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# Disulfonimides Versus Phosphoric Acids in Brønsted Acid Catalysis: The Effect of Weak Hydrogen Bonds and Multiple Acceptors on Complex Structures and Reactivity

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## ABSTRACT

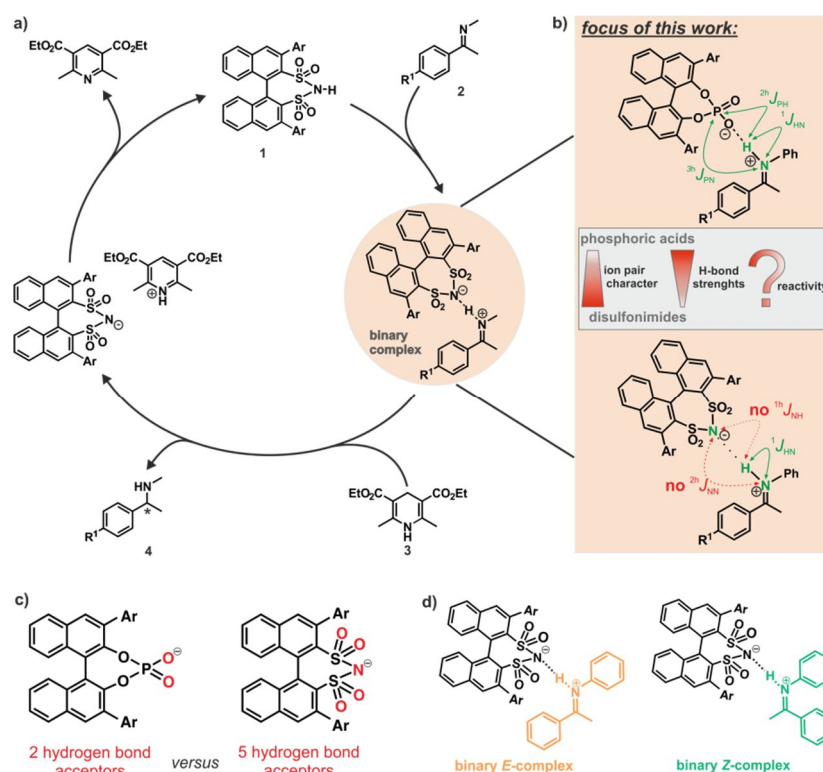
In Brønsted acid catalysis, hydrogen bonds play a crucial role for reactivity and selectivity. However, the contribution of weak hydrogen bonds or multiple acceptors has been unclear so far, since it is extremely difficult to collect experimental evidence for weak hydrogen bonds. Here, our hydrogen bond and structural access to Brønsted acid/imine complexes was used to analyse BINOL-derived chiral disulfonimide (DSI)/imine-complexes.  $^1\text{H}$  and  $^{15}\text{N}$  chemical shifts as well as  $^1J_{\text{NH}}$  coupling constants revealed for DSI/imine-complexes ion pairs with very weak hydrogen bonds. The high acidity of the DSIs leads to a significant weakening of the hydrogen bond as structural anchor. In addition, the five hydrogen bond acceptors of DSI allow an enormous mobility of the imine in the binary DSI-complexes. Theoretical calculations predict the hydrogen bonds to oxygen to be energetically less favored, however their considerable population is corroborated experimentally by NOE and exchange data. Furthermore, an *N*-alkyl-imine, which shows excellent reactivity and selectivity in reactions with DSI, reveals an enlarged structural space in complexes with the chiral phosphoric acid TRIP as potential explanation of its reduced reactivity and selectivity. Thus, considering factors such as flexibility and possible hydrogen bond sites is essential for catalyst development in Brønsted acid catalysis.

## INTRODUCTION

In asymmetric synthesis, the substrate activation by a chiral catalyst has been established as a powerful strategy.<sup>1</sup> Particularly, BINOL-derived Brønsted acids constitute a class of robust, highly enantioselective and extremely active catalysts available for many asymmetric transformations, including transfer hydrogenations, Strecker reactions, carbonyl additions and many others.<sup>1,2</sup> One prominent example of these organocatalysts are chiral phosphoric acids

(CPAs).<sup>1</sup> Extensive NMR-studies of the binary complexes between different CPAs and aromatic *N*-aryl imines proved the formation of strong, charge-assisted hydrogen bonds in these catalysts/substrate-complexes, supported by a network of CH- $\pi$ - and  $\pi$ - $\pi$ -interactions.<sup>3-5</sup> Thus, the induced stereoselectivity stems from the non-covalent interactions.<sup>6,7</sup> However, for some transformations, even stronger Brønsted acids are required or at least show higher activities.<sup>8-12</sup>

For this purpose, the groups of List and others reported the synthesis<sup>13-15</sup> of disulfonimide catalysts (DSIs),<sup>16</sup> which are more acidic than the CPAs and were successfully applied as catalysts for the transfer hydrogenation of *N*-alkyl imines.<sup>9</sup> Compared to *N*-aryl amines, the formed products are more basic and slow down the reaction by inhibiting the catalyst. In addition to the poor conversion, for the combination of CPA-catalysts and *N*-alkyl imines also disappointing stereoselectivities were observed. In contrast, the more acidic DSI-catalysts provided both high turnovers and astonishingly good enantioselectivities.<sup>9</sup> In general, DSIs and other highly acidic catalysts have been applied in various reactions, in which the substrates are difficult to activate and the acidity of the CPAs is not sufficient.<sup>17-19</sup>



**Figure 1.** a) Assumed catalytic cycle for the DSI-catalyzed asymmetric transfer hydrogenation of *N*-alkyl imines **2** derived from that of CPAs. b) Focus of this study was a hydrogen bond as well as a structural analysis of DSI/imine-complexes regarding the influence of the weakened hydrogen bonds and the increased ion pair character. All results were compared to the previously investigated less acidic CPAs.<sup>3-5,20</sup> Finally, the internal acidity of these different classes of catalysts was correlated to the

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3 reactivity in the transfer hydrogenation. c) In contrast to the CPAs, not only two but five possible hydrogen bond acceptors exist  
4 for the DSIs. d) The investigated binary *E*- and *Z*-complexes are shown.  
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8 The assumed catalytic cycle for the transfer hydrogenation with *N*-alkyl imines and DSI catalysts is similar to the  
9 proposed mechanism of the CPA-catalyst transfer hydrogenation<sup>21</sup> and is shown in Figure 1. In the first step, the  
10 Brønsted acid catalyst **1** protonates the imine **2** and a pre-catalytic species, the binary complex, is formed.  
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12 Subsequently, the Hantzsch ester **3** reduces the imine and the chiral amine **4** is formed as product. Finally, the  
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14 catalyst **1** is regenerated by proton transfer.  
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18 In a Brønsted acid catalyzed Nazarov cyclization, a direct correlation between the  $pK_a$ -values of the catalysts and the  
19 observed reaction rate was found.<sup>22</sup> For the cyclization, a faster reaction was observed for more acidic catalysts.<sup>22</sup> In  
20 one of our previous studies, the internal acidity of different CPAs was compared with the reactivity in the transfer  
21 hydrogenation of *N*-aryl imines.<sup>5</sup> There, it was shown that the reaction with the least acidic CPA was the fastest,  
22 while the slowest reaction was observed with the most acidic CPA.<sup>5</sup> However, the most sterically hindered catalyst  
23 showed a drastic drop in reactivity. Since the formation of the binary complex (i.e. the binding of the imine) was  
24 similar to the other catalysts, most probably the binding of the Hantzsch ester is hindered.<sup>5</sup> This suggested that the  
25 reaction rate of the transfer hydrogenation is not only dependent on the internal acidity of the catalyst but can be also  
26 modulated by other factors such as the steric demand of the 3,3'-substituents and the corresponding size of the  
27 binding pocket.<sup>5</sup>  
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37 However, the use of stronger Brønsted acids rise the question, whether still binary complexes with charge-assisted  
38 hydrogen-bonds are present similar to the CPA/imine-complexes<sup>3,5</sup> or whether pure ion pairs without hydrogen bond  
39 contribution are formed. As shown previously, the potential hydrogen bond is such a sensitive experimental indicator  
40 that the a hydrogen bond analysis can give information about the binding situation and even small structural changes  
41 within the binary complexes can be derived.<sup>3,5</sup>  
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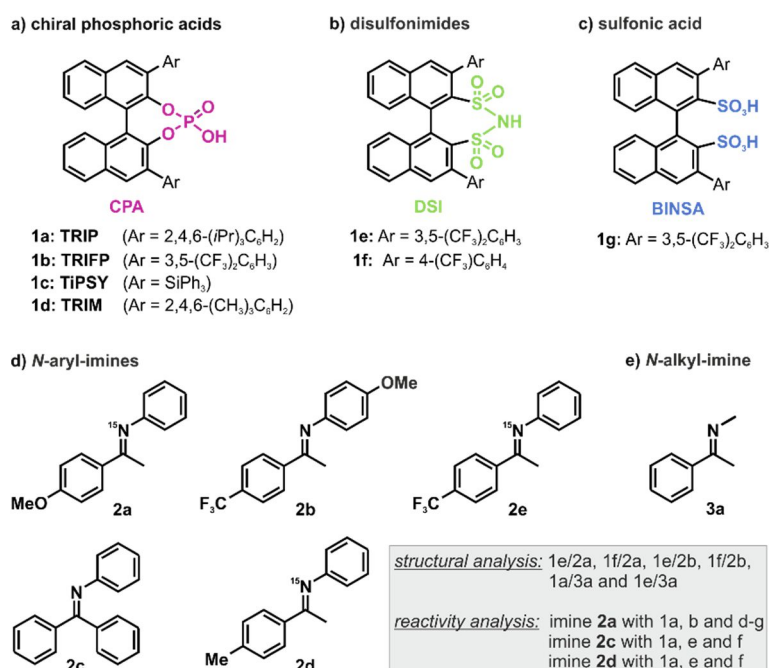
47 For CPA/imine-complexes, four highly conserved core structures were observed experimentally. Thus, in solution  
48 two different orientations (*type I* and *type II*) of each imine isomer (*E* and *Z*) inside the binary complex were  
49 detected.<sup>4</sup> The structural investigations of various CPA complexes showed that the 3,3'-substituents affect the  
50 relative population of these core structures but not their existence.<sup>20</sup> Despite the fact that low-temperature NMR  
51 spectroscopy was proven to be an excellent tool to investigate the occurring intermediates in Brønsted acid catalysis  
52 as well as the interactions between catalyst and substrates, up to now most of the NMR investigations are confined  
53 to CPAs or their derivatives.<sup>3–5,20,23,24</sup> Similarly, the extensive computational studies within Brønsted acid catalysis  
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focused mainly on CPAs.<sup>7,25–32</sup> However, to our knowledge, other acidic motifs and especially the promising DSI-catalysts have not been examined.

