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Fast Racemisation of Chiral Amines and Alcohols by Using Cationic Half-Sandwich Ruthena- and Iridacycle Catalysts

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Abstract: The lipase-catalysed resolution of alcohols and amines yields only 50% of the desired enantiopure product. However, addition of a racemisation catalyst leads to 100% yield in what is called a dynamic kinetic resolution (DKR). There is a need for new racemisation catalysts that are fast and compatible with the conditions of the

enzymatic reaction. We show that cationic half-sandwich ruthena- and iridacycle complexes are highly active and efficient in the racemisation of chiral alcohols and amines. Upon activation

with base, these complexes are able to selectively racemise alcohols, whereas the non-activated complexes are selective catalysts for the racemisation of amines. We have applied the iridacycles in the DKR of racemic β -chloroalcohols to produce chiral epoxides in a biphasic system in good yields and high *ee* (*ee* = enantiomeric excess).

Keywords: alcohols • amines • iridium • metallacycles • racemisation

Introduction

Enantiomerically pure amines and alcohols are important building blocks for pharmaceutical and agrochemical products.^[1] Although several catalytic methods exist for their preparation in an enantiopure form,^[2] one of the most frequently used production methods involves the classical resolution by crystallisation of diastereomeric salts.^[3] Enzymatic resolution is also frequently used.^[4] The drawback of these resolution methods lies in the fact that only 50% of the de-

sired enantiomer is produced; the other 50% of the non-desired enantiomer being mere waste. Designing catalysts that are capable of rapidly racemising the non-desired enantiomer and that are compatible with these enzymes enables a dynamic kinetic resolution (DKR) that can give a 100% yield of the desired enantiomer (Scheme 1).^[5] Relatively few

Scheme 1. DKR of alcohols and amines.

catalytic systems are available that can achieve this. The groups of Williams^[6] and Bäckvall^[7] developed the DKR of alcohols by using a combination of lipases and ruthenium catalysts. The latter used the dimeric Ru catalyst developed by Shvo.^[8] These catalysts function through a dehydrogenation–hydrogenation sequence. DSM Pharmaceutical Products has further developed the Bäckvall system to allow industrial production of alcohols.^[9]

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The racemisation of amines is much more challenging. Raney cobalt, Raney nickel or alkali metal hydroxide have been used at high temperatures for the racemisation of amines.^[10] In addition, aldehydes or thiols have been used as catalysts at lower temperatures.^[11] The first DKR of amines was achieved by Reetz et al. who managed to acylate (rac)- α -methylbenzylamine by using a combination of Pd/C and *Candida antarctica* lipase B (CALB, Novozym-435) in refluxing triethylamine,^[12] although rather long reaction times were needed for complete conversion. Jacobs and de Vos used a basic support, such as BaSO₄, for the palladium catalyst, which increased the catalyst activity and allowed the racemisation to proceed under milder conditions. Thus, the time of the DKR reaction was reduced to three days.^[13] In addition, these authors found that application of a low pressure of dihydrogen suppressed the formation of secondary amines in the racemisation of primary amines. Palladium nanoparticles developed by Park et al. led to excellent yields and enantioselectivities in the DKR of primary amines with a reaction time of three days.^[14] These nanoparticles could be recycled without any loss of activity for 10 consecutive runs. The Bäckvall group made several contributions to this area.^[15] They used the Shvo catalyst^[15a] and showed that better results were obtained when using an electron-rich variant thereof in the DKR of alcohols and amines.^[15b,c] Recently they reported the use of the transfer hydrogenation catalysts developed by Baratta for the racemisation of amines. No DKR could be achieved, though.^[15d] They applied this methodology in the synthesis of Norsetraline.

In general, the sensitivity of the metal catalyst for the enzyme seems to play an important role in the reactions since the dimeric iridium complex [Ir(Cp*)(I₂)]₂ (Cp* = pentamethylcyclopentadiene) was successfully used by Blacker as a fast racemisation catalyst for the dynamic kinetic resolution of 6,7-dimethoxy-1-methyl-tetrahydroisoquinoline in combination with immobilized *Candida antarctica* lipase, whereas palladium and ruthenium complexes showed much lower reactivity.^[16] The development of fast racemisation catalysts for alcohols and amines continues to be a major challenge. As we have developed the use of ruthenacycles as asymmetric transfer-hydrogenation catalysts, we were interested in studying these catalysts, and, in particular, the analogous iridacycles, as racemisation catalysts.^[17] The synthesis of iridacycles based on the reaction between [Ir(Cl₂)(Cp*)]₂ and benzylamines has been described by Davies^[18] and Pfeffer et al.^[19] Ikariya recently reported the use of iridacycles as alcohol oxidation catalysts.^[20]

Results and Discussion

We started by investigating the behaviour of half-sandwich metallacycles in the racemisation of (*S*)-1-phenylethanol (**S1**) and (*R*)-2-chloro-1-phenylethanol (**S2**). Cycloruthenated complexes of the type [Ru(η^6 -C₆H₆)(C-N)(CH₃CN)]-(PF₆), in which C-N is a chiral primary or secondary amine attached to the metallated aromatic ring through an alkyl group, have been shown to be very effective for the asymmetric transfer hydrogenation of aromatic ketones.^[17] We therefore decided to prepare an analogous complex, but with an achiral amine, and to test its activity for the racemisation of both alcohols (Scheme 2). Complex **1** was obtained analytically pure according to the transformation shown in Scheme 2.

Scheme 2. Synthesis of ruthenacycle complex **1**.

It is noteworthy that, due to the presence of stereogenic centres on the Ru and N atoms, **1** consists of two pairs of enantiomers $R_{Ru}S_N/S_{Ru}R_N$ and $R_{Ru}R_N/S_{Ru}S_N$, which show well-separated signals in their ¹H- and ¹³C NMR spectra and are found in a diastereomeric ratio of 56:44 (*de* = 12%; *de* = diastereomeric excess) in CD₃CN (Scheme 3). Considering

Scheme 3. Stereoisomers of **1**.

the sterically less-constrained structure of the $R_{Ru}S_N/S_{Ru}R_N$ pair (the NMe group is further away from the CH₃CN ligand than in the other pair) it is most probably the major one. These diastereomers rapidly interconvert in solution.^[21]

The catalytic activity of **1** was examined in the racemisation of (*S*)-**S1** and (*R*)-**S2** in the presence of KO^{*t*}Bu as an activator (Scheme 4). Complex **1** gave very poor results in di-

Scheme 4. Racemisation of chiral alcohols by using ruthenacycle catalyst **1**.

Table 1. Racemisation of alcohol (*S*)-**S1** with ruthenacycle **1**.

Entry ^[a]	Solvent	<i>c</i> [mol L ⁻¹]	Reaction time [h]	<i>ee</i> [%]
1	CH ₂ Cl ₂	0.25	19	70
2	PhMe	0.1	7	8
3 ^[b]	PhMe	0.1	3	2
4	<i>i</i> PrOH	0.05	20	50
5	<i>i</i> PrOH	0.25	7	6
6	<i>i</i> PrOH	1.0	1	2
7 ^[c]	<i>i</i> PrOH	1.0	0.5	0
8 ^[d]	H ₂ O	0.5	46	8
9 ^[d,e]	H ₂ O	0.5	5	6

[a] Reaction conditions: 0.20 mmol of enantiomerically pure substrate (*ee* > 99%), 4 mol% of **1**, 5 mol% of KOtBu, RT. [b] Reaction at 60 °C. [c] Reaction at 80 °C. [d] Reaction carried out with an additional 1.0 equiv of acetophenone. [e] Reaction at 40 °C.

chloromethane with only 30% of racemisation of **S1** after 19 h at RT (Table 1, entry 1). Even though much better results were observed in toluene at RT (8% *ee* after 7 h, entry 2; *ee* = enantiomeric excess), it required 3 h at 60 °C to observe almost complete racemisation of **S1** (entry 3). In *iso*-propanol, the reaction rate was found to be strongly dependent on the substrate concentration.

