Stereoselectivity in the mass-spectral fragmentation of palladium phosphinamine complexes

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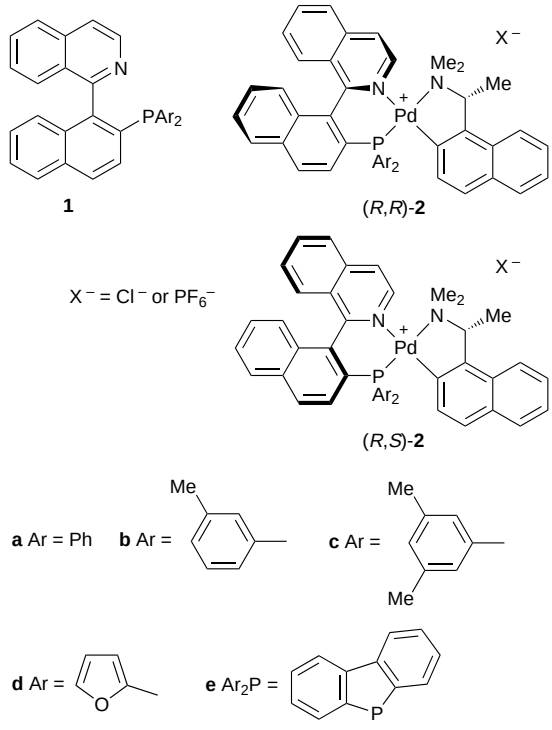
The diastereoisomers of cyclopalladated 1-naphthyldimethylethylamine complexes of several phosphinoarylisoquinolines demonstrate distinct fragmentation in their electrospray MS, diagnostic of the ligand enantiomer.

In previous work we have described the synthesis and resolution of a class of P–N chelating ligands based on 2-aza-1,1′-binaphthyl, the parent being **1a**.[1] These P–N chelates have proved useful for catalytic hydroboration and for allylic alkylation and considerable structure variation in the ligand is afforded by minor synthetic variations.[2] The chloropalladium complex derived (*R*)- or (*S*)-*N*,*N*-dimethyl-1-naphthylethylamine[3] proved to be uniquely effective for resolution of the racemic ligand, and this was rationalised in terms of an enforced conformational rigidity in the chelate ring of the complexed resolving agent.[4]



With a number of the resolution intermediates isolated in pure state as chloride or hexafluorophosphate salts, we were interested in making fuller spectroscopic comparisons. A difference became apparent on comparing electrospray MS of the diastereomeric pairs of the parent (*R*,*R*)-**2a** and (*R*,*S*)-**2a** at a standard cone voltage of 55 V. For the (*R*,*R*)-diastereomeric salt, the parent peak of the cation is evident, and a fragment $[LPdH]^+$ where the naphthylamine entity has been lost is also present with around twice the intensity of the parent peak. For the (*R*,*S*)-diastereomer, the same two peaks are observed but now the parent peak is about twice the intensity of the fragment peak. This pattern is repeated with related complexes at the same cone voltage, and under these conditions the spectrum is clean. More profound fragmentation to $[Ar_2PPd]^+$ occurs above 90 V.

In order to obtain more systematic information, three pairs of complexes of known configuration were subjected to electrospray MS over a range of cone voltages where both $[M^+]$ and $[M - 197]^+$ were evident, and the results are shown in Fig. 1. For **2a**, the parent compounds in the series, it can be seen that fragmentation is more pronounced for the (*R*,*R*)-enantiomer than for the (*R*,*S*)-enantiomer across the range of cone voltages [Fig. 1(*a*)]. The diastereomers of the phenanthridine analogue **3** behave quite similarly [Fig. 1(*b*)], although here the counter ion is Cl^- for the (*R*,*R*)-isomer and PF_6^- for the (*R*,*S*)-isomer.[5] For the phenylethylamine analogue **4** [Fig. 1(*c*)], where both complexes are PF_6^- salts, it can be seen that the (*R*,*S*)-diastereomer fragments to a lesser degree than does the (*R*,*R*)-diastereomer.† However the difference is much smaller here; the ease of fragmentation is comparable for all the (*R*,*S*)-diastereomers in the series but the (*R*,*R*)-diastereomer of **3** is

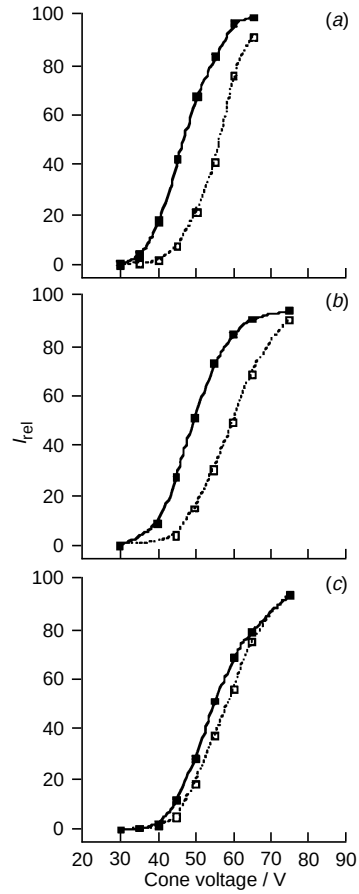
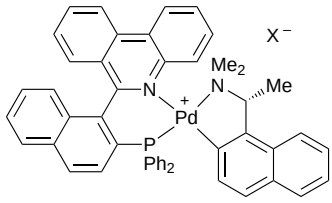
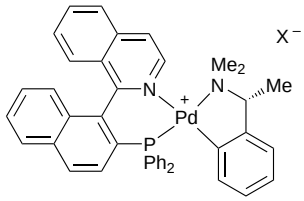


