Organic & Biomolecular Chemistry

Cite this: *Org. Biomol. Chem.*, 2012, **10**, 7763

www.rsc.org/obc

PAPER

Models for incomplete nucleophilic attack on a protonated carbonyl group and electron-deficient alkenes: salts and zwitterions from 1-dimethylamino-naphthalene-8-carbaldehyde†

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Received 14th May 2012, Accepted 11th July 2012
DOI: 10.1039/c2ob25929j

The X-ray crystal structures of salts and zwitterionic Knoevenagel products from 1-dimethylamino-naphthalene-8-carbaldehyde show long N–C bonds between *peri*-groups which provide models for incomplete nucleophilic attack on a protonated carbonyl group and electron-deficient alkenes respectively. For the salts the N–C bonds lie in the range 1.625–1.638 Å with C–OH bonds intermediate in length between single and double bonds, while for the zwitterions the N–C bonds lie in the range 1.612–1.660 Å. The structural assignment of the former is supported by solid state ^{13}C and ^{15}N NMR studies on doubly isotopically-labelled material. Several zwitterions were converted to naphtha[1,8-*bc*]-azepines by a mechanism involving the tertiary amino effect.

Introduction

peri-Substituted naphthalene derivatives have been used to investigate interactions between pairs of functional groups since this substitution pattern places the groups within van der Waals separation and without the possibility of conjugation with each other through the aromatic π-system. The *peri*-interactions of a dimethylamino groups with a wide variety of groups have been studied, as in proton sponges ($–Me_2N^+–H\cdots NMe_2–$)[1] but also with many electron deficient groups.[2] Of particular relevance to organic chemistry is the possibility of observing incipient bond formation in such systems, for example between a dimethylamino group and various carbonyl containing groups[3] or electron-deficient alkenes[4,5] as in **1–4**. We have reported that for two particularly electron deficient alkenes, this process goes further with a significant bonding interaction between the groups and formation of a zwitterionic structure, as in **5** and **6**. The activating groups on the alkene in these cases were a cyclic diester derived from Meldrum's acid, and a pair of nitro and benzoyl groups.[4,5] The bonds between the two functional groups are 1.651(3) and 1.6397(17) Å long in **5** and **6** and are not fully formed. We were interested in preparing further compounds which could show different degrees of bond formation between two *peri* groups for subsequent investigations, *e.g.* by experimental X-ray charge density measurements, to map how the charge density formation is related to the change in separation between the atoms involved. Here we report the structure of cation **7** which corresponds to the attack of a dimethylamino group on a protonated carbonyl group, and a family of zwitterionic structures (**8–14**) related to **5** and **6** but with different groups stabilising the negative charge or, in one case, different *N*-substituents. Finally, an alternative intramolecular reaction between these groups under microwave conditions is reported yielding fused azepine derivatives.

Discussion

Structure of cation 7

The trifluoroacetate and chloride salts of cation **7** were precipitated by treating the *peri*-aldehyde **1** with trifluoroacetic acid or HCl in ether and crystals grown from acetonitrile and methanol, respectively. The crystal structures show that protonation has taken place on oxygen with formation of a long N–C bond between the *peri* groups. For the two independent cations in the trifluoroacetate salt (Fig. 1 and 2), these bonds are 1.624(4) and 1.628(4) Å long, and the former carbonyl bonds are lengthened to 1.352(4) and 1.362(4) Å, intermediate between a carbonyl group (1.20 Å) and a single C–O bond (1.43 Å).[6] The N–C–O angles in each case are both 112.2(3)°. Thus, the structure corresponds to the partial addition of the dimethylamino group to a

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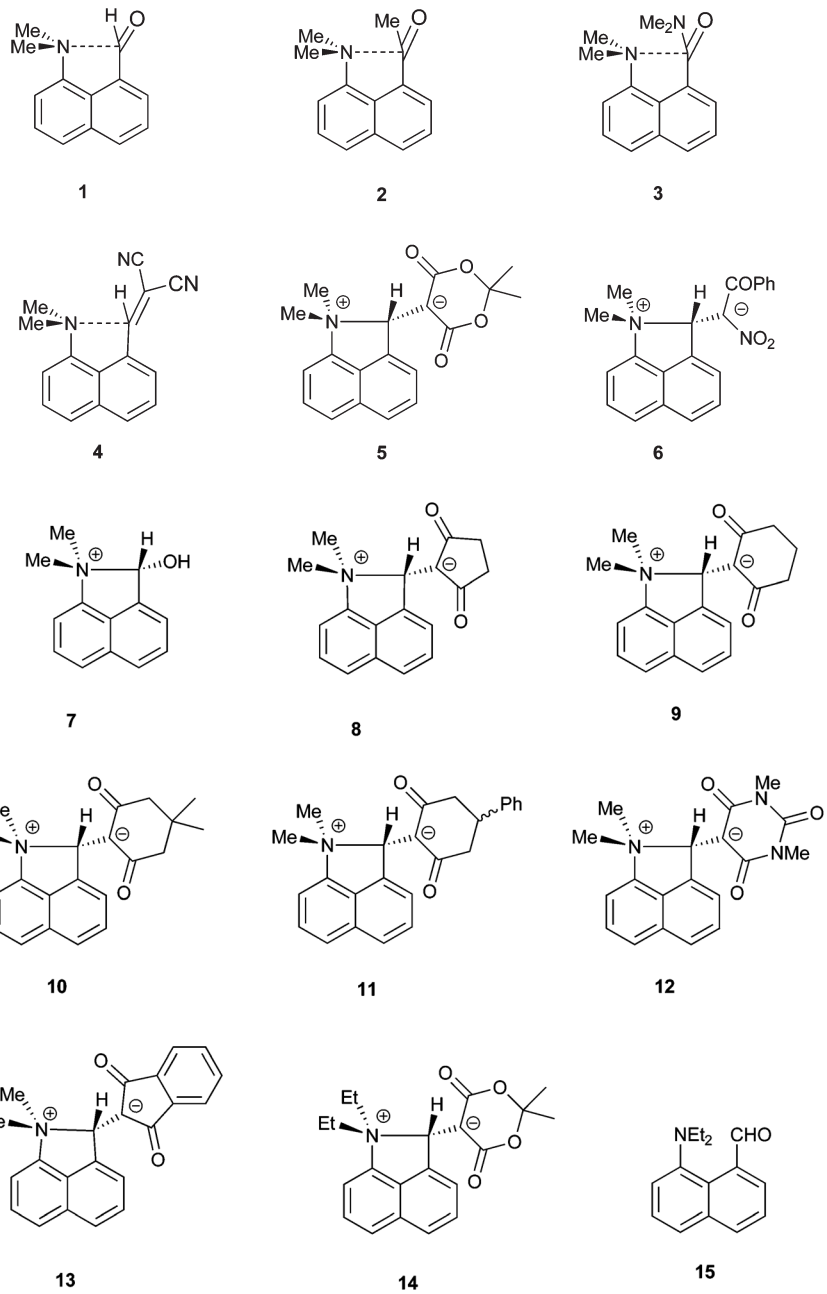


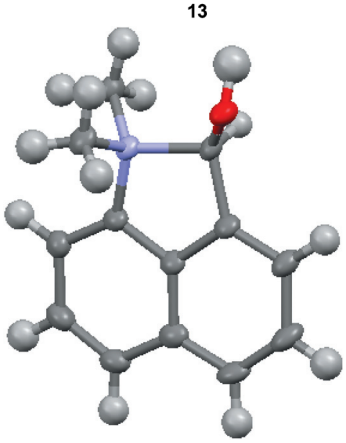


Fig. 1 Crystal structure of one of the two crystallographically unique cations in $7{\cdot}CF_3CO_2^-$, with atomic displacement parameters drawn at the 50% level.

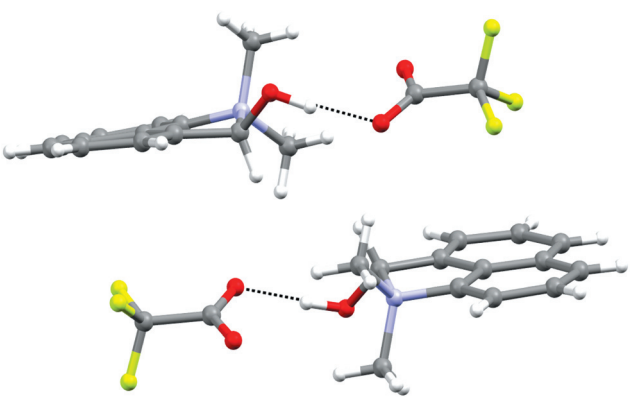


Fig. 2 Contents of the asymmetric unit of the trifluoroacetate salt of cation **7** showing hydrogen bonding within the cation/anion pairs.

protonated carbonyl bond within the restraints of the naphthalene framework. Both hydroxyl groups are hydrogen bonded to a trifluoroacetate anion (O···O: 2.581 and 2.604 Å, angle at H: 169 and 175°). The H_3C–N bond lengths lie in the range 1.496(4)–1.501(4) Å, much closer to those of the $(CH_3)_3N^+$- group in cation **16**[7] (1.500 Å) than those of the dimethylamino group (1.465 Å). This suggests that a considerable part of the positive charge on cation **7** is located at the N atom.

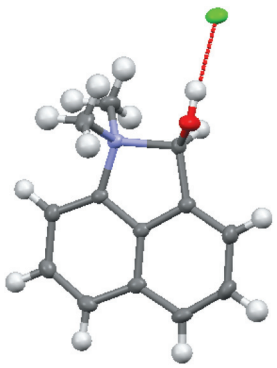


Fig. 3 Molecular structure of **7**·Cl with atomic displacement parameters drawn at the 50% level viewed down the *b* axis.

In the chloride salt of **7** the cation has a similar structure to that in the trifluoroacetate salt (Fig. 3 and 4, Table 1). The N–C bond between *peri* groups is slightly longer (1.638(2) Å) but the C–O bond length (1.353(2) Å) is similar. The hydroxyl group is hydrogen bonded to the chloride ion (O···Cl: 2.9301(13) Å, O–H···Cl angle 166°). The other three contacts of the chloride ion are with naphthalene or methyl H atoms (C–H···Cl: 2.69–2.89 Å), with the shortest distance being that to the H atom *ortho* to the positively charged N atom.

Changing the anion produced a different N–C bond length and this may be related to the different strength of O–H···anion hydrogen bonding, which may influence slightly the anomeric interaction of the oxygen lone pair with the N–C bond, or may just be down to the effects of crystal packing on the not fully formed N–C bond. Salts of this type are thus interesting targets for accurate charge density measurements to probe how bonding density changes with interatomic separation.

There are a number of structures in the Cambridge Structural Database[8] containing the fragment $(C)_3N^+$–C–OH, though most are room temperature measurements. In the five structural

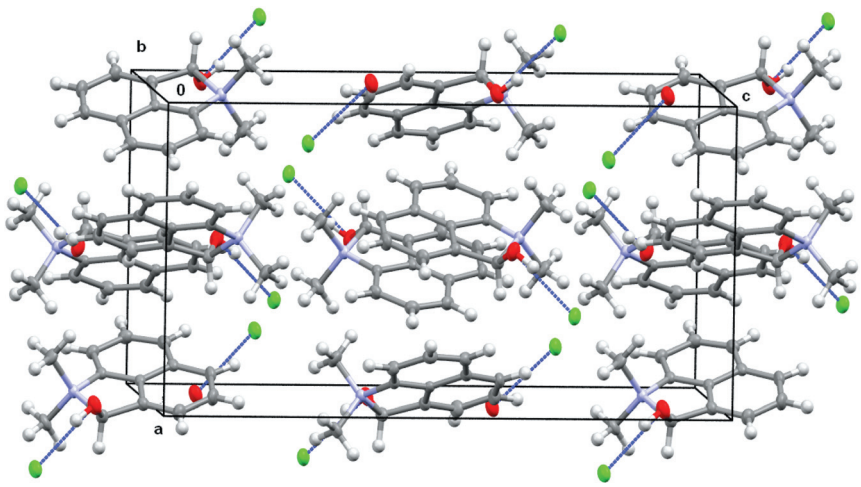
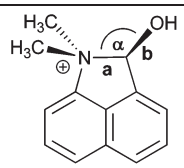


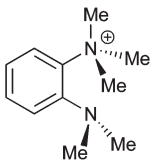
Fig. 4 Crystal packing arrangement for **7**·Cl.