While the reaction was very slow at a concentration of 0.05 M (Table 1, entry 4), it was almost complete (*ee* = 2%) after 1 h at a concentration of 1.0 M with 4 mol% of **1** and 5.2 mol% of KOtBu (entry 6). When run at 80 °C under otherwise similar conditions, racemisation was complete in 30 min (entry 7). In water, although poorly soluble, **1** racemised (*S*)-**S1** with a reasonable rate at 40 °C in the presence of one equivalent of acetophenone.

Unfortunately, **1** showed no activity for the racemisation of (*R*)-**S2** in the presence of KOtBu in various solvents. A control experiment showed that a reaction conducted at RT with a 1.0 M solution of (*S*)-**S1** in *i*PrOH in the presence of 4 mol% of **1** and 5.2 mol% of KOtBu was inhibited by the addition of 5 mol% of 2-chloroacetophenone (Scheme 5).

Scheme 5. Inhibition of the racemisation of (*S*)-**S1** by 2-chloroacetophenone.

This indicated that catalyst deactivation in the racemisation attempts of (*R*)-**S2** was due to the formation of small amounts of 2-chloroacetophenone, the dehydrogenation product of **S2**, which reacted with the active species. A similar behaviour had already been observed in the transfer hydrogenation of functionalised β -keto-esters catalysed by (β -amino-alcohol)(arene)ruthenium(II) complexes.^[22]

The active species **1'**, generated by the action of KOtBu on **1**, has been identified by ¹H NMR spectroscopy in CD₃CN (see the Experimental Section) as a neutral cyclometallated ruthenium hydride complex in which the NH proton is NMR silent, presumably due to rapid exchange with CD₃CN under basic conditions (Scheme 6). Like **1**,

Scheme 6. Formation of active species **1'**.

complex **1'** displays two sets of signals in its ¹H NMR spectrum, which indicates the presence of two diastereomers. The diastereoisomers are found in an approximate ratio of 1:1, and the ruthenium hydride signals are detected at δ = -7.13 and -7.85 ppm. The chemical shifts corresponding to the η^6 -benzene units and the aryl protons are strongly shielded in comparison to those of the cationic species **1**, which is characteristic of a neutral cycloruthenated complex.^[23] Presumably, deprotonation of **1** leads to the formation of the neutral complex, which reacts with *iso*-propanol to form **1'**.

2-Chloroacetophenone reacts almost instantaneously with **1'** (or with **1** in the presence of KOtBu) to give the inhibited species. Unfortunately, the latter could not be isolated due to decomposition during the workup. The ¹H NMR spectroscopic analysis of a crude reaction mixture points at the formation of a new cycloruthenated species that is present in solution in only one diastereomeric form. However, the exact structure remains unclear.

We next focused on the synthesis of electron-rich half-sandwich iridacycle complexes, as these complexes were expected to have a higher stability toward air and moisture compared to ruthenacycles. A first set of cationic iridacycles **2–4** (Scheme 7) was synthesized from [Ir(Cp*)(Cl₂)₂] and two equivalents of benzylamine, *N*-methylbenzylamine or *N,N*-dimethylbenzylamine, respectively, in the presence of sodium hydroxide and potassium hexafluorophosphate in acetonitrile at 45 °C for 16 h (Scheme 5). After filtration of the reaction mixture through alumina, the complexes **2–4** were obtained as yellowish powders in high yields (up to 92%). Contrary to ruthenacycle **1** (Scheme 3), the two pairs of enantiomers *R*_{Ir}*S*_N/*S*_{Ir}*R*_N and *R*_{Ir}*R*_N/*S*_{Ir}*S*_N were not observed by ¹H NMR spectroscopy at RT for iridacycle **3**,

Scheme 7. Synthesis of iridacycle complexes.

which might be due to the faster inversion of configuration at the iridium centre.

This hypothesis was confirmed by studying the behaviour of **3** by using variable-temperature ^1H NMR spectroscopy in CD_3CN (Figure 1a,b). The *N*-methyl and Cp^* moieties give very broad signals at 20°C . At 0°C , the two diastereoisomeric *N*-methyl groups are clearly observed as are the two Cp^* -methyl moieties (Figure 1a and b, respectively). This effect was more pronounced at -10 and -20°C . The coalescence temperature of the Cp^* -methyl signals is 3°C .

Figure 1. a) Variable-temperature ^1H NMR spectra of the *N*-methyl signals of **3** in CD_3CN . 1: $+20$, 2: $+10$, 3: 0, 4: -10 , 5: -20°C . b) Variable-temperature ^1H NMR spectra of the Cp^* -methyl signals of **3** in CD_3CN . 1: $+20$, 2: $+10$, 3: 0, 4: -10 , 5: -20°C .

Iridacycle complexes **2–4** were studied in the catalytic racemisation of (*S*)-phenylethanol (**S1**) and (*R*)-2-chloro-1-phenylethanol (**S2**). We soon observed a key role for the *N*-substituent on the ligand in complexes **2–4**. First investigations were done by using 5 mol % of **4** at 70°C in toluene.

As observed with the ruthenacycles, complex **4** was not able to racemise chiral alcohols without activation with base (Table 2, entries 1–2). Activa-

Table 2. Racemisation of alcohols **S1** and **S2** with iridacycles **2–4**.

Entry ^[a]	[Ir]	Substrate	T [$^\circ\text{C}$]	ee [%]	Ketone [%]
1 ^[b]	4	S1	70	100	9
2 ^[b]	4	S2	70	97	–
3	4	S1	70	34	15
4	4	S2	70	29	–
5	4	S1	RT	83	10
6	4	S2	RT	8	–
7	3	S1	RT	3	13
8	3	S2	RT	0	–
9	2	S1	RT	100	12
10	2	S2	RT	3	–

[a] Reaction conditions: 0.2 mmol of enantiomerically pure substrate (*ee* > 99%), 5 mol % of [Ir], 6 mol % KOtBu, 2 mL of PhMe at RT for 24 h. [b] Without KOtBu.

tion with 1.2 equivalents of potassium-*tert*-butoxide led to a highly efficient catalyst for the racemisation of **S1** since 34% *ee* was obtained in 24 h at 70°C in toluene (entry 3). Acetophenone (15%) was also observed by GC analysis. Under the same reaction conditions, 29% *ee* was obtained in the racemisation of (*S*)-**S2** with complete selectivity since no corresponding ketone was found (entry 4). Lowering the temperature to RT had the expected effect on the rate of racemisation of (*S*)-**S1** (83% *ee*, entry 5). Surprisingly, the rate of racemisation of (*R*)-**S2** was higher at RT compared to 70°C . Indeed, after 24 h, **S2** was obtained quantitatively in 8% *ee* (entry 6). Complexes **2** and **3** were then tested at RT in the racemisation of (*S*)-**S1** and (*R*)-**S2**. Complex **2** was inactive in the presence of (*S*)-**S1**, but was able to racemise (*S*)-**S2** almost to completion (100 and 3% *ee*, respectively, entries 9–10). Mono-*N*-methyl-substituted iridacycle **3** was the most efficient catalyst since complete racemisation of both (*S*)-**S1** and (*R*)-**S2** was observed after 24 h at RT (3 and 0% *ee*, respectively, entries 7–8).

