Rhodium promoted isomerisation of allylic alkoxides: a new method for enolate anion formation

Lewis J. Gazzard,[a] William B. Motherwell*[a] and David A. Sandham[b]

[a] *Christopher Ingold Laboratories, Department of Chemistry, University College, 20 Gordon Street, London, UK WC1H 0AJ*
[b] *Department of Chemistry, Imperial College of Science, Technology and Medicine, South Kensington, London, UK SW7 2AY*

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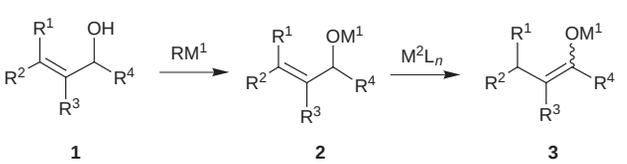
Transition metal mediated isomerisation of allylic alkoxides is presented as a new method for enolate anion generation. The scope and limitations of enolate formation with the catalysts $[Rh(dppe)(THF)_2]^+ClO_4^-$ and $(Ph_3P)_3RhCl$ are explored and the synthetic potential of the methodology demonstrated in the stereoselective formation and reactions of certain ketone and aldehyde enolates.

Introduction

The enolate anion is undoubtedly the premier reactive intermediate in synthetic organic chemistry, being the most accessible and versatile of all such species and historically providing one of the most reliable methods of carbon–carbon bond formation.[1–3] The ever-increasing number of enolate-based transformations is evident in the synthetic literature, yet new approaches to enolates themselves are rare and inevitably based upon the reactivity of the carbonyl group. We have communicated an alternative strategy, in which the inextricable link between keto–enol tautomerism and enolate formation was finally severed.[4] Herein we wish to report full details of our initial studies in this area.

Our approach hinges on the employment of an allylic alcohol **1** as a direct synthon for an enolate anion, as depicted in Scheme 1. Treatment of **1** with a suitable base RM^1 would

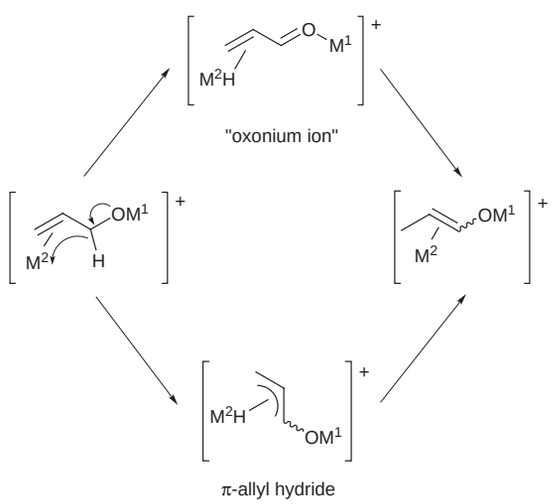


1 **2** **3**

Scheme 1

furnish the alkoxide **2**. Relocation of the double bond to give the thermodynamically stable enolate **3** would be effected under the catalytic influence of a transition metal complex M^2L_n. In choice of base and catalyst there are a number of criteria to consider. The base RM^1 must be far stronger than the alkoxide or enolate product so that deprotonation is irreversible and also the resultant conjugate acid RH must not interfere with subsequent isomerisation to, or reaction of the enolate **3**. Furthermore, M^1 must provide an alkoxide that cannot function as an *irreversible* ligand for M^2L_n, as well as producing an enolate of controllable and predictable reactivity. Enolates prepared by this method would be free of the amine by-products arising from strong base enolisation methods, which are known to interact with enolate oligomers and affect reactivity.[5] Similarly, more esoteric enolates hitherto prepared by transmetallation methods would now be accessible under 'salt-free' conditions.[6] Lithium was our choice of M^1; use of *n*-butyllithium would effect alkoxide formation and the literature abounds with the chemistry of the ubiquitous lithium enolate.[1–3] In selection of M^2L_n, our *a priori* expectation was that isomerisation would define enolate regiochemistry, whereas enolate stereochemistry might be influenced and possibly controlled by the geometry and substituents of the double bond in the alkoxide. As a further long-term goal, inspired by the seminal work of Noyori and co-workers,[7] an alkoxide having R^1 and R^2 as different alkyl groups would create a new chiral centre, allowing enantioselective isomerisation with an appropriate chiral ligand.

The isomerisation of both allylic ethers to enolic derivatives and allylic alcohols to carbonyl compounds is well-documented.[8] We reasoned that a transition metal complex having three vacant coordination sites would promote isomerisation *via* the π-allyl hydride mechanism[9–11] or 'oxonium ion' equivalent, in which the migrating hydride could benefit energetically from the indicated oxygen lone pair participation (Scheme 2). Our initial catalyst was the cationic complex [Rh-



Scheme 2

$(dppe)(THF)_2]ClO_4$[12]† (hereafter abbreviated to $[Rh(dppe)]^+$), conveniently prepared by the controlled hydrogenation of the cycloocta-1,5-diene (COD) derivative.

During the early stages of our own work Bosnich[13] confirmed our mechanistic approach with the remarkable observation of the persistence of simple enols formed by isomerisation of allylic alcohols with the same rhodium complex.

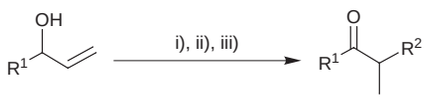
† dppe = 1,2-bis(diphenylphosphino)ethane.

The demonstration of irreversible hydride abstraction and delivery, coupled with the non-equilibration of π-allyl hydride intermediates reported in this work augured well for our new approach to enolate generation. We need hardly emphasise however, that the present work was undertaken with the fundamentally different objective of generating a *synthetically useful* enolate, avoiding the phenomenon of facile tautomerism that destroys the inherent potential of enols for stereocontrolled carbon–carbon bond formation.

Results and discussion

Formation of trisubstituted ketone enolates and a mechanistic refinement

Validation of the isomerisation concept on a simple substrate was our initial task (Scheme 3). Thus, treatment of a THF



4a R^1 = Ph; **4b** R^2 = Et **5a–e** see Table 1; **5f** R^1 = Ph, R^2 = H

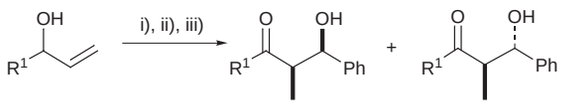
Scheme 3 *reagents:* i) *n*-BuLi, THF, 0 °C; ii) $[Rh(dppe)]^+$ (2 mol%), 60 °C, 7 h; iii) R_2X, 0 °C.

solution of **4a** with 1–1.05 equivalents of *n*-butyllithium was followed by addition of the pre-hydrogenated catalyst solution. After thermal isomerisation for 7 hours, addition of a range of electrophiles provided good yields of the corresponding α-alkylated ketones (Table 1). Notably, with pent-1-en-3-ol **4b** as substrate, it was demonstrated that the presence of an activated benzylic hydride was not a pre-requisite driving force for enolate formation. In all isomerisations of **4a**, a varying amount (*ca.* 10–15%) of protonated enolate **5f** was also isolated, notwithstanding the use of excess electrophile. As we shall see, this observation would be of importance in subsequent experiments.

Turning our attention to the question of enolate geometry, the trapping of isomerisation products derived from **4** with benzaldehyde[14] (Scheme 4) provided an initial, albeit indirect stereochemical probe, as well as demonstrating the further synthetic potential of this methodology. As we have reported,[4] the practically more convenient Wilkinsons catalyst $(Ph_3P)_3RhCl$ also functioned as an isomerisation catalyst for allylic alkoxides. A comparison of this catalyst with $[Rh(dppe)]^+$ in terms of activity and stereocontrol was now appropriate, the results of which are indicated in Table 2. Consideration of the Zimmerman–Traxler transition state model[14,15] reveals both catalysts selectively promoted *Z*-enolate formation. The extent of this selectivity may be judged by the literature report[14] that the

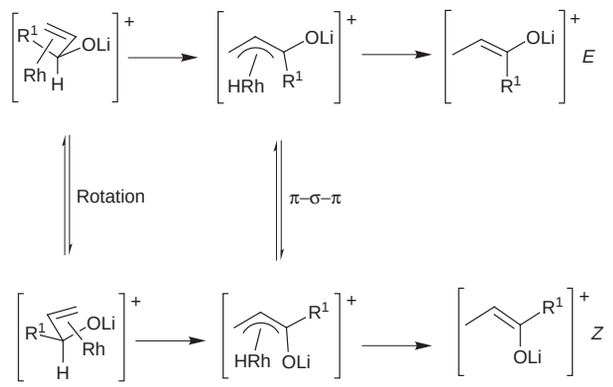
Table 1 Formation of trisubstituted ketone enolates

Substrate	Electrophile	Product	Yield (%)
4a	Allyl bromide	**5a**	82
4a	Benzyl bromide	**5b**	75
4a	Methyl iodide	**5c**	62
4a	*n*-Butyl iodide	**5d**	60
4b	Benzyl bromide	**5e**	48



4a R^1 = Ph; **4b** R^1 = Et **6a** R^1 = Ph; **6b** R^1 = Et

Scheme 4 *reagents*: i) *n*-BuLi, THF, 0 °C; ii) catalyst; iii) PhCHO, −78 °C.



Scheme 5

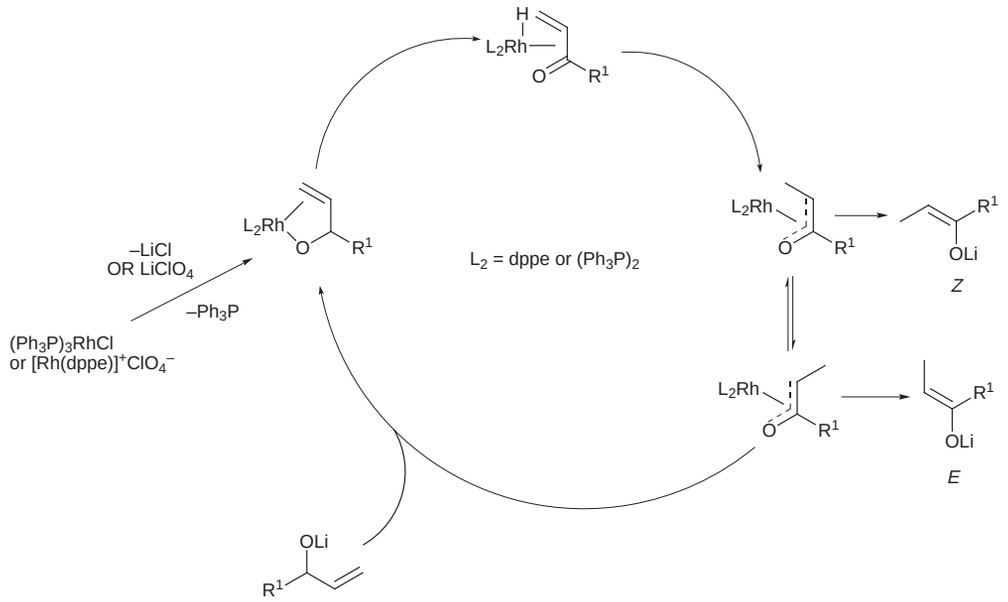
Z-enolate of 98% isomeric purity (prepared by deprotonation of **5f**) gave a 7.3 : 1 *syn* : *anti* ratio of aldols **6a**. Scheme 5 depicts the possibilities for stereocontrol arising from isomerisation *via* the π-allyl hydride mechanism. It is tempting, *a posteriori*, to invoke rhodium–oxygen coordination as a controlling factor leading to a '*cisoid*' intermediate. Equilibration of the π-allyl hydride intermediates[16] although not observed in the $[Rh(dppe)]^+$-mediated isomerisation of free alcohols[13] may also be possible.

There is a further mechanistic pathway arising from our 'oxy-anion effect' proposal in Scheme 2 which also allows a rhodium–oxygen interaction, namely isomerisation *via* a rhodium alkoxide–rhodium enolate conversion, as shown in Scheme 6. Precedent for this proposal arises from the work of Trost[17] and Bäckväll[18] who have both proposed similar alkoxide-based mechanisms for the ruthenium-promoted isomerisation of free alcohols to carbonyl compounds. Moreover, recent crystallographic and NMR studies by Slough on discrete rhodium enolates[19] have unambiguously established their fluxional η^3 nature, providing another potential equilibration pathway to which we shall return later. Of course, besides the *intermediate* equilibration pathways in either of these two mechanisms, there also remains the possibility of *enolate* equilibration catalysed by an adventitious proton source such as **5f**. It is notable that the *Z*-enolate is the more thermodynamically stable isomer.[20]

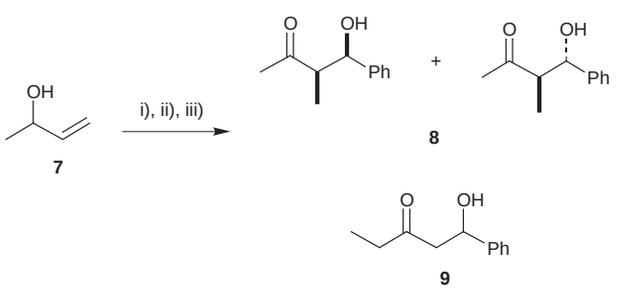
We now moved on to the issue of regiocontrol in enolate formation by examining the reactivity of the lithium alkoxide of but-1-en-3-ol **7** (Scheme 7). Isomerisation was again readily achieved with either catalyst and maintenance of *Z*-enolate selectivity was indicated by the diastereomeric ratios of aldol products **8** derived from the initially formed enolate (Table 3). We were slightly concerned that the overall ratio **8**:**9** corresponded to that obtained on enolisation of the parent ketone under 'thermodynamic' conditions.[21] Our concerns were ampli-

Table 2 A comparison of the effect of catalyst on the formation of aldols

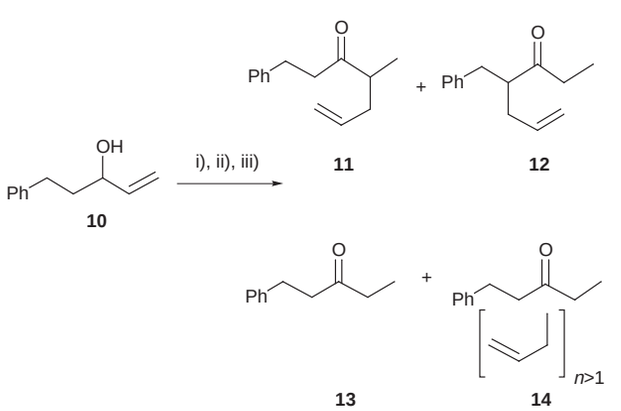
	Substrate	Catalyst and conditions	Aldol	*syn* : *anti*	Yield (%)
	4a	$[Rh(dppe)]^+$ (2 mol%, 60 °C, 7 h)	**6a**	8.6 : 1	84
	4a	$(Ph_3P)_3RhCl$ (2 mol%, reflux, 1.5 h)	**6a**	8.3 : 1	70
	4b	$[Rh(dppe)]^+$ (2 mol%, 60 °C, 9.5 h)	**6b**	3.9 : 1	79
	4b	$(Ph_3P)_3RhCl$ (2 mol%, reflux 10 h)	**6b**	3.5 : 1	80



Scheme 6



Scheme 7 *reagents*: i) *n*-BuLi, THF, 0 °C; ii) catalyst; iii) PhCHO, −78 °C.



