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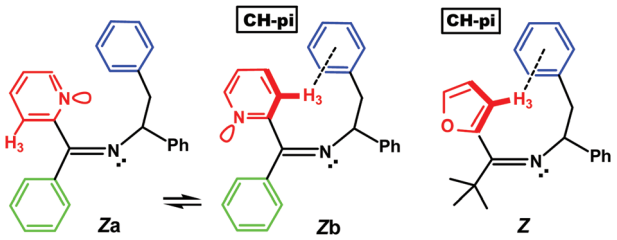
M. Eugenia González-Rosende,* Encarna Castillo, W. Brian Jennings* and John F. Malone

Imino models show that 6 and 5-membered heterocyclic rings can engage in attractive edge-to-face interactions with an adjacent phenyl ring.



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Organic & Biomolecular Chemistry

PAPER

Stereodynamics and edge-to-face CH–π aromatic interactions in imino compounds containing heterocyclic rings†‡

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By comparison with close contact interactions between benzene rings there is a paucity of experimental data available for attractive interactions involving aromatic heterocyclic rings, especially for small molecules in solution. Herein we describe aromatic heterocyclic and carbocyclic edge-to face interactions and conformational stereodynamics of *N*-1,2-diphenylethyl imines bearing a phenyl group and either a 2-pyridyl, 3-pyridyl, 2-thiophene or 2-furanyl moiety on the imino carbon. X-ray crystal structures have been determined for two compounds. Slow rotation about the phenyl–imino bond in the *E*-isomers and around the heterocycle–imino bond in the *Z*-isomers of the pyridyl compounds was observed at low temperatures by NMR. Abnormally large shielding of one *ortho* hydrogen indicates that both the imino phenyl and heterocycle rings can engage in an edge-to-face interaction with the N-terminal phenyl moiety in the appropriate isomer. Some rotational barriers around the phenyl–imino and heterocycle–imino bonds were measured.

Introduction

Attractive interactions between aromatic rings were initially thought to be largely restricted to face to face parallel "sandwich" compounds between a ring containing electron withdrawing substituents and a second ring bearing electron donating substituents[1] (Fig. 1a).

However X-ray investigations on crystals of benzene as early as 1958 indicated that unsubstituted rings can unexpectedly stack in close proximity but in an alternative edge-to-face T-shaped geometry (Fig. 1b).[2] Interest in this topic blossomed when it became evident that aromatic residues in amino acids such as phenylalanine and tyrosine can engage in close contact interactions.[3] Subsequently it was realised that these interactions can also be involved in host–guest macrocycles,[4] molecular recognition[5] and as control elements in stereoselective synthesis[6] and crystal engineering.[7] These developments stimulated theoretical groups to attempt to assess the origin and strengths of these weak interactions,[8] and synthetic chemists to design model systems for more detailed investigations.[9] Three further potentially attractive geometries have

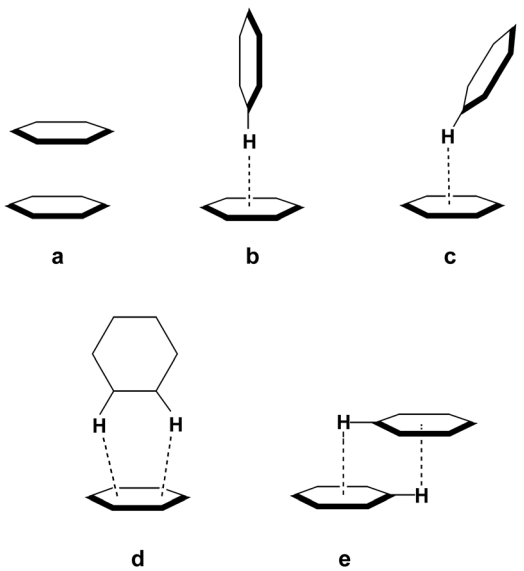

Fig. 1 Attractive geometries of the benzene dimer.

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† This paper is dedicated to the memory of our dear friend and former colleague the late Professor José Sepúlveda-Arques, University of Valencia, who facilitated this international collaboration.

‡ Electronic supplementary information (ESI) available: Additional dynamic NMR data, ^{1}H NMR, ^{13}C NMR and mass spectra for compounds **1–8**. CCDC 1518494 and 1518495 for compounds **1** and **5**. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c6ob02618d

been identified, namely the face tilted-T (c), the edge tilted-T (d) and the parallel displaced (e) (Fig. 1). Molecular orbital calculations differ somewhat on the size of the interaction energy, but calculations indicate that structures b, d and e have similar interaction energies in the range −2.4 to −2.8 kcal mol^{-1} while the parallel sandwich (a) has a lower interaction energy (*ca.* −1.5 to −2.0 kcal mol^{-1}).[10,11] The face tilted-T (c) which has been observed in our imino[12–14] and biaryl[15] model systems and in the cyclophanes reported by Kim *et al.*,[16] Fukazawa *et al.*[17] and Schladetsky *et al.*[18] is a distortion of the T-structure (b) produced by limitations of the linker groups. It is probably not quite an energy minimum for the benzene dimer and therefore probably has a reduced interaction energy. Experimental estimates suggest a binding enthalpy value of *ca.* −1.4 kcal mol^{-1} for the face tilted-T structure (c) which may reflect some strain in the linker.[12,14] In geometries b, c, d, and e there is a potentially stabilising CH–π interaction[19] (two in the case of structures d and e). However MO calculations indicate that less specific dispersive forces are involved and may well make a large contribution to the binding energy.[8] Interactions involving heterocyclic rings have been less intensively investigated. Cockroft and Hunter[20] have investigated parallel stacking of nucleoside bases, Gung *et al.*[21] have investigated parallel displaced stacking of pyridyl rings using a triptycene model system and Sherrill *et al.*[22] have reported theoretical calculations on the parallel pyridine dimer. Benaglia and coworkers[23] have investigated edge-to-face and parallel interactions between thiophene and furan rings and a benzene ring in paracyclophanes using molecular orbital calculations and NMR spectroscopy. Frontera and coworkers[24] have performed *ab initio* calculations on the T-shaped pyridine-benzene dimer with the *para* pyridyl hydrogen directed towards the face of the benzene ring. There have been a few other reports of edge-to-face interactions involving a heterocyclic ring, mainly in crystal structures.[25,26] We now report some edge-to-face interactions in a stereodynamically restricted imino based model system containing a six or five-membered heterocyclic ring.

Results and discussion

Model compounds 1 and 2 possessing a 3-pyridyl ring

Imines with different substituents on the imino carbon can exhibit *E*–*Z* isomerism at ambient temperature, but at elevated temperatures rapid isomerisation is often observed.[13,14,27] When crystals of imine **1** were dissolved in deuteriochloroform and the ^{1}H NMR spectrum recorded immediately a single set of signals was observed consistent with the proposed structure. However an aromatic doublet signal (^3J 6.9 Hz) which integrated for two hydrogens was abnormally shielded at δ 6.50. This signal was assigned to the two *ortho* protons (2Ho) on the imino phenyl ring. In contrast the NMR spectrum of compound **2** which has a similar structure but is lacking the N-terminal phenyl group showed no shielded aromatic signals in the range δ 5.5–7.0.

Previous investigations of a related imine derived from benzophenone and phenylalanine methyl ester have shown that the *ortho* protons (Ho) on a phenyl ring *cis* to the *N*-substituent are usually shielded due to close proximity of the N-terminal phenyl ring.[13] The *ortho* (2Ho) doublet in **1** was slightly broadened suggesting that there may be some residual exchange broadening, hence a lower temperature investigation was conducted in deuteriodichloromethane. On lowering the temperature to −30 °C the *ortho* Ho doublet signal at δ 6.45 broadened further and by −46 °C it had essentially collapsed into the baseline (Fig. 3). On further cooling two new equally intense broad signals appeared and by −80 °C these new signals at δ 5.68 (Ho) and δ 6.95 (Ho′) had sharpened considerably (Fig. 3). By analogy with related imines derived from benzophenone[13] it can be concluded that rotation about the phenyl–imino bond has become slow on the NMR timescale below −46 °C. The observation that one *ortho* signal (Ho) was abnormally shielded (δ 5.68) and well out of the usual aromatic region indicated that it was positioned close to the face of the N-terminal phenyl ring in an edge-to-face CH–π interaction. Hence this isomer can be confidently assigned the *E*-configuration where the imino phenyl ring is *syn* to the nitrogen substituent (Fig. 2). The other *ortho* signal (Ho′) at δ 6.95 lies in the normal aromatic range as it is directed away from the terminal phenyl ring and is not subjected to ring current shielding.