Table 1 Selected molecular geometry for cation **7** in its trifluoroacetate and chloride salts



	a (Å)	*b* (Å)	*α* (°)	N–CH_3 (Å)	(C_{ar}–N–C–C_{ar}) torsion (°)	(H_3)C–N–C–O torsion (°)
$7^+ \cdot CF_3CO_2^-$	1.624(4)	1.352(4)	112.2(3)	1.500(4)	18.6(3)	24.9(4)
				1.499(4)		96.7(3)
	1.628(4)	1.362(4)	112.2(3)	1.501(4)	11.6(3)	15.9(3)
				1.496(4)		105.8(3)
$7^+ \cdot Cl^-$	1.638(2)	1.353(2)	111.64(12)	1.497(2)	7.06(15)	9.94(18)
				1.498(2)		110.37(15)

measurements of the hexamethylenetetraminium-*N*-methanol cation **17**, in which the $^{+}$N–C(H$_2$OH) bond is unconstrained, the $^{+}$N–C(OH) bond lies in the range 1.509–1.534 Å, and the C–OH bond is 1.369–1.389 Å long.[9] Thus, in cation **7**, the N–C bond is longer and the C–O bond shorter, consistent with an incomplete formation of the addition reaction. In structures **18–20**, the N–C(OH) bond is constrained in a ring, and this group shows similar bonding features to cation **7**.[10]



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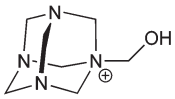

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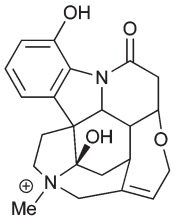

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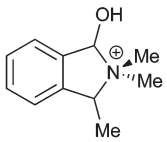

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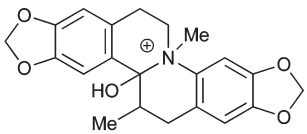

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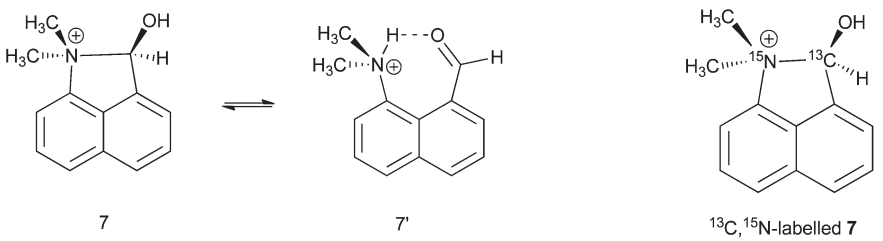
The ^{1}H and ^{13}C NMR of **7**·Cl are consistent with a ring closed structure in solution with the (N)–CH–(O) group giving signals at δ_H: 7.11 and δ_C: 112.2 in CD$_3$OD solution with a slightly broadened *N*-methyl carbon resonance at δ_C: 50.7. In DMSO-d$_6$, the methine signals are in similar positions at δ_H: 7.24 and δ_C: 114.1 but the latter is very broad indeed. Furthermore, the signals from the dimethylamino group are strongly broadened at room temperature, suggestive of a rapid opening and closing of the bond between *peri* substituents (Scheme 1). The *N*-methyl signals sharpen substantially on heating to 60 °C in DMSO-d$_6$. In the NMR spectra of the **7**·CF$_3$CO$_2$ salt in CD$_2$Cl$_2$, the methine group shows broadened signals at δ_H: 8.39 and δ_C: 140.2. The latter is very broad (over 3 ppm), and intermediate in chemical shift between what might be expected for the ring closed structure and the open structure **7′**, suggesting that the equilibrium between closed and open structures is shifted towards the open structure in this case. The structure of the open chain form may be protonated on the nitrogen and stabilised by an internal hydrogen bond to the carbonyl as in 1-hydroxynaphthalene-8-carbaldehyde.[11] Earlier NMR studies on aldehyde **1** in CF$_3$CO$_2$D have been interpreted in terms of two species.[12]

The solid state NMR of the chloride salt of cation **7** with isotopic enrichment of the *peri* nitrogen (^{15}N, 60%) and carbon (^{13}C, 99%) atoms (Scheme 1) was also studied to determine whether the powder isolated from the reaction had the same composition as the crystal prepared from it. The ^{13}C CPMAS NMR data (Fig. 5(a)–(c)) shows a single resonance at δ_{iso} = 111 ppm dominating these data, consistent with a carbon attached to nitrogen and oxygen atoms. A carbonyl group would be expected to appear at δ_{iso} > 180 ppm, therefore this result eliminates the possibility of the **7′** structure being formed. The chemical shift (CS) interaction parameters determined from the variable MAS frequency data reported in Table 2 are given in the IUPAC, Haeberlen and Herzfeld–Berger conventions. The magnitude of the measured ^{13}C chemical shift anisotropy (CSA) $\Delta\delta$ or chemical shift span (CSS) Ω of −77 ppm or 89 ppm, respectively, is also indicative of a species attached to two electronegative atoms and is much smaller than typically expected for a carbonyl species, thus providing additional evidence for the presence of compound **7** in preference to **7′**. Furthermore, from Table 2, the reported CS tensor values (δ_{11} = 149, δ_{22} = 124 and δ_{33} = 60 ppm) show that a non-axially symmetric site (*i.e.* $\delta_{11} \neq \delta_{22} \neq \delta_{33}$ or $\eta \neq 0$) is described, where the bridging *peri*-bond is lowering any point symmetry that may exist at the ^{13}C–OH position. From Table 2 it can be observed that excellent agreement



7 **7′** ^{13}C,^{15}N-labelled **7**

Scheme 1 left: Equilibrium between ring closed and open ring forms of cation **7**; right: location of isotopic labels in **7** used in the SS-NMR study of **7**·Cl.

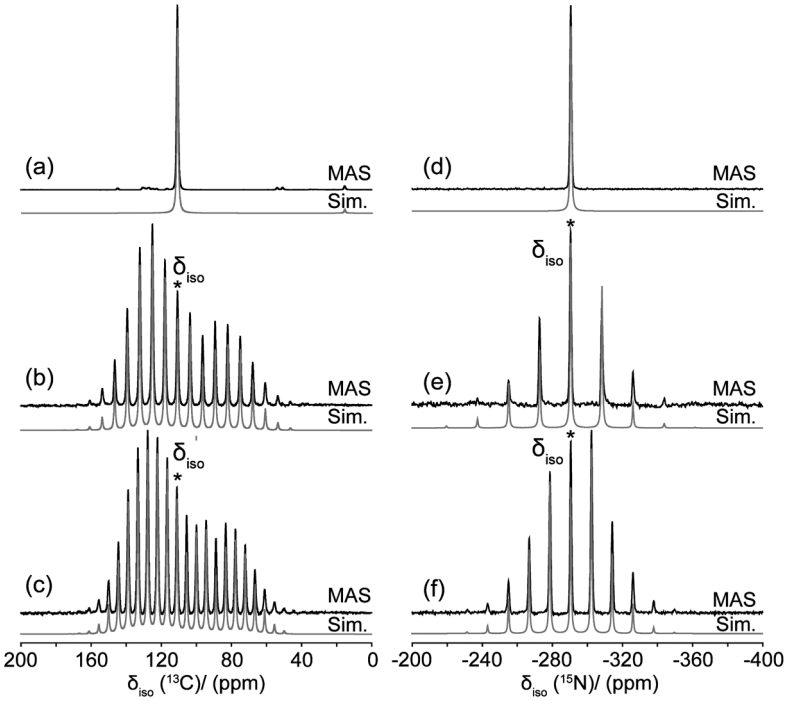


Fig. 5 A cross polarisation (^{1}H–$^{13}C/^{15}N$) experiment of $^{15}N(60\%)^{13}C(99\%)$ labelled **7** with varying magic angle spinning (MAS) frequencies (a)(d) 12 kHz, (b)(e) 900 Hz and (c)(f) 700 Hz. The isotropic shifts are labelled by $*\delta_{iso}$. The simulations (sim.) are shown below each spectrum in grey.

exists between the experimentally measured NMR parameters and the DFT calculated NMR parameters using the NMR-CASTEP code and the GIPAW approach.[13] This level of agreement for the basic chemical shift tensor values δ_{11}, δ_{22} and δ_{33}, and the more arithmetically convoluted parameters such as δ_{iso}, $\Delta\delta/\eta$, Ω/κ, demonstrates that a high degree of precision is associated with the single crystal X-ray structural solution of compound **7**. For these calculations, the generated unit cell H positions are geometry optimised using the energy minimization algorithms within the CASTEP program prior to NMR parameter computation.

The corresponding ^{15}N CPMAS NMR data from the $^{13}C/^{15}N$ labelled compound **7** are also shown in Fig. 5(d)–(f). The isotropic shift δ_{iso} −290.6 ppm emphasized in the data acquired with ν_r = 12.0 kHz is referenced against $MeNO_2$, however, upon conversion to the protein chemical shift range (by adding 379.5 ppm to this value), an isotropic shift of δ_{iso} 88.9 ppm is obtained. Reported ^{15}N chemical shift values for tetramethylammonium (solution) and trimethylammonium (solid state) cations are in the region 43–45 ppm[14] so it is not possible to unambiguously discriminate between the formation of compound **7** or **7′**. However, strongly supportive of structure **7** is the excellent agreement between measured ^{15}N NMR parameters and those calculated using the GIPAW approach and based on the crystal structure data for **7** (Table 2).

