


 Cite this: *RSC Adv.*, 2020, 10, 42164

# Preferential N–H⋯:C< hydrogen bonding involving ditopic NH-containing systems and N-heterocyclic carbenes†

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Hydrogen bonding plays a critical role in maintaining order and structure in complex biological and synthetic systems. N-heterocyclic carbenes (NHCs) represent one of the most versatile tools in the synthetic chemistry toolbox, yet their potential as neutral carbon hydrogen bond acceptors remains underexplored. This report investigates this capability in a strategic manner, wherein carbene-based hydrogen bonding can be assessed by use of ditopic NH-containing molecules. N–H bonds are unique as there are three established reaction modes with carbenes: non-traditional hydrogen bonding adducts (X–H⋯:C<), salts arising from proton transfer ([H–C<]<sup>+</sup>[X]<sup>–</sup>), or amines from insertion of the carbene into the N–H bond. Yet, there are no established rules to predict product distributions or the strength of these associations. Here we seek to correlate the hydrogen bond strength of symmetric and asymmetric ditopic secondary amines with 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene (IPr, a representative NHC). In symmetric and asymmetric ditopic amine adducts both the solid-state (hydrogen bond lengths, NHC interior angles) and solution-state (<sup>1</sup>H Δδ of NH signals, <sup>13</sup>C signals of carbenic carbon) can be related to the pK<sub>a</sub> of the parent amine.

 Received 5th October 2020  
 Accepted 5th November 2020

DOI: 10.1039/d0ra08490e

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## Introduction

Hydrogen bonding interactions play a vital role throughout nature and are central to our understanding of complex biological systems.<sup>1</sup> The biological examples of such systems are incalculable, but prominent examples such as DNA, RNA, and enzymatic processes deserve mention.<sup>2–4</sup> Non-biological examples are equally diverse, ranging from controlling the reactivity of small molecules,<sup>5</sup> being central to the unique properties of water,<sup>6,7</sup> to being a key mechanism for generating complex folded structures.<sup>8,9</sup> While the role of hydrogen bonding in complex systems is indisputable, the development of methods to predict and assess the strengths of these interactions are vital to rationally designing novel systems.<sup>10,11</sup>

Hydrogen bond adducts X–H⋯A involve three-center four-electron bonds formed by interaction of lone pair electrons on a hydrogen bond acceptor (A) with a σ\* orbital of a hydrogen bond donor (X–H).<sup>12</sup> In traditional hydrogen bonding, X is an electronegative atom (such as N, O, S, or F) which sufficiently

polarizes the X–H bond leading to a reduction of the σ\* orbitals energy; and A is generally an electronegative atom (N, O, or halogens) having accessible lone pair electrons.<sup>12–14</sup> Non-traditional hydrogen bonds involving carbon centers are known but relatively rare, with association strengths that are generally weaker than conventional hydrogen bonds.<sup>15</sup> Most often these non-traditional species are mediated *via* formally charged carbon centers (such as isonitriles and carbanions) as the hydrogen bond acceptor.<sup>16,17</sup>

Since the first isolation of singlet carbenes their proliferation to all corners of chemistry are readily apparent.<sup>18–22</sup> Though a variety of singlet carbenes are now synthetically accessible,<sup>23,24</sup> N-heterocyclic carbenes (NHCs) based on an imidazole core remain one of the most well-studied and utilized class of carbenes.<sup>21,22,25–27</sup> Shortly after the discovery of isolable NHCs, it was postulated that these compounds could serve as strong hydrogen bond acceptors: with their divalent carbon bearing a lone pair (σ-donor) to interact with a myriad of Brønsted acid X–H species.<sup>28,29</sup> Arduengo described the first example of a carbene-centered hydrogen bond between 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ium hexafluorophosphate and 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene (IMes).<sup>30</sup> Clyburne and Davidson later expanded these findings to amine-based non-traditional hydrogen bonding between diphenylamine (DPA) and IMes (DPA⋯IMes, Fig. 1a), showing these species can be structurally authenticated.<sup>31</sup> Movassaghi and Schmidt also identified a MeOH⋯IMes adduct in their efforts to catalyze