Computer aided lineshape analysis at −46 °C, just below the coalescence temperature, gave a phenyl–imino bond rotational rate of 1031 s^{-1} corresponding to a free energy barrier $\Delta G^{\ddagger}$ = 10.0 kcal mol^{-1} (see ESI,‡ p. S-3). This is slightly lower than that the reported barrier of 10.5 kcal mol^{-1} in a related imine derived from benzophenone.[13] A more extensive computer analysis of the exchange mediated lineshape over the temperature range −40 to −80 °C gave a rotational enthalpy of activation ($\Delta H^{\ddagger}$) of 7.6 ± 0.4 kcal mol^{-1} and an entropy of activation ($\Delta S^{\ddagger}$) of −10.5 ± 2.0 cal mol^{-1} K^{-1} (see ESI,‡ p. S-4 for details). The negative entropy factor reflects the

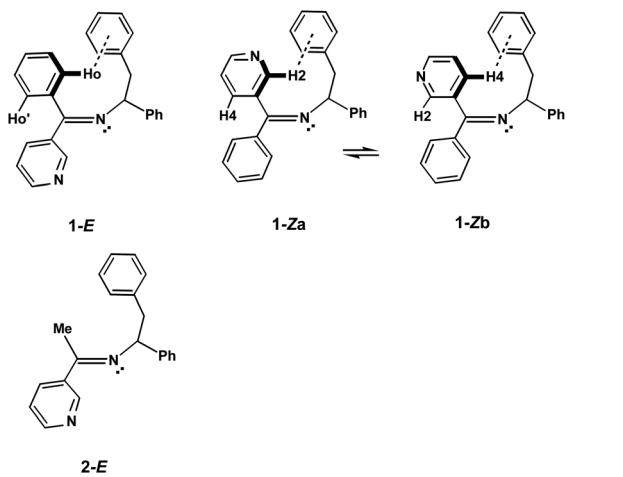

Fig. 2 Structures of compounds **1**-*E*, **1**-*Z*a, **1**-*Z*b and **2**-*E*.

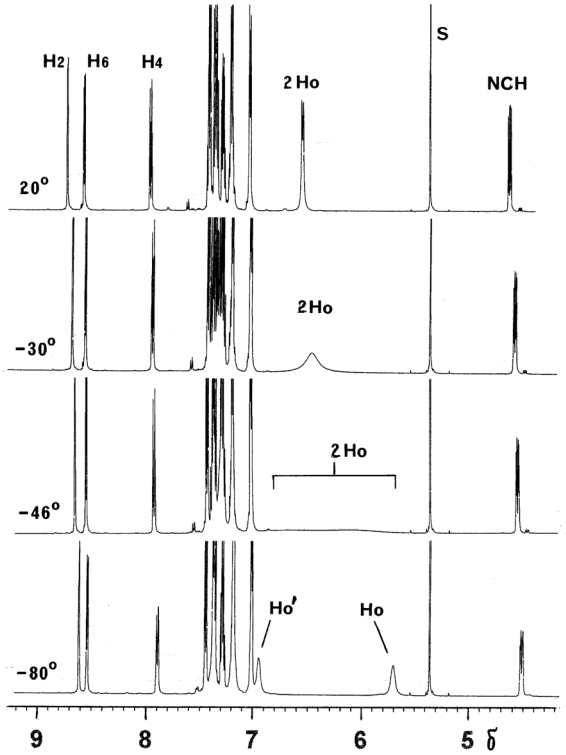

Fig. 3 Variable temperature ^{1}H NMR spectra (500 MHz) of compound **1*E*** in CD_2Cl_2 (S denotes residual solvent).

steric restrictions of freedom in the congested rotational transition state as the imino phenyl ring passes through the imino plane flanked by the *syn N*-3-pyridyl substituent and the geminal imino phenyl group. Although the imino-phenyl rotational barrier is mostly due to steric factors in the crowded transition state, the stabilisation of the ground state by the CH–π interaction will contribute a small amount (*ca.* 0.2–0.6 kcal mol^{-1}) to the free energy of activation $\Delta G^{\ddagger}$ based on previous estimates of the CH–π interaction free energy (ΔG) in related compounds.[12,13] However the contribution to raising the activation enthalpy ($\Delta H^{\ddagger}$) is likely to be much larger (*ca.* 1.3–1.8 kcal mol^{-1}) based on reported estimates of the CH–π interaction enthalpy[13,14] in related compounds.

An X-ray crystal structure analysis of **1** confirmed the *E*-configuration (Fig. 4). Furthermore it showed that the imino phenyl ring A is twisted by 67° out of the imino plane and engages in a face tilted-T arrangement with the N-terminal phenyl ring C. The interacting Ho hydrogen is at a perpendicular distance of 3.09 Å from the face of the terminal ring C and is offset from the ring centre by 0.73 Å (Table 1). These distances are longer than most of those previously reported for molecules with face tilted-T geometry.[9,12–15] The inter ring tilt angle A–C (36°) is also unusually low, hence the geometry lies slightly closer to a parallel displaced structure (tilt angle 0°) than a T-shaped structure (tilt angle 90°). The distance of Ho above the ring C plane is likely to increase as the tilt angle decreases from 90° in the T-structure to 0° in the parallel displaced structure. However the ring current shielding of Ho is

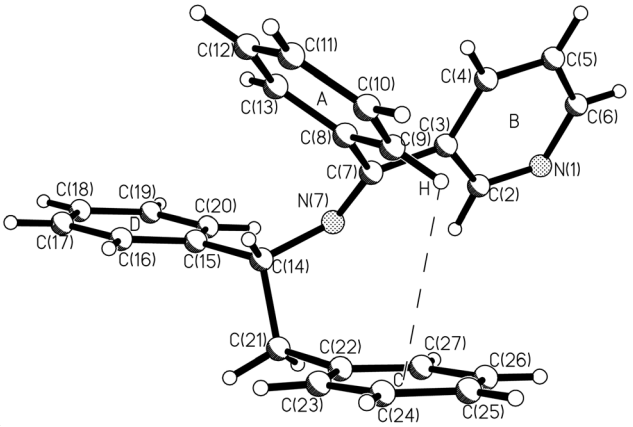

Fig. 4 X-ray crystal structure of compound **1**.

Table 1 Selected contact distances and twist angles from X-ray crystal data

Parameter	Compd **1**	Compd **5**[a]
Ho – ring C centre[b] (Å)	3.17	2.95, 3.07
Ho – ring C plane[b] (Å)	3.09	2.88, 3.06
Ho offset from ring C centre[b] (Å)	0.73	0.63, 0.29
Rings A and C inter-plane tilt angle (°)	36.3	55.6, 40.3
Phenyl (A)–imino interplane angle[c] (°)	66.6	82.8, 80.9
Heterocycle–imino interplane angle[c] (°)	13.5	4.6, 10.8
C═N–CH–CH_2 torsion angle[d] (°)	−116.5	−123.4, −122.9

[a] Values listed are for the two crystallographically independent molecules of this racemic crystal. [b] Calculated using a standard aromatic C–H bond length of 1.083 Å. [c] An interplane angle of 0° would denote that the aromatic ring lies in the imino plane. [d] Torsion angles in each case relate to the (*R*) (−) enantiomer (shown in Fig. 4 and 11).

similar to that reported in related imino compounds which have shorter Ho to phenyl distances and larger tilt angles.[13] The calculated vertical distance from the closest hydrogen to the face of the second ring in the parallel displaced benzene dimer (*ca.* 3.5 Å) is considerably longer than that in the alternative T-structure (*ca.* 2.5 Å).[8–11] Accordingly it is possible that crystal packing forces somewhat distort the geometry of compound **1**. Molecular orbital calculations[10] also indicate that the potential well for T-shaped aromatic edge-to-face interactions is very shallow, hence an appreciable interaction probably exists at H to ring face distances significantly greater that the calculated optimum (*ca.* 2.5 Å) for the T-dimer.

