64	10.6
$[Rh_4(CO)_{12}]/2Cl^-$ [e]	60	125	8	33 [c]	10.6	82	5.4
$[Rh_4(CO)_{12}] + PPh_3$ [f]	60	150	5	20	52	46	< 1
$[Rh_4(CO)_{12}] + PPh_3$ [g]	60	100	5	62	94	2	< 1
$[Rh_4(CO)_{12}] + PPh_3$ [g]	60	125	5	96	94	4	< 1
$[Rh_4(CO)_{12}] + PCy_3$ [h]	60	125	5	51	85	12	2
$[Rh_4(CO)_{12}] + dppe$ [i]	60	150	5	15	93 [j]	4 [j]	< 1

[a] $[M] = 5 \times 10^{-3}$ M, [pinene] = 1 M, toluene as solvent and $CO/H_2 = 1$, if not otherwise stated.
[b] A difference from 100% selectivity is due to the presence of hydrogenated products.
[c] Due to isomerization of β- to α-pinene, only conversion into oxygenated products is given.
[d] $CO/H_2 = 2$.
[e] THF as solvent.
[f] $PPh_3/M = 4$; the activity dropped after ca. 3 h due to progressive deactivation of the catalyst.
[g] $PR_3/M = 100$.
[h] $PR_3/M = 20$.
[i] $dppe/Rh = 2$; dppe = bis(diphenylphosphine)ethane.
[j] Approximately 1 : 1.5 mixture of aldehyde and alcohol.

by Co is relatively slow [12], could facilitate an efficient and diastereoselective synthesis of 10-formylpinanes.

A few selected results obtained with the above mixed metal catalysts in the 70–150°C temperature range and under 60 atm of syngas in the hydroformylation of $(1S,5S)$-$(-)$- and $(1R,5R)$-$(+)$-2-methylene-6,6-dimethyl-bicyclo[3.1.1]heptane [1, $(1S,5S)$-$(-)$-β-pinene and 1', $(1R,5R)$-$(+)$-β-pinene] enantiomers are collected in Tables 1 and 2, respectively.

First, the overall catalysis of preformed $[Co_2Rh_2-(CO)_{12}]$ and of 2:1 molar mixtures of $[Co_2(CO)_8]$ and $[Rh_4(CO)_{12}]$ were very similar in activity and selectivity. In both cases, after depressurization and cooling to ambient temperature at the end of each catalytic run, the rhodium was recovered almost quantitatively as a crystalline precipitate essentially of pure $[Rh_6(CO)_{16}]$ while most of the cobalt remained in solution as a mixture of carbonyl compounds. The segregation of the two metals when also starting from $[Co_2Rh_2(CO)_{12}]$, and the consequent loss of heterometallic Co–Rh bonds, is in keeping with the known reactivity of both $[Co_2Rh_2(CO)_{12}]$ and $[CoRh(CO)_7]$ under CO and H_2 [19,20]. Secondly, the performances of the above catalytic systems were almost unchanged upon adding fresh substrate, repressurization to 60 atm with syngas and heating at 100°C. In contrast, in both cases the reaction solutions separated from $[Rh_6(CO)_{16}]$ precipitate showed very poor activity upon addition of fresh substrate and recycling. As a consequence, only 2:1 molar mixtures of $[Co_2(CO)_8]$ and $[Rh_4(CO)_{12}]$ were routinely used for most of the subsequent experiments.

As shown in Tables 1 and 2, under 60 atm of syngas the activity of these systems increases with temperature. The average hydroformylation TF values with a 1 M concentration of $(1S,5S)$-$(-)$-β-pinene and a 5×10^{-3} M overall concentration of metal were 5–6 h^{-1} at 70°C, ca. 50–60 h^{-1} at 100°C and in the 100–120 h^{-1} range at 125°C. Unfortunately, under these conditions the rate of isomerization of β- to α-pinene is about twice as fast

and the yields of hydroformylated products never exceed 30–35%. Both the reaction rates and the selectivities are insensitive to the composition of the gas composition over a wide range of CO/H_2 molar ratios. Significant drops in activity were only observed on increasing the CO/H_2 molar ratio to 4–6. It appears likely that the hydroformylation is almost exclusively carried out by $[HRh(CO)_x]$ rather than by $[HCo(CO)_x]$ species (see below), otherwise the selectivity of the bimetallic Co–Rh system would be surprising in view of the reported [8,12] performances of $[Co_2(CO)_8]$ in related experiments. Evidently, under the experimental conditions adopted hydroformylation at cobalt is almost completely depressed by the combination of mild temperature and relatively high CO partial pressure. It is well known that the apparent order of CO partial pressure in Co-catalyzed hydroformylation reactions is -1 at $p_{CO} > 10$ atm and is > 0 only for $p_{CO} < 10$ atm, whereas rhodium shows a similar inversion of the apparent reaction order of CO at ca. 40 atm [21,22].

