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## COMMUNICATION

## Step-wise induction, amplification and inversion of molecular chirality through the coordination of chiral diamines with Zn(II)bisporphyrin

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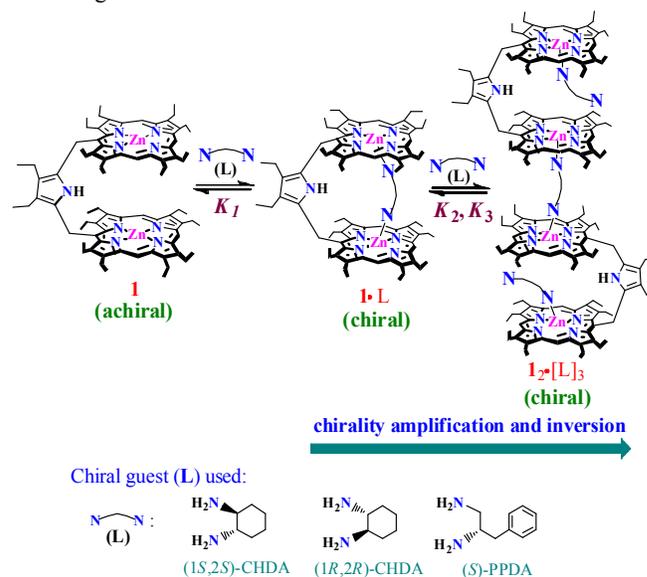
For the first time, a clear and unambiguous rationalization of chirality induction, inversion and subsequent amplification process has been demonstrated for the 1:1 sandwich and 2:3 host-guest supramolecular complexes consisting of Zn(II) bisporphyrin host and chiral diamines as guest that has so far remained the most outstanding issue for the chirogenic process.

Modulation of chirality contains chirality induction, amplification, reduction and inversion phenomena, which are important for understanding the asymmetry of various systems. Chirality induction in supra- and macromolecular systems, which are associated with chirality inversion due to conformational changes in intrinsically achiral components upon interactions with chiral guest ligands, are important topic to be looked into.<sup>1</sup> Porphyrins are of particular interest for detailed investigations for their interesting photophysical properties, versatile modification, great biological importance and wide applicability.<sup>1-7</sup> Upon formations of a chiral host-guest supramolecular complex between an achiral bismetalporphyrin derivative and a chiral guest, a bisignate CD curve (so-called exciton couplet) is observed in the porphyrin spectral region, which is diagnostic of the guest's absolute configuration.<sup>1</sup>

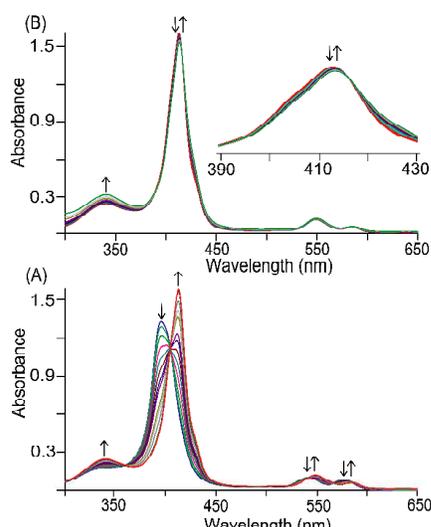
Stoichiometry controlled supramolecular chirality induction with bifunctional ligands are known to occur via stepwise 1:1 and 1:2 host-guest complexation mechanism.<sup>1-5,7</sup> However, no structural report is there so far which rationalize both the processes with the same host-guest system. In the present work, we investigate the effect of stoichiometry on the chirality induction process using highly flexible achiral Zn(II) bisporphyrin host with chiral diamine guests in the host-guest supramolecular complex. For the first time, a clear rationalization of chirality induction, inversion and amplification phenomena have been demonstrated during the formation of 1:1 sandwich and 2:3 host-guest supramolecular complexes which are supported by single crystal X-ray structures and DFT calculation.

