A concise synthesis of carpanone using solid-supported reagents and scavengers

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Polymer-supported reagents have been applied to the synthesis of the natural product carpanone resulting in a clean and efficient synthesis without the requirement for conventional purification techniques. A new polymer-supported transition metal isomerisation catalyst is also reported.

Introduction

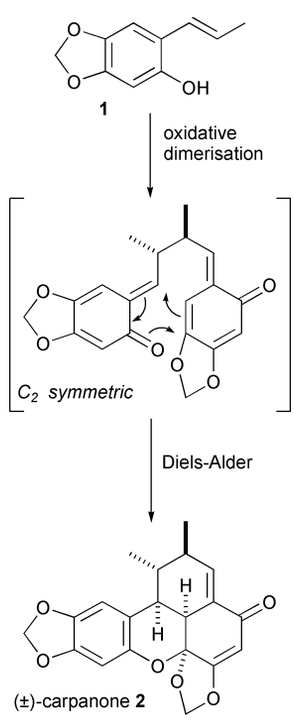
The utilisation of solid-supported reagents in chemical synthesis has been shown to markedly improve productivity in many critical aspects of the generation of new chemical entities and complex target molecules. The potential to configure the reactions in both a serial and convergent fashion offers many distinct advantages compared to solid-phase synthesis. In addition the simple removal of spent reagents through filtration enables reactions to be driven to completion through the addition of excess reagents and for lower yielding reactions to be cleaned-up using scavenger resins.

We have previously reported on the use of these concepts in the sequential multi-step synthesis of various natural products using solid-supported reagents and scavengers to effect all the individual steps.[1] As a consequence, no chromatographic purification procedures were necessary and all stages proceeded with simple and rapid optimisation. Here we report in full on the concise preparation of carpanone **2** using these methods and also describe the development of two new solid-supported reagents used in the synthesis.[2,3]

The natural product carpanone **2** was first isolated from the bark of the carpano tree from the island of Bouganville in the Pacific Ocean.[4] Carpanone is a hexacyclic molecule with five contiguous stereogenic centres, no formal element of symmetry and shows no optical activity. The elegant biomimetic synthesis of carpanone (Scheme 1) was first accomplished by Chapman and occurs through a diastereoselective oxidative dimerization of **1** using $PdCl_2$ followed by rapid *exo*-selective inverse electron demand Hetero-Diels–Alder cycloaddition.[5] More recently, Shair and co-workers have synthesised carpanone-like molecules on solid-support using the same biomimetic approach.[6]

Table 1 Claisen rearrangement of substrate **4**

Microwave at 220 °C	Conversion (%)
3 × 15 min	97
30 min continuous	78
45 min continuous	86
2 + 2 + 2 + 1 + 1 + 15 + 15 + 15 min	85



Scheme 1 Synthetic pathway to (±)-carpanone.

Results and discussion

The synthesis begins from commercially available sesamol **3**† which is readily allylated in acetonitrile containing a small quantity of dimethylformamide, using allyl bromide and a polymer-supported phosphazene base (PS–BEMP)[7] to give the aryl ether **4** in 98% yield (Scheme 2). The product **4** was then subjected to Claisen rearrangement. This was best achieved using a toluene–ionic liquid (1-ethyl-3-methyl-1*H*-imidazolium hexafluorophosphate) biphasic system and heating in a focused microwave well system[8] (3 × 15 min) at 220 °C. The reaction proceeded smoothly to give **5** in 97% conversion and the ionic liquid was removed by a simple filtration through a plug of silica. It was interesting to note that neither a 1 × 45 min burst nor many short bursts of microwave irradiation at the same temperature (220 °C) managed to give better conversions (86 and 85% respectively, Table 1). However, the reaction was found to be sensitive to concentration. A clean conversion was only obtained with a concentration of ~0.2 mmol ml^{-1} of substrate in toluene. When the concentration was increased to 0.6 mmol ml^{-1}, the reaction gave a complex mixture of products.

† The IUPAC name for sesamol is 3,4-(methylenedioxy)phenol.

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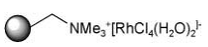
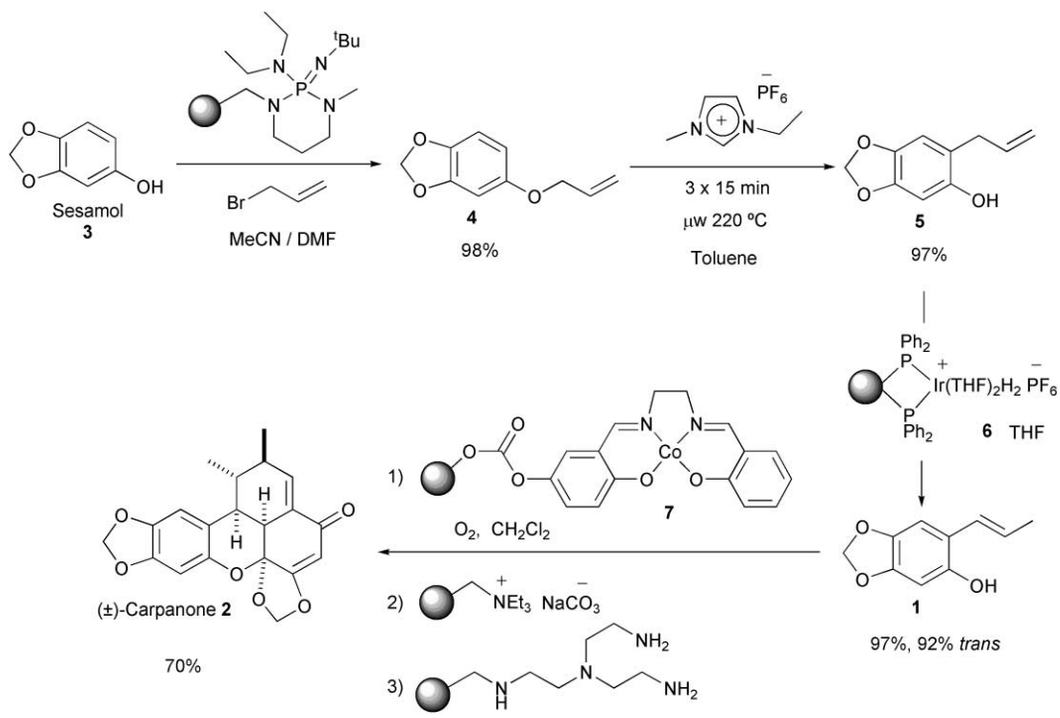
Table 2 Isomerisation of substrate **5** to **1**

