How Do They Know? Influencing the Relative Stereochemistry of the Complex Units of Dinuclear Triple-Stranded Helicate-Type Complexes

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Abstract: Dinuclear triple-stranded helicates or *meso*-helicates are formed by self-assembly of linear ligand strands with appropriate metal ions. Very often this self-assembly proceeds with high diastereoselectivity leading either to the helicate or the *meso*-helicate. The stereoselectivity of the self-assembly process can be influenced by different factors such as the rigidity of the ligand (→helicate), the number of methylene units in the alkyl spacers (even number of CH_2 units → helicate; odd number → *meso*-helicate), template effects, or chiral substituents.

Keywords: coordination compounds · helicates · *meso*-helicates · stereochemistry

Introduction

The interaction of two or more molecular moieties, each of which contains stereochemical information, plays a crucial role in the selectivity of self-assembly processes leading to stereochemically defined supramolecular structures. This means that the chiral units somehow have to communicate to influence the formation of a specific structure. A simple class of compounds in which the interaction of two different chiral units can easily be investigated are triple-stranded dinuclear coordination compounds: the helicates or *meso*-helicates.

The first triple-stranded helicate was structurally characterized in 1985 by Raymond and co-workers.[1, 2] It forms by self-assembly of three bis(1-hydroxy-2(1*H*)-pyridinone) ligands and two iron(III) ions. In the solid state it encapsulates a water molecule which by hydrogen bonding is fixed in the interior of the dinuclear complex. Both of the complex units were shown to possess the same configuration and therefore a chiral triple-helical complex was obtained in its racemic form.[3] Ten years later, in 1995, we described the first example for the alternative diastereoisomeric form of a dinuclear triple-stranded complex which we termed "*meso*-helicate"[4, 5] (in the meantime additionally the terms "side-by-side complex"[7] or "mesocate"[8] were introduced for this kind of coordination compound). In the helicates the ligands adopt a more linear "S"-type conformation in which they are more or less wrapped around the metal centers, while in the *meso*-helicates a "C"-type conformation of the ligand is observed.

It could be shown that the formation of the dinuclear complexes very often proceeds with high diastereoselectivity and that in the solid state as well as in solution only one of the two possible diastereoisomers is present (Figure 1).[7, 9]

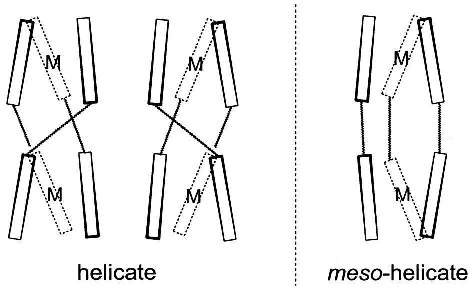

Figure 1. Schematic representation of the two enantiomeric forms of a dinuclear triple stranded helicate (left: ΔΔ; center: ΛΛ) and of the achiral *meso*-helicate (right: ΔΛ). In the helicates the ligands adopt an "S"-type geometry in the *meso*-helicate a "C"-type geometry.

Which influences control the high diastereoselectivity of the self-assembly processes of helicate-type coordination compounds? Or to put it in more simply: *How does one complex unit know which configuration the other one possesses?* This is the question which we address in this concept article. We will discuss different approaches to how the stereoselectivity of the formation of dinuclear complexes can be influenced and which problems arise by the interaction of different control mechanisms.

Control of the relative stereochemistry of two complex units by rigid ligands

The tetraanionic di(catechol) ligands $\mathbf{1}^{4-}$ [10–12] and $\mathbf{2}^{4-}$ [13] are very rigid ligand systems. In the ligands $\mathbf{1}^{4-}$ the rigidity is

