Insights on the synthesis and organisational phenomena of twisted pyrazine–pyridine hybrids

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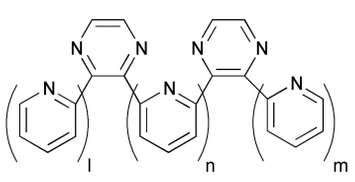
Pyrazine–pyridine hybrids containing two different oligopyridyl chains, 2,3-disubstituted onto the pyrazine ring nucleus are prepared from appropriate mixed α-diketone precursors. The latter were obtained by epoxidation of the enols of corresponding 1,2-disubstituted ethanones. The structures of the pyrazine derivatives were investigated by detailed proton NMR spectroscopic and X-ray crystallographic methods. These indicated a twisting of the oligopyridyl chains about one another to result in a pre-double helical topology. This phenomenon occurred up to two pyridin-2,6-diyl groupings from the pyrazine ring and is accompanied by edge-on-face stacking of spatially proximate pyridyl rings. Parallel stacking of pyrazine and weak C–H ··· N acid interactions are significant in their crystal lattices and may also figure in their metallosupramolecular self-assembly behaviour patterns.

Introduction

The physical properties of pyrazine derivatives—*e.g.* dipole moments, multipole-based or π-stacking interactions, conjugative effects and base strength—differ from those of other electron-deficient aza-aromatics.[1] This forms the basis of their eventual use in light-harvesting systems,[2] conducting materials[3] and polymers,[4] liquid crystalline substances,[5] dyes[6] and metallo-organics.[7] Our work is in the synthesis of 2,3-disubstituted pyrazine–pyridine hybrids, *e.g.* compound **1**, and exploration of their supramolecular chemistry.[8] Unlike the plethora of different types of "pure" oligopyridine-type compounds, for which mature synthetic methodologies are available,[9] the preparation of such pyrazine–pyridine hybrids requires the development of original methods,[10,1b] and this has arguably[11] held back their development. Prior to our work, a total of three pyrazine–pyridine hybrids having relatively simple and regular structures were known.[12]



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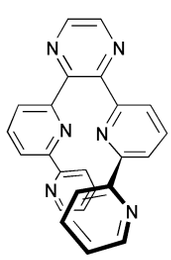

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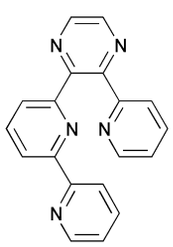
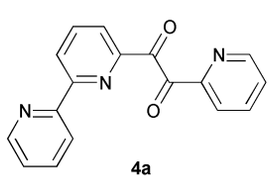


3a



4a

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Our pyrazine–pyridine hybrids self-assemble to form dimeric complexes with appropriate labile metal centres. By studying the organisational patterns of the native ligands in the solid state, particularly those involving ligand geometry/electronegativity, π-stacking effects and the weak acidity of sp^2-hybridised C–H bonds,[13] inferences concerning this behaviour may be possible. Of further interest is the topology of extended pyrazine–pyridine hybrids. Vicinal positioning of two 2,2′-bipyridyl moieties such as in **2** inclines them to twist about one another, both in solution and the solid state.[8f] In view of the current interest in helically self-organising molecules,[14] some of which are also based on electron-deficient aza-aromatics, it is valid to assess **1** for evidence of extended *double* helicity. Finally, methods are needed for the preparation of functionally elaborate pyrazine–pyridine hybrids. These will provide the molecular scaffolding upon which light-harvesting systems can be based.[15]

We have recently issued a preliminary communication on the preparation of such *unsymmetrical* pyrazine–pyridine hybrids, *e.g.* **3a** *via* α-diketones like **4a**.[8b] We now address the outstanding synthetic work in this context, and consider their topological and self-organisational properties.

Results and discussion

Claisen–Rubottom α-diketone synthesis

Esters **6** were prepared by basic methanolysis of the corresponding carbonitriles, and those compounds were in turn prepared by a modified Reissert–Henze reaction[16] of the oligopyridine *N*-oxides as previously described.[8b] Treatment of 6-methylpyridine derivatives **5** with 2 equiv. LDA, followed by addition of **6** afforded the condensation products **7** (Scheme 1). For **7d**–**f**, and **h**, this amide base reacted directly with the ester to form side-products that were tentatively identified on the basis of their ^{1}H NMR spectra as *N*,*N*-diisopropyl amides. The formation of these materials can be rationalised on the basis of the increased electrophillic reactivity of the α-position of 2-pyridyl derivatives.[17] The chromatographic separation of those diisopropyl amides was only possible in the synthesis of **7h**. For **7d**–**f**, the more sterically hindered base, lithium tetramethylpiperidide (LTMP) precluded formation of these side-products. As was previously alluded to,[8b] the stability of all

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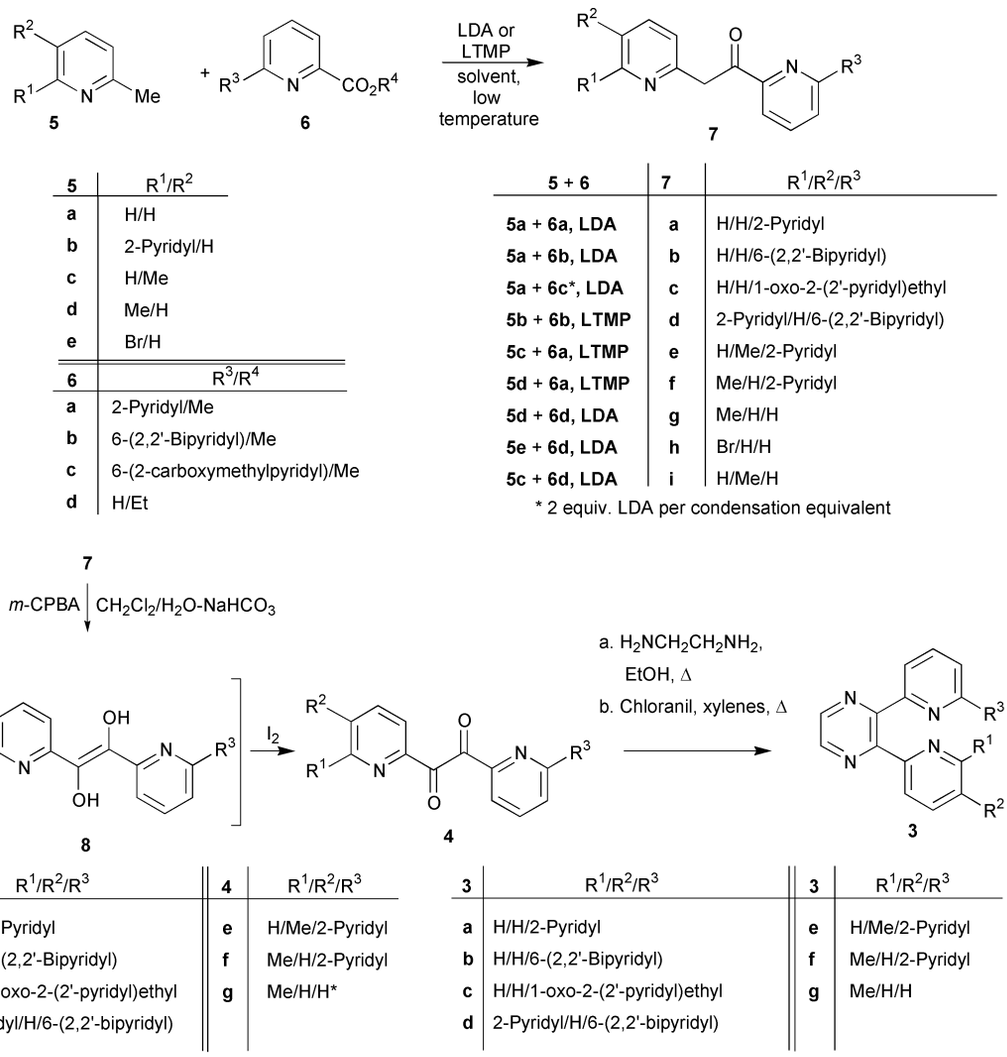


5	R^1/R^2
a	H/H
b	2-Pyridyl/H
c	H/Me
d	Me/H
e	Br/H

6	R^3/R^4
a	2-Pyridyl/Me
b	6-(2,2'-Bipyridyl)/Me
c	6-(2-carboxymethylpyridyl)/Me
d	H/Et

5 + 6	7	$R^1/R^2/R^3$
5a + 6a, LDA	a	H/H/2-Pyridyl
5a + 6b, LDA	b	H/H/6-(2,2'-Bipyridyl)
5a + 6c*, LDA	c	H/H/1-oxo-2-(2'-pyridyl)ethyl
5b + 6b, LTMP	d	2-Pyridyl/H/6-(2,2'-Bipyridyl)
5c + 6a, LTMP	e	H/Me/2-Pyridyl
5d + 6a, LTMP	f	Me/H/2-Pyridyl
5d + 6d, LDA	g	Me/H/H
5e + 6d, LDA	h	Br/H/H
5c + 6d, LDA	i	H/Me/H

* 2 equiv. LDA per condensation equivalent

4	$R^1/R^2/R^3$	4	$R^1/R^2/R^3$
a	H/H/2-Pyridyl	e	H/Me/2-Pyridyl
b	H/H/6-(2,2'-Bipyridyl)	f	Me/H/2-Pyridyl
c	H/H/1-oxo-2-(2'-pyridyl)ethyl	g	Me/H/H*
d	2-Pyridyl/H/6-(2,2'-bipyridyl)		

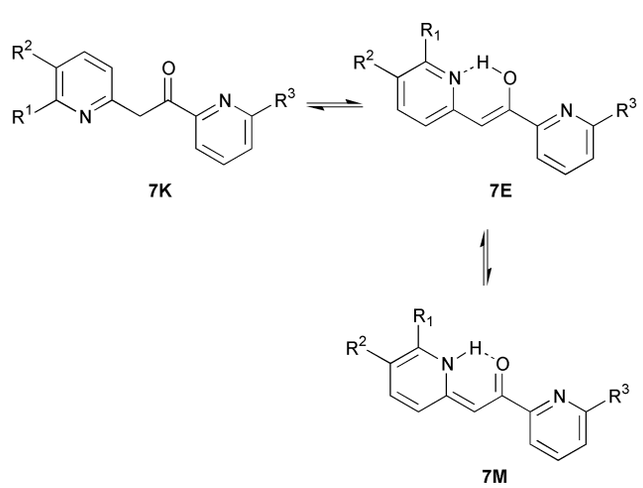
3	$R^1/R^2/R^3$	3	$R^1/R^2/R^3$
a	H/H/2-Pyridyl	e	H/Me/2-Pyridyl
b	H/H/6-(2,2'-Bipyridyl)	f	Me/H/2-Pyridyl
c	H/H/1-oxo-2-(2'-pyridyl)ethyl	g	Me/H/H
d	2-Pyridyl/H/6-(2,2'-bipyridyl)		

* reaction with 2 equiv. *m*-CPBA; no I_2.

Scheme 1 Claisen–Rubottom synthesis of α-diketones **4** and thus pyrazines **3**. MCPBA: *m*-chloroperbenzoic acid.

of these condensation products varied approximately inversely with their solubilities.