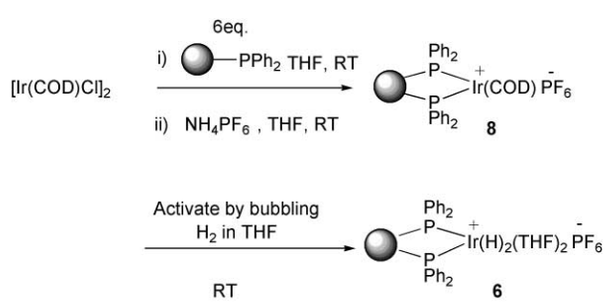
Reagents	Conditions	Time	Results
PS-Wilkinson's catalyst	Reflux in THF	24 h	No reaction
PS-Wilkinson's catalyst	Microwave in THF, 100 °C	15 min	No reaction
Wilkinson's catalyst	DABCO, ethanol (eq), reflux	2 h	No reaction
NaOEt–EtOH	Microwave 140 °C	30 min	No reaction
PS–BEMP	Microwave in MeCN 130 °C	30 min	No reaction
TFA	Reflux in CH_2Cl_2	2 h	No reaction
	Heat to 80 °C in aq. ethanol	30 min	No reaction
	Microwave at 85 °C in aq. ethanol	20 min	No reaction
$RhCl_3 \cdot nH_2O$	Ethanol, RT	2.5 h	10% conversion
KO^{t}Bu–DMSO	Microwave at 100 °C	15 min	3 : 1 mixture of *trans–cis* products
$Ir(COD)(PPh_2Me)_2PF_6$	Activated with H_2, THF, RT	1 h	85–88% isolated yield, 127 : 1 *trans–cis* ratio



Scheme 2 Synthesis of carpanone using polymer-supported reagents and scavengers.

The isomerisation of **5** to **1** proved to be more difficult than initially anticipated. Polystyrene-supported $RhCl_3$-quarternary ammonium ion pair catalyst,[9] Wilkinson's catalyst, polymer-supported Wilkinson's catalyst,[10] PS–BEMP and TFA all failed to effect the isomerisation. $RhCl_3 \cdot nH_2O$ gave a maximum of 10% conversion while the KO^{t}Bu–DMSO system gave a low 3 : 1 *trans–cis* selectivity (Table 2). Felkin's iridium catalyst,[11] which is formed by bubbling hydrogen through a THF suspension of $[Ir(COD)(PPh_2Me)_2]PF_6$, was discovered to be an excellent reagent for this selective transformation. In addition the conditions are mild compared to traditional base induced isomerisations and the *trans–cis* ratio was an excellent 127 : 1 for the isomerisation of **5**. We therefore developed a polymer-supported version of the Felkin iridium catalyst.

Scheme 3 shows the synthesis and proposed structure of the polymer-supported iridium catalyst, **6**.[6] A 6 : 1 molar ratio of polymer-supported triphenylphosphine[12] and $[(COD)IrCl]_2$ was agitated in THF at room temperature for 24 h. Addition of ammonium hexafluorophosphate as a solution in THF and agitation for a further 24 h produced a red polymer with the proposed structure **8**.[13] Elemental analysis indicated 12.5% iridium, corresponding to a theoretical loading of 0.65 mmol g^{-1}. Hydrogen activation of catalyst **8** produces a chrome yellow polymer of suggested structure **6** which isomerised substrate **5** at room temperature to give an 11 : 1 *trans–cis* ratio of **1**. Catalyst **8** was also prepared using a 2 : 1 molar ratio of

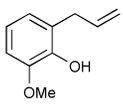
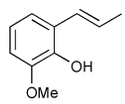
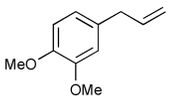
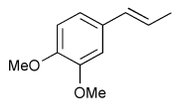
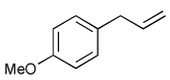
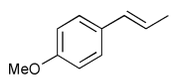
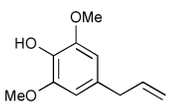
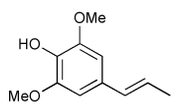
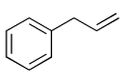
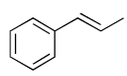
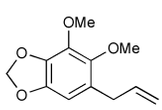
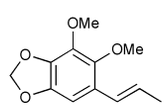
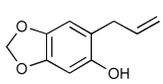
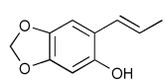
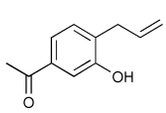
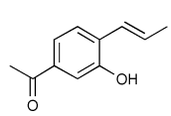
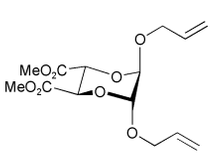
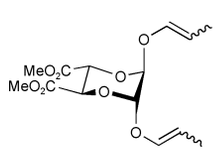
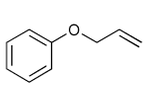
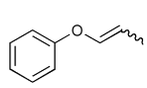
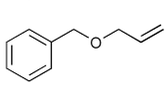
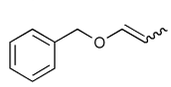
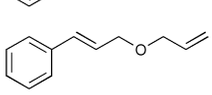
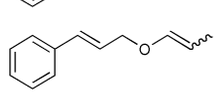
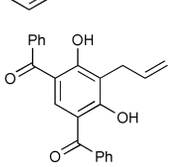
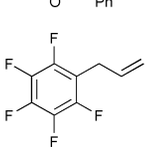
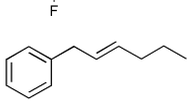


Scheme 3 Preparation of catalyst **6**.

polymer-supported triphenylphosphine and $[(COD)IrCl]_2$. This batch was found to be less active despite having a higher iridium loading of 1 mmol g^{-1}.