Therefore, in this study, we investigated the binary complexes of two DSIs with two *N*-aryl imines by low-temperature NMR-spectroscopy. A detailed hydrogen bond analysis, regarding <sup>1</sup>H and <sup>15</sup>N chemical shifts and coupling constants, as well as structural investigations were conducted. These results are compared with the corresponding CPA/imine complexes. Particularly, the effect of the increased number of hydrogen bond acceptors of the DSI compared to the CPA is addressed (Figure 1c). In addition, the differences of the more basic *N*-alkyl-imine in binary complexes with TRIP and DSI were compared. Finally, the expanded acidity range is correlated to the observed reaction rate in the transfer hydrogenation of imines.

## RESULTS AND DISCUSSION

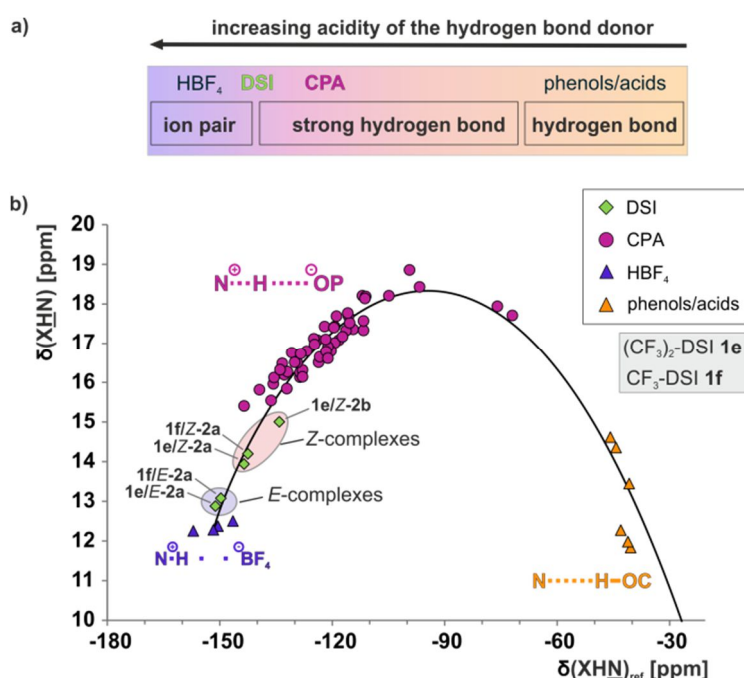
**Model system.** In order to compare the NHN hydrogen bonds of binary DSI/imine-complexes with our previously investigated POHN hydrogen bonds of CPA/imine-complexes<sup>3,4,20</sup> a detailed hydrogen bond and structural analysis was conducted. As catalysts we selected the commercially available DSIs **1e** and **1f** (Figure 2). To enable a comparison with our previous structural investigations on CPA/imine complexes<sup>3–5,20</sup> and to reduce the severe chemical shift overlap the methoxy-substituted *N*-aryl imines **2a** and **2b** were chosen. <sup>15</sup>N labeling of the imine **2a** allowed to access <sup>1</sup>J<sub>HN</sub> coupling constants. Furthermore, the imines **2a**, **2c** and **2d** were chosen for reactivity studies to consider the influence of electronic effects as well as isomerization. In addition, the highly acidic sulfonic acid (BINSAs) **1g** was used in the reactivity comparison to expand the p*K*<sub>a</sub>-range of the catalysts even more. Finally, the more basic *N*-alkyl imine **3a** was included into the structural investigations to address the special effects of *N*-alkyl versus *N*-aryl imines known from synthetic applications.<sup>9</sup> To achieve the smallest possible signal linewidths, all NMR measurements were conducted in CD<sub>2</sub>Cl<sub>2</sub>. All NMR spectra were recorded at 180 K to minimize exchange processes of the hydrogen-bonded protons.



**Figure 2.** The binary complexes of different BINOL-derived Brønsted acids were analyzed. a) While the phosphoric acids (CPAs) **1a-1d** were the main focus of our previous works,<sup>3-5,20</sup> b) in this study the binary complexes between with the disulfonimides catalysts (DSIs) **1e** and **1f** were investigated. c) In addition, the sulfonic acid (BINSA) **1g** was used for the reactivity analysis. d) The hydrogen bond and structural analysis was done with imine **2a** and **2b**. Whereas, the reaction kinetics of imines **2a**, **2c** and **2d** were investigated. e) Additionally, also the hydrogen bonds between the *N*-alkyl imine **3a** and CPA **1a** as well as DSI **1e** were investigated.

**Hydrogen bond analysis of the *N*-aryl-imine-complexes.** In general, the position of the proton within a hydrogen bond is dependent on the acidity of the hydrogen bond donor and the basicity of the acceptor. Thus, with increasing acidity of the donor the proton is initially shifted towards the center of the hydrogen bond, where the strongest hydrogen bonds are formed, then further on to the hydrogen bond acceptor resulting in a hydrogen bond assisted ion pairs, and finally completely to the acceptor forming pure ion pairs (Figure 3a). To define the position of the proton within OHN hydrogen bonds in pyridine/acid-complexes Steiner and Denisov developed an empirical correlation of <sup>1</sup>H- and the <sup>15</sup>N-chemical shifts.<sup>33,34</sup> Recently, we showed that this correlation is also applicable to the POHN hydrogen bonds in CPA/imine-complexes.<sup>3,5</sup> For most of the binary CPA/imine-complexes, the <sup>1</sup>H chemical shifts of the hydrogen-bonded protons are above 16 ppm and follow a parabolic curve revealing very strong hydrogen bonds (Figure 3b).<sup>3,5</sup> The position on the left upper half of the parabolic curve indicates hydrogen bond assisted ion pairs. In contrast to these CPA-complexes, those with DSIs exhibit high field shifts for both <sup>1</sup>H and <sup>15</sup>N. As a result, the DSI/imine-complexes are positioned far down on the left side of the Steiner-Limbach curve close to the almost pure ion pair with HBF<sub>4</sub> (Figure 3b). This position of the DSI-complexes on the curve shows that the proton within the

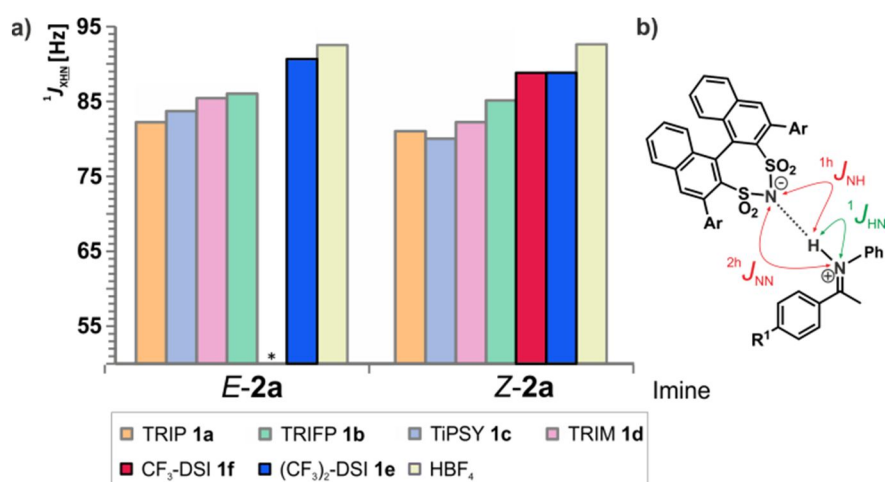
hydrogen bond is significantly shifted towards the nitrogen as expected for the more acidic DSI-catalysts (Figure 3a). In general,  $^1\text{H}$  and  $^{15}\text{N}$  chemical shifts as well as the  $^1J_{\text{NH}}$  coupling constants can be used to determine the hydrogen bond strengths. However, the  $^1\text{H}$  chemical shift of the CPA/imine-complexes was significantly influenced by neighbourhood and shielding effects, whereas the  $^{15}\text{N}$  chemical shift, which was directly correlated with the  $^1J_{\text{HN}}$  coupling constant, is not so sensitive for these effects and could be used as an appropriate descriptor for the hydrogen bond strengths.<sup>3,5</sup> For this reason the hydrogen bond analysis of the DSI-complexes was based on the  $^{15}\text{N}$  chemical shifts. Especially, the *E*-configured DSI/**2a**-complexes show a  $^{15}\text{N}$  chemical shift, which is similar to the  $\text{HBF}_4$ -model system for purely ionic complexes, suggesting none or an extremely weak hydrogen bond. In contrast, for the investigated *Z*-complexes with DSI a position on the curve significantly closer to the CPA catalysts was found indicating a substantial contribution of a hydrogen bond within in these ion pairs (Figure 3b). Thus, the smaller sterical demand of the *Z*-imine leads to stronger hydrogen bonds in DSI-complexes compared to the corresponding *E*-complexes. This observation is in accordance with the previously investigated CPA-complexes, where calculated as well as experimentally derived atomic distances corroborated the assumption of a reduced steric hindrance of the *Z*-imine allowing for a closer approach to the catalyst.<sup>3,5</sup> However, from chemical shifts alone it is difficult to distinguish between hydrogen bond assisted ion pair and pure ion pair. Therefore, next the scalar couplings within and through the hydrogen bonds were investigated.