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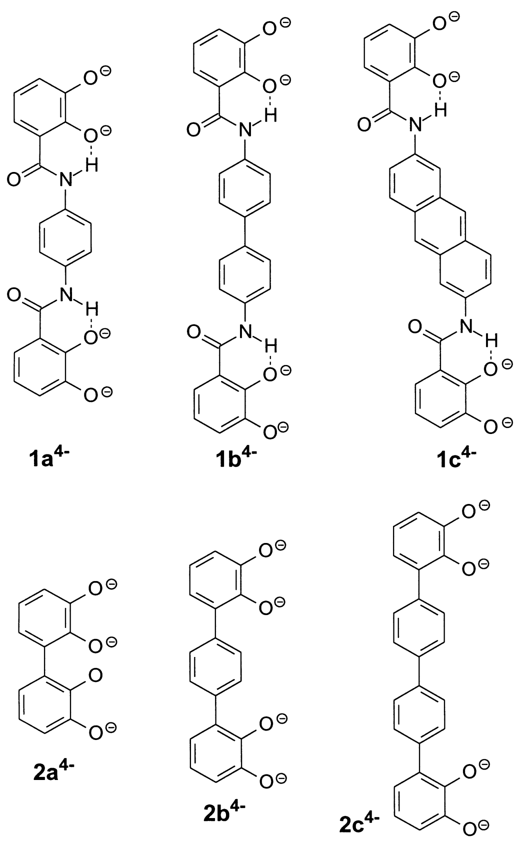


$1a^{4-}$ $1b^{4-}$ $1c^{4-}$

$2a^{4-}$ $2b^{4-}$ $2c^{4-}$

obtained upon complex formation due to intramolecular hydrogen bonding between the amide protons and the internal catecholato oxygen atoms. The ligands 2^{4-} possess a rigid linear oligo-*p*-phenylene structure.

Only triple-stranded helicates were observed for metal complexes of the rigid ligands **1** and **2**. Owing to the linear geometry of the ligands, the chiral information of one complex unit is transferred directly to the second one leading to helicates such as $[(\mathbf{1})_3Ga_2]^{6-}$ and $[(\mathbf{2})_3Ti_2]^{4-}$.[10–13] A bent ("C"-type) geometry of the ligand would be a requirement for the formation of the *meso*-helicate. This is disfavored due to steric strain.[10] However, for derivatives of $[(\mathbf{1a})_3Ga_2]^{6-}$ the *meso*-helicate was shown to be a high-energy intermediate in the stepwise inversion ("racemization") of the triple-stranded helix.[10]

Control of the relative stereochemistry of two complex units by the ligand spacer (even versus odd)

If alkyl chains are introduced as spacers between ligand moieties a transfer of the stereochemical information can proceed through the alkyl chain. Hereby the control of the relative stereochemistry of the complex units depends on the number of methylene units in the spacer. In a linear alkyl chain the preferred orientation of the alkyl substituents at a σ bond is antiperiplanar, leading to a zigzag conformation of the strand. This zigzag influences the preferred conformation of the ligand and thus its predisposition for complex formation. The zigzag conformation of the alkyl chain leads in the case of an even number of methylene units to an "S"-type structure of the ligand, supporting the formation of a dinuclear helicate. On the other hand, an odd number of methylene units leads to a "C"-type geometry of the ligand which is required for the *meso*-helicate (Figure 2).[9]

The ligands **3**–**6** have a CH_2 group as a spacer that connects the metal binding units. The protons of this spacer act as a