It was observed that when an NMR sample of **1** in deuteriochloroform was allowed to stand a second set of NCH and CH_2 signals began to appear adjacent to those of the **1**-*E* isomer and some new signals appeared in the aromatic region. These signals were assigned to the *Z*-isomer (Fig. 5). Interest centred on a new slightly broadened shielded doublet at δ 6.68 (^3J 7.5 Hz) assigned to H4 on the pyridyl ring of the *Z*-isomer and a new broadened singlet at δ 7.78 from the *Z*-pyridyl H2. These signals are much more shielded than the corresponding H4 and H2 signals at δ 8.02 (^3J 7.6 Hz) and δ 8.87 (^4J 2.1 Hz) respectively in the related model compound **2** where the imino

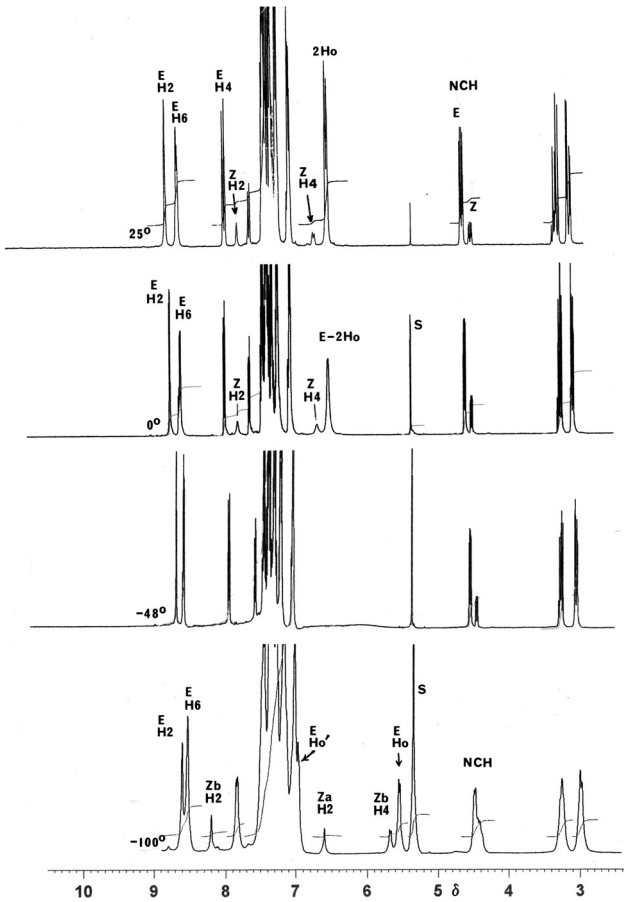

Fig. 5 Variable temperature ^{1}H NMR spectra (400 MHz) of an *EZ* isomeric mixture of compound **1** in CD_2Cl_2 (S denotes residual solvent).

phenyl group has been replaced by a smaller methyl group. Previous work has shown that imines derived from aryl methyl ketones exist predominantly or exclusively in the *E*-configuration unless the aryl group contains an *ortho* substituent.[27] Hence the 3-pyridyl ring in compound **2** cannot engage in an edge-to-face interaction with the *trans* N-terminal phenyl ring.

On warming a sample of **1** in deuteriochloroform to 40–50 °C equilibrium was eventually attained at an *E* : *Z* ratio of 62 : 38 accompanied by some thermal decomposition. A partly equilibrated (*E* : *Z* 74 : 26) sample in deuteriodichloromethane was subjected to low temperature NMR to see if rotation of the 3-pyridyl ring in the minor *Z*-isomer could be frozen. On cooling to 0 °C the *Z*-H2 and *Z*-H4 signals broadened (Fig. 5). At −48 °C both signals had collapsed into the baseline and merged with the exchange broadened Ho signal of the *E*-isomer. On further cooling three new broadened signals appeared and at −100 °C they were well resolved (Fig. 5, lower spectrum). The new strongly shielded doublet signal at δ 5.70 was assigned to H4 of the major *Z*b-isomer, and the new singlet signals of slightly different intensity at δ 6.61 and δ 8.20 were assigned to H2 in the minor (*Z*a) and major (*Z*b) rotamers respectively. The non-shielded exchanging partner (*Z*a-H4) of *Z*b-H4 evidently lies hidden under the main aromatic envelope between δ 7.0 and δ 7.5. Clearly at low temperature rotation around the 3-pyridyl–imino bond in the *Z*-isomer has become slow on the NMR time-scale leading to the observation of separate signals from the two *Z*-rotamers. In principle all signals should be differentiated in these isomers, but at this level of resolution only the H2 and H4 signals are resolved due to the large differential ring current effect of the terminal phenyl ring on these hydrogens. In the minor rotamer (*Z*a) the more shielded H2 hydrogen engages in an edge-to-face interaction with the N-terminal phenyl ring whereas in the major rotamer (*Z*b) the more shielded H4 hydrogen engages with the terminal phenyl and lies under the main aromatic envelope. The rotamer ratio *Z*a : *Z*b was estimated to be *ca.* 43 : 57. This indicates a small thermodynamic preference for the 3-pyridyl *Z*b rotamer where H4 interacts with the terminal phenyl ring. On a simple electrostatic model it might be expected that H2 would have the stronger CH–π interaction due to the adjacent pyridyl nitrogen rendering H2 more electropositive. Evidently other factors are involved such as the overall charge distribution of the pyridyl ring and dispersive interactions.

In the *EZ* mixture near coalescence the broad *Z*-pyridyl H2 signals were completely overlapped by the coalescing phenyl Ho signal preventing evaluation of the rate of pyridyl rotation. However at −74 °C and −65 °C the exchange broadened shielded *Z*b-H4 and shielded phenyl Ho signals were only partly overlapping. Hence computer aided lineshape fitting of these combined signals was feasible (eight site coalescence including the doublet splitting). The results (Table 2) gave an excellent fit with $\Delta G^{\ddagger}$ = 9.73 kcal mol^{-1} (*Z*a → *Z*b) and 9.81 kcal mol^{-1} (*Z*b → *Z*a) at −74 °C (see Fig. 6), and $\Delta G^{\ddagger}$ = 9.86 kcal mol^{-1} (*Z*a → *Z*b) and 9.94 kcal mol^{-1} (*Z*b → *Z*a) at −65 °C (see ESI,‡ p. S-5). These barriers are very close to those for the phenyl ring rotation in the *E*-isomer at the same temperatures ($\Delta G^{\ddagger}$ 9.69 kcal mol^{-1} and 9.81 kcal mol^{-1} respectively, see ESI‡ p. S-4) reflecting the very similar passing interactions of the 3-pyridyl and phenyl rings in their respective rotational transition states.

Model compounds 3 and 4 possessing a 2-pyridyl ring

The ^{1}H NMR spectrum of compound **3** (Fig. 7) in deuteriochloroform at ambient temperature exhibited two sets of NCH

Table 2 Kinetic data for rotation around the 3-pyridyl–imino and the phenyl–imino bonds in **1***Z* and **1***E* respectively

T/°C	Δν/Hz	St. Dev.[a]/%	*k*/s^{-1}	$\Delta G^{\ddagger}$/kcal mol^{-1}
−74	680[b]	0.97	85[c]/69[d]	9.73[c]/9.81[d]
−65	680[b]	0.47	190[c]/155[d]	9.86[c]/9.94[d]
−74	610[e]	0.97	96[f]	9.69[f]
−65	590[e]	0.47	215[f]	9.81[f]

[a] Standard deviation (%) between the best fit calculated lineshape and the experimental lineshape. [b] Separation of the *Z*a and *Z*b pyridyl H4 signals at 500 MHz used in the lineshape analysis. [c] *Z*a → *Z*b process. [d] *Z*b → *Z*a process. [e] Separation of the *ortho*-phenyl signals at 500 MHz used in the lineshape analysis. [f] Imino-phenyl rotation.

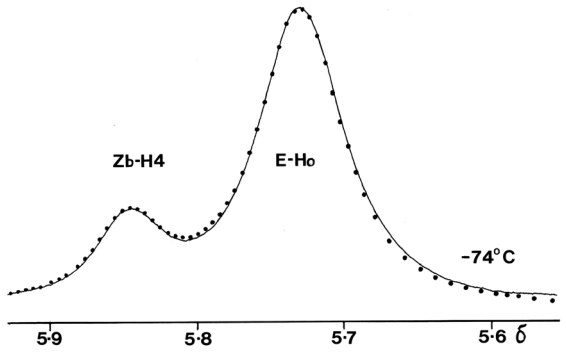

Fig. 6 Experimental (---) and best fit calculated (●) ^{1}H NMR lineshapes of the partly overlapping *E*-Ho and *Z*b-H3 NMR signals of compound **1** at −74 °C in CD_2Cl_2.

