

A widely applicable concept for predictable induction of preferred configuration in C_3 -symmetric systems†

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Starting from a single chiral platform a widely applicable concept to introduce the preferred configuration of octahedral and tetrahedral centres in C_3 -symmetric systems is described.

In recent years, chiral systems showing C_3 symmetry have created much interest and found application in several areas, including molecular receptors,¹ dendrimers,² organometallic ligands^{1k,3} and asymmetric catalysis.^{1k,4} C_3 -symmetric tripodal ligands, which in octahedral centres render the remaining three coordination sites identical, have a major contribution to make to asymmetric catalysis.^{1k}

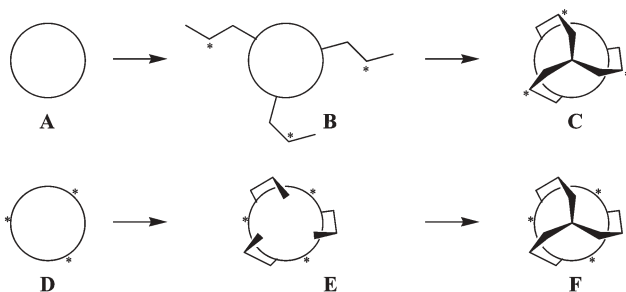
The formation of a C_3 -symmetric centre, especially one with a predetermined configuration (C in Scheme 1), usually starts from tripodal systems (B) assembled from an achiral platform or an achiral centre and three chiral arms. To our knowledge, there is only one case where a scaffold (E) assembled from a chiral platform and three achiral arms predetermines the configuration at a C_3 -symmetric centre to be formed (F in Scheme 1), namely enterobactin, where the corresponding Δ -Fe(III) complex is formed stereoselectively.⁵ However, the energy difference between the Λ - and the Δ -isomer of about 2.1 kJ mol⁻¹ is low,⁶ which may be explained by the high flexibility of the lactone platform. In our opinion, it is therefore impossible to make any predictions about the configuration when the centre and/or the arms of this system are varied.

Nevertheless, the predictable induction of the preferred configuration in C_3 -symmetric systems by a chiral platform is of great interest. This concept would be of a very general applicability because starting from a single platform (D) (which carries the complete chiral information) one would only have to attach achiral

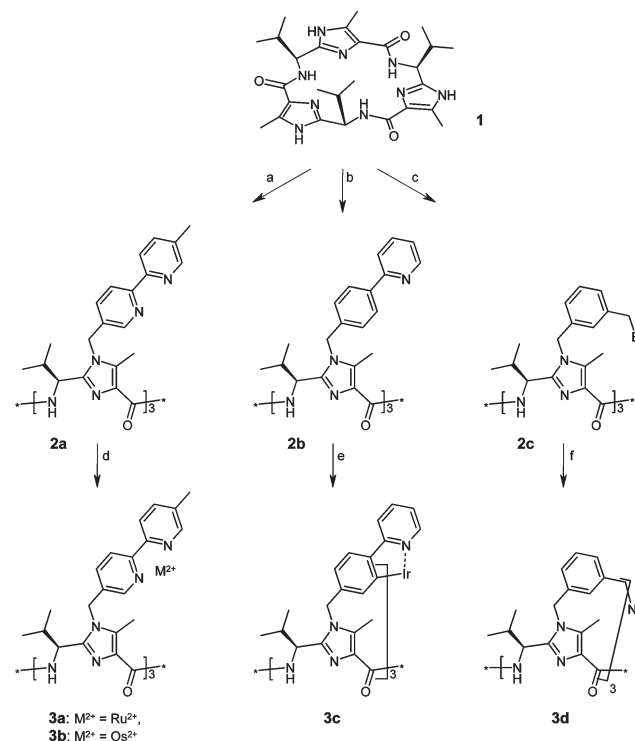
arms to it (E). The fixation of the arms on a centre would then predetermine the configuration of the latter (F).

Recently, we synthesized an imidazole platform (1) to which three arms can be attached by simple alkylation reactions.⁷ The X-ray structure of a substituted platform shows that due to the chirality of the platform the arms are oriented opposite to the isopropyl groups of the adjacent α -C-atoms and moreover do not point perpendicularly downward, but are arranged in a triple helix-like structure like E in Scheme 1.⁷ The preorganisation of the arms enabled us to suppose that it should be possible to realize the above-described concept, *i.e.* a predictable induction of preferred configuration in C_3 -symmetric systems, by using the said imidazole platform.