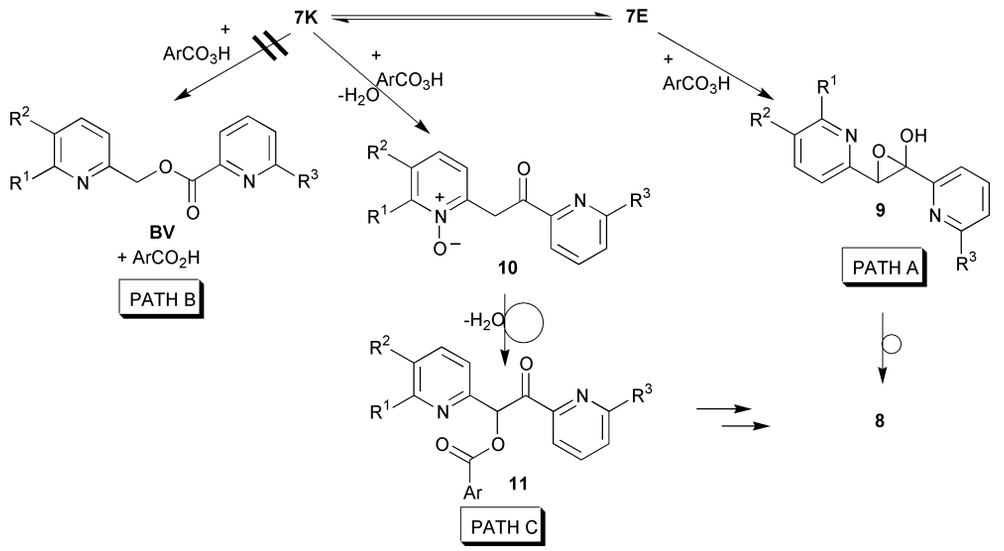
The condensation products occur as dynamic mixtures of two tautomers. Their ^{1}H NMR spectra display two closely overlapping sets of resonances and their proton-decoupled ^{13}C NMR spectra generally show double sets of lines. By comparison of the magnitudes of the enolic and ketonic shifts at δ_H = 6.82–7.12 and δ_C = 198.2–202.6, to values from the literature,[18] they could be identified as the ketimine and enolimine forms **7K** and **7E**; enaminone tautomers **7M** were not observed.



Integration of the proton NMR spectra indicated the enolimine forms to predominate by 66–86%. This finding is in accord with hydrogen-bonding reinforced tautomeric effects.[19] It also agrees with the proposed destabilisation of ketimine tautomers observed for highly electronegative aryl groups that are attached to the carbonyl carbon.[19] An X-ray crystal structure determination carried out on the bis-condensation product **7c** supports these findings. The tautomer of **7c** observed in the solid state is also the majority form in solution.[20]

The crucial part of the pyrazine synthesis was the transformation of the condensation products **7** into the α-diketones **4**. Treatment of **7a**–**f** under Rubottom conditions[21]—*i.e.* 1 equivalent of *m*-chloroperbenzoic acid (MCPBA) in a biphasic aqueous sodium bicarbonate–dichloromethane system—afforded the dihydroxyolefins **8**. These were expeditiously oxidised to **4** using a dichloromethane solution of one equivalent iodine. Clean formation of α-diketone **4g** could only be accomplished by treatment of **7g** with two equivalents of *m*-CPBA. Ethanones **7h**,**i** did not form the corresponding α-diketones under diverse conditions.

This synthetic sequence deserves comment. On one hand, it circumvents the low reactivity and scrambling[22] of Umpolung reagents prepared from pyridine-2-carbaldehyde derivatives.[23] Formation of α-diketones by direct α-oxygenation of ketones[24] or their silyl enol ethers,[25] as well as α-halogenation[26] are all well-established procedures that did not function for the bis-pyridyl-substituted condensation products **7**. Other peracids, *e.g.* peracetic acid and magnesium monoperoxyphthalate



Scheme 2 Reaction pathways for treatment of condensation products with *meta*-chloroperbenzoic acid. BV = Baeyer–Villiger-type product; Ar = *m*-ClC_6H_4.

(mmpp) were likewise unsuitable. The most likely mechanistic explanation for the formation of **8** would involve epoxidation of the enolimine tautomer **7E** to form intermediate **9** (Scheme 2, Path A). This must occur significantly more rapidly than the competing Baeyer–Villiger oxidation of the ketimine tautomer, since none of the ester products to be expected from that reaction [27] were detected in the crude reaction mixtures (Path B). An alternate mechanism would involve the formation of a pyridine *N*-oxide derivative **10** from the ketimine tautomer, and its subsequent rearrangement [28] to the α-hydroxyketone ester **11** (Path C). This would, however require that *N*-oxidation occur only on the pyridyl ring adjacent to the oxidisable site.

The unsymmetrical α-diketones could all be isolated as crystalline solids, although the stability of the methylpyridyl bipyridyl compounds **4e**, **f** dictated that they be further reacted in a synthetically pure state. Like the parent 1,2-di-2′-pyridylethan-1,2-dione,[29] upon prolonged exposure to light in the solid state, they decompose to green-coloured materials. The ^{1}H NMR spectra of **4** were assigned through various combinations of COSY, NOESY, selective proton decoupling, DIFNOE and long-range HETCOR experiments. Generally, δ_H of the pyridyl, 2,2′-bipyridyl (bpy) and 2,2′:6′,2″-terpyridyl (terpy) ring systems occurred at values that were unique and characteristic of a given position in a fragment, *e.g.* H-5 of C_5H_4N appeared at δ_H 7.47–7.48, 7.21–7.24 and 7.30–7.32 respectively. This provides an additional level of certainty in their assignments, as well as indicating the absence of interactions across the diketone bridge. In the cases of **4a**, **c** and **d**, complete assignment of ^{13}C NMR spectra were also carried out. All α-diketone spectra exhibited the expected numbers of signals, displaying two carbonyl carbon resonances.

The final two steps in the reaction sequence were conceptually straightforward. After condensation of the diketones with an appropriate molar equivalent of ethylenediamine, the intermediate dihydropyrazines (not shown) were conveniently oxidised to pyrazines **3** by treatment with chloranil in xylene under reflux.

The solution-state structures of the pyrazine derivatives **3** were thoroughly analysed using ^{1}H NMR spectroscopy (Fig. 1). In contrast to the situation for the α-diketones, these shift patterns occurred with partial signal overlap. Nevertheless, although complete assignment of the J_{HH} coupling patterns was sometimes not possible, the shift magnitudes could be accurately localised through a combination of 2D and proton–proton decoupling techniques (*vide supra*). In the cases of compounds **3d**, **f**, complete assignment of the ^{13}C NMR spectra was carried out. Of special note was the observation of four-bond coupling J_{CH}^4 = *ca.* 4 Hz between 2-C and H-5 on each of the mono-substituted pyridyl groups of the bpy-terpy-substituted **3d**. This phenomena permitted the establishment of the connectivity through each of those oligopyridyl groups, and thus through the entire molecule. In the remaining compounds the correct numbers of signals as expected from their structures were observed.

Twisting in solution and solid state

A prominent feature of the ^{1}H NMR spectra of compounds **3** is the pronounced upfield shifting of H-3 on the second pyridyl ring separated from pyrazine. In those containing the bipyridyl(pyridyl)pyrazine scaffolding (**3a**, **e** and **f**), this shift is at δ_H 7.22–7.38. On one hand, this is more than 1.1 ppm upfield from calculated values. On the other hand, it contributes to the conspicuous reversal of expected shift magnitude patterns, *i.e.* usually $\delta_{H\text{-}4} < \delta_{H\text{-}3}$.[30] Since the ^{1}H shift magnitudes from the bpy portions of all three of these compounds closely resemble each other, their conformations must also be similar. Also, the 5-methylpyridyl derivative **3e** displays non-overlapping absorptions on that solitary ring. Thus, it was possible to observe NOE effects between H-3 (*vide infra*) and H-3, H-6 of $C_5H_3N(CH_3)$. We therefore attribute this upfield shifting to non-bonding interactions involving H-3.

The shift magnitudes of positions on the 6-methylpyridyl ring of **3f** closely match those on the unsymmetrical model compound **3g**. In **3g**, through-space effects are expected to be considerably less pronounced. After correlating these findings back to **3a**, **e** and **f**, one can therefore deduce that in **3a**, the C_5H_4N rings of bpy and solitary pyridyl groups respectively form the base and top of a "T-like" edge-on-interaction, in particular one in which H-3 experiences magnetic anisotropic effects. Interestingly, the strength of the interactions among **3a**, **e** and **f** is greater than that originally observed for compound **2** (H-3 at δ_H 8.02).[8f]

While compounds **3a** and **e** exhibit similar melting points, isomeric **3f** could not be isolated as a solid. In spite of repeated column chromatography, merely an oil was obtained that, according to thin layer chromatographic and NMR spectroscopic analysis, was nonetheless pure. We considered two rationalisations for this phenomena: the presence of multiple conformational equilibria *or* severe (intermolecular) packing defects that inhibited crystallisation. The absence of both strong temperature-dependence in the ^{1}H NMR spectra of **3f** and

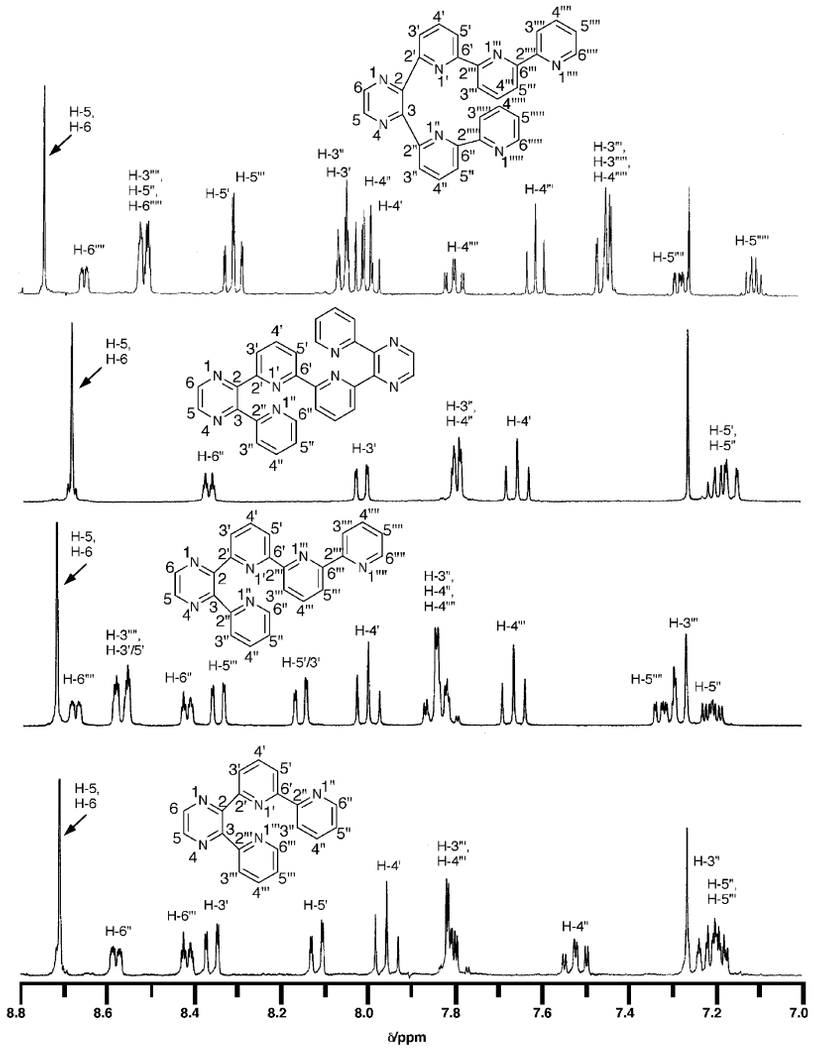


Fig. 1 Proton NMR overlay of pyrazine–pyridine hybrids **3a**–**d**.

spatial NOE effects between the 6-C methyl group and positions in the bpy ring system in that compound imply the latter.

The remaining three pyrazine derivatives **3b**–**d** showed similar ^{1}H NMR spectroscopic phenomena. Dipyrazine **3c** exhibited a shift assigned to H-5 at δ_H 7.15–7.22, or *ca.* 0.8 ppm upfield from calculated values. The number of signals in the spectrum of that same compound (also in its ^{13}C NMR) bespeaks of a symmetrical *meso* or C_2 structure. In the terpy-substituted derivatives **3b** and **d** display analogous phenomena, since H-3 on the second C_5H_3N ring removed from pyrazinyl appears upfield by *ca.* 0.75 ppm. The bpy-terpy derivative **2d** additionally gives rise to shielding phenomena associated with twisting of the bpy flank, H-3 appearing at δ_H 8.06, or *ca.* 1 ppm upfield from expected values. The orthogonal shielding arrangement does not extend to the terminal terpy pyridyl ring, since all these protons absorb at frequencies close to expected values.