The catalyst **6** was also tested on various aryl allylic derivatives and aryl ethers (Table 3). In general the isomerisation of electron-rich aromatic compounds by catalyst **6** results in products with predominantly the *trans* alkene geometry (entries 1–7). However, electron-poor derivatives (entries 13 and 14) are substantially less prone to rearrangement. Isomerisations of aryl ethers (entries 9–12) also proceeded smoothly, though these were not *trans* selective. However, catalyst **6** may still find an application in allyl ether deprotections where *trans* selectivity is not relevant.[14]

Table 3 Isomerisations using reagent **6**

Entry	Substrate	Product[a]	*Trans–cis* ratio[b]
1			>95% *trans*
2			>95% *trans*
3			>97% *trans*
4			>96% *trans*
5			*trans* only
6			>98% *trans*
7			~92% *trans*
8			~92% *trans*
9			Mixture of *trans* and *cis* products
10			1 : 1
11			1 : 1
12			1 : 1
13		Recovered starting material with <4% isomerised product	—
14		50% conversion	—
15		Recovered starting material	—

[a] Recovered yields are essentially quantitative although ^{1}H-NMR analysis indicate up to 4% of the hydrogenated alkene product present in small scale reactions. [b] Determined by ^{1}H-NMR.

In another experiment we determined whether the isomerisations were solely due to **6** or to a species that may have leached into the solution from the support during the course of the reaction. To test this, the reaction with dillapiole ‡ (entry 6) was stopped after 15 minutes of reaction by filtration. Analysis showed a 60% conversion to the desired product. The filtrate was then allowed to stir for a further 12 h. No further

‡ The IUPAC name for dillapiole is 1-allyl-2,3-dimethoxy-4,5-(methylenedioxy)benzene.

Table 4 Oxidative coupling of **1** to form carpanone, **2**

Entry	Oxidising agent	eq.	TLC monitoring	Yield[a]	Conditions	Solvent
1	$PhI(OAc)_2$	1.1		45%	RT	TFE[d]
2	$PhI(OAc)_2$	1.1		52%	−40 °C to RT	CH_2Cl_2
3	$PhI(OAc)_2$	0.5		26%	−40 °C O/N[c]	CH_2Cl_2
4	PS–$PhI(OAc)_2$(soluble)	~2	Mixture of products	low	RT	CH_2Cl_2
5	PS–$PhI(OAc)_2$(soluble)	~2	Mixture of products	~7%	−40 °C to RT	CH_2Cl_2
6	PS–$PhI(OAc)_2$(soluble)	~1.1	Mixture of products	17%	−40 °C to RT	CH_2Cl_2
7	PS–$PhI(OAc)_2$(insoluble)	~1.3	Complex mixture of products	low	−28 °C to −20 °C O/N	TFE and CH_2Cl_2
8	$PhI(OCOCF_3)$	~1.0	Complex mixture of products		−40 °C O/N	CH_2Cl_2
9	PS–$PhI(OCOCF_3)$	~1.0	Complex mixture of products	low	RT	CH_2Cl_2
10	TPAP, O_2	Catalytic	Complex mixture of products		RT	CH_2Cl_2
11	Co(salen), O_2	Catalytic	**2** is main product	78%	RT	CH_2Cl_2
12	Co(salen), chiral, O_2	Catalytic	**2** is main product	85%[b]	RT	CH_2Cl_2

[a] Together with carpanone, a small amount of another product, which is likely to be a configurational isomer, was formed. This has been reported previously.[16] [b] $[\alpha]_D = 0$. [c] O/N = overnight reaction. [d] TFE = 2,2,2-trifluoroethanol.

reaction was observed, suggesting that the active catalyst remains associated with the support during the course of the reaction.

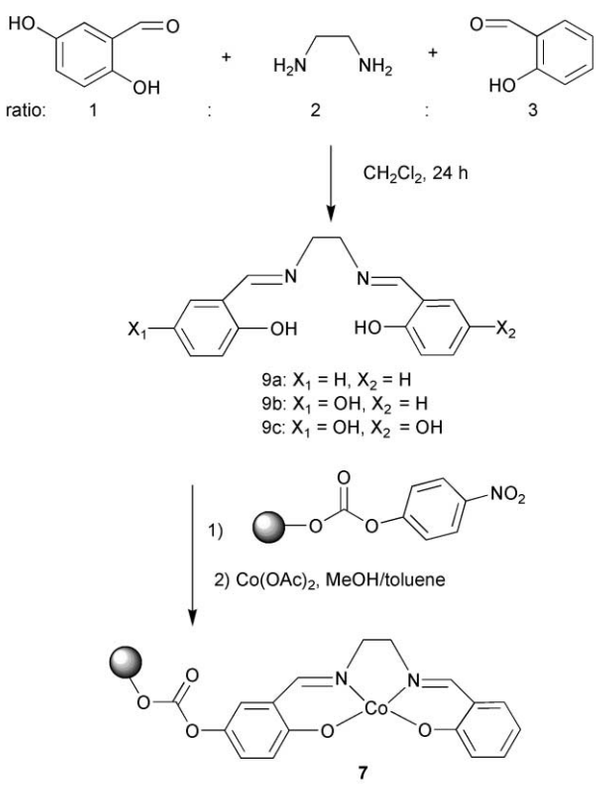
In an attempt to show that **6** can be recycled, we carried out a sequence of reactions on allylbenzene. The recovered polymer from the first conversion was reactivated with hydrogen and reused for a further three runs.[15] The conversion dropped from quantitative to 95%, 91% and 75% in each subsequent run, suggesting some degradation of the catalyst (the *cis–trans* ratio remained constant). A recycling test was also carried out on dillapiole (entry 6) since this substrate required a shorter reaction time of 1.5 h for each run. The sequence proceeded from quantitative to 91% to 70%. The reaction did however proceed to completion on the fourth run after it was allowed to react overnight.