Preparation and structures of zwitterions 8–14

A range of zwitterions related to examples **5** and **6** was prepared by Knoevenagel reactions of aldehyde **1** with cyclic methylene derivatives activated by two carbonyl groups which could both conjugate with the carbanionic centre in the final product. The aim was to produce materials with different bond distances between the *peri* groups by changing the cyclic diester to a cyclic diketone or a cyclic amide, where the stabilisation of the carbanionic centre would be expected to be greater or less than in the Meldrum's acid derivative respectively. Thus, aldehyde **1** was reacted with a variety of cyclic 1,3-diketones and with *N*,*N*-dimethylbarbituric acid under Knoevenagel conditions and the products **8–13** were obtained in 38–81% yield. Meldrum's acid was also reacted with 1-diethylamino-8-naphthaldehyde to give zwitterion **14**, the *N*,*N*-diethyl analogue of **5**, in 35% yield. Solution NMR studies support the assignment of zwitterionic structures to **8–14**. Crystals were grown of six of these zwitterionic structures, **8–10** and **12–14**, and their structures determined by X-ray crystallography at 120 K. The structures are shown in Fig. 6–8, and selected molecular geometry is given in Table 3. All six structures show a significant degree of bond formation between the functional groups, with N–C bond lengths in the range 1.612–1.661 Å. These can be viewed as corresponding to somewhat different late stages of the partial addition of the dimethylamino group to an activated alkene. Compounds **12** and **13** have been recently reported by Mátyus *et al.*[15]

Reaction of **1** with cyclopentane-1,3-dione or cyclohexane-1,3-dione in methanol yielded zwitterions **8** and **9** whose crystals are monohydrates, with **8** crystallising in space group $P2_1/c$ with two molecules of **8** and two water molecules in the asymmetric unit, and **9** crystallising in space group $P\bar{1}$ with one molecule of **9** and one water molecule crystallographically unique. None of the other zwitterions studied is solvated in the solid state. For zwitterion **8** (Fig. 6), there is a hydrogen bond between the two independent water molecules and their remaining three hydrogen

Table 2 Experimentally measured and NMR-CASTEP DFT calculated ^{13}C and ^{15}N NMR interaction parameters for compound **7**

Compound **7** Nucleus Observed	$\delta_{iso,mas}$ (ppm) (±0.5)	$\Delta\delta_{iso}$ [a] (ppm) (±0.5)	δ_{11} [a] (ppm) (±0.5)	δ_{22} [a] (ppm) (±0.5)	δ_{33} [a] (ppm) (±0.5)	$\Delta\delta^b$(ppm)	η^b	Ω^c (ppm)	κ^c	$\Delta\delta_{iso}$ [a] (ppm) CASTEP	δ_{11} [a] (ppm) CASTEP	δ_{22} [a] (ppm) CASTEP	δ_{33} [a] (ppm) CASTEP	$\Delta\delta^b$ (ppm) CASTEP	η^b CASTEP	Ω^c (ppm) CASTEP	κ^c CASTEP
^{13}C	111	111	149	124	60	−77	0.49	89	0.44	112	153	122	60	−78	0.60	93	0.33
^{15}N	−291	−290	−250	−293	−328	60.5	0.87	78	0.10	−285	−246	−282	−327	63	0.86	81	0.11

[a] IUPAC isotropic shift convention: $\delta_{11} \geq \delta_{22} \geq \delta_{33}$ where $\delta_{iso} = (\delta_{11} + \delta_{22} + \delta_{33})/3$. [b] Haeberlen shift convention: $|\delta_{33} - \delta_{iso}| \geq |\delta_{11} - \delta_{iso}| \geq |\delta_{22} - \delta_{iso}|$ (tensorial representation not shown above), $\delta_{iso} = (\delta_{11} + \delta_{22} + \delta_{33})/3$, $\Delta\delta = \delta_{33} - 1/2(\delta_{11} + \delta_{22}) = 3/2(\delta_{33} - \delta_{iso})$, $\eta_\delta = (\delta_{22} - \delta_{11})/(\delta_{33} - \delta_{iso})$ $(1 \geq \eta_\delta \geq 0)$. [c] Herzfeld–Berger shift convention: $\delta_{11} \geq \delta_{22} \geq \delta_{33}$ (tensorial representation shown above), $\delta_{iso} = (\delta_{11} + \delta_{22} + \delta_{33})/3$, $\Omega = (\delta_{11} - \delta_{33})$, $\kappa = 3(\delta_{22} - \delta_{iso})/(\delta_{11} - \delta_{33})$ $(1 \geq \kappa \geq -1)$.

atoms form hydrogen bonds to three of the four carbonyl groups of the two molecules of **8**. The carbonyl group which is not hydrogen bonded is the shortest of the four: 1.249(2), *cf.* 1.253(2)–1.256(2) Å. Thus, one of the two unique zwitterion molecules **A** has both carbonyl groups hydrogen bonded to water molecules and the N–C bond between the *peri* groups is 1.612(2) Å, while the second molecule **B** is only hydrogen bonded at one carbonyl group and the N–C bond is longer, 1.626(2) Å. This is consistent with the hydrogen bonding promoting the delocalisation of the zwitterion's anionic charge and thus promoting the formation of the N–C bond. Increased formation of this bond would be expected to be correlated with lengthening of the exocyclic C–C bond to the carbanionic centre which is indeed observed: 1.478(2) Å for **A** and 1.471(2) Å for **B**. In molecule **B**, the carbonyl group which is not hydrogen bonded to water lies adjacent to three electron deficient *N*-methyl groups: rotation of the five-membered ring leads to approach to an *N*-methyl group from the same molecule ($H_3C\cdots C(=O)$: 3.211 and $H_3C\cdots O(=C)$: 3.322 Å, H···O 2.58 Å), and the carbonyl group lies near to the $^{+}NMe_2$ group of another molecule ($H_3C\cdots O(=C)$: 3.318 and 3.329 Å).

In the crystal structure of **9** (Fig. 7), bridging water molecules between carbonyl groups link the molecules into rows. The N–C bond length is 1.6310(19) Å. Compared to the bis-hydrated molecule **8A** the three bonds along the N–CH–C^-–C(=O) pathway are all longer (Table 3). However, it is important to note that the six-membered ring projects the carbonyl groups closer to the *N*-methyl groups than does the five-membered ring, so that optimisation of the $O\cdots CH_3$ interactions may play a larger role in determining the structure of **9** than for **8**. Thus, in **9** each *N*-methyl group lies closer to a carbonyl oxygen atom (O···C: 3.187 and 3.295 Å) than in the corresponding bis-hydrated molecule **8A** (3.385 and 3.488 Å). The structure of molecule **10** (Fig. 8) differs from **9** only by the presence of two methyl groups on the extremity of the dione ring, and is not hydrated in the crystalline state. The molecular geometry is, however, very similar to that of **9** with a bond of 1.636 Å between the *peri* groups.

Reactions of **1** with *N*,*N*′-dimethylbarbituric acid or indanone, in which the carbonyl groups are conjugated to nitrogen or a benzene ring respectively, led to the production of crystalline zwitterions **12** and **13** (Fig. 8). In zwitterion **12**, where the carbanionic centre is part of a barbiturate group, the N–C bond between *peri*-groups is 1.6266(19) Å long and the bond to the carbanionic centre is 1.477(2) Å. The two pyrimidine N atoms are both flanked by two carbonyl groups. The central urea-like carbonyl group is the shortest of the three (1.2324(17) Å, *cf.* 1.2395(17) and 1.2451(17) Å). It might have been expected that the other two carbonyl groups would have a reactivity akin to esters, since the attached N atoms must share their lone pair with two carbonyl groups, yet the pyridinetrione group seems to be as effective as the cyclic diketones **9** and **10** in promoting the reaction between the two *peri* groups. Indeed it is of note that these two N atoms make significantly shorter bonds to the urea-like carbonyl group (1.3762(18) and 1.3771(18) Å) than to the other two carbonyl groups (1.4167(18) and 1.4208(18) Å), emphasizing their preferential interaction with the central carbonyl group, leaving the other two carbonyls to stabilise the carbanion. The through-space interactions between these carbonyl

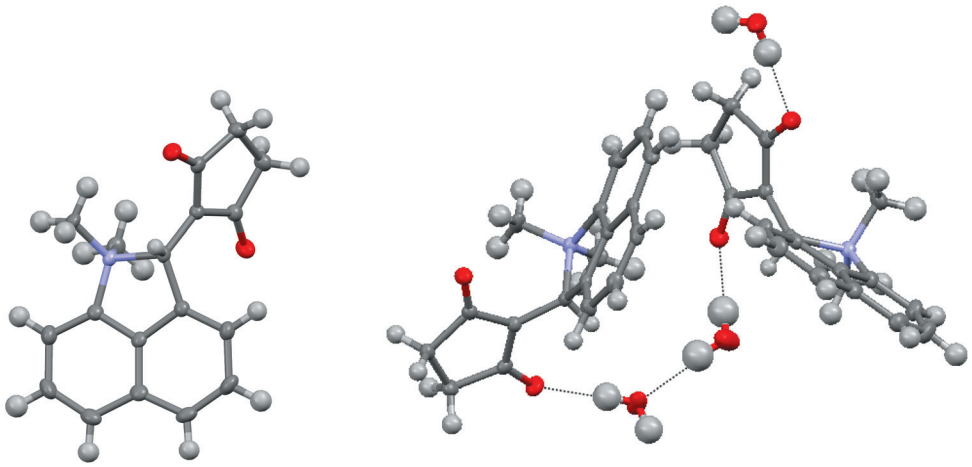


Fig. 6 One of two crystallographically independent molecules of zwitterion **8** (left); crystal structure of **8**·H_2O showing the different hydrogen bonding arrangements for the two unique molecules of **8** (right).

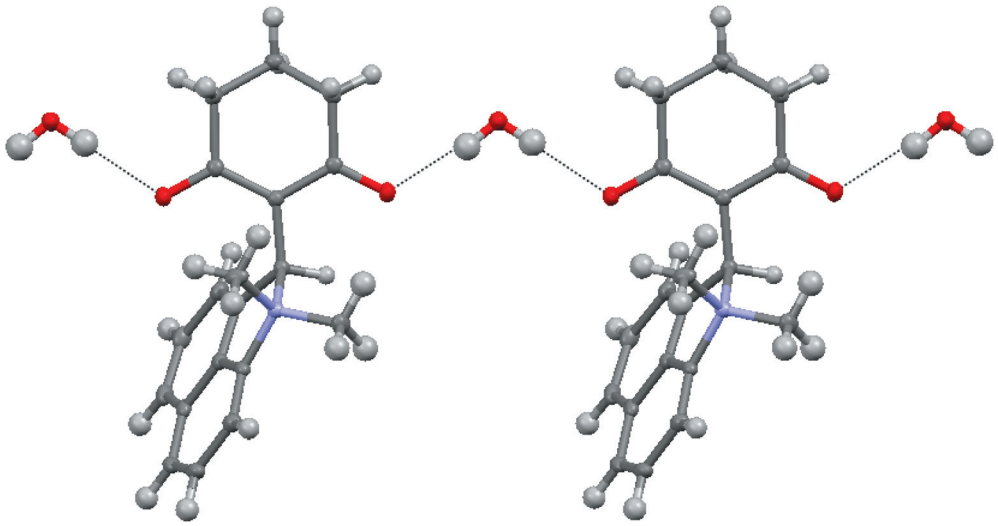


Fig. 7 Crystal structure of **9**·H_2O showing the water molecules bridging the zwitterions.

oxygens and the two N–CH_3 groups are similar to those in **9** (O···C 3.122 and 3.366 Å).

In the indanone derivative **13** (Fig. 8), the N–C bond between *peri* groups is 1.6536(14) Å – considerably longer than in diketones **8–10** (1.612–1.636 Å), and the C–C bond to the carbanionic centre is correspondingly shorter (1.4640(16) Å) than in the other two cases (1.471–1.486 Å). This relates to the lower efficacy of the indanone group in stabilising the developing carbanionic charge. Indeed, there is evidence of less delocalisation from the carbanion into the carbonyl groups, with longer bonds between them: 1.4275(16) and 1.4292(17) Å compared to 1.413–1.419 Å in **8** in which the carbanion is also in a five-membered ring. Conjugation of the carbonyls with the fused phenyl group lowers the capacity of the carbonyl groups to stabilise the carbanionic centre. Aldehyde **15**, with a *peri*-diethylamino group rather than the smaller dimethylamino group, also reacted with Meldrum's acid to give the expected zwitterion **14** whose structure was determined (Fig. 8). The structure is very similar to the *N*,*N*-dimethylamino analogue, with the ethyl groups organised so that the peripheral methyl groups are turned away from the anionic portion of the molecule, so reducing any extra steric repulsion between the groups.