In order to compare the solution-state structures with the solid state, crystal structure determinations were carried out. For compound **3a**, the inter-annular angle between the pyrazinyl and the bpy C_5H_3N ring is *ca.* 28°, whilst the solitary C_5H_4N ring is correspondingly rotated by 42° (Fig. 2A). The angle between the two C_5H_4N rings is 69°. Thus, H-3 does, indeed undergo an edge-on interaction. The crystal structure of **3c** is similar, but less pronounced (Fig. 3A)—the planes of the C_5H_4N and adjacent C_5H_3N rings are rotated 44° and 31° with respect to the pyrazinyl ring. The angle between the mean planes of both of these rings is 54°. The same compound furthermore possesses an overall *meso*-stereochemistry, since the twist of each pyridyl pyrazine fragment is in the opposite direction.

For **3d**, a double-helical geometry is observed up to the second pyridyl ring removed from pyrazine (Fig. 4A). Beyond this point, the preferred *transoid* arrangement characteristic of 2,2′-oligopyridyl ring systems[31] prevails, and the terminal ring of terpy is directed away from the approximate helical axis. Two independent but geometrically similar molecules of **3d** occur within the unit cell. The average angles by which the bpy C_5H_3N and terpy C_5H_3N rings are deflected from the plane of the adjoining pyrazinyl ring are 46 and 30° respectively.

Both π-electronic and torsional steric/C=N dipole effects are possible explanations for the preference of the pyrazine derivatives for twisted geometries.[32] According to current theory,[33] interaction between two orthogonal electron-poor aromatic systems can be stabilising. Furthermore, a hydrogen donor–π-electron acceptor interaction is quantified by the distance of H from the π-electron system *and* the deflection, α, of the attached C–H bond from the individual atoms.[13] Thus, for d defined as the distance between H and π_C, the centre of the π-electron system, $d < 3.05$ Å is crucial, since this value corresponds to the sum of the van der Waals radius of hydrogen plus the Pauling one-half thickness of benzene. Additionally, the condition $150° < \alpha < 180°$ must be met, since only then is the C–H bond deflected towards the p-orbitals of the π-electron system. These calculated parameters are summarised for **3a**, **c** and **g** in Table 1; data for compound **2**[8f] are included for comparison.

For all compounds except **3d**, the approach of H-3 to π_C is closer than to any ring atoms. However, it is only for **3a**

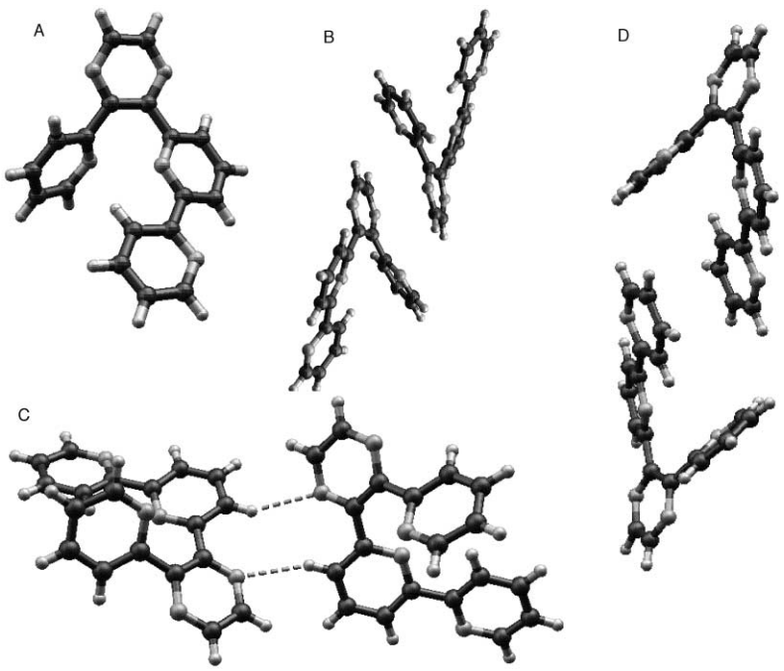


Fig. 2 Depiction of intra- and intermolecular interactions for **3a** in the crystal lattice. A. intramolecular twisting; B. pyrazine stacking; C. dimeric C–H ··· N interactions; D. pyridine stacking.

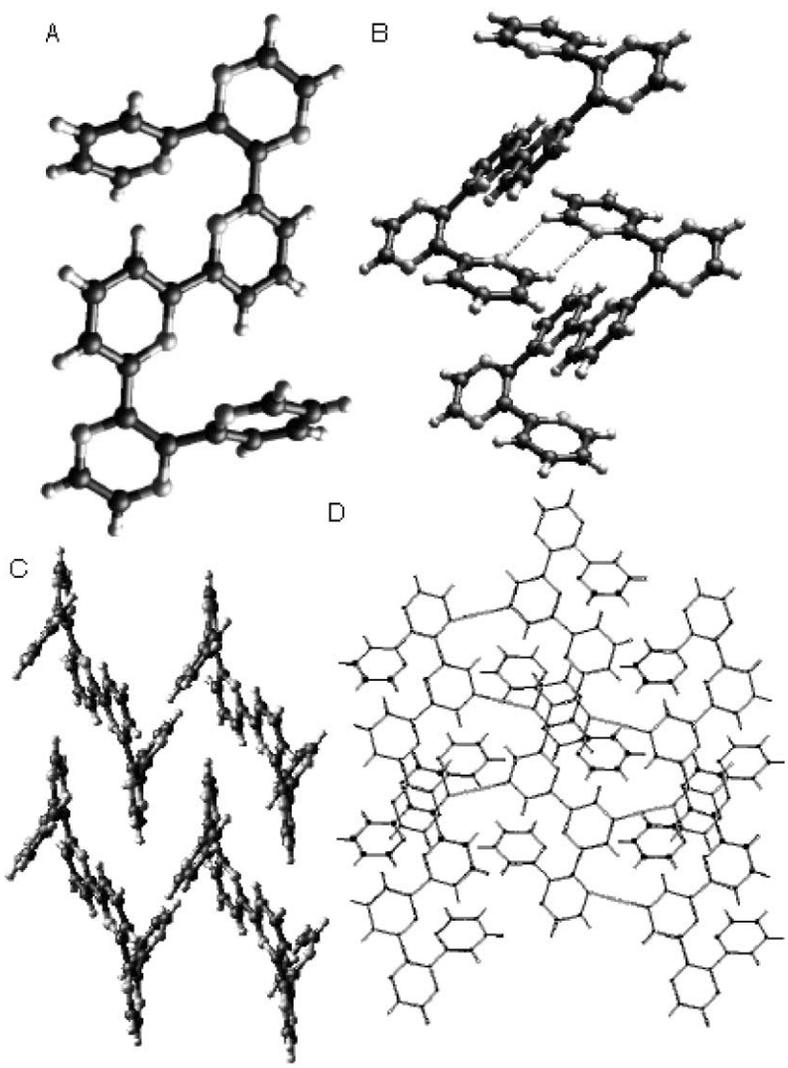


Fig. 3 Solid-state structure and lattice interactions in **3c**. A. *Meso-twisted* conformation; B. catenating C–H ··· N interactions; C. columnar stacking of intermeshed pyrazinyl rings; D. cross-linking of sheets of columns through C–H ··· N interactions.

Table 1 Geometrical parameters of pyrazine–pyridine hybrids related to C–H · · · π interactions

	3a	**3c**	**3d** Bpy C_5H_4N– Tpy C_5H_3N	**3d** Tpy C_5H_3N– Bpy C_5H_3N	**3d′** [c] Bpy C_5H_4N– Tpy C_5H_3N	**3d′** [c] Tpy C_5H_3N– Bpy C_5H_3N	**2**
$d\pi_C$(–H-3)/Å	2.87	3.16	3.78	3.16	3.23	3.01	3.23
α/° [a]	158	134	141	134	138	131	143
d'(N-1)/Å [b]	3.14	3.53	3.76	3.85	3.57	3.49	3.53
d'(C-2)/Å [b]	3.09	3.31	3.73	3.28	3.39	3.22	3.43
d'(C-3)/Å [b]	3.16	3.23	4.02	3.14	3.38	3.05	3.42
d'(C-4)/Å [b]	3.23	3.36	4.29	3.31	3.48	3.13	3.49
d'(C-5)/Å [b]	3.24	3.57	4.29	3.61	3.60	3.38	3.67
d'(C-6)/Å [b]	3.18	3.61	4.02	3.70	3.64	3.64	3.57

[a] α = 3-C–H-3–π_C. [b] d' = Separation from H-3 to indicated position on the orthogonal ring. [c] Two independent molecules in unit cell.

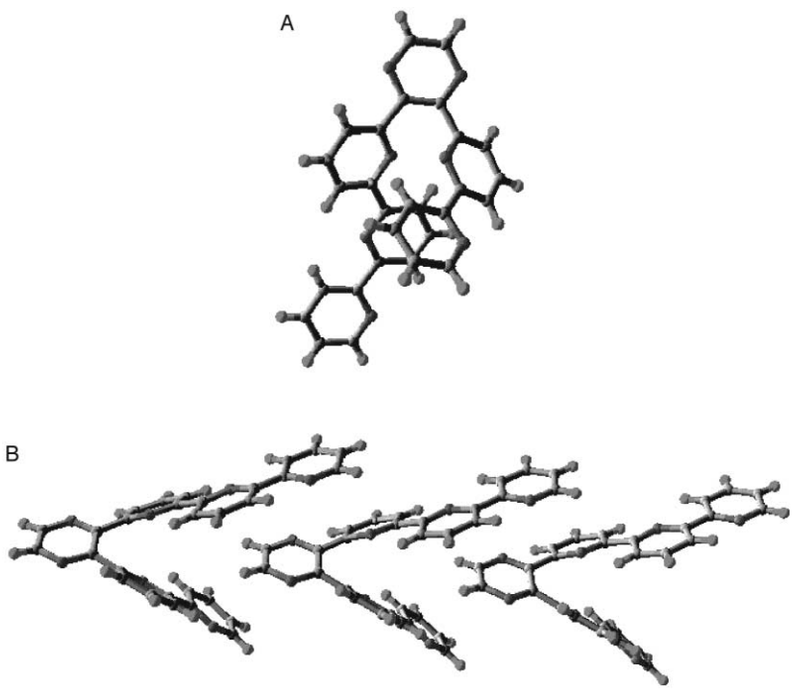


Fig. 4 Solid-state structure of terpyridyl bipyridyl **3d**. A. overall twisting of Bpy ring systems around terpy; B. weak parallel interpyridine stacking.

that *both* of the aforementioned criteria are met. The tentative conclusion is that although C–H · · · π interactions may *reinforce* the orthogonal interactions of the pyridyl groups, they do not *per se induce* them. The double-helical twisting in these pyrazine-pyridine hybrids is therefore principally of steric–dipole origin.

Lattice and stacking interactions

It was also of interest to determine whether the lattice interactions in **3a** had any bearing on the poor crystallinity of derivative **3f** or the low solubility and high melting point of **3c**. In **3a**, two sorts of intermolecular parallel stacking effects are apparent (Fig. 2B). In the first, pyrazine rings are aligned in antiparallel columns. This overlap is, however not perfect and adjacent pyrazine rings are slipped offset by 32° in an alternating fashion. Adjacent molecules are also enantiomerically related with respect to their sense of helical twisting. This results in different separations between the centroids of the pyrazine rings, 3.67 and 4.55 Å for the ring faces bearing the bpy and pyridyl substituents respectively. Stepping back yet again, one sees that neighbouring stacks are aligned through dimeric C–H · · · N hydrogen bond donor–acceptor interactions (2.67 Å) between H-4 of bpy and N-1 of pyrazine (Fig. 2C). The second parallel stacking effect involves the C_5H_4N rings of bpy, which exhibit a slipped anti-parallel alignment (Fig. 2D). The centroid of one ring efficiently overlaps with 4-C of its neighbour, and distances of 3.69 Å are thereby observed. Overlaps of a similar magnitude between 2-C and the adjacent H-4 are also observed.