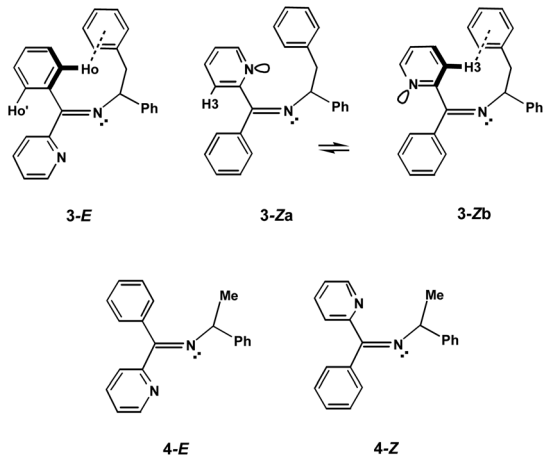

Fig. 7 Structures of compounds **3**-*E*, **3**-*Z*a, **3**-*Z*b, **4**-*E* and **4**-*Z*.

signals at δ 4.64 (major isomer) and δ 4.48 (minor isomer) attributed to a mixture of *E* and *Z*-isomers in the ratio 67 : 33 (Fig. 8). Some other signals were also duplicated in the same ratio. Interest was centred on two abnormally shielded aromatic doublet signals at δ 6.58 (^3J 6.9 Hz, ^4J 1.5 Hz, 2H, major isomer) and δ 6.29 (^3J 7.7 Hz, 1H, minor isomer). On the basis of multiplicity, coupling constants and 2D COSY spectra these were respectively assigned to the *ortho* hydrogens (2Ho) on the imino phenyl ring of the *E*-isomer and the single H3 hydrogen on the 2-pyridyl ring of the minor *Z*-isomer. By comparison H3 in the 2-pyridyl ring of the major *E*-isomer which cannot engage in close contact with the *trans* N-terminal phenyl ring was strongly deshielded at δ 8.22 (^3J 7.9 Hz). Similarly the proton NMR spectrum of the related 2-pyridyl compound **4** which was obtained as an approximately equal mixture of *E* and *Z* isomers showed two equally intense strongly deshielded pyridyl H3 signals at δ 8.04 (^3J 7.1 Hz, *E* or *Z*) and δ 8.18 (^3J 7.1 Hz, *Z* or *E*). This compound cannot engage in edge-to-face interactions as the N-terminal CH_2Ph moiety has been replaced by a methyl group.

The ^{1}H NMR spectrum of **3** recorded in deuteriodichloromethane at 0 °C exhibited similar features (Fig. 8, inset). The

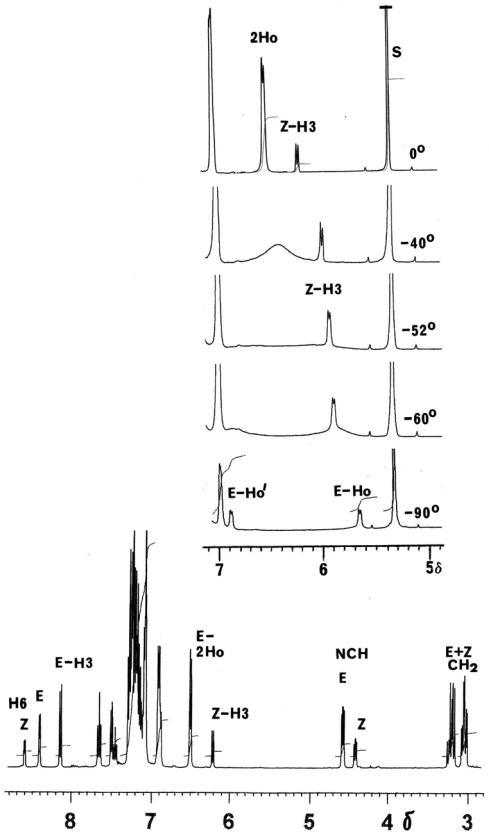

Fig. 8 ^{1}H NMR spectra (400 MHz) of compound **3** in $CDCl_3$ at 25 °C and in CD_2Cl_2 (S) at low temperatures (inset).

major *E*-isomer had a slightly broadened 2Ho doublet at δ 6.55 (^3J 6.8 Hz) arising from the imino phenyl ring which engages in an edge-to-face fashion with the *cis* N-terminal phenyl ring as in the 3-pyridyl compound **1**. The second lower intensity shielded pyridyl signal at δ 6.23 (^3J 7.6 Hz) arises from H3 in the minor *Z*-isomer which also engages in an edge-to-face interaction with the N-terminal phenyl group. On cooling the sample of **3** in deuteriodichloromethane below 0 °C the *E*-Ho phenyl signal (2H) steadily broadened and by −52 °C it had essentially collapsed into the baseline (Fig. 8). At −60 °C two new widely separated equally intense broad signals (Ho and Ho′) appeared at δ 5.9 and δ 6.9 (each 1H) due to slow rotation around the phenyl–imino bond in the major *E*-isomer (Fig. 8). At −90° C the Ho and Ho′ signals had sharpened sufficiently to resolve the doublet splitting. Computer analysis of the broad signal at coalescence (−52 °C) afforded a rate constant of 731 s^{-1} corresponding to a free energy barrier ($\Delta G^{\ddagger}$) of 9.91 kcal mol^{-1} for rotation around the phenyl–imino bond in the *E*-isomer (see ESI,‡ p. S-6). This barrier is of similar magnitude to that in the 3-pyridyl compound **1** (10.0 kcal mol^{-1}). On lowering the temperature the pyridyl H3 signal steadily decreased in chemical shift from δ 6.22 at 0 °C to δ 5.92 at −60 °C but remained fairly sharp (Fig. 8). This behaviour is normal for these imino systems as the edge-to-face interaction entropy contribution ($T\Delta S$) which favours alternative open

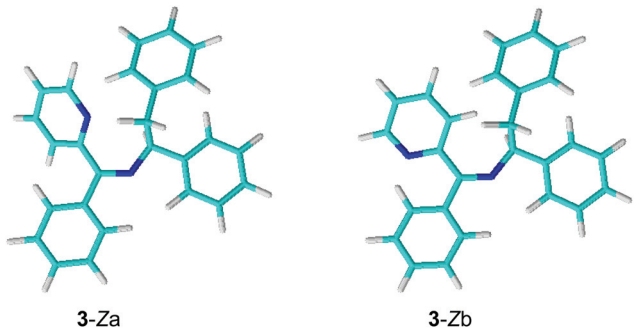

Fig. 9 3D Structures of the *Z*a and *Z*b rotamers of compound **3**.

conformations at higher temperature decreases with temperature.[12–15] However on further cooling the H3 signal rapidly broadened and by −90 °C it had collapsed into the baseline (Fig. 8) due to slowing of rotation around the pyridyl–imino bond in the minor *Z*-isomer. Unfortunately the individual component signals of the *Z*a and *Z*b rotamers (Fig. 9) had not reappeared at the point where the solvent froze (*ca.* −100 °C). Hence the rotational barrier around the 2-pyridyl–imino bond cannot be accurately determined, but it probably lies in the range 7.0–8.0 kcal mol^{-1} based on a coalescence temperature of *ca.* −100 °C. The H3 signal of the *Z*b rotamer (Fig. 7 and 9) is strongly shielded and becomes more shielded as the temperature decreases (Fig. 8). This indicates that the *Z*b rotamer where H3 is directed towards the face of the N-terminal ring is considerably thermodynamically favoured over the alternative *Z*a rotamer where the pyridyl lone pair formally points towards the terminal *N*-phenyl group and there is no possible CH–π interaction (Fig. 9).

The lower barrier to 2-pyridyl rotation in this compound compared with that in the 3-pyridyl analogue is probably due to reduced steric interactions with the *cis* imino nitrogen substituent in the rotational transition state as one *ortho* position in the 2-pyridyl compound is occupied by the less sterically demanding nitrogen lone pair. Hence the passing interactions are significantly reduced.

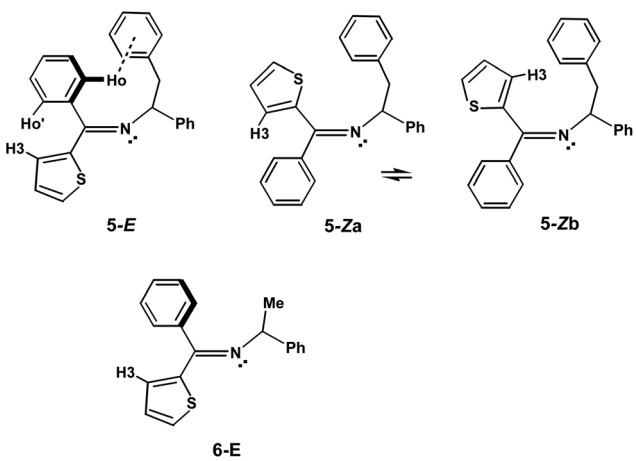

Fig. 10 Structures of compounds **5**-*E*, **5**-*Z*a, **5**-*Z*b and **6**-*E*.