**Figure 3.** a) With increasing acidity of the hydrogen bond donor, the proton is shifted toward the nitrogen of the hydrogen bond acceptor until an ion pair is formed. b) Plot of  $\delta_{(\text{OHN})}$  against  $\delta_{(\text{OHN})_{\text{ref}}}$  of the hydrogen-bonded complexes. The binary complexes of DSIs **1e** and **1f** with the imines **2a** and **2b** (green diamonds) are complemented with the binary imine-complexes of  $\text{HBF}_4$  (purple

triangles), CPAs (pink cycles) and some carboxylic acids and phenols (orange triangles) from previous studies.<sup>3,5</sup> All  $^{15}\text{N}$  chemical shifts are referenced  $[\delta(\text{OHN})_{\text{ref}} = \delta(\text{OHN})_{\text{exp}} - 340\text{ppm}]$  (for details and exact values see SI).

The observed  $^1J_{\text{HN}}$  coupling constants are a measure for the binding strengths between proton and nitrogen of the imine, i.e. the larger the  $^1J_{\text{HN}}$  the higher the ion pair character of the binary complex. The  $^1J_{\text{HN}}$  coupling constants of the DSI/**2a**-complexes are larger than for all CPA-complexes ( $^1J_{\text{HN}}$  between 82 and 86 Hz), but still slightly smaller than the  $^1J_{\text{HN}}$  coupling constants of the completely protonated imine with  $\text{HBF}_4$  (Figure 4). Due to signal broadening caused by exchange processes, for the *E*-imine **2a** only the  $^1J_{\text{HN}}$  of the complex with  $(\text{CF}_3)_2\text{-DSI } \mathbf{1e}$  was experimentally available ( $^1J_{\text{HN}} = 90.6 \text{ Hz}$ ). This coupling constant differs about 2 Hz from that observed for the completely protonated  $\text{HBF}_4/\text{E-2a}$ -complex ( $^1J_{\text{HN}} = 92.5 \text{ Hz}$ ) and thus reveals a very weak hydrogen bond for the  $(\text{CF}_3)_2\text{-DSI } \mathbf{1e}/\mathbf{2a}$ -complex. Also the  $^1J_{\text{HN}}$  coupling constants for the DSI/*Z*-imine-complexes are slightly smaller than for the *E*-complexes. This confirms the stronger hydrogen bonds of the *Z*-imines, which were already discussed within the chemical shift analysis section. In accordance with this trend and the high acidity of DSI, the coupling constants for both *Z-2a*-complexes with DSIs **1e** and **1f** ( $^1J_{\text{HN}} = 88.8 \text{ Hz}$  for both) are larger than those of the CPA-complexes ( $^1J_{\text{HN}}$  between 80 and 85 Hz) and smaller than the respective *E*-complexes as well as the protonated imine with  $\text{HBF}_4$  ( $^1J_{\text{HN}} = 92.6 \text{ Hz}$ ). These observations show unambiguously that for the *Z*-complexes a hydrogen bond assisted ion pair is present.



**Figure 4.** a) The experimental  $^1J_{\text{HN}}$  coupling constants are shown for *E*- and *Z*-imine **2a** with the CPAs **1a-1d**,<sup>3,5</sup>  $\text{HBF}_4$ <sup>3</sup> and the DSIs **1e** and **1f** (for values see SI). Due to fast chemical exchange the  $^1J_{\text{HN}}$  of **1f**/*Z-2a* could not be determined (marked by an asterisk). b) Except the (green)  $^1J_{\text{HN}}$  also trans-hydrogen bond scalar couplings (red  $^1J_{\text{NH}}$  and  $^2J_{\text{NN}}$ ) were addressed.

Next potential trans-hydrogen bond scalar couplings ( $^1J_{\text{NH}}$  and  $^2J_{\text{NN}}$ ) were addressed, since for magnetization transfers *via*  $^2J_{\text{NN}}$  scalar couplings across NHN hydrogen bonds large coupling constants are expected. The first trans-hydrogen bond scalar coupling was measured across such hydrogen bonds between the nitrogen atoms of



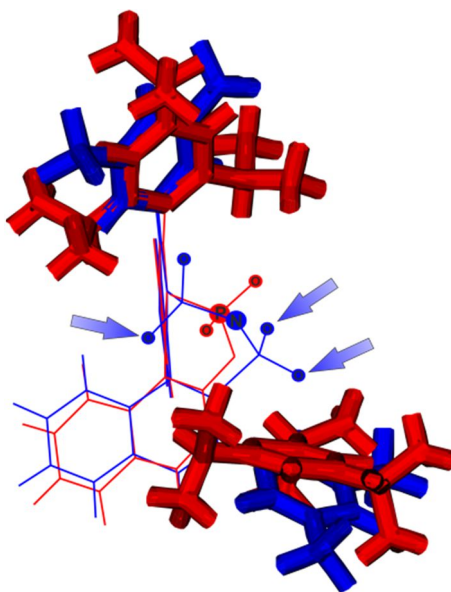
Watson-Crick base pairs in  $^{15}\text{N}$ -labeled RNA and showed unexpectedly large through hydrogen bond scalar couplings of  $^2J_{\text{NN}} \approx 7 \text{ Hz}$ .<sup>35</sup> Later also  $^3J_{\text{NC}}$  scalar couplings through COHN hydrogen bonds could be detected in proteins. Due to the additional bond the observed scalar coupling constants were one order of magnitude smaller (i.e.  $^3J_{\text{CN}} = 0.2 - 0.9 \text{ Hz}$ )<sup>36</sup> than the  $^2J_{\text{NN}}$  coupling constants. Surprisingly, in our previous study of the CPA/imine-complexes for the POHN hydrogen bonds (similar to the protein situation) very large trans-hydrogen bond scalar couplings of  $^3J_{\text{PN}} \approx 2\text{-}3 \text{ Hz}$  were measured, indicating the formation of strong, charge assisted hydrogen bonds.<sup>3</sup> Comparable to the situation in RNA also in the DSI-complexes the additional oxygen atom within the hydrogen bond is missing. Therefore, compared to the  $^3J_{\text{PN}}$  coupling constants of the CPA-complexes, by far stronger trans-hydrogen bond  $^2J_{\text{NN}}$  scalar couplings were expected for hydrogen bonds with similar strengths. For more ionic DSI-complexes these through hydrogen bond scalar couplings should be the best sensor to probe the existence of weak hydrogen bonds. However, even with  $^{15}\text{N}$ -labelled DSI **1e** neither the  $^2J_{\text{NN}}$  coupling nor the  $^1J_{\text{NH}}$  coupling between the acidic proton and DSI-nitrogen (see Figure 4b) were detectable in a 1D  $^{15}\text{N}$  or 2D  $^1\text{H},^{15}\text{N}$ -HSQC spectrum. Therefore, theoretical calculations were conducted and revealed for the **1e/E-2a**-complex a very small  $^1J_{\text{NH}}$  coupling constant of 0.5 Hz, and a  $^2J_{\text{NN}}$  coupling constant of 7 Hz. These values are in accordance with the previously found through hydrogen bond scalar couplings of Watson-Crick base pairs in  $^{15}\text{N}$ -labeled RNA.<sup>35</sup> However, considering the linewidths of the hydrogen bonded proton of the Z-complex in the  $^1\text{H}$ -spectrum (half line widths  $\approx 22.9 \text{ Hz}$ ), it is typical for conformational exchange and in none of the  $^1\text{H},^{15}\text{N}$ -spectra through hydrogen bond cross peaks are detectable. Additionally, the  $^{15}\text{N}$ -signal of the free labeled DSI is sharp (half line widths  $\approx 3.5 \text{ Hz}$ ), while the  $^{15}\text{N}$ -signal of the DSI in the binary complex is broadened significantly (for spectra see SI). Again, this line broadening suggests exchange processes, which would also explain the missing cross peaks *via* partial decoupling.

Overall the hydrogen bond analysis based on  $^1\text{H}$  and  $^{15}\text{N}$  chemical shift as well as  $^1J_{\text{HN}}$  coupling constant revealed in all investigated DSI-complexes the formation of weak charge-assisted hydrogen bonds. Due to the higher acidity of the catalyst, the hydrogen bonds and the related effect as structural anchor is weakened compared to the CPAs. However, even with  $^{15}\text{N}$ -labelled DSI it was not possible to detect any through hydrogen bond coupling (neither the  $^2J_{\text{NN}}$  coupling nor the  $^1J_{\text{NH}}$  coupling). This observation in combination with the line broadening of the  $^{15}\text{N}$ -signal of the DSI in the binary complex suggests several exchange processes.

**Structural investigations of the *N*-aryl-imine-complexes.** To address the potential exchange processes suggested by the hydrogen bond analysis, next structural investigations of the DSI/imine-complexes were conducted. In this way the structural changes caused by the transition from strong to weak hydrogen bonds in the

binary Brønsted acid/imine-complexes should be revealed. Furthermore, in this manner the differences of a single *versus* a multiple hydrogen bond acceptor catalyst within this system should become obvious.