The crystal lattice of **3c** displays progressively interwoven degrees of organisation. Molecules are interconnected through dimeric C–H · · · N interactions between H-6 and N of the C_5H_4N rings (2.76 Å), forming achiral ribbons (Fig. 3B). Although this effect has been observed in other nitrogen-containing arenes,[34] to our knowledge, it has not yet been documented from positions directly adjacent to pyridine nitrogen. Neighbouring ribbons are interdigitated through offset stacking of the pyrazine rings, which thus form columns running through the lattice (Fig. 3C). The centroid-to-centroid distances between the pyrazine rings are 3.92 and 3.79 Å. Judged from these derived values, the offset between the rings is 15.54°, or 0.53 Å. A similar feature occurs in the crystal structure of pyrazine itself.[35] Additional C–H · · · N interactions existing between N of C_5H_4N and H-5 of the pyrazine ring (2.79 Å) may also contribute towards stabilisation of this array. The interdigitated ribbons together form pleated sheets, and these sheets are interconnected by contacts between H-4 of bpy and N-1 of pyrazine of 2.61 Å (Fig. 3D). This is below the sum of the concerned van der Waals radii[36] and the vector represented by the 4-C–H-4 bond deviates by *ca.* 36° from the mean plane of the pyrazine ring. Therefore, this relationship meets the criteria outlined for a C–H · · · N hydrogen bonding interaction.[37] Furthermore, comparison between these

interactions in compounds **3a** and **3c** shows that for the former a *dimeric* supramolecular synthon results, whereas for the latter a *catenated* supramolecular synthon results.

In contrast, the lattice of **3d** is distinguished by the *absence* of inter-pyrazine stacking interactions. The only parallel π-stacking evident involves the first and third pyridyl rings of the terpy ring system in one of the two molecules present in the asymmetric cell (Fig. 4B). This occurs through parallel (not anti-parallel) orientation of the two concerned rings. The overlapping terpy systems are also inclined 19° to one other.

Conclusions

A convergent synthesis of unsymmetrical pyrazine–pyridine hybrids using mixed α-diketones as immediate precursors has been presented. A novel epoxidation reaction of keto–enol tautomeric ethanones affords those diketones.

On the basis of solid- and solution-state studies, the pyrazine–pyridine hybrids can be described as preferentially twisted, pre-double helically shaped compounds occurring on a relatively small scale molecular format. Proton NMR spectroscopic evidence indicates that the second pyridyl ring out from pyrazine orthogonally juts into the first pyridyl ring of the other group attached to pyrazine. Uniformly, H-3 on that second ring is shifted upfield by δ 1.0 ppm, indicating that in solution, the average twisting is comparable for all compounds. The same geometry *can* also enable C–H ⋯ π stacking interactions—at least in the solid state—however, the extent to which this is possible is subordinate to steric effects manifested by the pendant *transoid* oligopyridyl substituents.

Additionally, the solid-state structures illustrated several supramolecular synthons: offset stacking of pyrazine rings, weak C–H ⋯ N hydrogen bonding and trans-annular distortion of oligopyridyl ring systems from transoid-coplanar conformity. Pyrazine stacking appears to be favoured in those hybrids having relatively high pyrazine content. It is also a central self-organising feature of the dicopper(I) complex of **3a**.[8d] Thus, the manifestation of these features in their metallo–organic supramolecular complexes is a topic of future and ongoing interest.

Experimental

Infrared spectra were recorded on Mattson Genesis Fourier-transform spectrophotometers with samples in compressed KBr discs. Proton and carbon NMR spectra were recorded on Varian Gemini (300, 75 MHz), Bruker DRX 500 (500, 125 MHz) or JEOL GX (270, 67.5 MHz) spectrometers. δ_H and δ_C values are referenced to Me_4Si and $CHCl_3$, respectively. *J* values are given in Hz. Unless otherwise indicated, δ_C assignments refer to single, magnetically equivalent carbon atoms. For the ethanone derivatives, key resonances in their NMR spectra are reported for identification of the ketimine and enolimine tautomers and to establish the positions of their keto–enol tautomeric equilibria. Unless indicated otherwise, all mass spectra were recorded as electron-impact (EI) spectra (including relative intensities) on VG 70–250, Kratos MS-902 or Finnigan 8430 spectrometers at 70 eV. Column chromatography was performed with silica gel (70–230 mesh, Fluka) or aluminium oxide/activity III (Fluka). Anhydrous diethyl ether, tetrahydrofuran, 1,2-dimethoxyethane and toluene were freshly distilled from sodium–benzophenone ketal under dry nitrogen gas. Dry dichloromethane was freshly distilled from P_4O_{10}. Diisopropylamine and tetramethylpiperidine were distilled from CaH_2 and stored over activated 5 Å molecular sieves. Methanol was distilled from iodine-activated magnesium turnings and stored over freshly-activated 5 Å molecular sieves. Unless indicated, all other chemicals were commercially available and used as received.

Pyrazine 3a

Pyrazine **3a** has been previously reported:[8b] ν_{max}/cm^{-1} (KBr) 3055 (w, Ar C–H), 1581 (s, Ar C=C), 1560 (s, Ar C=C), 837 (m, Ar C–H), 781 (s, Ar C–H); δ_C($CDCl_3$, 75 MHz) 158.14 (C), 155.67 (C), 155.52 (C), 154.63 (C), 152.86 (C), 151.99 (C), 148.96 (CH), 148.90 (CH), 142.62 (CH), 137.85 (CH), 136.39 (CH), 136.30 (CH), 124.06 (CH), 123.86 (CH), 123.64 (CH), 122.77 (CH), 120.75 (CH), 120.48 (CH); λ_{max}(MeCN)/nm = 237 (log ε/dm^3 mol^{-1} cm^{-1} 4.30 sh), 248 (4.32), 282 (4.43).

3b

Analogous to the synthesis of **3a**, **4b** afforded **3b** in 48% yield after recrystallisation (heptane–CH_2Cl_2) as colourless rhombohedral crystals. ν_{max}/cm^{-1} (KBr) 3060 (m, Ar C–H), 1579 (s, Ar C=C), 1564 (s, Ar C=C), 810 (m, Ar C–H), 783 (s, Ar C–H), 744 (m, Ar C–H); δ_H($CDCl_3$, 300 MHz) 8.71 (s, 2H, H-5, H-6), 8.68 (br d, *J* 4.8, 1H, H-6‴″), 8.55–8.59 (m, 2H, H-3′,5′, H-3‴″), 8.42 (dt, *J* 1.3, 4.9, 1H, H-6″), 8.35 (dd, *J* 1.0, 7.8, 1H, H-5‴″), 8.16 (dd, *J* 1.0, 7.7, 1H, H-5′,3′), 8.00 (t, *J* 7.8, 1H, H-4′), 7.79–7.87 (m, 3H, H-3″, H-4″, H-4‴″), 7.66 (t, *J* 7.8, 1H, H-4‴″), 7.32 (ddd, *J* 1.2, 4.8, 7.5, 1H, H-5‴″), 7.28 (br d, *J* 7.1, 1H, H-3‴″), 7.20 (ddd, *J* 2.5; 4.9, 7.2, 1H, H-5″); δ_C($CDCl_3$, 75 MHz) 158.10 (C), 156.08(C), 155.41(C), 155.06 (C), 154.78 (C), 154.59 (C), 152.86 (C), 151.91 (C), 149.07 (CH), 148.92 (CH), 142.61 (CH), 142.58 (CH), 137.77 (CH), 137.37 (CH), 136.82 (CH), 136.34 (CH), 124.02 (CH), 123.83 (CH), 123.72 (CH), 122.81 (CH), 121.06 (CH), 120.89 (CH), 120.62 (CH), 120.51 (CH); *m*/*z* 388 ([M]$^+$, 100%), 387 ([M − H]$^+$, 100), 336 ([M − NCCN]$^+$, 4), 334 ([M − $C_2H_2N_2$]$^+$, 3), 233 ([M − $C_{10}H_7N_2$]$^+$, 7), 194 ([M − $C_{10}H_7N_2$ − C_2HN]$^+$, 12). Found: C, 74.16; H, 4.27; N, 21.54. Calc. for $C_{24}H_{16}N_6$: C, 74.21; H, 4.15; N, 21.64%.

3c

Analogous to the synthesis of **3a**, **4c** afforded **3c** in 44% yield after reaction with 2 equiv. each of ethylenediamine and chloranil. Recrystallisation (CH_2Cl_2–Me_2CHOH) afforded colourless small blocks for combustion analysis. Mp > 400 °C; ν_{max}/cm^{-1} (KBr) 3060 (w, Ar C–H), 1587 (m, Ar C=C), 1577 (s, Ar C=C), 1566 (s, Ar C=C), 831 (m, Ar C–H), 802 (s, Ar C–H), 779 (s, Ar C–H), 744 (s, Ar C–H); δ_H($CDCl_3$, 300 MHz) 8.69 (s, 4H, H-5, H-6), 8.37 (br d, *J* 4.8, 2H, H-6″), 8.02 (dd, *J* 1.0, 7.7, 2H, H-3′), 7.79–7.81 (m, 2H, H-3″, H-4″), 7.66 (t, *J* 7.9, 1H, H-4′), 7.15–7.22 (m, 2H, H-5′, H-5″); δ_C($CDCl_3$, 75 MHz) 158.02 (C, 1C), 155.20 (C, 1C), 154.11 (C, 1C), 152.70 (C, 1C), 151.81 (C, 1C), 148.77 (CH, 1C), 142.61 (CH, 2C), 137.37 (CH, 1C), 136.41 (CH, 1C), 124.05 (CH, 1C), 123.74 (CH, 1C), 122.84 (CH, 1C), 120.20 (CH, 1C); *m*/*z* 466 ([M]$^+$, 100%), 414 ([M − NCCN]$^+$, 4), 412 ([M − HNCCNH]$^+$, 3), 388 ([M − C_5H_4N]$^+$, 94), 335 ([M − C_5H_4N − C_2HN_2]$^+$, 7), 233 ([M/2]$^+$, 33), 232 ([M/2 − H]$^+$, 53). Found: C, 70.56; H, 4.10; N, 23.58. Calc. for $C_{28}H_{18}N_8$·½H_2O: C, 70.73; H, 4.03; N, 23.56%.

3d

Analogous to the synthesis of **3a**, **4d** afforded **3d** in 67% yield after recrystallisation (heptane–$CHCl_3$) in the form of colourless rhombohedral crystals. ν_{max}/cm^{-1} (KBr) 3055 (w, Ar C–H), 1576 (m, Ar C=C), 1566 (s, Ar C=C), 821 (m, Ar C–H), 780 (s, Ar C–H); δ_H($CDCl_3$, 500 MHz) 8.74 (s, 2H, H-5, H-6), 8.65 (br d, *J ca.* 4.8, 1H, H-6‴″), 8.50–8.52 (m, 3H, H-5″, H-3‴″, H-6‴″), 8.32 (dd, *J* 1.1, 7.8, 1H, H-5′), 8.30 (dd, *J* 1.1, 7.8, 1H, H-5‴″), 8.060 (dd, *J* 1.2, 7.7, 1H, H-3″), 8.054 (dd, *J ca.* 1.2, 7.7, 1H, H-3′), 8.01 (t, *J* 7.6, 1H, H-4″), 7.99 (t, *J* 7.6, 1H, H-4′), 7.80 (br t, *J* 7.7, 1H, H-4‴″), 7.62 (t, *J* 7.8, 1H, H-4‴″), 7.45–7.48 (m, 3H, H-3‴″, H-3‴″, H-4‴″), 7.27–7.30 (m, 1H, H-5‴″), 7.11–7.13 (m, 1H, H-5‴″); δ_C($CDCl_3$, 125 MHz, 280 K) 156.45 (C, 1C, 6″-C), 156.38 (C, 1C, 6′-C), 155.89 (C, 1C, 2‴″-C), 155.43 (C, 1C, 2‴″-C), 154.97, 154.92, 154.91, 154.65 (C, 4C, 2′-C, 2″-C, 2″-C, 6‴″-C), 152.49 (C, 1C, 3-C), 152.44 (C, 1C, 2-C), 149.00 (6‴″-C),

148.79 (6′′′′-C), 142.59 (CH, 1C, 5/6-C), 142.58 (6/5-C), 137.67 (CH, 1C, 4′′-C), 137.57 (CH, 1C, 4′′′-C), 137.54 (CH, 1C, 4′-C), 136.75 (CH, 1C, 4′′′′-C), 136.57 (CH, 1C, 4′′′′-C), 123.68 (CH, 2C, 3′′-C, 3′-C), 123.63 (CH, 1C, C-5′′′′), 123.61 (CH, 2C, 3′,3′′-C, 5′′′′-C), 120.96 (CH, 1C, 5′,3′′′′-C), 120.84 (CH, 1C, 5′′′-C), 120.70 (CH, 1C, 3′′′,3′′′′-C), 120.64 (CH, 1C, 3′′′,3′′′-C), 120.28 (CH, 1C, 3′′′,5′-C), 120.19 (CH, 1C, 5′′-C); *m*/*z* 465 ($[M]^+$, 100%), 464 ($[M - H]^+$, 85), 387 $[M - C_5H_4N]^+$, 12), 310 ($[M - C_{10}H_7N_2]^+$, 9), 233 ($[M - C_{15}H_{11}N_3]^+$, 20), 155 ($[C_{10}H_7N_2]^+$, 6). Found: C, 73.54; H, 4.23; N, 20.82. Calc. for $C_{29}H_{19}N_7O \cdot ½ H_2O$: C, 73.40; H, 4.25; N, 20.66%.