Subsequently, we studied the kinetics of the racemisation of chiral α -aryl and alkyl alcohols **S1–S8** by using the optimised reaction conditions (5 mol % of catalyst **3**, 6 mol % of

KOtBu, PhMe, RT; Table 3). With **S1**, 50% and complete racemisation was achieved in 1 and 7 h, respectively (Table 3, entry 1). A tremendous increase of reaction rate

Table 3. Racemisation of alcohols with iridacycle **3** at room temperature.

Entry ^[a]	Substrate	$t_{1/2(\text{rac})}$ [min]	$t_{\text{compl.}(\text{rac})}$ [min]	Ketone [%]
1	S1	60	420	6
2	S2	–	5	–
3 ^[b]	S2	20	180	–
4 ^[c]	S2	–	1080	–
5 ^[d]	S2	–	60	–
6	S3	20	240	10
7	S4	120	720	12
8	S5	17	200	8
9 ^[e]	S6	360	1440	20
10	S7	150	960	7
11	S8	240	1440	12

[a] Reaction conditions: 0.75 mmol of enantiomerically pure substrate ($ee > 99\%$), 5 mol % of **3**, 6 mol % KOtBu, 2.4 mL of PhMe. [b] With 1 mol % of **3**. [c] After 16 h, 0.2 mmol of (*S*)-**S2** was added and the reaction mixture was stirred for an additional 2 h, 6% ee after 18 h. [d] Reaction achieved in a mixture of PhMe/H₂O 1:1. [e] 10% ee after 24 h.

was observed with **S2** since complete racemisation was achieved within 5 min at RT (entry 2). Similar high rates have only recently been reported by Bäckvall and co-workers for this substrate.^[24] Decreasing the catalyst loading to 1 mol % allowed complete racemisation to be reached in 3 h with a half-life time of racemisation of 20 min (entry 3). The catalyst was still active after 16 h. Indeed, when a new batch of (*R*)-**S2** was added only 6% ee was observed 2 h after the addition (entry 4). Furthermore, complete racemisation of (*R*)-**S2** was obtained in 1 h in a mixture of toluene/water as the solvent (entry 5), which showed the high tolerance of **3** to aqueous media.

Compared to substrate (*S*)-**S1**, the presence of an electron-withdrawing group at the *para* position of (*S*)-1-(4-fluorophenyl)ethanol (**S3**) strongly decreased the time of complete racemisation to 4 h, with a time of half-racemisation of 20 min (Table 3, entry 6). Compared to **S1**, a longer reaction time was needed to perform the complete racemisation of

(*S*)-1-phenylbutanol (**S4**) possessing a longer alkyl chain (entry 7). Racemic 1-(2-naphthyl)ethanol (**S5**) was obtained from (*S*)-**S5** in 200 min with a $t_{1/2}$ of racemisation of 17 min (entry 8). The rate of racemisation decreased with a more rigid substrate structure, such as (*R*)-1-indanol (**S6**), since complete racemisation was obtained after 24 h (entry 9). Iridacycles also showed activity in the catalytic racemisation of aliphatic alcohols. However lower reactivity was observed in the racemisation of (*S*)-2-butanol (**S7**) and (*R*)-2-hexanol (**S8**) with a $t_{1/2}$ of racemisation of 150 and 240 min and complete racemisation in 16 and 24 h, respectively (entries 10–11). In all cases, when using α -methyl-substituted alcohols, the formation of the corresponding ketone was observed, showing that the rate-determining step is the reduction of the ketone to the corresponding racemic alcohol. This is also corroborated by the faster racemisation of **S2**. The reduction rate is enhanced by the presence of electron-withdrawing groups. Based on these results, we suggest that the substrate dissociates from the metal centre after dehydrogenation. This was also shown by adding one equivalent of 2-bromoacetophenone to (*S*)-**S1** in the presence of 5 mol % of **3** and 5.2 mol % of base in toluene (Scheme 8). Only acetophenone and the corresponding racemic bromoalcohol were detected quantitatively by GC analysis.

The tolerance of half-sandwich iridacycle **3** towards aqueous media and its high efficiency in the racemisation of (*R*)-2-chloro-1-phenylethanol (**S2**) at RT led us to combine this racemisation reaction with an enzymatic kinetic resolution process. Janssen et al. found that haloalcohol dehalogenase Hhec is very efficient in the resolution of β -chloroalcohols to afford enantiopure epoxides.^[25] By using the double mutant Hhec C153S W249F and catalytic amounts of the activated iridacycle **3**, enantioenriched epoxides were obtained

by dynamic kinetic resolution of racemic substituted 2-chloro-1-phenylethanol in a one-pot reaction in high yields and with excellent enantioselectivities (up to 90 and 98% ee , respectively; Scheme 9).^[26] Unfortunately, only enzymatic

Scheme 9. Chemoenzymatic DKR of β -chloroalcohols to chiral epoxides.

resolution and no racemisation was observed when using aliphatic β -chloroalcohols.

Thus, iridacycle complexes **1–3** have shown their efficiency in the catalytic racemisation of chiral alcohols. In addition, they can be combined with aqueous enzymes for a dynamic kinetic resolution.

Amine racemisation: We also investigated the behaviour of these complexes in the catalytic racemisation of chiral amines, such as (*S*)- α -methylbenzylamine (**S9**) and (*S*)-*N*, α -dimethylbenzylamine (**S10**), as model substrates in toluene (0.25 M) at 100 °C when using 2 mol % of iridacycle (Scheme 10). In contrast to the corresponding reaction with alcohols, no racemisation was observed after activating **1–3** with potassium-*tert*-butoxide.

Scheme 10. Racemisation of α -methylbenzylamine derivatives.

Without activation, preliminary tests with (*S*)- α -methylbenzylamine (**S9**) showed that only slow racemisation of this substrate was observed and mainly formation of side products was detected. The side products are formed by the condensation reaction of the imine intermediate with the substrate to form dimers.^[27] This result shows that, in the case of substrate **S9**, the rate-determining step in the catalytic cycle is the reduction of the imine to the racemic amine.

Iridacycles **2–4** showed good reactivity with (*S*)- α -methyl-*N*-methylbenzylamine (**S10**) since a decrease of enantiomeric excess down to 10 % *ee* was obtained in toluene at 100 °C when using 2 mol % of catalyst after 16 h. Moreover, no side products were observed. Kinetic studies showed that catalysts **2** and **4** have the same activity after 3 h ($t_{1/2(\text{rac})}$ = 200 min), but catalyst **2** is more active than **4** after 8 h (15 and 26 % *ee*, respectively; Figure 2). A different behaviour was observed with iridacycle **3** synthesised from *N*-methylbenzylamine: the racemisation rate is higher than with catalysts **2** and **4** (41 % *ee* after 1 h). After the initial fast racemisation, catalyst **3** seems to be deactivated after 2 h since only a decrease of less than 13 % *ee* was detected in the next 6 h (34 % *ee* after 2 h and 21 % *ee* after 8 h).