Zn(II) bisporphyrin, **1**, has been synthesized following the reported procedure.<sup>8</sup> Upon addition of chiral diamines such as (1*S*,2*S*)-cyclohexane diamine, (1*S*,2*S*)-CHDA and (*S*)-phenylpropane diamine, (*S*)-PPDA into **1**, two stepwise UV-visible spectral changes were observed depending on the concentration of the guest ligand. For example, the addition of (1*S*,2*S*)-CHDA to the dichloromethane solution of **1**, results, at first, large red shifts of the Soret (from 395 to 412 nm) and Q

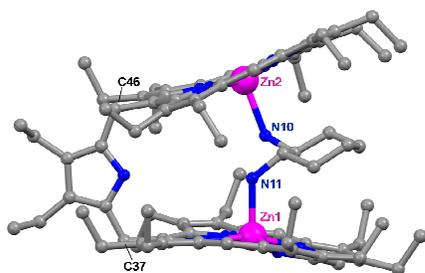
bands (from 542 to 549 and 577 to 585 nm) along with an increase in Soret band intensity (Fig. 1) due to the formation of 1:1 sandwich complex **1**•(1*S*,2*S*)-CHDA, which has been isolated in solid and structurally characterized. Upon further additions of (1*S*,2*S*)-CHDA, more red shifts of Soret (from 412 to 413 nm) and Q bands (from 549 to 550 and 585 to 586 nm) have been observed due to conversion of 1:1 sandwich to 2:3 host-guest oligomeric complex which has also been isolated in solid and structurally characterized. Similar changes in the UV-visible spectra of **1** in dichloromethane was also observed with (*S*)-PPDA due to the formations of **1**•(*S*)-PPDA and **1**<sub>2</sub>•[(*S*)-PPDA]<sub>3</sub>, respectively (Fig. S1). ESI-MS spectra reveals peak at *m/z* 1490.7858 which is assigned for [**1**•(*S*)-PPDA+H]<sup>+</sup> (Fig. S2), confirming the formation of 1:1 sandwich complex. In sharp contrast, monoamines such as (*S*)-2-aminobutane, (*R*)-1-phenethylamine and cyclohexylamine also bind with **1** but produce 1:2 host-guest complexes only (Figs S3-S5). Scheme 1 shows the complexes reported here along with the list of chiral diamine guests used here and their abbreviations.



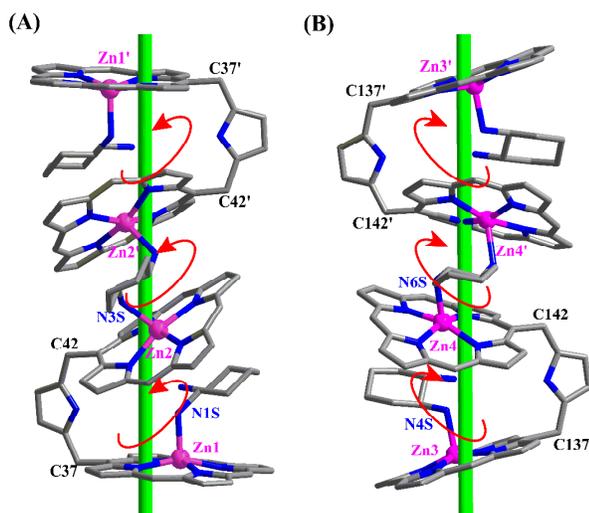
Scheme 1: Step-wise regulation of molecular chirality



**Fig. 1** UV-visible (in  $\text{CH}_2\text{Cl}_2$  at 295 K) spectral change of **1** (at  $5 \times 10^{-6}$  M) upon addition of (1*S*,2*S*)-CHDA as the host-guest molar ratio changes from (A) 1:0 to 1:10 and (B) 1:15 to 1:600. Inset shows the expanded Soret band region.



**Fig. 2** Molecular structure (at 100 K) of **1**•(1*S*,2*S*)-CHDA (H atoms have been omitted for clarity).



**Fig. 3** Molecular structures (at 100 K) of (A) molecule I (anticlockwise) and (B) molecule II (clockwise) component of  $\text{I}_2 \cdot [(1*S*,2*S*)-\text{CHDA}]_3$  (H atoms and ethyl groups have been omitted for clarity).