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† Electronic supplementary information (ESI) available: Experimental procedures, supplemental figures and analysis, NMR spectra, and crystallographic results. CCDC 2011390, 2011391 and 2011392. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d0ra08490e



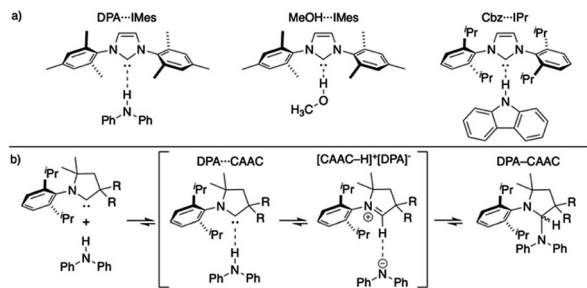


Fig. 1 (a) Representative authenticated  $X-H\cdots C<$  systems;<sup>31–33</sup> (b) general reaction progression elucidated by Bertrand of CAAC inserting into a N–H bond.<sup>34</sup>

amidation reactions with carbenes, authenticating the adduct both in solid- and solution-state (Fig. 1a).<sup>32</sup>

In addition to these reports, other computational<sup>35–39</sup> and experimental<sup>33,40–50</sup> studies on non-traditional  $X-H\cdots C<$  hydrogen bonding have emerged ( $C<$  is neutral carbene species). The balance between non-traditional hydrogen bonding and proton transfer relies on the weak nucleophilicity but high Lewis basicity of NHCs, which can be further modulated *via* variation of the substituents on the imidazole-core.<sup>51,52</sup> Comparison of the available solid-state structures of  $X-H\cdots C<$  hydrogen bonding reveal significant differences can occur. An example of this can be realized in comparing the hydrogen bond lengths ( $H\cdots C<$  distance) in secondary amine-based adducts of carbazole (Cbz) and DPA with common NHCs 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene (IPr) and IMes. The hydrogen bond lengths of  $Cbz\cdots IPr$  (2.07(3) Å)<sup>33</sup> and  $DPA\cdots IMes$  (2.30(2) Å)<sup>31</sup> suggest a stronger interaction for the carbazole *NH* than for the DPA *NH* when employing similar NHCs.<sup>53</sup> The interior N–C–N angles of the imidazole-2-ylidene units are slightly distorted as well, where  $Cbz\cdots IPr = 102.2(2)^\circ$  and  $DPA\cdots IMes = 101.7(1)^\circ$ .

These differences might be attributed to the differing steric profiles of IMes and IPr (2,4,6-trimethylphenyl, Mes *versus* 2,6-diisopropylphenyl, Dipp), though more probably these differences are due to the acidities of DPA ( $pK_a \approx 25.0$  in DMSO)<sup>54</sup> *versus* Cbz ( $pK_a \approx 19.9$  in DMSO).<sup>55</sup> Consistent with the latter hypothesis, MeOH...IMes adduct (Fig. 1a) displays a shorter hydrogen bond length (1.96(2) Å) and a more pronounced N–C–N angle of  $102.5(1)^\circ$  (MeOH  $pK_a \sim 29.0$  in DMSO)<sup>56,57</sup> than the amine-based species depicted in Fig. 1a. Although making comparisons between the reactivities of different NHCs can be troublesome, relatively minor differences in the basicity of IPr and IMes can be assumed, for the  $pK_a$  of their parent imidazoliums' are within error ( $pK_a$  IPr·HCl =  $19.29 \pm 0.07$ ,  $pK_a$  IMes·HCl =  $19.40 \pm 0.12$ ).<sup>58,59</sup>

Though the isolation and authentication of hydrogen bonding adducts of carbenes has thus far been limited to imidazolylidene-based carbenes, hydrogen bonding adducts role in catalysis<sup>60–63</sup> and X–H insertion chemistry has been postulated for some time. Bertrand recently provided computational evidence for these non-traditional hydrogen bonded species as key intermediates for the reversible insertion of cyclic (alkyl)(amino)(carbene)s (CAACs) into the N–H bond of DPA (Fig. 1b).<sup>34</sup> The calculations



Chart 1 Ditopic secondary amines.

suggested that the process of a CAAC inserting into an N–H bond proceeds *via* non-traditional hydrogen bonded and proton transfer intermediates.