The use of more polar solvents, such as chlorobenzene, allowed an increase of the reaction rate (Figure 3). This effect might be due to the enhanced solubility of these complexes in this solvent. Complete racemisation of (*S*)- α -methyl-*N*-methylbenzylamine (**S10**) was obtained with catalysts **3** and **4** in 8 h, ($t_{1/2(\text{rac})}$ = 30 and 90 min, respectively). Although catalyst **3** seems to be deactivated after 2 h, the effect is less prominent than in toluene. No improvement was observed with catalyst **2** since the time of half-racemisation was about 180 min as in toluene and complete racemisation was obtained after 16 h.

Figure 2. Enantiomeric excess versus time in the racemisation of **S10** (0.75 mmol, 0.25 M) with 2 mol % of [Ir] at 100 °C in toluene. ♦: **2**; ■: **3**; △: **4**.

Figure 3. Enantiomeric excess versus time in the racemisation of **S10** (0.75 mmol, 0.25 M) with 2 mol % of [Ir] at 100 °C in chlorobenzene. ♦: **2**; ■: **3**; △: **4**.

Catalysts **2–4** were efficient in the racemisation of (*S*)- α -methyl-*N*-methylbenzylamine since complete racemisation was observed within 8 h in chlorobenzene and within 16 h in toluene at 100 °C when using 2 mol % of catalyst. However, the most active catalyst **3** possessing a secondary amine as the ligand again seems to be deactivated under the reaction conditions. The deactivation of catalyst **3** might be due to the oxidation of the *N*-methylbenzylamine ligand to *N*-benzylidenemethylamine in solution, resulting in less-active catalyst **5** (Scheme 11). This was confirmed by studying the sta-

Scheme 11. Oxidation of iridacycle **3** into **5** in CDCl_3 .

bility of **3** in CDCl_3 . It was found that complex **3** slowly oxidized to imine-complex **5**. Moreover, iridacycle **5** synthesized from $[\text{Ir}(\text{Cp}^*)(\text{Cl}_2)_2]$ and *N*-benzylidenemethylamine showed lower reactivity relative to complex **3** since only 55% *ee* was obtained in 16 h in the racemisation of **S10**.

The presence of a secondary amine moiety in the ligand, as in **3**, seems to be important in terms of reactivity during the racemisation reaction since **3** is initially the most active. To counter the oxidation of the ligand, iridacycles **6** and **7**

were synthesized with ligands containing an sp^2 carbon centre at the benzylic position and a secondary amine, such as phenylimidazoline and phenylimidazole. To compare with **6** and **7**, iridacycle **8** possessing a 2-phenyloxazoline ligand was also synthesized (Figure 4). These complexes were obtained analytically pure in excellent yields (up to 95%) and show a high stability towards air and moisture.

Figure 4. ORTEP style plot of cationic iridacycle **8**. Thermal ellipsoids are drawn at the 50% probability level and hydrogen atoms are omitted for clarity.

Iridacycle **8** is able to racemize (*S*)-**S10** but no enhancement of reactivity was observed (26% *ee* after 16 h at 100°C when using 2 mol% of catalyst in toluene). On the contrary, both catalysts **6** and **7** showed very high activities in the racemisation of **S10** with 2 mol% of iridacycle at 100°C. Complete racemisation was obtained in chlorobenzene within 40 and 180 min with **6** and **7**, respectively, with a remarkably short time of half-racemisation of 4 min and less than 20 min, respectively (Figure 5). As expected, no deactivation of the catalysts was observed. By using the same conditions, the reaction was scaled-up to 2 g of enantiopure substrate

Figure 5. Kinetic studies of the racemisation of (*S*)-**S10** (0.75 mmol) in chlorobenzene (0.25 M) at 100°C by using 2 mol% of **6** and **7**. ▲: **6**; □: **7**.

S10 without any loss of activity. It is noteworthy that the presence of a NH group in the ligand of iridacycle complexes **6** and **7** is necessary to increase the racemisation rate (compared to **8**). This effect was already observed with complexes **3** and **5** (Scheme 11).

The effect of the temperature on the reaction rate of the racemisation of **S10** in toluene and chlorobenzene was investigated with catalyst **6** (Table 4). In toluene at 100°C, the

Table 4. Temperature effect in the racemisation of (*S*)-**S10** with iridacycle **6**.

Entry ^[a]	Solvent	<i>T</i> [°C]	<i>t</i> _{1/2(rac)} [min]	<i>t</i> _{compl.(rac)} [min]
1 ^[b]	PhMe	40	—	—
2	PhMe	60	160	960
3	PhMe	80	45	360
4	PhMe	100	20	180
5 ^[c]	PhCl	40	—	—
6	PhCl	60	90	960
7	PhCl	80	25	280
8	PhCl	100	4	40

[a] Reaction conditions: 0.25 mmol of substrate, 2 mol% of [Ir], 1 mL of PhMe. [b] 63% *ee* observed after 16 h. [c] 68% *ee* observed after 16 h.

racemisation is complete in 3 h with a time of half-racemisation of 20 min. At 80°C the time of half-racemisation is about 45 min with a complete racemisation in 6 h. Decreasing the temperature to 60°C reduces the rate of the reaction (*t*_{1/2(rac)} = 160 min and complete racemisation in 16 h) but only a low turnover was observed at 40°C since a loss of enantiomeric excess of less than 10% was observed after 4 h.

In chlorobenzene at 100°C, the rate of the reaction increases relative to toluene since complete racemisation was obtained in 40 min (*t*_{1/2(rac)} = 4 min; Table 1). At 80°C, the rate of the reaction is slightly higher than in toluene

($t_{1/2(\text{rac})}$ = 25 min). It is expected that the reactivity of the catalytic system decreases with the temperature, but it is still efficient at 60°C ($t_{1/2(\text{rac})}$ = 90 min). As in toluene, only slow racemisation is obtained at 40°C (less than 12% in 4 h). However, iridacycle **6** has been shown to be very efficient in racemising (*S*)- α -methyl-*N*-methylbenzylamine since racemic product **S10** was obtained in 40 min at 100°C in chlorobenzene.

To demonstrate the robustness of catalyst **6** in the racemisation of (*S*)-**S10**, we added new batches of enantiopure **S10** every 40 min (Figure 6). By starting from a reaction mixture

Figure 6. Kinetic studies of the racemisation of (*S*)-**S10** with 2 mol % of **6** by the sequential addition 0.25 mmol of (*S*)-**S10** every 40 min.

of 0.25 mmol of **S10** in chlorobenzene ([**S10**] = 0.25 M) in the presence of 2 mol % of **6** at 100°C, complete racemisation was obtained after 40 min. At this time, 0.25 mmol of (*S*)-**S10** was added to the reaction, increasing the concentration of the reaction mixture to [**S10**] = 0.5 M and the substrate/catalyst ratio to 100. Just after addition, the ee was 50%, as expected. After 2 min, the ee of the product already dropped to 42%, which shows the high activity of the catalyst under these conditions. Almost complete racemisation was obtained after 80 min (1.5% ee). A new batch of (*S*)-**S10** was added at 80 min ([**S10**] = 0.75 M, s/c = 150) and a sample analysed 2 min after the addition gave 44% ee for **S10**. At 120 min, the rate of racemisation slowed down since the ee of **S10** was 11%. Final addition of (*S*)-**S10** ([**S10**] = 1 M, s/c = 200) highly influenced the catalytic system in terms of reactivity. At 2 min, after addition, only 48% ee was observed and 18% ee after 160 min. Complete racemisation was obtained after 6 h.