Scheme 8 *reagents*: i) *n*-BuLi, THF, 0 °C; ii) catalyst; iii) allyl bromide, 0 °C.

fied with the less biased allylic alcohol **10**, (Scheme 8) which with either catalyst under the standard conditions delivered an essentially unselective mixture of products **11** and **12** (Table 4).

Detailed study of this process revealed that the same ratio of enolate regioisomers was present at *all* stages of the isomerisation. Attempts to enhance the rate of the initial isomerisation to the enolate precursor of **11** (concordant with the 'oxy-anion' effect postulated in Scheme 2) by addition of complexing agents such as TMEDA, DMPU, HMPA, crown ethers and podand ligands were uniformly unsuccessful. We had considered that the participation of oxygen lone pairs in the formation of an aggregated alkoxide[22] would be suppressed by such additives.

Besides a second, rhodium promoted isomerisation, there remained the possibility that the small amount of the protonated enolate **13** formed *in situ* could function as a catalyst for

Table 3 An examination of regiocontrol in enolate formation from but-1-en-3-ol

Catalyst and conditions	Yield of **8** (%), *syn*:*anti*	Yield of **9** (%)
$[Rh(dppe)]^+$ (2 mol%, 60 °C, 8 h)	62, 4:1	10
$(Ph_3P)_3RhCl$ (2 mol%, reflux, 3 h)	56, 3:1	10

enolate scrambling.[23] Therefore, the alkoxide was formed with 1.5 equivalents of butyllithium, in the hope that the excess would sequester any of the protonated enolate as soon as it was formed, although ring opening of THF would obviously be a competing process.[24] Under these conditions with the $[Rh(dppe)]^+$ catalyst, no change in the ratio and yield of **11**:**12** was observed. Contrastingly, with Wilkinsons catalyst and 1.5 equivalents of butyllithium (Table 4, entry 3), despite a high initial rate of reaction (as evidenced by TLC monitoring), isomerisation did not proceed to completion, with metallic rhodium being deposited. However, **11** *was* formed selectively. We speculate that a short-lived hydridorhodium species, produced by β-elimination of a butylrhodium complex[25] may have induced isomerisation *via* the hydride addition–elimination mechanism[26–28] Indeed, since the completion of this work, a similar catalytic system has been shown to be effective for the isomerisation of allylic ethers.[29] Although the yield of this regioselective transformation was unacceptably low, we have since demonstrated efficient selective formation of **11** with what may be an analogous hydridonickel complex generated from $(Cy_3P)_2NiCl_2$ *in situ*.[30]

Influence of double bond geometry and substitution

While isomerisation of simple monosubstituted allylic derivatives is readily achieved by a range of transition metal catalysts, additional substitution around the double bond is known to dramatically lower the rate of reaction or suppress it totally.[17] In the context of our approach to enolate generation, this issue was clearly of paramount importance and called for a systematic study of the effect of double bond geometry and substitution in a range of allylic alkoxides.

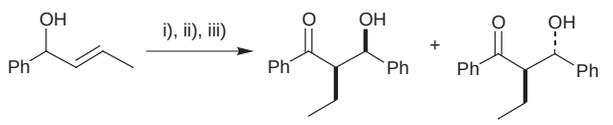
The lithium alkoxide of the *E*-allylic alcohol **15** was subjected to the usual isomerisation and aldol reactions with Wilkinson's catalyst and $[Rh(dppe)]^+$ (Scheme 9). Although the *syn*:*anti* ratio of **16** still indicated selective *Z*-enolate formation (Table 5), this represented a significant erosion of selectivity compared

Table 4 An examination of regiocontrol in enolate formation from 5-phenylpent-1-en-3-ol

Equiv. *n*-BuLi	Catalyst and conditions	Ratio **11**:**12**	Yield **11** + **12** (%)	Yield **13** (%)	Yield **14** (%)
1.05	$[Rh(dppe)]^+$ (2 mol%, 60 °C, 7 h)	1:1.2	79	7	5
1.05	$(Ph_3P)_3RhCl$ (2 mol%, reflux, 3 h)	1:1.3	54	6	5
1.50	$(PH_3P)_3RhCl$ (2 mol%, reflux, 8.5 h)	9.7:1	39	6	2

Table 5 An examination of regiocontrol in enolate formation from 4-phenylbut-2-en-4-ol

Catalyst and conditions	Yield of **16** (%) *syn*:*anti*
$[Rh(dppe)]^+$ (2 mol%, 3 h)	71, 3.0:1
$(Ph_3P)_3RhCl$ (2 mol%, 5.5 h)	92, 3.0:1



15 **16**

Scheme 9 *reagents*: i) *n*-BuLi, THF, 0 °C; ii) catalyst, reflux; iii) PhCHO, −78 °C.

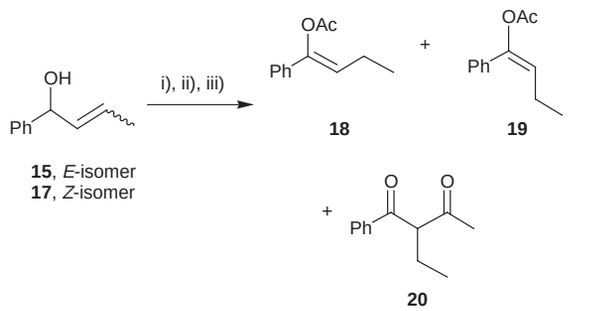
with the enolate derived from **4a**. Our concerns rested on the fact that the benzaldehyde quench did not differentiate between a loss of stereoselectivity in the isomerisation or the aldol process itself. Shortfalls in the latter were amplified by Heathcock's report that lithium aldolates derived from 1-phenyl substituted ketones underwent rapid *syn–anti* equilibration (*via* a retro aldol process) at −78 °C.[14]

We reasoned that formation of hydrolytically stable enol acetate derivatives by trapping the enolate on oxygen would provide us with a more subtle stereochemical probe (Scheme 10). With this in mind, the isomeric *Z*-allylic alcohol **17** allowed a comparison of the reactivity of the two isomers. The derived enolates were quenched with either acetyl chloride or acetic anhydride at low temperature to yield the enol acetates **18** and **19**, with minor quantities of the C-acylation product **20** (Table 6). We do not have a satisfactory explanation for the inefficiency of the acylation in the presence of Wilkinson's catalyst, especially given the efficiency of enolate formation evidenced by the excellent yields of aldol product **16**. Nevertheless, the uniformly excellent *Z*-selectivity appears to validate the aldolate equilibration concept.

Assuming the isomerisation proceeds *via* the π-allyl hydride or rhodium enolate mechanism, one can envisage how the

Table 6 An examination of regiocontrol in enolate formation from the *E* and *Z* isomers **15** and **17**

Substrate	Catalyst and conditions	Ratio **18**:**19** and yield (%)	Yield of **20** (%)
15	$[Rh(dppe)]^+$ (2 mol%, 3 h)	25:1, 64	10
15	$(Ph_3P)_3RhCl$ (2 mol%, 7 h)	>25:1, 32	7
17	$[Rh(dppe)]^+$ (2 mol%, 4 h)	25:1, 64	13
17	$(Ph_3P)_3RhCl$ (2 mol%, 8 h)	>25:1, 45	12



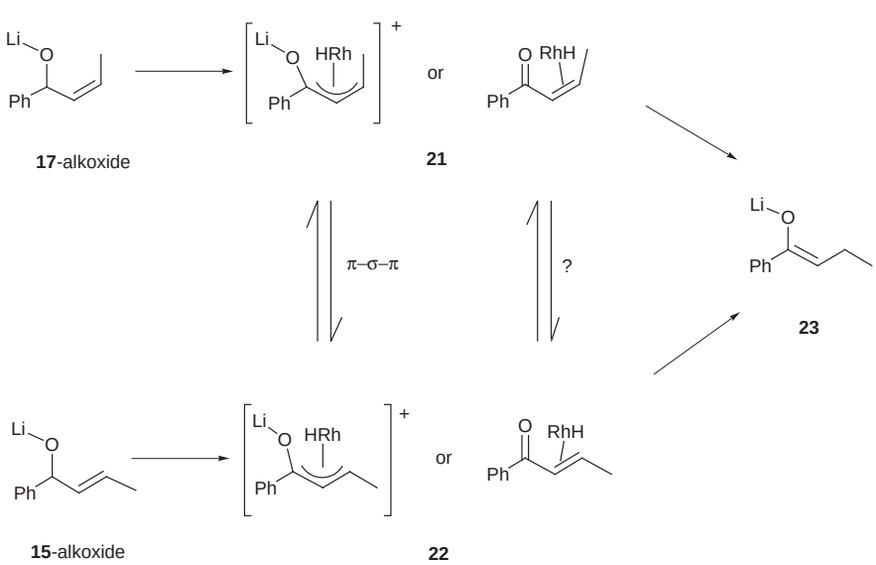
15, *E*-isomer
17, *Z*-isomer

18 **19** **20**

Scheme 10 *reagents*: i) *n*-BuLi, THF, 0 °C; ii) catalyst, reflux; iii) Ac_2O or AcCl, −78 °C.

Z-methyl group in **17** may sterically retard formation of π-allyl hydride or oxabutadiene complex **21** (Scheme 11). Indeed, the slightly longer isomerisation time required with this substrate compared to **15** is possibly evidence for this. However, this experiment is mute on whether conversion to the less-hindered intermediate **22** occurs, since *both* intermediates lead to the same *Z*-enolate **23**.

Continuing to probe the effect of *E*-olefin geometry, the lithium alkoxide of cyclohex-2-en-1-ol **24** proved unreactive towards $[Rh(dppe)]^+$. With Wilkinson's catalyst, very poor conversion to the enolate occurred, evidenced by the low yield of aldols **25** (Scheme 12). Both these results underscored the apparent requirement for access to a *cisoid* alkoxide conformation and are in contrast to the ready isomerisation of this substrate using the alternative nickel catalyst.[30]



17-alkoxide **21** **23**

15-alkoxide **22**

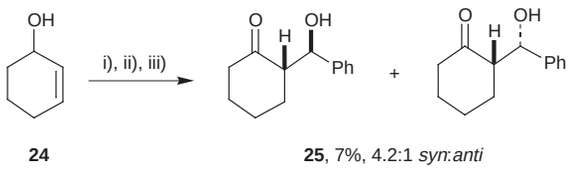
Scheme 11

Table 7 An examination of regiocontrol in enolate formation from allylic alcohols **26** and **27**

Substrate	Catalyst and conditions	Ratio **28**:**29**	Yield **28** + **29** (%)	Yield **30** (%)
26	$[Rh(dppe)]^+$ (5 mol%, 24 h)	not determined	<5	—
26	$(Ph_3P)_3RhCl$ (2 mol%, 16 h)	3.5:1	33	17
27	$[Rh(dppe)]^+$ (5 mol%, 6 h)	2.9:1	70	0
27	$(Ph_3P)_3RhCl$ (2 mol%, 24 h)	3.0:1	59	15

Table 8 An examination of regiocontrol in enolate formation from **31**

Catalyst and conditions	Ratio **28**:**29**	Yield **28** + **29** (%)	Yield **30** (%)
$[Rh(dppe)]^+$ (5 mol%, 3 h)	3.7:1	56	17
$(Ph_3P)_3RhCl$ (2 mol%, 21 h)	3.5:1	40	3



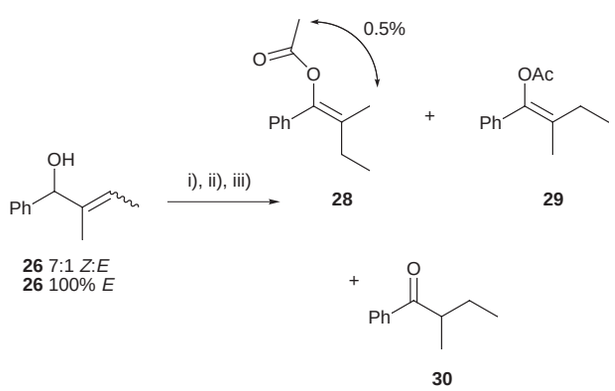
24 **25**, 7%, 4.2:1 *syn*:*anti*

Scheme 12 *reagents*: i) *n*-BuLi, THF, 0 °C; ii) $(P_3P)_3RhCl$ (5 mol%), reflux, 48 h; iii) PhCHO, −78 °C.

Formation of tetrasubstituted ketone enolates

The stereoselective formation of tetrasubstituted enolates is one area where recourse to carbonyl group chemistry often fails to provide a satisfactory synthetic method. Previous examples of tetrasubstituted enolate formation have either relied on addition of alkyllithium reagents to ketenes[31,32] or transmetallation of geometrically pure silyl enol ethers obtained by conjugate addition processes.[33] Clearly, production of a tetrasubstituted enolate *via* our isomerisation approach calls for the use of a trisubstituted allylic alkoxide, the potential difficulties of which have been noted above.

