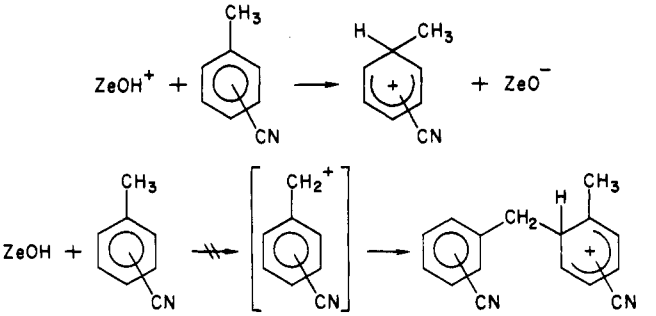
out. The apparent direct interconversion could involve 3,5-DMB which never desorbs to be observed in the gas phase. In principle, these two alternatives could be distinguished by labeling one of the two methyl groups and observing the label in the products at very low conversions.

While CN migration is unlikely, the possibility cannot be excluded without labeling studies in the toluonitriles. Isomerizations of DMB's require methyl migrations.

Large port zeolites such as faujasites transalkylate xylenes to toluene and trimethylbenzenes.[10] Smaller zeolites such as HZSM-5 and mordenite are more selective and are useful to disroportionate toluene to *p*-xylene and benzene.[11] HZSM-5 has shape selective sites which preclude the formation of the branched diphenylmethane intermediates proposed for the intermolecular exchange process.[2] That the products are formed in this reaction by intramolecular 1,2-shifts rather than an intermolecular, electrophilic mechanism is an example of transition-state selectivity.

The acid sites of HZSM-5 are unusually strong.[11] Thus even though large zeolites such as Y and Omega can accommodate all the substrates and transition states, they are not effective catalysts because the acid sites are not strong enough to form the intermediate carbenium ions from the deactivated methylbenzonitriles.



Experimental Section

3,4-Dimethylbenzoic acid was converted to 3,4-DMB by treatment with chlorosulfonyl isocyanate.[12,13] The sample of 2,5-DMB obtained from Pfaltz and Bauer had some 2,4-isomer as an impurity. All other nitriles were obtained from commercial sources and used without additional purification. The GC analyses were done by using a FI detector and a 12 ft × $^1/_8$ in. column of 2% UCON 40 HB 5100 1% KOH on CWHP 80-100 at 120 °C. The elution order for the toluonitriles was ortho < meta < para and for the dimethylbenzonitriles 2,5 < 2,4 < 3,4.

Registry No. *o*-Toluonitrile, 529-19-1; *m*-toluonitrile, 620-22-4; *p*-toluonitrile, 104-85-8; 2,4-dimethylbenzonitrile, 21789-36-6; 2,5-dimethylbenzonitrile, 13730-09-1; 3,4-dimethylbenzonitrile, 22884-95-3.

(10) Lanewalda, M. A.; Bolton, A. P. *J. Org. Chem.* **1969**, *34*, 3107.
(11) Wang, I.; Chen, T. J.; Chaa, K. J.; Tsai, T. C. *J. Catal.* **1979**, *60*, 140.
(12) Lohaus, G. *Org. Synth.* **1970**, *50*, 18.
(13) Friedman, L.; Shechter, H. *J. Org. Chem.* **1961**, *26*, 2522.

Directing Effects in Homogeneous Hydrogenation with $[Ir(cod)(PCy_3)(py)]PF_6$

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The presence of a ligating group, e.g., OH, CO_2Me, C=O, or OMe, on an olefinic substrate is shown to direct the attack of the hydrogenation catalyst $[Ir(cod)(PCy_3)(C_6H_5N)]PF_6/H_2/CH_2Cl_2$ from the face of the molecule containing the directing group. Isomerization is a minor side reaction in the cases studied. The origin of this effect is discussed and a model intermediate isolated.

One of the important advantages of homogenous over heterogeneous catalysis is selectivity. This has been strikingly shown by the achievement of both stereo- and enantioselective control in a number of organic transformations, of which the Sharpless[1] asymmetric epoxidation is perhaps the most significant. We report here on the way that a ligating group, particularly OH, in certain olefinic substrates can bind the catalyst and so direct addition of H_2 from that face of the molecule which contains the ligating group. This has only been reported for a restricted range of catalysts, including our own $[Ir(cod)(PCy_3)(py)]PF_6$, which are sufficiently coordinatively unsaturated in their active form to be able to bind the ligating group as well as H_2 and the C=C double bond. Heterogeneous catalysts have also been known to show directing effects, but these are much less strong and much less predictable than those described here.[2]

The first observation of a directing effect in homogeneous hydrogenation was reported by Thompson,[3] who showed, as early as 1974, that directed reduction of a tricyclic homoallylic alcohol, stigmasterol, was possible using the lithium salt of the alcohol with $RhCl(PPh_3)_3$ as catalyst. In 1982, Brown and Naik[4a] described the reduction of various unmodified acyclic chiral allylic and homoallylic alcohols with $[(nbd)Rh(dppb)]PF_4$ (dppb = $PPh_2P(CH_2)_4PPh_2$) in CH_2Cl_2 to give product diastereomer ratios as high as 97:3.