We reinvestigated the racemisation of primary amine (*S*)- α -methylbenzylamine (**S9**) by using 2 mol % of iridacycle **6** in toluene at 100°C. The decrease of enantioselectivity was found to be low and corresponds to the formation of side products. A way to overcome the formation of byproducts might be the addition of dihydrogen during the reaction. However, the hydrogen pressure must not be too high otherwise it could inhibit the dehydrogenation step during the catalysis. A significant improvement was indeed achieved. Upon using a hydrogen atmosphere of 1 atm in toluene at

100°C with 2 mol % of **6** for 16 h ee values down to 34% were reached, but the selectivity of the reaction was still low (36%).

To extend the scope of the reaction, we investigated the catalytic racemisation of a series of chiral amines including primary, secondary and tertiary amines by using 2 mol % of **6** as the catalyst in toluene (Table 5).

Table 5. Racemisation of amines **S9**–**S15** with 2 mol % of iridacycle **6** in toluene (0.25 M).

Entry ^[a]	Substrate	T [°C]	$t_{1/2(\text{rac})}$ [min]	$t_{\text{compl}(\text{rac})}$ [min]
1 ^[b]	S9	100	dimers	–
2	S10	80	45	360
3	S10	100	15	180
4 ^[c]	S10	100	4	40
5	S11	100	< 5	15
6 ^[d]	S12	100	–	960
7 ^[b]	S13	100	120	300
8 ^[b]	S14	100	< 90	600
9	S15	100	–	960

[a] Reaction conditions: 0.75 mmol of substrate, 2 mol % of [Ir], 3 mL of PhMe. [b] More than 60% of dimers were observed. [c] in PhCl. [d] ee of (*S*)-**S12** = 86%.

With primary amine (*S*)-**S9**, only dimer formation was observed (Table 5, entry 1).^[27] Racemisation of (*S*)- α -methyl-*N*-methylbenzylamine (**S10**) was fast in toluene at 100°C with 2 mol % of **6** ($t_{1/2(\text{rac})}$ = 15 min, entry 3). By using chlorobenzene instead of toluene, $t_{1/2(\text{rac})}$ was decreased to 4 min and complete racemisation was obtained after 40 min (entry 4). (*S*)-*N*-benzyl- α -methylbenzylamine (**S11**) showed the highest reactivity since complete racemisation was obtained after 15 min ($t_{1/2(\text{rac})}$ < 5 min, entry 5). Quinoline was also investigated as a substrate. Complete racemisation of (*S*)-2-methyl-1,2,3,4-tetrahydroquinoline (**S12**) was obtained overnight (entry 6).^[28] Further studies on the racemisation of cyclic benzylic primary amines, such as (*S*)-1-aminointhane (**S13**) and (*S*)-1,2,3,4-tetrahydro-1-naphthylamine (**S14**), gave good results with complete racemisation in 6 and 10 h, respectively ($t_{1/2(\text{rac})}$ = 120 min, entry 7; $t_{1/2(\text{rac})}$ < 90 min, entry 8). In these cases, major formation of dimers was also observed. Finally, iridacycle **6** was able to racemise tertiary amine (*S*)- α ,*N,N*-trimethylbenzylamine (**S15**) overnight (entry 9).

Iridacycles are very efficient in the catalytic racemisation of chiral secondary and tertiary amines. However, dimer formation was observed during the racemisation of primary amines. This suggests that the imine resulting from the dehy-

drogenation of the chiral amine does not stay coordinated to the iridium centre and that the rate-determining step might be the hydrogenation of the imine derivative.

Conclusion

We have synthesized and characterized a small library of half-sandwich cationic ruthena- and iridacycle complexes and studied their behaviour in the catalytic racemisation of chiral amines and alcohols. We found that readily synthesized electron-rich iridacycles **2–8**, obtained from commercial available metal precursors and aromatic secondary amines, are able to racemize both chiral alcohols and amines. These complexes are among the fastest racemisation catalysts described. Moreover, they show an unexpected switchable behaviour. Without activation of iridacycle complexes by KOtBu, no activity towards chiral alcohols was observed, whereas complete racemisation of amines occurred in the best case in 15 min. The reverse effect was observed as well since base-activated iridacycles were efficient only with chiral alcohols; (*R*)-2-chloro-1-phenylethanol (**S2**) was racemized within 5 min at RT, but no reaction occurred with amines. Alkyl alcohols can also be racemized with longer reaction times. Mechanistic aspects and applications of these iridacycles in other chemo-enzymatic dynamic kinetic resolutions are currently being investigated by our group.

Experimental Section

General: Starting materials were purchased from Acros, Sigma–Aldrich, Strem, Merck or Alfa Aesar, and were used as received unless stated otherwise. All solvents were reagent grade and, if necessary, dried and distilled prior to use. Toluene and diethylether were distilled over Na/benzophenone. Column chromatography was performed on silica gel (Aldrich 60, 230–400 mesh) or activated neutral aluminium oxide (Merck aluminium oxide 90 neutral activated). TLC was performed on silica gel 60/Kieselguhr F₂₅₄ or neutral aluminium oxide 60 F₂₅₄. ¹H and ¹³C NMR spectra were recorded in CDCl₃ on a Varian VXR300 (299.97 MHz for ¹H, 75.48 MHz for ¹³C) or a Varian AMX400 (399.93 MHz for ¹H, 100.59 MHz for ¹³C) spectrometer. Chemical shifts are reported in δ values (ppm) relative to the solvent peak (CHCl₃, δ = 7.26 (¹H), 77.0 ppm (¹³C)). The following abbreviations are used to indicate multiplicity: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad). Mass spectra (HRMS) were performed on a Jeol JMS-600H. GCMS spectra were recorded on a Hewlett Packard HP6890 equipped with a HP1 column and an HP 5973 Mass Selective Detector. GC analysis was performed on a Shimadzu GC-17 A or a Hewlett Packard HP6890 chromatograph equipped with the columns indicated for each compound separately. HPLC analysis was performed on a Shimadzu HPLC system equipped with two LC-10AD *vp* solvent delivery systems, a DGU-14 A degasser, a SIL-10AD *vp* auto injector, an SPD-M10 A *vp* diode array detector, a CTO-10 A *vp* column oven and an SCL-10A *vp* system controller by using the columns indicated for each compound separately. Elemental analyses were carried out on a EuroVector Euro EA elemental analyser.

Synthesis and characterisation of the cationic ruthenacycle complex: The procedure described by Pfeffer et al. was used.^[19] A suspension of [Ru-(Cl₂)(η⁶-C₆H₆)] (200 mg, 0.4 mmol), *N*-methylbenzylamine (72 μL, 0.56 mmol), NaOH (32 mg, 0.8 mmol) and KPF₆ (294 mg, 1.6 mmol) in CH₃CN (6 mL) was stirred at RT for 3 d. The resulting dark-yellow sus-

pension was filtered over Al₂O₃ by using CH₃CN as the eluent. A yellow fraction was collected and concentrated under vacuum to 1–2 mL. Addition of Et₂O (4 mL) gave **1** as a yellow solid that was washed with Et₂O (3 × 2 mL) and pentane (3 × 2 mL). Yield: 200 mg, 0.30 mmol, 74 %.