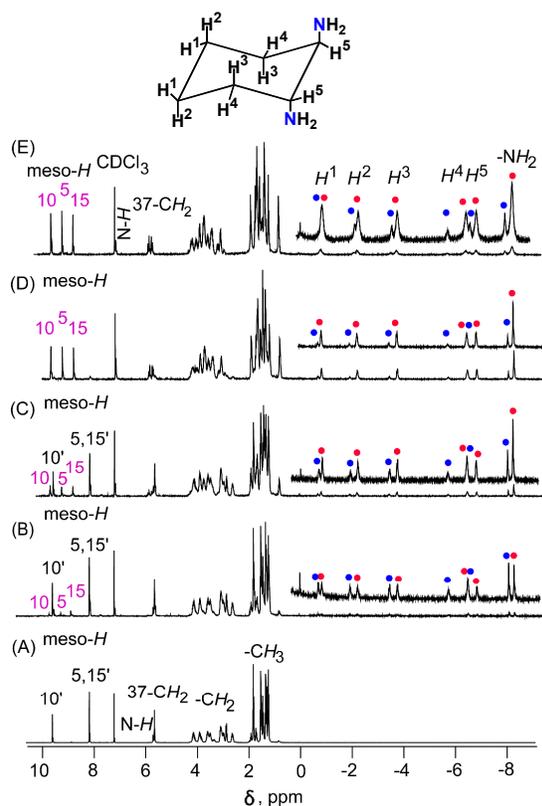
Dark purple square shaped crystals of **1**•(1*S*,2*S*)-CHDA are grown via slow diffusion of acetonitrile into the chloroform solution of the 1:1 mixture of **1** and (1*S*,2*S*)-CHDA at room temperature in air. The molecule crystallizes in the triclinic

crystal system with *P1* chiral space group (Table S1), a perspective view of the molecule and its packing are depicted in Figs 2 and S6, respectively. There are two molecules in the asymmetric unit which are also structurally different (Table S2). Cyclohexane ring is in chair conformation and lies parallel to the two porphyrin rings, thus allowing attractive CH- $\pi$  interactions between the ligand and the porphyrin moieties which further stabilize the 1:1 sandwich complex (Fig. S7). Interestingly, the induction of asymmetry information of the enantiomerically pure chiral guest to an achiral host is highly anticipated from the unidirectional screw observed in the bisporphyrin moiety in order to minimize the host-guest steric interactions. Because of the pre-organized binding sites of the (*S*) guest ligand, the two porphyrin rings are compelled to have stereospecific twist in a clockwise orientation around the pyrrole bridge, with a torsional angles  $\Phi$  (Zn1-C37-C46-Zn2) of 23.75° and 26.89° for molecules-I and II, respectively.

Needle shaped purple crystals of  $\text{I}_2 \cdot [(1*S*,2*S*)-\text{CHDA}]_3$  are grown via slow diffusion of acetonitrile into the chloroform solution of **1** and (1*S*,2*S*)-CHDA in 1: >10 molar ratio at room temperature in air. The molecule crystallizes in *P2* chiral space group, the structure is shown in Fig. 3 and packing in Fig. S8. (1*S*,2*S*)-CHDA ligand coordinate to one Zn-center inside the jaw of each bisporphyrin host (*endo*-form), followed by another (1*S*,2*S*)-CHDA ligand which binds as an *exo*-form and bridges two Zn(II) bisporphyrin to form 2:3 host-guest oligomer. Interestingly, the asymmetric unit contains two such bisporphyrin oligomers; one (molecule I) with anticlockwise twist around the pyrrole bridge which contains an intramolecular torsional angle of -4.72° (Zn1-C37-C42-Zn2) and intermolecular torsional angle (between two repetitive units) of -148.30° (C42-Zn2-Zn2'-C42') while other molecule (molecule II) have clockwise twist with intramolecular torsional angle of 3.61° (Zn3-C137-C142-Zn4) and intermolecular torsional angle of 147.08° (C142-Zn4-Zn4'-C142'). According to the projection of chiral ligand's two amino groups, there could have been unidirectional molecule of right-handed screw sense as observed in molecule II, however, opposite directional molecule (molecule I) is also apparent as evident in the X-ray crystallography. It is because ligand's accommodation in the left-handed screw (molecule I) is more suitable in order to minimize host-guest steric interactions which eventually transfer the chirality information from the enantiomeric guest to the achiral host (*vide infra*).