Related zwitterionic structures in the biphenyl series (*e.g.* **21**) have been reported,[16,17] but in these less strained cases the N–C bonds between *ortho* substituents lie in the range 1.58–1.61 Å. The importance of having both carbonyl groups able to fully conjugate the carbanionic centre for formation of the zwitterionic structure is illustrated by the molecular structure of **22** where this is not so. The latter is shown by X-ray crystallography to exist in the ring open form (Fig. 9). The two carbonyl groups make torsion angles of 2.31(16) and 61.7(2)° with the alkene bond, so only the *trans* carbonyl group fully conjugates with it. The dimethylamino nitrogen lone pair is directed towards the other *peri* group: the N···CH═ separation is 2.632(2) Å, the N···C═C angle is 117.73(12)° and the Me_2N···H(C═C) separation is 2.42 Å. The N···C separation and the orientation of the

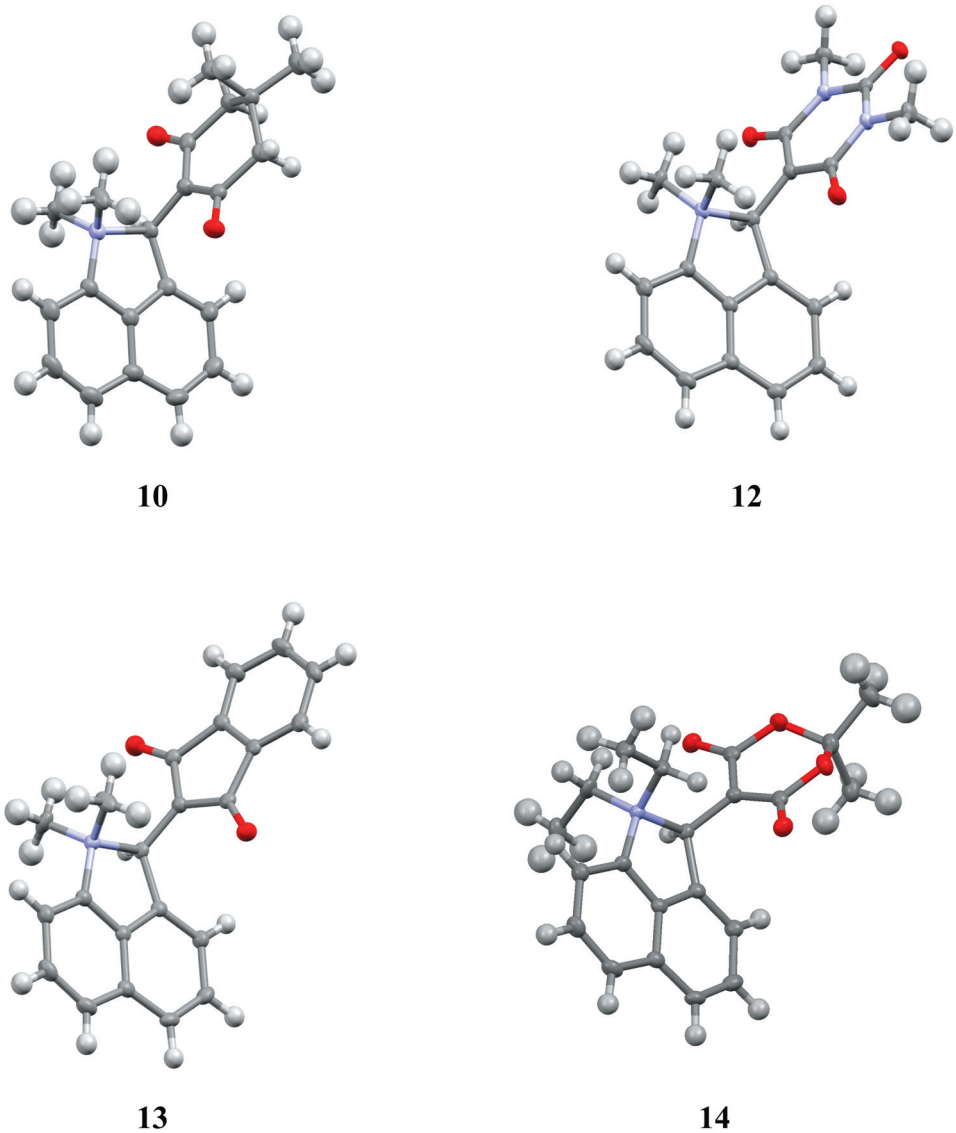
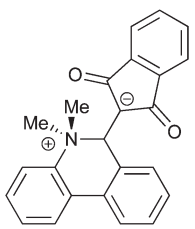


Fig. 8 Molecular structures of **10** and **12–14** with anisotropic displacement parameters drawn at the 50% level.

dimethylamino group is intermediate between those seen for the corresponding dibenzoyl (2.679(2) Å) and dinitrile analogues (2.413(2) Å),[4] suggesting that in the conformations observed in the crystal structures two acetyl groups are more effective than two benzoyl groups in activating the alkene bond to the approach of a nucleophile.



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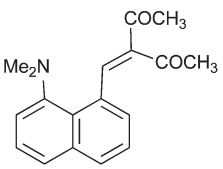


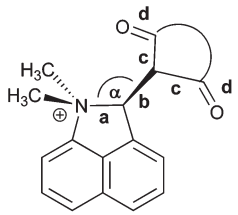
22

Solution NMR studies on 8–14

Investigations of the solution state structures of the zwitterions **8–13** were made by variable temperature NMR. The evidence supports the adoption of the zwitterionic structures, but at ambient temperatures it appears that the bond between *peri* substituents is rapidly opening and closing, with only a very low concentration of the open chain form. The discussion will be divided between those molecules with carbanionic centres in five-membered rings (**8**, **13**) and those in six-membered rings (**9–12**). Selected data for ^{13}C shifts of *peri* groups is given in Table 4.

At −48 °C, the ^{1}H and ^{13}C spectra of **8** in $CDCl_3$ both show two peaks for the dimethylamino group (δ_H: 3.13 and 3.57; δ_C: 52.6 and 51.8) and the methine signals occur at δ_H: 6.49 and δ_C: 86.9 consistent with the ring closed structure in which the two methyl groups lie either *cis* or *trans* to the cyclopentanide group. Furthermore, the two carbonyl carbons show different

Table 3 Selected molecular geometry for cations **8–10** and **12–14**. Data for **5**[4] are provided for reference



	a (Å)	*b* (Å)	*c* (Å)	*d* (Å)	*α* (°)
8·H_2O	1.612(2)	1.478(2)	1.418(2) 1.413(2)	1.256(2) 1.2539(19)	114.75(13)
	1.626(2)	1.471(2)	1.415(2) 1.419(2)	1.2527(18) 1.2489(18)	114.57(12)
9·H_2O	1.6310(19)	1.4863(19)	1.4281(17) 1.4211(18)	1.2532(16) 1.2566(16)	113.99(10)
10	1.636(3)	1.479(4)	1.422(4) 1.424(4)	1.253(3) 1.257(3)	116.4(2)
12	1.6266(19)	1.477(2)	1.4229(19) 1.4113(19)	1.2395(17) 1.2451(17)	115.54(11)
13	1.6536(14)	1.4640(16)	1.4275(16) 1.4292(17)	1.2441(14) 1.2391(14)	114.40(9)
14	1.6603(15)	1.4691(16)	1.4214(16) 1.4152(17)	1.2235(15) 1.2254(14)	116.70(9)
5[4]	1.651(3)	1.471(3)	1.409(3) 1.428(2)	1.224(2) 1.236(2)	114.9(2)

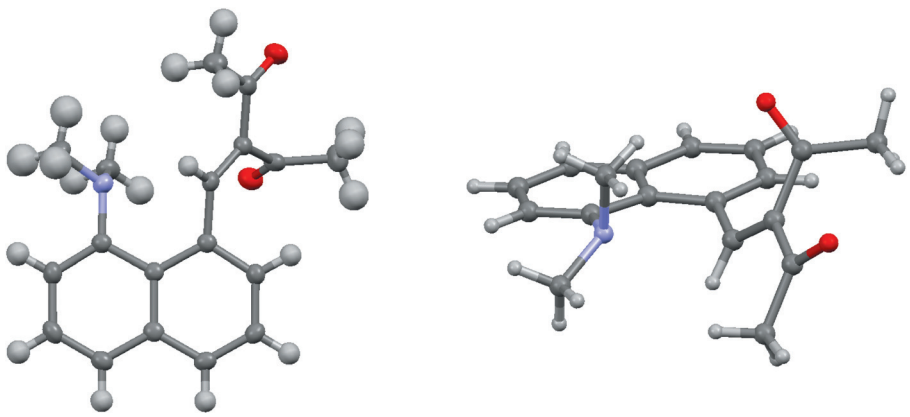


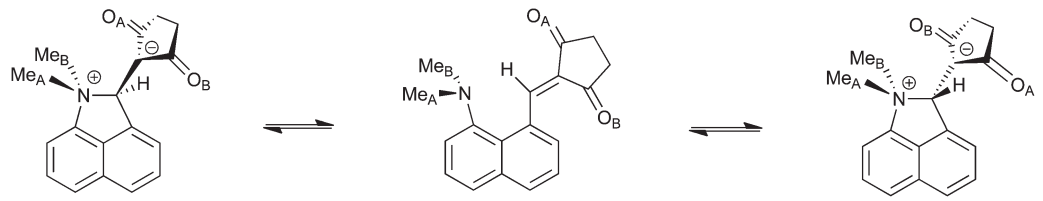
Fig. 9 Molecular structure of **22** with anisotropic displacement parameters drawn at the 50% level (left), and showing relative orientation of *peri* groups (right).

shifts (δ_C: 204.6 and 203.0), as do the two methylene groups (δ_C: 33.4 and 33.1), indicating that the cyclopentanide group is not rotating at this temperature. The carbanionic centre resonates at δ_C: 99.4. On warming to room temperature, the ring opening/ring closing process is activated, and since on ring opening there is also rotation of one *peri* group relative to the other, the *cis* and *trans* relationship of each *N*-methyl group to the cyclopentanide ring is scrambled (Scheme 2). Thus, at 24 °C the methyl signals coalesce to δ_H: 3.31 and δ_C: 52.2. Furthermore, there is evidence at 24 °C that the cyclopentanide group is starting to rotate about the C^-–CH bond, in particular the two carbonyl resonances are replaced with a single broad resonance, and the resonances of the two methylene carbons coalesce. In DMSO-d_6, the carbonyl signal in **8** sharpens on heating to 65 °C consistent with a faster rotation of this group. The NMR spectrum of the indanone derivative **13** at −60 °C in CD_2Cl_2 is consistent with the frozen zwitterionic structure, with the methine and carbanionic carbons resonating at δ_C: 92.4 and 90.4. Distinct resonances for all 16 aromatic carbons are observed. However, on warming to room temperature, the ring opening and closing process begins, along

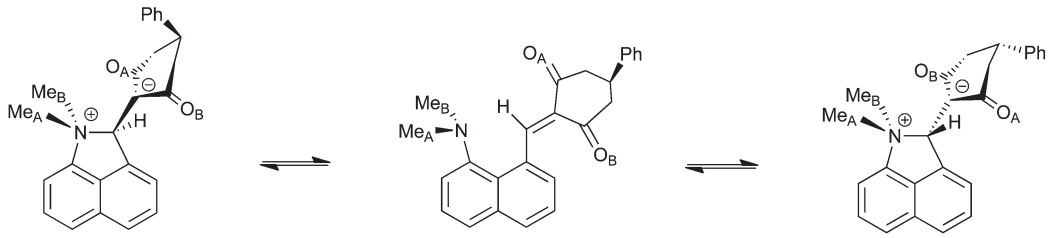
Table 4 Selected ^{13}C NMR shifts for zwitterions **8–13**

	8	**9**	**11**[a]	**12**	**13**
T (K)	225	243	233	297	213
Solvent	$CDCl_3$	$CDCl_3$	CD_2Cl_2	DMSO-d_6	CD_2Cl_2
N–CH	86.9	91.2	89.1 (88.6)	93.5	92.4
C^-	99.4	102.0	99.7 (98.5)	77.7	90.4

[a] Major and minor conformers.