The two isomeric allylic alcohols **26** and **27** provided our initial substrates for isomerisation to tetrasubstituted enolates (Scheme 13), as well as indicating the first major difference

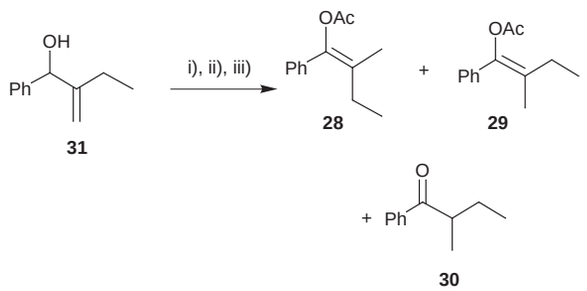


26 7:1 *Z*:*E*
26 100% *E*

Scheme 13 *reagents*: i) *n*-BuLi, THF, 0 °C; ii) catalyst, reflux; iii) Ac_2O or AcCl, −78 °C.

in activity between the catalysts. With $[Rh(dppe)]^+$ and **26**, negligible conversion to the enolate occurred, starting material being recovered with an unchanged *Z*:*E* ratio (Table 7). Contrastingly, Wilkinsons catalyst promoted isomerisation with increased efficiency, although 36% starting material was still recovered. The slight dependence of reaction rate on olefin geometry noted earlier was greatly amplified in the case of **27**: isomerisation with either catalyst proceeded to completion, giving comparable *E*:*Z* selectivity to **26**. Stereochemistry of the products was assigned by the indicated NOE enhancement.

Although the enolate geometry observed in the isomerisation of **26** and **27** was apparently at variance with the rhodium–oxygen coordination hypothesis advanced earlier, the hope remained that enolate geometry could be pre-ordained by selection of an appropriate substrate. However, isomerisation of the *exo*-methylene substrate **31** (Scheme 14), while readily achieved



31

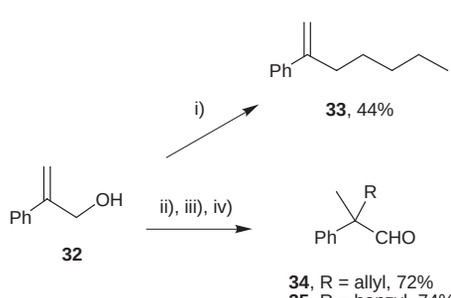
Scheme 14 *reagents*: i) *n*-BuLi, THF, 0 °C; ii) catalyst, reflux; iii) Ac_2O, −78 °C.

with either catalyst, afforded essentially the same ratio of enolates as **26** and **27** (Table 8). Taken in conjunction with the fact that the *E*:*Z* ratio was independent of time and unaffected by addition of TMEDA or 12-crown-4, we were led to the conclusion that the enolates underwent equilibration under the reaction conditions. Clearly, the formation of **30** in these isomerisations (even in the presence of a large excess of acetylating agent) renders it a likely catalyst for such a process, either *via* simple proton exchange or an aldol–retro-aldol sequence.[34] However a rhodium-promoted interconversion of enolate stereoisomers *via* fluxional rhodium enolates as outlined in Scheme 6 cannot be excluded.[19]

Formation of aldehyde enolates

The generation of aldehyde enolates represents a long-standing problem in synthetic chemistry. Low molecular weight aldehydes themselves are not always satisfactory precursors, given their tendency to oligomerise. Furthermore, attempted deprotonation with the ubiquitous LDA may result in a hydride transfer reduction.[35] As a consequence of these difficulties, aldehyde enolate equivalents, such as metallated imines[36] and hydrazones[37] have been developed. However, the multistep nature of these protocols renders them inconvenient and we felt our isomerisation methodology would present an appropriate 'one-pot' alternative.

Our initial substrate was the primary alcohol **32** (Scheme 15). Surprisingly, treatment with *n*-butyllithium did not provide the alkoxide. Instead the olefin **33**, derived from a formal S_N2' pro-



32

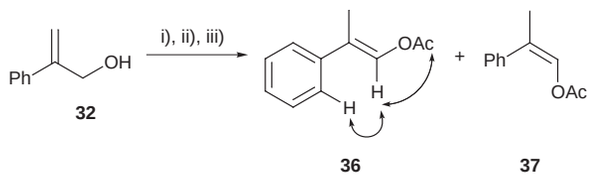
34, R = allyl, 72%
35, R = benzyl, 74%

Scheme 15 *reagents*: i) *n*-BuLi, THF, 60 °C, 6 h; ii) *t*-BuLi, THF, 0 °C; iii) $[Rh(dppe)]^+$ (2 mol%), 60 °C, 3 h; iv) allyl or benzyl bromide, 0 °C.

Table 9 An examination of regiocontrol in enolate formation from **32**

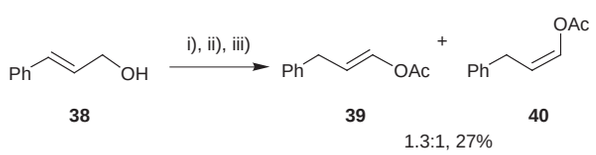
Catalyst and conditions	Ratio **36**:**37**	Yield **36** + **37** (%)
$[Rh(dppe)]^+$ (2 mol%, 30 min)	10:1	78
$(Ph_3P)_3RhCl$ (2 mol%, 40 min)	13:1	83

cess, was isolated in 49% yield. Recourse to the more hindered *tert*-butyllithium did form the alkoxide cleanly, which underwent rapid isomerisation with $[Rh(dppe)]^+$ to provide good yields of the aldehydes **34** and **35** after alkylation. Enolate geometry was probed by the stereoselective formation of enol acetates **36** and **37** using both catalysts (Scheme 16 and Table 9),



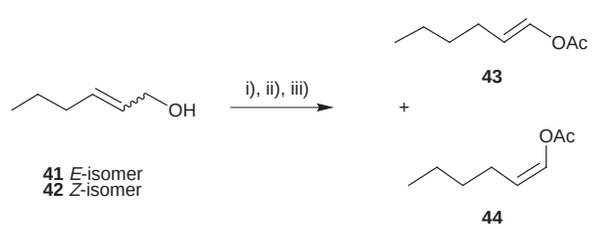
Scheme 16 *reagents*; i) *n*-BuLi, THF, 0 °C; ii) catalyst, reflux; iii) Ac_2O, −78 °C.

with the structure of the major product assigned by the indicated NOE. Relocation of the phenyl group to the terminus of the double bond had a drastic effect on both the rate and selectivity of the isomerisation. The lithium alkoxide of cinnamyl alcohol **38** (Scheme 17) gave a complex mixture of unidentified



Scheme 17 *reagents*: i) *n*-BuLi, THF, 0 °C; ii) $[Rh(dppe)]^+$ (5 mol%), reflux, 24 h; iii) Ac_2O −78 °C.

products with Wilkinson's catalyst. However, $[Rh(dppe)]^+$ *did* promote partial conversion over 24 hours and after acetic anhydride quench a low yield of enol acetates **39** and **40** was isolated, with a slight preference for the *E*-isomer. This result contrasts the ready isomerisation of the free alcohol to give a predominance of the *Z*-enol.[13] Clearly, deconjugation of the styrene chromophore presented a large barrier to isomerisation and we decided to investigate the isomerisation of simpler, alkyl-substituted primary allylic alkoxides, as shown in Scheme 18.



Scheme 18 *reagents*: i) *n*-BuLi, THF, 0 °C; ii) catalyst; iii) Ac_2O, −78 °C.

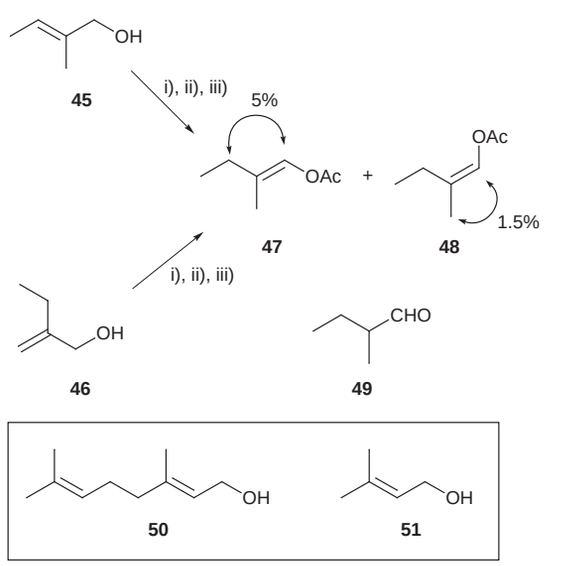
Both the *E* and *Z*-isomers of hex-2-en-1-ol **41** and **42** underwent facile isomerisation with $[Rh(dppe)]^+$ to afford near-identical ratios of the volatile enol acetates **43** and **44** (Table 10). Surprisingly, Wilkinson's catalyst gave no isomerisation products. Notably, the *E*-selectivity could be increased to 2.8:1 by lowering the reaction temperature from reflux to 40 °C, albeit at the expense of incomplete conversion after 24 hours. This temperature-dependent stereoselectivity was not observed in the isomerisation of secondary alkoxides, nor indeed with the more highly substituted primary alkoxides (*vide infra*).

Table 10 An examination of regiocontrol in enolate formation from **41** and **42**

Substrate	Catalyst and conditions	Ratio **43**:**44**	Yield **43** + **44** (%)
41	$(Ph_3P)_3RhCl$ (10 mol%, reflux, 24 h)	—	0
41	$[Rh(dppe)]^+$ (5 mol%, reflux, 6 h)	1.8:1	43
42	$[Rh(dppe)]^+$ (5 mol%, reflux, 6 h)	2.0:1	41
41	$[Rh(dppe)]^+$ (5 mol%, 40 °C, 24 h)	2.8:1	18

Table 11 An examination of regiocontrol in enolate formation from **45** and **46**

Substrate	Catalyst and conditions	Ratio **47**:**48**	Yield **47** + **48** (%)
45	$[Rh(dppe)]^+$ (5 mol%, reflux, 1 h)	3.0:1	46
45	$(Ph_3P)_3RhCl$ (2 mol%, reflux, 24 h)	—	0
46	$[Rh(dppe)]^+$ (5 mol%, reflux, 45 min)	3.0:1	60
46	$(Ph_3P)_3RhCl$ (2 mol%, reflux, 9 h)	3.0:1	49



Scheme 19 *reagents*: i) *n*-BuLi, THF, 0 °C; ii) catalyst; iii) Ac_2O, −78 °C.

The two substrates **45** and **46** (Scheme 19) provided an appropriate comparison with the phenyl-substituted secondary alkoxides **27** and **31** in terms of enolate equilibration. With $[Rh(dppe)]^+$, isomerisation of either alkoxide was readily achieved and quenching with acetic anhydride gave an identical ratio of the very volatile enol acetates **47** and **48** (Table 11), the stereochemistry of which was assigned by the indicated NOE enhancements. Turning to Wilkinson's catalyst, **45** once again gave no identifiable products derived from isomerisation, although the *exo*-methylene substrate **46** gave a similar result to $[Rh(dppe)]^+$. None of the aldehyde **49** could be isolated in these experiments, although we cannot rule out its formation in small amounts and subsequent loss on evaporation. These experiments therefore appeared to validate the concept of enolate stereoisomer equilibration in the primary alkoxide series.

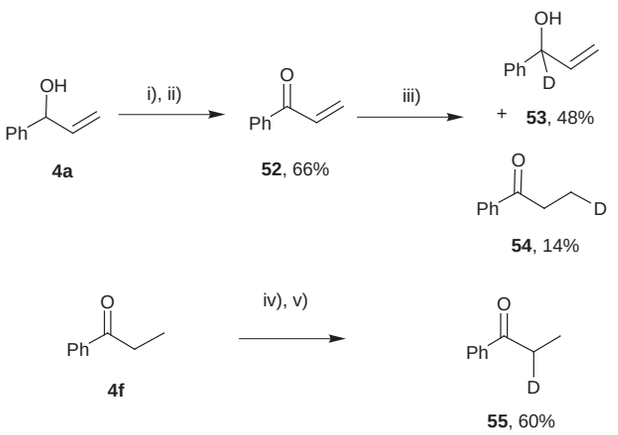
The logical progression in terms of substitution pattern now called for the addition of a second alkyl substituent at the olefin terminus. However, literature precedent for the isomerisation of geraniol **50** or the simpler alcohol **51** (Scheme 19) did not auger well[17] and prolonged exposure of either lithium alkoxide to $[Rh(dppe)]^+$ or Wilkinson's catalyst did not induce isomerisation.

Table 12 Isomerisation of **53**

Catalyst and conditions	Ratio **54**:**55**
$[Rh(dppe)]^+$ (10 mol%, 30 min)	>50:1
$(Ph_3P)_3RhCl$ (10 mol%, 30 min)	>50:1
$(Ph_3P)_3RhCl$ + 1 equiv. *n*-BuLi (10 mol%, 30 min)	30:1

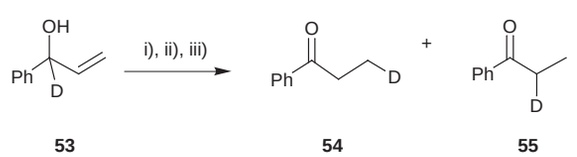
Mechanistic studies

Having probed the limitations of substrate structure applicable to the two rhodium catalysts, it remained to verify that isomerisation was occurring *via* either of the two 1,3-hydride shift mechanisms. Accordingly, the deuterated substrate **53** was prepared according to Scheme 20, along with authentic samples



Scheme 20 *reagents*: i) $(COCl)_2$, DMSO, CH_2Cl_2, −78 °C; ii) Et_3N; iii) $LiAlD_4$, Et_2O, 0 °C; iv) LDA, THF, −78 °C; v) add to D_2O–THF, 0 °C.

of the 2- and 3-deuterio ketones **55** and **54**. Careful analysis of the ^2H NMR spectra of the isomerisation of **53** (Scheme 21)



Scheme 21 *reagents*: i) *n*-BuLi, THF, 0 °C; ii) catalyst, reflux; iii) aq NH_4Cl.

promoted by either catalyst revealed the sole presence of 3-deuterio ketone **54** indicating a specific 1,3 migration of deuterium.[9] However, isomerisation with Wilkinson's catalyst pre-treated with an equivalent of *n*-butyllithium did result in formation of a small detectable amount of the 2-deuterio ketone **55** (Table 12), suggesting that a hydrometallation–elimination process[26–28] was at least partially operative under these conditions. It is emphasised that these experiments cannot differentiate between the π-allyl hydride and the closely related rhodium alkoxide mechanism; only differentiation between either one of these routes and the hydrometallation mechanism is possible.