Prompted by the work of Brown and Naik, we,[5] Evans and Morrisey,[6] and Stork and Kahne[7] have recently

(1) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974.
(2) Thompson, H. W.; Naipawer, R. E. *J. Am. Chem. Soc.* **1973**, *95*, 6379 and references therein.
(3) Thompson, H. W.; McPherson, E. *J. Am. Chem. Soc.* **1974**, *96*, 6232.
(4) (a) Brown, J. M.; Naik, R. G. *J. Chem. Soc., Chem. Commun.* **1982**, 348. (b) Brown, J. M.; Hall, S. A. *Tetrahedron Lett.* **1981**, *25*, 1393; (c) *J. Organomet. Chem.* **1985**, *285*, 333.
(5) Crabtree, R. H.; Davis, M. W. *Organometallics* **1983**, *2*, 681.
(6) Evans, D. A.; Morrisey, M. M. *Tetrahedron Lett.* **1984**, *25*, 4637; *J. Am. Chem. Soc.* **1984**, *106*, 3866.
(7) Stork, G.; Kahne, D. E. *J. Am. Chem. Soc.* **1983**, *105*, 1072.

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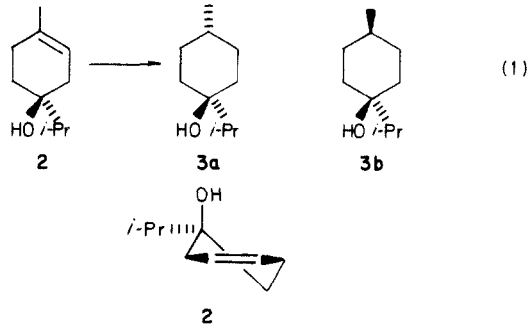
studied directing effects and published brief papers on the results. Both our own [Ir(cod)(PCy_3)py]PF_6 (1)[8] as well as the related [(diene)M(dppb)]BF_4 catalysts (M = Rh or Ir) have been studied.[4-7] The directing effect of the iridium catalyst 1 has also been used in syntheses of daunomycin[9a] and pumilitoxins.[9b] More recently, Brown and Hall[4b,c] have amplified their earlier work with studies on unsaturated cyclic alcohols and esters with both Rh and Ir catalysts.

Results and Discussion

Our initial work was carried out on the commercially available terpinen-4-ol (2). This is reduced by 5% Pd/C in ethanol to give a 20:80 ratio of the two possible products **3a** and **3b**. A slight directing effect, often called the



"haptophilic effect",[2] operates even in this heterogeneous case because in cyclohexane a 53:47 ratio is obtained. It appears that these results can probably be best understood on the basis of the conformational preference of **2** shown in eq 1. The bulky *i*-Pr group must take up a pseudoequatorial orientation, making the OH pseudoaxial. The substrate can now be thought of as having two faces: the upper face is polar while the other is not. When adsorbed on to the catalyst surface, the adsorbed face interacts with the surface and the other with the solvent. In a nonpolar solvent, such as cyclohexane, the polar face of the substrate will tend to interact with the weakly polar catalyst surface. On the other hand, in a polar solvent, the polar face of the molecule will show a greater preference to interact with the solvent side, resulting in a greater tendency for catalyst adsorbtion on the nonpolar face. The effect is usually small, and the heterogenous directing effect[2] is correspondingly of limited practical use. It would also be hard to predict the outcome in advance of experiment, especially in a molecule containing several functional groups.

In contrast, our homogeneous catalyst 1 in CH_2Cl_2 at 0 °C gives essentially only **3a**. The upper limit of **3b** can be set at ≤0.1%. This is a very large directing effect and clearly has practical utility.[9] Furthermore, because this catalyst seems to depend on coordination chemistry rather than surface adsorbtion for its directing properties, the stereochemical outcome is likely to be much more predictable.[7] This is, of course, a great advantage in planning a synthetic strategy.

We looked at a number of different substrates shown in Table I to see if directivity effects could be extended to allylic alcohols.[7] Excellent results were obtained (entries 2–7). In four cases the product isomeric ratio exceeds 99:1 of directed to counterdirected product, and in the other two cases it exceeds 96:4. In each case Pd/C(EtOH) gives a mixture that usually favors the counterdirected product, presumably for the reasons suggested earlier. This is very convenient from a synthetic point of view, but the Pd/C(EtOH) system cannot be relied upon to furnish the counterdirected product as shown in entry 7. Here the bulky isopropyl group must hinder adsorbtion of the corresponding face of the substrate. The predicted directed product is obtained with the Ir catalyst in this case too.

The yields of product are usually good or excellent. Isomerization of the allylic alcohols to the corresponding ketones occurs to a minor extent (≤3%). This is discussed further below.

In Table I, the products observed are listed together with the percentage of each found by GC. The directivity, *D*, follows from the observed percentages of directed (A) and counterdirected isomer (B), as defined in eq 2. The

$$D = \frac{[A] - [B]}{[A] + [B]} \qquad (2)$$

possible values of *D* range from +1 to −1. Using *D* makes it easier to compare the directivities of two entries which differ significantly in percentage of isomerization or starting material remaining.

A striking feature of the Ir results is that the directivity lies in the range 0.92–1.0, broadly in line with the results obtained by Stork et al.[7] A notable difference between their conditions and our is that we use 2.5% catalyst rather than their 20% loading. As shown by Evans et al.,[6] the directivity decreases with increasing catalyst concentration, an effect which they ascribe to the presence of several catalyst species in solution. In only one case have we studied exactly the same substrate at 2.5% catalyst loading that had previously been studied at 20%: our entry 2. The directivity rose from 0.973 at the higher loading to 0.99 at the lower. More importantly, the yield rose from 48% to 98.8%. As has been shown previously, an important deactivation pathway for the catalyst involves the formation of a trinuclear cluster complex and so is expected to be much faster at higher catalyst loading.[8a] We also observe some isomerization, not reported previously.