Our recent work has established that Cbz and IPr form a hydrogen bonding adduct ( $Cbz\cdots IPr$ , Fig. 1a) that has a strength of association in solution ( $C_6D_6$ ) of  $-2.8$  kcal mol<sup>-1</sup>.<sup>33</sup> Previous studies of non-traditional  $X-H\cdots C<$  hydrogen bonding ( $X = N$  (ref. 31) or O (ref. 32, 47, 48 and 64)) did not quantitate the strengths of interaction. Interestingly, the corresponding reaction of Cbz with CAAC from this study is reversible and yields the product of insertion of the carbene into the N–H bond of Cbz. The use of more strongly acidic N–H species with CAACs however results in proton transfer to forms salts.<sup>33,65</sup> Collectively, these experimental efforts help “visualize” the proposed intermediates for insertion reactions of CAACs into X–H bonds.

While these efforts have proven fruitful in identifying new species with unique hydrogen bonds, there are no steadfast rules to predict reactivity or product distribution. Crystallographic information on  $H\cdots C<$  hydrogen bonds shed some insight into the strength of these associations, but there are no obvious ways to correlate these metrics to solution-state measurements. Computational efforts have been made to determine the hydrogen bond basicity of carbenes, but thus far these measures have been purely theoretical.<sup>66,67</sup>

It is of interest therefore to gain further insights into the factors that determine when hydrogen bonding occurs in preference to proton transfer or N–H insertion for reactions between isolable carbenes and *NH*-containing molecules. An important part of this effort involves delineating the strengths of non-conventional hydrogen bonding. In order to probe this latter question in more detail, a series of symmetric and asymmetric ditopic *NH*-containing systems consisting of Cbz and DPA units (Chart 1; 3,3'-bicarbazole,<sup>68</sup> BC; *N,N'*-diphenylbenzidine, DPB; *N,N'*-diphenyl-*p*-phenylenediamine, DPPD, 4-(carbazol-3-yl)-*N*-phenylaniline, CD), which are structurally similar with differing acidities, will be reacted with a single NHC (IPr). These unusual platforms will allow for the gradual tuning of a single component (X–H) while having the carbene (A) remain consistent. This array of hydrogen bonded adducts will be used to assess how a NHC participates in non-traditional hydrogen bonding when presented with multiple reactive sites within single molecules.

## Results and discussion

### BC...2IPr adduct

Previous studies on a  $Cbz\cdots IPr$  hydrogen bonded adduct suggested that IPr could form a di-hydrogen bonded adduct with BC, and that this adduct should be labile and display





Fig. 2 Partial  $^1\text{H}$  NMR spectra (500 MHz,  $\text{THF}-d_8$ ) of **BC** (50 mM) and **BC** $\cdots$ **2IPr**. Dashed lines indicate chemical shift changes upon hydrogen bonding to **IPr**.

concentration dependent behavior.  $^1\text{H}$  NMR analysis of a 1 : 2 mixture of **BC** and **IPr** in  $\text{THF}-d_8$  reveals that significant shifts ( $\Delta\delta > 0.05$  ppm) occur for all proton resonances of the individual components, as highlighted in Fig. 2. In particular, the drastic downfield shift of  $\text{H}_\alpha$  ( $\Delta\delta \approx +1.7$  ppm) is indicative of hydrogen bonding, and is similar to the corresponding shift of  $\text{H}_\alpha$  during formation of **Cbz** $\cdots$ **IPr**. The number of resonances indicate a symmetric structure for the **BC** $\cdots$ **2IPr** di-hydrogen bonded adduct. Consistent with this formulation, signals 1b and 2b show a substantial upfield shift ( $\Delta\delta \approx -0.9$  ppm), since upon complexation they are positioned directly into the face of the Dipp groups on **IPr**. Inspection of the  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of **BC** $\cdots$ **2IPr** reveals a single carbenic resonance ( $\delta$  215.2 ppm) that is noticeably upfield relative to the carbenic resonance of **IPr** ( $\delta$  221.1 ppm in  $\text{THF}-d_8$ ).