As a further investigation, the catalytic potential of **6** was tested using the dimethoxy substrate (entry 2). Employing catalyst **6** (2 mol%) for the isomerisation of 800 mg of the substrate resulted in 77% conversion after 24 h. Subsequent monitoring over an additional 3 day period showed a slow but steady progression to 84% conversion (day 2; 80%, day 3; 82%). The addition of a further batch of freshly prepared catalyst (1 mol%) allowed the reaction to proceed to completion over a further 48 h period.

Felkin's catalyst was reported to be selective towards primary allyl ethers and so far only primary allyl ethers and aryls have been tested. To test the selectivity of catalyst **6**, the non-primary allyl aryl (entry 15) was subjected to isomerising conditions with **6**. No isomerisation was observed, suggesting that catalyst **6** is also selective towards primary allyls.

Finally, the coupling of **1** to form carpanone **2** was carried out using hypervalent iodine reagents (Table 4). The transformation was successful using solution phase $PhI(OAc)_2$, yielding carpanone in 52% after chromatographic purification (entry 2). The reaction proceeded within minutes at room temperature but was found to give much cleaner transformations at lower temperatures. Encouraged by this result, the insoluble[16a] and soluble[16b] polymer-supported $PhI(OAc)_2$ were used to attempt this coupling under various conditions (entries 4–9). Although these reactions did form carpanone, the isolated yields were generally low and the reactions were not clean, and therefore were not acceptable.

In 1981, Matsumoto and Kuroda successfully synthesised carpanone in excellent yield (94%) by the oxidation of **1** with molecular oxygen in the presence of Co(salen).[17] A polymer-supported version of Co(salen) was therefore synthesised using a slight modification of Anis and Jacobsen's method for making polymer-supported chiral Co(salen) complexes for hydrolytic kinetic resolution of terminal epoxides (Scheme 4).[18] The synthesis starts from readily available salicylaldehyde, gentisaldehyde and diethylamine. The reaction

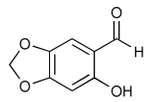


Scheme 4 Preparation of the Co(salen) catalyst **7**.

of these three starting materials produced a mixture of ligands. The hydroxy-terminated ligands were selectively captured by addition of hydroxymethylpolystyrene, derivatised as the corresponding 4-nitrophenyl carbonate, while the non-hydroxy-terminated ligand was washed away from the polymer-bound product. Finally, cobalt complexation was achieved by the addition of $Co(OAc)_2{\cdot}4H_2O$. Elemental analysis indicated 2.2% Co which corresponds to a theoretical loading of 0.37 mmol g^{-1}.

Reagent **7** was used in catalytic amounts to transform **1** to carpanone **2** successfully by agitating a suspension of **7** and **1** in CH_2Cl_2 at room temperature under an atmosphere of O_2 (Scheme 2). However, a minor side product, the aldehyde **10** formed in this reaction. This side product was scavenged from the reaction mixture using polymer-supported trisamine scavenger. This procedure successfully converted **1** to carpanone in 80% yield and 98% HPLC purity without any aqueous work up or chromatographic purification. When a crude mixture of 11 : 1 *trans–cis* **1** and 4,5-methylenedioxy-2-propenylphenol was used, a further step was necessary to

remove the unreacted phenol. This was achieved using polymer-supported Na_2CO_3 to give carpanone in 70% yield.



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In summary, the work reported above illustrates further the power of using immobilised systems in a multi-step fashion to produce complex products without the need for conventional work-up methods.

Experimental

Unless otherwise specified, all reactions involving polymers were carried out on a laboratory shaker IKA 125 at 250 rpm. All moisture sensitive reactions were carried out under an argon atmosphere using oven-dried glassware. All commercially available resins were washed and dried *in vacuo* prior to use. Diethyl ether (Et_2O) and tetrahydrofuran (THF) were distilled from sodium benzophenone ketyl; acetonitrile, benzene, dichloromethane, methanol and toluene from calcium hydride. All other solvents and reagents were used as supplied unless otherwise specified. Analytical TLC was performed using precoated glass-backed plates (Merck Kieselgel 60 F254) and visualised by ultra-violet radiation, acidic ammonium molybdate(IV) or potassium permanganate. Infra-red spectra were obtained on Perkin–Elmer Spectrum One FT-IR spectrometer. Single-bead infra-red spectra were recorded on a Perkin–Elmer Autoimage system with a spectrum 1000 IR bench. Samples for single bead IR spectroscopy were flattened using a Specac diamond compression cell. ^{1}H-NMR spectra were recorded in $CDCl_3$ on a Bruker Advance DPX-400 spectrometer at 400 MHz with residual chloroform as the internal reference (δ_H = 7.26 ppm) and J values are given in Hz. ^{13}C-NMR spectra were recorded in $CDCl_3$ on the same spectrometer at 100 MHz with the central peak of chloroform as the internal reference (δ_C = 77.0 ppm). DEPT 135 and two-dimensional (COSY, HMQC and HMBC) NMR spectroscopy were used, where appropriate, to aid in the assignment of signals in the ^{1}H-NMR and ^{13}C-NMR spectra. Mass spectra were obtained using electrospray techniques on a Bruker BIOAPEX 4.7 T FTICR spectrometer at the Department of Chemistry, University of Cambridge. Microanalyses were performed by Medac Ltd., Surrey. X-Ray crystal structures were determined at the Department of Chemistry, Lensfield Road, Cambridge. The microwave used was a prototype *Smith Synthesizer* supplied by Personal Chemistry, Sweden.