All efforts to obtain directing effects with catalysts less coordinatively unsaturated than 1 such as $RhCl(PPh_3)_3$ or $RuCl_2(PPh_3)_3$ were fruitless. Direction requires binding of the ligating group, H_2, and C=C all to the metal, for a total electron count of 6. The ML_n metal fragment must presumably have a 12-electron structure so that the total sum is 18. This may be the reason for the failure of "$RhCl(PPh_3)_2$", the 14-electron species believed to derive from $RhCl(PPh_3)_3$ under reaction conditions, to give directing effects. In contrast, the 12-electron "RhL_2" or "IrL_2^+" systems do direct. Efficient asymmetric hydrogenation also requires chelation by the substrate via C=C and amide C=O and is only known to be efficient for the 12-electron "RhL_2^+" fragment.

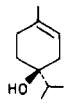
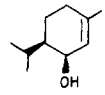
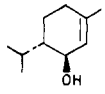
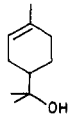
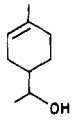
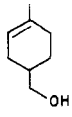
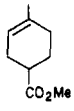
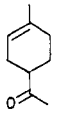
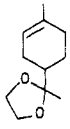
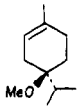
The interesting feature of the iridium catalyst, shared to some extent by RhL_2^+ is that it can bind both the soft ligands H_2 and C=C as well as the hard OH group. The existence of isolable complexes such as [$IrH_2(ROH)_2(PPh_3)_2$]BF_4 (R = H or Et)[10b,c] demonstrates the ability

(8) (a) Crabtree, R. H.; Felkin, H.; Morris, G. E. *J. Organomet. Chem.* **1977**, *141*, 205. (b) Several syntheses of 1 have been described.[8c-e] (c) Crabtree, R. H.; Morris, G. E. *J. Organomet. Chem.* **1977**, *135*, 395. (d) Suggs, J. W.; Cox, S. D.; Crabtree, R. H.; Quirk, J. M. *Tetrahedron Lett.* **1981**, *22*, 303. (e) Crabtree, R. H.; Morehouse, S. M.; Quirk, J. M. *Inorg. Synth.*, in press.

(9) (a) Mashado, A. S.; Olesker, A.; Castillon, S.; Lukacs, G. *J. Chem. Soc., Chem. Commun.* **1985**, 330. (b) Schultz, A. G.; McCloskey, P. J., submitted for publication in *J. Am. Chem. Soc.*

(10) (a) Crabtree, R. H.; Davis, M. W.; Mellea, M. F.; Mihelcic, M. *Inorg. Chim. Acta* **1983**, *72*, 223. (b) Crabtree, R. H.; Demou, P. C.; Eden, D.; Mihelcic, J. M.; Parnell, C.; Quirk, J. M.; Morris, G. E. *J. Am. Chem. Soc.* **1982**, *104*, 6994. (c) Shapley, J. R.; Schrock, R. R.; Osborn, J. A. *J. Am. Chem. Soc.* **1969**, *91*, 2816. (d) Crabtree, R. H. *Ann. N. Y. Acad. Sci.* **1984**, *415*, 268.

Table I. Results of Some Directed Hydrogenations[a]

entry	substrates	hydrogenation, %	directed isomer, %	counter-directed isomer, %	directivity	directivity change[b]	isomerization, %	starting material, %
1		>99.9	>99.9 (20)	<0.1 (80)	>0.998 (−0.6)	1.6		<0.1
2		98.8	97.1 (18.4)	0.7 (81.6)	0.99 (−0.63)	1.63	2.2	<0.1
o		98.5	98.5 (27.4)	<0.1 (72.6)	>0.998 (−0.452)	1.45	1.4	<0.1
4		99.4	98.5 (38.4)	0.9 (61.6)	0.98 (−0.23)	1.23	0.5	0.1
5		97.3	97.3 (16.7)	<0.1 (83.3)	>0.998 (−0.67)	1.67	2.5	0.1
6		97.7	96.2 (15.4)	1.5 (84.6)	0.97 (0.69)	1.66	2.3	<0.1
7		>99.9	962 (85)	3.8 (15)	0.92 (0.7)	0.22	<0.1	<0.1
8		85.3	66.2 (68)	19.1 (32)	0.55 (0.36)	0.19	<0.1	14.7
9		99.2	91.0 (73.6)	8.2 (26.4)	0.83 (0.47)	0.36	<0.1	0.8
10		>99.9	89.6 (70.6)	10.4 (29.4)	0.79 (0.41)	0.38	<0.1	<0.1
11		96.7	95.0 (57.5)	1.7 (42.5)	0.96 (0.15)	0.81	<0.1	3.3
12		>99.9	99.2 (53.8)	0.8 (42.6)	0.98 (0.08)	0.90	<0.1	<0.1
13		45.2[c]	62.4 (55.0)	37.6 (45.0)	(0.25) 0.1	0.15	<0.1	54.8
14		>99.9	>99.9 (15)	<0.1 (85)	>0.998 (−0.7)	1.7	<0.1	<0.1
15		>99.9	>99.9 (20)	<0.1 (80)	>0.998 (−0.6)	1.6		<0.1

[a] Values for Pd/C(EtOH) in parentheses. [b] On going from Pd to Ir. [c] It is not clear why we see such poor yield and directivity. Possibly the slightly acidic Ir catalyst may have opened the heterocyclic ring to some extent, and this could lead to catalyst deactivation. We were not able to determine the relative stereochemistry in the two products in an unambiguous way but suggest the most likely one here.