3e

Analogous to the synthesis of **3a**, **4e** afforded **3e** in 31% yield as a viscous oil; recrystallised (heptane–$CHCl_3$) for analytical purposes. ν_{max}/cm^{-1} (KBr) 3042 (w, Ar C–H), 1579 (s, Ar C=C), 1562 (s, Ar C=C), 837 (m, Ar C–H), 779 (s, Ar C–H); δ_H($CDCl_3$, 400 MHz) 8.69 (s, 2H, H-5, H-6), 8.59 (br d, *J* 4.7, 1H, H-6′′′), 8.35 (dd, *J* 1.1, 7.9, 1H, H-3′), 8.24 (br s, 1H, H-6′′), 8.08 (dd, *J* 1.1, 7.8, H-5′), 7.94 (t, *J* 7.8, 1H, H-4′), 7.70 (d, *J* 7.5, 1H, H-3′′), 7.60 (br dd, *J* 1.8, 7.9, 1H, H-4′′), 7.52 (dt, *J* 1.8, 7.6, 1H, H-4′′′), 7.38 (dt, *J* 1.0, 6.9, 1H, H-3′′′), 7.20 (ddd, *J* 0.9, 4.0, 7.5, 1H, H-5′′′), 2.27 (s, 3H, H-7′′); δ_C($CDCl_3$, 100 MHz) 155.74 (C), 155.66 (C), 155.31 (C), 154.60 (C), 152.86 (C), 151.84 (C), 149.31 (CH), 148.86 (CH), 142.60 (CH), 142.39 (CH), 137.72 (CH), 136.69 (CH), 136.22 (C), 132.49 (CH), 123.85 (CH), 123.57 (2CH), 120.76 (CH), 120.35 (CH); *m*/*z* 324 ($[M]^+$, 100%), 247 ($[M - C_5H_3N]^+$, 8), 245 ($[M - C_5H_5N]^+$, 7). *m*/*z* Found: 325.132. $C_{20}H_{15}N_5$ requires 325.133.

3f

Analogous to the synthesis of **3a**, **4f** afforded **3f** in 22% yield as a golden-coloured oil that was a single substance according to thin-layer chromatography and ^{1}H NMR spectroscopic analysis. ν_{max}/cm^{-1} (film) 3056 (m, Ar C–H), 2924 (w, aliphatic C–H), 1579 (s, Ar C=C), 1564 (s, Ar C=C), 1429 (m, C–H), 789 (s, Ar C–H), 777 (s, Ar C–H), 746 (m, Ar C–H); δ_H($CDCl_3$, 400 MHz) 8.69–8.71 (m, 2H, H-5, H-6), 8.59 (br d, *J* 4.7, 1H, H-6′′′), 8.35 (dd, *J* 1.1, 7.9, 1H, H-3′), 8.06 (dd, *J* 1.1, 7.7, 1H, H-5′), 7.94 (dt, *J* 1.5, 7.8, 1H, H-4′), 7.63 (dt, *J* 1.5, 7.7, 1H, H-4′′), 7.52–7.56 (m, H-3′′, H-4′′′), 7.34 (br d, *J* 7.9, 1H, H-3′′′), 7.20 (ddd, *J* 1.2, 4.7, 7.4, 1H, H-5′′′), 7.04 (d, *J* 7.7, 1H, H-5′′), 2.32 (s, 3H, H-7′′); δ_C($CDCl_3$, 100 MHz) 157.76 (C, 1C, 2′′′-C), 157.15 (C, 1C, 2-C′′), 155.69 (C, 2C, 2′-C; 2′′′-C), 154.52 (C, 1C, 6′-C), 152.96 (C, 1C, 3-C), 151.93 (C, 1C, 2-C), 148.82 (CH, 1C, 6′′′-C), 142.68 (CH, 1C, 5,6-C), 142.49 (CH, 1C, 6,5-C), 137.54 (CH, 1C, 4′-C), 136.45 (CH, 1C, 4′′-C), 136.30 (CH, 1C, 4′′′-C), 123.83 (CH, 1C, 3′-C), 123.56 (CH, 1C, 5′′′-C), 122.24 (CH, 1C, 5′′-C), 120.92 (CH, 1C, 3′′-C), 120.80 (CH, 1C, 3′′′-C), 120.19 (CH, 1C, 5′-C), 24.20 (CH_3, 1C, 7′′-C); *m*/*z* 325 ($[M]^+$, 91%), 324 $[M - H]^+$, 100), 310 ($[M - CH_3]^+$, 5), 247 ($[M - C_5H_4N] - 11$), 220 ($[M - C_5H_4N - HCN]^+$, 9), 206 ($[M - C_5H_4N - CH_3CN]^+$, 7). *m*/*z* Found: 325.132. $C_{20}H_{15}N_5$ requires 325.133.

3g

Analogous to the synthesis of **3a**, **4g** afforded **3g** in 30% yield; recrystallised (CH_2Cl_2–heptane) to give colourless crystals for combustion analysis. ν_{max}/cm^{-1} (KBr) 3051 (m, Ar C–H), 2922 (w, C–H), 1587 (s, Ar C=C), 1574 (m, Ar C=C), 1444 (m, C–H), 796 (s, Ar C–H); δ_H($CDCl_3$, 300 MHz) 8.67–8.69 (m, 2H, H-5, H-6), 8.41 (br d, *J* 4.8, H-6′′), 7.70–7.73 (m, 2H, H-3′′, H-4′′), 7.61 (t, *J* 7.4, 1H, H-4′), 7.55 (br d, *J* 6.4, 1H, H-3′), 7.22–7.24 (m, 1H, H-5′′), 7.08 (d, *J* 6.5, 1H, H-5′), 2.28 (s, 3H, H-7′); δ_C($CDCl_3$, 75 MHz) 157.56 (C, 1C), 157.27 (C, 1C), 155.82 (C, 1C), 152.52 (C, 1C), 152.43 (C, 1C), 148.73 (CH, 1C), 142.82 (CH, 1C), 142.63 (CH, 1C), 136.66 (CH, 1C), 136.22 (CH, 1C), 124.23 (CH, 1C), 122.80 (CH, 1C), 122.65 (CH, 1C), 121.12 (CH, 1C), 24.21 (CH_3, 1C, 7′-C); *m*/*z* 247 ($[M]^+$, 100%). Found: C, 72.38; H, 4.82; N, 22.18. Calc. for $C_{15}H_{12}N_4$: C, 72.56; H, 4.87; N, 22.57%.

Diketone 4a

Diketone **4a** has been previously reported:[8b] ν_{max}/cm^{-1} (KBr) 3054 (w, Ar–H), 1709 (s, C=O), 1691 (s, C=O), 1581 (s, Ar C=C), 789 (m, Ar–H), 756 (m, Ar–H); δ_H($CDCl_3$, 300 MHz) 8.64 (dd, *J* 1.1, 8.0, 1H, H-5), 8.60 (ddd, *J* 0.9, 1.8, 4.8, 1H, H-6′′), 8.57 (ddd, *J* 0.9, 1.7, 4.7, 1H, H-6′), 8.26 (dt, *J* 1.1, 7.8, 1H, H-3′), 8.21 (dd, *J* 1.1, 7.6, 1H, H-3), 8.04 (t, *J* 7.8, H-4), 7.96 (dt, *J* 1.7, 7.8, 1H, H-4′), 7.86 (dt, *J* 0.9, 8.0, 1H, H-3′′), 7.62 (dt, *J* 1.8, 7.8, 1H, H-4′′), 7.47 (ddd, *J* 1.2, 4.8, 7.7, 1H, H-5′), 7.24 (ddd, *J* 1.2, 4.8, 7.5, 1H, H-5′′); δ_C($CDCl_3$, 100 MHz) 197.18 (8-C), 196.78 (7-C), 155.65 (6-C), 154.49 (2′′-C), 151.98 (2′-C), 151.00 (2-C), 149.52 (6′-C), 148.97 (6′′-C), 138.10 (CH, 4-C), 137.12 (CH, 4′-C), 136.82 (CH, 4′′-C), 127.69 (CH, 5′-C), 125.09 (CH, 5-C), 124.13 (CH, 5′′-C), 122.00 (CH, 3-C), 121.79 (CH, 3′-C), 120.99 (CH, 3′′-C); λ_{max}(hexane)/nm 231 (log ε/dm^3 mol^{-1} cm^{-1} 4.49), 255 (4.18 sh), 277 (4.29).

4b

Analogous to the synthesis of **4a**, **7b** afforded **4b** in 40% yield; recrystallisation ($CHCl_3$–pentane, light exclusion) for combustion analysis. Mp 207.5–208.5 °C; ν_{max}/cm^{-1} (KBr) 3062 (w, Ar–H), 1709 (s, C=O), 1695 (m, C=O), 1583 (m, Ar C=C), 1562 (m, Ar C=C), 781 (w, Ar–H), 764 (m, Ar–H); δ_H($CDCl_3$, 300 MHz) 8.82 (dd, *J* 1.1, 7.9, 1H, H-5), 8.68 (br d, *J ca.* 4, 1H, H-6′′′), 8.58 (br d, *J ca.* 5, 1H, H-6′), 8.55 (br d, *J* 8.0, 1H, H-3′′′), 8.39 (dd, *J* 1.0, 7.8, 1H, H-3′′,5′′), 8.28 (dt, *J* 1.0, 7.8, 1H, H-3′), 8.24 (dd, *J* 1.1, 7.6, 1H, H-3), 8.08 (t, *J* 7.8, 1H, H-4), 7.97 (dt, *J* 1.7, 7.8, 1H, H-4′), 7.81–7.90 (m, 2H, H-3′′,5′′, H-4′′′), 7.76 (t, *J* 7.8, 1H, H-4′′), 7.48 (ddd, *J* 1.2, 4.7, 7.5, 1H, H-5′), 7.32 (ddd, *J* 1.2, 4.8, 7.5, 1H, H-5′′′); δ_C($CDCl_3$, 75 MHz) 197.25 (C), 196.88 (C), 155.87 (C), 155.79 (C), 155.34 (C), 153.78 (C), 152.02 (C), 151.03 (C), 149.57 (CH), 149.14 (CH), 138.05 (CH), 137.80 (CH), 137.19 (CH), 136.84 (CH), 127.75 (CH), 125.16 (CH), 123.84 (CH), 122.06 (CH), 121.85 (CH), 121.42 (CH), 121.04 (CH), 120.94 (CH); *m*/*z* 366 (M^+, 59%), 338 ($[M - CO]^+$, 60), 310 ($[M - 2CO]^+$, 67), 309 ($[M - C_2H_3N]^+$, 68), 232 ($C_{15}H_{10}N_3$, 100), 155 ($C_{10}H_7N_2$, 29); λ_{max}(MeCN)/nm 227 (log ε/dm^3 mol^{-1} cm^{-1}, 4.56), 264 (4.28 sh), 283 (4.35), 302 (4.20 sh). Found: C, 71.94; H, 3.90; N, 15.31. Calc. for $C_{22}H_{14}N_4O_2$: C, 72.12; H, 3.85; N, 15.29%.