Vapor diffusion of hexanes into a solution of **BC** $\cdots$ **2IPr** in THF yielded pale yellow crystals suitable for X-ray diffraction. Crystallographic analysis of one such crystal of **BC** $\cdots$ **2IPr** is portrayed in Fig. 3 (see ESI† for full details). The structure confirms a two-fold hydrogen bonding adduct, with an average  $\text{H1}\cdots\text{C13}$  distance of 2.10 Å and a  $\text{N2}-\text{C12}-\text{N3}$  angle of  $102.2^\circ$ ,

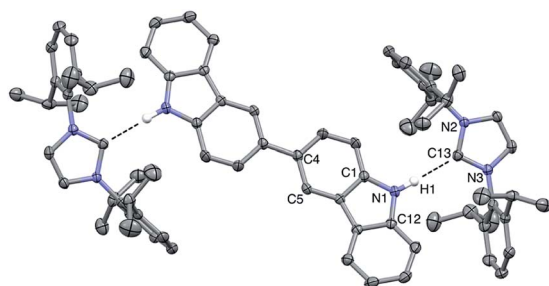


Fig. 3 ORTEP diagram (ellipsoids drawn at 50% probability) of **BC** $\cdots$ **2IPr**. Non-hydrogen bonding hydrogens and co-crystallized THF are omitted for clarity. Average select bond lengths (Å) and angles ( $^\circ$ ):  $\text{H1}\cdots\text{C13}$ , 2.10;  $\text{N1}\cdots\text{C13}$ , 2.96;  $\text{N2}-\text{C13}-\text{N3}$ ,  $102.2^\circ$ ;  $\text{N2}-\text{N3}-\text{C12}-\text{C1}$ ,  $13.5^\circ$ .

which are nearly identical to corresponding parameters for the mono-functional counterpart **Cbz** $\cdots$ **IPr**. Interestingly, the imidazole-2-ylidene  $\text{C}_3\text{N}_2$  and **Cbz** ring systems are nearly coplanar as indicated by  $\phi$   $\text{N2}-\text{N3}-\text{C12}-\text{C1} = 13.5^\circ$ , which is in line with the monotopic **Cbz** $\cdots$ **IPr** system ( $\phi = 11.0^\circ$ ).

### Model **DPA** $\cdots$ **IPr** adduct

Structural data for a **DPA** $\cdots$ **IPr** hydrogen bonded adduct were previously reported,<sup>31</sup> but for the present study related details on the corresponding **DPA** $\cdots$ **IPr** adduct are necessary so that closer comparisons can be made. This material was synthesized by the addition of **IPr** to a THF solution of **DPA**. Removal of solvent, followed by recrystallization from toluene at  $-35^\circ\text{C}$  affords pure **DPA** $\cdots$ **IPr** as white crystals. Hydrogen bond formation is clearly indicated in  $\text{C}_6\text{D}_6$  by an upfield shift of the carbenic carbon resonance (218.2 ppm) compared to parent **IPr** (220.6 ppm in  $\text{C}_6\text{D}_6$ ).<sup>69</sup> Preliminary  $^1\text{H}$  NMR analysis of this material showed concentration dependent behavior. To ascertain the strength of this association a  $^1\text{H}$  NMR concentration dependent study of **DPA** $\cdots$ **IPr** was performed in  $\text{C}_6\text{D}_6$  over a broad concentration range (75–1 mM). Benzene is an ideal solvent in such an analysis as its impact on hydrogen bonding is minimal,<sup>70</sup> while also allowing for comparison to our previous measurements on **Cbz** $\cdots$ **IPr** ( $\text{C}_6\text{D}_6$ , concentration range of 50–1 mM).<sup>33</sup> This analysis revealed the association strength of **DPA** $\cdots$ **IPr** to be substantially weaker than **Cbz** $\cdots$ **IPr** ( $K_d = 105 \pm 3 \text{ M}^{-1}$ ;  $\Delta G \approx -2.8 \text{ kcal mol}^{-1}$ ), with only the *NH* resonance being significantly influenced upon complexation ( $K_d = 0.85 \pm 1.05 \text{ M}^{-1}$  and  $\Delta G \approx -0.10 \text{ kcal mol}^{-1}$ , see ESI† for full details).<sup>71</sup> This drastic preference for the more acidic amine of **Cbz** was also verified *via* an exchange reaction (eqn (1)):