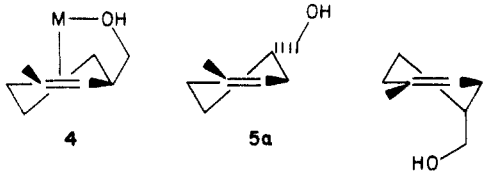
of what might have been expected to be a relatively soft Ir(III) system to bind hard ligands. We have proposed that two factors are involved, an antisymbiotic effect between the ROH group and the trans hydrides[10a] and the net positive charge on the complex as a whole.[10d] The Rh(III) complexes are much less stable.

The most probable form of the catalyst at high concentration is a hydride-bridged dimer. It is now well established that the M–H group can act as a two-electron ligand to fill a vacant coordination site on a second metal center (eq 3).[11] Such binding, by the arguments given

$$M{-}H + M{-}\square \rightarrow M{-}H{-}M \qquad (3)$$

above, could prevent directivity, being observed by reducing the unsaturation of the "IrL_2^+" group. Decreased directivity is indeed observed at higher catalyst concentrations.

We wanted to see whether exocyclic OH groups would also direct.[7] Entries 8–10 show that the directed product is obtained for three homoallylic alcohols, but not very much more of it than is obtained with Pd/C(EtOH). Stork's[7] examples (involving allylic alcohols) are much more convincing in this respect (e.g., 1-methyl-3-(hydroxymethyl)cyclohexene, D = 0.83(Ir) vs. 0.66(Pd/C)).

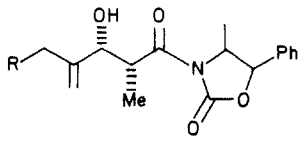


4 5a 5b

We can rationalize this difference on the basis of the expected groundstate conformations of the two species **4** and **5a**. Models show that **4** can chelate to Ir via the OH and (C=C) groups, as shown, with unexceptional bond angles and distances; conformer **5a** in contrast cannot do so. Even the higher energy pseudoaxial conformer **5b** does not chelate well, the Ir–O–C bond angles being unsatisfactory. Such directivity as is observed probably arises from **5b**; if so, we can identify this as the directing conformer. This is suggested by the fact that progressive substitution of the hydroxymethyl group (entries 9 and 8) leads to progressively lower directivity differences between the Ir and Pd cases. Substitution of the CH_2OH group should also make the directing conformer **5b** more unstable with respect to the ground-state conformer **5a**.

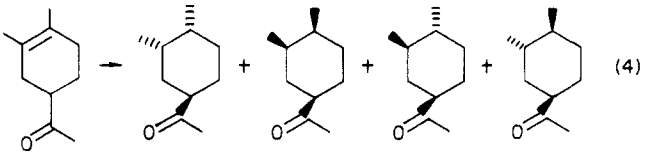
Other functionalities than OH also direct. For example CO_2Me (entry 11), COMe (entry 12), and OMe (entries 14 and 15). This was not unexpected since we have observed ether, ketone, and ester complexes of related cationic iridium species.[10] After our own work was completed, Brown and Hall[4c] also observed directivity in the case of entry 11 and related esters. Our conditions appear to give better directivities, however.

The fact that these other functionalities also bind may have a bearing on Evans and Morrisey's failure to observe directivity with our catalyst in the acyclic substrate shown.



This substrate has multiple potentially ligating groups including amide carbonyl at which the catalyst might bind. Schultz et al. have shown that amide carbonyl is a very efficient directing group for catalyst 1.[9b] Such binding might cloud the interpretation of the results.

A particularly interesting substrate was **6**. Here, all four possible products **7a–d** were obtained on Pd/C (EtOH) reduction; but essentially only one of these, **7a**, was formed with the iridium catalyst, together with a trace of **7b**. We



(4)

6	7a	7b	(7c)	(7d)
Ir	99	1	<0.01	<0.01
Pd/C(EtOH)	38.9	46.7	(8.1)	(6.3)

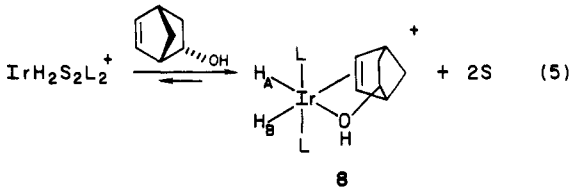
were not able to find a way of identifying the stereochemistries of **7a–d**. We were therefore forced to invoke the postulate that when an iridium reduction of a compound of this type gives essentially only one product then that product is the directed product. This suggests that **7a** has the structure shown in eq 4. We believe **7b** is the counterdirected product, since it is the major product of Pd/C(EtOH) reduction and the minor product from iridium. The two remaining isomers **7c** and **7d**, minor products from Pd/C(EtOH) and not formed at all in the iridium reduction, could not be assigned. An arbitrary choice has been made for these isomers in eq 4, as indicated by enclosing the labels and data for these isomers in parentheses. If this postulate is confirmed by future work, it may prove useful in making stereochemical assignments of compounds in cases where the corresponding olefin is available and shows high directivity. This example confirms that even tetrasubstituted olefins can be smoothly reduced by the iridium catalyst without isomerization. This Ir catalyst is unusual in that, unlike those derived from $[Rh(diene)L_2]^+$, it reduces even simple tetrasubstituted alkenes in the absence of a directing effect.[8a,d]

We also looked at reduction of an equimolar mixture of a ketone (entry 12) and an alcohol (entry 10). The C=C group of the ketone was reduced slightly more rapidly than the alcohol, but each was successfully reduced and in each case the products were formed in the same ratio found when each compound was reduced separately.