Fig. 1 Relative signal intensity I_{rel} *vs*. cone voltage for complexes **2a** (*a*), **3** (*b*) and **4** (*c*); intensity expressed as $(M - 197)^+/[M^+ + (M - 197)^+]$ for the ^{106}Pd isotopomer. The upper trace is the (*R*,*R*)-diastereomer (■) and the lower trace the (*R*,*S*)-diastereomer (□).



(*R*,*R*)- or (*R*,*S*)-**3**

$X^- = Cl^-$ or PF_6^-



(*R*,*R*)- or (*R*,*S*)-**4**

more stable to ESI cone voltage fragmentation than the other (*R*,*R*)-complexes.

A series of related ligands **1b–e** have been prepared in order to elucidate aryl substituent effects on asymmetric catalysis.[6] The resolution protocol was successful in separating enantiomers of each ligand, but the order of crystallisation was not predictable and in some cases the PF_6^- salt was formed but in others the Cl^- salt was isolated. Whilst it was possible to infer the absolute configuration in other cases by an accumulation of evidence (sign of optical rotation, sense of rhodium catalytic asymmetric hydroboration[7]) the furylphosphine **1d** proved anomalous. The (+)-isomer gave closely similar results in rhodium-catalysed asymmetric hydroboration to the (*R*)-(+)-isomer of **1a**, but the opposite hand of secondary alcohol was formed, indicating the (*S*)-(+) configuration for **1d**. This was confirmed by comparative CD spectra of (*S*)-(−)-**1a** and (−)-**1d** in $CHCl_3$ which are similar but mirror-related. It was observed that all the four pairs of diastereomeric complexes **2b–e** showed clear-cut behaviour in their electrospray mass spectra of 55 V; one of the pair was dominated by the parent M^+ and the other by the fragment $[M - 197]^+$. In each case it was the compound inferred to be the (*R*,*S*)-diastereomer which showed the strong parent peak and correspondingly the compound inferred to be the (*R*,*R*)-diastereomer which showed the strong fragment (Fig. 2). Hence the electrospray MS provides a simple and general method for defining the absolute configuration of the ligand. This is consistent with our earlier suggestions that the success of the palladium–naphthylamine resolving agent is due to enforced rigidity in the resolution complexes which specifically destabilises one diastereomer through unfavourable steric interactions.[4] Although these examples relate to P–N chelate ligands, some preliminary observations have been made which indicate that chiral diphosphines exhibit similar behaviour.[8]

The application of mass spectrometry to stereochemical problems is uncommon, although there are established cases where diastereomers can be identified from differences in their fragmentation patterns. For example, collision-induced dissociation is capable of defining ring-junction stereochemistry where that is the site of a retro-Diels–Alder reaction.[9] Electrospray MS in tandem with cone-voltage CID has been used to distinguish between C_2-epimeric pairs of ammine–nickel glycoside complexes.[10] The present case provides a simple method for direct assay of the configuration of a family of ligands useful in asymmetric catalysis, which may have more general applicability.

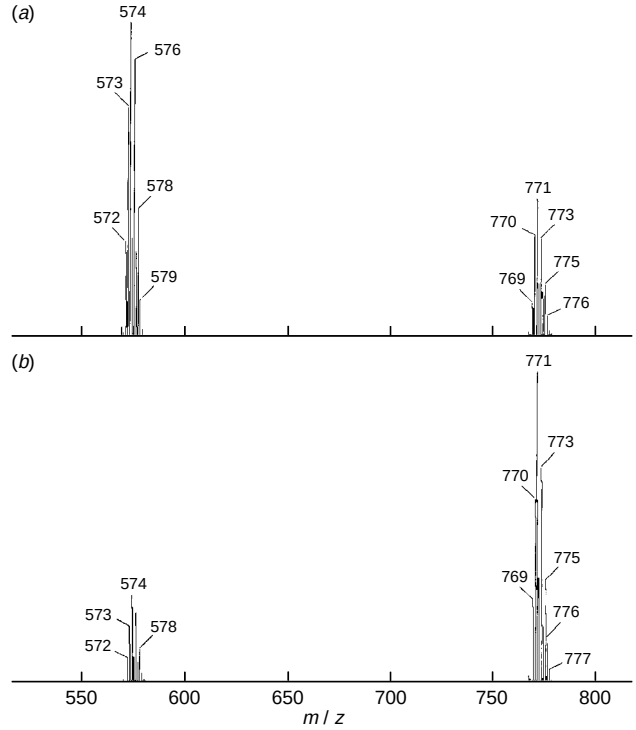


Fig. 2 The electrospray mass spectra of (*a*) the (*R*,*R*) and (*b*) the (*R*,*S*) isomers of complex **2b** taken at a cone voltage of 55 V from a *ca.* 1% solution in MeCN–MeOH

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Footnotes and References

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† In this case the (*S*)-enantiomer of the resolving agent was used, but the chirality is reversed in the discussion for consistency.

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