The bimetallic Co–Rh system under 60 atm of syngas starts to lose its high selectivity only at reaction temperatures above 125°C, and this is only partially offset by a concomitant increase of the partial pressure of syngas or of CO. In all conditions, the major product (85%–96%) of the catalysis consists of $(1S,2R,5S)$-$(-)$-10-formylpinane (5) from $(-)$-β-pinene and $(1R,2R,5R)$-$(+)$-10-formylpinane (5') from $(+)$-β-pinene. The products were isolated in a pure state by fractional distillation under vacuum. The epimeric $(1S,2S,5S)$-(4) and $(1R,2R,5R)$-10-formylpinane (4') are only detected in small amounts (gas chromatographic analysis) and are undetectable in the ^1H and ^{13}C NMR spectra of distilled samples. These attributions are based on full spectroscopic characterization (see below) and retention times, since 4 and 5 (as well as 4' and 5'), often referred to as cis and trans diastereomers, can be separated by gas chromatography using capillary columns.

Table 2
Hydroformylation of $(1R,5R)$-$(+)$-β-pinene [a]

Catalyst	Pressure (atm)	Temp. (°C)	Time (h)	Conversion (%)	Selectivity (%) [b]		
					4'	5'	3 + 6 + 7
$[Rh_4(CO)_{12}] + [Co_2(CO)_8]$	60	100	5	21 [c]	2.1	87	8
$[Rh_4(CO)_{12}] + [Co_2(CO)_8]$	60	125	2	34 [c]	3.3	82	12.5
$[Rh_4(CO)_{12}]/2Cl^-$ [d]	60	125	8	27 [c]	4.5	78	12.1
$[Rh_4(CO)_{12}] + PPh_3$ [e]	60	125	8	94	95	4	< 1
$[Rh_4(CO)_{12}] + PCy_3$ [f]	60	125	8	28	93	4	< 1

[a] [M] = 5×10^{-3} M, [pinene] = 0.5 M, toluene as solvent and CO/H_2 = 1, if not otherwise stated.
[b] A difference from 100% selectivity is due to hydrogenated products.
[c] Due to isomerization of β- to α-pinene, only conversion into oxygenated products is given.
[d] THF as solvent.
[e] PPh$_3$/Rh = 100.
[f] PCy$_3$/Rh = 20.

In addition to alcohols, the impurities which accompany 5 (or 5') are isomeric aldehydes which show rather different retention times and slightly different fragmentation patterns but identical mass peaks in the mass spectrum. For instance, the $M - 15$ fragment is systematically more abundant in these aldehydes than in 4 and 5. Consequently, structures such as 3, 6 and, to a minor extent 7, appear the most likely. Unfortunately, since these isomeric aldehydes were always produced in small amounts in mixtures, our attempts at fractional distillation under vacuum to isolate a sample suitable for NMR spectroscopy failed.

Since our attribution of a *trans* stereochemistry to 5 was in contrast with previous findings in the hydroformylation of β-pinene with $[Rh_6(CO)_{16}]$ [12], we extended our investigations to a second active catalytic system, which can be generated from $[Rh_4(CO)_{12}]$ by addition of stoichiometric amounts of halide ions. CIR studies have shown that under syngas (60–150 atm) and in the presence of 1–3 equiv. of chloride ions, $[Rh_4(CO)_{12}]$ and $[Rh_6(CO)_{16}]$ readily disproportionate to mixtures of $[Rh(CO)_2Cl_2]^-$, $[Rh(CO)_4]^-$, $[Rh_5-(CO)_{15}]^-$ and, possibly, $[HRh(CO)_4]$ [16]. The above mixtures are active in the hydroformylation of formaldehyde to glycolaldehyde [16]. As shown in Tables 1 and 2, the above mixtures with an $[N(PPh_3)_2]Cl/[Rh_4(CO)_{12}]$ molar ratio of 1:2 were also active in the hydroformylation of β-pinene both in toluene and in THF solution. Although their activity is less than that of the Co–Rh bimetallic system, the selectivity is comparable. The *trans* diastereomers 5 and 5' are obtained stereoselectively. As with the Co–Rh system, and in keeping with the acidity of the rhodium carbonyl hydride derivatives, the hydroformylation yields do not exceed ca. 30% because of concomitant isomerization of β- to α-pinene.