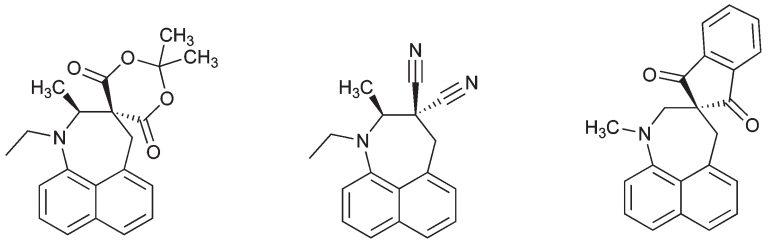
Scheme 2



Scheme 3 Equilibration of the two zwitterionic structures of **12**, showing the probable transition state for the relative rotation of the *peri* groups in the open chain form (centre).

with rotation of the indanonide group. The methine and carbanionic carbon shift downfield to δ_C: 118.6 and 105.5 and the four indanone aromatic methine carbons give just two signals.

In contrast, the NMR spectra of the six-membered ring cases are somewhat simpler, since there is no rotation of the cyclohexanide ring, due to the increased steric interaction of the carbonyl O atoms with the *N*-methyl groups as the ring attempts to rotate. Thus, at −30 °C in $CDCl_3$ compound **9** is frozen in the zwitterionic form with methine and carbanionic carbons resonating at δ_C: 91.2 and 102.0 respectively. The two *N*-methyl groups show separate resonances (δ_H: 3.57 and 3.14, δ_C: 55.2 and 49.6), as do the two carbonyl groups (δ_C: 196.2 and 194.4) and their neighbouring methylene carbons (δ_C: 37.6 and 36.6). On warming to room temperature, the rate of the ring opening/ring closing process increases and the *N*-methyl groups give just one broad resonance in both the ^1H and ^{13}C NMR spectra (δ_H: 3.31 and δ_C: 52.2). The NMR spectra of the 4-phenylcyclohexanide derivative **11** in CD_2Cl_2 are very instructive. At low temperature (−40 °C) they show two isomeric species present in ratio *ca.* 2 : 1, with very similar ^1H and ^{13}C NMR spectra. This is indeed what would be expected if the zwitterionic structure is frozen out, since the phenyl group can either be directed towards or away from the other *peri* group (Scheme 3). Thus each isomer shows a pair of distinct *N*-methyl resonances (δ_H: 3.57 and 3.13 major isomer, δ_H: 3.54 and 3.17 minor isomer). On warming to room temperature, and onset of ring opening/closing the pairs of *N*-methyl, carbonyl and methylene carbon resonances are all replaced by single signals.



23 **24** **25**

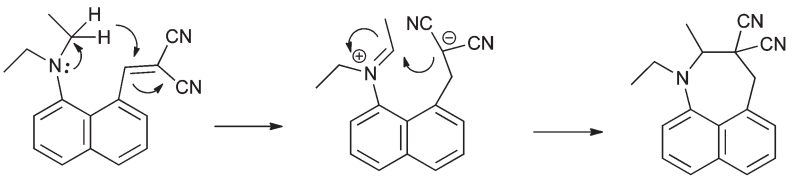
Formation of naphtho[1,8-*bc*]azepines

When some of the zwitterion-forming Knoevenagel reactions were carried out under microwave conditions, a different type of product was obtained. Reaction of the diethylamino aldehyde **15** with Meldrum's acid or malonitrile under microwave conditions (typically 200 W, 100 °C, 10 min) yielded **23** and **24** in which the functional groups had reacted together to form a seven-membered ring. Similarly, reaction of the dimethylamino aldehyde **1** with indanone under these conditions yielded azepine **25**, rather than the zwitterion **13**. Interestingly, when the diethylamino aldehyde was reacted with malonitrile in refluxing methanol, compound **24** was also obtained, in contrast to the reaction with the dimethylamino aldehyde **1** which gives the normal Knoevenagel product **4**. The structures of **23–25** were confirmed by X-ray crystallography. It is proposed that after formation of the initial Knoevenagel product, an *N*-methylene or *N*-methyl group donates a hydride to the alkene, an

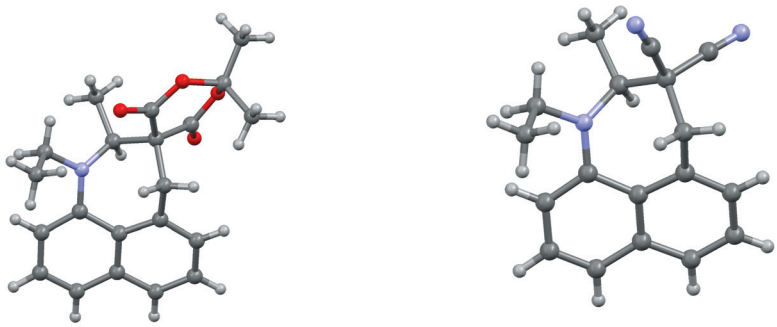
example of the tertiary amino effect,[18] forming an iminium cation and a stabilised carbanion which then react together to form the azepine ring, as outlined in Scheme 4 for **24**. We observed this reaction earlier for zwitterion **6**,[5] and Mátyus and co-workers[15,16] have reported similar reactions between *ortho* groups in the biphenyl series and between *peri* groups in the naphthalene series for which they have reported mechanistic evidence of intramolecular hydride transfer from deuterium labelling experiments. Pozharskii[19] has recently reported such reactions between *ortho* groups on naphthalene rings.

The molecular structures of the fused azepines **23–25** were determined by X-ray crystallography (Fig. 10). The structures of **23** and **24** are well resolved, but that for **25**, while confirming the molecular structure, is not so accurate.[20] Selected molecular geometry is shown in Table 5. The molecular conformations are similar and the azepine ring show some signs of strain. In the more highly substituted structures **23** and **24**, the two bonds to the quaternary centre are just over 1.57 and 1.55 Å long, respectively. The naphthalene skeleton is twisted so that there is a significant torsion between the bonds to the *peri*-substituents (23.47 and 24.83° in **23** and **24**). In the azepine ring, the sp^3 carbon atoms α and β to the nitrogen atom are displaced to the same side of the naphthalene plane with the α-carbon displaced more than the quaternary β-carbon (by 1.343 and 1.364 Å, *cf.* 1.001 and 0.933 Å for **23** and **24**), to give a roughly staggered conformation about the bond that links them. The bonding geometry of the nitrogen atoms in **23–25** is not far from planar (Table 5).

Solution ^{1}H NMR spectra indicate that there is a conformational equilibrium at 24 °C for compounds **24** and **25** due to flexing of the seven-membered ring to either side of the naphthalene plane (Scheme 5). For example, for **25** at 25 °C in CD_2Cl_2 the two ring methylene groups appear as a broad signal at δ_H: 3.44, but on cooling down to −65 °C these resolve into four doublets: δ_H: 4.17 and 2.69 from the aryl-methylene group and



Scheme 4



23 **24**

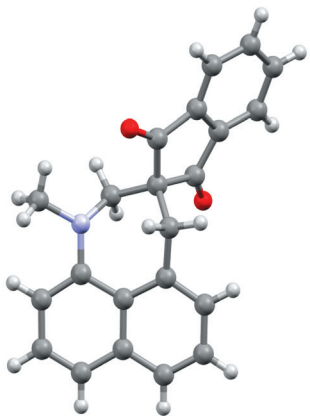


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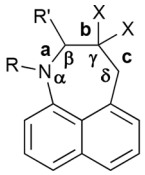
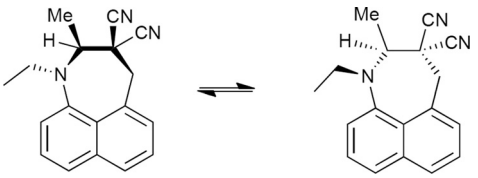
Fig. 10 Molecular structures of **23–25** drawn in the ball and stick style.

Table 5 Selected molecular geometry for fused azepines **23–25**



23 R = Et, R' =Me, X,X = $(C(=O)O)_2CMe_2$
24 R = Et, R' =Me, X = CN
25 R = Me, R'=H, X,X = $(CO)_2C_6H_4$

	a/Å	*b*/Å	*c*/Å	*β*–*δ*/°	*α*/°	Σ angles at N/°
23	1.4593(16)	1.5746(18)	1.5577(18)	105.61(10)–114.46(10)	116.22(11)	355.98
24	1.4644(13)	1.5708(14)	1.5538(14)	107.87(8)–114.09(9)	115.75(9)	356.22
25	1.450(2)	1.541(2)	1.545(2)	108.18(13)–115.69(11)	115.57(14)	350.91



Scheme 5 Conformational equilibrium for **24**.

δ_H: 3.31 and 3.50 from the methylene group next to nitrogen. In contrast, in **23** ring flexing is inhibited, because this process would move the ring methyl group from a pseudo-equatorial position to a pseudo-axial one and in close steric contact to a carbonyl group of the cyclic bis-lactone.

Conclusions

A range of compounds with N–C bonds between *peri*-substituents in the range 1.612 to 1.661 Å have been prepared, which can be interpreted as models for the incomplete addition of a dimethylamino group to a protonated carbonyl group or an electron-deficient alkene. This family of compounds is of particular interest for investigations by accurate X-ray crystallography and solid state NMR methods, to follow the bond formation process by measuring the characteristics of the bond electron density and the NMR signals of the nuclei involved as the bond forms. This work is in progress.

Experimental

General

NMR spectra were measured on a Jeol ECLIPSE 400 spectrometer at 400 MHz for ^{1}H and at 100.6 MHz for ^{13}C using $CDCl_3$ as solvent and tetramethylsilane (TMS) as standard unless otherwise stated, and measured in ppm downfield from TMS with coupling constants reported in Hz. IR spectra were recorded on a Perkin Elmer Spectrum 100 FT-IR Spectrometer using Attenuated Total Reflection sampling unless otherwise stated, and are reported in cm^{-1}. Mass spectra were recorded at the EPSRC Mass Spectrometry Centre at the University of Swansea. Chemical analysis data were obtained from Mr Stephen Boyer, London Metropolitan University. X-ray diffraction datasets were measured either on an Oxford Diffraction Xcalibur diffractometer equipped with a Sapphire detector and an Oxford Cryosystems 700 series Cryostream low temperature system at NTU, or at the EPSRC National Crystallography Service (NCS) at Southampton University. Flash chromatography was performed on 40–63 silica gel (Merck).

Preparation of (1,1-dimethyl-1,2-dihydro-2-hydroxybenzo[*cd*]-indol-1-ium trifluoroacetate, 7·CF_3CO_2

Three drops of trifluoroacetic acid were added to a solution of the aldehyde **1** (100 mg, 0.5 mmol) in ether (5 ml) to give a precipitate which was collected, washed with ether and dried to give **7**·trifluoroacetate (92 mg, 58%), a white solid, m.p. 99–101 °C; δ_H (CD_2Cl_2, 24 °C): 9.12 (1H, v br, *OH*), 8.39 (1H, br, 2-*H*), 7.88 (1H, d, *J* = 8.0 Hz, Ar-H_1), 7.79 (1H, d, *J* = 8.2 Hz, Ar-H_1), 7.61 (1H, t, *J* = 7.6 Hz, Ar-H_1), 7.55 (2H, m, Ar-H_2), 7.41 (1H, d, *J* = 7.4 Hz, Ar-H_1), 3.11 (6H, s, N(CH_3)$_2$); δ_C (CD_2Cl_2, 24 °C): 162.1 (q, $J_{C,F}$ = 34.3 Hz, *C*=O), 146.8 (Ar-C_1), 140.2 (v br, 2-*C*), 134.4, 133.0, 129.1, 128.6, 128.5, 128.0, 126.7 and 123.9 (Ar-C_8), 117.4 (q, $J_{C,F}$ = 292 Hz, *C*F_3), 115.8 (Ar-C_1), 48.4 (N(CH_3)$_2$); ν_{max}: 2566 br, 1658, 1631, 507, 1472, 1420, 1332, 1307, 1154, 1135, 1123, 999, 894, 833, 806, 797, 785, 776, 717, 707, 541, 524, 389; *HRMS*: (LTQ Orbitrap XL, MeOH/H_2O) found 200.1071, $C_{13}H_{14}NO^+$ requires 200.1070.