The Isolation of Model Complexes. Although we were not able to isolate catalyst–substrate complexes for the "$Ir(PCy_3)py^+$" system, the more stable "$Ir(PPh_3)_2^+$", a much poorer catalyst, did give some useful results. Under H_2, $[Ir(cod)L_2]BF_4$ (L = PPh_3) and 4-terpineol give a complex of the familiar $[IrH_2S_2L_2]^+$ type.[10] (S = solvent or other weakly binding ligand). These can be detected by ^1H NMR. Thanks to the sensitivity of the Ir–H chemical shift to the nature of the trans ligand, S, general conclusions can be drawn about the nature of the species formed. C=C and OH give rise to very different trans Ir–H shift ranges: δ −9 to −14 and −29 to −32, respectively. That the product shows an Ir-H chemical shift at δ −29 suggests that the OH but not C=C group of the terpineol is bound. To the extent that this picture is applicable to the real system, this in turn suggests that the OH has a higher binding constant than the C=C group. The substrate may therefore be bound initially via the OH, only subsequently chelating via the C=C group to lead to hydrogenation. This helps to explain the high directivites that can be achieved. If much binding to the C=C group occurred independently of binding to the OH then counterdirected product would be observed in substantial amounts.

(11) Bau, R.; Teller, R. G. *Struct. Bonding (Berlin)* **1981**, *44*, 1.

We thought that we might be able to make the unsaturated alcohol prefer to chelate by increasing the strength of the interaction between the metal and the C=C group by introducing strain into the latter group of the substrate. This is favorable to binding because the strain tends to be relieved on moving to the bound state in which the vinyl carbons relax somewhat in the direction of sp_3 hybridization. *endo*-5-Norbornene-2-ol proved to be a successful chelating ligand. This chelated to the "IrL_2^+" system at 0 °C to give essentially pure 8 in solution. No other hydride-containing species could be detected by ^1H NMR. On the other hand, the norbornenol was competitively displaced by acetone, 2 mol equiv of the latter displacing 30% of the norbornenol. This means that even here the binding is not as strong as we had expected.



(5)

8

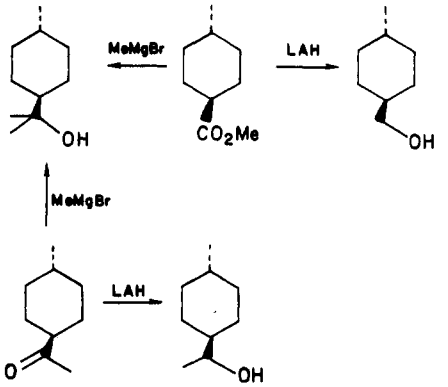
(S = Me_2CO; L = PPh_3)

The complex has the same configuration at the metal as the nonchelating analogues[11b] such as $[IrH_2(H_2O)(C_2H_4)L_2]^+$. Two Ir–H resonances are observed. One, H_A, has a chemical shift (δ −29.4) characteristic of H trans to an oxygen ligand and the other, H_B, a shift (δ −9.6) characteristic for an Ir–H trans to an olefin. The two resonances show the same $^1J(H,H')$ of 5.5 Hz. Coupling to two inequivalent phosphorus nuclei is also present (e.g., $^2J(H_A,P)$ = 11 and 24 Hz). This is expected on the basis of structure 8 since the norborneol ligand breaks the symmetry present in $[IrH_2S_2L_2]^+$. On warming to 30 °C, complex 8 decomposed by simple H_2 loss rather than by hydrogenation of the olefin.

While the OH group in the directing substrates is responsible for the selectivity, it also protects the catalyst from deactivation. 1-Methylcyclohexene is reduced much faster than the terpinenol (4000 vs. mol of H_2 (mol of Ir)$^{-1}$ h^{-1}). The second important difference is that while the latter went essentially to completion, the unsubstituted olefin, in contrast, was only reduced to the extent of 75% under the same conditions (0.1% catalyst, 0 °C, CH_2Cl_2) because the catalyst underwent deactivation.[8a] We have not examined the possibility that the catalyst might direct toward attack of a nearby (C=C) group over a distant one, but it seems likely that this would happen.