The most notable difference in selectivity between the unsubstituted bimetallic Co–Rh carbonyl, as well as the $Cl^-[Rh_4(CO)_{12}]$ catalytic system investigated by us, and the homometallic carbonyl-substituted or unsubstituted rhodium catalysts previous investigated is the almost exclusive formation of the *trans* isomer 5 (or 5') in our experiments, rather than the *cis* isomer 4 (or 4') generally obtained by other workers [1,8,10,12]. To gain some understanding of the factors effecting selectivity, as well as to evaluate their effect on activity, we investigated the hydroformylation of β-pinene with $[Co_2(CO)_8]/[Rh_4(CO)_{12}]$ mixtures or with $[Rh_4(CO)_{12}]$ in the presence of phosphines. Since the phosphine-modified bimetallic system did not display any significant synergetic effect attributable to the presence of both Co and Rh, only the homometallic rhodium system was investigated in detail. A few significant results are collected at the bottom of Tables 1 and 2. First, the triphenylphosphine-modified $[Rh_4(CO)_{12}]$ catalytic systems, under experimental conditions identical to those

adopted for the $[Co_2(CO)_8]$-modified $[Rh_4(CO)_{12}]$ catalyst, display less activity. For instance, with PPh_3/Rh molar ratios ≤ 4, the observed initial *TF* values were in the range 8–30 h^{-1}. Furthermore, within 3 or 4 h significant deactivation of all catalysts occurred. Concomitantly, the selectivity toward the *trans* diastereomer 5 decreased on increasing the PPh_3/Rh molar ratio, so that with $PPh_3/Rh = 4$ a ca. 1:1 mixture of the diastereomers 4 and 5 is obtained. As expected from previous reports [1], upon increasing the PPh_3/Rh ratio to 100, an almost complete switch of selectivity towards the *cis* diastereomer 4 (or 4') was observed, with *TF* values of ca. 20 h^{-1}. Although the activities are not directly comparable with those observed with $[HRh(PPh_3)_3(CO)]$ in the presence of free PPh_3 as catalyst, due to differences in the experimental conditions [1], the selectivities observed with $[Rh_4(CO)_{12}]$ modified with triphenylphosphine are exactly the same. This is in keeping with the known chemistry of $[Rh_4(CO)_{12}]$ and triphenylphosphine. Indeed, it has been reported that progressive substitution of the carbonyls of $[Rh_4(CO)_{12}]$ gives $[Rh_4(CO)_8(PPh_3)_4]$ [23]. Further addition of triphenylphosphine results in degradation to the binuclear $[Rh_2(CO)_4(PPh_3)_4]$ that oxidatively adds dihydrogen to give $[HRh(CO)_2(PPh_3)_2]$ [24].

As shown in Tables 1 and 2, diastereomers 4 and 4' were also obtained with a selectivity up to 93% on replacing the unidentate triphenylphosphine with the bidentate bis(diphenylphosphine)ethane (dppe) even at relatively low dppe/Rh molar ratios (dppe/Rh ≥ 2). However, on increasing the temperature to 150°C, the activity of the catalyst remains rather low, with average *TF* values of 4–10 h^{-1}.

An enhanced selectivity toward the *cis* isomer was also observed on increasing the cone angle of the unidentate phosphine, as when using the tricyclohexylphosphine (PCy_3) instead of PPh_3. For instance, the stereoselectivity toward *cis*-10-formylpinane of the $[Rh_4(CO)_{12}]/PCy_3$ catalytic system is 85% with an L/Rh ratio of 20. Unfortunately, the activity of the system drops significantly as the L/Rh ratio is increased and, under the experimental conditions used, this system was practically inactive for a ratio of 100.

In addition to the switch from *trans* to *cis* selectivity, the addition of phosphine also prevents catalysis of the isomerization of β- to α-pinene at the lowest L/Rh ratios. This is attributed to the decreased acidity of the phosphine-modified carbonyl hydrides $[HRh(CO)_{3-x}-L_x]$.