Model compounds 5 and 6 possessing a 2-thiophene ring

The proton NMR spectrum of freshly dissolved crystals of compound **5** (Fig. 11) in deuteriochloroform at room temperature showed one set of alkyl and aromatic signals consistent with a single isomer. By analogy with the pyridyl compounds this compound was expected to prefer the *E*-configuration with the imino phenyl group *cis* to the nitrogen substituent. There were two unusually shielded aromatic signals evident in the NMR spectrum, namely a very broad two proton signal at δ 6.50 and a sharp one proton doublet of doublets (^3J 3.6 Hz and ^4J 1.1 Hz) at δ 6.55 (Fig. 11). The latter signal can be assigned to H3 on the thiophene ring by comparison with the three and four bond coupling constants in thiophene (J 3.6 Hz and 1.1 Hz respectively[28]). The exchange broadened signal at δ 6.50 can be assigned to the two *ortho* protons on the imino phenyl ring as observed in the *E*-pyridyl compounds **1** and **3**. On cooling a sample of **5** in deuteriodichloromethane to 7 °C this signal essentially disappeared into the baseline and by −13 °C it had

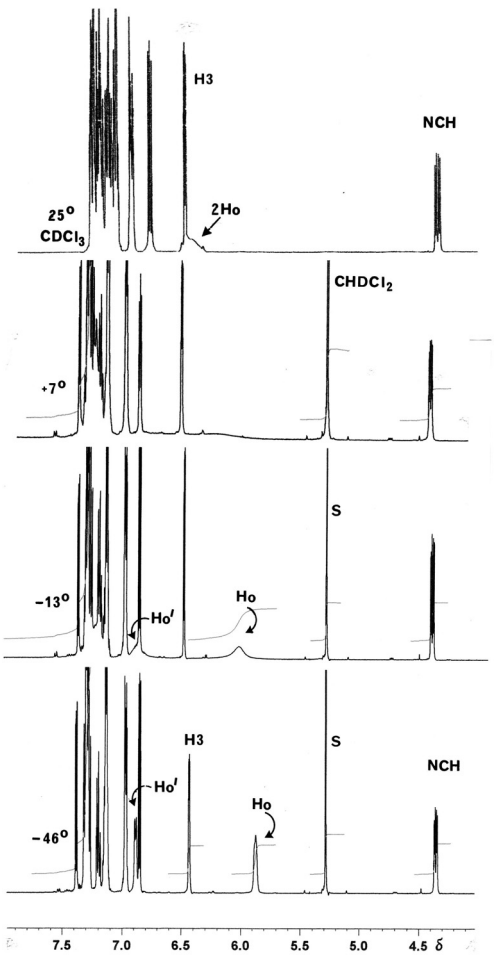

Fig. 11 ^{1}H NMR spectrum (300 MHz) of compound **5**-*E* in $CDCl_3$ at 25 °C and in CD_2Cl_2 at low temperatures (500 MHz).

resolved into two widely separated broad signals of equal intensity at δ 6.09 and δ 6.94 (Fig. 11). On further cooling these signals gradually sharpened and the more shielded signal steadily moved to lower δ values. At −46 °C the more shielded component (Ho) had sharpened and reached δ 5.96 whereas the other component (Ho′) remained within the normal aromatic range at δ 6.96. No further changes were observed down to −76 °C except that the Ho signal had moved to δ 5.76. Computer assisted lineshape analysis of the exchanging Ho and Ho′ signals at 7 °C (just below coalescence) gave a good lineshape fit (see ESI,‡ p. S-7) with k = 640 s^{-1} and $\Delta G^{\ddagger}$ = 12.76 kcal mol^{-1} for rotation around the phenyl–imino bond. A second analysis at −13 °C gave k = 148 s^{-1} and $\Delta G^{\ddagger}$ = 12.57 kcal mol^{-1}. Combination of these data afforded an estimate of the rotational entropy $\Delta S^{\ddagger}$ = −9.5 ± 4 cal mol^{-1} K^{-1} similar to that in the 3-pyridyl compound **1** ($\Delta S^{\ddagger}$ = −10.5 ± 2 cal mol^{-1} K^{-1}). This barrier is markedly higher than those for phenyl rotation in the pyridyl compounds **1** and **3** ($\Delta G^{\ddagger}$ 10.0 and 9.9 kcal mol^{-1} respectively). This is probably due to increased passing interactions between the imino phenyl *ortho* hydrogens and the 2-thiophene ring in the rotational transitional state. Unlike the pyridyl compounds the 2-thiophene ring is a fairly strong π-donor and will conjugate strongly with the imino double bond as observed in 2-thiophene aldehyde and 2-acetyl thiophene.[29–32] Hence the thiophene ring resists twisting out of the imino plane as the geminal imino phenyl ring rotates through the imino plane. This will increase the passing interactions of the imino phenyl group in the rotational transition state thereby raising the barrier to rotation of the imino phenyl ring.

An X-ray crystal structure analysis of **5** (Fig. 12) showed the presence of two crystallographically independent molecules (A and B) in the asymmetric unit. Both have the *E*-configuration but display small differences in conformation (Table 1). The imino phenyl ring A is almost orthogonal to the imino plane with interplane angles of 83° and 81° for the two crystalline forms. In both molecules the *ortho* hydrogen Ho on the imino

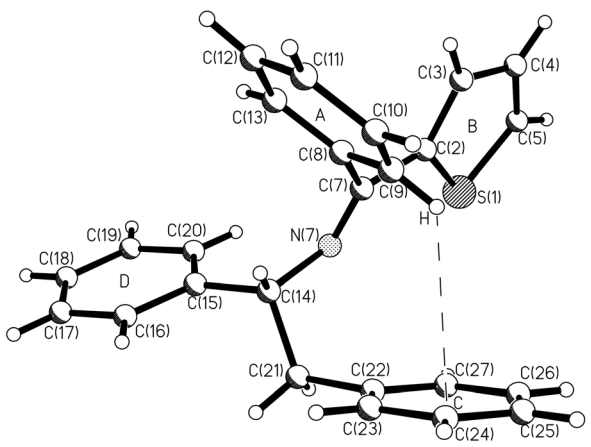

Fig. 12 X-ray structure of one of the two crystallographically independent molecules of compound **5**.

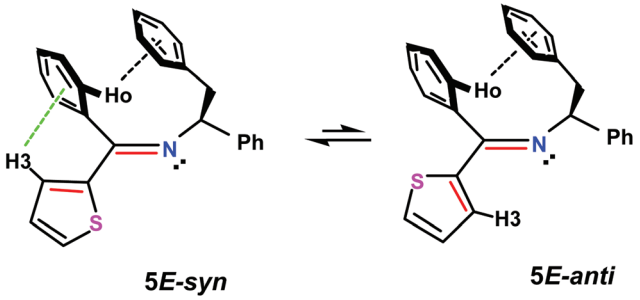

Fig. 13 Structures of **5**-*E syn* and **5**-*E anti*.

phenyl ring is in a face tilted-T relationship with the N-terminal ring. The perpendicular distance of Ho above the terminal ring face is 2.88 Å (molecule A) and 3.08 Å (molecule B) with relatively small projected horizontal offsets of 0.63 Å and 0.29 Å, respectively, from the terminal ring centre. The ring A–ring C tilt angles are 56° and 40° for the two independent molecules, hence the edge-to-face geometry has some structural flexibility and lies between the T-shaped and parallel displaced structures. It is also evident from the crystal structure that the thiophene sulphur is directed *syn* to the imino nitrogen as depicted in Fig. 13, with the thiophene ring twisted by only 4.6° (molecule A) and 10.8° (molecule B) out of the imino plane. Thiophene-2-carbaldehyde, 2-acetylthiophene and 2-benzoylfuran also favour this conformation where the carbonyl oxygen lies *syn* to ring sulphur or oxygen.[33–37] Possibly this is because in the S/N *syn* conformation the C═O bond is in a favoured *s-trans* relationship with the heterocyclic C═C bond. Recent molecular orbital calculations on 2-benzoylthiophene indicate that that the S/O *syn* conformer is 1.7 kcal mol^{-1} more stable than S/O *anti*.[38]

As a result the thiophene H3 hydrogen in **5** points away from the deshielding imino group towards the face of the geminal imino phenyl ring A which is nearly orthogonal to the thiophene moiety (Fig. 13). Although the in-plane offset of the thiophene H3 from the imino phenyl ring centre (1.8 Å) places it just outside the edge of the imino phenyl ring (A), the perpendicular distance of H3 above the ring A face is only 2.75 Å. Ring current shift tables[39] for this geometry predict a ring current shielding of *ca.* −0.4 ppm. This may explain why the thiophene H3 in compound **5** is unusually shielded at δ 6.55, compared to H3 in thiophene (δ 7.1). In the model compound **6** (Fig. 10) where the N-terminal benzyl moiety has been replaced by a methyl group H3 is also somewhat shielded at δ 6.65. Hence the remote benzyl ring in **5** is not involved in the shielding of H3.