To verify this hypothesis, we reacted the tris(bipyridine) platform 2a⁷ with ruthenium(II)⁸ and osmium(II)⁹ ions (Scheme 2). From the hereby formed octahedral complexes 3a and 3b only one diastereomer could be isolated. Our prediction, which was based



Scheme 1



Scheme 2 Reagents and conditions: (a) C₁₁H₉N₂CH₂Br, K₂CO₃, CH₃CN, Δ , 65%; (b) C₁₁H₈NCH₂Br, K₂CO₃, CH₃CN, Δ , 77%; (c) *m*-(BrH₂C)C₆H₄(CH₂Br), K₂CO₃, CH₃CN, Δ , 55%; (d) Ru(DMSO)₄Cl₂, EtOH, Δ , 55% for 3a and (NH₄)₂OsCl₆, ethylene glycol, Δ , 50% for 3b; (e) Ir(acac)₃, ethylene glycol, Δ , 49%; (f) NH₃, K₂CO₃, CH₃CN, Δ , 90%.

† Electronic supplementary information (ESI) available: experimental preparations for 2b, 2c, and 3a–d. See <http://www.rsc.org/suppdata/cc/b5/b502158h/>

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on the orientation of the arms into one direction in space, was that the Λ -isomers had been formed. The X-ray structure of the isolated ruthenium complex **3a** (Fig. 1) proved that the prediction had been correct. Of particular interest is the fact that the newly-formed ruthenium centre is more than 7 Å away from the configuration-determining α -carbon atoms of the platform. Moreover, DFT-based calculations were carried out in order to determine the extent of stereoselectivity by the chiral platform. The full geometry optimization computations were performed for the Λ - and the Δ -complexes of **3a** and **3b** applying the DFT-B3LYP^{10,11} method and 3-21G*¹² or LanL2DZ¹³ basis set. The energy difference between the stereoisomers is 105.8 kJ mol⁻¹ (B3LYP/3-21G*) or 139.2 kJ mol⁻¹ (B3LYP/LanL2DZ) for **3a** and 144.7 kJ mol⁻¹ (B3LYP/LanL2DZ) for **3b**, in favour of the clearly preferred Λ -isomers. The very high energy difference explains why only the Λ -isomers are formed. In our opinion, this high difference is due to the strong repulsive steric interactions between the methyl groups on the imidazole rings and the bipyridine arms (Fig. 1).

To verify the general applicability of the concept, we further investigated whether the predictable induction of the preferred configuration can be realized with other arms and centres. In the first case, tolyl pyridine arms were attached to the scaffold **1** and the resulting platform **2b** was reacted with Ir(acac)₃¹⁴ to give the octahedral iridium complex **3c** (Scheme 2). In the second case, the platform **1** was converted into the tribromide **2c**, which was subsequently treated with ammonia to give the tertiary amine **3d**.

Here too, in both cases, only one diastereomer could be isolated. The X-ray structures of these diastereomers show that both correspond to the predicted configuration (Fig. 2). The isolated octahedral iridium complex **3c** proved to be the Λ -isomer, whereas the isolated tetrahedral tertiary amine **3d** forms a right-handed rotation, as shown in Fig. 2 (right view).

To investigate the extent of stereoinduction by the chiral platform for a tetrahedral centre, the energy of the isolated amine **3d** and of the isomer with inverse configuration at the nitrogen atom was calculated by applying the DFT method. The energy difference between the two configuration isomers is 47.2 kJ mol⁻¹ (B3LYP/3-21G*) or 21.6 kJ mol⁻¹ (B3LYP/LanL2DZ), in favour of the isolated amine **3d**.

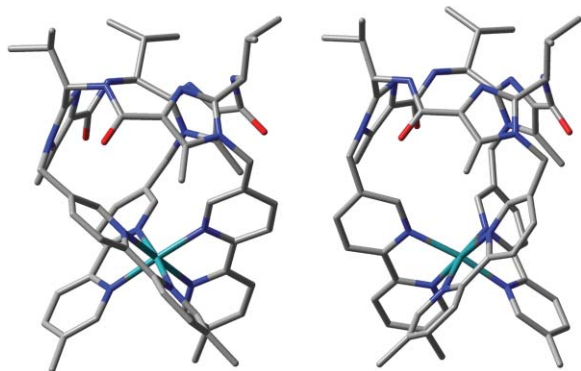


Fig. 1 Crystal structure of the isolated Λ -isomer of **3a** (left) and calculated molecular structure of the Δ -isomer of **3a** (right). View perpendicular to the molecular three-fold axis; all hydrogen atoms and in the case of Λ -**3a** the two PF₆⁻ ions (one of them was found to be disordered) have been omitted for clarity.