2.2. Spectroscopic characterization of the (1S, 2R, 5S)-, (1S, 2S, 5S)-, (1R, 2R, 5R)- and (1R, 2S, 5R)-10-formylpinanes

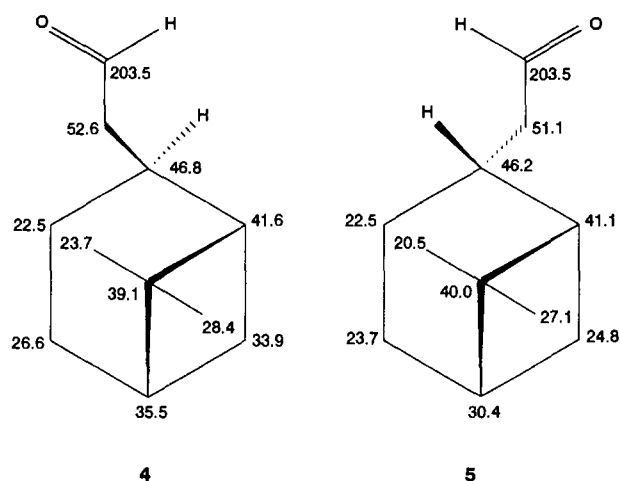As previously reported, the *trans*- and *cis*-10-formylpinanes are clearly distinguishable by ^1H NMR

Fig. 3. ^{13}C NMR data for the (1S,2S,5S)- (4) and (1S,2R,5S)- (5) epimers of 10-formylpinane. The corresponding (1R,2R,5R)- (4') and (1R,2S,5R)- (5') enantiomers of 10-formylpinane show identical chemical shifts to within experimental error.

spectroscopy, through the chemical shifts of the methyl protons (δ 1.05 ppm for 4 and 4', δ 0.9 ppm for 5 and 5') [1], and by ^{13}C NMR spectroscopy. The ^{13}C chemical shifts have been assigned guided by those of the related cis- and trans-myrtenal [25]. As shown in Fig. 3, where the assignments of the ^{13}C resonances of the two diastereomers are reported, the most significant difference between the (1S,2R,5S)-(−)- and (1S,2S,5S)-(−)-10-formylpinane epimers consists in the chemical shift of carbon atom 7. This in the cis diastereomer 4, because the methylene bridge is trans to the −CH$_2$−C(=O)H moiety which lies on the same side of the gem-dimethyl carbon bridge and falls in a region where the trans isomer 5 does not show any absorption. The corresponding (1R,2R,5R)-(+)- and (1R,2S,5R)-(+)-10-formylpinane enantiomers show identical NMR spectra to the above, as expected. Consistent with the capillary column gas chromatography results, the ^{13}C NMR spectra allow us to calculate ca. 95% optical purity for the various distilled samples.

The optical rotatory powers (α_D) of the above diastereomers are collected in Table 3. As expected, the introduction of a third asymmetric carbon has little effect on the optical rotatory power. Therefore, the α_D values allow us to distinguish between each pair of diastereomers (4–4' or 5–5'), but do not enable us to discriminate between the 4–5, and presumably 4'–5', pair of epimers which derive from the hydroformylation of (−)- or (+)-β-pinene, respectively. This led us to study their optical behaviour in more detail.

The spectroscopic behaviour of aldehydes has been investigated both experimentally and theoretically [26,27] but, to our knowledge, no circular dichroism (CD) study of asymmetric aldehydes has so far been reported [28]. For instance, the isotropic ultraviolet and visible (UV–vis) spectra of formaldehyde and higher aldehydes show absorptions at ca. 300 and 190 nm. Both absorptions have been assigned to excitations to triplet valence and Rydberg states, although the particular transition involved may be controversial [26,27]. Thus, while there is complete agreement in assigning the weak absorption at ca. 300 nm (molar extinction coefficient $\varepsilon = 100$ in formaldehyde) to a symmetry forbidden n → π* transition, several controversial single–triplet promotions (e.g. valence n → σ*, n → π* or π → π*, as well as n → 3s Rydberg transitions) have been proposed in the past as being responsible for the second excitation at ca. 190 nm. Nowadays, the latter absorption is thought to arise from a mixing of π → π* and n → 3s Rydberg transitions [27].