[Ru(η⁶-C₆H₆)(2-(CH₂NHMe)-C₆H₄)(NCMe)](PF₆) (1**):** ¹H NMR analysis revealed the presence of two pairs of enantiomers, *R*_{Ru}*S*_N/*S*_{Ru}*R*_N and *R*_{Ru}*R*_N/*S*_{Ru}*S*_N, in a 56:44 ratio in CD₃CN. Enantiomer *R*_{Ru}*S*_N/*S*_{Ru}*R*_N: ¹H NMR (400.0 MHz, CD₃CN, 298 K): δ = 7.72 (d, ³*J*_{H–H} = 7.6 Hz, 1H; C₆H₄), 7.04–6.90 (m, 3H; C₆H₄), 5.57 (s, 6H; C₆H₆), 4.04 (m, 1H; NH), 3.94 (dd, ²*J*_{H–H} = 13.6, ³*J*_{H–H} = 4.4 Hz, 1H; CH₂N), 3.61 (dd, ²*J*_{H–H} = 13.6, ³*J*_{H–H} = 11.2 Hz, 1H; CH₂N), 3.06 (d, ³*J*_{H–H} = 6.0 Hz, 3H; NCH₃), 2.15 ppm (s; CH₃CN); ¹³C NMR (100.6 MHz, CD₃CN, 298 K): 166.4, 147.6, 140.2, 127.4, 124.2, 122.0 (C₆H₄), 118.3 (CH₃CN), 87.9 (C₆H₆), 67.8 (CH₂N), 47.3 (NCH₃), 1.3 ppm (CH₃CN); enantiomer *R*_{Ru}*R*_N/*S*_{Ru}*S*_N: ¹H NMR (400.0 MHz, CD₃CN, 298 K): δ = 7.96 (d, ³*J*_{H–H} = 7.6 Hz, 1H; C₆H₄), 7.04–6.90 (m, 3H; C₆H₄), 5.61 (s, 6H; C₆H₆), 4.04 (m, 1H; NH), 3.77 (dd, ²*J*_{H–H} = 14.0, ³*J*_{H–H} = 5.6 Hz, 1H; CH₂N), 3.47 (dd, ²*J*_{H–H} = 14.0, ³*J*_{H–H} = 9.0 Hz, 1H; CH₂N), 2.84 (d, ³*J*_{H–H} = 6.0 Hz, 3H; NCH₃), 2.15 ppm (s; CH₃CN); ¹³C NMR (100.6 MHz, CD₃CN, 298 K): δ = 162.7, 148.3, 139.9, 127.1, 124.5, 122.4 (C₆H₄), 118.3 (CH₃CN), 88.3 (C₆H₆), 63.2 (CH₂N), 45.7 (NCH₃), 1.3 ppm (CH₃CN); elemental analysis calcd (%) for C₁₆H₁₉N₂RuPF₆: C 39.59, H 3.95, N 5.77; found: C 39.91, H 3.93, N 5.71.

[Ru(η⁶-C₆H₆)(2-(CH₂NHMe)-C₆H₄)] (1'**):** KOtBu (9 mg, 0.077 mmol) was added to an orange suspension of **1** (25 mg, 0.052 mmol) in *i*PrOH (2.5 mL). After 20 min, of stirring at RT, all compounds were dissolved leading to a dark-orange solution. An aliquot was then removed by syringe, immediately dried in vacuo, and redissolved in CD₃CN for ¹H NMR spectroscopic analysis, which revealed the presence of two pairs of enantiomers in an approximate ratio of 1:1. ¹H NMR (400.0 MHz, CD₃CN, 298 K): δ = 7.48 (d, ³*J*_{H–H} = 7.5 Hz, 1H; C₆H₄), 6.83–6.62 (m, 3H; C₆H₄), 5.09 (s, 6H; C₆H₆), 3.74, 3.09 (AB, ²*J*_{H–H} = 12.6 Hz, 2H; CH₂N), 2.61 (s, 3H; NCH₃), –7.13 ppm (s, 1H; RuH); ¹H NMR (400.0 MHz, CD₃CN, 298 K): δ = 7.35 (d, ³*J*_{H–H} = 7.5 Hz, 1H; C₆H₄), 6.83–6.62 (m, 3H; C₆H₄), 5.09 (s, 6H; C₆H₆), 3.79, 3.46 (AB, ²*J*_{H–H} = 12.0 Hz, 2H; CH₂N), 2.64 (s, 3H; NCH₃), –7.85 ppm (s, 1H; RuH).

Synthesis and characterisation of cationic iridacycle complexes: The procedure described by Pfeffer et al. for analogous compounds was used.^[19] In a typical experiment, a 50 mL Schlenk tube was thoroughly flame-dried and put under an atmosphere of nitrogen, after which the following compounds were added, respectively, in acetonitrile (5 mL): [Ir(Cl₂)-(Cp*)]₂ (159 mg, 0.2 mmol), amine (0.40 mmol), NaOH (16 mg, 0.4 mmol) and KPF₆ (147 mg, 0.8 mmol). This mixture was stirred at 45 °C for 16 to 50 h. The mixture was then cooled down to RT, washed with hexane and filtered over neutral aluminium oxide (eluent: MeCN). The resulting solution was concentrated in vacuo. Subsequent stripping with dry Et₂O yielded the desired iridacycle complex.

[Ir(η⁵-C₅Me₅)(C₆H₄-2-CH₂NH₂)(NCCH₃)](PF₆) (2**):** Complex **2** was obtained as a brown-solid precipitate (216 mg, 0.35 mmol, 87 %) by using benzylamine (43 mg). ¹H NMR (400.0 MHz, CDCl₃, 298 K): δ = 7.40 (dd, ³*J*_{H–H} = 1.4, 7.1 Hz, 1H; Ph-H), 7.12 (d, ³*J*_{H–H} = 7.6 Hz, 1H; Ph-H), 6.98 (td, ³*J*_{H–H} = 1.3, 7.2 Hz, 2H; Ph-H), 4.35 (s, 2H; NH₂), 4.24 (m, 1H; CH₂), 3.86 (m, 1H; CH₂), 2.39 (s, 3H; NCCH₃), 1.75 ppm (s, 15H; C₅-(CH₃)₅); ¹³C NMR (100.6 MHz, CDCl₃, 298 K): δ = 150.2, 149.1, 135.9, 127.4, 123.9, 121.3 (CH₃CN), 89.6, 56.1, 9.1 ppm (CH₃CN); HRMS (EI⁺): *m/z*: calcd. for C₁₇H₂₃Ni⁺: 434.1460 (–CH₃CN/PF₆, [M]⁺); found: 434.1441; elemental analysis calcd (%) for C₁₆H₁₉F₆N₂PIr: C 39.59, H 3.95, N 5.77; found: C 39.91, H 3.93, N 5.71.