Determination of the Stereochemistry of the Organic Products. The stereochemical identification of the products in Table I is clearly the key element of the argument of this paper. In the case of **3a** and **3b**, this was achieved by isolating a sample of each isomer. In the case of **3a** we simply distilled the products from the Ir-catalyzed hydrogenation of the parent terpinen-4-ol (**2**). **3b** was isolated by preparative GC from the Pd/C(EtOH) reduction product of **2**. **3a** was identified as *cis*-*p*-menthan-4-ol (the directed product) by microanalysis and ^1H NMR spectral data (500 MHz, $CDCl_3$, see Experimental Section) and by its mp of 51–51.5 °C (lit.[12] mp 51–52 °C). **3b** was shown to be the trans or counterdirected product by ^1H NMR and its refractive index n^{25}_D 1.459 (lit.[13] mp n^{20}_D = 1.461). The stereochemistries of the allylic alcohols

Scheme I. The Transformations Used To Establish the Stereochemistries of Entries 9–12 (Table I)



relies in part on the work of Eliel et al.[14] who measured the chemical shifts of the carbinol protons in each case for each isomer. The differences observed between the two isomers are substantial and characteristic.

The stereochemistry of the *cis*- and *trans*-*p*-menthan-8-ols follows from the work of Eastman and Quinn[15] who showed that the higher melting isomer has the cis configuration. The stereochemistries of all of the next four compounds (entries 9–12 in Table I) was related to that of the *p*-menthan-8-ol by the standard transformations shown in Scheme I. Epimerization problems prevented us from determining the stereochemistries of the products in the case of entry 13. In view of the poor directivity in this case we did not pursue the question. Finally, the stereochemistry of the ether of entries 14 and 15 were determined by conversion of directed hydrogenation products of the terpineol (entry 1) and cyclohexenol (entry 2) to the ether with NaH and MeI.

Isomerization. Isomerization of the allylic alcohols to the corresponding ketones was a minor pathway (≤2.5%) in all the cases studied. Simple olefins seem to give more isomerization with this catalyst[8a] so the heteroatom functionality may help suppress isomerization. Evans et al. have used higher H_2 pressures to suppress isomerization in the Rh series.[6] Brown and Hall[4c] described isomerization reactions accompanying directed reduction in unsaturated esters. Felkin[16] described the use of the related catalyst $[Ir(cod)(PPh_3)_2]PF_6$ under conditions designed to enhance isomerization (absence of excess H_2) for the conversion of allyl alcohols to ketones. We hope in the future to examine the possibility of a directed isomerization reaction.

Mechanisms. An important criterion that a catalyst has to be able to meet to give efficient directing effects is that it binds to the directing group in preference to the reactive group (in this case, C=C). The behavior of the cationic Ir catalysts and to some extent their Rh analogues conforms to this expectation. Experimentally, it was difficult to find a substrate that would chelate via the OH and the C=C in the model study; normally binding only to the OH group was observed. This is an unusual property for a homogeneous hydrogenation catalyst and may have its origin in the net positive charge on the metal. This tends to make the metal a harder Lewis acid. Ligating groups other than those used in this paper are likely to be successful, e.g., SR, halide.[10a] Groups which might deprotonate intermediate dihydrides, e.g., NR_2, or to de-

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carbonylate, e.g., CHO, might cause problems, however. The approximate order of binding ability[10b] is likely to be $CONH_2 < OH < C{=}O < CO_2R < OMe$, this may help in predicting the outcome in cases where several groups are present.

The second feature of the successful catalysts may be the 12-electron configuration of the metal fragments involved: "IrL_2^+" and "RhL_2^+". This allows binding of H_2, C=C, and the directing group. Most hydrogenation catalysts involve 14-electron catalyst fragments, e.g., "$RhCl(PPh_3)_2$", "$RuHCl(PPh_3)_2$"; these do not give directing effects.

Finally, it is important that the product of the catalytic reaction does not bind to the catalyst site too strongly and poison the system. In our case this seems to be true: the directing effect does not change with the percentage conversion of the substrate. Even the rate of reduction falls off only very late in the reaction. The exchange of ROH and R_2CO groups is fast on the ^1H NMR time scale, at least in the model system $[IrH_2S_2(PPh_3)_2]^+$ (S = ROH or R_2CO),[10b] so this step is unlikely to be rate-limiting.

It is likely that directed versions of other common homogeneous catalytic processes will be discovered in the next few years. They will probably find many applications in organic synthesis.

Experimental Section

Melting points were determined on a Mel-Temp melting point apparatus and are uncorrected. ^1H NMR and ^{13}C NMR spectra were recorded on a JEOL FX90Q instrument (89.55 and 22.5 MHz, respectively) unless otherwise noted. IR spectra were obtained on a Nicolet 5 SX FTIR. GC analysis were performed on a Varian Model 3700 capillary gas chromatograph using a 25-m Carbowax 20M or 50-m SE 30 column. Solvents were distilled immediately before use. Dichloromethane was distilled from calcium hydride. Diethyl ether, THF, and benzene were distilled from sodium benzophenone ketyl. Terpinen-4-ol, methylcyclohexene, *endo*-5-norboren-2-ol, 3-methyl-2-cyclohexen-1-ol, 3,5,5-trimethyl-2-cyclohexen-1-ol, α-terpineol, and 10% Pd/C were purchased from Aldrich and used without further purification. $[Ir(cod)(PPh_3)_2]PF_6$,[16] $[IrH_2(MeCO)_2(PPh_3)_2]PF_6$,[10b] and $[Ir(cod)PCy_3(py)]PF_6$[8] were prepared according to the literature methods.

Rate Studies. Rate studies were carried out in an all-glass constant-pressure apparatus as previously described.[8a] A solution of 7.5 mmol of substrate in dichloromethane (15 mL) was degassed in a 250-mL round-bottom flask by three freeze/pump/thaw cycles. The solution was frozen a fourth time, the flask was filled with dry nitrogen, and the catalyst (7.5 μmol) was introduced as a solid. The flask was then attached to the hydrogenation apparatus and the system evacuated. The solution was allowed to thaw in the closed apparatus in vacuo and cooled to 0 °C. Hydrogen, which had been passed through dichloromethane at 0 °C was then introduced into the system, stirring commenced, and hydrogen uptake monitored.