The availability of the trans (5) and cis- (4 and 4') 10-formylpinane diastereomers in a satisfactory optical purity made possible an investigation of their chiroptical behaviour to further confirm the assigned absolute configuration. In any case, a study of the aldehydic chromophore by UV–vis and CD spectra appeared desirable in view of the lack of previous studies.

The UV and CD spectra of 5, 4 and 4' are shown in Fig. 4 and selected parameters for 4, 4' and 5 are listed in Table 3. The UV spectrum of 5 in the top part of Fig.

Table 3
Chiroptical behaviour of the 4, 4' and 5 diastereomers [a]

Compound	Solvent	M × 10^2	[α_D] (wt.%)	ε (λ,nm)	$\Delta\varepsilon$ (λ,nm)	g × 10^3
4	CHCl$_3$		−17.1 (1.2%)			
	heptane	0.759	−15.4 (1.0%)	30 (300)	+0.127 (300)	+6.0
					−0.438 (193)	
4'	CHCl$_3$		+15.2 (1.2%)			
	heptane	1.217	+15.0 (1.0%)	31 (300)	−0.143 (300)	−5.0
				1314 (192)	+0.468 (191)	+0.4
5	CHCl$_3$			20 (298)	−0.082 (298)	−4.0
	heptane	0.985	−17.4 (1.0%)	18 (300)	−0.092 (300)	−5.1
					−0.150 (192)	
5* [b]	heptane	3.28		148 (212)	−0.187 (212)	

[a] Slight discrepancies between the ε and $\Delta\varepsilon$ values for the diastereomeric aldehydes are due partially to air oxidation during prolonged handling in dilute solution.
[b] Compound 5* is the acid obtained by oxidation of 5.

4 shows one band at ca. 300 nm and one inflection lower than 200 nm, corresponding to two electronic transitions, as evident in the isotropic spectra. The bottom part of the figure, which reports the CD spectrum of 5, shows two corresponding Cotton effects. The first band at ca. 300 nm shows vibronic structure with an apparent progression of ca. 900 cm^{-1}. The absorption of ca. 300 nm is unambiguously due to the n → π* electronic transition of the –C(=O)H chromophore in an aliphatic chiral substrate, since upon oxidation of the aldehyde to the corresponding acid, this absorption is replaced by a new, more intense absorption at ca. 220 nm (dotted plot in Fig. 4) arising from the –C(=O)OH chromophore. As a result of the observed induction of optical activity by the chiral aliphatic radical on the n → π* electronic transition of the formyl chromophore, the negative sign of the corresponding multiple Cotton effect seems to relate mainly to the absolute configuration, R, of the asymmetric carbon atom in position 2 of the aliphatic cycle. Thus, both 5 (Fig. 4) and 4′ (Fig. 5) show a negative sign. In contrast, the second band, only noticeable as an inflection in the continuously rising energy curve of the isotropic spectra, is partly resolved into a Cotton effect at ca. 190 nm in the CD experiments. The related sign of the Cotton effect seems to be determined mainly by the absolute configurations of carbon atoms 1 and 5 of the aliphatic cycle, since it is negative for both 4 and 5 (1S,5S), and positive for 4′ (1R,5R). The octant rule, which has been often successfully applied to interpret the sign of the Cotton effect in cyclic ketones such as (S)-(+)-3-meth-
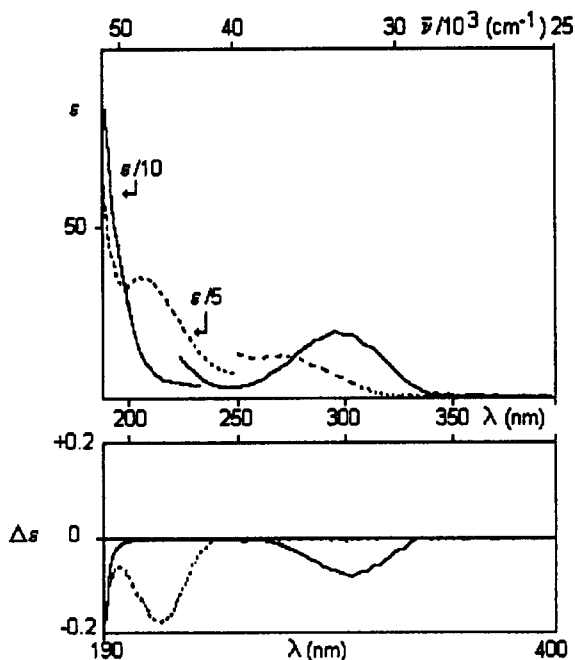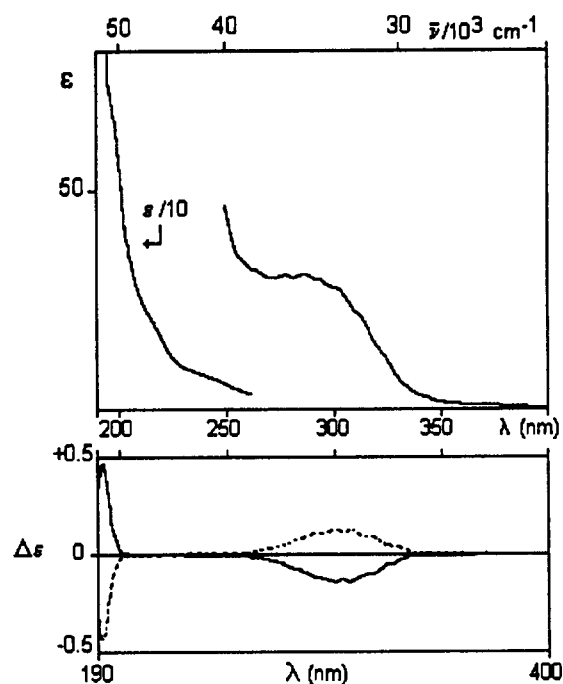