4c

Analogous to the synthesis of **4a**, but using 2 equiv. each of MCPBA and I_2 **7c** afforded **4c** in 39% yield; recrystallisation ($CHCl_3$–heptane, light exclusion) for combustion analysis. Mp 229.5–230.0 °C; ν_{max}/cm^{-1} (KBr) 3060 (w, Ar–H), 1718 (s, C=O), 1682 (m, C=O), 1581 (m, Ar C=C), 758 (w, Ar–H), 764 (m, Ar–H), 1562 (m, Ar C=C), 781 (w, Ar–H), 742 (w, Ar–H); δ_H($CDCl_3$, 300 MHz) 8.55 (br d, *J ca.* 4.7, 2H, H-6′), 8.25 (dt, *J* 1.1, 7.8, 2H, H-3′), 8.16 (dd, *J* = 1.1, 6.6, 2H, H-3,5), 8.06 (dd, *J* 1.1, 6.6, 2H, H-5,3), 7.96 (dt, *J* 1.7, 6.0, 2H, H-4′), 7.87 (t, *J* 7.8, 2H, H-4), 7.48 (ddd, *J* 1.2, 4.8, 7.6, 2H, H-5′); δ_C($CDCl_3$, 75 MHz) 196.91 (C, 8-C), 196.54 (C, 7-C), 154.23 (C-6), 151.90 (C-2′), 150.97 (C-2), 149.59 (CH, 6′-C), 138.21 (CH, 4-C), 137.23 (CH, 4′-C), 127.84 (CH, 5′-C), 125.08 (CH, 5-C), 122.47 (CH, 3-C), 121.88 (CH, 3′-C); *m*/*z* 422 (M^+, 66%), 394 ($[M - CO]^+$, 20), 366 ($[M - 2CO]^+$, 15), 365 ($[M - CO - CHO]^+$, 42), 338 ($[M - 3CO]^+$, 11), 337 ($[M - 2CO - CHO]^+$, 28), 310 ($[M - 4CO]^+$, 36), 309 ($[M - 3CO - CHO]^+$, 100); λ_{max}(MeCN)/nm 225 (log ε/dm^3 mol^{-1} cm^{-1} 4.61), 268 (4.28), 281 (4.20 sh), 293 (4.10 sh), 375 (2.65). Found: C, 67.94; H, 3.47; N, 13.17. Calc. for $C_{24}H_{14}N_4O_4$: C, 68.24; H, 3.34; N, 13.26%.

4d

Analogous to the synthesis of **4a**, **7d** afforded **4d** in 35% yield; recrystallisation ($CHCl_3$–pentane, light exclusion) of colourless rhombohedral crystals for combustion analysis. Mp 151.5–152.5 °C; ν_{max}/cm^{-1} (KBr) 3059 (w, Ar–H), 1707 (s, C=O), 1689 (s, C=O), 1579 (s, Ar C=C), 1562 (s, Ar C=C), 781 (m, Ar–H), 754 (m, Ar–H); δ_H($CDCl_3$, 300 MHz) 8.81 (dd, *J* 1.1, 7.9, 1H, H-5), 8.66 (dq, *J* 0.9, 4.8, 1H, H-6‴), 8.63 (dd, *J* 1.1, 7.9, 1H, H-5′), 8.57 (dq, *J* 0.8, 4.6, 1H, H-6‴), 8.52 (dt, *J* 1.0, 7.9, 1H, H-3‴), 8.37 (dd, *J* 1.0, 7.8, 1H, H-5″,3″), 8.29 (m, 2H, H-3′, H-3), 8.12 (t, *J* 7.8, 1H, H-4), 8.09 (t, *J* 7.8, 1H, H-4′), 7.90–7.93 (m, 2H, H-3‴, H-3″/5″), 7.82 (dt, *J* 1.8, 7.2, 1H, H-4‴), 7.76 (t, *J* 7.8, 1H, H-4″), 7.62 (dt, *J* 1.8, 7.8, 1H, H-4‴), 7.30 (ddd, *J* 1.2, 4.8, 7.5, 1H, H-5‴), 7.22 (ddd, *J* 1.2, 4.8, 7.6, 1H, H-5‴); δ_C($CDCl_3$, 100 MHz) 197.17 (C, 2C, 7-C, 8-C), 155.92 (C, 1C, 2‴-C), 155.90 (C, 1C, 2′-C), 155.84 (C, 1C, 6-C), 155.36 (C, 1C, 6‴-C), 154.52 (C, 1C, 2″-C), 153.71 (C, 1C, 2‴-C), 151.35 (C, 2C, 6′-C, 2-C), 149.16 (CH, 1C, 6‴-C), 149.03 (CH, 1C, 6″-C), 138.16 (CH, 1C, 4-C), 138.04 (CH, 1C, 4′-C), 137.86 (CH, 1C, 4″-C), 136.83 (CH, 1C, 4‴,4″-C), 136.77 (CH, 1C, 4″,4‴-C), 125.02 (CH, 1C, 5′-C), 124.99 (CH, 1C, 5-C), 124.16 (CH, 1C, 5″-C), 123.80 (CH, 1C, 5‴-C), 121.52 (CH, 3C, 3-C, 3-C, 5‴,3‴-C), 121.08 (CH, 1C, 3″-C), 121.02 (CH, 1C, 3‴,5‴-C), 121.00 (CH, 1C, 3‴-C); λ_{max}($CHCl_3$)/nm 256 (log ε/dm^3 mol^{-1} cm^{-1} 4.43 sh), 284 (4.53), 387 (2.13 sh); *m*/*z* 443 (M^+, 21%), 415 ([M − CO]$^+$, 93), 387 ([M − 2CO]$^+$, 64), 386 ([M − CO − CHO]$^+$, 100), 232 ($C_{15}H_{10}N_3$, 64), 155 ($C_{10}H_7N_2$, 64). Found: C, 72.76; H, 3.97; N, 15.80. Calc. for $C_{27}H_{17}N_5O_2$: C, 73.13; H, 3.86; N, 15.79%.

4e

Analogous to the synthesis of **4a**, **7e** afforded **4e** in 63% yield as a red-coloured solid without column chromatography. Mp 121–122 °C; ν_{max}/cm^{-1} (KBr) 3058 (w, Ar–H), 1710 (s, C=O), 1691 (s, C=O), 1582 (s, Ar C=C), 783 (m, Ar–H), 769 (s, Ar–H), 746 (m, Ar–H); δ_H($CDCl_3$, 400 MHz) 8.60 (dd, *J* 1.1, 7.9, 1H, H-5), 8.57 (br d, *J ca.* 5, 1H, H-6″), 8.36 (br s, 1H, H-6′), 8.18 (dd, *J* 1.1, 7.7, 1H, H-3), 8.14 (d, *J* 7.9, 1H, H-3′), 8.01 (t, *J* 7.8, H-4), 7.89 (d, *J* 7.9, 1H, H-3″), 7.71 (dd, *J* 1.5, 8.0, 1H, H-4′), 7.60 (dt, *J* 1.8, 7.8, 1H, H-4″), 7.21 (ddd, *J* 1.2, 4.8, 8.8, H-5″), 2.37 (s, 3H, H-7′); δ_C($CDCl_3$, 100 MHz) 196.96 (C), 196.90 (C), 155.65 (C), 154.52 (C), 151.02 (C), 150.05 (CH), 149.71 (C), 148.96 (CH), 138.02 (CH), 137.37 (CH), 136.73 (CH), 124.94 (CH), 124.06 (CH), 121.93 (CH), 121.57 (CH), 120.99 (CH), 18.80 (CH_3); *m*/*z* 303 (M^+, 65%), 275 ([M − CO]$^+$, 59), 247 ([M − 2 CO]$^+$, 69), 246 ([M − CO − COH]$^+$, 77), 155 ([$C_{10}H_7N_2$]$^+$, 100), 92 ([5 − Me − C_5H_3N]$^+$, 84); λ_{max}(MeOH)/nm 232 (log ε/dm^3 mol^{-1} cm^{-1} 4.13), 246 (4.06 sh), 252 (4.04 sh), 279 (4.08). Found: 303.10. $C_{18}H_{13}N_3O_2$ requires 303.10.

4f

Analogous to the synthesis of **4a**, **7f** afforded **4f** in 32% yield as a yellow-coloured oil that solidified. Mp 116–117 °C; ν_{max}/cm^{-1} (KBr) 3064 (w, Ar–H), 1710 (s, C=O), 1691 (m, C=O), 1598 (m, Ar C=C), 1588, (m, Ar C=C), 756 (w, Ar–H), 740 (m, Ar–H); δ_H($CDCl_3$, 270 MHz) 8.59–8.64 (m, 2H, H-5, H-6″), 8.19 (dd, *J* 1.0, 7.6, H-3), 8.01–8.06 (m, 2H, H-3′, H-4), 7.92 (d, *J* 7.9, 1H, H-3″), 7.80 (t, *J* 7.8, 1H, H-4′), 7.63 (dt, *J* 1.8, 7.7, 1H, H-4″), 7.30 (d, *J* 9.3, 1H, H-5′), 7.24 (ddd, *J* 1.1, 4.8, 7.5, 1H, H-5″), 2.39 (s, 3H, H-7′); δ_C($CDCl_3$, 75 MHz) 197.46 (C), 197.04 (C), 158.76 (C), 155.43 (C), 154.54 (C), 151.44 (C), 151.22 (C), 148.88 (CH), 138.07 (CH), 137.02 (CH), 136.98 (CH), 127.52 (CH), 124.89 (CH), 124.16 (CH), 121.84 (CH), 121.18 (CH), 119.01 (CH), 24.10 (CH_3); *m*/*z* 303 ([M]$^+$, 25), 275 ([M − CO]$^+$, 66), 247 ([M − 2CO]$^+$, 60), 246 ([M − CO − CHO]$^+$, 100), 155 ([$C_{10}H_7N_2$]$^+$ 82). Found: 303.1008. $C_{18}H_{13}N_3O_2$ requires 303.10.

4g

To a vigorously stirred solution of 3.78 g (17.8 mmol) **18g** in CH_2Cl_2 (100 cm^3) was added an aq. 1.5 M $NaHCO_3$ solution (200 cm^3) and then *m*-chloroperbenzoic acid (55% pure, 12.3 g, 39.2 mmol) over *ca.* 2 h at 0 °C. The resulting mixture was stirred for 5.5 h at 0 °C, whereupon water (100 cm^3), a saturated $NaHCO_3$ solution (100 cm^3) and CH_2Cl_2 (50 cm^3) were added. This mixture was briefly stirred, the phases separated, the organic layer washed with water (4 × 50 cm^3) and dried (Na_2SO_4). After rotary evaporation of the solvent and column chromatography (SiO_2, CH_2Cl_2), 1.46 g (36%) of a pale orange crystalline solid was isolated, and that could be recrystallised from CH_2Cl_2–heptane. Mp 138–139 °C; ν_{max}/cm^{-1} (KBr) 3072 (w, Ar–H), 1711 (s, C=O), 1693 (m, C=O), 1593 (m, Ar C=C), 758 (w, Ar–H), 742 (w, Ar–H); δ_H($CDCl_3$, 300 MHz) 8.58 (br d, *J ca.* 4.8, 1H, H-6′), 8.18 (dt, *J* 1.0, 7.7, 1H, H-3′), 7.50 (br d, *J* 7.7, 1H, H-3), 7.92 (dt, *J* 1.7, 7.7, 1H, H-4′), 7.77 (t, *J* 7.7, 1H, H-4), 7.48 (ddd, *J* 1.2, 4.7, 7.4, 1H, H-5′), 7.32 (br d, *J* 7.7, 1H, H-5), 2.41 (s, 3H, H-7); δ_C($CDCl_3$, 75 MHz) 197.17 (C), 197.13 (C), 158.72 (C), 151.96 (C), 151.21 (C), 149.42 (CH), 137.10 (CH), 137.06 (CH), 127.70 (CH), 127.67 (CH), 122.14 (CH), 119.55 (CH), 24.11 (CH_3); *m*/*z* 226 (M^+, 49%), 198 ([M − CO]$^+$, 49), 170 ([M − 2 CO]$^+$, 41), 169 ([M − CO − CHO]$^+$, 100), 92 ([6-Me-C_5H_4N]$^+$, 97). Found: C, 68.73; H, 4.61; N, 12.28. Calc. for $C_{13}H_{10}N_2O_2$: C, 69.02; H, 4.46; N, 12.38.