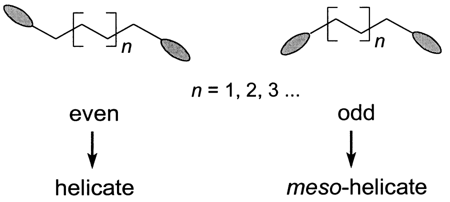
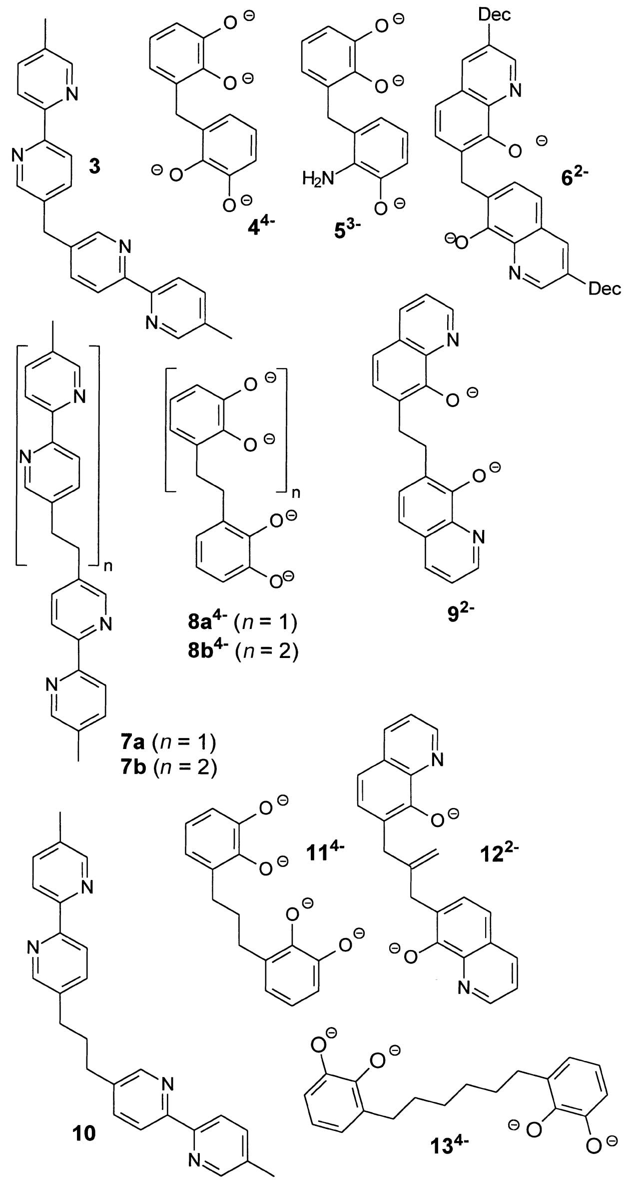


Figure 2. Schematic representation of the preferred conformation of alkyl-bridged ligands. Ligands with an even number of methylene groups in the spacer lead to the formation of the helicates, while the assembly of a *meso*-helicate is preferred if ligands with an odd number of CH_2 groups are used.



3 4^{4-} 5^{3-} 6^{2-}

7a (*n* = 1)
7b (*n* = 2)

$8a^{4-}$ (*n* = 1)
$8b^{4-}$ (*n* = 2)

9^{2-}

10 11^{4-} 12^{2-} 13^{4-}

stereochemical probe. In a helicate structure the two protons would be homotopic and would show only one singlet by ^{1}H NMR spectroscopy. If a *meso*-helicate is formed, the protons would be diastereotopic and thus would lead to two doublets. For all ligands **3**–**6**, doublets are observed by NMR spectroscopy of the metal complexes showing the formation of *meso*-helicates[14–16] or in the case of the dinuclear Ga^{III}, Ti^{IV}, or Ga^{III}/Ti^{IV} complexes of the directional ligand $\mathbf{5}^{3-}$ chiral complexes (as racemates) with a *meso* relation of the two complex units.[17] For Li$_4$[(**4**)$_3$Ti$_2$][15] and K$_2$[(**5**)$_3$GaTi][17] X-ray structures were obtained which show that *meso*-helicate-type complexes are present in the solid state (Figure 3).

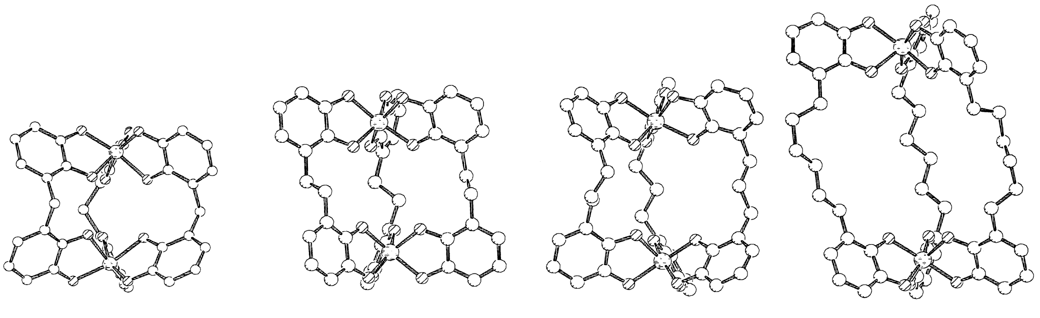
The ligands **7**–**9** possess ethylene linkages as spacers. Owing to the zigzag conformation of the spacer, these ligands lead to dinuclear or trinuclear helicates. For the trinuclear nickel(II) complex of **7b**,[18] the titanium(IV) and vanadium(IV) complex of **8a**,[19] and the gallium(III) complex of **9**,[20] X-ray structures were obtained which show the triple-stranded helical structures of the coordination compounds. However, a differentiation of the helicate and the *meso*-helicate in solution by simple ^{1}H NMR spectroscopy is not possible for (CH$_2$)$_2$-bridged complexes. The helicate as well as the *meso*-helicate lead to signals of diastereotopic spacer protons. However, NMR spectroscopy reveals that only one of the two diastereoisomers is present. A chiral derivative of **8a** and its dinuclear titanium(IV) complex were synthesized and NMR spectroscopy indicates that the helical structure (which for related complexes is observed in the solid state) also seems to be the geometry in solution.[21]