Preparation of 5-allyloxybenzo[1,3]dioxole 4

A solution of sesamol (1 g, 7.24 mmol) in acetonitrile–DMF 9 : 1 (40 ml) was added to PS–BEMP (Fluka, 2.2 mmol base g^{-1}, 9.87 g, 21.7 mmol). Allyl bromide (0.876 g, 7.24 mmol) was added and the resulting mixture agitated under an argon atmosphere at RT for 3 h. The polymer was removed by filtration and the resulting filtrate was filtered through a plug of silica and concentrated *in vacuo* to yield **4** as a colourless oil (1.27 g, 7.1 mmol, 98%); ν_{max}/cm^{-1} 1630 (C=C), 1501 (Ar C=C), 1242 & 1038 (C–O); δ_H(400 MHz, $CDCl_3$) 6.69 (1H, d, J 8.42, H-3), 6.51 (1H, d, J 2.56, H-6), 6.36 (1H, dd, J 8.42, 2.56, H-2), 6.00 (1H, m, CH_2CHCHH'), 5.91 (2H, s, OCH_2O), 5.39 (1H, dd, J 17.2, 1.83, $CH_2CHCH'H$), 5.27 (1H, dd, J 10.25, 1.83, $CH_2CHCH'H$), 4.47 (2H, d, J 5.49, OCH_2CH); δ_C($CDCl_3$) 154.15, 148.27, 141.76, 133.50+, 117.45−, 107.89+, 106.01+, 101.08−, 98.31+, 69.73−.

Preparation of 6-allylbenzo[1,3]dioxol-5-ol (5) [19]

A mixture of **4** (200 mg, 1.12 mmol), 1-ethyl-3-methyl-1*H*-imidazolium hexafluorophosphate (280 mg) and toluene (3 ml) was placed in a sealed tube heated with stirring at 220 °C for 3 × 15 min using microwave radiation. The mixture was cooled to RT in the microwave using a stream of pressurised (4 bar) nitrogen before filtration through a pad of silica using Et_2O as the eluent. The filtrate was concentrated *in vacuo* to yield **5** as a yellow solid (97% conversion); ν_{max}/cm^{-1} 3235 (OH), 1636 (C=C), 1504 (Ar C=C), 1205 & 1054 (C–O); δ_H(400 MHz, $CDCl_3$) 6.58 (1H, s, H-2), 6.43 (1H, s, H-5), 5.96 (1H, m, CH_2CHCHH'), 5.88 (2H, s, OCH_2O), 5.16 (1H, m, CH_2CHCHH'), 5.13 (1H, m, CH_2CHCHH'), 4.68 (1H, s, OH), 3.35 (2H, dt, J 6.22, 1.46, CH_2CHCHH'); δ_C($CDCl_3$) 149.05, 147.16, 141.91, 136.81+, 117.20, 116.77−, 109.49+, 101.38−, 99.08+, 35.43−.

Polymer-supported iridium isomerisation catalyst (8)

Triphenylphosphine on polymer support (Fluka, 3 mmol g^{-1}, 1.49 g, 4.47 mmol) was added to a suspension of chloro-(cycloocta-1,5-diene)iridium(I)dimer (500 mg, 0.744 mmol) in THF (10 ml). The resulting suspension was agitated under an atmosphere of argon at RT for 24 h. The polymer turned dark red–brown. A solution of ammonium hexafluorophosphate (970 mg, 5.95 mmol) in THF (14 ml) was then added and the resulting suspension was agitated under an atmosphere of argon at RT for 24 h. The resulting red–brown polymer was washed sequentially with MeOH and CH_2Cl_2 and dried *in vacuo*. Elemental analysis indicated 12.5% iridium was present, corresponding to a theoretical loading of 0.65 mmol g^{-1}.

Preparation of *trans*-6-propenylbenzo[1,3]dioxol-5-ol (1) [2]

Solution phase. An oven dried Schlenk flask was charged with a suspension of $[Ir(COD)(PPh_2Me)_2]PF_6$ (138 mg, 0.16 mmol) in THF (10 ml). Hydrogen gas was bubbled through the solution until the red catalyst dissolved completely to give a pale yellow catalyst solution of $[Ir(THF)_2H_2(PPh_2Me)_2]PF_6$. The flask was evacuated and filled with argon 3 times. A solution of **5** (0.97 g, 5.4 mmol) in THF (10 ml) was cannulated into the catalyst solution and the resulting mixture was stirred under an atmosphere of argon for 1 h. The reaction was quenched with a buffer solution (pH 7), the organic layer extracted with Et_2O, dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (SiO_2, 3 : 2 petroleum ether–diethyl ether) to give **1** (0.82 g, 85%) as a pale yellow solid; ν_{max}/cm^{-1} 3324 (OH), 1635 (C=C), 1508 (Ar C=C), 1245 & 1032 (C–O); δ_H(400 MHz, $CDCl_3$) 6.76 (1H, s, H-2), 6.48 (1H, dd, J 15.73, 1.83, $CHCHCH_3$), 6.39 (1H, s, H-5), 6.02 (1H, dq, J 15.73, 6.59, H-8), 5.88 (2H, s, OCH_2O), 4.90 (1H, s, OH), 1.881 (3H, dd, J 6.59, 1.83, CH_3); δ_C($CDCl_3$) 147.23, 147.00, 128.10, 126.39+, 124.90+, 117.43, 105.88+, 101.01−, 98.19+, 18.70+.

Using polymer-supported reagent 8. An oven-dried flask was charged with catalyst **8** (150 mg) and THF (3 ml). Hydrogen gas was bubbled through the resulting suspension until the polymer turned from red to chrome yellow. The suspension was flushed with argon before a solution of **5** (35 mg, 0.20 mmol) in THF (1.5 ml) was cannulated into it. The resulting suspension was agitated under an atmosphere of argon at RT for 24 h. The polymer was removed *via* filtration and washed sequentially with Et_2O and CH_2Cl_2. The filtrate was concentrated *in vacuo* and filtered through a plug of silica to give **1** with a *trans–cis* ratio of 11 : 1, and a small amount (<3%) of the hydrogenated product, 4,5-methylenedioxy-2-propenylphenol. Mass recovery was essentially quantitative.

Polystyrene-bound 4-nitrophenyl carbonate [18]

Hydroxymethyl polystyrene (Advanced Chemtech, 1% cross-linked, 1 mmol g^{-1}, 1.0 g), 4-nitrophenyl chloroformate (0.81 g, 4 mmol) and DMAP (0.12 g, 1 mmol) were combined, CH_2Cl_2 (14 ml) was added, and the resulting suspension agitated at RT for 1.5 h. Filtration and rinsing with anhydrous CH_2Cl_2

followed by drying *in vacuo* yielded white beads; ν_{max} (single bead)/cm^{-1} 1768 (C=O), 1527 (C–NO_2).