wherein addition of **Cbz** to **DPA** $\cdots$ **IPr** results in near complete conversion to **Cbz** $\cdots$ **IPr** and displacement of **DPA**. The dynamic (on the NMR timescale) nature of the mixture is indicated by the fact that a single hydrogen bonding *NH* resonance is observed (albeit not to the extent of the pure adducts, see ESI†) for each of the reaction pairs (**DPA** $\cdots$ **IPr**/**DPA** and **Cbz** $\cdots$ **IPr**/**Cbz**).

### Ditopic **DPB** $\cdots$ **2IPr** and **DPPD** $\cdots$ **2IPr** adducts

Both ditopic **DPB** and **DPPD** yield 1 : 2 adducts **DPB** $\cdots$ **2IPr** and **DPPD** $\cdots$ **2IPr**, respectively, upon reaction with two equivalents of **IPr** (Fig. 4, top) in THF. As previously observed, **DPB** $\cdots$ **2IPr** and **DPPD** $\cdots$ **2IPr** are in equilibrium with their individual components, and at higher NMR concentrations these solutions exist predominately as the di-hydrogen bonded species.  $^1\text{H}$  NMR analyses (**DPB** $\cdots$ **2IPr**, **DPPD** $\cdots$ **2IPr**), as shown in Fig. 4, highlights the subtle chemical shift changes ( $\Delta\delta < 0.20$  ppm) for resonances compared to **BC** $\cdots$ **2IPr** ( $\Delta\delta > 0.15$  ppm). Though these shifts in proton resonances are smaller, the overall directionality matches that observed for **BC** $\cdots$ **2IPr**. This is best realized in the *NH* signal,  $\text{H}_\beta$ , which shifts by  $\Delta\delta = 0.20$  ppm (**DPB** $\cdots$ **2IPr**) and  $\Delta\delta = 0.15$  ppm (**DPPD** $\cdots$ **2IPr**), indicative of a significantly weaker hydrogen bond.





Fig. 4 Partial  $^1\text{H}$  NMR spectra (500 MHz,  $\text{THF-d}_8$ ) of DPB (50 mM),  $\text{DPB}\cdots 2\text{IPr}$ ,  $\text{DPPD}\cdots 2\text{IPr}$ , and DPPD (50 mM). Dashed lines highlight the chemical shift changes upon hydrogen bonding to IPr.

Crystals of  $\text{DPPD}\cdots 2\text{IPr}$  suitable for a X-ray diffraction studies were obtained by chilling a solution of  $\text{DPPD}\cdots 2\text{IPr}$  in a 3 : 2 hexanes : THF solvent mixture at  $-35^\circ\text{C}$  for several days. The resulting solid-state structure of  $\text{DPPD}\cdots 2\text{IPr}$  is portrayed in Fig. 5. The  $\text{H1}\cdots\text{C24}$  distance of 2.30(2) Å matches that found for the  $\text{DPA}\cdots\text{IMes}$  adduct, as is the interior  $\text{N2-C13-N3}$  angle of  $101.9(1)^\circ$ . The dihedral between the pseudo-planes of  $\text{DPPD}\cdots 2\text{IPr}$  ( $\phi$   $\text{N2-N3-C2-C4} = 17^\circ$ ) are in agreement with  $\text{BC}\cdots 2\text{IPr}$ , and slightly less pronounced than  $\text{DPA}\cdots\text{IMes}$  ( $\phi = 38^\circ$ ). The  $\text{N1-H1}\cdots\text{C24}$  bond angle is nearly linear ( $171^\circ$ ), albeit quite bent relative to  $\text{DPA}\cdots\text{IMes}$  ( $\text{N-H}\cdots\text{C} = 179^\circ$ ). The hydrogen bond distances are within the sum of the van der Waal radii, and display closer contacts than the hydrogen bond