Preparation of (1,1-dimethyl-1,2-dihydro-2-hydroxybenzo[*cd*]-indol-1-ium chloride, 7·Cl

A stirred solution of aldehyde **1** (53 mg, 0.27 mmol) in dry ether (3 ml) under nitrogen was treated with a 1 M solution of HCl in ether (0.4 ml, 0.40 mmol) at room temperature to give a white precipitate. After stirring for 30 min, the solid was filtered off and washed with ether, and dried *in vacuo* to give **7**·Cl as a white solid (54 mg, 86%) m.p. 194–196 °C dec. δ_H (CD_3OD, 24 °C): 8.10 (1H, d, *J* = 8.2 Hz, Ar-H_1), 8.08 (1H, d, *J* = 8.3 Hz, Ar-H_1), 7.95 (1H, d, *J* = 7.3 Hz, Ar-H_1), 7.85 (1H, t, *J* = 7.8 Hz, Ar-H_1), 7.80 (2H, m, Ar-H_2), 7.11 (1H, s, 2-*H*), 3.48 (6H, s, N(CH_3)$_2$); δ_C NMR (CD_3OD, 24 °C): 146.0 (Ar-C_1), 132.9 (Ar-C_2), 131.3, 129.8, 128.7, 128.4, 128.3, 123.8 and 116.1 (Ar-C_7), 112.2 (2-*C*), 50.7 slightly br (N(CH_3)$_2$); δ_H (DMSO-d_6, 24 °C): 10.45 (1H, br, O*H*), 8.09 (1H, m, Ar-H_3), 7.81 (2H, m, Ar-H_2), 7.71 (1H, d, *J* = 6.9 Hz, Ar-H_1), 7.24 (1H, s, 2-*H*), 3.55 (6H, br, N(CH_3)$_2$); δ_C (DMSO-d_6, 24 °C): 145.1, 132.4, 130.7, 129.6, 128.4, 127.1, 126.6, 126.4, 122.2, and 115.2 (Ar-C_{10}),

114.1 (v. br., 2-*C*), 49.4 slightly br (N(*C*H$_3$)$_2$); ν_{max}: 2799, 2690, 2614, 2585, 1504, 1477, 1460, 1450, 1327, 1302, 1203, 1194, 1169, 1137, 985, 826, 806, 797, 773, 767, 717, 697, 543, 524, 395; *HRMS*: (LTQ Orbitrap XL, MeOH/H$_2$O) found 200.1064, $C_{13}H_{14}NO^+$ requires 200.1070. The doubly labelled salt was prepared in the same way from (Me$_2$^{15}N(60%))-naphthalene-8-(^{13}C(99%)) carbaldehyde by the above method.

Preparation of zwitterions 8–13

General procedure A: Aldehyde **1** (102 mg, 0.51 mmol), the appropriate cyclic 1,3-dicarbonyl compound (0.52 mmol) and ethylenediaminium diacetate (12 mg) were refluxed in dry methanol (25 ml) for 6 h. Reduction of the solvent volume and addition of ether, or evaporation of solvent and trituration with ether, gave the product.

General procedure B: Aldehyde **1** (102 mg, 0.51 mmol), the appropriate cyclic 1,3-dicarbonyl compound (0.52 mmol) and ethylenediaminium diacetate (12 mg) in dry DMSO (2 ml) were reacted at 100 °C for 10 min under microwave conditions (200 W). After cooling to room temperature, water (5 ml) was added and the mixture was extracted with ethyl acetate (3 × 10 ml). The organic extract was washed with water (3 × 15 ml) and brine (3 × 15 ml) and dried over MgSO$_4$. Evaporation of solvent and trituration with ether gave the product.

1-(1′,1′-Dimethyl-1′,2′-dihydrobenzo[*cd*]indol-1′-ium-2′-yl)-2,5-dioxocyclo-pentan-1-ide, 8. Method A, yield 81%, cream powder, m.p. 135–137 °C; δ_H (CDCl$_3$, 24 °C): 7.89 (1H, d, *J* = 8.3 Hz, Ar-*H*$_1$), 7.77 (1H, d, *J* = 8.2 Hz, Ar-*H*$_1$), 7.64 (1H, t, *J* = 7.6 Hz, Ar-*H*$_1$), 7.52 (1H, t, *J* = 7.8 Hz, Ar-*H*$_1$), 7.37 (1H, d, *J* = 7.4 Hz, Ar-*H*$_1$), 7.15 (1H, d, *J* = 6.8 Hz, Ar-*H*$_1$), 6.53 (1H, s, 2′-*H*), 3.31 (6H, s, 2 × NC*H*$_3$), 2.48 (2H, br s, 3-,4-*H*$_2$); δ_C (CDCl$_3$, 24 °C): 203.0 br (2 × *C*═O), 146.3, 133.7, 131.8, 130.5, 128.7, 127.3, 126.9, 124.2, 121.2, 112.3 (Ar-*C*$_{10}$), 99.3 (1-*C*), 88.9 (2′-*C*), 52.2 (N(*C*H$_3$)$_2$), 33.4 (3-,4-*C*); δ_H (CDCl$_3$, −48 °C): 7.93 (1H, d, *J* = 8.3 Hz, Ar-*H*$_1$), 7.81 (1H, d, *J* = 8.2 Hz, Ar-*H*$_1$), 7.67 (1H, t, *J* = 7.6 Hz, Ar-*H*$_1$), 7.60 (1H, t, *J* = 7.8 Hz, Ar-*H*$_1$), 7.42 (1H, d, *J* = 7.3 Hz, Ar-*H*$_1$), 7.29 (1H, d, *J* = 6.9 Hz, Ar-*H*$_1$), 6.49 (1H, s, 2′-*H*), 3.57 (3H, s, NC*H*$_3$), 3.13 (3H, s, NC*H*$_3$), 2.49 (4H, br m, 3-,4-*H*$_2$); δ_C (CDCl$_3$, −48 °C): 204.6 and 203.0 (2 × *C*═O), 145.8, 133.3, 131.5, 130.4, 128.3, 127.3, 126.9, 124. 2, 120.2, 112.3 (Ar-*C*$_{10}$), 99.4 (1-*C*), 86.9 (2′-*C*), 52.6 and 51.8 (2 × N-*C*H$_3$), 33.4 and 33.1 (3-,4-*C*); δ_C (DMSO-d$_6$, 65 °C): 199.7 (2 × *C*═O), 146.9, 135.2, 130.8, 129.4, 128.2, 127.3, 126.0, 123. 2, 119.7, 113.8 (Ar-*C*$_{10}$), 98.2 (1-*C*), 87.8 (2′-*C*), 51.5 (2 × N-*C*H$_3$), 32.7 (3-,4-*C*); at 24 °C, the spectrum is very similar, apart from the carbonyl C resonance appears as a broad signal at 200.1 ppm; ν_{max}: 3396, 3173, 3018, 2908, 1547, 1498, 1446, 1435, 1369, 1347, 1283, 1263, 1234 1024, 994, 906, 833, 826, 807, 785, 778, 749, 703, 640, 632, 610, 530, 478, 411; *HRMS*: (LTQ Orbitrap XL, DCM/MeOH/NH$_4$OAc) found 280.1330, $C_{18}H_{17}NO_2 + H^+$ requires 280.1332; found: C 77.58, H 5.94, N 4.86%, $C_{18}H_{17}NO_2$ requires C 77.40, H 6.13, N 5.01%.

1-(1′,1′-Dimethyl-1′,2′-dihydrobenzo[*cd*]indol-1′-ium-2′-yl)-2,6-dioxocyclo-hexan-1-ide, 9. Method A, yield 46%, cream powder, m.p. 154–155 °C; δ_H (CDCl$_3$, 24 °C): 7.85 (1H, d, *J* = 8.6 Hz, Ar-*H*$_1$), 7.70 (1H, d, *J* = 8.2 Hz, Ar-*H*$_1$), 7.60 (1H, t, *J* = 7.8 Hz, Ar-*H*$_1$), 7.52 (1H, t, *J* = 8.0 Hz, Ar-*H*$_1$), 7.31 (1H, d, *J* = 7.3 Hz, Ar-*H*$_1$), 7.15 (1H, d, *J* = 6.9 Hz, Ar-*H*$_1$), 7.11 (1H, s, 2′-*H*), 3.31 (6H, br s, 2 × NC*H*$_3$), 2.78 (2H t, *J* = 6.4 Hz,) and 2.50 (2H t, *J* = 6.2 Hz) (3-,5-*H*$_2$), 1.97 (2H, quin, *J* = 6.3 Hz, 4-*H*$_2$); δ_C (CDCl$_3$, 24 °C): 196.0 and 194.0 (2 × *C*═O), 146.9, 137.1, 131.7, 130.3, 128.6, 127.0, 126.6, 123. 0, 119.1, 111.8 (Ar-*C*$_{10}$), 102.0 (1-*C*), 93.1 (2′-*C*), 52.2 br (N(*C*H$_3$)$_2$), 37.6 and 36.6 (3-,5-*C*), 21.2 (4-*C*); δ_H (CDCl$_3$, −30 °C): 7.88 (1H, d, *J* = 8.1 Hz, Ar-*H*$_1$), 7.73 (1H, d, *J* = 8.1 Hz, Ar-*H*$_1$), 7.63 (1H, t, *J* = 7.6 Hz, Ar-*H*$_1$), 7.55 (1H, t, *J* = 7.8 Hz, Ar-*H*$_1$) 7.33 (1H, d, *J* = 7.3 Hz, Ar-*H*$_1$), 7.18 (1H, d, *J* = 6.8 Hz, Ar-*H*$_1$), 7.11 (1H, s, 2′-*H*), 3.57 (3H, s, NC*H*$_3$), 3.14 (3H, s, NC*H*$_3$), 2.53 (2H, m) and 2.33 (2H, m, 3-,5-*H*$_2$), 1.97 (2H, m, 4-*H*$_2$); δ_C (CDCl$_3$, −30 °C): 196.2 and 194.4 (2 × *C*═O), 146.6, 136.9, 131.5, 130.4, 128.3, 127.0, 126.7, 123.0, 118.7, 111.8 (Ar-*C*$_{10}$), 102.0 (1-*C*), 91.2 (2′-*C*), 55.2 and 49.6 (N(*C*H$_3$)$_2$), 37.6 and 36.6 (3-,5-*C*), 21.2 (4-*C*); ν_{max}: 2930, 2870, 1606, 1587 w, 1521, 1500 sh, 1462, 1442, 1397, 1382, 1183, 1173, 1120, 1007, 980, 830, 777, 768, 736, 661, 624, 551, 529, 511, 434, 417; *HRMS*: (LTQ Orbitrap XL, DCM/MeOH/NH$_4$OAc) found: 294.1491 [M + H]$^+$; $C_{19}H_{19}NO_2 + H^+$ requires 294.1489; found C, 77.63; H, 6.48; N, 4.76%, $C_{19}H_{19}NO_2$ requires C, 77.78; H, 6.53, N: 4.78%.