Dissymmetric salen ligand (9a, 9b, 9c)

Ethylenediamine (0.39 g, 6.4 mmol) was added to a solution of salicylaldehyde (1.17 g, 9.6 mmol) and 2,5-dihydroxybenzaldehyde (0.44 g, 3.2 mmol) in CH_2Cl_2 (50 ml). The reaction mixture was stirred under an atmosphere of argon at RT for 24 h, then concentrated *in vacuo* to yield a yellow solid. This product was used without further purification in the synthesis of **7** by resin-capture. The expected statistical yield of **9b** in this step is 2.4 mmol assuming equal reactivity of the two aldehydes, based on work by Jacobsen and co-workers;[18] ν_{max}/cm^{-1} 3284 (OH), 1633 (C=N).

Polystyrene-bound salen ligand

Dissymmetric salen ligand **9** (0.225 g, 0.3 mmol), DMAP (25 mg, 0.2 mmol) and diisopropyl ethylamine (DIPEA) (50 mg, 0.4 mmol) was added to a suspension of polystyrene-bound 4-nitrophenyl carbonate (0.250 g, ~0.2 mmol) in anhydrous DMF (5 ml). The resulting orange–yellow suspension was agitated at RT for 3 h, then filtered and rinsed sequentially with DMF, CH_2Cl_2, MeOH, CH_2Cl_2 and dried *in vacuo* to yield the product as yellow beads; ν_{max} (single bead)/cm^{-1} 1763 (C=O), 1635 (C=N). The absorbance at 1527 (C–NO_2) has disappeared completely.

Polystyrene-bound Co(salen) complex (7)

A solution of $Co(OAc)_2 \cdot 4H_2O$ (99 mg, 0.4 mmol) in 1 : 1 MeOH–toluene (4 ml) was added to the polystyrene-bound salen ligand (0.25 g) with agitation at RT. After 2 h, the beads were filtered, rinsed sequentially with MeOH and CH_2Cl_2 and dried *in vacuo* to yield dark brown beads; ν_{max} (single bead)/cm^{-1} 1763 (C=O), 1635 (C=N). Elemental analysis indicated 2.2% Co corresponding to a loading of 0.37 mmol g^{-1}.

Preparation of carpanone (2)[1,2]

Polystyrene-bound Co(salen) **7** (49 mg) was added to a solution of 6-propenylbenzo[1,3]dioxol-5-ol **1** (34 mg, 0.19 mmol) in CH_2Cl_2 (2.5 ml). The resulting suspension was agitated under an atmosphere of oxygen at RT for 3 h. The polymer was removed by filtration and washed sequentially with CH_2Cl_2 and Et_2O. The filtrate was concentrated *in vacuo* and the resulting residue was dissolved in CH_2Cl_2 (2.5 ml). Polymer-supported trisamine (90 mg) was added and the resulting suspension agitated under an atmosphere of argon at RT for 2 h. The polymer was removed by filtration and the filtrate was filtered through a plug of silica with Et_2O as eluent. The solvent was evaporated *in vacuo* to yield carpanone (27 mg, 80%, HPLC purity, 98.10%) as a white solid. Recrystallisation from carbon tetrachloride gave white crystals; mp 185 °C [lit.[2] mp 185 °C]; δ_H(400 MHz, $CDCl_3$) 7.02 (1H, ddd, *J* 2.3, 0.9, 5.0, H-7′), 6.80 (1H, s, H-6), 6.33 (1H, s, H-3), 5.90 (1H, d, *J* 1.5, OC_aHHO), 5.87 (1H, d, *J* 1.5, OC_aHHO), 5.69 (1H, s, H-3′), 5.67 (1H, s, OC_bHHO), 5.63 (1H, s, OC_bHHO), 3.28 (1H, dd, *J* 7.4, 2.1, H-7), 3.17 (1H, ddd, *J* 7.4, 2.3, 2.3, H-6′), 2.52 (1H, m, H-8), 2.22 (1H, m, H-8′), 1.14 (3H, d, *J* 7.2, H-9), 0.71 (3H, d, *J* 7.6, H-9′); Found (ESI): $[M + Na]^+$ 377.1001, $C_{20}H_{18}O_6Na$ requires 377.1001. Data are consistent with those reported previously.[1,2]

Crystal data§: $C_{20}H_{18}O_6$, M = 354.34, monoclinic, a = 8.3846 (4), b = 27.9562 (17), c = 7.1987(4), β = 107.629(3)°, U = 1608.14(15) Å^3, T = 180(2) K, space group $P2_1$, Z = 4, μ = 0,109 mm^{-1}, 8235 reflections collected, 2752 independent reflections (R_{int} = 0.0463). The final $wR(F^2)$ was 0.0873.[5]

§ CCDC reference number 187437. See http://www.rsc.org/suppdata/p1/b2/b203388g for crystallographic files in .cif or other electronic format.

When using a crude mixture of 11 : 1 *trans–cis* **1** and 4,5-methylenedioxy-2-propenylphenol, a further step was required to scavenge out the phenolic impurities: polymer-supported carbonate (Fluka, 3.5 mmol g^{-1}, 40 mg) and CH_2Cl_2 (2 ml) were added to the crude product and the resulting suspension was agitated at RT for 3 h. The polymer was removed by filtration and filtrate was concentrated *in vacuo* to give carpanone (24 mg, 70%) as a white solid.

General procedure for isomerisation reactions using reagent 8

An oven-dried flask was charged with catalyst **8** (150 mg) and THF (2.5 ml). Hydrogen gas was bubbled through the resulting suspension until the polymer turned from red to chrome yellow. The suspension was flushed with argon before a solution of the aryl allylic derivative or allyl ether (0.25 mmol) in THF (2.5 ml) was cannulated into it. The resulting suspension was agitated under an atmosphere of argon at RT for 24 h. The polymer was removed *via* filtration and washed sequentially with THF and CH_2Cl_2. The filtrate was concentrated *in vacuo*. Crude mass recovery was essentially quantitative and ^{1}H NMR spectroscopy was used to determine the *trans–cis* ratio. In these small scale reactions, ^{1}H NMR analysis also indicates up to 4% hydrogenated alkene product.