In our previous studies of the CPA-complexes for each imine-isomer two different orientations of the imine (*type IE*, *type IIE*, *type IZ* and *type IIZ*) in the binary complex were found.<sup>4,20</sup> These core structures are independent of the CPA and the substitution of the *N*-aryl-imine. In principle, two different exchange pathways between *type I* and *type II* are possible: Either the imine tilts inside the binary complex and switches the oxygen that constitutes the hydrogen bond, or the imine rotates around 180° under retention of the hydrogen bond. Although *type I* and *type II* are in fast exchange on the NMR time scale even at 180 K, it was possible to identify the effective exchange modes between the two orientations experimentally.<sup>4,20</sup> For the *E*-imine in most of the investigated complexes exclusively the tilting-pathway was observed (with exception of TRIM), whereas for the *Z*-imines a combination of tilting and rotation was found.<sup>4,20</sup> These tilting and rotation processes are fast on the NMR time scale. In contrast, the exchange of the free imine with the imine in the binary CPA-complex (dissociation/association of the imine) is slow on the NMR time scale.<sup>4,20</sup>

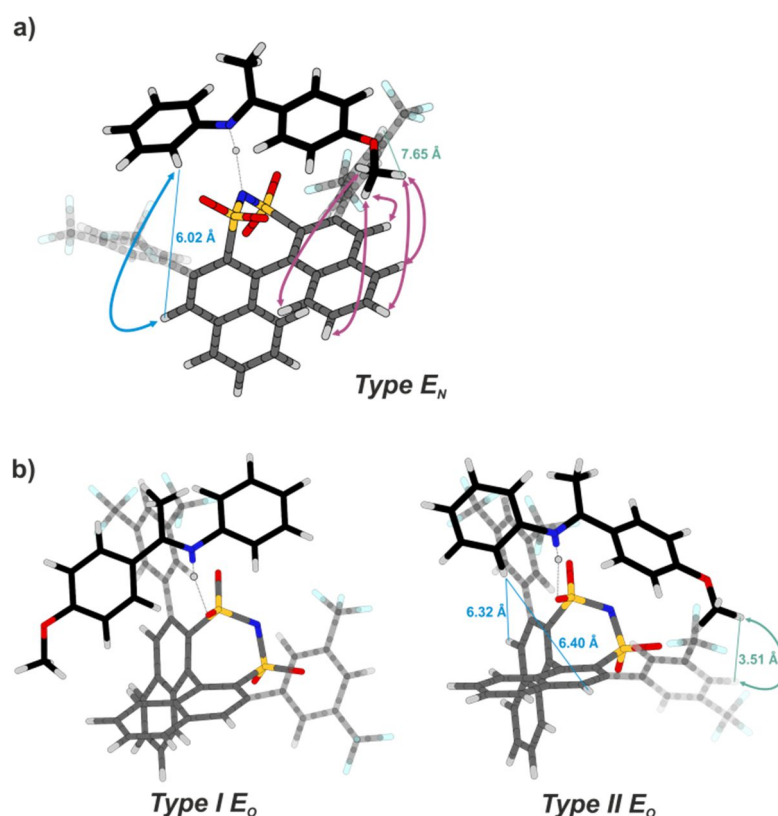


**Figure 5.** Overlay of TRIP **1a** (red) and (CF<sub>3</sub>)<sub>2</sub>-DSI **1e** (blue) showing the differences of the binding pockets (oxygen, phosphorus and nitrogen atoms are marked in respective colors). Indeed, the binding pocket of DSI is just slightly larger, but the hydrogen binding sites of the DSI (denoted with blue arrows) stick out of the binding pocket and are easier available for the substrate compared to TRIP. This in combination with the increased number of hydrogen bond acceptors may result in a higher mobility of the substrate.

Due to the significant weaker hydrogen bonds in the DSI/imine-complexes and the five readily accessible hydrogen binding sites of the DSI (Figure 5), additional exchange processes compared to CPAs were expected. Thus, for the

first time a fast exchange between the free imine and the *E*-imine in the binary complex was observed in the  $^1\text{H}$  spectrum at 180 K (for spectra see SI), indicating a fast dissociation/association process of the *E*-imine. In addition, different sets of signals are observed for the *E*- and *Z*-imines within the complexes, but only one set of chemical shifts for the DSI-catalyst. This hints at a slow *E/Z*-isomerization in combination with various complex structures leading to an assimilation of the catalyst chemical shifts. Therefore, theoretical calculations were used to explore the structural space of the DSI/imine-complexes. These calculations predict for the *E*-imine one most stable complex structure, in which a hydrogen bond between the imine and the nitrogen of the DSI (*type E<sub>N</sub>*) is formed (Figure 6a). The orientation of the imine in *type E<sub>N</sub>* is equivalent to the *type IE*-structure of the CPA-complexes. In addition, various structures with a hydrogen bond to one of the oxygens (*type E<sub>O</sub>*) were found, whereby two of these orientations are energetically preferred. One of them corresponds to *type IE* (here *type IE<sub>O</sub>*) and the other to *type IIE* (here *type IIE<sub>O</sub>*) of the CPA complexes (Figure 6b). In general, the calculations predict a stronger hydrogen bond to the nitrogen than to the different oxygens. Furthermore, initial molecular dynamic calculations predict that for the exchanges between the different orientations of the imine not only the tilting-pathway (such as for most of the CPA-complexes) but also the rotation-mechanism is active.

To confirm the predicted structures experimentally, selective 1D  $^1\text{H}$ ,  $^1\text{H}$ -NOESY as well as 2D NOESY spectra were recorded. The intense intermolecular NOEs between the *p*-methoxy group of the imine **2a** and the BINOL backbone of the DSI corroborate the existence of the energetically most favored structure (*type E<sub>N</sub>*). Furthermore, the existence of the *type IIE<sub>O</sub>* orientation was confirmed by a NOE between the *p*-methoxy group of the imine **2a** and the 3,3'-substituents of the DSI (green arrow in Figure 6b, for spectra see SI). Overall, the line broadening of the  $^{15}\text{N}$  signal of the labeled  $(\text{CF}_3)_2$ -DSI **1e** in the binary complex with imine **2a** (see the discussion about hydrogen bonds above), the detection of a single set of chemical shifts for the catalyst and the observed NOEs showed experimentally, that the hydrogen bond is not only formed to the strongest (here nitrogen), but also to the weaker hydrogen bond acceptors (here oxygen). Similar experimental data were found for the binary **1f/2a**- as well as the **1f/2b**-complex (for spectra and assignment see SI).



**Figure 6.** Calculations predict for the DSI/imine **2a**-complexes the existence of a) one stable structure, where a hydrogen bond to the nitrogen of the DSI-catalyst (*type E<sub>N</sub>*), is formed and b) several orientations with a hydrogen bond to one of the oxygens. The two most stable structures are shown. *type II E<sub>o</sub>* could be identified by the green NOE. All distances given in this figure were obtained from calculations.

Next, the structures of the DSI/Z-complexes were addressed. The theoretical calculations predict no structural preference for the Z-complexes despite the stronger hydrogen bonds compared to the *E*-complexes (see hydrogen bond analysis above). Thus, the sterically less demanding Z-imine seems to enable even more structural orientations within the binary complex than the corresponding *E*-complexes. This was confirmed by various sel. NOESY experiments, in which the NOE is transferred from the  $\alpha$ -methyl-group to the whole catalyst-backbone as well as to the protons on the 3,3'-substituents (for spectra see SI). Even at smaller mixing times ( $\tau_{\text{mix}} = 25$  ms) the same NOE pattern was observed, indicating a fast exchange between several hydrogen bonded species, which could not be identified unambiguously.

Overall the structural investigations of three different binary DSI-complexes showed a high mobility of the substrate inside the binding pocket of the DSI-catalyst due to the presence of five hydrogen bond acceptors. Despite theoretical calculations propose significantly weaker hydrogen bonds to the oxygens, these hydrogen bonds and the corresponding structures are considerably populated even at 180 K. Thus, the weaker and more diverse hydrogen

within DSI/imine complexes do not longer act as tight structural anchor. Finally, in the *E*-complex the energetically most stable structure (*type E<sub>N</sub>*) as well as another, where the hydrogen bond is formed to one of the oxygens (*type E<sub>O</sub>*), was identified experimentally. On the other hand, for the complexes with the sterically less demanding *Z*-imines no structural preference was found. Despite this enormous flexibility of the binary complexes, the (*R*)-product is achieved in excess (imine **2a**: 70-78% ee with DSIs **1e** and **1f**, imine **2d**: 32-40% ee with DSIs **1e** and **1f**; see SI). Maybe also in DSI complexes the conformational and structural dynamics stabilize non-covalent interactions or minimize steric repulsion to achieve high selectivities, as proposed previously.<sup>37</sup>

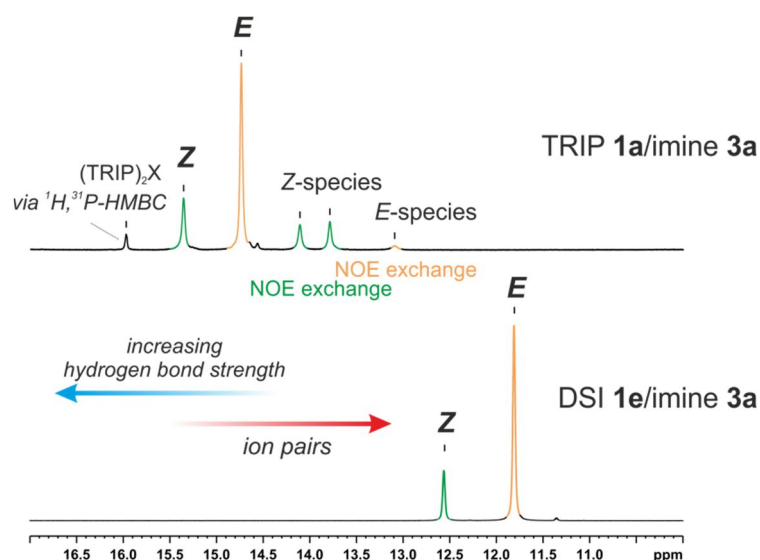
**Reactivity analysis of CPAs, DSIs and BINSAs in transfer hydrogenations.** Recently, for the CPA-catalyzed transfer hydrogenation of *N*-aryl-imines an inverse correlation between reactivity and internal acidity was obtained.<sup>5</sup> This means that TRIP with the strongest hydrogen bond (i.e. the least acidic catalyst) shows the fastest overall reaction rate. Hence, we investigated whether this correlation is also applicable for catalysts with different acidic functionalities and acidities, specifically on combinations of BINSAs **1g**, (CF<sub>3</sub>)<sub>2</sub>-DSI **1e**, (CF<sub>3</sub>)-DSI **1f** and TRIP **1a** with imine **2a** (calculated pK<sub>a</sub> values in DMSO: BINSAs **1g** -9, (CF<sub>3</sub>)<sub>2</sub>-DSI **1e** 0.05, TRIP **1a** 3 – 4).<sup>38</sup> The most acidic BINSAs revealed the lowest reactivity, while the reactivity of the least acidic TRIP was found to be between the two DSIs (imine **2a**: (CF<sub>3</sub>)<sub>2</sub>-DSI **1e** > TRIP **1a** > (CF<sub>3</sub>)-DSI **1f** > BINSAs **1g**; for data see SI). This shows that in case of significantly different hydrogen bond motifs the reactivity is not following the acidity of the catalysts. The same catalyst acidity–reactivity trend was also found with the structural similar imine **2d** in combination with the two DSIs and TRIP. Next, the effect of a bulkier imine **2c** was investigated in combination with (CF<sub>3</sub>)<sub>2</sub>-DSI **1e**, (CF<sub>3</sub>)-DSI **1f** and TRIP **1a**. However, with the bulkier imine **2c** the relative reactivity is different (imine **2c**: (CF<sub>3</sub>)-DSI **1e** > (CF<sub>3</sub>)<sub>2</sub>-DSI **1f** > TRIP **1a**). This indicates that the reactivity is determined by both the structure of the catalyst (size of the binding pocket and acidic motif) and the properties of the substrate.