Hydrogenations with $[Ir(cod)PCy_3(py)]PF_6$. All hydrogenations were carried out with 25 mmol of substrate (except entries 4–7 which were carried out with 0.1 mmol) using 2.5 mol % catalyst in each case. In a 250-mL round-bottom flask was placed a solution of the substrate in dichloromethane (5 mL). The solution was frozen in liquid nitrogen, the flask evacuated and filled with dry nitrogen followed by the catalyst as a solid. The flask was attached to the hydrogenation apparatus, the system evacuated, and the solution brought to room temperature with a water bath under a static vacuum. Hydrogen was introduced and stirring commenced immediately. After 30 min, the dichloromethane was evaporated and the residue treated with diethyl ether (5 mL) and filtered through a column of Florosil and Celite to remove the precipitated metal salts. Samples were used immediately for GC analysis. [Note: Special care must be taken to ensure that hydrogen is added immediately because the catalyst deactivates slowly in the presence of olefins; possibly dehydrogenation of the substrate may be taking place. The catalyst also deactivates in the presence of H_2 if substrate is not present. In this case a metal cluster complex is formed.[8a]]

Hydrogenations with 10% Palladium on Carbon. A solution of substrate (0.5 mmol) in absolute ethanol (10 mL) containing 0.05 g of 10% Pd/C was stirred under an atmosphere of hydrogen for 1 h. The solution was filtered through a column as above to give an essentially quantitative yield of the diastereomeric pair of reduction products. Samples were taken immediately for GC analysis.

Preparation of Substrates. All the substrates are known, but three were prepared by new applications of known general routes.

***cis*- and *trans*-3,6-Dimethyl-2-cyclohexen-1-ol.** These were prepared from the corresponding ketone[17] by the method of Luche.[18] To the ketone (0.25 g, 2.0 mmol) in EtOH (5 mL) were added $CeCl_3{\cdot}7H_2O$ (0.75 g, 2.0 mmol) and then $NaBH_4$ (0.076 g, 2.0 mmol). After 5 min of being stirred, the reaction mixture was quenched with H_2O (10 mL) and extracted with Et_2O (3 × 15 mL), and the combined extracts were washed with brine, dried over Na_2SO_4 and evaporated to give 0.2 g (78%) of the cis and trans products. The diastereomers were separated by preparative GC (10 ft × 1/4 in. Carbowax 20 M, 75 °C), the cis isomer eluting first. The compounds were identified, and their stereochemistry was confirmed by conversion to the acetates with Ac_2O and DMAP and observing the ^1H NMR spectrum and in particular the residual coupling of the carbinol proton resonance when the vinyl proton is irradiated:[14] Cis isomer, δ 5.14 (d, J = 3.6 Hz); trans isomer, δ 4.95 (d, J = 6.5 Hz).

***cis*- and *trans*-3-Methyl-5-(methylethyl)-2-cyclohexen-1-ol** were prepared by the same route from piperitone (Pfaltz and Bauer) and identified by ^1H NMR.[19]

α,4-Dimethyl-3-cyclohexene-1-methanol was prepared by LAH reduction of 1-methyl-3-acetyl-1-cyclohexene in 91% yield to give an inseparable mixture of diastereomers, identified by ^1H NMR:[19] ^1H NMR δ 1.14 and 1.15 (d, J = 6.2 Hz, diastereotopic Me), 1.62 (s, C=CMe).

4-Methyl-3-cyclohexene-1-methanol,[20] methyl-4-methyl-3-cyclohexene-1-carboxylate,[21] 1-(4-methyl-3-cyclohexen-1-yl)-ethanone,[22] 3-methoxy-1-methylcyclohexene,[23] 1-(3,4-dimethyl-3-cyclohexen-1-yl)ethanone,[24] and 4-(methyl-3-cyclohexene-1-carboxaldehyde)[25] were prepared by the literature methods and identified by ^1H NMR and, for ketone 6, by the melting point of the semicarbazones.

Determination of the Stereochemistries of the Reduction Products. Entry 1, Table I. The directed isomer eluted second on Carbowax 20M and was identified by the mp of 51.0–51.5 °C (lit.[26] mp 51–52 °C); the counterdirected isomer was a liquid at room temperature n^{25}_D 1.459 (lit.[26] n^{25}_D 1.461). In confirmation of this assignment, the ^{13}C NMR spectrum of the directed isomer shows the C-7 resonance at 20.0 ppm (lit.[27] 20.5 ppm) rather than 22.5 ppm (lit.[27] 22.5 ppm) for the other isomer.

Entry 2. The trans isomer elutes before the cis isomer on Carbowax 20M. They were identified from the positions of the carbinol resonances in the ^1H NMR ($CDCl_3$): *trans*, δ 4.03 (lit.[14] δ 3.97); *cis*, δ 3.53 (lit.[14] δ 3.45).

Entry 3. The trans isomer was eluted before the cis isomer and was identified as above: trans, δ 4.13 (lit.[14] δ 4.1).

Entry 4. The directed product eluted before the other isomer and was identified as above: δ 3.79 (lit.[14] δ 3.78).