[Ir(η⁵-C₅Me₅)(C₆H₄-2-CH₂NHCH₃)(NCCH₃)](PF₆) (3**):** Complex **3** was obtained as a yellow powder (233 mg, 0.37 mmol, 92 %) by using *N*-methylbenzylamine (49 mg). ¹H NMR (400.0 MHz, CDCl₃, 298 K): δ = 7.36 (d, ³*J*_{H–H} = 6.9 Hz, 1H; Ph-H), 7.07 (d, ³*J*_{H–H} = 6.9 Hz, 1H; Ph-H), 7.00 (t, ³*J*_{H–H} = 7.2 Hz, 1H; Ph-H), 6.92 (t, ³*J*_{H–H} = 7.0 Hz, 1H; Ph-H), 4.40 (s, 1H; NH), 4.17 (s, 1H; CH₂), 3.68 (s, 1H; CH₂), 3.11 (s, 3H; NCH₃), 2.38 (s, 3H; NCCH₃), 1.68 ppm (s, 15H; C₅(CH₃)₅); ¹³C NMR (100.6 MHz, CDCl₃, 298 K): δ = 150.2, 146.6, 135.2, 134.4, 127.4, 123.6, 121.0, 119.1 (CH₃CN), 89.8, 67.2, 44.7, 9.0 ppm (CH₃CN); HRMS (EI⁺): *m/z*: calcd. for C₁₈H₂₃Ir⁺: 448.1616 (–CH₃CN/PF₆, [M]⁺); found: 448.1617; elemen-

tal analysis calcd (%) for $C_{20}H_{28}F_6N_2PIr$: C 37.91, H 4.45, N 4.42; found: C 38.64, H 4.54, N 3.99.

[Ir(η^5 -C₅Me₅)(C₆H₄-2-CH₂N(CH₃)₂)(NCCH₃)](PF₆) (4): Complex **4** was obtained as a yellowish powder (212 mg, 0.33 mmol, 82%) by using *N,N*-dimethylbenzylamine (54 mg). ¹H NMR (400.0 MHz, CDCl₃, 298 K): δ = 7.43 (d, ³J_{H-H} = 7.6 Hz, 1H; Ph-H), 7.13 (d, ³J_{H-H} = 6.8 Hz, 1H; Ph-H), 7.05 (t, ³J_{H-H} = 6.4 Hz, 1H; Ph-H), 7.00 (t, ³J_{H-H} = 7.2 Hz, 1H; Ph-H), 3.79 (s, 2H; CH₂), 2.94 (brs, 6H; NC(CH₃)₂), 2.55 (brs, 3H; NCCH₃), 1.67 ppm (s, 15H; C₅(CH₃)₅); ¹³C NMR (100.6 MHz, CDCl₃, 298 K): δ = 149.3, 146.7, 134.7, 127.4, 123.8, 122.4, 120.1 (CH₃CN), 90.7, 76.2, 57.5, 9.0 ppm (CH₃CN); HRMS (EI+): *m/z*: calcd for C₁₉H₂₇IrN⁺: 462.1773 (–CH₃CN/PF₆, [M]⁺); found: 462.1751.

[Ir(η^5 -C₅Me₅)(C₆H₄-2-CHNCH₃)(NCCH₃)](PF₆) (5): Complex **5** was obtained as a yellow powder (227 mg, 0.36 mmol, 91%) by using *N*-benzylidenemethylamine (48 mg). ¹H NMR (400.0 MHz, CDCl₃, 298 K): δ = 8.37 (s, 1H; CH), 7.69 (d, ³J_{H-H} = 7.6 Hz, 1H; Ph-H), 7.58 (d, ³J_{H-H} = 7.6 Hz, 1H; Ph-H), 7.21 (t, ³J_{H-H} = 9.4 Hz, 1H; Ph-H), 7.11 (t, ³J_{H-H} = 7.2 Hz, 1H; Ph-H), 3.94 (s, 3H; CH₃), 2.37 (s, 3H; NCCH₃), 1.77 ppm (s, 15H; C₅(CH₃)₅); ¹³C NMR (100.6 MHz, CDCl₃, 298 K): δ = 178.4, 161.7, 146.8, 139.1, 134.4, 132, 129.6, 128.9, 128.7, 123.5, 118.9 (CH₃CN), 91.0, 51.2, 8.8 ppm (CH₃CN); HRMS (EI+): *m/z*: calcd for C₁₈H₂₃IrN⁺: 446.1460 (–CH₃CN/PF₆, [M]⁺); found: 446.1455; elemental analysis calcd (%) for C₂₀H₂₆F₆N₂PIr: C 38.03, H 4.15, N 4.44; found: C 38.04, H 4.24, N 4.26.

[Ir(η^5 -C₅Me₅)(C₆H₄-2-C₃H₅N₂)(NCCH₃)](PF₆) (6): Complex **6** (237 mg, 0.36 mmol, 91%) was obtained as a yellowish powder by using 2-phenyl-2-imidazoline (59 mg). ¹H NMR (400.0 MHz, CDCl₃, 298 K): δ = 7.67 (d, ³J_{H-H} = 7.6 Hz, 1H; Ph-H), 7.33 (d, ³J_{H-H} = 7.6 Hz, 1H; Ph-H), 7.20 (t, ³J_{H-H} = 7.4 Hz, 1H; Ph-H), 7.07 (t, ³J_{H-H} = 7.6 Hz, 1H; Ph-H), 5.91 (s, 1H; NH), 3.97 (s, 4H; (CH₂)₂), 2.33 (s, 3H; NCCH₃), 1.78 ppm (s, 15H; C₅(CH₃)₅); ¹³C NMR (100.6 MHz, CDCl₃, 298 K): δ = 177.7, 157.3, 135.3, 134.8, 131.8, 125.5, 123.2, 117.5 (CH₃CN), 89.8, 51.8, 45.9, 9.2 ppm (CH₃CN); HRMS (EI+): *m/z*: calcd for C₁₉H₂₄IrN₂⁺: 473.1563 (–CH₃CN/PF₆, [M]⁺); found: 473.1542; elemental analysis calcd (%) for C₂₁H₂₇F₆N₃PIr: C 38.29, H 4.13, N 6.38; found: C 37.93, H 4.07, N 6.18.

[Ir(η^5 -C₅Me₅)(C₆H₄-2-C₃H₅N₂)(NCCH₃)](PF₆) (7): Complex **7** was obtained as a yellowish powder (249 mg, 0.38 mmol, 95%) by using 2-phenylimidazole (58 mg). ¹H NMR (400.0 MHz, CDCl₃, 298 K): δ = 10.55 (s, 1H; NH), 7.65 (d, ³J_{H-H} = 7.6 Hz, 1H; Ph-H), 7.56 (d, ³J_{H-H} = 7.2 Hz, 1H; Ph-H), 7.07 (m, 4H), 2.24 (s, 3H; NCCH₃), 1.74 ppm (s, 15H; C₅(CH₃)₅); ¹³C NMR (100.6 MHz, CDCl₃, 298 K): δ = 158.6, 152.9, 135.5, 135.0, 129.9, 123.8, 122.2, 118.2 (CH₃CN), 89.9, 8.9 ppm (CH₃CN); HRMS (EI+): *m/z*: calcd for C₁₉H₂₂IrN₂⁺: 471.1412 (–CH₃CN/PF₆, [M]⁺); found: 471.1409.