**Analysis of the binary *N*-alkyl-imine-complexes.** Interestingly, the reaction outcome of the transfer hydrogenation of the more basic *N*-alkyl imines is extremely dependent on the used catalyst. While the highly acidic DSI catalysts were applied successfully and give the product in excellent yields and stereoselectivities, the less acidic CPA catalysts provided only disappointing enantioselectivities and low conversions.<sup>9</sup> To figure out if exclusively the high differences in acidity of the catalysts are responsible for these observations, also the pre-catalytic, binary complexes of imine **3a** with TRIP **1a** and (CF<sub>3</sub>)<sub>2</sub>-DSI **1e** at 180 K were analyzed.

Initially, the analysis of the binary TRIP/**3a**-complex revealed that apart from the *E*- and *Z*-complexes, various other hydrogen bonded species are present (Figure 7, top spectrum). The additional species were not identified, but selective 1D <sup>1</sup>H,<sup>1</sup>H-NOESY experiments showed that in two of these species the *Z*-imine and in the third the *E*-imine

is involved (for spectra see SI). Most probably some of these complexes are dimeric species, which were observed previously in the TRIP/*N*-aryl-imine-complexes.<sup>20</sup> The population of the additional *Z*-species is significantly higher compared to the complemented *E*-species, most likely due to the less sterical demand of the *Z*-imine. Furthermore, a dimeric species of the phosphoric acid was identified.<sup>3</sup> Under the assumption that the transfer hydrogenation of the *N*-alkyl-imines also proceeds through the transition states of the *Z*-imine, as previously proposed for the *N*-aryl-imines,<sup>39</sup> these off-cycle equilibria of the *Z*-imine reduce the amount of the reactive species and may result in a reduced reactivity. Furthermore, this is the first time that we observed an enlarged structural space (two additional *Z*-imine and one additional *E*-imine complex) in the core structures of TRIP/imine complexes in comparison to our previously reported *N*-aryl imine complexes,<sup>3–5,20</sup> which may explain the low enantioselectivity with TRIP (26 % *ee*).

Furthermore, for the CPA-catalysts a correlation between their reactivity in the transfer hydrogenation of *N*-aryl-imines and the internal acidity was found: The least acidic TRIP (i.e. forming the strongest hydrogen bond) shows the fastest overall reaction rate.<sup>5</sup> Thus, also the hydrogen bonds of the TRIP/**3a**-complex were analyzed. The position of the TRIP/**3a**-complexes on the Steiner-Limbach curve (see SI) and the  $^1J_{\text{HN}}$  coupling constant of the binary *E*-complex ( $^1J_{\text{HN}} \approx 85$  Hz) revealed the formation of a charge-assisted hydrogen bond. However, the observed hydrogen bond is weakened compared to the CPA/*N*-aryl-imine-complexes. The weakening of the hydrogen bond is also indicated by the fact, that for the major *E*- and *Z*-complexes no magnetization is transferred from the hydrogen bonded proton to the phosphorus in a  $^1\text{H}, ^{31}\text{P}$ -HMBC spectrum. In contrast, for the CPA/*N*-aryl-imine-complexes, which form stronger hydrogen bonds, this magnetization transfer was observed. Since, the weakening of a hydrogen bond comes along with an increased distance between the hydrogen bonded proton and proton-donor (TRIP), the through hydrogen bond magnetization transfer is complicated. Taking into account, that for weaker hydrogen bonds lower reactivities in the CPA-catalysed transfer hydrogenation of *N*-aryl imines were observed,<sup>5</sup> the even more weakened hydrogen bonds of the TRIP/*N*-alkyl-imine-complex may also be a reason for the disappointing reactivity.



**Figure 7.**  $^1\text{H}$  NMR spectra of the hydrogen bond region of the TRIP **1a/3a** and DSI **1e/3a** binary complexes in  $\text{CD}_2\text{Cl}_2$  at 180 K, showing the presence of various hydrogen bonded species with TRIP. In contrast with the  $(\text{CF}_3)_2\text{-DSI}$  only the major *E*- and *Z*-complexes were observed. On the left side of the Steiner-Limbach curve higher  $^1\text{H}$  chemical shifts reveal increasing hydrogen bond strength, while smaller  $^1\text{H}$  chemical shifts indicate an enhanced ion pair character.

In contrast, in the  $^1\text{H}$ -spectrum of the binary  $(\text{CF}_3)_2\text{-DSI 1e/3a}$ -complex only two hydrogen bonded species, which could be assigned as binary *E*- and *Z*-complex, were observed (Figure 7, bottom spectrum). The analysis of the Steiner-Limbach curve showed that these *E*- and *Z*-complexes are positioned in the region of the pure ion pairs (see SI). Nevertheless, the  $^1J_{\text{HN}}$  coupling constant of the  $(\text{CF}_3)_2\text{-DSI 1e/E-3a}$ -complex (around 91 Hz) is still slightly lower than the coupling constant in the pure ion paired  $\text{HBF}_4/\text{E-2a}$ -complex (92.5 Hz, see above), indicating a very minor contribution of the hydrogen bond. Thus, also for the DSI/*N*-alkyl-imine-complex the hydrogen bond is still present and can be decisive for the reactivity and selectivity. Again, a weak hydrogen bond, possible switching between various DSI hydrogen bond donors and a large binding pocket allow the mobility of the imine. These properties, coupled to the smaller size of the *N*-methyl substituent compared to *N*-phenyl, result in a fast exchange between all the possible complex structures and give only averaged NMR signals for each *E*- and *Z*-configurations even at 180 K. In addition, an *N*-tosylimine in a binary complex with TRIP was investigated to test the effect of multiple H-bond acceptors on the substrate side. Unexpectedly, no POHN hydrogen bond but instead several POHO bonds were found. This shows that multiple acceptors also on the substrate side create structural diversity (for details, see SI section 11).

Overall, the analysis of TRIP **1a/N**-methyl imine complex showed the presence of various hydrogen-bonded species, which might lower the reactivity and selectivity due to the competition and off-cycle equilibria. For highly acidic DSI **1e/ N**-methyl imine complex, only two structures, specifically an *E*- and a *Z*-complex, were observed. In this case,

off-cycle equilibria were not detectable. This may give a hint that the change in core structures could be decisive for the reaction outcome.

## CONCLUSION

A hydrogen bond analysis of the binary complexes consisting of imines and disulfonimide (DSI) catalysts is performed and compared to chiral phosphoric acid (CPA) catalysts. With the highly acidic DSI catalysts, complexes with a high ion pair character were formed, but unexpectedly still weak hydrogen bonds were detected. By means of NMR spectroscopy, these hydrogen bonds were analyzed using the Steiner-Limbach curve and the chemical shifts as well as the observed  $^1J_{\text{NH}}$  coupling constants suggest the formation of very weak hydrogen bonds. Exchange line broadening and the lack of magnetization transfers across hydrogen bonds indicate several exchange processes of the imine.

The weakening of the structural anchor allows a high mobility of the substrate inside the pocket. Additionally, the presence of multiple hydrogen bonding sites (four oxygens and one nitrogen) results in increased structural flexibility and reveals additional entropic contributions in the DSI-complexes. To identify the present species in the binary complex a structural analysis was conducted. Calculations predicted out of a multitude of structures three energetically most favored *E*-imine complexes (*type E<sub>N</sub>*, *type IE<sub>O</sub>* and *type IIE<sub>O</sub>*) in a fast exchange *via* rotation and dissociation. Even though, these processes are fast on the NMR time scale, the existence of at least two structures with a hydrogen bond to the nitrogen or oxygen (*type E<sub>N</sub>* and *type IIE<sub>O</sub>*) were confirmed by various NOESY measurements. Thus, the experiments show that not only the strongest possible hydrogen acceptor (nitrogen) is engaged in hydrogen bonding, which should be considered in the future development of catalyst design.

In the transfer hydrogenation of *N*-alkyl imines, CPAs exhibit low activity and selectivity compared to DSIs. In comparison to the previously investigated *N*-aryl-imines, for an *N*-alkyl-imine several additional complex structures with TRIP were found. These additional structures and their equilibria may contribute to the poor performance of TRIP. In contrast, for the corresponding DSI-complexes only the typical binary *E*- and *Z*-complexes were observed. Overall this study shows that a high structural flexibility is not in contrast to a good performance of a catalytic system.

## EXPERIMENTAL SECTION



Deuterated solvents were purchased from Deutero or Sigma Aldrich. Where anhydrous solvents were essential, CD<sub>2</sub>Cl<sub>2</sub> was freshly distilled over CaH<sub>2</sub> under argon atmosphere. The catalysts were purchased from Sigma Aldrich.