Fig. 5. UV (top) and CD (bottom, dotted plot) spectra of (1S,2S,5S)-10-formylpinane (4), and CD spectrum (bottom, continuous plot) of (1R,2R,5R)-10-formylpinane (4′) in heptane.

ylcyclopentanone [28] seems to be of little use in this case.

3. Discussion

The hydroformylation results reported here clearly show that as the steric hindrance of the probable active species [HRh(CO)$_{3-x}$L$_x$] increases on progressive replacement of carbonyl groups by bulkier triphenylphosphine and tricyclohexylphosphine, the activity drops and the stereoselectivity switches from 5 to 4 (or from 5′ to 4′). The stereochemistry of hydroformylation has been shown to result from a formal *syn* addition of a H–M moiety in all cases involving both cobalt and rhodium investigated [22], and, more recently, in the case of a platinum catalyst [29]. Either π-complexation of the olefin to the metal followed by insertion into the H–M bond or direct *syn* addition of a H–M moiety to the O=C double bond in a 4-centre transition state should have identical stereochemical consequences. As inferred from Fig. 2, steric considerations suggest that π-complexation *anti* to the *gem*-dimethyl carbon bridge (attack from the bottom or to the least hindered face of the olefin) should always be the most favourable. Such an attack would give rise to the *cis* 4 and 4′ diastereomers, as occurs with the bulkier [HRh(CO)$_{3-x}$L$_x$] catalysts. In contrast, the least bulky [HRh(CO)$_3$] species, generated in situ via fragmentation either of heterometallic Co–Rh clusters or of [Rh$_4$(CO)$_{12}$], evi-

Fig. 4. UV (top) and CD (bottom) spectra of (1S,2R,5S)-10-formylpinane (5, continuous plot) and its corresponding acid (5*, dotted plot) in heptane.

dently attacks from the top on to the most hindered face of the olefin, as shown by the stereoselectivity of the hydroformylation in the *trans* 5 and 5' diastereomers. Moreover, it has also been reported that the hydrogenated pinane obtained as a by-product of the hydroformylation of β-pinene with $[Rh_6(CO)_{16}]$ consists only of the diastereomer having the methyl group *anti* to the *gem*-dimethyl carbon group [12]. Although it is reasonable that such an attack should be available preferentially only to the least crowded carbonyl $[HRh(CO)_3]$, it raises the question of why the expected products from the addition on to the opposite least-hindered face of the olefin are so disfavoured. A greater electron density or the *exo* face of the endocyclic double bond of norbornene [30] has been suggested to be the origin of the preference for *exo* attack in its hydroformylation reactions [29]. Such an unbalance in the electron density on the two faces of an exocyclic double bond appears less probable and is contradicted by the results of the hydroformylation of *R*-(+)-camphene which show very little discrimination between the two faces [31]. We therefore suggest that in the case of β-pinene, discrimination between the two enantiotopic faces of the substrate made by an unsubstituted $[HRh(CO)_3]$ species is not only a straightforward consequence of the different steric hindrance which they present to approach of the catalyst, but is also greatly influenced by the relative energies of the transition states which are traversed on the way to the corresponding σ-alkylrhodium derivatives. In other words, attack from the bottom should give rise to a π-complex which is more favoured thermodynamically than that derived from a top addition. However, the former leads to the σ-alkyl intermediate complex more slowly than the latter, probably because it forces the methylene group closer to the methyl of the *gem*-dimethyl group, rather than away, and traverses a higher-energy transition state. A related crossing of the reaction profiles of diastereomers has been demonstrated to be at the origin of the stereospecific hydrogenation of olefinic substrates [32].