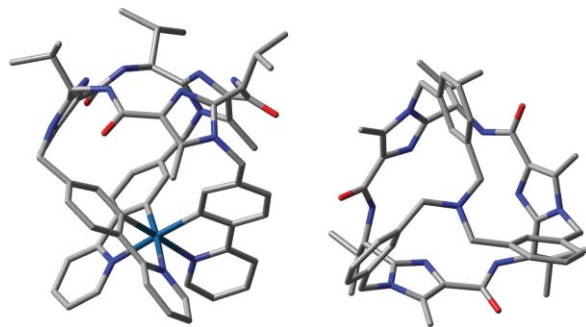


Fig. 2 Crystal structures of **3c** (left, view perpendicular to the molecular three-fold axis) and **3d** (right, view along the molecular three-fold axis). All hydrogen atoms and some solvent molecules have been omitted for clarity.

In summary, we describe for the first time a predictable induction of the preferred configuration by a platform, *via* three arms, to a newly-formed C₃-symmetric centre. The presented concept is of a very general applicability because, starting from a single platform (which carries the complete chiral information), different achiral arms and centres can be used. For the future we plan to predictably induce the configuration at a C₃-symmetric octahedral or tetrahedral catalytic centre over a wide distance, *e.g.* over seven and more bonds.†

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Notes and references

† *Crystal data:* for C₆₃H₆₉N₁₅O₃Ru·2PF₆ (**3a**): *M* = 1475.34, orange crystal (irregular), dimensions 0.17 × 0.10 × 0.09 mm³, crystal system cubic, space group *P*2₁3, *Z* = 4, *a* = 18.999(1) Å, *V* = 6858.1(6) Å³, ρ = 1.429 g cm⁻³, *T* = 100(2) K, $\theta_{\max}$ = 20.79°, radiation Mo K α , λ = 0.71073 Å, μ = 0.36 mm⁻¹, 36787 reflections measured, 2388 unique [*R*(int) = 0.097], 2311 observed [*I* > 2 σ (*I*)], *R*₁(*F*) = 0.044, *wR*(*F*²) = 0.102, residual electron density -0.32 to 0.67 e Å⁻³.

For C₆₃H₆₃IrN₁₂O₃·7.8H₂O (**3c**): *M* = 1368.98, yellow crystal (irregular), dimensions 0.16 × 0.12 × 0.04 mm³, crystal system rhombohedral, space group *R*3, *Z* = 3, *a* = 16.214(1) Å, *c* = 22.071(2) Å, *V* = 5024.7(7) Å³, ρ = 1.357 g cm⁻³, *T* = 100(2) K, $\theta_{\max}$ = 28.32°, radiation Mo K α , λ = 0.71073 Å, μ = 2.06 mm⁻¹, 17200 reflections measured, 5546 unique [*R*(int) = 0.052], 5518 observed [*I* > 2 σ (*I*)], *R*₁(*F*) = 0.047, *wR*(*F*²) = 0.111, residual electron density -0.73 to 2.72 e Å⁻³.

For C₅₁H₆₀N₁₀O₃·2CH₂Cl₂ (**3d**): *M* = 1030.94, colorless crystal (polyhedron), dimensions 0.28 × 0.24 × 0.12 mm³, crystal system monoclinic, space group *P*2₁, *Z* = 2, *a* = 13.0619(2) Å, *b* = 15.4301(3) Å, *c* = 13.6751(1) Å, β = 92.0570(10)°, *V* = 2754.39(7) Å³, ρ = 1.243 g cm⁻³, *T* = 200(2) K, $\theta_{\max}$ = 21.50°, radiation Mo K α , λ = 0.71073 Å, μ = 0.26 mm⁻¹, 16688 reflections measured, 6327 unique [*R*(int) = 0.097], 4978 observed [*I* > 2 σ (*I*)], *R*₁(*F*) = 0.060, *wR*(*F*²) = 0.149, residual electron density -0.58 to 0.92 e Å⁻³. CCDC 257958–257960. See <http://www.rsc.org/suppdata/cc/b5/b502158h/> for crystallographic data in CIF or other electronic format.

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