The ligands **10**–**12** with three carbon atoms in the spacer lead to triple-stranded dinuclear complexes with *meso*-helicate structure. For the complexes of $[(\mathbf{10})_3\mathrm{Fe}_2]^{4+}$ and $[(\mathbf{11})_3\mathrm{Ti}_2]^{4-}$ this could be shown by NMR spectroscopy by observing the diastereotopic protons of the central methylene group of the spacer.[4, 6] X-ray structures were obtained for the *meso*-helicates Na$_4$[(**11**)$_3$Ti$_2$][4] and [Cs{(**12**)$_3$Ga$_2$}]Cl.[22]

In addition to the examples already discussed, the solid-state structure of K$_4$[(**13**)$_3$Ti$_2$] with six methylene units in the spacer was determined (Figure 3). Following the "zigzag" concept, the complex adopts the helicate structure in the solid state. However, owing to the very flexible and long spacers it is assumed that a helicate/*meso*-helicate equilibrium is present in solution.[23]

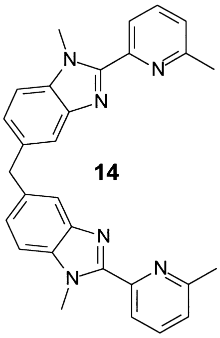
In summary, in linear ligands with two chelating binding sites for metal ions which bear alkyl chains as spacers the stereochemical information is transferred between the complex units by the preferred zigzag conformation of the spacer. An even number of methylene units in the spacer leads to the helicate, while a *meso*-helicate is formed when an odd number of CH$_2$ groups is present. However, there are some requirements for the control of the relative stereochemistry of the dinuclear complexes by alkyl spacers: i) the aromatic ligand units have to be attached linearly to the spacer (that means, that the line connecting the two ligand donor atoms and the vector of the σ bond that attaches the aromatic ligand moieties to the spacer have to be parallel), ii) the spacer should be a "pure" alkyl chain: heteroatoms have to be avoided, iii) other influences on the stereochemistry which are discussed herein are capable of suppressing (overriding) the control by the alkyl chain. *Exceptions*: Some representative examples are discussed here to show the influence of factors like i) or ii) on the relative stereochemistry of the complex units (for iii) see below).

The ligands **14**–**18** all lead upon formation of metal complexes to the homochiral helicates. In the case of **14** the stereochemistry is influenced by the connection of the methylene spacer to the ligand units. The attachment is not linear and leads to a predisposition of the ligand which is ideal for the formation of a helicate.[24] Ligand **15** possesses two *p*-phenylene units in the spacer which have some rotational freedom and thus disturb the transfer of the chiral information through the alkyl group of the spacer.[25] The dinuclear iron(II) complexes of the ligands **16** and **17** represent very interesting examples. Both complexes show a helicate structure although one of the ligands has a (CH$_2$)$_2$ (even) the other one a (CH$_2$)$_3$ group (odd) as spacer. However, again the spacers are not connected to the ligand units in a linear fashion.[26] In the case of the ligand **18** the transfer of the chiral information from one chelating unit to the other is disturbed by the presence of the amide linkages which are able to freely rotate around the σ bonds.[27]



$[(\mathbf{4})_3\mathrm{Ti}_2]^{4-}$ $[(\mathbf{8a})_3\mathrm{Ti}_2]^{4-}$ $[(\mathbf{11})_3\mathrm{Ti}_2]^{4-}$ $[(\mathbf{13})_3\mathrm{Ti}_2]^{4-}$