Fig. 5 ORTEP diagram (ellipsoids drawn at 50% probability) of  $\text{DPPD}\cdots 2\text{IPr}$ . Non-hydrogen bonding hydrogens are omitted for clarity. Select bond lengths (Å) and angles ( $^\circ$ ):  $\text{H1}\cdots\text{C24}$ , 2.30(2);  $\text{N1}\cdots\text{C24}$ , 3.174(2);  $\text{N2-C13-N3}$ , 101.9(1);  $\text{N2-N3-C4-C2}$ ,  $-17.41(7)$ .

adducts of the Ong group, where carbenes with pendant secondary amines form dimers in the solid-state.<sup>44,45</sup> By contrast, all attempts to crystallize  $\text{DPB}\cdots 2\text{IPr}$  resulted in dissociation of the adduct into individual components. It appears that the poor solubility of DPB leads to preferential precipitation/crystallization of DPB, which is in facile equilibrium with IPr and  $\text{DPB}\cdots 2\text{IPr}$  (*vide infra*).

Analysis of the metric data obtained for the symmetric ditopic  $\text{NH}$ -bearing adducts in both solid- and solution-state reveals several interesting insights. In the solid-state the  $\text{N-C-N}$  angles within IPr ( $101.5^\circ$ )<sup>69</sup> relax upon formation of hydrogen bonded species  $\text{DPPD}\cdots 2\text{IPr}$  ( $101.9^\circ$ ) and  $\text{BC}\cdots 2\text{IPr}$  ( $102.2^\circ$ ). A greater distortion of the  $\text{N-C-N}$  angle is thus associated with greater interaction, and if taken to an extreme would result in proton transfer (where imidazolium salts typically feature  $\text{N-C-N}$  angles of  $\sim 108^\circ$ ).<sup>30</sup> The length of the hydrogen bonds ( $\text{H}\cdots\text{C}$  distance;  $\text{DPPD}\cdots 2\text{IPr}$ , 2.30 Å;  $\text{BC}\cdots 2\text{IPr}$ , 2.10 Å) also correlate well with the presumed strength of association based on measurements on the monofunctional amine counterparts (*vide supra*).

While  $^1\text{H}$  NMR spectra show that the changes in the chemical shifts for protons involved in hydrogen bonding can be predictive of association strengths, the shifts observed in the  $^{13}\text{C}\{^1\text{H}\}$  NMR spectra for the carbenic carbon are also quite sensitive to these external interactions. As the strength of the hydrogen bond increases the carbenic carbon shifts upfield.<sup>30</sup>

Specifically, the  $^{13}\text{C}\{^1\text{H}\}$  NMR spectra of  $\text{BC}\cdots 2\text{IPr}$  (215.2 ppm) shows a greater  $\Delta\delta$  (free IPr  $\delta$  221.1 ppm) than either  $\text{DPB}\cdots 2\text{IPr}$  ( $\delta$  220.1 ppm) and  $\text{DPPD}\cdots 2\text{IPr}$  ( $\delta$  220.3 ppm).  $^{13}\text{C}$  spectroscopy might thus serve as a new tool for assessing the strength of the hydrogen bond in non-traditional systems, adding to other experimental measures used to assess the properties of carbenes as ligands (*i.e.* measuring  $\pi$ -acidity *via*  $^{31}\text{P}$  or  $^{77}\text{Se}$  NMR spectroscopy<sup>72</sup> and carbene-metal ligand strength assessed *via*  $^{13}\text{C}$  spectroscopy<sup>73</sup>).

### Internal competitive hydrogen bonding

To probe the competitive nature of these hydrogen bonding adducts mixed carbazole-diphenylamine species CD was synthesized *via* Suzuki-Miyaura cross-coupling in modest yield (55% isolated, see ESI† for details). Reactions of CD with one and two equivalents of IPr were thus examined (Fig. 6, upper). As expected, formation of the mono- and di-carbene adducts  $\text{CD}\cdots\text{IPr}$  and  $\text{CD}\cdots 2\text{IPr}$  is observable by NMR spectroscopy at elevated concentrations. Fig. 6 compares partial  $^1\text{H}$  NMR spectra of these products contrasted against CD, highlighting the proton resonances impacted by NHC association. In alignment with the findings above, preferential interaction of the NHC occurs with the carbazole unit of CD upon addition of one equivalent of IPr (black dotted lines in Fig. 6). This assessment is confirmed by the signals for carbazole fragment of CD shifting in the same fashion as the symmetric  $\text{BC}\cdots 2\text{IPr}$ , with the caveat that shifts are only  $\sim 65\%$  the overall  $\Delta\delta$  of their symmetric counterpart. This may reflect the fact that IPr equilibrates between both carbazole and diphenylamine  $\text{NH}$  residues to some extent. The perturbations of the proton