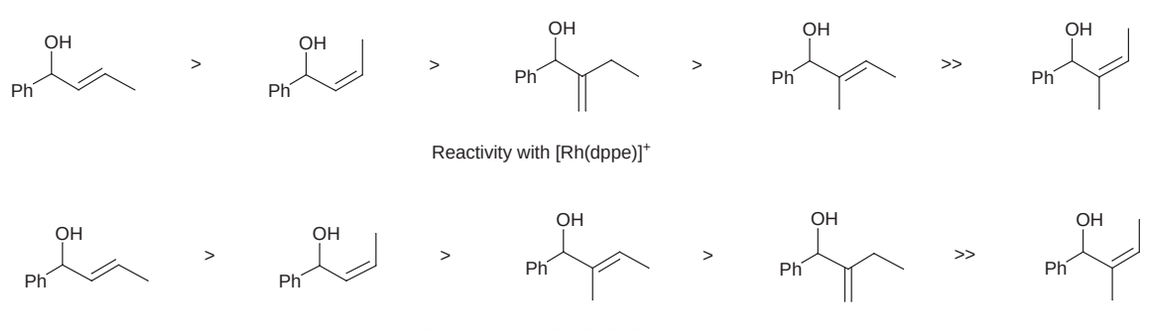
Conclusions

This work has demonstrated that, given certain structural limitations, an allylic alcohol may serve as a direct synthon for an enolate anion. In comparison with enolate generation from the carbonyl group, a similar sense and level of stereocontrol to strong base technology was achieved in formation of trisubstituted ketone enolates. Increasing substitution around the double bond slowed the rate of isomerisation and a general order of reactivity was observed as shown in Scheme 22. With either of the two catalysts examined, undesired equilibration of enolate regioisomers took place, although this problem was subsequently solved using a nickel-based catalyst system.[30] Moderate levels of stereocontrol were observed in the formation of tetrasubstituted enolates, although again apparently hampered by enolate stereoisomer equilibration. In formation of aldehyde enolates, isomerisation with the $[Rh(dppe)]^+$ catalyst represented a significant advance in terms of stereocontrol and facility of operation. Mechanistically, specific 1,3-migration of the hydride was demonstrated experimentally for both catalysts, although the precise nature of the isomerisation mechanism and a full stereochemical *rationale* awaits further study.

Experimental

General considerations

^1H NMR spectra were recorded at 270 MHz on a JEOL GSX-270 instrument and at 500 MHz on a Bruker AM-500 instrument (270 MHz unless otherwise noted), with *J* values in Hz. ^{13}C NMR spectra were recorded at 67.9 MHz on a JEOL GSX-270 and ^2H NMR 76.8 MHz on a Bruker WM-250 instrument, all spectra being run in $CDCl_3$ unless otherwise noted. Infrared spectra were recorded as thin films on NaCl plates on a Perkin-Elmer 983G or 881 instrument. Mass spectra were recorded on a VG 7070B or Autospec Q instrument under electron impact conditions at 70 eV. Elemental analysis was performed by Imperial College Microanalytical Laboratory. Petrol refers to light petroleum ether (bp 40–60 °C) and 30/40 petrol refers to light petroleum ether (bp 30–40 °C), both of which were distilled prior to use. Ether refers to diethyl ether, which when used as a reagent was distilled under argon from sodium–benzophenone ketyl, as was tetrahydrofuran (THF). Dichloromethane was distilled under argon from P_2O_5. Commercially available allylic alcohols were dried over K_2CO_3, prior to distillation on to 4 Å molecular sieves. Other reagents were purified by standard methods.[38] $[Rh(dppe)COD]ClO_4$ and $(Ph_3P)_3RhCl$ were prepared by literature methods.[12,39] All isomerisation reactions were carried out in flame-dried Schlenk glassware under a dry deoxygenated argon atmosphere



Scheme 22

and solutions were degassed by the freeze–pump–thaw cycle method. Analytical TLC was performed on pre-coated glass plated (Merck 60 F_{254}) and preparative chromatography was performed at low positive pressure on Merck Kieselgel 60.

Standard procedure for $[Rh(dppe)]^+$ catalysed isomerisation

A solution of [Rh(dppe)COD]ClO_4 (2–5 mol%) in THF was degassed twice, then stirred under a positive pressure of hydrogen for 20 min and purged with argon. *n*-Butyllithium (*ca.* 2.5 mol dm^{-3} in hexanes, 1–1.05 equiv.) was added dropwise to a cooled (0 °C) solution of allylic alcohol in THF. The resultant alkoxide solution was degassed twice, prior to addition of the catalyst solution *via* a cannula and the reaction was then heated (60 °C or reflux as appropriate) until TLC showed consumption of starting material.

Standard procedure for $(Ph_3P)_3RhCl$ catalysed isomerisation

A solution of $(Ph_3P)_3RhCl$ (2–5 mol%) in THF was degassed twice. *n*-Butyllithium (*ca.* 1.6 mol dm^{-3} hexanes, 1–1.05 equiv.) was added dropwise to a cooled (0 °C) solution of allylic alcohol in THF. The resultant alkoxide solution was degassed twice, prior to addition of the catalyst solution *via* a cannula and the reaction mixture was then heated at reflux until TLC showed consumption of starting material.

Standard enolate quench and work-up procedures

Alkylation. The reaction mixture was cooled to 0 °C, the alkylating agent (10 equiv.) was added *via* a syringe in one portion and the reaction mixture allowed to warm to ambient temperature overnight. Excess saturated aqueous NH_4Cl was then added, followed by water to dissolve any precipitated solids. The mixture was extracted with ether (3 × 10 cm^3), the combined organic phases were washed with brine (10 cm^3), dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product.

Aldol.[14] The reaction mixture was cooled to −78 °C and benzaldehyde (1.1 equiv.) was added in one portion as rapidly as possible, followed exactly 5 s later by excess saturated aqueous NH_4Cl. The mixture was allowed to warm to ambient temperature and water was added to dissolve any precipitated solids. After extraction with ether (3 × 10 ml), the combined organic phases were washed with brine (10 ml), dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product.

Acetylation. The reaction mixture was cooled to −78 °C and acetyl chloride or acetic anhydride (10 equiv.) was added *via* a syringe in one portion as rapidly as possible. After 15–20 min at −78 °C, excess $NaHCO_3$ was added and the mixture allowed to warm to ambient temperature and stir for a further 20 min. Water was added to dissolve any precipitated solids and the mixture was extracted with ether (3 × 10 cm^3), the combined organic phases were washed with brine (10 cm^3), dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product.

Preparation of 4a

A solution of benzaldehyde (3 cm^3, 29 mmol) in THF (20 cm^3) was added dropwise over 10 min to a stirred solution of vinylmagnesium bromide (1 mol dm^{-3} THF, 30 cm^3, 30 mmol) at 0 °C. The reaction mixture was stirred for a further 15 min at 0 °C, then at RT for 2 h. Saturated aqueous NH_4Cl (25 cm^3) was then added, followed by water (5 cm^3) to dissolve excess magnesium salts. The layers were separated and the aqueous phase extracted with ether (2 × 20 cm^3), the combined organic phases were washed with brine (20 cm^3), dried ($MgSO_4$) and evaporated. Flash chromatography (4:1 petrol–ether elution) afforded *1-phenylprop-2-en-1-ol* **4a**[40] as a clear colourless oil (2.96 g, 76%); ν_{max}/cm^{-1}: 3399, 2958, 2926, 1674, 1600, 1450, 1026, 991, 927, 739, 700; δ_H: 1.97 (1 H, d, *J* 3.7), 5.06–5.16 (2 H, m), 5.27 (1 H, dd, *J* 17.1 and 1.0), 5.97 (1 H, ddd, *J* 17.1, 10.0 and 1.0), 7.2–7.4 (5 H, m); *m/z*: 134 (M^+), 133, 115, 105, 92, 77, 55, 51.

Isomerisation of 4a with $[Rh(dppe)]^+$: alkylation to give 5a

A degassed solution of alkoxide prepared from **4a** (0.324 g, 2.41 mmol) and *n*-butyllithium (2.5 mol dm^{-3} hexanes, 1 cm^3, 2.5 mmol) in THF (15 cm^3) was treated with catalyst prepared from [Rh(dppe)COD]ClO_4 (38 mg, 0.05 mmol) in THF (8 cm^3) and heated at 60 °C for 7 h. Quench with allyl bromide (2 cm^3, 23 mmol) followed by standard work-up and flash chromatography (20:1 petrol–ether elution) afforded *2-methyl-1-phenylpent-4-en-1-one* **5a**[41] as a clear colourless oil (0.347 g, 82%); ν_{max}/cm^{-1}: 2972, 1676, 1637, 1595, 1447, 1208, 975, 705; δ_H: 1.21 (3 H, d, *J* 6.8), 2.20 (1 H, m), 2.60 (1H, m), 3.55 (1 H, sextet, *J* 6.8), 5.10 (2H, m), 5.79 (1 H, ddt, *J* 17.8, 10.3 and 6.6), 7.80 (5H, m) and *1-phenylpropan-1-one* **5f**[42] as a clear colourless oil (30 mg, 10%); δ_H: 1.20 (3 H, t, *J* 7.3), 2.94 (2 H, q, *J* 7.3), 7.60 (5 H, m); *m/z*: 134 (M^+), 122, 106, 105, 91, 77.

Isomerisation of 4a with $[Rh(dppe)]^+$: alkylation to give 5b

The enolate was prepared as described above and quenched with benzyl bromide (3 cm^3, 25 mmol). Standard work-up and flash chromatography (20:1 petrol–ether elution) afforded *1,3-diphenyl-2-methylpropan-1-one* **5b**[43] as a clear colourless oil (0.420 g, 75%): ν_{max}/cm^{-1}: 2968, 1676, 1595, 1447, 1229, 973, 698; δ_H: 1.12 (3 H, d, *J* 6.8), 2.87 (1 H, dd, *J* 13.7 and 7.8), 3.08 (1 H, dd, *J* 13.7 and 6.4), 3.65 (1 H, sextet, *J* 6.8) 7.0–7.85 (5 H, m); *m/z*: 224 (M^+), 209, 151, 133, 118, 105, 91, 77 and *1-phenylpropan-1-one* **5f** (57 mg, 18%).

Isomerisation of 4a with $[Rh(dppe)]^+$: alkylation to give 5c

The enolate was prepared as described above and quenched with methyl iodide (1.50 cm^3, 23 mmol). Standard work-up and flash chromatography (20:1 petrol–ether elution) afforded *2-methyl-1-phenylpropan-1-one* **5c**[44] as a clear colourless oil which discoloured on standing (0.229 g, 62%): ν_{max}/cm^{-1}: 2972, 1684, 1595, 1446, 1220, 979, 703; δ_H: 1.22 (6 H, d, *J* 6.8), 3.56 (1 H, septet, *J* 6.8), 7.40–7.90 (5 H, m); *m/z*: 148 (M^+), 134, 105, 77 and *1-phenylpropan-1-one* **5f** (54 mg, 17%).

Isomerisation of 4a with $[Rh(dppe)]^+$: alkylation to give 5d

A degassed solution of alkoxide prepared from **4a** (0.166 g, 1.24 mmol) and *n*-butyllithium (1.6 mol dm^{-3} hexanes, 0.80 cm^3, 1.28 mmol) in THF (8 cm^3) was treated with catalyst prepared from [Rh(dppe)COD]ClO_4 (17 mg, 0.024 mmol) in THF (5 cm^3) and heated at 60 °C for 7 h. Quench with *n*-butyl iodide (1.20 cm^3, 11 mmol) followed by standard work-up and flash chromatography (40:1 petrol–ether elution) afforded *2-methyl-1-phenylhexan-1-one* **5d**[45] as a clear colourless oil (0.142 g, 60%): ν_{max}/cm^{-1}: 2930, 1676, 1594, 1447, 1229, 970, 704; δ_H: 0.87 (3 H, t, *J* 6.8), 1.19 (2 H, d, *J* 6.8), 1.30 (6 H, m), 3.43 (1 H, sextet, *J* 6.8), 7.40–7.80 (5 H, m); *m/z*: 190 (M^+), 176, 162, 147, 139, 105 and *1-phenylpropan-1-one* **5f** (22 mg, 13%).

Isomerisation of 4b with $[Rh(dppe)]^+$: alkylation to give 5e

A degassed solution of alkoxide prepared from **4b** (0.255 cm^3, 2.49 mmol) and *n*-butyllithium (2.5 mol dm^{-3} hexanes, 1.0 cm^3, 2.50 mmol) in THF (8 cm^3) was treated with catalyst prepared from [Rh(dppe)COD]ClO_4 (35 mg, 0.049 mmol) in THF (5 cm^3) and heated at 60 °C for 9.5 h. Quench with benzyl bromide (3 cm^3, 25 mmol), followed by standard work-up and flash chromatography (40:1 petrol–ether elution) afforded *2-methyl-1-phenylpentan-3-one* **5e**[46] as a clear colourless oil (0.210 g, 48%): ν_{max}/cm^{-1}: 2971, 1706, 1602, 1583, 1450, 1371, 742, 700; δ_H(500 MHz): 0.97 (3 H, t, *J* 7.3), 1.08 (3 H, d, *J* 6.9), 2.25 (1 H, dq, *J* 17.8, 7.3), 2.43 (1 H, dq, *J* 17.8, 7.3), 2.57 (1 H, dd, *J* 13.4, 7.4), 2.84 (1 H, sextet, *J* 7.0), 2.97 (1 H, dd, *J* 13.4, 7.2), 7.20 (5 H, m); *m/z*: 190 (M^+), 176, 162, 147, 139, 105.

Isomerisation of 4a with [Rh(dppe)]$^+$: aldol to give 6a

A degassed solution of alkoxide prepared from **4a** (0.160 g, 1.19 mmol) and *n*-butyllithium (2.5 mol dm^{-3} hexanes, 0.50 cm^3, 1.25 mmol) in THF (8 cm^3) was treated with catalyst prepared from [Rh(dppe)COD]ClO_4 (17 mg, 0.024 mmol) in THF (5 cm^3) and heated at 60 °C for 7 h. Quench with benzaldehyde (0.126 cm^3, 1.26 mmol) followed by standard work-up and flash chromatography (4 : 1 petrol–ether elution) afforded an inseparable mixture of *syn* and *anti-1,3-diphenyl-3-hydroxy-2-methylpropan-1-one* **6a**[47] (8.6 : 1, 0.240 g, 84%) as a clear colourless viscous oil: ν_{max}/cm^{-1}(mix): 3467, 2973, 2933, 1674, 1595, 1575, 1448, 1214, 971, 702; δ_H(*syn*, $CDCl_3$+D_2O): 1.19 (3 H, d, *J* 7.3), 3.69 (1 H, m), 5.29 (1 H, d, *J* 3.2), 7.20–8.0 (10 H, m); *anti*: 1.07 (3 H, d, *J* 7.1), 3.69 (1 H, m), 4.99 (1 H, d, *J* 7.8), 7.20–8.0 (10 H, m); *m*/*z*: 240 (M$^+$), 222, 134, 105, 77.