[Ir(η^5 -C₅Me₅)(C₆H₄-2-C₃H₅NO)(NCCH₃)](PF₆) (8): Complex **8** was obtained as a yellowish powder (171 mg, 0.26 mmol, 65%) by using 2-phenyloxazoline (58 mg). ¹H NMR (400.0 MHz, CDCl₃, 298 K): δ = 7.70 (d, 1H, ³J_{H-H} = 7.5 Hz; Ph-H), 7.47 (d, ³J_{H-H} = 7.3 Hz, 1H; Ph-H), 7.29 (t, ³J_{H-H} = 7.3 Hz, 1H; Ph-H), 7.13 (t, ³J_{H-H} = 7.8 Hz, 1H; Ph-H), 5.03 (m, 1H; CH₂), 4.89 (m, 1H; CH₂), 4.29 (m, 1H; CH₂), 4.04 (m, 1H; CH₂), 2.41 (s, 3H; NCCH₃), 1.81 ppm (s, 15H; C₅(CH₃)₅); ¹³C NMR (100.6 MHz, CDCl₃, 298 K): δ = 177.5, 153.4, 131.6, 129.4, 127.4, 123.3, 119.4, 117.2, 86.3, 68.7, 47.2, 5.5 ppm; elemental analysis calcd (%) for C₂₁H₂₆F₆N₂OPIr: C 38.24, H 3.97, N 4.25; found: C 38.88, H 4.03, N 4.08. *Crystal data for 8*: C₂₁H₂₆F₆IrN₂O; *M_r* = 659.53; monoclinic; space group *P*2₁/*n*; *a* = 12.7656(13), *b* = 13.8437(14), *c* = 13.4841(14) Å; β = 103.1777(13)°; *V* = 2320.2(4) Å³; *Z* = 4; *D_x* = 1.888 g cm^{–3}; *F*(000) = 1280; μ = 58.87 cm^{–1}; λ (MoK α) = 0.71073 Å; *T* = 100(1) K; 17885 reflections measured; *GoF* = 1.064, *wR*(*F*²) = 0.0751 for 4910 unique reflections and 295 parameters, and *R*(*F*) = 0.0308 for 4151 reflections obeying *F_o* ≥ 4.0 σ (*F_o*) criterion of observability.

Typical procedure for catalytic racemisation of alcohols: In a thoroughly flame-dried Schlenk flask under an atmosphere of nitrogen, catalyst (37.5 μ mol) and KO^tBu (41.2 μ mol) were dissolved in freshly distilled toluene (2.4 mL), after which chiral alcohol (0.75 mmol) was added. The reaction was monitored by periodically taking 0.1 mL aliquots from the mixture, filtering them over silica gel (eluent: Et₂O) and analysing the resulting samples by chiral GC. For the reactions performed in the presence of water: in a typical experiment, in a thoroughly flame-dried

Schlenk flask under an atmosphere of nitrogen, **3** (6.3 mg, 10 μ mol) and KO^tBu (1.3 mg, 12 μ mol) were dissolved in freshly distilled toluene (3 mL), after which the mixture was stirred for 15 min at RT. The resulting solution was slowly transferred by syringe into another Schlenk tube containing water (3 mL) and a chiral alcohol (1200 μ mol). Care was taken not to disturb phase separation, since this resulted in deactivation of the catalyst. The reaction was monitored by periodically taking 0.1 mL aliquots from the mixture, filtering them over silica gel (eluent: Et₂O) and analysing the resulting samples by chiral GC. Chirasil-Dex CB column (25 m × 0.25 mm × 0.25 μ m), gas vector: helium, flow = 1 mL min^{–1}, injector: 250 °C, program: 100 °C for 3 min, 120 °C (15 °C min^{–1}) for 15 min, 140 °C (15 °C min^{–1}) for 15 min, 100 °C (15 °C min^{–1}): 1-phenylethanol (**S1**): *t*_(R) = 12.8, *t*_(S) = 13.7 min; program: 100 °C for 5 min, 160 °C (12 °C min^{–1}) for 10 min, 100 °C (10 °C min^{–1}): 1-(4-fluorophenyl)ethanol (**S3**): *t*_(R) = 10.5, *t*_(S) = 10.8 min; program: isotherm 60 °C: 2-butanol (**S7**): *t*_(S) = 11.5, *t*_(R) = 13.1 min; program: isotherm 80 °C, 2-hexanol (**S8**): *t*_(S) = 12.7, *t*_(R) = 15.5 min; GTA column (30 m × 0.25 mm × 0.25 μ m), gas vector: helium, flow = 1 mL min^{–1}, injector 250 °C, program: 50 °C, for 3 min, 95 °C (10 °C min^{–1}) for 10 min, 125 °C (10 °C min^{–1}) for 20 min, 50 °C (10 °C min^{–1}): 2-chloro-1-phenylethanol (**S2**): *t*_(R) = 12.8, *t*_(S) = 13.7 min; program: isotherm 100 °C: 1-phenylbutanol (**S4**): *t*_(R) = 15.9, *t*_(S) = 16.4 min; HPLC, OD-H column, hexane/isopropanol 95:5, flow = 0.5 mL min^{–1}: 1-(2-naphthyl)ethanol (**S5**): *t*_(S) = 28.6, *t*_(R) = 29.8 min; OD-H column (25 cm), hexane/isopropanol 98:2, flow = 0.5 mL min^{–1}: 1-indanol (**S6**): *t*_(S) = 30.4, *t*_(R) = 34.2 min.

Typical procedure for catalytic racemisation of amines: In a thoroughly flame-dried Schlenk flask under a nitrogen atmosphere, amine (0.75 mmol) was added to a solution of iridacycle (0.015 mmol, 2 mol %) and dodecane (100 μ L) in dry and degassed toluene (3 mL) at the desired temperature. The reaction mixture was then stirred at this temperature. For GC analysis, samples were taken (100 μ L), filtered over silica gel (eluent: Et₂O) and diluted in dichloromethane (1.0 mL) after adding 2 drops of triethylamine and acetic anhydride and were analysed by chiral GC analysis. CP Chirasil-Dex CB column (25 m × 0.25 mm × 0.25 μ m), gas vector: helium, flow: 1 mL min^{–1}, injector: 250 °C, program: 125 °C for 4 min, 140 °C (3 °C min^{–1}), 180 °C (10 °C min^{–1}) for 30 min, 125 °C (10 °C min^{–1}): acylated α -methylbenzylamine (**S9**): *t*_(S) = 12.3, *t*_(R) = 12.5 min; acylated α ,*N*-dimethylbenzylamine (**S10**): *t*_(S) = 12.8, *t*_(R) = 12.9 min; acylated *N*-benzyl- α -methylbenzylamine (**S11**): *t*_(S) = 33.4, *t*_(R) = 33.9 min; acylated aminoindane (**S13**): *t*_(S) = 16.0, *t*_(R) = 16.3 min; acylated 1,2,3,4-tetrahydronaphthylamine (**S14**): *t*_(S) = 18.8, *t*_(R) = 19.4 min; program: 95 °C for 15 min, 180 °C (5 °C min^{–1}) for 10 min, 95 °C (10 °C min^{–1}): 1-methyltetrahydroquinoline (**S12**): *t*_(S) = 25.7, *t*_(R) = 26.0 min; HPLC, OD-H column (25 cm), hexane/isopropanol 99.8:0.2, flow = 1.0 mL min^{–1}: *N,N*, α -trimethylbenzylamine (**S15**): *t*_(R) = 5.4, *t*_(S) = 6.2 min.

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