Figure 3. The structures of the tetraanions of the *meso*-helicate $[(\mathbf{4})_3\mathrm{Ti}_2]^{4-}$, the helicate $[(\mathbf{8a})_3\mathrm{Ti}_2]^{4-}$, the *meso*-helicate $[(\mathbf{11})_3\mathrm{Ti}_2]^{4-}$, and the helicate $[(\mathbf{13})_3\mathrm{Ti}_2]^{4-}$ as found in the solid state (representation: SCHAKAL 97, E. Keller, Freiburg im Breisgau).



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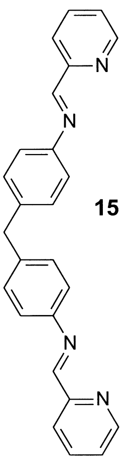

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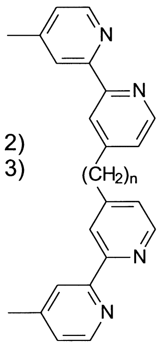
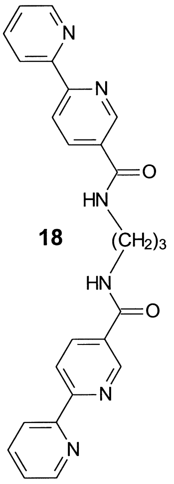


16 ($n = 2$)
17 ($n = 3$)



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Control of the relative stereochemistry of two complex units by templates

Just recently an example was described in which the formation of the helicate *versus* the *meso*-helicate was controlled by the presence or absence of an appropriate template. Ligand **19**$^{2-}$ forms dinuclear triple-stranded *meso*-helicates $[(\mathbf{19})_3M_2]$ (M = Al, Ga) with gallium(III) or aluminum(III) ions in the absence of water (Figure 4).[8]

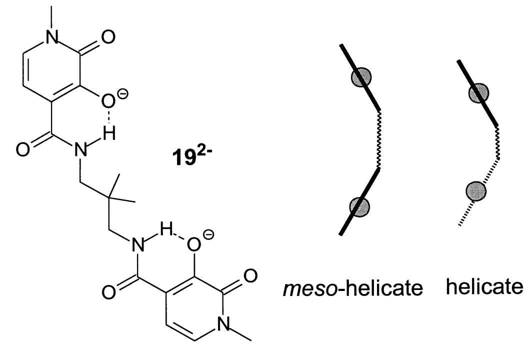
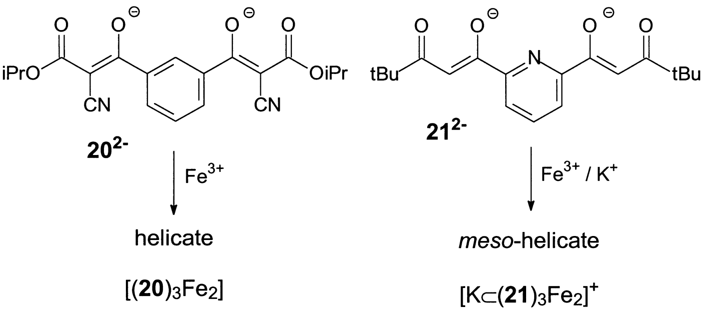


Figure 4. Schematic representation of the *meso*-helicate (left) and the helicate (right) which are formed from ligand **19**$^{2-}$ showing the different sizes of the cavities of the two diastereomeric complexes (only one of the three ligand strands is shown).

This again can be rationalized by the preferred zigzag conformation of the spacer which possesses an odd number of carbon atoms and is linearly attached to the amide of the ligand unit which is planar and geometrically fixed by intramolecular hydrogen bonding. If water is present, in addition the helicate can be observed by NMR spectroscopy (no diastereotopic CH_3 groups!) and the X-ray structure of $[(H_2O)\subset\{(\mathbf{19})_3Al_2]$ was obtained. In the solid state, water is encapsulated in the interior of the helicate and is fixed there by hydrogen bonding. The interior of the *meso*-helicate seems to be too big to effectively bind the water molecules; therefore, the complex has to adjust its structure to the guest. As shown schematically in Figure 4, this can take place by a change from the *meso*-helicate to the helicate which possesses a more condensed structure with a smaller cavity.[8] In this example switches between the diastereomeric complexes can be made very elegantly by simply adding or removing a guest such as water. Hereby either the spacer (→ *meso*-helicate) or the size of the template (→ helicate) control the relative stereochemistry of the two complex units. Inclusion of water probably also is the driving force for the formation of an analogous helicate that was described earlier.[3]