When the NMR sample of **5** was examined after standing in deuteriochloroform solution, a trace amount (*ca.* 2%) of additional NMR signals were noticed at δ 6.33 (^3J 3.5 Hz, ^4J 1.2 Hz) and δ 4.80 (doublet of doublets, ^3J 4.8 and 8.6 Hz). These signals are believed to arise from the thiophene H3 and the NCH protons respectively in a trace of the *Z*-isomer. On warming a sample in deuteriochloroform at 50 °C the relative intensity of these minor signals increased until equilibrium

was attained at *ca.* 7%, although the equilibration was accompanied by some thermal decomposition. The selective shielding of the *Z*-thiophene H3 could arise from an edge-to-face CH–π interaction with the *syn* N-terminal phenyl ring as in the *Z*-pyridyl compounds if it adopts the *Z*b conformation (Fig. 10). In contrast to the behaviour of the pyridyl compounds this minor signal did not broaden significantly or split on cooling to −80 °C in deuteriodichloromethane. However, unlike the situation in the pyridyl compounds strong conjugation of the thiophene ring with the C=N bond in the coplanar rotational transition state is likely to considerably lower the pyridyl–imino rotational barrier. An alternative rationale could be that the thiophene ring of the minor *Z*-isomer prefers a near coplanar *Z*a conformation around the thiophene imino bond due to the strong conjugation with the imino C=N bond. As a result the thiophene H3 could be shielded by the geminal phenyl ring current as in the *E*-isomer. We consider this explanation to be less likely due to an expected additional steric interactions in the *E*-isomer between a near coplanar thiophene ring and the adjacent *syn N*-substituent.

Model compounds 7 and 8 possessing a 2-furanyl ring

Imines bearing a very bulky *t*-butyl substituent on the imino carbon normally exist exclusively as the isomer where the *N*-substituent is directed *trans* to the *t*-butyl group.[14,27] Accordingly it can be concluded that compound 7 which showed only one set of NMR signals adopts the *Z*-configuration with the smaller 2-furanyl ring *cis* to the *N*-alkyl moiety (Fig. 14). The proton NMR spectrum of 7 in deuteriochloroform showed a very highly shielded furanyl doublet of doublets signal at δ 5.44. The magnitude of the coupling constants (^3J 3.4 Hz, ^4J 0.8 Hz) establishes that this signal is from H3 on the furanyl ring (*cf.* furan where the ^3J and ^4J couplings are 3.4 Hz and 0.9 Hz respectively for H3). Remarkably the H3 signal in 7 is 1.0 ppm more shielded than H3 in furan (δ 6.4) and 1.3 ppm more shielded than H3 in the model compound **8** (δ 6.73). Compound **8** is expected to favour the *E*-configuration (Fig. 14) due to the replacement of the very bulky *t*-butyl group by the much less sterically demanding methyl group.

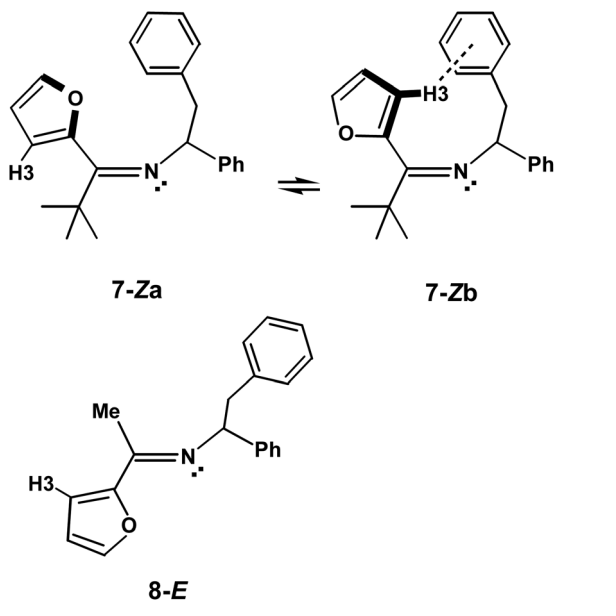

Fig. 14 Structures of 7-*Z*a, 7-*Z*b and 8-*E*.

The very large selective shielding of H3 in compound 7 clearly demonstrates that this compound exists predominantly or exclusively in the twisted *Z*b conformation around the furanyl–imino bond (Fig. 14). This arrangement projects H3 towards the face of the N-terminal phenyl ring as opposed to the twisted *Z*a rotamer where the furanyl oxygen is directed towards the N-terminal phenyl. Accordingly the aromatic CH–π interaction in the *Z*b conformer probably makes an appreciable contribution to the binding energy between the two rings. Additionally a repulsive interaction between the furanyl oxygen and the phenyl π-cloud could destabilise the alternative *Z*a rotamer.

Conclusion

The present results demonstrate that six and five-membered aromatic heterocyclic rings can engage in tilted T-shaped interactions with proximate phenyl rings in a similar fashion to a phenyl–phenyl interaction in an isomer of the same molecule. Although the binding energies for the current compounds cannot be determined due to the low temperatures needed to slow the ring rotations, the similar temperature dependence of the shielded interacting heterocyclic hydrogens and the phenyl Ho signals indicate that the binding enthalpies are of similar magnitude to those previously reported for phenyl–phenyl interactions (*ca.* −1.3 to −1.7 kcal mol^{-1}).[12–15] Frontera *et al.*[24] have calculated the interaction energy for the *para* pyridine-benzene T-shaped dimer to be *ca.* −2.3 kcal mol^{-1}. The interaction energies of the face tilted-T structures observed in this work are likely to be weaker than those in the ideal T-geometry. It should be noted that the interaction free energy (ΔG) for these type of weak interactions in solution at ambient temperature is much lower (only *ca.* −0.1 to −0.5 kcal mol^{-1}) for this model system.[12,14,15] Hence, as we have pointed out previously (since 1990),[12] measured free energies (ΔG) at ambient temperature for these type of interactions often grossly underestimate their energetic (enthalpic) strength. It has recently been demonstrated that in the much studied Wilcox torsion balance model system entropy contributions are also very significant.[40] This is due to the considerable temperature dependent entropy factor ($-T\Delta S$) which strongly favours free non-bound conformations and thereby considerably reduces the magnitude of the interaction free energy (ΔG) at ambient temperature.

It was initially believed that the main factors involved in edge-to-face aromatic interactions were electrostatic interactions between an electropositive hydrogen atom on the edge orientated ring and the aromatic π-cloud of the face directed

ring.[40] Hence the term "CH–π" interaction was introduced.[7] However, high quality *ab initio* molecular orbital calculations combined with symmetry-adapted perturbation analysis (SAPT)[41] or molecular interaction potential with polarization (MIPp) partition analysis[24] indicate that less specific dispersion and induction forces are also involved in these interactions and may have a significant role. The edge-to-face interactions observed in the present compounds are generally consistent with a significant electrostatic interaction between the hydrogen on the edge directed heterocyclic or carbocyclic ring and the face of the proximate phenyl ring. However the modest preference in the 3-pyridyl compound **1** for a stronger interaction involving the *para* hydrogen of the *Z*b rotamer rather than the *ortho* hydrogen of the *Z*a rotamer is difficult to explain on a simple electrostatic basis unless there is a small repulsive interaction between the pyridyl nitrogen lone pair and the phenyl π-cloud in the *Z*a rotamer. A reported[24] MIPp analysis on the *para* pyridyl-benzene T-shaped dimer indicates that the electrostatic interactions are much larger than the dispersion–repulsion or polarisation contributions to the binding energy.