Isomerisation of 4a with $(Ph_3P)_3RhCl$: aldol to give 6a

A degassed solution of alkoxide prepared from **4a** (0.200 g, 1.49 mmol) and *n*-butyllithium (1.49 mol dm^{-3} hexanes, 1.0 cm^3, 1.49 mmol) in THF (6 cm^3) was treated with catalyst prepared from $(Ph_3P)_3RhCl$ (27 mg, 0.029 mmol) in THF (4 cm^3) and heated at reflux for 1.5 h. Quench with benzaldehyde (0.166 cm^3, 1.64 mmol) followed by standard work-up and flash chromatography afforded an inseparable mixture of *syn* and *anti-1,3-diphenyl-3-hydroxy-2-methylpropan-1-one* **6a** (8.3 : 1, 0.250 g, 70%).

Isomerisation of 4b with [Rh(dppe)]$^+$: aldol to give 6b

A degassed solution of alkoxide prepared from **4b** (0.255 cm^3, 2.49 mmol) and *n*-butyllithium (2.5 mol dm^{-3} hexanes, 1.0 cm^3, 2.50 mmol) in THF (8 cm^3) was treated with catalyst prepared from [Rh(dppe)COD]ClO_4 (35 mg, 0.049 mmol) in THF (5 cm^3) and heated at 60 °C for 9.5 h. Quench with benzaldehyde (0.252 cm^3, 2.49 mmol), followed by standard work-up and flash chromatography (3 : 1 petrol–ether elution) afforded an inseparable mixture of *syn* and *anti-1-hydroxy-2-methyl-1-phenylpentan-3-one* **6b**[14] as a clear colourless viscous oil (3.9 : 1, 0.378 g, 79%): ν_{max}/cm^{-1}(mix): 3452, 2935, 1706, 1602, 1491, 1406, 1375, 1015, 975, 762, 702; δ_H(*syn*, $CDCl_3$+D_2O): 1.00 (3 H, t, *J* 7.2), 1.08 (3 H, d, *J* 7.3), 2.40 (2 H, m), 3.84 (1 H, m), 5.06 (1 H, d, *J* 3.9), 7.30 (5 H, m); *anti*: 0.94 (3 H, d, *J* 7.1), 1.00 (3 H, t, *J* 7.2), 2.40 (2 H, m), 3.84 (1 H, m), 4.75 (1 H, d, *J* 8.1), 7.30 (5 H, m); *m*/*z*: 192 (M$^+$), 177, 163, 159, 145, 117, 106, 86, 77.

Isomerisation of 4b with $(Ph_3P)_3RhCl$: aldol to give 6b

A degassed solution of alkoxide prepared from **4b** (0.135 g, 1.57 mmol) and *n*-butyllithium (1.49 mol dm^{-3} hexanes, 1.05 cm^3, 1.57 mmol) in THF (6 cm^3) was treated with catalyst prepared from $(Ph_3P)_3RhCl$ (29 mg, 0.032 mmol) in THF (4 cm^3) and heated at reflux for 10 h. Quench with benzaldehyde (0.176 cm^3, 1.72 mmol) followed by standard work-up and flash chromatography afforded an inseparable mixture of *syn* and *anti-1-hydroxy-2-methyl-1-phenylpentan-3-one* **6b** (3.5 : 1, 0.240 g, 80%).

Isomerisation of 7 with [Rh(dppe)]$^+$: aldol to give 8 and 9

A degassed solution of alkoxide prepared from **7** (0.204 cm^3, 2.34 mmol) and *n*-butyllithium (2.5 mol dm^{-3} hexanes, 1.0 cm^3, 2.50 mmol) in THF (8 cm^3) was treated with catalyst prepared from [Rh(dppe)COD]ClO_4 (36 mg, 0.051 mmol) in THF (10 cm^3) and heated at 60 °C for 8 h. Quench with benzaldehyde (0.252 cm^3, 2.49 mmol), followed by standard work-up and flash chromatography (2 : 1 petrol ether elution) afforded an inseparable mixture of *syn* and *anti-1-hydroxy-2-methyl-1-phenylbutan-3-one* **8**[48] and *1-hydroxy-1-phenylpentan-3-one* **9**[49] as a clear colourless oil (5.0 : 1.3 : 1, 0.312 g, 72%): ν_{max}/cm^{-1}(mix): 3438, 2975, 1702, 1602, 1491, 1450, 1356, 901, 762; δ_H(*syn*-**8**, $CDCl_3$+D_2O): 1.02 (3 H, d, *J* 7.3), 2.09 (3 H, s), 2.80 (1 H, m), 5.05 (1 H, d, *J* 3.9), 7.20 (5 H, m); *anti*-**8**: 0.87 (3 H, d, *J* 7.1), 2.16 (3 H, s), 2.80 (2 H, m), 4.68 (1 H, d, *J* 8.3), 7.20 (5 H, m); **9**: 1.0 (3 H, t, *J* 7.3), 2.4 (2 H, q, *J* 7.3), 2.80 (2 H, m), 5.09 (1 H, m), 7.20 (5 H, m); *m*/*z*: 178 (M$^+$), 160, 133, 122, 117, 106, 79, 77.

Isomerisation of 7 with $(Ph_3P)_3RhCl$: aldol to give 8 and 9

A degassed solution of alkoxide prepared from **7** (0.123 g, 1.70 mmol) and *n*-butyllithium (1.63 mol dm^{-3} hexanes, 1.05 cm^3, 1.71 mmol) in THF (6 cm^3) was treated with catalyst prepared from $(Ph_3P)_3RhCl$ (32 mg, 0.034 mmol) in THF (5 cm^3) and heated at reflux for 3 h. Quench with benzaldehyde (0.190 cm^3, 1.87 mmol) followed by standard work-up and flash chromatography afforded an inseparable mixture of *syn* and *anti-1-hydroxy-2-methyl-1-phenylbutan-3-one* **8** and *1-hydroxy-1-phenylpentan-3-one* **9** (5.6 : 1.4 : 1, 0.312 g, 66%).

Preparation of 10

3-Phenylpropanal (2.90 cm^3, 22 mmol) was added dropwise over 30 min to a cooled (0 °C) stirred solution of vinylmagnesium bromide (1 mol dm^{-3} THF, 20 cm^3, 20 mmol) in THF (40 cm^3). The reaction was allowed to warm to RT and stirred for 1.5 h, prior to addition of saturated aqueous NH_4Cl (50 cm^3). The layers were separated and the aqueous phase was extracted with ether (3 × 25 cm^3), the combined organic phases were washed with water (50 cm^3), brine (50 cm^3) and dried ($MgSO_4$). Evaporation and purification by flash chromatography afforded *1-phenylpent-4-en-3-ol* **10**[17] as a clear colourless oil (2.47 g, 74%): ν_{max}/cm^{-1}: 3406, 2932, 1635, 1602, 1431, 1036, 928, 700; δ_H: 1.50 (1 H, br s), 1.85 (2 H, m), 2.70 (2 H, m), 4.14 (1 H, q, *J* 6.0), 5.15 (1 H, d, *J* 10.4), 5.15 (1 H, d, *J* 17.4), 5.92 (1 H, ddd, *J* 17.4, 10.4 and 6.1), 7.20–7.40 (5 H, m); *m*/*z*: 162 (M$^+$), 144, 133, 129, 105, 91, 77, 57.

Isomerisation of 10 with [Rh(dppe)]$^+$: alkylation to give 11 and 12

A degassed solution of alkoxide prepared from **10** (0.199 g, 1.23 mmol) and *n*-butyllithium (2.5 mol dm^{-3} hexanes, 0.55 cm^3, 1.30 mmol) in THF (8 cm^3) was treated with catalyst prepared from [Rh(dppe)COD]ClO_4 (18 mg, 0.023 mmol) in THF (5 cm^3) and heated at 60 °C for 7 h. Quench with allyl bromide (1 cm^3, 11 mmol) and standard work-up followed by flash chromatography (100 : 3–5 : 1 petrol–ether gradient elution) afforded *4-(phenylmethyl)hept-6-en-3-one* **12** and *4-methyl-1-phenylhept-6-en-3-one* **11**, an inseparable mixture as a clear colourless oil (1.2 : 1, 0.196 g, 79%): ν_{max}/cm^{-1}(mix): 2973, 2932, 1707, 1637, 1602, 1493, 1450, 1373, 1083, 748, 700; δ_H(**12**): 0.90 (3 H, t, *J* 7.1), 2.0–2.45 (2 H, m), 2.65–2.75 (1 H, m), 2.75–3.0 (4 H, m), 4.95–5.10 (2 H, m), 5.60–5.80 (1 H, m), 7.10–7.35 (5 H, m); **11**: 1.05 (3 H, d, *J* 6.8), 2.0–2.45 (2 H, m), 2.58 (1 H, sextet, *J* 7.1), 2.65–2.80 (2 H, m), 2.80–3.0 (2 H, m), 4.95–5.1 (2 H, m), 5.60–5.80 (1 H, m), 7.10–7.35 (5 H, m); *m*/*z*: 242 (M$^+$, %), 202, 173, 161, 145, 133, 111, 105, 91, 77; HRMS: $C_{14}H_{18}O$ requires *M* = 202.1357, found M$^+$ = 202.1343, *1-phenylpentan-3-one* **13**[50] as a clear colourless oil (14 mg, 7%): ν_{max}/cm^{-1}: 2973, 2932, 1707, 1602, 1493, 1449, 1370, 1083, 740, 689; δ_H: 0.97 (3 H, t, *J* 7.3), 2.33 (2 H, q, *J* 7.3), 2.66 (4 H, m), 7.15–7.35 (5 H, m); *m*/*z*: 162 (M$^+$, %), 161, 145, 133, 111, 105, 91, 77 and the intractable mixture of *polyalkylated ketones* 14 (15 mg, *ca.* 5%): ν_{max}/cm^{-1}: 2973, 2932, 1708, 1638, 1602, 1493, 1450, 1373, 1083, 748, 700; δ_H(*inter alia*): 0.68 (d, *J* 6.8), 1.10 (s), 2.8–3.0 (m), 5.0 (m), 5.40–5.80 (m), 7.10–7.30 (m); *m*/*z*: 282 (triallyl M$^+$), 242 (diallyl M$^+$); HRMS: diallyl compound $C_{17}H_{22}O$ requires *M* = 242.1671, found M$^+$ = 242.1671.

Isomerisation of 10 with $(Ph_3P)_3RhCl$: alkylation to give 11 and 12

A degassed solution of alkoxide prepared from **10** (0.211 g, 1.30 mmol) and *n*-butyllithium (1.51 mol dm^{-3} hexanes, 0.86 cm^3, 1.30 mmol) in THF (6 cm^3) was treated with catalyst prepared from $(Ph_3P)_3RhCl$ (25 mg, 0.027 mmol) in THF (5 cm^3) and heated at reflux for 3 h. Quench with allyl bromide (1.0 cm^3, 11 mmol) and standard work-up followed by flash chromatography afforded *4-(phenylmethyl)hept-6-en-3-one* **12**, *4-methyl-1-phenylhept-6-en-3-one* **11** (1.3:1, 0.143 g, 54%), *1-phenylpentan-3-one* **13** (14 mg, 6%) and the intractable mixture of *polyalkylated ketones* 14 (15 mg, *ca.* 5%).

Isomerisation of 10 with $(Ph_3P)_3RhCl$ and excess BuLi: alkylation to give 11 and 12

A degassed solution of alkoxide was prepared from **10** (0.211 g, 1.30 mmol) and *n*-butyllithium (1.51 mol dm^{-3} hexanes, 1.31 cm^3, 1.95 mmol) in THF (6 cm^3) was treated with catalyst prepared from $(Ph_3P)_3RhCl$ (24 mg, 0.026 mmol) in THF (5 cm^3) and heated at reflux for 8.5 h. The reaction mixture was initially very deep red in colour and metallic rhodium was deposited on the stirrer bead by the end of the isomerisation. Quench with allyl bromide (1.0 cm^3, 11 mmol) and standard work-up followed by flash chromatography afforded *4-(phenylmethyl)hept-6-en-3-one* **12**, *4-methyl-1-phenylhept-6-en-3-one* **11** (1:9.7, 0.102 g, 39%), *1-phenylpentan-3-one* **13** (12 mg, 6%), the intractable mixture of *polyalkylated ketones* 14 (2 mg, *ca.* 2%) and starting material (18 mg, 6%).

Preparation of 15

Mg turnings (1.46 g, 61 mmol) were dry stirred under argon for 2.5 h then suspended in THF (40 cm^3). A small crystal of iodine was added, followed by a solution of bromobenzene (5.30 cm^3, 50 mmol) in THF (20 cm^3) over 20 min so as to maintain gentle reflux. The reaction mixture was refluxed for a further 20 min and then cooled to 5 °C. A solution of freshly distilled crotonaldehyde (4.15 cm^3, 50 mmol) in THF (20 cm^3) was added over 10 min and the reaction allowed to warm to ambient temperature over 2 h. Saturated aqueous NH_4Cl (50 cm^3) was added and the two-phase mixture stirred for a further 30 min. The layers were separated and the aqueous phase was extracted with ether (2 × 25 cm^3). The combined organic phases were washed with brine (25 cm^3) dried ($MgSO_4$) and evaporated. Flash chromatography (4:1 petrol–ether elution) afforded (*E*)-*1-phenylbut-2-en-1-ol* **15**[51] as a clear colourless oil (5.0 g, 68%): ν_{max}/cm^{-1}: 3345, 3028, 2916, 1660, 1600, 1491, 1451, 1069, 964, 846, 754, 699; δ_H: 1.73 (3 H, dd, *J* 5.1, 0.7), 1.88 (1 H, m), 5.16 (1 H, m), 5.70 (1 H, m), 7.20–7.40 (5 H, m); *m/z*: 148 (M^+), 133, 129, 115, 105, 77.