Ethanone 7a

Ethanone **7a** was prepared as previously reported:[8b] ν_{max}/cm^{-1} (KBr) 1646 (m, C=O), 1601 (s, C=C), 1578 (s, C=C), 1560 (m, C=C), 1551 (m, C=C), 1430 (s, O–H bend), 1258 (m, enol C–O), 813 (s, Ar–H), 781 (s, Ar–H), 742 (m, Ar–H); δ_H($CDCl_3$, 300 MHz) 8.68–8.70 (H-6^E + H-6^K or H-6″^{E} + H-6″^{K}), 8.35–8.36, 4.90 (s, H-7^K) (H-6″^{E} or H-6^E), from the integrals of {H-6^E + H-6^K} and H-6″^{E} (39 and 32, respectively) 18% : 82% keto–enol content was calculated; δ_C($CDCl_3$, 75 MHz) 198.24 (C, 7-C^K), 95.77 (CH, C-8^E), 46.87 (CH_2, C-8^E); λ_{max}(MeOH)/nm 228 (log ε/dm^3 mol^{-1} cm^{-1} 4.20), 245 (4.10 sh), 279 (4.18), 343 (4.13), 411 (3.66), 432 (3.51 sh); *m*/*z* 275 ([M]$^+$, 46%), 247 ([M − CO]$^+$, 85), 246 ([M − CHO]$^+$, 100), 156 ([$C_{10}H_8N_2$]$^+$, 44), 155 ([$C_{10}H_7N_2$]$^+$, 73), 120 ([M − $C_{10}H_7N_2$]$^+$, 21).

7b

Prepared in an analogous manner to **7a**, using inverse addition of lithiated α-picoline–LDA to a suspension of **6b** and in 78% yield; recrystallised ($CHCl_3$–pentane) for combustion analysis. Mp 171.5–172.5 °C; ν_{max}/cm^{-1} (KBr) 3051 (w, alkene C–H), 1645 (m, C=O), 1603 (m, C=C), 1577 (m, C=C), 1566 (s, C=C), 1552 (m, C=C), 1427 (s, O–H bend), 806 (m, Ar–H), 777 (s, Ar–H), 734 (m, Ar–H); δ_H($CDCl_3$, 300 MHz) 8.37 (br d, *J* 5.0, H-6″^{E}), 7.03–7.07 (m, 2H, H-8^E, H-5″^{E}, H-5‴^{E}), 4.92 (s, 2H, H-8^K), from the integrals of {H-8^E, H-5″^{E}}, H-6″^{E} and H-8^K (85, 44 and 41, respectively) 34% : 66% keto–enol content was calculated; δ_C($CDCl_3$, 75 MHz) 198.48 (C, 7-C^K), 95.75 (CH, 8-C^E), 47.15 (CH_2, 8-C^K); λ_{max}(MeOH)/nm 223 (log ε/dm^3 mol^{-1} cm^{-1} 4.50), 238 (4.40 sh), 260 (4.32 sh), 285 (4.37), 301 (4.33 sh), 316 (4.23 sh), 343 (4.24), 350 (4.22 sh), 411 (3.81), 428 (3.73 sh); *m*/*z* 352 ([M]$^+$, 46%), 324 ([M − CO]$^+$, 100), 323 ([M − CHO]$^+$, 86), 233 ([$C_{15}H_{11}N_3$]$^+$, 63), 155 ([$C_{15}H_{10}N_3$]$^+$, 82), 120 ([M − $C_{10}H_7N_2$]$^+$, 5). Found: C, 74.75; H, 4.65; N, 15.96. Calc. for $C_{22}H_{16}N_4O$: C, 74.98; H, 4.58; N, 15.90%.

7c

Prepared in an analogous manner to **7b** and from **6c**, but using two-fold amounts of LDA and α-picoline, giving 92% of a yellow-coloured solid that could be recrystallised ($CHCl_3$–pentane) to afford yellow blocks for analytical purposes. Mp 198–199 °C; ν_{max}/cm^{-1} (KBr) 3053 (w, alkene C–H), 1637 (s, C=O), 1599 (s, C=C), 1570 (s, C=C), 1550 (s, C=C),

1433 (s, O–H bend), 1294 (m, enol C–O), 1082 (m, enol C–O), 802 (s, Ar–H); δ_H($CDCl_3$, 300 MHz) 8.35–8.39 (m, H-6$^{E/K}$), 7.08–6.99 (m, H-5$^{E/K}$, H-8^E), 4.93 (s, H-8^K), from the integrals of H-6$^{E/K}$, {H-5$^{E/K}$, H-8^E} and H-8^K (12.5, 23.0 and 10, respectively) and the correllation of the signal at δ_H 8.35–8.39 to that at δ_H 7.08–6.99, 32% : 68% ratio of total keto–enol content was estimated; δ_C($CDCl_3$, 75 MHz, total of 35 signals resolved) 198.48 (C, 7-C^K), 95.74 (CH, 8-C^E), 47.15 (CH_2, 8-C^K); λ_{max}(MeOH)/nm 222 (log ε/dm^3 mol^{-1} cm^{-1} 5.06 sh), 258 (3.93), 268 (3.91 sh), 284 (3.88 sh), 349 (4.16), 411 (3.70), 430 (3.63 sh); *m*/*z* 394 ([M]$^+$, 82%), 366 ([M − CO]$^+$, 100), 365 ([M − CHO]$^+$, 58), 338 ([M − 2 CO]$^+$, 3), 337 ([M − CO − CHO]$^+$, 7), 288 ([M − CO − C_5H_4N]$^+$, 10), 274 ([M − $C_5H_4NCH_2CO$]$^+$, 26), 247 ([M − C_5H_4NCHO − CO]$^+$, 30), 246 ([M − $C_5H_4N_2$-CH_2O − CO]$^+$, 68), 92 ([$C_5H_4NCH_2$]$^+$, 38). Found: C, 72.70; H, 4.71; N, 14.08. Calc. for $C_{24}H_{18}N_4O_2$: C, 73.08; H, 4.60; N, 14.20%.

7d

Prepared in an analogous manner to **7b**, but using **5b**,[38] **6b**, and 2 equiv. each of tetramethylpiperidine and ^{n}BuLi in 28% yield (rel. to **6b**); recrystallisation ($CHCl_3$–pentane) for analytical purposes. Mp 182.5–183.5 °C; ν_{max}/cm^{-1} (KBr) 3054 (w, alkene C–H), 1637 (m, C=O), 1577 (s, C=C), 1566 (s, C=C), 1542 (s, C=C), 1428 (s, O–H bend), 1265 (m, enol C–O), 792 (m, Ar–H), 775 (s, Ar–H), 742 (m, Ar–H); δ_H($CDCl_3$, 300 MHz) 7.12 (s, 1H, H-7^E), 4.97 (s, 2H, H-7^K) from integrals of H-7^E and H-7^K (1.02 and 0.96, respectively) 32% : 68% keto–enol content was calculated; λ_{max}($CHCl_3$)/nm 285 (log ε/dm^3 mol^{-1} cm^{-1} 4.42), 302 (4.33 sh), 318 (4.19 sh), 361 (4.14), 437 (3.03 sh), 606 (1.84); *m*/*z* 429 ([M]$^+$, 100%), 401 ([M − CO]$^+$, 38), 400 ([M − CHO]$^+$, 34), 233 ([$C_{15}H_{11}N_3$]$^+$, 50), 232 ([$C_{15}H_{10}N_3$]$^+$, 56), 197 ([$C_{10}H_7N_2CH_2CO$]$^+$, 77), 169 ([$C_{10}H_7N_2$]$^+$, 19). Found C, 74.21; H, 4.54; N, 16.10. Calc. for $C_{27}H_{19}N_5O$: C, 75.51; H, 4.46; N, 16.31; O, 3.73%.

7e

Prepared in an analogous manner to **7d**, but using **5c**, **6a**, 1 equiv. tetramethylpiperidine and 2 equiv. ^{n}BuLi in 39% yield; recrystallisation (hexanes) for analytical purposes, although with considerable loss. Mp 92–93 °C; ν_{max}/cm^{-1} (KBr) 2924 (w, C–H), 1639 (s, alkene C=C), 1608 (m, Ar C=C), 1570 (s, Ar C=C), 1560 (s, Ar C=C), 1429 (m, O–H), 1257 (m, C–O), 839 (m, Ar–H), 773 (s, Ar–H); δ_H($CDCl_3$, 300 MHz) 6.98 (s, 1H, H-8^E), 4.90 (s, 2H, H-8^K), from the integrals of H-8^E and H-8^K (0.87 and 0.99, respectively) 64% : 36% keto–enol content was calculated; δ_C($CDCl_3$, 75 MHz) 198.51 (C, 1C, 7-C^K), 95.88 (CH, 1C, 8-C^E), 46.47 (CH_2, 1C, 8-C^K), 18.23 (CH_3, 1C, 7′-C^E), 18.04 (CH3, 1C, 7′-C^K); *m*/*z* 289 ([M]$^+$, 69%), 261 ([M − CO]$^+$, 92), 260 ([M − CHO]$^+$, 100), 156 ([$C_{10}H_8N_2$]$^+$, 62), 155 ([$C_{10}H_7N_2$]$^+$, 96), 134 ([M − $C_{10}H_7N_2$]$^+$, 46). Found: C, 74.76; H, 5.36; N, 14.66. Calc. for $C_{18}H_{15}N_3O$: C, 74.72; H, 5.23 N, 14.52%.

Ethanone 7f

Analogous to the preparation of **7a**, but using **5d**, **6a**, 1 equiv. tetramethylpiperidine and 2 equiv. ^{n}BuLi to give after flash chromatography 71% yield **7f** as a synthetically pure red oil. ν_{max}/cm^{-1} (KBr) 3057 (w, Ar–H), 2924 (m, C–H), 1702 (w, C=O), 1639 (m, alkene C=C), 1595 (m, Ar C=C), 1577 (s, Ar C=C), 1558 (s, Ar C=C), 1452 (s, O–H), 1427 (m, O–H); δ_H($CDCl_3$, 270 MHz, enol form) 8.70 (br d, *J* 3.8, 1H, H-6″), 8.59 (br d, *J* 7.9, 1H, H-3″), 8.40 (dd, *J* 1.2, 7.8, 1H, H-3/5), 8.01 (dd, *J* 1.2, 7.8, 1H, H-5,3), 7.92 (t, *J* 7.8, 1H, H-4), 7.87 (dt, *J* 1.6, 7.7, 1H, H-4″), 7.57 (t, *J* 7.8, 1H, H-4′), 7.33 (ddd, *J* 1.2, 4.8, 7.4, 1H, H-5″), 7.06 (*J* 7.9, 1H, H-5′), 6.98 (s, 1H, H-8), 2.05 (s, 3H, H-7′), from the integrals of H-8^E and H-8^K (3.40 and 1.54, respectively) 18% : 82% keto–enol content was calculated; δ_C($CDCl_3$, 75 MHz) 198.45 (C, 1C, 7-C^K), 94.81 (CH, 1C, 8-C^E), 47.23 (CH_2, 1C, 8-C^K), 24.39 (CH_3, 1C, 7′-C^K), 23.11 (CH_3, 1C, 7′-C^E); *m*/*z* 289 ([M]$^+$, 83%), 261 ([M − CO]$^+$, 100), 260 ([M − CHO]$^+$, 89), 155 ([$C_{10}H_7N_2$]$^+$, 98), 134 ([M − $C_{10}H_7N_2$], 62).

7g

Analogous to the preparation of **7b** from **5d** and **6d** in 46% yield as an orange solid; recrystallisation (hexanes) afforded yellow blocks for analytical purposes. Mp 68–68.5 °C; ν_{max}/cm^{-1} (KBr) 3055 (w, alkene C–H), 1595 (m, C=C), 1583 (m, C=C), 1556 (s, C=C), 1452 (s, O–H bend), 1261 (m, enol C–O), 795 (s, Ar–H), 742 (m, Ar–H); δ_H($CDCl_3$, 300 MHz) 8.63 (br d, *J* = 4.8, 1H, H-6′^{E}), 7.98 (br d, *J* 7.9, 1H, H-3′^{E}), 7.78 (dt, *J* 1.8, 7.7, 1H, H-4′^{E}), 7.54 (t, *J* 7.8, 1H, H-4^E), 7.24–7.29 (m, 1H, H-5′^{E}), 6.99 (d, *J* 8.0, 1H, H-3^E), 6.84 (d, *J* 7.4, 1H, H-5^E), 6.78 (s, 1H, H-8′^{E}), 2.56 (s, 3H, H-7^E), shifts of ketone tautomer visible at δ_H 4.74 (s, 2H, H-8^K), 2.53 (s, 3H, H-7′^{K}), from integrals of H-8′^{E} and H-8^K (42 and 12, respectively) 90% : 10% enol–keto content was calculated; δ_C($CDCl_3$, 75 MHz) 202.57 (C, 1C, 7-C^K), 94.83 (CH, 1C, 8-C^E), 47.02 (CH_2, 1C, 8-C^K); λ_{max}-(hexane)/nm 229 (log ε/dm^3 mol^{-1} cm^{-1} 3.78 sh), 234 (3.78), 241 (3.75 sh), 285 (3.96), 344 (4.37); *m*/*z* 212 ([M]$^+$, 84%), 184 ([M − CO]$^+$, 29), 183 ([M − CHO]$^+$, 51), 134 ([M − C_5H_4N]$^+$, 100), 106 ([$C_5H_4NCH_2$]$^+$, 63). Found: C, 73.27; H, 5.78; N, 13.28. Calc. for $C_{13}H_{12}N_2O$: C, 73.56; H, 5.70; N, 13.20%.