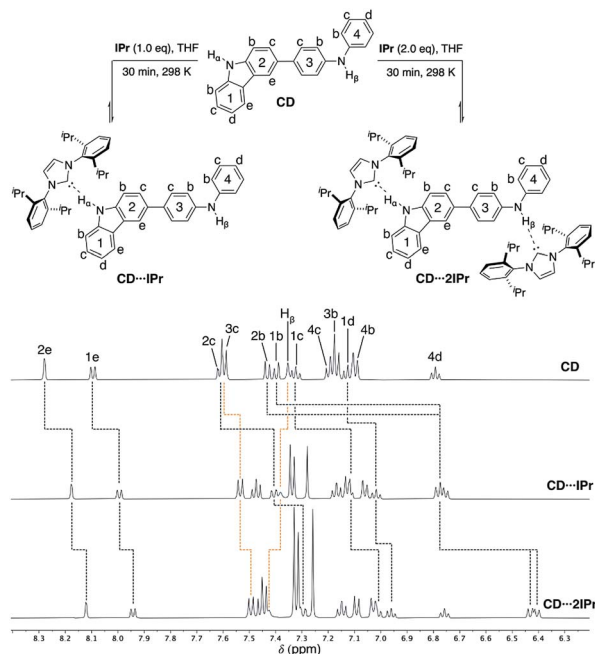


Fig. 6 Partial  $^1\text{H}$  NMR spectra (500 MHz,  $\text{THF-}d_8$ ) of CD (50 mM),  $\text{CD}\cdots\text{IPr}$ , and  $\text{CD}\cdots 2\text{IPr}$ , highlighting the chemical shift changes upon hydrogen bonding to **IPr**. CD  $\text{H}_z$  (10.25 ppm),  $\text{CD}\cdots\text{IPr}$   $\text{H}_z$  (11.30 ppm), and  $\text{CD}\cdots 2\text{IPr}$   $\text{H}_z$  (12.40 ppm) are broadened due to exchange, see ESI† (rings 1 and 2 = black dotted lines, rings 3 and 4 = orange dotted lines).

resonances on rings 3 and 4 (orange dotted lines) are reminiscent of  $\text{DPB}\cdots 2\text{IPr}$  and  $\text{DPPD}\cdots 2\text{IPr}$ , albeit only minor in comparison to rings 1 and 2.

Upon addition of two equivalents of **IPr** to **CD**, the  $^1\text{H}$  NMR chemical shifts of  $\text{CD}\cdots 2\text{IPr}$  are a near match to the symmetric diamine counterparts,  $\text{BC}\cdots 2\text{IPr}$  and  $\text{DPB}\cdots 2\text{IPr}$  respectively. The realignment of the  $^1\text{H}$  spectra to mirror the symmetric analogues confirms formation of  $\text{CD}\cdots 2\text{IPr}$ . Due to the rapid exchange of **IPr** between both *NH* sites on **CD** the  $^{13}\text{C}\{^1\text{H}\}$  NMR spectra yield a singular shift for the carbenic resonance. The observed shifts for asymmetric  $\text{CD}\cdots 2\text{IPr}$  ( $\delta$  217.4 ppm) and  $\text{CD}\cdots\text{IPr}$  ( $\delta$  216.4 ppm) fall between their respective symmetric counterparts ( $\text{BC}\cdots 2\text{IPr}$ ,  $\delta$  215.2 ppm,  $\text{DPB}\cdots 2\text{IPr}$ ,  $\delta$  220.1 ppm). Unsurprisingly the  $^{13}\text{C}\{^1\text{H}\}$  NMR signal in  $\text{CD}\cdots\text{IPr}$  resides closer to  $\text{BC}\cdots 2\text{IPr}$ , verifying our  $^1\text{H}$  measurements which show that **IPr** preferentially binds to the carbazole side of the ditopic system. When both *NH* sites are satisfied in  $\text{CD}\cdots 2\text{IPr}$  the carbenic carbon resonance is a near perfect average of the observed resonances for the symmetric species ( $\text{BC}\cdots 2\text{IPr}$  and  $\text{DPB}\cdots 2\text{IPr}$  average resonance carbenic resonance  $\approx$  217.6 ppm).