Isomerisation of 15 with $[Rh(dppe)]^+$: aldol to give 16

A degassed solution of alkoxide prepared from **15** (0.183 g, 1.24 mmol) and *n*-butyllithium (2.5 mol dm^{-3} hexanes, 0.50 cm^3, 1.25 mmol) in THF (8 cm^3) was treated with catalyst prepared from $[Rh(dppe)COD]ClO_4$ (20 mg, 0.028 mmol) in THF (5 cm^3) and heated at reflux for 3 h. Quench with benzaldehyde (0.126 cm^3, 1.25 mmol) and standard work-up followed by flash chromatography (3:1 petrol–ether elution) afforded an inseparable mixture of *syn* and *anti-2-[hydroxy(phenyl)methyl]-1-phenylbutan-1-one* **16**[52] as a clear colourless viscous oil (3.0:1, 0.226 g, 71%): ν_{max}/cm^{-1}(mix): 3449, 2964, 1668, 1597, 1491, 1447, 1359, 1267, 1027, 760, 702; δ_H(*syn*): 0.73 (3 H, t, *J* 7.6), 2.80 (2 H, m), 3.16 (1 H, d, *J* 2.0), 3.74 (1 H, quintet, *J* 4.6), 5.03 (1 H, dd, *J* 4.6, 2.0), 7.10–7.90 (10 H, m); *anti*: 0.76 (3 H, t, *J* 7.6), 2.80 (2 H, m), 3.02 (1 H, d, *J* 5.4), 3.78 (1 H, td, *J* 7.1, 5.2), 4.97 (1 H, dd, *J* 7.1, 5.4), 7.10–7.90 (10 H, m); *m/z*: 254 (M^+), 236, 225, 148.

Isomerisation of 15 with $(Ph_3P)_3RhCl$: aldol reaction to give 16

A degassed solution of alkoxide prepared from **15** (0.223 g, 1.50 mmol) and *n*-butyllithium (1.49 mol dm^{-3} hexanes, 1.01 cm^3, 1.50 mmol) in THF (6 cm^3) was treated with catalyst prepared from $(Ph_3P)_3RhCl$ (28 mg, 0.03 mmol) in THF (5 cm^3) and heated at reflux for 5.5 h. Quench with benzaldehyde (0.168 cm^3, 1.65 mmol) and standard work-up followed by flash chromatography afforded an inseparable mixture of *syn* and *anti-2-[hydroxy(phenyl)methyl]-1-phenylbutan-1-one* **16** (3.0:1, 0.351 g, 92%).

Preparation of 17

Li shot (0.86 g, 123 mmol) and anhydrous $FeCl_3$ (40 mg, cat) were added to liquid ammonia (*ca.* 50 cm^3) at −78 °C. The deep blue solution was stirred at −78 °C for 5 min, then allowed to reflux without external cooling for 2 h, during which time it became grey. A solution of 1-phenylprop-2-yn-1-ol (6.63 g, 50 mmol) in THF (50 cm^3) was added *via* a cannula to give a brown slurry which was stirred at RT for 1.5 h. Iodomethane (3.10 cm^3, 50 mmol) was added and the reaction mixture stirred for a further 1 h, prior to evaporation of excess ammonia. The residue was partitioned between ether (100 cm^3) and saturated aqueous NH_4Cl (100 cm^3). The layers were separated, the aqueous phase was extracted with ether (2 × 100 cm^3) and the combined organic phases were washed with brine (50 cm^3) and dried ($MgSO_4$). After evaporation, flash chromatography (2:1 petrol–ether elution) afforded *1-phenylbut-2-yn-1-ol*[53] as a clear colourless oil (6.14 g, 85%): ν_{max}/cm^{-1}: 3360, 2919, 2288, 1603, 1492, 1450, 1136, 1002, 694; δ_H: 1.91 (3 H, d, *J* 2.2), 2.17 (1 H, m), 5.43 (1 H, q, *J* 2.2), 7.40 (5 H, m); *m/z*: 146 (M^+, %), 131, 115, 105, 77. A suspension of Pd–$BaSO_4$ (73 mg) in hexane (2 cm^3) was treated with quinoline (2 drops) and stirred under a low positive pressure of hydrogen at 0 °C for 30 min. A solution of 1-phenylbut-2-yn-1-ol (0.70 g, 4.70 mmol) in hexane–ether (9:1 v/v, 10 cm^3) was added *via* a cannula and the reaction mixture stirred under hydrogen for 2 h, prior to filtration through a Celite® pad. After washing with ether, the combined filtrate and washings were evaporated to afford (*Z*)-*1-phenylbut-2-en-1-ol* **17** as a clear colourless oil (0.65 g, 93%): ν_{max}/cm^{-1}: 3359, 3025, 1676, 1601, 1493, 1449, 1033, 910, 844, 698; δ_H: 1.80 (3 H, dd, *J* 4.6, 0.9), 1.90 (1 H, s), 5.60 (3 H, m), 7.40 (5 H, m); *m/z*: 148 (M^+), 133, 129, 115, 105, 77.

Isomerisation of 15 with $[Rh(dppe)]^+$: acetylation to give 18 and 19

A degassed solution of alkoxide prepared from **15** (0.178 g, 1.20 mmol) and *n*-butyllithium (2.5 mol dm^{-3} hexanes, 0.50 cm^3, 1.25 mmol) in THF (8 cm^3) was treated with catalyst prepared from $[Rh(dppe)COD]ClO_4$ (20 mg, 0.028 mmol) in THF (5 cm^3) and heated at reflux for 3 h. Quench with acetyl chloride (0.80 cm^3, 11 mmol) and standard work-up followed by flash chromatography (10:1 petrol–ether elution) afforded an inseparable mixture of (*Z*)- and (*E*)-*1-phenylbut-1-en-1-yl acetate* **18** and **19** as a clear colourless oil (25:1, 0.147 g, 64%): ν_{max}/cm^{-1}(mix): 3034, 2968, 2936, 1760, 1665, 1601, 1494, 1447, 1370, 1207, 1035, 751, 691; δ_H(**18**, 500 MHz): 1.08 (3 H, t, *J* 7.6), 2.16 (2 H, quintet, *J* 7.5), 2.30 (3 H, s), 5.83 (1 H, t, *J* 7.3), 7.27 (1 H, br t, *J* 7.0), 7.33 (2 H, br t, *J* 7.0), 7.41 (2 H, br d, *J* 7.0); **19**: 1.73 (3 H, dd, *J* 6.3, 0.7), 2.10 (3 H, s), 5.68 (1 H, ddd, *J* 15.3 and 6.9, 1.4), 5.77 (1 H, ddd, *J* 15.3, 6.3 and 0.7), 6.23 (1 H, br d, *J* 7.0), 7.25–7.45 (5 H, m); *m/z*: 190 (M^+), 148, 133, 105; HRMS: $C_{12}H_{14}O_2$ requires $M = 190.0994$, found $M^+ = 190.1002$ and *2-ethyl-1-phenylbutane-1,3-dione* **20**[54] as a clear colourless oil (22 mg, 10%): ν_{max}/cm^{-1}: 2969, 2936, 1722, 1675, 1597, 1448, 1357, 1273, 1211, 735, 695; δ_H: 0.95 (3 H, t, *J* 7.3), 2.0 (2 H, m), 2.14 (3 H, s), 4.35 (1 H, t, *J* 6.8), 7.28–8.0 (5 H, m).

Isomerisation of 15 with $(Ph_3P)_3RhCl$: acetylation to give 18 and 19

A degassed solution of alkoxide prepared from **15** (0.199 g, 1.34 mmol) and *n*-butyllithium (1.63 mol dm^{-3} hexanes, 0.824 ml, 1.34 mmol) in THF (6 ml) was treated with catalyst prepared from $(Ph_3P)_3RhCl$ (24 mg, 0.027 mmol) in THF (5 cm^3) and heated at reflux for 6 h. Quench with acetic anhydride (1.21 cm^3, 12.8 mmol) and standard work-up followed by flash chromatography afforded an inseparable mixture of (*Z*)- and (*E*)-*1-phenylbut-1-en-1-yl acetate* **18** and **19** (>25:1, 0.102 g, 32%) and *2-ethyl-1-phenylbutane-1,3-dione* **20** (16 mg, 7%).

Isomerisation of 17 with $[Rh(dppe)]^+$: acetylation to give 18 and 19

A degassed solution of alkoxide prepared from **17** (0.176 g, 1.19 mmol) and *n*-butyllithium (2.5 mol dm^{-3} hexanes, 0.50 cm^3, 1.25 mmol) in THF (8 cm^3) was treated with catalyst prepared from [Rh(dppe)COD]ClO_4 (20 mg, 0.028 mmol) in THF (5 cm^3) and heated at reflux for 4 h. Quench with acetyl chloride (0.80 cm^3, 11 mmol) and standard work-up followed by flash chromatography afforded an inseparable mixture of (*Z*) and (*E*)-*1-phenylbut-1-en-1-yl acetate* **18** and **19** (25:1, 0.145 g, 64%) and *2-ethyl-1-phenylbutane-1,3-dione* **20** (30 mg, 13%).

Isomerisation of 17 with $(Ph_3P)_3RhCl$: acetylation to give 18 and 19

A degassed solution of alkoxide prepared from **17** (0.199 g, 1.34 mmol) and *n*-butyllithium (1.63 mol dm^{-3} hexanes, 0.824 cm^3, 1.34 mmol) in THF (6 cm^3) was treated with catalyst prepared from $(Ph_3P)_3RhCl$ (25 mg, 0.027 mmol) in THF (5 cm^3) and heated at reflux for 7 h. Quench with acetyl chloride (0.95 cm^3, 13.4 mmol) and standard work-up followed by flash chromatography afforded an inseparable mixture of (*Z*) and (*E*)-*1-phenylbut-1-en-1-yl acetate* **18** and **19** (>25:1, 0.115 g, 45%) and *2-ethyl-1-phenylbutane-1,3-dione* **20** (31 mg, 12%).

Isomerisation of 24 with $(Ph_3P)_3RhCl$: aldol to give 25

A degassed solution of alkoxide prepared from **24** (0.139 g, 1.42 mmol) and *n*-butyllithium (1.63 mol dm^{-3} hexanes, 0.871 cm^3, 1.42 mmol) in THF (6 cm^3) was treated with a catalyst prepared from $(Ph_3P)_3RhCl$ (65 mg, 0.071 mmol) in THF (5 cm^3) and heated at reflux for 48 h. Quench with benzaldehyde (0.159 ml, 1.56 mmol) and standard work-up followed by flash chromatography (5:1–2:1 petrol–ether gradient elution) afforded an inseparable mixture of *anti* and *syn-2-[hydroxy(phenyl)methyl]-cyclohexanone* **25**[14] as a clear colourless oil (4.2:1, 20 mg, 7%): ν_{max}/cm^{-1}(mix): 3502, 2937, 2864, 1699, 1604, 1450, 1130, 1042, 776, 702; δ_H(*anti*): 1.20–2.60 (8 H, m), 2.55–2.70 (1 H, m), 3.95 (1 H, d, *J* 0.7), 4.78 (1 H, d, *J* 8.8), 7.20–7.40 (5 H, m); *syn*:1.20–2.70 (9 H, m), 3.0 (1 H, d, *J* 3.0), 5.39 (1 H, m), 7.20–7.40 (5 H, m); *m/z*: 204 (M^+), 186, 175, 157, 147, 77.

Preparation of 26

Mg turnings (1.46 g, 60 mmol) were dry-stirred under argon for 3 h, then suspended in THF (20 cm^3) and a crystal of iodine was added. A solution of 2-bromobut-2-ene (6.75 g, 50 mmol) in THF (20 cm^3) was added over 30 min so as to maintain gentle reflux. The reaction mixture was then refluxed for a further 30 min, prior to cooling to 5 °C. A solution of benzaldehyde (6.0 cm^3, 60 mmol) in THF (20 cm^3) was added over 20 min and the reaction allowed to warm to RT over 1 h. Saturated aqueous NH_4Cl (50 cm^3) was added and the two-phase mixture stirred for a further 30 min, after which the layers were separated. The aqueous phase was extracted with ether (2 × 25 cm^3) and the combined organic phases washed with brine (25 cm^3), then dried ($MgSO_4$). Evaporation and flash chromatography (4:1 petrol–ether elution) afforded (*Z*)-*2-methyl-1-phenylbut-2-en-1-ol* **26** as a clear colourless oil (7:1 *Z*:*E*, 4.90 g, 60%): ν_{max}/cm^{-1}: 3383, 2974, 2925, 1665, 1603, 1492, 1449, 1377, 1187, 1105, 1070, 1013, 734, 699; δ_H: 1.58 (3 H, m), 1.81 (3 H, d, *J* 6.9), 5.47 (3 H, qq, *J* 6.9, 0.5), 5.81 (1 H, s), 7.20–7.40 (5 H, m); *m/z*: 162 (M^+), 147, 129, 107, 105, 91, 77.

Isomerisation of 26 with $(Ph_3P)_3RhCl$: acetylation to give 28 and 29

A degassed solution of alkoxide prepared from **26** (0.201 g, 1.24 mmol) and *n*-butyllithium (1.63 mol dm^{-3} hexanes, 0.761 cm^3, 1.24 mmol) in THF (6 cm^3) was treated with catalyst prepared from $(Ph_3P)_3RhCl$ (23 mg, 0.025 mmol) in THF (5 cm^3) and heated at reflux for 16 h. Quench with acetic anhydride (1.17 cm^3, 12.4 mmol) and standard work-up followed by flash chromatography (20:1–5:1 petrol–ether gradient elution) afforded *2-methyl-1-phenylbutan-1-one* **30**[55] as a clear colourless oil (34 mg, 17%): ν_{max}/cm^{-1}: 3060, 2969, 2934, 2875, 1680, 1597, 1581, 1448, 1378, 1263, 1219, 972, 702; δ_H: 0.92 (3 H, t, *J* 7.4), 1.19 (3 H, d, *J* 6.8), 1.50 (1 H, m), 1.84 (1 H, m), 3.39 (1 H, sextet, *J* 6.8), 7.46 (2 H, br t, *J* 7.0), 7.55 (1 H, br t, *J* 7.0), 7.96 (2 H, br d, *J* 7.0); *m/z*: 162 (M^+, %), 149, 134, 120, 107, 77, an inseparable mixture of (*E*) and (*Z*)-*2-methyl-1-phenylbut-1-en-1-yl acetate* **28** and **29** as a clear colourless oil (3.5:1, 84 mg, 33%): ν_{max}/cm^{-1}(mix): 2970, 2936, 1753, 1601, 1574, 1493, 1215, 1116, 1026, 700; δ_H(**28**): 1.05 (3 H, t, *J* 7.6), 1.72 (3 H, s), 2.10 (5 H, m), 7.20–7.40 (5 H, m); **29**: 1.07 (3 H, t, *J* 7.6), 1.78 (3 H, s), 2.10 (5 H, m), 7.20–7.40 (5 H, m); *m/z*: 204 (M^+), 162, 147, 129, 105, 77; HRMS: $C_{13}H_{16}O_2$ requires *M* = 204.1150, found M^+ = 204.1154 and *starting material* (7:3 acetylated: free OH, 93 mg, 36%).