$^1\text{H}$  NMR spectra plays an important role in establishing structure of 1:1 *sandwich* and 2:3 oligomeric host-guest complex in solution. Fig. 4 shows the  $^1\text{H}$  NMR spectra (in  $\text{CDCl}_3$ ) resulting out of the titration between **1** and (1*S*,2*S*)-CHDA. Trace A shows the well resolved  $^1\text{H}$  NMR spectra of **1**, while traces B, C, D and E show the spectra generated after additions of 0.25, 0.5, 1.0, and 2.0 equivalent of (1*S*,2*S*)-CHDA, respectively. Most interesting feature is the large upfield shift of the guest ligand protons in the host-guest complex which generates two set of 6 resonances due to the presence of both 1:1 *sandwich* and 2:3 host-guest oligomer in solution (*vide infra*). In the 1:1 *sandwich* complex, (1*S*,2*S*)-CHDA protons resonate at -0.66 ( $\text{H}^1$ ), -1.89 ( $\text{H}^2$ ), -3.41 ( $\text{H}^3$ ), -5.72 ( $\text{H}^4$ ), -6.47 ( $\text{H}^5$ ) and -8.06 ( $\text{NH}_2$ ) ppm. In the 2:3 oligomeric host-guest complex, however, two (1*S*,2*S*)-CHDA bind inside the two bisporphyrin cavity, while another (1*S*,2*S*)-CHDA ligand

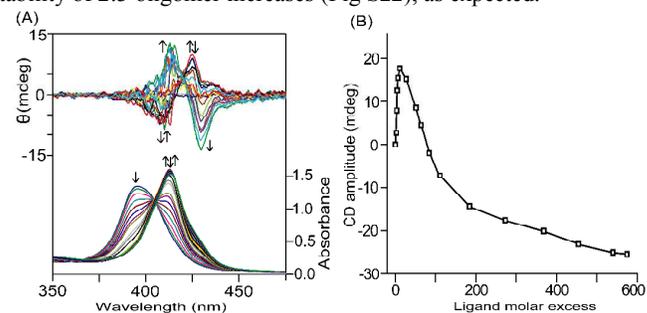
bridging two bisporphyrin units. As a result, guest ligand in oligomeric complex experiences stronger shielding effect compared to discrete 1:1 *sandwich* complex, resulting relatively larger upfield shifts of  $^1\text{H}$  NMR resonances at  $-0.80$  ( $\text{H}^1$ ),  $-2.18$  ( $\text{H}^2$ ),  $-3.72$  ( $\text{H}^3$ ),  $-6.47$  ( $\text{H}^4$ ),  $-6.84$  ( $\text{H}^5$ ) and  $-8.28$  ( $\text{NH}_2$ ) ppm. In contrast, the addition of cyclohexylamine produces only 1:2 host-guest complex that gives upfield-shifts of the guest protons also but to a smaller extent (Fig. S9). As can be seen in Fig. 4, 1:1 *sandwich* complex is produced in larger ratio at lower concentration of the guest ligand, while increasing the guest ligand concentration, the populations of 2:3 oligomer increases. The identical 5,15-*meso* protons are downfield shifted and split into two resonances at 8.84 and 9.28 ppm while 10-*meso* and NH protons are also shifted downfield due to the strong chiral environment generated by the stereospecific twisting of the porphyrin units in oligomer. Similar  $^1\text{H}$  NMR spectral changes are also observed when **1** is titrated with (*S*)-PPDA (Fig. S10). Complete assignments of the resonances of the guest protons have been made by the relative intensity of the signals and  $^1\text{H}$ - $^1\text{H}$  COSY (Figs. S11 and S12).



**Fig. 4**  $^1\text{H}$  NMR (at 295 K in  $\text{CDCl}_3$ ) spectral changes of **1** ( $\sim 10^{-3}$  M) upon gradual addition of (*1S,2S*)-CHDA as the host-guest molar ratio of (A) 1 : 0, (B) 1 : 0.25, (C) 1 : 0.5, (D) 1 : 1.0 and (E) 1 : 2.0. The ratio of **1**:(*1S,2S*)-CHDA (●) :  $1_2$ :(*1S,2S*)-CHDA $_3$  (●) are (B) 3:1, (C) 1.5:1, (D) 1.3:1, and (E) 1:1.2. Meso-*H* signals for unbound ( $10'$ ,  $5, 15'$ ) and bound ( $10$ ,  $5$ ,  $15$ ) bisporphyrin are shown separately. Inset shows the proton numbering scheme of (*1S,2S*)-CHDA.