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Entry 5. The directed product eluted second on Carbowax and was identified as above: δ 3.49 (lit.[14] δ 3.48). The other product gave a resonance at δ 3.09 (lit.[14] δ 3.02).

Entry 6. The directed product eluted first and was identified by ^{1}H NMR: δ 4.09 (lit.[14] δ 4.02).

Entry 7. The directed product eluted second and was identified by ^{1}H NMR: δ 3.78 (lit.[14] δ 3.75).

Entry 8. The directed isomer eluted before the other and was identified from the mp of 37–38 °C (lit.[15] mp 34.5–35 °C). The other isomer melted at 47–48 °C (lit.[15] mp 46–47 °C).

Entry 9. The directed product eluted before the other and was shown to be identical (GC, NMR) with the LAH reduction product of the directed product of entry 12. The counterdirected products were also identical.

Entry 10. The directed product eluted before the other and was identified from its ^{13}C NMR (22.4, 29.4, 32.6, 34.5, 39.9, 68.0 ppm) by comparison with the literature[28] data (40.8, 30.0, 35.1, 33.3, 22.8, 68.9 ppm).

Entry 11. The directed isomer eluted second (^{13}C NMR 42.1, 28.2, 33.5, 31.2, 21.5, 175.1, 50.1 ppm)[29] and was identified by ^{13}C NMR as above. In addition, MeMgBr converted this directed isomer to the directed isomer obtained in entry 8 (GC, NMR).

Entry 12. The directed product eluted second [^{1}H NMR ($CDCl_3$) δ 2.09 (s, COMe), 0.85 (d, J = 5.7 Hz, CHMe)] and was converted with MeMgBr to the directed isomer obtained in entry 8 (GC NMR).

Entry 13 (See Text). We were not able to determine the stereochemistry in this case, but the isomer which predominates on reduction with the iridium catalyst is probably the directed product. This isomer eluted second on Carbowax.

Entry 14. The directed isomer [^{1}H NMR δ 3.15 (s, OMe), 0.85 (d, J = 6.6 Hz, CHMe)] eluted second and was identical with the methyl ether of the directed product formed for entry 1.

Entry 15. The directed isomer eluted first [^{1}H NMR ($CDCl_3$) δ 3.30 (s, OMe), 0.90 (d, J = 5.5 Hz, CHMe)] and was identical with the methyl ether of the directed product formed in entry 2.

From 6. We postulate that the isomer formed to the extent of 99% with the iridium catalyst is the directed isomer [^{1}H NMR ($CDCl_3$) δ 0.83 (d, J = 6.6 Hz, CHMe), 2.09 (s, COMe)].

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Metal Catalysis in Oxidation by Peroxides.[1] Molybdenum- and Tungsten-Catalyzed Oxidations of Alcohols by Diluted Hydrogen Peroxide under Phase-Transfer Conditions

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A synthetic procedure is described which allows the oxidation of primary and secondary alcohols to the corresponding carbonyl compounds with dilute hydrogen peroxide, employing Mo(VI) and W(VI) as catalysts, under phase-transfer conditions (Aliquat 336), characterized by high yields and selectivities.

Transition-metal-catalyzed oxidations with dilute hydrogen peroxide under phase-transfer conditions are increasingly attractive synthetic procedures[2] overcoming most of the drawbacks of homogeneous systems[2b] and allowing the use of dilute aqueous solutions of the oxidant.

In a previous paper[2b] we described a two-phase method of oxidation of organic sulfides and alkenes with 30% w/v hydrogen peroxide, molybdenum (VI) or tungsten (VI) catalysts, and neutral lipophilic ligands as extracting agents characterized by high yields and selectivities. By means of the ligand, *neutral* peroxo complexes $MO(O_2)_2$, which formed in water[1] by addition of an excess of H_2O_2 to H_2MO_4 (M = Mo, W), were extracted in the organic phase. Owing to the acidic character of MO_5, addition of acid was required to neutralize[1,3] the anionic form.

Table I. Effect of the Acidity of the Aqueous Phase on the Oxidation of Cyclohexanol to Cyclohexanone with H_2O_2 Catalyzed by Mo(VI) or W(VI) Complexes in the Presence of Aliquat 336, at 60 °C, under Phase-Transfer Conditions (10 mL of DCE–1 mL of H_2O)

run[a]	catalyst	pH[b]	time, min	cyclohexanone, mmol
1	Mo(VI)	4.50	60[c]	(4.2)[c]
2	Mo(VI)	3.10	120	5.0
3	Mo(VI)	2.95	120	5.5
4	Mo(VI)	2.60	120	3.0
5	Mo(VI)	2.10	120	1.1
6	W(VI)	2.85	50	4.0
7	W(VI)	2.05	50	8.2
8	W(VI)	1.40	50	9.8
9	W(VI)	1.25	50	6.2

[a] Cyclohexanol (50 mmol), H_2O_2 (10.1 mmol), Aliquat 336 (0.5 mmol), WO_4^{2-} or MoO_4^{2-} (0.25 mmol), and added acid, H_2SO_4. [b] Reference 6. [c] Complete consumption of H_2O_2.

On the other hand, the occurrence of acid–base equilibria of MO_5 implies that, at lower acidities (i.e., higher pH), it should be possible to transfer anionic peroxo compounds from an aqueous to an organic phase by using cationic phase-transfer agents. Anionic Mo(VI) and W(VI)

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