The various hindrances that the catalyst should experience on approaching the two faces of the olefin become most different on increasing the crowding at the metal centre. In this case, energy differences between π-complexes arising from bottom and top attack may become so large that only the former remains possible. As a consequence, selectivity should switch from the *trans* to the *cis* diastereomers and the rate of hydroformylation should slow down because of steric hindrance of the π-complex, and within the transition state. Accordingly, at relatively low PPh_3/Rh molar ratios, which should favour the presence of $[HRh(CO)_2(PPh_3)]$, a mixture of 4 and 5 is obtained, with a rate lower than those displayed by the Co–Rh and the Rh–Cl$^-$ systems. Moreover, with high PPh_3/Rh molar ratios (70–100) or with bidentate ligands, which should favour

disubstituted $[HRh(CO)(PPh_3)_2]$ [33], diastereomer 4 was obtained stereoselectively, although at an even lower rate.

4. Experimental details

All preparations of reaction solutions were performed under dinitrogen or using a standard Schlenk tube technique. $[Rh_4(CO)_{12}]$ and $[Co_2Rh_2(CO)_{12}]$ were prepared by literature methods [34,35]. $[Co_2(CO)_8]$ was purchased from Strem and crystallized from heptane. $(1S,5S)-(-)-\beta$-Pinene and $(1R,5R)-(+)-\beta$-pinene were obtained from Fluka and used as purchased. Toluene was dried over sodium and distilled prior to use.

4.1. Hydroformylation reactions

Hydroformylation reactions were carried out in 250 ml Parr autoclave reactors equipped with mechanical stirrers, internal thermocouples, addition ports, sampling valves and a cooling coil. In a typical experiment, the autoclave was charged with a solution made as following: $[Co_2(CO)_8]$ (43 mg), $[Rh_4(CO)_{12}]$ (47 mg), mesitylene (2 g, as internal standard), and olefin (16 g) were dissolved in toluene (ca. 50 ml). The resulting solution was brought to a final volume of 100 ml with toluene and charged into the autoclave glass reactor. The autoclave was pressurized to 60 atm with a 1:1 mixture of CO and H_2, and thermostatted at 100°C. The hydroformylation reactions were run at constant pressure and were stopped by rapid cooling to ca. 20°C and depressurization.

4.2. Analysis of the products

The product distributions of each olefin during the catalytic reactions were analyzed every 30 min by sampling. Analyses were performed on Hewlett Packard HP5890 GC-FID and 5971 GC-MSD instruments. Standard and capillary (50 m) Carbowax 20M columns were used respectively.

The final diastereomeric distribution was determined by ^1H and ^{13}C NMR spectroscopy after vacuum distillation. NMR spectra were recorded for $CDCl_3$ solutions containing TMS as internal standard on Varian Gemini 200 and 300 spectrometers. The assignments are based on DEPT studies and comparisons with related derivatives [25].

The IR spectra were recorded on a Perkin-Elmer 1600 interferometer. Ultraviolet and visible spectra (UV–vis) were measured on a Jasco UVIDEC-650 spectrophotometer between 20000 and 52600 cm^{-1} (400–190 nm), both in heptane and chloroform solutions. Circular dichroism (CD) spectra were obtained from the same solutions on a Jasco 500A spectropo-

larimeter equipped with a Jasco Data Processor, by repeated scannings (60 times) and averaging of the accumulated data. Optical rotation (α_D) was measured with a Bendix 143C polarimeter.

Acknowledgment

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