### Synthesis of Imine Substrates

The imines were prepared according to a modified literature procedure.<sup>3,39</sup> The toluene was used either in p.A. quality or was dried by refluxing over sodium. The used <sup>15</sup>N-enriched aniline was purchased from Sigma Aldrich. All imines were synthesized in accordance to our previous publications.<sup>3,39</sup>

**(E)-1-(4-methoxyphenyl)-N-phenylethan-1-imine (98% <sup>15</sup>N) (2a).** Molecular sieves 4 Å (9.8 g) were activated by 450°C under reduced pressure. Under argon atmosphere 4-methoxyacetophenone (2.16 g, 14.3 mmol, 1.3 eq) and aniline (98% <sup>15</sup>N, 1 ml, 1.02 g, 11.0 mmol) were added to the Schlenk flask and dissolved in 33 ml toluene. The solution was heated to reflux in an oil bath overnight with a drying tube filled with CaCl<sub>2</sub>. The molecular sieves were removed, and the orange solution was concentrated under reduced pressure. The remaining solid was recrystallized from diethylether at -20°C. The product was obtained as yellow solid. <sup>1</sup>H-NMR (400.1 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ<sub>H</sub> [ppm] = 7.95 (m, 2H, Aryl-H), 7.35 (m, 2H, Aryl-H), 7.07 (m, 1H, Aryl-H), 6.96 (m, 2H, Aryl-H), 6.77 (m, 2H, Aryl-H), 3.86 (s, 3H, -OCH<sub>3</sub>), 2.18 (d, <sup>3</sup>J<sub>HN</sub> = 1.76 Hz, -CH<sub>3</sub>). <sup>13</sup>C-NMR {<sup>1</sup>H} (100.6 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ<sub>C</sub> [ppm] = 164.5, 161.9, 152.5, 132.5, 129.3, 129.2, 123.2, 119.9, 113.9, 55.8, 17.2. <sup>15</sup>N-NMR (40.5 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ<sub>N</sub> [ppm] = 325.5. <sup>1</sup>H- and <sup>13</sup>C-spectra were in accordance with the literature.<sup>40</sup> For the reaction kinetics the imine **2a** was used in its unlabeled form. The synthesis was done according to this procedure only by using unlabeled aniline.

**(E)-1-(4-trifluoromethyl)-N-phenylethan-1-anisidine (2b).** Molecular sieves 4 Å (9.7 g) were activated by 450°C under reduced pressure. Under argon atmosphere 4-trifluoromethylacetophenone (2.72 g, 14.3 mmol, 1.3 eq) and 4-anisidine (1.37 g, 11.0 mmol) were added to the Schlenk flask and dissolved in 33 ml toluene. The solution was heated to reflux in an oil bath overnight with a drying tube filled with CaCl<sub>2</sub>. The molecular sieves were removed, and the reaction solution was concentrated under reduced pressure. The remaining solid was recrystallized from a diethylether/pentane-mixture (1:1) at -20°C. The product was obtained as yellow needles. <sup>1</sup>H-NMR (400.1 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ<sub>H</sub> [ppm] = 8.10 (d, <sup>3</sup>J<sub>HH</sub> = 8.1 Hz, 2H), 7.71 (d, <sup>3</sup>J<sub>HH</sub> = 8.3 Hz, 2H), 6.93 (m, 2H), 6.76 (dm, 2H), 3.81 (s, 3H), 2.27 (s, 3H). <sup>13</sup>C-NMR {<sup>1</sup>H} (100.6 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ<sub>C</sub> [ppm] = 164.5, 156.7, 144.6, 143.5, 127.9, 125.6, 121.0, 114.6, 55.8, 17.4. <sup>19</sup>F-NMR {<sup>1</sup>H} (376 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ<sub>F</sub> [ppm] = - 62.9. <sup>15</sup>N-NMR (40.5 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ<sub>N</sub> [ppm] = 337.3

**N,1,1-triphenylmethanimine (2c).** Molecular sieves 4 Å (10.0 g) were activated by 450°C under reduced pressure. Under argon atmosphere benzophenone (2.5 g, 14.0 mmol, 1.3 eq) and aniline (1 ml, 1.02 g, 11.0 mmol) were added to the Schlenk flask and dissolved in 33 ml toluene. The solution was heated to reflux in an oil bath overnight

with a drying tube filled with CaCl<sub>2</sub>. The molecular sieves were removed, and the reaction solution was concentrated under reduced pressure. The remaining solid was recrystallized from diethyl ether at -20°C. The product was obtained as a yellow solid. **<sup>1</sup>H-NMR** (400.1 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ<sub>H</sub> = 7.77 (m, 2H, Aryl-H), 7.50 (m, 1H, Aryl-H), 7.42 (m, 2H, Aryl-H), 7.33 - 7.26 (m, 3H, Aryl-H), 7.18 - 7.10 (m, 4H, Aryl-H), 6.95 (m, 1H, Aryl-H), 6.78 (m, 2H, Aryl-H). **<sup>13</sup>C-NMR {<sup>1</sup>H}** (100.6 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ<sub>C</sub> [ppm] = 168.3, 151.9, 139.9, 136.7, 131.1, 129.7, 129.6, 128.8, 128.8, 128.5, 128.2, 122.2, 121.0. **<sup>15</sup>N-NMR** (60.8 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ<sub>N</sub> [ppm] = 330.2

**(E)-1-(4-methylphenyl)-N-phenylethan-1-imine (98% <sup>15</sup>N) (2d).** Molecular sieves 4 Å (9.8 g) were activated by 450°C under reduced pressure. Under argon atmosphere 4-methylacetophenone (2.27 mL, 2.28 g, 17.0 mmol, 1.6 eq) and aniline (98% <sup>15</sup>N, 1 mL, 1.02 g, 11.0 mmol) were added to the Schlenk flask and dissolved in 33 mL toluene. The solution was heated to reflux in an oil bath overnight with a drying tube filled with CaCl<sub>2</sub>. The molecular sieves were removed, and the reaction solution was concentrated under reduced pressure. The remaining solid was recrystallized from petroleum ether at -20°C. The product was obtained as yellow needles. **<sup>1</sup>H-NMR** (400.1 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ<sub>H</sub> [ppm] = 7.86 (m, 2H, Aryl-H), 7.34 (m, 2H, Aryl-H), 7.25 (m, 2H, Aryl-H), 7.06 (m, 1H, Aryl), 6.76 (m, 2H), 2.40 (s, 3H, -CH<sub>3</sub>) 2.18 (d, <sup>3</sup>J<sub>HN</sub> = 1.76 Hz, 3H, -CH<sub>3</sub>). **<sup>13</sup>C-NMR {<sup>1</sup>H}** (100.6 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ<sub>C</sub> [ppm] = 165.3, 152.4, 141.2, 133.9, 129.5, 129.3, 127.5, 123.3, 119.7, 21.5, 17.4. **<sup>15</sup>N-NMR** (40.5 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ<sub>N</sub> [ppm] = 328.9 <sup>1</sup>H- and <sup>13</sup>C-spectra were in accordance with the literature.<sup>41</sup>

**(E)-1-(4-trifluoromethylphenyl)-N-phenylethan-1-imine (98% <sup>15</sup>N) (2e).** Molecular sieves 4 Å (5 g) were activated by 350°C under reduced pressure. Under argon atmosphere 4-trifluoromethylacetophenone (3.66 g, 19.5 mmol, 1.3 eq) and aniline (98% <sup>15</sup>N, 1.40 mL, 1.40 g, 15.0 mmol) were added to the Schlenk flask and dissolved in 25 mL toluene. The solution was heated to reflux in an oil bath overnight with a drying tube filled with CaCl<sub>2</sub>. The molecular sieves were removed, and the reaction solution was concentrated under reduced pressure. The remaining solid was recrystallized from methanol at -20°C. The product was obtained as yellow needles. **<sup>1</sup>H-NMR** (400.1 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ<sub>H</sub> [ppm] = 8.11 (m, 2H, Aryl-H), 7.72 (m, 2H, Aryl-H), 7.37 (m, 2H, Aryl-H), 7.11 (m, 1H, Aryl), 6.79 (m, 2H), 2.25 (s, 3H, -CH<sub>3</sub>). **<sup>13</sup>C-NMR {<sup>1</sup>H}** (100.6 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ<sub>C</sub> [ppm] = 164.5, 151.7, 143.2, 132.1, 129.4, 128.0, 125.6, 124.6, 123.9, 119.5, 17.5. **<sup>15</sup>N-NMR** (40.5 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ<sub>N</sub> [ppm] = 338.2. **<sup>19</sup>F-NMR {<sup>1</sup>H}** (376 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ<sub>F</sub> [ppm] = - 63.1. <sup>1</sup>H- and <sup>13</sup>C-spectra were in accordance with the literature.<sup>42</sup>

**(E)-N-methyl-1-phenylethan-1-imine (3a).** N-Methyl imine **3a** was synthesized following the literature procedure.<sup>9</sup> A solution of methylamine (33 % in EtOH, 5 mL, 40 mmol, 4 eq.) was added to a flask containing molecular sieves 4 Å (2.5 g). The mixture was cooled to 0° C, and freshly distilled acetophenone (1.2 mL, 10 mmol) was added. The mixture was stirred at rt for 3 days, filtered, and the solid residue washed with DCM. The solvents were then

evaporated under reduced pressure to give the product as a clear yellow oil (0.88 g, 66 % yield). **<sup>1</sup>H-NMR** (400.1 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> [ppm] 7.82 – 7.75 (m, 2H), 7.42 – 7.33 (m, 3H), 3.33 (s, 3H), 2.23 (s, 3H). **<sup>13</sup>C-NMR {<sup>1</sup>H}** (100.6 MHz, CDCl<sub>3</sub>) δ<sub>C</sub> [ppm] 167.2, 141.2, 129.4, 128.0, 126.5, 39.5, 15.1. <sup>1</sup>H- and <sup>13</sup>C-spectra were in accordance with the literature.<sup>9</sup>

### Sample preparation of binary complexes in CD<sub>2</sub>Cl<sub>2</sub>

The DSI-catalyst was weighted directly into a 5 mm NMR-tube and dried for 20 min at 120°C under reduced pressure. Under argon atmosphere the imine was added. CD<sub>2</sub>Cl<sub>2</sub> (0.6 ml) and 1.0 ml of tetramethylsilane atmosphere were added to the tube. If not mentioned a 1:1 catalyst/imine-ratio was used. Despite careful sample preparation hydrolysis of the imine could not be completely prevented. Therefore, the catalyst/imine-ratios are slightly different than 1:1. A concentration 50 mmol/L was used for all samples, except the sample with the <sup>15</sup>N-labeled DSI (30 mM). Between the measurements the samples were stored at -80°C.