Unfortunately attempts to obtain single crystals of either  $\text{CD}\cdots\text{IPr}$  and  $\text{CD}\cdots 2\text{IPr}$  were thwarted by the preferential crystallization of **CD** from solutions of these materials (see ESI† for crystallographic details). While this may be due to the reduced solubility of **CD** relative to **IPr**, the probable cause is the labile nature of the  $\text{N-H}\cdots\text{C}$  bond not being conducive to solid-state analysis.

Table 1 Summation of solid- and solution-state metrics<sup>a</sup>

	N–C–N (°)	$^{13}\text{C}$ $\delta$ (ppm)	$^1\text{H}$ $\Delta\delta$ (ppm)	$\text{pK}_a$
<b>IPr</b>	101.5 <sup>b</sup>	221.1	—	19.3 <sup>c</sup>
<b>BC</b> $\cdots 2\text{IPr}$	102.2	215.2	1.66	19.9
<b>DPB</b> $\cdots 2\text{IPr}$	—	220.1	0.20	25.0
<b>DPPD</b> $\cdots 2\text{IPr}$	101.9	220.3	0.15	25.0
<b>CD</b> $\cdots 2\text{IPr}$	—	217.4	0.99 <sup>d</sup>	22.5 <sup>d</sup>

<sup>a</sup>  $^1\text{H}$   $\Delta\delta$  is calculated relative to each adducts parent species at 50 mM in  $\text{THF-}d_8$ . <sup>b</sup> See ref. 69. <sup>c</sup>  $\text{pK}_a$  of the conjugate acid (**IPr** $\cdot\text{HCl}$ ).<sup>58,59</sup> <sup>d</sup> Average values.

## Conclusion

Through a series of symmetric and asymmetric ditopic secondary amines the strength of a  $\text{X-H}\cdots\text{C}$  hydrogen bond can be directly assessed *via* several solid- and solution-state factors, summarized in Table 1. Paramount in predicting the strength of the association is the  $\text{pK}_a$  of the parent X–H species, which in these examples correlates well with both solid- and solution-state metrics. In the solid-state limiting the degrees of freedom in the parent molecule is vital, wherein systems with even weak hydrogen bonds can be crystallized in their adduct form ( $\text{DPPD}\cdots 2\text{IPr}$ ). In **BC**, **DPB**, and **DPPD** systems solution-state analysis is simplified due their high degree of symmetry and rapid equilibrium of the  $\text{N-H}\cdots\text{IPr}$  interaction. In each of these species both the  $\Delta\delta$  of the proton participating in hydrogen bonding and the  $^{13}\text{C}$  resonance of the carbenic carbon are indicators of hydrogen bond strength.  $^1\text{H}$  NMR spectra show that upon hydrogen bonding with **IPr** the monomers are rigidified, with proton resonances far removed from area of interaction changing significantly in comparison to the unhindered molecules. When starving the asymmetric **CD** system of **IPr**, the carbene primarily interacts with the more acidic carbazole residue as evidenced by both  $^1\text{H}$  and  $^{13}\text{C}$  spectroscopy. When enough **IPr** is supplied to satisfy both *NH* sites the carbenic carbon resonance falls directly between the symmetric  $^{13}\text{C}$  residues, indicating a system that is in rapid equilibrium on the NMR timescale. The reversible nature of these systems and the ability to predict hydrogen bond strength through both solid- and solution-state metrics could lead to further developments in systems chemistry. Efforts to explore higher functionality *NH*-containing systems and carbenes are currently underway.

## Conflicts of interest

The authors declare no conflicts of interest.

## Acknowledgements

We thank the National Science Foundation (CHE-1464855 and CHE-1955845) for their support of this work.

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