Preparation of 2-methoxy-6-(*E*)-prop-2-enylphenol.[20] Following the procedure above, *o*-eugenol¶ (41 mg, 0.25 mmol) was isomerised by reagent **8** to give the title compound as a yellow solid with a 19 : 1 *trans–cis* selectivity; ν_{max}/cm^{-1} 3416 (OH), 1656 (C=C), 1612, 1586, 1475 (Ar C=C), 1270, 1064 (C–O–C), 973 (*trans* HC=CH); δ_H(400 MHz, $CDCl_3$) 6.98 (1H, d, *J* 7.68, Ar–H_3), 6.85–6.70 (2H, m, Ar–H), 6.68 (1H, dq, *J* 17.56, 1.83, C*H*=CHCH_3), 6.29 (1H, dq, *J* 17.56, 6.59, CH=C*H*CH_3), 5.82 (1H, s, O*H*), 3.87 (3H, s, OCH_3), 1.90 (3H, dd, *J* 6.59, 1.83, CH=CHCH_3); δ_C($CDCl_3$) 146.63, 142.57, 126.87, 125.12, 124.34, 119.37, 118.85, 108.71, 56.06, 18.87.

Preparation of 1,2-dimethoxy-4-(*E*)-prop-2-enylbenzene.[21] Following the procedure above, 4-allyl-1,2-dimethoxybenzene (45 mg, 0.25 mmol) was isomerised by reagent **8** to give the title compound as a colourless liquid with a 19 : 1 *trans–cis* selectivity; ν_{max}/cm^{-1} 1603, 1583, 1512 (Ar C=C), 1230, 1026 (C–O–C), 962 (*trans* HC=CH); δ_H(400 MHz, $CDCl_3$) 6.69–6.83 (3H, m, Ar–H), 6.26 (1H, dq, *J* 15.73, 1.83, C*H*=CHCH_3), 6.02 (1H, dq, *J* 15.73, 6.59, CH=C*H*CH_3), 3.81 (3H, s, OCH_3), 3.78 (3H, s, OCH_3), 1.79 (3H, dd, *J* 6.59, 1.83, CH=CHCH_3); δ_C($CDCl_3$) 148.97, 148.16, 131.15, 130.58, 123.72, 118.62, 111.22, 108.52, 55.87, 55.73, 18.28; Found (ESI): $[M + Na]^+$ 201.0892, $C_{11}H_{14}O_2Na$ requires 201.0891.

Preparation of 1-methoxy-4-(*E*)-prop-2-enylbenzene.[22] Following the procedure above, 4-allylanisole (37 mg, 0.25 mmol) was isomerised by reagent **8** to give the title compound as a colourless liquid with a 97 : 3 *trans–cis* selectivity; δ_H(400 MHz, $CDCl_3$) 7.27 (2H, d, *J* 8.78, Ar–H), 6.84 (2H, d, *J* 8.78, Ar–H), 6.36 (1H, dq, *J* 15.72, 1.83, C*H*=CHCH_3), 6.10 (1H, dq, *J* 15.73, 6.59, CH=C*H*CH_3), 3.80 (3H, s, OCH_3), 1.87 (3H, dd, *J* 6.59, 1.83, CH=CHCH_3); δ_C($CDCl_3$) 158.58−, 130.82−, 130.34+, 126.85+, 123.44+, 113.89+, 55.24+, 18.35+; Found (ESI): $[M]^+$ 148.08942, $C_{10}H_{12}O_1$ requires 148.08878.

Preparation of 2,6-dimethoxy-4-(*E*)-prop-2-enylphenol.[23] Following the procedure above, 4-allyl-2,6-dimethoxyphenol (49 mg, 0.25 mmol) was isomerised by reagent **8** to give the title compound as a yellow liquid with a 24 : 1 *trans–cis* selectivity; ν_{max}/cm^{-1} 3470 (OH), 1653 (C=C), 1603, 1516 (Ar C=C), 961 (*trans* HC=CH); δ_H(400 MHz, $CDCl_3$) 6.55 (2H, s, Ar–H), 6.29

¶ The IUPAC name for *o*-eugenol is 2-allyl-6-methoxyphenol.

(1H, dq, *J* 15.73, 1.83, C*H*=CHCH$_3$), 6.07 (1H, dq, *J* 15.73, 6.59, CH=C*H*CH$_3$), 5.46 (1H, s, O*H*), 3.87 (6H, s, OCH$_3$), 1.85 (3H, dd, *J* 6.59, 1.83, CH=CHC*H*$_3$); δ_C(CDCl$_3$) 147.07, 134.00, 130.92, 129.57, 123.76, 102.67, 56.19, 18.22.

Preparation of (*E*)-prop-2-enylbenzene.[24] Following the procedure above, allylbenzene (30 mg, 0.25 mmol) was isomerised by reagent **8** to give the title compound as a colourless liquid; ν_{max}/cm^{-1} 1598, 1578, 1496 (Ar C=C), 960 (*trans* HC=CH); δ_H(400 MHz, CDCl$_3$) 7.47–7.20 (5H, m, Ar–H), 6.46 (1H, dq, *J* 15.73, 1.46, C*H*=CHCH$_3$), 6.28 (1H, dq, *J* 15.73, 6.59, CH=C*H*CH$_3$), 1.93 (3H, dd, *J* 6.59, 1.46, CH=CHC*H*$_3$); δ_C(CDCl$_3$) 137.94, 131.05, 128.44, 126.70, 125.81, 125.62, 18.44.