### Spectrometer data

NMR experiments were performed on Bruker Avance III HD 400 MHz spectrometer, equipped with 5 mm BBO BB-1H/D probe head with Z-Gradients and a Bruker Avance III HD 600 MHz spectrometer, equipped with a 5 mm CPPBBO BB-<sup>1</sup>H/<sup>19</sup>F. Temperature was controlled in the VT-experiments by BVT 3000 and BVTE 3900. For NMR measurements employing standard NMR solvents 5 mm NMR tubes were used. All pulse programs used are standard Bruker NMR pulse programs. NMR Data were processed, evaluated and plotted with TopSpin 3.2. Further plotting of the spectra was performed with Corel Draw X7. <sup>1</sup>H and <sup>13</sup>C chemical shifts were referenced to TMS or the respective solvent signals. The heteronuclei <sup>15</sup>N and <sup>19</sup>F and were referenced, employing  $\nu(X) = \nu(\text{TMS}) \times \Xi_{\text{reference}} / 100$  % according to Harris *et al.*<sup>43</sup> The following frequency ratios and reference compounds were used:  $\Xi(^{15}\text{N}) = 10.132912$  (lq. NH<sub>3</sub>) and  $\Xi(^{19}\text{F}) = 94.094011$  (CCl<sub>3</sub>F). All pulse programs used are standard Bruker NMR pulse programs.

**Synthesis of (R)-3,3'-Bis[3,5-bis(trifluoromethyl)phenyl]-1,1'-binaphthyl-2,2'-diyl-O,O'-bis(N,N-dimethylthiocarbamate) (6).** To a suspension of NaH (60 % suspension in mineral oil, 72 mg, 1.75 mmol, 5 eq.) in anhydrous DMF (2 mL) was added solid diol (R)-5 (250 mg, 0.35 mmol). After the mixture turned red, N,N-dimethylthiocarbamoylchloride (189 mg, 1.53 mmol, 4.4 eq) was added and the mixture was stirred at 85 °C in an oil bath overnight. The mixture was cooled down, another portion of NaH (5 eq.) and N,N-dimethylthiocarbamoylchloride (5 eq.) was then added and the mixture was stirred at rt for 5 days. The reaction was quenched by the addition of 2 % aq. KOH (20 mL) and the precipitate was filtered. The solid residue was then dissolved in DCM (20 mL) and

washed with sat. aq. NaCl (20 mL). The layers were separated, and the aqueous layer extracted with DCM (20 mL). The combined organic layers were dried over MgSO<sub>4</sub>, filtered and the solvent evaporated under reduced pressure. The residue was purified by silica gel column chromatography (eluent hexanes/EtOAc 98:2 – 90:10) to give *O,O'*-thiocarbamate **6** (300 mg, 97 % yield) as a white solid. <sup>1</sup>H-NMR (400.3 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> [ppm] 8.17 – 7.70 (m, 10 H), 7.60 – 7.27 (m, 6H), 2.04 – 3.12 (m, 12H). <sup>19</sup>F-NMR {<sup>1</sup>H} (376.5 MHz, CDCl<sub>3</sub>) δ<sub>F</sub> [ppm] -63.21, -63.23, -63.3. <sup>1</sup>H- and <sup>19</sup>F-spectra were in accordance with the literature.<sup>13</sup> Compound exists as a mixture of rotamers.

**Synthesis of (R)-3,3'-Bis[3,5-bis(trifluoromethyl)phenyl]-1,1'-binaphthyl-2,2'-diyl-S,S'-bis(N,N-dimethylthiocarbamate) (7).** Solid **6** (300 mg, 0.34 mmol) was stirred at 250 °C for 75 min in an aluminium heating block. The flask was then cooled down and the residue was purified by silica gel column chromatography (eluent hexanes/EtOAc 95:5) to give *S,S'*-thiocarbamate **7** (237 mg, 79 % yield) as a white solid. <sup>1</sup>H-NMR (400.3 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> [ppm] 8.08 (br s, 4H), 7.98 (br s, 2H), 7.95 – 7.90 (m, 2H), 7.86 (br s, 2H), 7.54 – 7.48 (m, 2H), 7.34 – 7.28 (m, 2H), 7.28 – 7.22 (m, 2H), 2.47 (br s, 12H). <sup>19</sup>F-NMR {<sup>1</sup>H} (376.5 MHz, CDCl<sub>3</sub>) δ<sub>F</sub> [ppm] -62.6. <sup>13</sup>C-NMR {<sup>1</sup>H} (100.6 MHz, CDCl<sub>3</sub>) δ<sub>C</sub> [ppm] 165.1, 144.5, 143.4, 141.1, 133.4, 132.9, 130.6 (m), 130.5 (q, *J*<sub>CF</sub> = 32.8 Hz), 129.8, 127.9, 127.8, 127.6, 127.3, 127.2, 123.5 (q, *J*<sub>CF</sub> = 272.6 Hz), 120.3 (m), 36.9 – 36.0 (m). <sup>1</sup>H- and <sup>13</sup>C-spectra were in accordance with the literature.<sup>13</sup>

**Synthesis of the DSI-precursor BINSAs 1g.** The disulfonic acid BINSAs (**1g**) was synthesized according to the literature.<sup>13</sup> Hydrogen peroxide (30 % aq., 1 mL) was added to HCO<sub>2</sub>H (8 mL) and the mixture was stirred at rt for 1 h. A solution of **7** (227 mg, 0.257 mmol) in DCM (4 mL) was then added and the mixture was stirred at rt for 2 h. The mixture was then filtered through a pad of silica gel, washed with DCM, and the solvents were evaporated under reduced pressure. The residue was purified by silica gel column chromatography (eluent DCM/MeOH 20:1 – 10:1) to give **1g** (probably as a sodium salt, 100 mg, 46 % yield) as a white solid. The solid was dissolved in DCM (20 mL), washed with 6 M aq. HCl (12 mL), and the aqueous layer was extracted with DCM (2 x 15 mL). The organic layers were combined, the solvent evaporated under reduced pressure and the remaining water was removed by azeotropic distillation with toluene (3 x 20 mL) to give **1g** (BINSAs, 76 mg, 34 %) as a brown solid. <sup>1</sup>H-NMR (400.3 MHz, CD<sub>3</sub>OD) δ<sub>H</sub> [ppm] 8.23 (s, 4H), 7.94 (d, *J* = 8.2 Hz, 2H), 7.91 (s, 2H), 7.82 (s, 2H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 7.8 Hz, 2H), 7.09 (d, *J* = 8.6 Hz, 2H). <sup>19</sup>F-NMR {<sup>1</sup>H} (376.5 MHz, CD<sub>3</sub>OD) δ<sub>F</sub> [ppm] -63.9. <sup>13</sup>C-NMR {<sup>1</sup>H} (100.6 MHz, CD<sub>3</sub>OD) δ<sub>C</sub> [ppm] 147.0, 139.6, 137.8, 136.7, 134.6, 134.2, 132.6, 132.1, 131.0 (q, *J*<sub>CF</sub> = 33.0 Hz), 129.0, 128.8, 128.7, 128.3, 125.3 (q, *J*<sub>CF</sub> = 271.8 Hz), 121.3 (m). <sup>1</sup>H- and <sup>13</sup>C-spectra were in accordance with the literature.<sup>13</sup>

**Synthesis of the  $^{15}\text{N}$ -labeled DSI **1e**.** The  $^{15}\text{N}$ -DSI **1e** was synthesized from its precursor BINSAs **1g** using  $^{15}\text{NH}_3$  (aq.) (instead of 2 M  $\text{NH}_3$  in MeOH) by following the literature procedure.<sup>13</sup> BINSAs **1g** (90 mg, 0.110 mmol) was dissolved in thionylchloride (2.5 mL), anhydrous DMF (10  $\mu\text{L}$ ) was added and the mixture was refluxed for 2 h. The solvent was then evaporated under reduced pressure. The remaining solid was triturated with anhydrous  $\text{Et}_2\text{O}$  (2 x 1 mL) to give (*R*)-3,3'-bis[3,5-bis(trifluoromethyl)phenyl]-1,1'-binaphthyl-2,2'-disulfonyl dichloride **8** as a white solid, which was used further without any purification.