4,4-Dimethyl-1-(1′,1′-dimethyl-1′,2′-dihydrobenzo[*cd*]indol-1′-ium-2′-yl)-2,6-dioxocyclohexan-1-ide, 10. Method B, yield 81%, oily solid, δ_H (CDCl$_3$, 24 °C): 7.86 (1H, d, *J* = 8.2 Hz, Ar-*H*$_1$), 7.71 (1H, d, *J* = 8.2 Hz, Ar-*H*$_1$), 7.61 (1H, t, *J* = 7.4 Hz, Ar-*H*$_1$), 7.53 (1H, t, *J* = 7.8 Hz, Ar-*H*$_1$), 7.32 (1H, d, *J* = 7.4 Hz, Ar-*H*$_1$), 7.14 (1H, d, *J* = 7.2 Hz, Ar-*H*$_1$), 7.13 (1H, s, 2′-*H*), 3.32 (6H, br s, N-(C*H*$_3$)$_2$), 2.41 (s, 2H) and 2.19 (s, 2H) (3-,5-*H*$_2$), 1.12 (6H, s, 2 × 4-C*H*$_3$); δ_C (CDCl$_3$, 24 °C): 194.7 and 193.0 (2 × *C*═O), 146.8, 137.1, 131.7, 130.4, 127.7, 127.0, 126.6, 123.0, 119.2 and 111.8 (Ar-*C*$_{10}$), 100.6 (2-*C*), 93.4 (2′-*C*), 52.0 (br s, N-(*C*H$_3$)$_2$), 50.5 and 50.1 (3-,5-*C*), 31.3 (4-*C*), 28.8 (2 × 4-*C*H$_3$); ν_{max} (film): 3028, 2943, 2885, 2016, 1604, 1589, 1525, 1467, 1439, 1405, 1384, 1279, 1260,1156; *HRMS*: (LTQ Orbitrap XL, DCM/MeOH/NH$_4$OAc) found: 322.1805 [M + H]$^+$; $C_{21}H_{23}NO_2$ + H$^+$ requires 322.1805.

1-(1′,1′-Dimethyl-1′,2′-dihydrobenzo[*cd*]indol-1′-ium-2′-yl)-4-phenyl-2,6-dioxocyclohexan-1-ide, 11. Method B, 38%, cream solid, m.p. 142–144 °C; δ_H (CDCl$_3$, 24 °C): 7.90 (1H, d, *J* 8.2 Hz, Ar-*H*$_1$), 7.76 (1H, d, *J* 8.3 Hz, Ar-*H*$_1$), 7.66 (1H, t, *J* = 7.6 Hz, Ar-*H*$_1$), 7.56 (1H, t, *J* = 7.8 Hz, Ar-*H*$_1$), 7.33 (5H, m, *o*-, *m*-phenyl-*H*$_3$ + Ar-*H*$_2$), 7.22 (2H, m, *para*-Ph-*H*$_1$ + Ar-*H*$_1$), 7.16 (1H, s, 2′-*H*), 3.47 (1H, br s, 4-*H*), 3.31 (6H, br s, N(C*H*$_3$)$_2$), 2.83 (2H, m) and 2.60 (2H, m) (3-,5-*H*$_2$); δ_C (CDCl$_3$, 24 °C): 194.7 and 192.9 (2 × *C*═O), 146.9 (Ar-*C*$_1$), 144.4 (*ipso*-Ph-*C*$_1$), 136.9, 131.8, 130.5, 128.7 (Ar-*C*$_4$), 128.5 (Ph-*C*$_2$), 127.1 (Ar-*C*$_1$), 126.8 (Ph-*C*$_2$), 126.7 (Ar-*C*$_1$), 126.3 (*para*-Ph-*C*$_1$), 123.2, 119.2, 111.8 (Ar-*C*$_3$), 101.5 (br s, 1-*C*), 92.6 (2′-*C*), 52.0 (br s, 2 × N-*C*H$_3$), 44.8 and 43.9 (3-,5-*C*), 38.9 (4-*C*); δ_H (CD$_2$Cl$_2$, −40 °C): 7.94 (1H, d, *J* = 8.4 Hz, Ar-*H*$_1$), 7.79 (1H, t, *J* = 7.4 Hz, Ar-*H*$_1$), 7.65 (m), 7.44 (m), 7.33 (m), 7.22 (m) and 7.13(m) (Ar-*H*$_9$), 7.03 (7.09) (1H, s, 2′-*H*), 3.57 (3.54) (3H, s, N-C*H*$_3$), and 3.13 (3.17) (3H, s, N-C*H*$_3$), 2.71 (2H, m, 3-,5-*H*$_\alpha$), 2.47 (2H, m, 3-,5-*H*$_\alpha$); δ_C (CD$_2$Cl$_2$, −40 °C): 192.7 (192.2) and

190.6 (190.9) (2 × *C*═O), 145.2 (145.1), 143.1 (143.2), 135.8 (135.6), 129.8 (129.7), 128.5, 126.9, 125.6 (125.5), 125.2 (125.3), 124.7, 121.4 (121.3), 117.3, 111.0 (Ar-C_{14}), 99.7 (98.5) (2-*C*), 89.1 (88.6) (2′-C), 53.8 (53.0) and 48.2 (48.5) (2 × NCH_3), 42.9 (43.4) and 42.1 (4-,6-*C*), 37.6 (37.2) (5-*C*), values in brackets correspond to minor isomer when the resonances can be distinguished, resonance at *ca.* 131 not observed; ν_{max}: 1605, 1585, 1505, 1444, 1403, 1376, 1251, 1036, 989, 915, 826, 771, 699, 667, 608, 567, 532, 504, 438, 415; *HRMS*: (LTQ Orbitrap XL, DCM/MeOH/NH_4OAc) found 370.1804 $[M + H]^+$. $C_{25}H_{25}NO_2$–H^+ requires 370.1802.

1,3-Dimethyl-5-(1′,1′-dimethyl-1′,2′-dihydrobenzo[*cd*]indol-1′-ium-2′-yl)-2,4,6-trioxo-1*H*,3*H*,5*H*-pyrimidin-5-ide, 12. Method A, 54%, white solid, m.p. 190–192 °C; δ_H (DMSO-d_6, 24 °C): 8.01 (1H, d, J = 8.0 Hz, Ar-H_1), 7.94 1H, d, J = 7.4 Hz, Ar-H_1), 7.86 (1H, d, J = 8.2 Hz, Ar-H_1), 7.72 (1H, t, J = 7.8 Hz, Ar-H_1), 7.64 (1H, dd, J = 8.1, 7.1 Hz, Ar-H_1), 7.15 (1H, d, J = 6.9 Hz, Ar-H_1), 7.08 (1H, s, 2′-*H*), 3.48 and 3.16 (6H, 2 × v br s, (N(CH_3)$_2$), 3.21 and 2.95 (2 × 3H, s, 2 × NCH_3); δ_C (DMSO-d_6, 24 °C): 164.6 and 162.4 (4-,6-*C*), 152.8 (2-*C*), 147.2, 136.5, 131.0, 129.7, 128.1, 127.6, 126.2, 123.1, 119.0 and 113.9 (Ar-C_{10}), 93.5 (2′-*C*), 77.7 (5-*C*), 54.5 and 49.5 (2 × v br, (N(CH_3)$_2$), 27.4 and 26.7 (2 × N-CH_3); δ_H (DMSO-d_6, 80 °C): 7.99 (1H, d, J = 8.4 Hz, Ar-H_1), 7.88 1H, d, J = 7.4 Hz, Ar-H_1), 7.85 (1H, d, J = 8.2 Hz, Ar-H_1), 7.69 (1H, t, J = 7.8 Hz, Ar-H_1), 7.63 (1H, t, J = 7.6 Hz, Ar-H_1), 7.15 (1H, d, J = 7.2 Hz, Ar-H_1), 7.13 (1H, s, 2′-*H*), 3.33 (6H, s, N(CH_3)$_2$), 3.22 and 2.95 (2 × 3H, s, 2 × NCH_3); δ_C (DMSO-d_6, 80 °C):164.4 and 162.1 (2-,6-*C*), 152.5 (4-*C*), 146.8, 136.0, 130.8, 129.2, 128.0, 127.0, 125.9, 122.8, 118.9 and 113.5 (Ar-C_{10}), 95.6 (2′-*C*), 77.8 (5-*C*), 51.2 (N(CH_3)$_2$), 27.0 and 26.2 (2 × N-CH_3). ν_{max}: 1672, 1600, 1469, 1424, 1422, 1371, 1337, 832, 810, 790, 779, 769, 757, 677, 632, 616, 514, 495, 468, 428, 413; *HRMS*: (LTQ Orbitrap XL, MeOH/DCM/NH_4OAc) found 360.1324, $C_{19}H_{19}N_3O_3$ + Na^+ requires 360.1319.

2-(1′,1′-Dimethyl-1,2-dihydrobenzo[*cd*]indol-1′-ium-2′-yl)-1,3-dioxo-2,3-dihydro-1*H*-inden-2-ide, 13. Method A, 41%, yellow crystals, m.p. 144–146 °C; δ_H (CD_2Cl_2, 24 °C): 7.90 (1H, d) and 7.88 (1H, d) (J = *ca.* 8 Hz, naphth-H_2), 7.66 (1H, s, 2′-*H*), 7.63 (6H, br m, Ar-H_6), 7.42 (1H, d, J = 7.5 Hz, naphth-H_1), 7.39 (1H, d, J = 6.9 Hz, naphth-H_1), 2.99 (6H, s, (N(CH_3)$_2$); δ_C (CD_2Cl_2, 24 °C): 191.0 br (2 × *C*═O), 148.1 (Ar-C_1), 142.5 and 140.2 br (indanone-C_2), 133.7, 133. 1 (Ar-C_2), 132.7 (indanone-C_2), 130.3, 128.4, 127.2, 126.9, 126.7, 124. 3 (Ar-C_6), 120.8 (indanone-C_2), 116.2 (Ar-C_1), 118.6 br (2′-*C*), 105.5 br (2 -*C*), 49.0 (N(CH_3)$_2$); δ_H (CD_2Cl_2, −60 °C): 7.97 (1H, d, J = 8.3 Hz, napth-H_1), 7.88 (1H, d, J = 8.3 Hz, naphth-H_1), 7.61 (2H, Ar-H_2), 7.43 (5H, m, 2′-*H* and Ar-H_4), 7.31 (1H, d, J = 6.8 Hz, naphth-H_1), 7.25 (1H, d, J = 6.8 Hz, naphth-H_1), 3.28 (6H, slightly br s, (N(CH_3)$_2$); δ_C (CD_2Cl_2, −60 °C): 192.4 and 190.8 (2 × *C*═O), 145.8 (Ar-C_1), 139.6, 138.8 (indanone-C_2), 133.8, 131.3 (Ar-C_2), 130.7, 130.5 (indanone-C_2), 129.8, 128.5, 127.3, 126.9, 124.2, 121.1 (Ar-C_6), 118.5, 118.4 (indanone-C_2) and 113.5 (Ar-C_1), 92.4 (2′-C), 90.4 (2-C), 51.4 br (N(CH_3)$_2$); ν_{max}: 1613, 1563, 1430, 1373, 872, 822, 773, 746, 736, 721, 664, 620, 609, 558, 520, 501, 471, 427; *m*/*z*: 327 (M^+, 100), 312 (M–CH_3, 25), 181 (24), 168 (57); *HRMS*: (LTQ Orbitrap XL, MeOH) found 328.1336, $C_{22}H_{17}NO_2$ + H^+ requires 328.1332.