Experimental

All experiments were conducted under a nitrogen atmosphere. Melting points were determined with a Kofler hot-stage apparatus and are uncorrected. Flash column chromatography was performed using silica gel (Merck 60, 70–230 mesh). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-300 instrument unless otherwise indicated. Low temperature NMR spectra were recorded on Bruker spectrometers operating at 500 or 400 MHz. Analyses of exchange broadened lineshapes were performed using a semi-automatic computer program (INMR) which varies the exchange rate to optimize the lineshape fit.[42] Vicinal doublet couplings were treated as separate exchanging sites. Probe temperatures were calibrated using a digital thermometer with a long fine copper-constantan lead inserted into the sample. HRMS were obtained using a VG Autospec TRIO 1000 instrument. The ionization mode used in mass spectra was electron impact (EI) or fast atom bombardment (FAB). The 2-Pivaloylfuran used in the preparation of compound **8** was prepared by a Friedel–Crafts acylation of furan with pivaloyl chloride (2,2-dimethylethanoyl chloride) using boron trifluoride etherate as catalyst.[43]

General procedure for the synthesis of imines 1–8

The ketone (5.1 mmol) and the amine (5.1 mmol) in the presence of titanium ethoxide (5.8 mL, 25.5 mmol) were refluxed in 1,2-dichloroethane (10 mL) for 8 h under nitrogen. Water (10 mL) was added slowly and any solids formed were suction filtered through celite and washed with dichloromethane. The organic layer was separated and the aqueous layer was extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried and concentrated under reduced pressure. These imines slowly decompose on standing in solution.

(1,2-Diphenyl-ethyl)-(phenyl-pyridin-3-yl-methylene)-amine (1). The crude product (89%) contained a mixture of *Z* and *E* isomers (ratio 1 : 3 from ^{1}H NMR analysis). δ_H (300 MHz, $CDCl_3$) 3.10 (2H, m, CH_A, *Z* and *E*), 3.30 (2H, m, CH_B, *Z* and *E*), 4.46 (1H, dd, ^3J 9.4 and 3.8, NCH, *Z*), 4.59 (1H, dd, ^3J 9.2 and 4.1, NCH, *E*), 6.50 (2H, d, ^3J 6.9, Ph-Ho, *E*), 6.68 (1H, d, ^3J 7.5, Py-H_4, *Z*), 7.02 (4H, m, ArH, *Z* and *E*), 7.15–7.40 (24H, m, ArH, *Z* and *E*), 7.59 (2H, d, ^3J 7.0, Ph-Ho, *Z*), 7.78 (1H, br. s, Py-H_2, *Z*), 7.95 (1H, dt, ^3J 8.9, ^4J 1.8, Py-H_4, *E*), 8.61 (2H, m, Py-H_6, *Z* and *E*), 8.76 (1H, d, ^4J 1.9, Py-H_2, *E*). δ_C (75 MHz, $CDCl_3$) 46.1 (CH_2, *E* + *Z*), 69.0 (NCH, *E*), 69.4 (NCH, *Z*), 123.0, 126.0, 127.0, 127.1, 127.4, 128.2, 128.4, 128.5, 129.3, 130.3, 130.7, 135.4 (Py-C_4, *Z*), 135.7 (Py-C_4, *E*), 139.6, 139.9, 144.0, 148.2 (Py-C_6, *Z*), 149.4 (Py-C_2, *Z*), 150.0 (Py-C_6, *E*), 150.5 (Py-C_2, *E*), 164.7 (C=N, *E* + *Z*). HRMS (EI): found *m*/*z* 363.1864 $(M + H)^+$, $C_{26}H_{23}N_2$ requires 363.1861.Slow recrystallization from hexane afforded some colourless crystals of the pure major *E* isomer, mp 108–110 °C. δ_H (300 MHz, $CDCl_3$) 3.10 (1H, dd, ^2J 12.9, ^3J 4.1, CH_A), 3.29 (1H, dd, ^2J 12.9, ^3J 9.2, CH_B), 4.60 (1H, dd, ^3J 9.2 and 4.1, NCH), 6.50 (2H, d, ^3J 6.9, Ph-Ho), 7.03 (2H, dd, ^3J 7.5 and 3.0, ArH), 7.20–7.40 (12H, m, ArH), 7.96 (1H, dt, ^3J 8.9, ^4J 1.8, Py-H_4), 8.60 (1H, dd, ^3J 4.9, ^4J 1.8, Py-H_6), 8.76 (1H, d, ^4J 1.9, Py-H_2).

Crystal data for **1** ($C_{26}H_{22}N_2$) *M* = 362.5, orthorhombic, *a* = 19.746(8), *b* = 11.173(4), *c* = 9.393(4) Å, *U* = 2072.2(14) Å^3, *T* = 293(2) K, space group $Pna2_1$ (no. 33), Mo-Kα radiation, λ = 0.71073 Å, *Z* = 4, *F*(000) = 768, D_x = 1.162 g cm^{-3}, μ = 0.068 mm^{-1}, Bruker P4 diffractometer, ω scans, 4.1° < 2θ < 49°, measured/independent reflections: 1970/1650, R_{int} = 0.032, direct methods solution, full-matrix least squares refinement on F_o^2, anisotropic displacement parameters for non-hydrogen atoms; all hydrogen atoms located in a difference Fourier synthesis but included at positions calculated from the geometry of the molecules using the riding model, with isotropic vibration parameters. R_1 = 0.046 for 1160 data with $F_o > 4\sigma(F_o)$, 253 parameters, ωR_2 = 0.093 (all data), GoF = 1.05, $\Delta\rho_{min,max}$ = −0.16/0.12 e Å^{-3}. CCDC 1518494.

1,2-Diphenyl-*N*-(1-(pyridin-3-yl)ethylidene)ethanamine (2). The crude product was purified by column chromatography on neutral alumina using hexane–ethyl (9 : 1) as eluent to afford colourless crystals (80%), mp 53–55 °C. δ_H (300 MHz, $CDCl_3$) 1.75 (3H, s, CH_3), 3.11 (2H, m, CH_2), 4.79 (1H, dd, ^3J 8.0, ^3J 5.7, NCH), 7.0–7.3 (9H, m, ArH), 7.39 (2H, dd, ^3J 7.3, ^4J 1.3, ArH), 8.02 (1H, dt, ^3J 7.6, ^4J 1.8, Py-H_4), 8.51 (1H, dd, ^3J 4.7, ^4J 1.7, Py-H_6), 8.87 (1H, d, ^4J 2.1, Py-H_2). δ_C (75 MHz, $CDCl_3$) 15.2 (CH_3), 46.2 (CH_2), 67.2 (NCH), 123.0 (CHar), 126.1 (CHar), 126.9 (CHar), 127.1 (CHar), 128.1 (CHar), 128.4 (CHar), 129.7 (CHar), 134.1 (CHar), 136.4 (Car), 139.1 (Car), 144.0 (Car), 148.3 (CHar), 150.2 (CHar), 161.7 (C=N). HRMS (EI): found *m*/*z* 300.1623 (M^+), $C_{21}H_{20}N_2$ requires 300.1626.

***Z* and *E*-(1,2-Diphenyl-ethyl)-(phenyl-pyridin-2-yl-methylene)-amine (3).** The crude product (67%) contained a mixture of *Z* and *E* isomers. Recrystallization from hexane gave **3** as a colourless solid (*Z* : *E* ratio 33 : 67 from ^{1}H NMR analysis). δ_H (300 MHz, $CDCl_3$) 3.10 (2H, m, CH_A, *E* + *Z*), 3.26 (2H, m, CH_B, *E* + *Z*), 4.48 (1H, dd, ^3J 8.1 and 5.2, NCH, *Z*), 4.64 (1H, dd,

^3J 9.0 and 4.5, NCH, *E*), 6.29 (1H, d, ^3J 7.7, Py-H_3, *Z*), 6.58 (2H, dd, ^3J 6.9, ^4J 1.5, Ph-Ho, *E*), 6.90–7.40 (29H, m, ArH), 7.55 (2H, m, ArH, *E* + *Z*), 7.73 (1H, td, ^3J 7.5, ^4J 1.7, Py-H_4, *E*), 8.22 (1H, d, ^3J 7.9, Py-H_3, *E*), 8.49 (1H, ddd, ^3J 4.8, ^4J 1.7, ^5J 0.9, Py-H_6, *E*), 8.68 (1H, ddd, ^3J 4.5, ^4J 1.5, ^5J 0.9, Py-H_6, *Z*). δ_C (75 MHz, $CDCl_3$) 45.4 (CH_2, *Z*), 45.9 (CH_2, *E*), 68.3 (NCH, *Z*), 68.6 (NCH, *E*), 122.4 (Py-C_5, *E*), 123.0 (Py-C_5, *Z*), 123.2 (Py-C_3, *Z*), 123.9 (Py-C_3, *E*), 126.0, 126.1, 126.4, 126.8, 126.9, 127.0, 127.2, 127.3, 127.6, 127.8, 128.0, 128.1, 128.2, 128.3, 128.4, 129.8, 129.9, 130.0, 135.8, 136.1, 136.2, 138.9, 139.0, 143.7, 143.9, 148.8, 149.5, 155.8 (Py-C_2, *Z*), 157.9 (Py-C_2, *E*), 164.9 (C=N, *Z*), 167.4 (C=N, *E*). HRMS (EI): found *m*/*z* 363.1867 $(M + H)^+$, $C_{26}H_{23}N_2$ requires 363.1861.