Preparation of 27

To phenylmagnesium bromide (prepared as described for **15** above, *ca.* 0.83 mol dm^{-3} THF, 30 cm^3, 25 mmol) cooled to 0 °C was added dropwise a solution of (*E*)-2-methylbut-2-enal (2.3 cm^3, 24 mmol) in THF (10 cm^3) over 35 min. The reaction mixture was allowed to warm to RT over 1 h; saturated NH_4Cl (25 cm^3) was then added and the two-phase mixture stirred for a further 30 min. The layers were separated and the aqueous phase extracted with ether (2 × 25 cm^3). The combined organic phases were washed with brine (25 cm^3), dried ($MgSO_4$) and evaporated. Flash chromatography (4:1 petrol–ether elution) afforded (*E*)-*2-methyl-1-phenylbut-2-en-1-ol* **27** as a clear colourless viscous oil which crystallised on standing (3.20 g, 82%): mp 40–42 °C (Found C, 81.45%; H, 8.95%. $C_{11}H_{14}O$ requires C, 81.4%; H, 8.7%); ν_{max}/cm^{-1}: 3272, 2978, 2915, 1667, 1607, 1495, 1451, 1193, 1024, 809, 748; δ_H: 1.50 (3 H, m), 1.67 (3 H, d, *J* 6.8), 1.93 (1 H, d, *J* 3.4), 5.14 (1 H, d, *J* 2.9), 5.72 (1 H, q, *J* 6.8), 7.20–7.40 (5 H, m); *m/z*: 162 (M^+), 147, 129, 107, 105, 91, 79, 77.

Isomerisation of 27 with $[Rh(dppe)]^+$: acetylation to give 28 and 29

A degassed solution of alkoxide prepared from **27** (0.202 g, 1.24 mmol) and *n*-butyllithium (2.5 mol dm^{-3} hexanes, 0.50 cm^3, 1.25 mmol) in THF (8 cm^3) was treated with catalyst prepared from [Rh(dppe)COD]ClO_4 (43 mg, 0.06 mmol) in THF (5 cm^3) and heated at reflux for 6 h. Quench with acetic anhydride (0.60 cm^3, 6.3 mmol) and standard work-up followed by flash chromatography afforded an inseparable mixture of (*E*) and (*Z*)-*2-methyl-1-phenylbut-1-en-1-yl acetate* **28** and **29** (2.9:1, 0.177 g, 70%).

Isomerisation of 27 with $(Ph_3P)_3RhCl$: acetylation to give 28 and 29

A degassed solution of alkoxide prepared from **26** (0.202 g, 1.24 mmol) and *n*-butyllithium (1.63 mol dm^{-3} hexanes, 0.764 cm^3, 1.25 mmol) in THF (6 cm^3) was treated with catalyst prepared

from $(Ph_3P)_3RhCl$ (23 mg, 0.025 mmol) in THF (5 cm^3) and heated at reflux for 24 h. Quench with acetic anhydride (1.17 cm^3, 12.5 mmol) and standard work-up followed by flash chromatography afforded an inseparable mixture of (*E*) and (*Z*)-*2-methyl-1-phenylbut-1-en-1-yl acetate* **28** and **29** (3.0:1, 0.150 g, 59%) and *2-methyl-1-phenylbutan-1-one* **30** (34 mg, 17%).

Preparation of 31

To phenylmagnesium bromide (prepared as described for **15** above, *ca.* 1.25 mol dm^{-3} THF solution, 40 cm^3, 50 mmol) cooled to 0 °C was added dropwise a solution of freshly distilled 2-ethylprop-2-enal (4.90 cm^3, 50 mmol) over 20 min. The reaction was warmed to ambient temperature over 1 h, then saturated aqueous NH_4Cl (50 cm^3) was added and the layers were separated. The aqueous phase was extracted with ether (3 × 20 cm^3) and the combined organic phases washed with brine (20 cm^3), dried ($MgSO_4$) and evaporated. Flash chromatography (6:1 petrol–ether elution) afforded *2-ethyl-1-phenylprop-2-en-1-ol* **31** as a clear colourless oil (5.4 g, 67%): ν_{max}/cm^{-1}: 3372, 2966, 1646, 1603, 1491, 1450, 1025, 903, 700; δ_H: 1.0 (3 H, d, *J* 7.5), 1.95 (3 H, m), 4.99 (1 H, s), 5.17 (1 H, s), 5.27 (1 H, s), 7.20–7.40 (5 H, m); *m*/*z*: 162 (M^+), 147, 133, 107, 105, 79, 77; HRMS: $C_{11}H_{14}O$ requires M = 162.1044, found M^+ = 162.1054.

Isomerisation of 31 with [Rh(dppe)]$^+$: acetylation to give 28 and 29

A degassed solution of alkoxide prepared from **31** (0.196 g, 1.21 mmol) and *n*-butyllithium (2.5 mol dm^{-3} hexanes, 0.50 cm^3, 1.25 mmol) in THF (8 cm^3) was treated with catalyst prepared from [Rh(dppe)COD]ClO_4 (44 mg, 0.061 mmol) in THF (5 cm^3) and heated at reflux for 3 h. Quench with acetyl chloride (0.80 cm^3, 11.0 mmol) and standard work-up followed by flash chromatography afforded an inseparable mixture of (*E*) and (*Z*)-*2-methyl-1-phenylbut-1-en-1-yl acetate* **28** and **29** (3.7:1, 0.137 g, 56%) and *2-methyl-1-phenylbutan-1-one* **30** (34 mg, 17%).

Isomerisation of 31 with $(Ph_3P)_3RhCl$: acetylation to give 28 and 29

A degassed solution of alkoxide prepared from **31** (0.191 g, 1.18 mmol) and *n*-butyllithium (1.63 mol dm^{-3} hexanes, 0.722 cm^3, 1.18 mmol) in THF (6 cm^3) was treated with catalyst prepared from $(Ph_3P)_3RhCl$ (22 mg, 0.024 mmol) in THF (5 cm^3) and heated at reflux for 21 h. Quench with acetyl chloride (0.837 cm^3, 11.8 mmol) and standard work-up followed by flash chromatography afforded an inseparable mixture of (*E*) and (*Z*)-*2-methyl-1-phenylbut-1-en-1-yl acetate* **28** and **29** (3.5:1, 97 mg, 40%) and *2-methyl-1-phenylbutan-1-one* **30** (6 mg, 3%).

Preparation of 32

To a stirred suspension of SeO_2 (3.0 g, 27 mmol) in CH_2Cl_2 (10 cm^3) at RT was added a solution of *tert*-butyl hydroperoxide (3 mol dm^{-3} 2,2,4-trimethylpentane, 9.0 cm^3, 27 mmol). After 10 min a solution of 2-phenylpropene (2.11 g, 17.0 mmol) in CH_2Cl_2 (15 cm^3) was added and the mixture stirred at ambient temperature for 4 h. Saturated aqueous $NaHCO_3$ (25 cm^3) was added and the mixture was extracted with CH_2Cl_2 (3 × 25 cm^3). The combined organic phases were washed with water and brine, dried ($MgSO_4$) and evaporated. Flash chromatography (5:1 petrol–ether elution afforded *2-phenylprop-2-en-1-ol* **32**[56] as a clear colourless oil (1.18 g, 49%): ν_{max}/cm^{-1}: 3352, 3056, 2923, 1629, 1599, 1573, 1494, 1444, 1026, 906, 779, 708; δ_H: 2.03 (1 H, br s), 4.54 (2 H, s), 5.36 (1 H, d, *J* 0.7), 5.48 (1 H, d, *J* 0.7), 7.30–7.50 (5 H, m); *m*/*z*: 134 (M^+), 115, 105, 103, 92, 77.

Preparation of 33

n-Butyllithium (2.5 mol dm^{-3} hexanes, 0.5 cm^3, 1.25 mmol) was added dropwise to a cooled (0 °C) solution of alcohol **32** (0.165 g, 1.23 mmol) in THF (8 cm^3). The solution was heated at 60 °C for 6 h, then cooled to 0 °C and saturated aqueous NH_4Cl (5 cm^3) added. The layers were separated and the aqueous phase extracted with ether (3 × 10 cm^3). The combined organic phases were washed with brine (10 cm^3), dried ($MgSO_4$) and evaporated. Flash chromatography (neat petrol elution) afforded *2-phenylhept-1-ene* **33** as a clear colourless oil (94 mg, 44%): ν_{max}/cm^{-1}: 2954, 2927, 1624, 1598, 1570, 1491, 1459, 1027, 893, 776, 702; δ_H: 0.88 (3 H, t, *J* 7), 1.40 (6 H, m), 2.50 (2 H, t, *J* 6.6), 5.05 (1 H, d, *J* 1.5), 5.20 (1 H, d, *J* 1.5), 7.40 (5 H, m); δ_C: 14.2, 22.6, 28.1, 31.7, 35.4, 112.1, 126.2, 127.3, 128.3, 141.6, 148.9; *m*/*z*: 174 (M^+), 159, 145, 131, 118, 105, 103, 91, 77; HRMS: $C_{13}H_{18}$ requires M = 174.1409, found M^+ = 174.1410.

Isomerisation of 32 with [Rh(dppe)]$^+$: alkylation to give 34

A degassed solution of alkoxide prepared from **32** (0.164 g, 1.22 mmol) and *tert*-butyllithium (1.7 mol dm^{-3} pentanes, 0.75 cm^3, 1.27 mmol) in THF (8 cm^3) was treated with catalyst prepared from [Rh(dppe)COD]ClO_4 (18 mg, 0.025 mmol) in THF (5 cm^3) and heated at 60 °C for 3 h. Quench with allyl bromide (1.0 cm^3, 11 mmol) and standard work-up followed by flash chromatography (50:1 petrol–ether elution) afforded *2-methyl-2-phenylpent-4-enal* **34** as a clear colourless oil (0.53 g, 72%): ν_{max}/cm^{-1}: 3074, 2975, 2931, 2805, 2708, 1722, 1637, 1597, 1492, 1443, 1029, 997, 919, 761, 700; δ_H: 1.37 (3 H, s), 2.55 (1 H, dd, *J* 14.1, 7.6), 2.63 (1 H, dd, *J* 14.1, 6.9), 4.97 (2 H, m), 5.50 (1 H, ddt, 17.3, 9.9 and 7.2), 7.30 (5 H, m), 9.95 (1 H, s); *m*/*z*: 174 (M^+), 159, 156, 145, 117, 105, 91, 77; HRMS: $C_{12}H_{14}O$ requires M = 174.1045, found M^+ = 174.1050.

Isomerisation of 32 with [Rh(dppe)]$^+$: alkylation to give 35

A degassed solution of alkoxide prepared from **32** (0.164 g, 1.22 mmol) and *tert*-butyllithium (1.7 mol dm^{-3} pentanes, 0.75 cm^3, 1.27 mmol) in THF (8 cm^3) was treated with catalyst prepared from [Rh(dppe)COD]ClO_4 (18 mg, 0.025 mmol) in THF (5 cm^3) and heated at 60 °C for 3 h. Quench with benzyl bromide (0.75 cm^3, 6 mmol) and standard work-up followed by flash chromatography (40:1 petrol–ether elution) afforded *2-methyl-2,3-diphenylpropanal* **35** as a clear colourless oil (0.202 g, 74%): ν_{max}/cm^{-1}: 3026, 2930, 2806, 2708, 1718, 1598, 1492, 1450, 1370, 1030, 762, 700; δ_H: 1.38 (3 H, s), 3.17 (1 H, d, *J* 13.6), 3.24 (1 H, d, *J* 13.6), 6.90–7.20 (10 H, m), 9.64 (1 H, s); *m*/*z*: 224 (M^+), 206, 195, 133, 117, 105, 91: HRMS: $C_{16}H_{16}O$ requires M = 224.1202, found M^+ = 224.1201.

Isomerisation of 32 with [Rh(dppe)]$^+$: acetylation to give 36 and 37

A degassed solution of alkoxide prepared from **32** (0.155 g, 1.16 mmol) and *tert*-butyllithium (1.7 mol dm^{-3} pentanes, 0.68 cm^3, 1.16 mmol) in THF (8 cm^3) was treated with catalyst prepared from [Rh(dppe)COD]ClO_4 (17 mg, 0.023 mmol) in THF (5 cm^3) and heated at reflux for 30 min. Quench with acetic anhydride (0.60 cm^3, 6.3 mmol) and standard work-up followed by flash chromatography (20:1 petrol–ether elution) afforded an inseparable mixture of (*E*) and (*Z*)-*2-phenylprop-1-en-1-yl acetate* **36** and **37**[57] as a clear colourless oil (10:1, 0.159 g, 78%): ν_{max}/cm^{-1}(mix): 3085, 2924, 1757, 1656, 1600, 1496, 1446, 1370, 1285, 1221, 1121, 1069, 1028, 918, 837, 759, 697, 643; δ_H(**36**, 500 MHz): 2.12 (3 H, d, *J* 1.4), 2.23 (3 H, s), 7.28 (1 H, t, *J* 7.5), 7.35 (2 H, t, *J* 7.4), 7.40 (2 H, d, *J* 7.4), 7.54 (1 H, q, *J* 1.4); **37**: 2.04 (3 H, d, *J* 1.4), 2.13 (3 H, s), 7.20–7.45 (4 H, m), 7.48 (2 H, d, *J* 7.5); *m*/*z*: 176 (M^+), 134, 118, 105, 91, 79, 77.

Isomerisation of 32 with $(Ph_3P)_3RhCl$: acetylation to give 36 and 37

A degassed solution of alkoxide prepared from **32** (0.176 g, 1.31 mmol) and *tert*-butyllithium (1.7 mol dm^{-3} pentanes, 0.77 cm^3, 1.31 mmol) in THF (6 cm^3) was treated with catalyst prepared from $(Ph_3P)_3RhCl$ (24 mg, 0.026 mmol) in THF (5 cm^3) and heated at reflux for 40 min. Quench with acetic anhydride (1.24 cm^3, 13.1 mmol) and standard work-up followed by flash chromatography afforded an inseparable mixture of (*E*) and (*Z*)-*2-phenylprop-1-en-1-yl acetate* **36** and **37** (13:1, 0.192 g, 83%).