The binding constants between **1** and chiral diamines in solution are determined by both UV-visible and CD spectroscopic titration methods using the HypSpec computer program (Protonic Software, U.K.).<sup>9</sup> Each Zn(II)bisporphyrin unit binds with the guest ligand in a 1:1 *sandwich* complex first which, upon

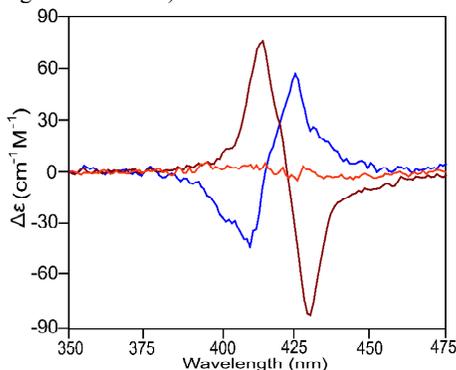
increasing guest concentration, converts to 1:2 host-guest complex that eventually transformed to more stable 2:3 oligomer (Scheme S1). Two sets of UV-visible titration data were analyzed considering three-step binding models<sup>10</sup> for 1:1 *sandwich*, 1:2 and 2:3 host-guest complexes with binding constants of  $K_1$ ,  $K_2$  and  $K_3$ , respectively. For complexation of **1** with (*1S,2S*)-CHDA, the values are found to be  $6.1 \pm 0.3 \times 10^5 \text{ M}^{-1}$ ,  $1.7 \pm 0.2 \times 10^4 \text{ M}^{-1}$  and  $1.4 \pm 0.2 \times 10^4 \text{ M}^{-1}$  (Fig. S13), respectively, while with (*S*)-PPDA, the values are  $8.2 \pm 0.2 \times 10^5 \text{ M}^{-1}$ ,  $3.2 \pm 0.1 \times 10^4 \text{ M}^{-1}$  and  $1.0 \pm 0.1 \times 10^4 \text{ M}^{-1}$  (Fig. S14). Similar binding constants are also obtained for the complexes using two set of CD titration data (Figs. S15 and S16). The relative population of the species has also been plotted in Fig. S13 in which the populations of the 1:1 *sandwich* and 2:3 oligomer are greater at lower and higher chiral diamine concentrations, respectively. 1:2 host-guest complexes, however, have been produced in between as an intermediate species. CD and UV-vis titration experiments have also been performed using higher concentration of **1** ( $\sim 5 \times 10^{-5}$  M), the stability of 2:3 oligomer increases (Fig S22), as expected.<sup>10</sup>



**Fig. 5** (A) CD and UV-visible spectral changes upon addition of (*1S,2S*)-CHDA to the  $\text{CH}_2\text{Cl}_2$  solution of **1** ( $5 \times 10^{-6}$  M) at 295 K as the host-guest molar ratio changes from 1:0 to 1:570. (B) CD amplitude change with substrate molar excess.

The interactions of the chiral diamine (*1S,2S*)-CHDA with **1** have also been investigated in details in dichloromethane at 295 K using CD spectroscopy. Similar to the observations found in the UV-visible spectra, there appear, in CD spectrum also, two spectral patterns at low and high ligand concentration regions associated with 1:1 *sandwich* and 2:3 host-guest complexes, respectively. Gradual addition of (*1S,2S*)-CHDA (upto 7 equivalent) into the dichloromethane solution of **1**, however, generates CD amplitude ( $A_{\text{cal}}$ ) of  $+105 \text{ M}^{-1} \text{ cm}^{-1}$  which is due to the formation of 1:1 *sandwich* complex (Fig. 5). Here, the pre-organized binding sites of the chiral (*S*) diamine have forced two porphyrin macrocycles to be oriented in a clockwise direction with the torsion angles of  $23.75^\circ$  and  $26.89^\circ$  observed in the X-ray structure for molecules I and II, respectively. With excess (*1S,2S*)-CHDA concentration (15 to 570 equivalent), however, the 1:1 *sandwich* complex eventually converted to 2:3 host-guest complex which displayed an enhanced CD couplet ( $A_{\text{cal}} = -168 \text{ M}^{-1} \text{ cm}^{-1}$ ) but with opposite sign (Fig. 6). Presence of both left-handed (molecule I) and right-handed (molecule II) helix as observed in the X-ray structure of the complex contribute to the CD amplitude to an unequal extent while left-handed conformer is more stable which eventually transfer the chirality information with negative first cotton effect in the 2:3 host-guest oligomer. Similar is the situation with (*1R,2R*)-CHDA also, however, the sign of the CD couplets for both 1:1 and 2:3 host-guest