Preparation of 4,5-dimethoxy-(*E*)-prop-2-enylbenzo[1,3]-dioxole.[25] Following the procedure above, dillapiole (56 mg, 0.25 mmol) was isomerised by reagent **8** to give the title compound as a colourless oil with a 39 : 1 *trans–cis* selectivity; δ_H(400 MHz, CDCl$_3$) 6.61 (1H, s Ar–H), 6.59 (1H, dq, *J* 15.73, 1.83, C*H*=CHCH$_3$), 6.05 (1H, dq, *J* 15.73, 6.59, CH=C*H*CH$_3$), 5.85 (2H, s, OC*H*$_2$O), 4.00 (3H, s, OC*H*$_3$), 3.74 (3H, s, OC*H*$_3$), 1.86 (3H, dd, *J* 6.59, 1.83, CH=CHC*H*$_3$); δ_C(CDCl$_3$) 145.04, 143.92, 137.53, 136.49, 125.17, 124.91, 124.84, 101.14, 98.34, 61,43, 60.02, 18.66; Found (ESI): [MH]$^+$ 223.09750, $C_{12}H_{15}O_4$ requires 223.0970.

Preparation of prop-2-enyloxybenzene.[26] Following the procedure above, allyl phenyl ether (20 mg, 0.15 mmol) was isomerised by reagent **8** to give the title compound as a colourless liquid as a mixture of 1 : 1 *trans–cis* isomers; δ_H(400 MHz, CDCl$_3$) 7.22 (4H, m, Ar–H), 6.92 (6H, m, Ar–H), 6.34 (1H, dq, *J* 12.08, 1.46, OC*H*=CHCH$_3$-*trans*), 6.30 (1H, dq, *J* 6.22, 1.83, OC*H*=CHCH$_3$-*cis*), 5.29 (1H, dq, *J* 12.08, 6.95, CH=C*H*CH$_3$-*trans*), 4.79 (1H, dq, *J* 6.22, 6.95, OCH=C*H*CH$_3$-*cis*), 1.64 (3H, dd, *J* 6.95, 1.83, C*H*$_3$-*cis*), 1.59 (3H, dd, *J* 6.95, 1.46, C*H*$_3$-*trans*).

Prop-2-enyloxymethylbenzene.[27] Following the procedure above, allyl benzyl ether (30 mg, 0.20 mmol) was isomerised by reagent **8** to give the title compound as a colourless liquid as a mixture of 1 : 1 *trans–cis* isomers; δ_H(400 MHz, CDCl$_3$) 7.34–7.16 (10H, m, Ar–H), 6.24 (1H, dq, *J* 12.44, 1.46, OC*H*=CHCH$_3$-*trans*), 5.96 (1H, dq, *J* 6.22, 1.83, OC*H*=CHCH$_3$-*cis*), 4.82 (1H, dq, *J* 6.59, 12.44, CH=C*H*CH$_3$-*trans*), 4.72 (2H, s, PhC*H*$_2$O), 4.63 (2H, s, PhC*H*$_2$O), 4.37 (1H, m, OCH=C*H*CH$_3$-*cis*), 1.83 (3H, dd, *J* 5.12, 1.83, C*H*$_3$-*cis*), 1.49 (3H, dd, *J* 6.59, 1.46, C*H*$_3$-*trans*).

(3-Allyloxy-(*E*)-prop-2-enyl)benzene.[28] Sodium hydride (60% w/w dispersion in oil) was added to a solution of cinnamyl alcohol (300 mg, 2.24 mmol) in dry DMF (5 ml) at 0 °C. The mixture was allowed to stir under argon for 30 min. Allyl bromide (0.23 ml, 2.68 mmol) was added dropwise and the reaction mixture was allowed to stir for a further 3 h. The reaction mixture was diluted with ether, quenched with water and the organic layer extracted with ether. The combined organic layers were washed with brine and dried (MgSO$_4$). The crude product was purified by column chromatography (4 : 1 petroleum ether–diethyl ether) to yield the title compound as a colourless liquid (324 mg, 83%); ν_{max}/cm^{-1} 1647, 1599, 1495 (Ar C=C), 1071 (C–O), 965 (RCH=CHR-*trans*), 921 (RCH=CH$_2$); δ_H(400 MHz, CDCl$_3$) 7.24–7.45 (5H, m, Ar–H), 6.65 (1H, d, *J* 16.10, H-1), 6.33 (1H, dt, *J* 16.10, 5.85, H-2), 5.99 (1H, m, C*H*=CH$_2$), 5.34 (1H, ddt, *J* 17.2, 1.46, 1.46, CH$_2$=C*H*H′), 5.23 (1H, ddt, *J* 10.25, 1.46, 1.46, CH$_2$=CH*H*′), 4.19 (2H, dd, *J* 5.85, 1.46, H-3), 4.07 (2H, ddd, *J* 5.85, 1.46, 1.46, OC*H*$_2$CH); δ_C(CDCl$_3$) 136.74, 134.74, 132.38, 128.52, 127.62, 126.46, 126.07, 117.07, 71.11, 70.70.

Preparation of (3-propenyloxyprop-2-enyl)benzene. Following the procedure above, (3-allyloxypropenyl)benzene (25 mg, 0.14 mmol) was isomerised by reagent **8** (70 mg) to give the title compound as a colourless liquid with as a mixture of 1 : 1 *trans–cis* isomers; δ_H(400 MHz, CDCl$_3$) 7.40–7.42 (10H, m, Ar–H), 6.62 (2H, dq, *J* 16.10, 1.83, H-1), 6.33–6.22 (3H, m, H-2, OC*H*=CHCH$_3$-*trans*), 6.02 (1H, dq, *J* 6.22, 1.46, OC*H*=CHCH$_3$-*cis*), 4.87 (1H, m, CH=C*H*CH$_3$-*trans*), 4.43 (1H, m, CH=C*H*CH$_3$-*cis*), 4.41 (2H, dd, *J* 16.10, 1.83, H-3-*cis*), 4.33 (2H, dd, *J* 16.10, 1.83, H-3-*trans*), 1.62 (3H, dd, *J* 5.12, 1.83, C*H*$_3$-*cis*), 1.56 (3H, dd, *J* 6.59, 1.46, C*H*$_3$-*trans*).

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