7h

Analogous to the preparation of **7a**, **5e** and **6d** gave **7h** in 40% yield as a yellow microcrystalline solid after column chromatography (2 × SiO_2, 10 : 90, EtOAc–PhMe); recrystallisation (CH_2Cl_2–EtOH, then CH_2Cl_2–heptanes) for analysis. Mp 95–96 °C; ν_{max}/cm^{-1} (KBr) 3101 (w, alkene C–H), 1639 (s, C=O), 1589 (vs, C=C), 1567 (m, C=C), 1531 (s, C=C), 1444 (s, O–H bend), 1280 (s, enol C–O), 789 (s, Ar–H), 718 (m, Ar–H), 675 (m, C–Br); δ_H($CDCl_3$, 300 MHz) 8.63 (br d, *J* 4.8, 1H, H-6′^{E}), 7.96 (br d, *J* 7.9, 1H, H-3′^{E}), 7.80 (dt, *J* 1.8, 7.8, 1H, H-4′^{E}), 7.52 (t, *J* 7.8, 1H, H-4^E), 7.29 (ddd, *J* 1.2, 4.8, 7.6, 1H, H-5′^{E}), 7.24 (d, *J* 7.8, 1H, H-3,5^E), 7.16 (d, *J* 7.9, 1H, H-5,3^E), 6.82 (s, 1H, H-7^E), 5.76 (s, 2H, H-7^K), other shifts from ketone tautomer obscured; from the integrals of H-7^E and H-7^K (1.02 and 1.81, respectively) a ratio of 53% : 47% was determined; δ_C($CDCl_3$, 67.5 MHz) 198.12 (C, 8-C^K), 96.91 (CH, 7-C^E), 46.61 (CH_2, 7-C^K); *m*/*z* 278, 276 ([M]$^+$, 54%), 248, 250 ([M − CO]$^+$, 14), 247, 249 ([M − CHO]$^+$, 17), 198, 200 ([M − C_5H_4N]$^+$, 32), 170, 172 ([M − CHO − C_5H_4N]$^+$, 14). Found: C, 52.06; H, 3.32; N, 10.11. Calc. for $C_{12}H_9BrN_2O$: C, 52.01; H, 3.27; N, 10.11%.

7i

Analogous to the preparation of **7b** using **5c**, **6d** and 2 equiv. LDA gave 70% yield of **7i**; recrystallisation (MeOH). Mp 92–93 °C; δ_H($CDCl_3$, 270 MHz) 8.71 (br d, *J* 4.9, 1H, H-6^K), 8.63 (br d, *J* 4.0, 1H, H-6^E), from the integrals of H-6^K and H-6^E (1.89 and 4.73, respectively) a ratio of 71% : 29% enol–ketone was calculated; δ_C($CDCl_3$, 67.5 MHz) 198.44 (C, 7-C^K), 96.17 (CH, 8-C^E), 40.06 (CH_2, 8-C^K), 18.35 (CH_3, 7′-C^K), 18.17 (CH_3, 7′-C^E); *m*/*z* 212 ([M]$^+$, 48%), 184 ([M − CO]$^+$, 8), 183 ([M − COH]$^+$, 33), 134 ([M − C_5H_4N]$^+$, 63), 106 ([C_5H_4NCO], 100).

6a

Compound **6a** has been previously reported.[8b] Mp 82–83 °C; ν_{max}/cm^{-1} (KBr) 2995 (w), 2951 (m), 1719 (s), 1593 (s), 1459 (m), 1432 (s), 1326 (s), 1136 (s), 1076 (m), 994 (m), 760 (s); δ_H($CDCl_3$, 300 MHz) 8.69 (br d, *J* ~ 4.4, 1H, H-6′), 8.61 (dd, *J* 1.1, 7.9, 1H, H-3), 8.54 (dd, *J* 1.0, 8.0, 1H, H-3′), 8.14 (dd, *J* 1.1, 7.7, 1H, H-5), 7.96 (t, *J* 7.8, 1H, H-4), 7.85 (dt, *J* 1.8, 7.8, 1H, H-4′), 7.34 (ddd, *J* 1.2, 4.6, 7.8, 1H, H-5′), 4.04 (s, 3H, H-8); δ_C($CDCl_3$, 75 MHz) 165.85 (C, 7-C), 156.47 (C), 155.24 (C), 149.19 (CH), 147.55 (C), 137.88 (CH), 137.06 (CH), 124.98

Table 2 Crystal data and parameters of data collection for **3a**, **c** and **d**

	3a	**3c**	**3d**
Formula	$C_{19}H_{13}N_5$	$C_{28}H_{18}N_8$	$C_{29}H_{19}N_7$
Mol. weight	311.35	466.508	465.52
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	C 2/c	P 21/c	P 21/a
a/Å	33.8039(31)	7.6365(5)	9.4955(1)
b/Å	7.8999(9)	15.3853(12)	27.5691(3)
c/Å	11.7328(9)	9.7993(6)	17.9795(2)
α/°	90	90	90
β/°	97.615	94.771(5)	92.8582(8)
λ/°	90	90	90
Volume/Å^3	3105.6(5)	1147.3(1)	4700.86
Z	8	2	8
F(000)	1296	484	1936
Calcd. density /g * cm^{-3}	1.33	1.35	1.32
μ /cm^{-1}	0.63	0.08	0.08
Crystal size /mm	0.20 * 0.50 * 0.55	0.20 * 0.25 * 0.40	0.05 * 0.10 * 0.22
Absorption correction	*φ-scans*	*φ-scans*	none
Radiation	Cu*K*α (λ = 1.54180)	Mo*K*α (λ = 0.71069)	Mo*K*α (λ = 0.71069)
Scan type	$\omega/2\theta$	$\omega/2\theta$	
θ_{max}[°]	74.33	26.32	25.03
# Measured reflections	3121	1866	51112
# Independent reflections	2866	1750	16190
# Reflns in refinement	2469	1077	10909
# Variables	218	164	991
Final *R*	0.0382	0.0386	0.0522
Final *R*w	0.0419	0.0401	0.0805
Last max/min in difference map (e × Å^{-3})	0.20/−0.12	0.14/−0.13	0.53/−0.58

(CH), 124.28 (CH), 124.20 (CH), 121.67 (CH), 52.82 (CH_3, 8-C); *m*/*z* 214 ([M]$^+$, 14%), 156 (100), 130 (9). Found: C, 67.23; H, 4.88; N, 12.88. Calc. for $C_{12}H_{10}N_2O_2$: C, 67.28; H, 4.71; N, 13.08.

6b

Analogous to **6a** using 6-cyano-2,2′:6′,2″-terpyridine,[8b] however under reflux conditions and nitrogen gas (10 h), column chromatography (Al_2O_3, activity grade III, CH_2Cl_2) gave 91% yield of a colourless solid, mp 192–193 °C; recrystallized (2 × CH_2Cl_2–heptane), for combustion analysis. Mp 193–194 °C; ν_{max}/cm^{-1} (KBr) 1722 (C=O, s), 1581 (Ar C=C, m), 1562 (C=C–N, m), 1427 (Ar C=C, s), 1136 (m), 1080 (ester C–O, w), 766 (Ar–H, s); δ_H($CDCl_3$, 300 MHz) 8.82 (dd, *J* 1.2, 8.0, 1H, H-3), 8.71 (br d, *J* ~ 4.8, 1H, H-6″), 8.61 (dd, *J* 1.0, 8.0, 1H, H-3″), 8.60 (dd, *J* 1.0, 7.8, 1H, H-3′/5′), 8.49 (dd, *J* 1.0, 7.9, 1H, H-5′/3′), 8.17 (dd, *J* 1.1, 7.7, 1H, H-5), 8.01 (t, *J* 7.8, 1H, H-4), 7.99 (t, *J* 7.8, 1H, H-4′), 7.87 (dt, *J* 1.8, 7.7, 1H, H-4″), 7.34 (ddd, *J* 1.2, 4.8, 7.5, 1H, H-5″), 4.07 (s, 3H, H-8); δ_C($CDCl_3$, 75 MHz) 165.86 (C), 156.48 (C), 156.06 (C), 155.42 (C), 154.39 (C), 149.17 (CH), 147.52 (C), 138.03 (CH), 137.77 (CH), 136.82 (CH), 125.01 (CH), 124.31 (CH), 123.80 (CH), 121.56 (CH), 121.49 (CH), 121.10 (CH), 52.83 (CH_3); *m*/*z* 291 ([M]$^+$, 44%), 233 (100), 232 (51), 193 (5), 155 (12). Found: C, 69.93; H, 4.58; N, 14.28. Calc. for $C_{17}H_{13}N_3O_2$: C, 70.09; H, 4.50; N, 14.42%.

6c

Analogous to **6a** using 2,2′-dicyano-6,6′-bipyridine[39] however in PhMe–MeOH under reflux conditions and nitrogen gas (10 h), hydrolysis by stirring overnight with a 1 : 2 : 1 CH_2Cl_2–MeOH–2 M. aq. HCl mixture, 87% yield; recrystallisation (CH_2Cl_2–EtOH) for combustion analysis. Mp 188–191 °C; ν_{max}/cm^{-1} (KBr) 2924 (w), 1739 (m, C=O), 1252 (s, C–O), 766 (Ar–H); δ_H($CDCl_3$, 300 MHz) 8.75 (dd, *J* 1.1, 7.8, 2H, H-5), 8.17 (dd, *J* 1.1, 7.8, 2H, H-5), 8.00 (t, *J* 7.9, 2H, H-3), 4.04 (s, 6H, H-8); δ_C($CDCl_3$, 75 MHz) 165.65 (C, 7-C), 155.44 (C), 147.50 (C), 138.06 (CH), 125.46 (CH), 124.82 (CH), 52.86 (CH_3); *m*/*z* 272 ([M]$^+$, 11%), 241 ([M − OCH_3]$^+$, 11), 240 ([M − MeOH]$^+$, 14), 214 ([M − CO_2CH_3]$^+$, 100). Found: C, 62.14; H, 4.65; N, 10.50. Calc. for $C_{14}H_{12}N_2O_4$: C, 61.76; H, 4.44; N, 10.29%.

X-Ray structural analyses ‡

A sample was stuck with glue on a glass fibre and mounted on the diffractometer. For **3a** and **c**, unit cell parameters were determined by careful centering of 25 independent, strong reflections. Data collection was carried out at 293 K on an Enraf–Nonius CAD4 diffractometer (**3a** and **3c**) or Kappa CCD area detector (**3d**), both with a graphite monochromator. The usual corrections were applied. For **3d**, unit cell determination and integration were carried out using the programs Denzo and Scalepack.[40] All structures were solved by direct methods using the program SIR92,[41] anisotropic least squares full matrix refinement was carried out on all non-hydrogen atoms using the program CRYSTALS[42] and positions of the hydrogen atoms determined geometrically. Parameter refinement included reflections with $I > 3\sigma(I)$ (**3a** and **c**) or $I > 2\sigma(I)$ (**3d**); Chebychev polynomial weights[43] were used to complete the refinements. Scattering factors have been taken from the International Tables.[44] Further techniques and measurement parameters that are particular to the individual compounds are presented in Table 2. Fractional co-ordinates have been deposited at the Cambridge Crystallographic Data Center.

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‡ CCDC reference number(s) 170985–170987. See http://www.rsc.org/suppdata/p1/b1/b107751a/ for crystallographic files in .cif or other electronic format.

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