complexes are just opposite (Fig. S17) to the respective signals observed for (1*S*,2*S*)-CHDA which suggest that the chirality is dictated solely by the stereographic projection of the chiral center. Both intra- and inter-molecular coupling are present in the 2:3 oligomeric host-guest complexes leading to larger CD intensity compared to 1:1 *sandwich* complex, which have only intramolecular coupling. Interaction of the bisporphyrin host **1** with (*S*)-PPDA guest in dichloromethane was also monitored by CD spectroscopy (Fig. S18) and Table S3 summarizes the spectral parameters for all the complexes reported here. CD spectra of **1**•(1*S*,2*S*)-CHDA and **1**<sub>2</sub>•[(1*S*,2*S*)-CHDA]<sub>3</sub> obtained from solid (using pure crystals in KBr matrix) and in dichloromethane solution at 295 K have similar spectral features; the solid state spectra is somehow broad and red shifted (Fig. S19). In contrast, enantiopure monoamines such as (*S*)-2-aminobutane and (*R*)-1-phenylethylamine produce 1:2 host-guest complex with **1** which, however, generate very weak chiroptical response (Figs S20 and S21).



**Fig. 6** CD spectra of **1** (red), **1**•(1*S*,2*S*)-CHDA (blue) and **1**<sub>2</sub>•[(1*S*, 2*S*)-CHDA]<sub>3</sub> (brown).

The oligomeric host-guest complex **1**<sub>2</sub>•[(1*S*, 2*S*)-CHDA]<sub>3</sub> contains two molecules in the asymmetric unit; one having clockwise and another having anticlockwise twist. Single point energy calculations on both clockwise and anticlockwise oligomers have been performed with the help of DFT method in which the oligomer having anticlockwise twist is found to be slightly more stable (by 2.8 kcal/mol) in dichloromethane and thus having more proportions as also obtained in the experiment. Geometry optimizations are also done on both clockwise and anticlockwise oligomers separately. The optimized structure of clockwise twisted oligomer shows intramolecular torsional angle of 17.29° and intermolecular torsional angle of 170.24° between two repeatative unit while anticlockwise twisted oligomer show intramolecular and intermolecular torsional angles of -14.1° and -168.9°, respectively, (Fig. S23 and Table S4).

In summary, the present work demonstrates a clear rationalization of the origin of chirality transfer from an optically active guest to an achiral host in a 1:1 and 2:3 host-guest supramolecular complex, for the first time. Pre-existing (*S*)-chirality of the chiral diamines has forced two porphyrin macrocycles to be oriented in a stereospecific clockwise orientation around the pyrrole bridge in order to minimize host-guest steric interactions which results positive CD couplet in the 1:1 *sandwich* complex. With excess guest ligand concentration, however, the 1:1 *sandwich* complex converted into 1:2 host-guest complex which eventually converts to 2:3 host-guest oligomer and displayed an enhanced CD couplet but with opposite sign. Although both left-handed (molecule I) and right-

handed (molecule II) helix are present in the asymmetric unit (X-ray structure) but left-handed conformer is more stable (and thus predominates) which eventually transfer the chirality information with overall negative CD couplet in the 2:3 host-guest oligomer. Both intra- and inter-molecular coupling are responsible for the highly enhanced CD couplet in the 2:3 oligomeric complexes as compared to 1:1 *sandwich* complexes which have only intramolecular coupling.

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## Notes and references

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<sup>†</sup> Electronic Supplementary Information (ESI) available: synthesis and characterization. Instrumentations, experimental details, spectroscopic characterizations, computational details, crystallographic data, DFT-optimized structures, Figs S1-S23, Scheme S1 and Tables S1-S4. CCDC 1023382 and 1023383 contain X-ray crystallographic details in CIF 70 format.

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