Isomerisation of 38 with $[Rh(dppe)]^+$: acetylation to give 39 and 40

A degassed solution of alkoxide prepared from **38** (0.167 g, 1.25 mmol) and *n*-butyllithium (2.5 mol dm^{-3} hexanes, 0.50 cm^3, 1.25 mmol) in THF (8 cm^3) was treated with catalyst prepared from [Rh(dppe)COD]ClO_4 (44 mg, 0.062 mmol) in THF (12 cm^3) and heated at reflux for 8 h. Quench with acetic anhydride (0.60 cm^3, 6.3 mmol) and standard work-up followed by flash chromatography (40:1 petrol–ether elution) afforded an inseparable mixture of (*E*) and (*Z*)-*3-phenylprop-1-en-1-yl acetate* **39** and **40** as a clear colourless oil (1.3:1, 59 mg, 27%): ν_{max}/cm^{-1}(mix): 3028, 2913, 1755, 1673, 1603, 1495, 1453, 1370, 1220, 1100, 747, 699; δ_H(**39**): 2.12 (3 H, s), 3.34 (2 H, dd, *J* 7.6, 0.7), 5.59 (1 H, dt, *J* 12.4, 7.6), 7.20–7.40 (6 H, m); **40**: 2.18 (3 H, s), 3.51 (2 H, dd, *J* 7.6, 1.0), 5.09 (1 H, td, *J* 7.6, 6.4), 7.20–7.40 (6 H, m); *m/z*: 176 (M^+), 134, 116, 105, 92, 78; HRMS: $C_{11}H_{12}O_2$ requires M = 176.0837, found M^+ = 176.0837.

Isomerisation of 41 with $[Rh(dppe)]^+$: acetylation to give 43 and 44

A degassed solution of alkoxide prepared from **41** (0.144 cm^3, 1.22 mmol) and *n*-butyllithium (2.5 mol dm^{-3} hexanes, 0.50 cm^3, 1.25 mmol) in THF (8 cm^3) was treated with catalyst prepared from [Rh(dppe)COD]ClO_4 (45 mg, 0.064 mmol) in THF (12 cm^3) and heated at reflux for 6 h. Quench with acetic anhydride (0.60 cm^3, 6.3 mmol) and standard work-up (after which the crude ethereal solution was carefully preadsorbed on to silica by evaporation below RT) was followed by flash chromatography (40:1 30/40 petrol–ether elution) to afford an inseparable mixture of (*E*) and (*Z*)-*hex-1-en-1-yl acetate* **43** and **44**[58] as a clear colourless oil (1.8:1, 75 mg, 43%): ν_{max}/cm^{-1}(mix): 2959, 2930, 1758, 1673, 1370, 1221, 1053, 937, 904; δ_H(**43**): 0.9 (3 H, br t, *J* 7.0), 1.30 (4 H, m), 2.0 (2 H, q, *J* 7.7), 2.10 (3 H, s), 5.41 (1 H, dt, *J* 12.5, 7.6), 7.06 (1 H, dt, *J* 12.5, 1.5); **44**: 0.9 (3 H, br t, *J* 7.0), 1.30 (4 H, m), 2.0 (2 H, q, *J* 7.7), 2.14 (3 H, s), 4.86 (1 H, dt, *J* 6.6, 7.4), 6.99 (1 H, dt, *J* 6.6, 1.5); *m/z*: 142 (M^+), 127, 114, 100.

Isomerisation of 42 with $[Rh(dppe)]^+$: acetylation to give 43 and 44

A degassed solution of alkoxide prepared from **42** (0.106 g, 1.23 mmol) and *n*-butyllithium (2.5 mol dm^{-3} hexanes, 0.50 cm^3, 1.25 mmol) in THF (8 cm^3) was treated with catalyst prepared from [Rh(dppe)COD]ClO_4 (46 mg, 0.064 mmol) in THF (12 cm^3) and heated at reflux for 1 h. Quench with acetic anhydride (0.60 cm^3, 6.3 mmol) and standard work-up was followed by flash chromatography to afford an inseparable mixture of (*E*) and (*Z*)-*hex-1-en-1-yl acetate* **43** and **44** (2.0:1, 71 mg, 41%).

Isomerisation of 45 with $[Rh(dppe)]^+$: acetylation to give 47 and 48

A degassed solution of alkoxide prepared from **45** (0.122 g, 1.22 mmol) and *n*-butyllithium (2.5 mol dm^{-3} hexanes, 0.50 cm^3, 1.25 mmol) in THF (8 cm^3) was treated with catalyst prepared from [Rh(dppe)COD]ClO_4 (45 mg, 0.064 mmol) in THF (12 cm^3) and heated at reflux for 1 h. Quench with acetic anhydride (0.60 cm^3, 6.3 mmol) and standard work-up (after which the crude ethereal solution was carefully preadsorbed on to silica by evaporation below RT) was followed by flash chromatography (40:1 30/40 petrol–ether elution) to afford an inseparable mixture of (*E*) and (*Z*)-*2-methylbut-1-en-1-yl acetate* **47** and **48**[59] as a clear colourless oil (3.0:1, 72 mg, 46%): ν_{max}/cm^{-1}(mix): 2969, 2939, 2878, 1753, 1685, 1451, 1370, 1309, 1225, 1117, 1078, 915, 823; δ_H(**47**): 1.02 (3 H, t, *J* 7.4), 1.67 (3 H, d, *J* 1.5), 1.99 (2 H, dq, *J* 7.4, 1.0), 2.13 (3 H, s), 6.88 (1 H, m); **48**: 1.02 (3 H, t, *J* 7.4), 1.63 (3 H, d, *J* 1.5), 2.15 (2 H, m), 2.12 (3 H, s), 6.80 (1 H, m); *m/z*: 128 (M^+), 86, 71.

Isomerisation of 46 with $[Rh(dppe)]^+$: acetylation to give 47 and 48

A degassed solution of alkoxide prepared from **46** (0.107 g, 1.24 mmol) and *n*-butyllithium (2.5 mol dm^{-3} hexanes, 0.50 cm^3, 1.25 mmol) in THF (8 cm^3) was treated with catalyst prepared from [Rh(dppe)COD]ClO_4 (34 mg, 0.048 mmol) in THF (12 cm^3) and heated at reflux for 45 min. Quench with acetic anhydride (0.60 cm^3, 6.3 mmol) and standard work-up was followed by flash chromatography to afford an inseparable mixture of (*E*) and (*Z*)-*2-methylbut-1-en-1-yl acetate* **47** and **48** (3.0:1, 95 mg, 60%).

Isomerisation of 46 with $(Ph_3P)_3RhCl$: acetylation to give 47 and 48

A degassed solution of alkoxide prepared from **46** (0.213 g, 2.47 mmol) and *n*-butyllithium (1.63 mol dm^{-3} hexanes, 1.52 cm^3, 2.47 mmol) in THF (6 cm^3) was treated with catalyst prepared from $(Ph_3P)_3RhCl$ (46 mg, 0.050 mmol) in THF (5 cm^3) and heated at reflux for 9 h. Quench with acetic anhydride (2.36 cm^3, 24.7 mmol) and standard work-up was followed by flash chromatography to afford an inseparable mixture of (*E*) and (*Z*)-*2-methylbut-1-en-1-yl acetate* **47** and **48** (3.0:1, 0.156 g, 49%).

Preparation of 52

DMSO (1.4 cm^3, 18 mmol) was added dropwise to a cooled (−78 °C) solution of oxalyl chloride (0.83 cm^3, 9.50 mmol) in CH_2Cl_2 (30 cm^3). After stirring for 5 min, a solution of alcohol **4a** (1.02 g, 7.60 mmol) in CH_2Cl_2 (10 cm^3) was added dropwise *via* a cannula and the reaction mixture stirred at −78 °C for 1 h. Triethylamine (3.80 cm^3, 27 mmol) was added, with formation of a dense white precipitate. The reaction mixture was warmed to ambient temperature and poured into water (50 cm^3). The layers were separated and the aqueous phase extracted with CH_2Cl_2 (3 × 30 cm^3). The combined organic phases were washed with brine (50 cm^3) and dried ($MgSO_4$). After preadsorption on to silica gel, purification by flash chromatography (10:1 petrol–ether elution) afforded *1-phenylprop-2-en-1-one* **52**[60] as a clear colourless oil which was used directly in the next step (0.661 g, 66%): ν_{max}/cm^{-1}: 3062, 1672, 1609, 1597, 1578, 1448, 1404, 1234, 993, 728, 688; δ_H: 5.93 (1 H, dd, *J* 10.7, 1.7), 6.43 (1 H, dd, *J* 17.1, 1.7), 7.15 (1 H, dd, *J* 17.1, 10.1), 7.50–8.20 (5 H, m).

Preparation of 53 and 54

A solution of the enone **52** (0.660 g, 5.0 mmol), in ether (10 cm^3) was added dropwise *via* a cannula to a cooled (0 °C) suspension of $LiAlD_4$ (98% atom D, 0.212 g, 5.0 mmol) in ether (10 cm^3). After warming to RT, the reaction mixture was stirred for 30 min, prior to the cautious addition of water (5 cm^3), followed by 1 mol dm^{-3} aqueous NaOH (10 cm^3). The layers were separated, the aqueous phase extracted with ether (4 × 10 cm^3) and the combined organic phases were washed with brine, dried ($MgSO_4$) and evaporated. Flash chromatography (4:1 petrol–ether elution) afforded *3-deuterio-1-phenylpropan-1-one*

54 as a clear colourless oil (>90% D, 0.10 g, 14%): ν_{max}/cm^{-1}: 3062, 2944, 1692, 1598, 1449, 1363, 1277, 1215, 949, 745, 719, 690; δ_H: 1.22 (2 H, tt *J* 7.3, 2.2), 3.0 (2 H, tt, *J* 7.3, 1.0), 7.20–7.40 (5 H, m); $\delta_D\{^1H\}$: 1.18; *m/z*: 135 (M^+), 118, 105, 77, 51; HRMS: C_9H_9OD requires *M* = 135.0794, found M^+ = 135.0789 and *1-deuterio-1-phenylprop-2-en-1-ol* **53** as a clear colourless oil (>90% D, 0.326 g, 48%): ν_{max}/cm^{-1}: 3364, 3060, 3027, 1640, 1602, 1494, 1449, 1064, 1015, 991, 926; δ_H: 1.50 (1 H, s), 5.21 (1 H, dd, *J* 10.4, 1.4), 5.36 (1 h, dd, *J* 17.2, 1.4), 6.06 (1 H, dd, *J* 17.2, 10.4), 7.20–7.40 (5 H, m); *m/z*: 135 (M^+), 134, 118. 105, 91, 80, 77; HRMS: C_9H_9OD requires *M* = 135.0794, found M^+ = 135.0791.

Preparation of 55

A cooled (−78 °C) solution of diisopropylamine (0.209 cm^3, 1.49 mmol) in THF (10 cm^3) was treated with *n*-butyllithium (1.49 mol dm^{-3} hexanes, 1.0 cm^3, 1.49 mmol) and stirred for 30 min. A solution of ketone **4f** (0.190 g, 1.42 mmol) in THF (5 cm^3) was added dropwise and the mixture stirred a further 30 min, prior to dropwise transfer over 10 min to a cooled (0 °C) solution of D_2O (3.0 cm^3, 170 mmol) in THF (7 cm^3). After 15 min ether (20 cm^3) was added, the layers were separated and the organic phase dried ($MgSO_4$). Evaporation and short-path distillation afforded *2-deuterio-1-phenylpropan-1-one* **55** as a clear colourless oil (*ca.* 60% D incorporation, 0.157 g): ν_{max}/cm^{-1}: 3063, 2978, 2939, 1966, 1910, 1818, 1688, 1598, 1583, 1450, 1333, 1267, 1181, 1076, 1002, 952, 746, 724, 691; δ_H: 1.21 (3 H, dt, *J* 7.3, 1.5), 2.98 (1 H, qt, *J* 7.3, 2.7), 7.45 (2 H, t, *J* 7.0), 7.52 (1 H, t, *J* 7.0), 7.96 (2 H, d, *J* 7.0); $\delta_D\{^1H\}$: 2.98; *m/z*: 135 (M^+), 134, 119, 105, 91, 77; HRMS: C_9H_9OD requires *M* = 135.0794, found M^+ = 135.0796.

Isomerisation of 53 with $[Rh(dppe)]^+$

A degassed solution of alkoxide prepared from **53** (85 mg, 0.63 mmol) and *n*-butyllithium (1.6 mol dm^{-3} hexanes, 0.38 cm^3, 0.63 mmol) in THF (5 cm^3) was treated with catalyst prepared from [Rh(dppe)COD]ClO_4 (44 mg, 0.062 mmol) in THF (12 cm^3) and heated at reflux for 30 min. Quench with saturated aqueous NH_4Cl (10 cm^3) and standard work-up was followed by flash chromatography (10 : 1 petrol–ether elution) to afford *3-deuterio-1-phenylpropan-1-one* **54** (50 mg, 59%) as the sole product by ^2H NMR.

Isomerisation of 53 with $(Ph_3P)_3RhCl$

A degassed solution of alkoxide prepared from **53** (32 mg, 0.24 mmol) and *n*-butyllithium (1.63 mol dm^{-3} hexanes, 0.15 cm^3, 0.24 mmol) in THF (2 cm^3) was treated with catalyst prepared from $(Ph_3P)_3RhCl$ (22 mg, 0.024 mmol) in THF (3 cm^3) and heated at reflux for 30 min. Quench with saturated aqueous NH_4Cl (2 cm^3) and standard work-up was followed by flash chromatography (10 : 1 petrol–ether elution) to afford *3-deuterio-1-phenylpropan-1-one* **54** (23 mg, 70%) as the sole product by ^2H NMR.

Isomerisation of 53 with $(Ph_3P)_3RhCl$–*n*-BuLi

A degassed solution of alkoxide was prepared from **53** (35 mg, 0.26 mmol) and *n*-butyllithium (1.63 mol dm^{-3} hexanes, 0.16 cm^3, 0.26mmol) in THF (2 cm^3). A solution of $(Ph_3P)_3RhCl$ (24 mg, 0.026 mmol) in THF (3 cm^3) was treated dropwise with *n*-butyllithium (1.63 M hexanes, 0.016 cm^3, 26 μmol) and degassed twice. This was then added to the alkoxide solution and the mixture heated at reflux for 30 min. Quench with saturated aqueous NH_4Cl (2 cm^3) and standard work-up was followed by flash chromatography (10 : 1 petrol–ether elution) to afford a mixture of *3-deuterio-1-phenylpropan-1-one* **54** and *2-deuterio-1-phenylpropan-1-one* **55** in the ratio 30 : 1 by ^2H NMR (23 mg, 66%).

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