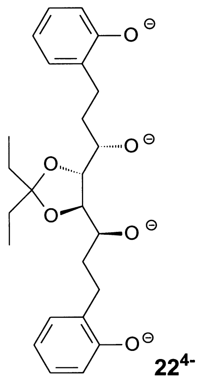
A very similar control mechanism seems to be active in the formation of iron(III) complexes from the ligands **20**$^{2-}$ and **21**$^{2-}$. The two geometrically very similar ligands form either the dinuclear helicate $[(\mathbf{20})_3Fe_2]$ or the corresponding *meso*-helicate $[K\subset\{(\mathbf{21})_3Fe_2]^+$ which encapsulates a potassium ion in its interior.[28] Effective binding of the potassium ion seems to be the driving force for the distortion of the rigid ligand **21** and the formation of the *meso*-helicate. *Exception:* The ligand **9**$^{2-}$ forms the cryptate-type helicates $[M\subset\{(\mathbf{9})_3Ga_2\}]^+$ (M = Na, K, Rb) with gallium(III) ions in the presence of Na^+, K^+, or Rb^+ ions. Although the NMR spectra of the three cryptates are significantly different, it could be shown that the neutral cryptand-type helicate $[(\mathbf{9})_3Ga_2]$ can adjust to the size of the guest by simple stretching or compression using the complex units as molecular hinges. A dramatic conformational change which leads to the *meso*-helicate is not observed here.[20]



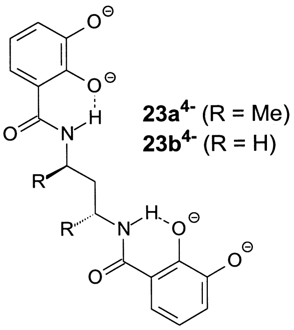
Control of the relative stereochemistry of two complex units by chiral spacers

Chiral groups in the ligand spacer are able to control the stereochemistry of the neighboring complex units. Thus, an enantiopure trinuclear triple-stranded helicate $[(\mathbf{22})_3Ti_3]$ assembles from three ligands **22**$^{4-}$ and three titanium(IV) ions.[29]

The C_3-linked dicatechol ligand **23a**$^{4-}$ bears two methyl groups in the spacer, leading to two *R* configurated centers. Upon coordination to gallium(III) ions, these chiral centers induce a Λ-configuration at the two complex units, leading to the enantiopure helicate $[(\mathbf{23a})_3Ga_2]^{6-}$. The *meso*-helicate is



22^{4-}



$23a^{4-}$ (R = Me)
$23b^{4-}$ (R = H)

probably formed if the corresponding *meso*-(*R*,*S*)-configurated ligand is used for complex formation.[30] Surprisingly, the analogous achiral $(CH_2)_3$-bridged ligand **$23b^{4-}$** also leads to the helicate $[(\mathbf{23b})_3Ga_2]^{6-}$. However, the authors do not comment on the possible inclusion of water in the interior of this complex (see for comparison[8]).[31]

Conclusion

In most cases the formation of triple-stranded dinuclear helicates or *meso*-helicates is highly stereoselective. The stereochemistry hereby is influenced by different control mechanisms or combinations thereof. Herein we have discussed that rigid linear ligands prefer to form helicates, while the relative stereochemistry in dinuclear complexes from ligands with flexible spacers depends on the nature of the spacer (even *versus* odd), spatial requirements of templates, or chiral substituents.

Other mechanisms to control the stereochemistry of dinuclear helicate-type complexes have not been found yet but might also play an important role. For example, it should be possible to influence the configuration of the complex units by chiral counterions.[32] Further investigations are necessary to get a more detailed insight into the control mechanisms of supramolecular stereochemistry.

Acknowledgements

Our work in this area was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft.

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