***Z* and *E*-(1-Phenyl-ethyl)-(phenyl-pyridin-2-yl-methylene)-amine (4).** This reference compound was isolated as a colourless oil (67%) containing a mixture of *Z* and *E* isomers (*ca.* 1 : 1 from ^{1}H NMR integration). δ_H (300 MHz, $CDCl_3$) 1.50 (3H, d, ^3J 6.5, Me, *Z* or *E*), 1.52 (3H, d, ^3J 6.5, Me, *E* or *Z*), 4.49 (1H, q, ^3J 6.5, NCH, *Z* or *E*), 4.66 (1H, q, ^3J 6.5, NCH, *E* or *Z*), 7.10–7.60 (20H, m, ArH, *Z* and *E*), 7.62 (2H, d, ^3J 6.6, ^4J 1.7, ArH, *Z* or *E*), 7.70 (2H, m, ArH, *Z* or *E*), 8.04 (1H, dd, ^3J 7.1, ^4J 1.3, Py-H_3, *Z* or *E*), 8.18 (1H, dd, ^3J 7.1, ^4J 0.9, Py-H_3, *E* or *Z*), 8.52 (1H, ddd, ^3J 4.8, ^4J 1.5, ^5J 0.9, Py-H_6, *Z* or *E*), 8.75 (1H, ddd, ^3J 4.8, ^4J 1.9, ^5J 0.9, Py-H_6, *E* or *Z*). HRMS (EI): found $(M + H)^+$ 287.1555, $C_{20}H_{19}N_2$ requires 287.1548.

1,2-Diphenyl-*N*-(phenyl(thiophen-2-yl)methylene)ethanamine (5). The crude product was purified by column chromatography on neutral alumina (eluent hexane–ethyl acetate 98 : 2) to afford a colourless solid (42%), mp 58–60°. δ_H (300 MHz, $CDCl_3$) 2.97 (1H, dd, ^2J 13.0, ^3J 4.0, CH_A), 3.16 (1H, dd, ^2J 13.0, ^3J 9.4, CH_B), 4.41 (1H, dd, ^3J 9.4, ^3J 4.0, NCH), 6.50 (2H, br s, phenyl-Ho), 6.55 (1H, dd, ^3J 3.6, ^4J 1.1, thiophene-H_3), 6.84 (1H, dd, ^3J 5.1, ^3J 3.6, thiophene-H_4), 6.98 (2H, m, ArH), 7.10–7.40 (12H, m, ArH). δ_C (75 MHz, $CDCl_3$) 46.5 (Me), 68.3 (NCH), 126.3, 127.2, 127.4, 127.8, 128.3, 128.4, 128.6, 128.7, 129.4, 130.4, 130.5, 136.3, 139.7, 144.8, 147.9, 163.0 (C=N). HRMS (EI): found *m*/*z* 367.1386 (M^+), $C_{25}H_{21}NS$ requires 367.1395.

Crystal data for **5** ($C_{25}H_{21}NS$) M = 367.5, monoclinic, a = 32.437(5), b = 7.626(2), c = 33.681(6) Å, U = 8244(3) Å^3, T = 293 (2) K, space group *C*2/*c* (no. 15), Mo-Kα radiation, λ = 0.71073 Å, Z = 16, F(000) = 3104, D_x = 1.184 g cm^{-3}, μ = 0.165 mm^{-1}, Bruker P4 diffractometer, ω scans, 4.9° < 2θ < 50°, measured/independent reflections: 8919/7238, R_{int} = 0.047, direct methods solution, full-matrix least squares refinement on F_o^2, anisotropic displacement parameters for non-hydrogen atoms; all hydrogen atoms located in a difference Fourier synthesis but included at positions calculated from the geometry of the molecules using the riding model, with isotropic vibration parameters. R_1 = 0.075 for 3077 data with $F_o > 4\sigma(F_o)$, 487 parameters, ωR_2 = 0.239 (all data), GoF = 0.99, $\Delta\rho_{min,max}$ = −0.29/0.22 e Å^{-3}. CCDC 1518495.

(1-Phenyl-ethyl)-(phenyl-thiophene-2-yl-methylene)-amine (6). The crude product was purified by column chromatography on neutral alumina using hexane–ethyl acetate (95 : 5) as eluent to afford **6** as a colourless oil (40%). δ_H (300 MHz, $CDCl_3$) 1.37 (3H, d, ^3J 6.6, Me), 4.41 (1H, q, ^3J 6.6, NCH), 6.65 (1H, dd, ^3J 3.6, ^4J 1.1, thiophene-H_3), 6.85 (1H, dd, ^3J 5.1, ^3J 3.6, thiophene-H_4), 7.12–7.38 (11H, m, ArH). δ_C (75 MHz, $CDCl_3$) 25.0 (Me), 60.6 (NCH), 125.5, 126.4, 127.0, 127.4, 128.2, 128.3, 128.5, 128.9, 130.2, 136.0, 145.9, 147.4, 160.9 (C=N). HRMS (EI): found *m*/*z* 291.1089 (M^+), $C_{19}H_{17}NS$ requires 291.1082.

(1,2-Diphenyl-ethyl)-(1-furan-2-yl-2,2-dimethyl-propylidene)-amine (7). To a stirred solution of 1-(2-furanyl)-2,2-dimethyl-propan-1-one[43] (0.4 g, 2.6 mmol), 1,2-diphenylethylamine (0.6 g, 3 mmol) and triethylamine (0.79 g, 7.8 mmol) in dichloroethane (6 mL) under nitrogen was added titanium(IV) chloride (0.24 g, 1.0 mmol) at 0 °C. The reaction mixture was heated at reflux for 15 h and cooled. Water (10 mL) was added slowly and any solids formed were suction filtered through celite and washed with dichloromethane. The organic layer was separated and the aqueous phase was extracted with dichloromethane. The combined organic layers were washed with brine, dried over magnesium sulfate, filtered and concentrated under reduced pressure to give **7** as a yellow oil (0.70 g, 81%). δ_H NMR (300 MHz, $CDCl_3$) 1.00 (9H, s, 3 × Me), 2.92 (1H, dd, ^2J 13.0, ^3J 4.9, CH_A), 3.01 (1H, dd, ^2J 13.0, ^3J 8.5, CH_B), 4.31 (1H, dd, ^3J 8.5, ^3J 4.9, NCH), 5.44 (1H, dd, ^3J 3.4, ^4J 0.8, furanyl-H_3), 6.20 (1H, dd, ^3J 3.2, ^3J 1.9, furanyl-H_4), 6.92 (2H, dd, ^3J 7.7, ^4J 1.7, *o*-Ph), 7.10–7.30 (9H, m, Ar). δ_C (75 MHz, $CDCl_3$) 27.8 (Me), 31.5 (Cq), 46.2 (CH_2), 68.2 (NCH), 109.4 (furanyl-C_3 or C_4), 109.5 (furanyl-C_4 or C_3), 125.9, 126.6, 126.9, 127.7, 128.1, 129.9, 139.1, 139.3, 141.5 (furanyl-C_5), 150.9 (furanyl-C_2), 160.6 (C=N). HRMS (EI): found *m*/*z* 331.1947 (M^+), $C_{23}H_{25}NO$ requires 331.1936.

***N*-(1-(Furan-2-yl)-ethylidene)-1,2-diphenylethanamine (8).** The product was isolated as a colourless oil (58%). δ_H (300 MHz, $CDCl_3$) 1.82 (3H, s, Me), 3.25 (2H, m, CH_2), 4.79 (1H, t, ^3J 6.6, NCH), 6.42 (1H, dd, ^3J 3.4 and 1.8, furanyl-H_4), 6.73 (1H, d, ^3J 3.4, furanyl-H_3), 7.10–7.30 (10H, m, ArH), 7.41 (1H, d, ^3J 1.8, furanyl-H_5). δ_C (75 MHz, $CDCl_3$) δ 14.8 (Me), 45.9 (CH_2), 66.7 (NCH), 111.2 (furanyl-C_3 and C_4), 126.0, 126.8, 127.3, 128.0, 128.4, 129.6, 139.3, 143.9, 146.4 (furanyl-C_5) 154.2 (furanyl-C_2), 155.5 (C=N). HRMS (EI): found *m*/*z* 290.1541 $(M + H)^+$, $C_{20}H_{20}NO$ requires 290.1545.

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