As no product was detected during a reaction of **8** with aq.  $^{15}\text{NH}_3$  using THF as the solvent, biphasic conditions were applied: Crude sulfonic acid dichloride **8** was dissolved in  $\text{CHCl}_3$  (35 mL), cooled to  $-15\text{ }^\circ\text{C}$  and 7 M aq.  $^{15}\text{NH}_3$  (4 mL) was added over 5 h. The mixture was stirred at  $-15\text{ }^\circ\text{C}$  for 24 h and then at rt for 2 days. Then 14 M aq.  $^{15}\text{NH}_3$  (2 mL) was added and the reaction stirred overnight. The reaction was quenched by the addition of 5 % aq.  $\text{KHSO}_4$  (15 mL) and extracted with  $\text{CHCl}_3$  (3 x 25 mL). The combined organic layers were dried over  $\text{MgSO}_4$ , filtered and the solvent evaporated under reduced pressure. The residue was purified by silica gel column chromatography (eluent DCM/MeOH 40:1). The purified product was dissolved in DCM (5 mL) and washed with 6 M aq. HCl (5 mL), and the aqueous layer was extracted with DCM (5 mL). The organic layers were combined and washed again with 6 M aq. HCl (10 mL). The aqueous layer was extracted with DCM (10 mL). The organic layers were combined, the solvent evaporated under reduced pressure and the remaining water was removed by azeotropic distillation with toluene (6 x 20 mL) to give DSI-**1e** (16 mg) as a brown solid.  $^1\text{H-NMR}$  (600.0 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta_{\text{H}}$  [ppm] = 8.18 – 8.11 (m, 4H), 8.07 (br s, 2H), 8.04 – 7.97 (m, 4H), 7.83 (t,  $J = 7.8\text{ Hz}$ , 2H), 7.56 (t,  $J = 7.8\text{ Hz}$ , 2H), 7.27 (d,  $J = 8.7\text{ Hz}$ , 2H), 4.30 – 5.60 (br s).  $^{13}\text{C-NMR}$   $\{^1\text{H}\}$  (100.6 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta_{\text{C}}$  [ppm] = 141.2, 138.6, 134.3, 134.2, 133.6, 132.2, 130.9 (m), 130.5, 129.2, 129.0 (m), 128.7, 128.1, 123.3 (q,  $J_{\text{CF}} = 273.0\text{ Hz}$ ), 122.4, 121.7 (m).  $^{19}\text{F-NMR}$   $\{^1\text{H}\}$  (376 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta_{\text{F}}$  [ppm] = -62.9, -63.0.  $^{15}\text{N-NMR}$  {inverse-gated  $^1\text{H}$ } (40.5 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{N}}$  [ppm] = 200.6. The spectral data of the purified product **1e** match the published data.<sup>13</sup>

## Structure identification of all binary complexes

The structural investigations of the binary DSI-complexes were done in analogous to our previous investigations.<sup>4,20</sup>

Selective  $^1\text{H}$  NOESY, 2D  $^1\text{H}$ ,  $^1\text{H}$ -NOESY and  $^1\text{H}$ ,  $^{19}\text{F}$ -HOESY spectra were used to identify the structures of complexes **E-2a-b/1e-f** in solution. All spectra were measured in  $\text{CD}_2\text{Cl}_2$  at 180 K. One orientation (**TYPE E<sub>N</sub>**) was identified by the NOE pattern between the varying *p*-methoxy-groups of the imines **2a** and parts of the BINOL backbone of **1e** and **1f**. In the complexes **E-2a/1e-f**, the *p*-methoxy-groups were excited in selective  $^1\text{H}$  NOESY

spectra. In the **E-2b/1f**-complex no characteristic NOEs were found to proof the existence of **TYPE E<sub>N</sub>**. But its existence was assumed due to the the computationally calculated preference for this structure. Nevertheless, one of the other orientations (**TYPE IIE<sub>O</sub>**) was identified by 2D <sup>1</sup>H,<sup>1</sup>H-NOESY spectra with a mixing time of 300 ms in all investigated complexes. Here the characteristic NOE between aniline moiety and the backbone was found. Nevertheless, in the **E-2a/1f**-complex the NOE between aniline moiety and the backbone can be assumed. In contrast to the TRIP **1a/2b**-complexes, it was not possible to excite selectively the methoxy-group of the anisidine moiety of the imine **2b** due to overlap. But in 2D <sup>1</sup>H,<sup>1</sup>H-NOESY the characteristic NOEs between the methoxy group and the BINOL backbone were found.

Selective <sup>1</sup>H NOESY and 2D <sup>1</sup>H,<sup>1</sup>H-NOESY spectra were used to identify the structures of complexes **Z-2a-b/1e-f** in solution. All spectra were measured in CD<sub>2</sub>Cl<sub>2</sub> at 180 K. The selective excitation of the α-methyl-group of both Z-imines **2a-2b** in selective <sup>1</sup>H NOESYs showed NOE transfer to the whole catalyst-backbone as well as to the protons on the 3,3'-substituents. Also with a mixing time of 25 ms this NOE pattern was observed. Therefore, it is impossible to identify **TYPE IZ<sub>N</sub>** and **TYPE IIZ<sub>N</sub>** unambiguous. Nevertheless, for the **1d/2b**-complex in the 2D <sup>1</sup>H,<sup>1</sup>H-NOESY some characteristic NOEs indicate the existence of **TYPE IZ<sub>N</sub>** and **TYPE IIZ<sub>N</sub>**.

## Reaction kinetics of the transfer hydrogenation

### *Representative procedure for the ex-situ kinetics with imine 2a*

A Schlenk tube with an additional attached septum was dried at 300 °C for 15 min under reduced pressure. The flask was left to cool down and was flushed with argon. Imine **2a** (73.7 mg, 327 μmol, 1.0 eq.) and Hantzsch Ester (116.0 mg, 457.8 μmol, 1.4 eq.) were weighed into the tube. The tube was evacuated and flushed with argon three times. A standard stock solution of 1,3,5-trimethoxybenzene (54 mM) in anhydrous toluene was prepared and 3 mL of the standard stock solution were added to the tube under argon flow. The setup was put into a metal-heating block and preheated to 35 °C. A catalyst stock solution was prepared by dissolving the catalyst (2.9 mM) in anhydrous toluene. To start the reaction, the catalyst stock solution (1.0 mL, 0.009 eq., 0.9 mol % catalyst) was added to the reaction solution. After 1, 5, 10, 15, 20, 25, 30, 45 and 60 min, samples of the reaction mixture (≈ 0.1 mL) were taken via a septum and quenched by adding to a solution of *n*-hexane (2.0 mL) and NEt<sub>3</sub> (10 μL, 7.3 μg, 0.072 mmol, 100 eq. based on the catalyst). The mixture was filtered through a PTFE syringe filter and analyzed by chiral HPLC. Previously, it was shown that the addition of NEt<sub>3</sub> quenches the reaction and that the standard does not interfere with the reaction. The kinetics with the imines **2c** and **2d** were performed at the same scale.

### *HPLC conditions*

**(E)-1-(4-methoxyphenyl)-N-phenylethan-1-imine (2a).** CSP-HPLC, CHIRALPAK IC column (4.6mm x 250 mm, particle size: 5  $\mu$ m), eluent *n*-hexane/*i*-propanol 99:1, flowrate 0.9 mL/min, column compartment temperature 20°C,  $\lambda$  = 220 nm. **Retention times:** toluene/NEt<sub>3</sub>:  $\tau_1$  = 3.7 min; major (*R*)-amine:  $\tau_2$  = 10.8 min; minor (*S*)-amine:  $\tau_3$  = 11.8 min; 1,3,5-trimethoxybenzene:  $\tau_4$  = 16.0 min; imine **2a**:  $\tau_5$  = 25.7 min; HE-pyridine:  $\tau_6$  = 42.9 min.

**N,1,1-triphenylmethanimine (2c).** CSP-HPLC, CHIRALPAK IC column (4.6mm x 250 mm, particle size: 5  $\mu$ m), eluent *n*-hexane/*i*-propanol 99:1, flowrate 0.9 mL/min, column compartment temperature 20°C,  $\lambda$  = 220 nm. **Retention times:** toluene/NEt<sub>3</sub>:  $\tau_1$  = 3.7 min; product **4c**:  $\tau_2$  = 5.1 min; imine **2c**:  $\tau_3$  = 8.6 min; 1,3,5-trimethoxybenzene:  $\tau_4$  = 16.0 min; HE-pyridine:  $\tau_5$  = 43.0 min. An aliquot from the quenched samples was diluted 4x with *n*-hexane before syringe filtering and HPLC analysis because of the high absorption of the product at higher conversion.

**(E)-1-(4-methylphenyl)-N-phenylethan-1-imine (98% <sup>15</sup>N) (2d).** CSP-HPLC, CHIRALCEL OD-H column (4.6mm x 250 mm, particle size: 5  $\mu$ m), eluent *n*-hexane/*i*-propanol 98:2, flowrate 0.9 mL/min, column compartment temperature 20°C,  $\lambda$  = 220 nm. **Retention times:** toluene/NEt<sub>3</sub>:  $\tau_1$  = 4.0 min; HE-pyridine:  $\tau_2$  = 6.3 min; minor (*S*)-amine **4d**:  $\tau_3$  = 9.2 min; 1,3,5-trimethoxybenzene:  $\tau_4$  = 9.4 min; major (*R*)-amine **4d**:  $\tau_5$  = 10.2 min; imine **2d**:  $\tau_6$  = 11.7 min. Because of the partially overlapping peaks of the minor enantiomer of the product and the standard, the enantiomeric ratio of the product was determined at 254 nm, where the standard absorbs minimally. The integral of the minor enantiomer at 220 nm was calculated from the *er* and the major enantiomer peak, and the integral of the standard was calculated by subtraction from the overlapping peak.

**(E)-1-(4-trifluoromethylphenyl)-N-phenylethan-1-imine (98% <sup>15</sup>N) (2e).** CSP-HPLC, CHIRALPAK IA column (4.6mm x 250 mm, particle size: 5  $\mu$ m), eluent *n*-hexane/*i*-propanol 99:1, flowrate 0.9 mL/min, column compartment temperature 20°C,  $\lambda$  = 220 nm. **Retention times:** toluene/NEt<sub>3</sub>:  $\tau_1$  = 7.7 min; imine **2e**:  $\tau_2$  = 15.2 min; minor (*S*)-amine **4e**:  $\tau_3$  = 16.8 min; major (*R*)-amine **4e**:  $\tau_4$  = 18.2 min; 1,3,5-trimethoxybenzene:  $\tau_5$  = 20.3 min; HE-pyridine:  $\tau_6$  = 21.9 min.

## SUPPORTING INFORMATION

The Supporting Information is available free of charge on the ACS Publications website.

The Supporting Information contains:

experimental  $^1\text{H}$  and  $^{15}\text{N}$  chemical shifts as well as the  $^1J_{\text{HN}}$  coupling constants, complete set of  $^1\text{H}$  and  $^{15}\text{N}$  spectra for the binary complexes, additional information about the Steiner-Limbach curve, assignments of all binary complexes in  $\text{CD}_2\text{Cl}_2$ , computational data, NOESY spectra used for the structure investigations, chromatograms of the ex-situ reaction kinetics, reaction profiles of the transfer hydrogenation.

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