2,2-Dimethyl-5-(1′,1′-diethyl-1′,2′-dihydrobenzo[*cd*]indol-1′-ium-2′-yl)-4,6-dioxocyclo-1,3-dioxan-5-ide, 14. Method A using aldehyde **15** but no catalyst, 35%, beige powder, m.p. 119–121 °C; δ_H ($CDCl_3$, 24 °C): 7.87 (1H, d, J = 8.2 Hz, Ar-H_1), 7.79 (1H, d, J = 8.2 Hz, Ar-H_1), 7.62 (1H, t, J = 7.6 Hz, Ar-H_1), 7.55 (1H, t, J = 7.8 Hz, Ar-H_1), 7.51 (1H, s, 2′-*H*); 7.25 (2H, d, J = 7.4 Hz, Ar-H_2), 3.74 (2H, approx dq, J = 13.6, 7.2 Hz, 2 × CH_αMe), 3.61 (2H, approx. dq, J = 13.6, 7.2 Hz, 2 × CH_βMe), 1.76 (6H, 4-,4-CH_3), 1.22 (6H, t, J = 7.2 Hz , 2 × (CH_2)CH_3); δ_C ($CDCl_3$, 24 °C): 168.2 and 165.0 (2 × *C*═O), 140.7, 134.6, 132.4 and 130.9, 129.2, 126.7, 126.1, 125.0, 121.3, 116.6 (Ar-C_{10}), 104.6 (2′-*C*), 102.7 (2-*C*), 74.8 (5-*C*), 53.0 (2 × NCH_2), 26.4 (4-,4-CH_3), 9.3 (2 × (CH_2)CH_3); ν_{max}: 1626, 1397, 1363, 1282, 1252, 1198, 1174, 1087, 1083, 930, 786, 752, 672, 635, 493, 481, 422, 404, 386; *HRMS*: (LTQ Orbitrap XL, MeOH/DCM/NH_4OAc) found 354.1704, $[C_{21}H_{23}NO_4 + H]^+$ requires 354.1700; found C: 71.09, H: 6.72, N: 3.85% $C_{21}H_{23}NO_4$ requires C: 71.37, H: 6.56, N: 3.96%.

2-Acetyl-1-(1′-dimethylaminonaphth-8′-yl)but-1-en-3-one 22. Method A using aldehyde **1** and pentane-2,4-dione, refluxing for 48 h, and chromatography (cyclohexane : ethyl acetate 1 : 1) of the reaction mixture gave **22** (9%) containing *ca.* 10% of **1**, and evaporation of an ether solution gave crystals of **22** for X-ray diffraction, m.p. 210–212 °C; δ_H ($CDCl_3$, 24 °C): 8.67 (1H, s, 1-*H*), 7.75 (1H, d, J = 8.0 Hz, Ar-H_1), 7.58 (1H, d, J = 8.1 Hz, Ar-H_1), 7.41 (1H, t, J = 7.8 Hz, Ar-H_1), 7.30 (2H, m, Ar-H_2), 7.12 (1H, d, J = 7.0 Hz, Ar-H_1), 2.69 (6H, s, N-(CH_3)$_2$), 2.40 (3H, s, CH_3CO), 2.08 (3H, s, CH_3CO); δ_C($CDCl_3$, 24 °C): 203.8 & 197.3 (2 × *C*═O). 151.2 (Ar-C_1), 147.7 (1-*C*), 137.1, 135.6 (Ar-C_2), 131.4 (2-C), 130.1, 129.3, 127.3, 126.5 (Ar-C_4), 125.4 (Ar-C_2), 119.4 (Ar-C_1), 46.0 (N-(CH_3)$_2$), 32.2 & 27.0 (2 × COCH_3).

Preparation of naphtho[1,8-*bc*]azepines

1′-Ethyl-2,2,2′-trimethyl-2′,4′-dihydro-1′*H*-spiro[[1,3]dioxane-5,3′-naphtho[1,8-*bc*]azepine]-4,6-dione, 23. Aldehyde **15** (200 mg, 0.88 mmol), Meldrum's acid (126 mg, 0.87 mmol) and ethylenediammonium diacetate (12 mg) in methanol (5.5 ml) were reacted under microwave conditions (200 W) for 10 min at 100 °C. After cooling to room temperature and stirring overnight, filtration gave the product (119 mg, 38%) as a cream solid, m.p. 158–159 °C; δ_H ($CDCl_3$, 24 °C): 7.71 (1H, d, J = 8.2 Hz, Ar-H_1), 7.47 (1H, d, J = 8.2 Hz, Ar-H_1), 7.32 (2H, m, Ar-H_2), 7.03 (1H, d, J = 6.9 Hz, Ar-H_1), 6.91 (1H, d, J = 7.4 Hz, Ar-H_1), 4.45 (1H, d, J = 13.3 Hz, 4′-H_α), 4.29 (1H, q, J = 7.1 Hz, 2′-*H*), 3.50 (2H, q, J = 6.9 Hz, NCH_2(CH_3)), 2.96 (1H, d, J = 13.3 Hz, 4′-H_β), 1.86 (3H, s) and 1.77 (3H, s) (2-,2-CH_3), 1.37 (3H, t, J = 6.9 Hz, (NCH_2)CH_3), 1.26 (3H, d, J = 7.1 Hz, 2′-CH_3); δ_C ($CDCl_3$, 24 °C): 169.5 and 168.0 (2 × *C*═O), 149.2, 136.3, 132.7, 128.2, 127.8, 127.7, 125.4, 125.1, 120.5 and 111.9 (Ar-C_{10}), 104.6 (2-*C*), 67.7 (2′-*C*), 60.8 (5-*C*), 42.8 (4′-*C*), 37.8 (N-CH_2), 30.0 and 28.5 (2-,2-CH_3), 14.6 (2′-CH_3), 13.3 ((NCH_2)CH_3); ν_{max}: 3034, 2972, 2936, 2869, 1766, 1730, 1581, 1460, 1383, 1319, 1274, 1242, 1227, 1203,

1153, 1125, 1108, 1080. 1059, 1046, 1015, 995, 956, 927, 893, 876, 823, 785, 768, 749, 729, 687, 663, 637, 628, 527, 513, 500, 474; *HRMS*: (LTQ Orbitrap XL, DCM/MeOH/NH_4OAc) found: 354.1701 $[M + H]^+$; $C_{21}H_{23}NO_4 + H^+$ requires 354.1700.

1-Ethyl-2-methyl-1,2,3,4-tetrahydro-naphtho[1,8-*bc*]azepine-3,3-dinitrile, 24. Aldehyde **15** (200 mg, 0.88 mmol), malonitrile (58 mg, 0.87 mmol) and ethylenediammonium diacetate (20 mg) in methanol (5.5 ml) were reacted under microwave conditions (200 W) for 2 × 10 min at 100 °C. After cooling to room temperature, the solvent was evaporated and the residue run through a short plug of silica (cyclohexane–ethyl acetate 3 : 1) to give the product as a white solid (120 mg, 43%), m.p. 101–103 °C, δ_C ($CDCl_3$, 24 °C): 7.75 (1H, d, J = 7.8 Hz, Ar-H_1), 7.43 (1H, d, J = 7.8 Hz, Ar-H_1), 7.35 (2H, m, Ar-H_2), 7.25 (1H, d, J = 6.9 Hz, Ar-H_1), 6.98 (1H, d, J = 7.3 Hz, Ar-H_1), 4.10 (1H, br, 4′-H_α), 4.04 (1H, q, J = 6.9 Hz, 2′-H), 3.50 (2H, m, N-CH_2Me), 3.44 (1H, br, 4′-H_β), 1.59 (3H, br, 2′-CH_3), 1.36 (3H, t, J = 6.9 Hz, (NCH_2)CH_3); δ_C ($CDCl_3$, 24 °C): 149.2 br, 135.9, 129.4, 129.0, 128.1, 128.0, 125.7, 121.8, 115.4 br (Ar-C_9), 114.9 (2 × CN), 113.4 br (Ar-C_1), 65.5 (2′-C), 43.1 (4′-C), 42.8 (3′-C), 39.3 br (N-CH_2), 15.1 (2′-CH_3), 14.5 ((NCH_2)CH_3); δ_C ($CDCl_3$, −30 °C): 7.69 (1H, d, J = 8.2 Hz, Ar-H_1), 7.36 (1H, d, J = 7.8 Hz, Ar-H_1), 7.29 (2H, m, Ar-H_2), 7.19 (1H, d, J = 6.9 Hz, Ar-H_1), 6.90 (1H, d, J = 7.5 Hz, Ar-H_1), 4.10 (1H, d, J = 13.5 Hz, 4′-H_α), 3.96 (1H, q, J = 6.9 Hz, 2′-H), 3.56 (1H, m) and 3.45 (1H, m) (N-CH_2Me), 3.40 (1H, d, J = 13.5 Hz, 4′-H_β), 1.57 (3H, d, J = 6.9 Hz, 2′-CH_3), 1.27 (3H, t, J = 7.0 Hz, (NCH_2)CH_3); δ_C ($CDCl_3$, −30 °C): 147.5, 135.7, 129.3, 128.7, 128.0, 127.9, 127.4, 125.6, 121.4 (Ar-C_9), 114.9 (2 × CN), 113.4 (Ar-C_1), 65.6 (2′-C), 43.0 (4′-C), 42.4 (3′-C), 38.0 (N-CH_2), 15.0 (2′-CH_3), 14.3 ((NCH_2)CH_3); ν_{max}: 2973, 2850, 2248, 1581, 1458, 1447, 1406, 1383, 1345, 1302, 1283, 1250, 1239, 1219, 1204, 1106, 1077, 1055, 823, 785, 747, 711, 660, 580, 552; *m/z*: 275 (M^+, 85), 196 (82), 195 (100), 167 (45); found C: 78.60, H: 6.29, N: 15.01% $C_{18}H_{17}N_3$ requires C: 78.52, H: 6.22, N: 15.26%. Reaction in refluxing methanol for 18 h without any catalyst gave the same product.

1′-Methyl-2′,4′-dihydro-1′*H*-spiro[indene-2,3′-naphtho[1,8-*bc*]-azepine]-1,3-dione, 25. Aldehyde **1** (121 mg, 0.61 mmol) and indanone (94 mg, 0.64 mmol) in methanol (5 ml) were reacted under microwave conditions (200 W) for 10 min at 120 °C. After cooling to room temperature, the methanol was evaporated, the residue triturated with ether and the precipitated solid collected to give the product as a yellow-orange powder (145 mg, 64%), m.p. 163–164 °C, δ_H ($CDCl_3$, 25 °C): 7.94 (2H, m, indanone-H_2), 7.81 (2H, m, indanone-H_2), 7.60 (1H, d, J = 8.4 Hz, Ar-H_1), 7.25 (3H, m, Ar-H_3), 6.92 (1H, d, J = 6.9 Hz, Ar-H_1), 6.74 (1H, d, J = 7.2 Hz, Ar-H_1), 3.43 (4H, br, 2 × CH_2), 3.08 (3H, s, NCH_3); δ_C (CD_2Cl_2, 25 °C): 202.4 (2 × C═O), 152.2 (Ar-C_1), 141.4 (indanone-C_2), 136.3 (indanone-C_2 + Ar-C_1), 135.0, 127.8, 127.4, 126.9, 126.0, 125.7 (Ar-C_6), 123.6 (indanone-C_2), 120.4, 109.4 (Ar-C_2), 60.0 (2-,3-C), 41.0 (N-CH_3), 40.1 (4-C); δ_H (CD_2Cl_2, −65 °C): 8.02 (br d, indanone-H_1), 7.92 (br m, indanone-H_3), 7.67 (1H, d, J = 8.2 Hz, Ar-H_1), 7.30 (m, Ar-H_3), 6.97 (1H, d, J = 6.9 Hz, Ar-H_1), 6.80 (1H, dd, J = 6.6, 1.8 Hz, Ar-H_1), 4.17 (1H, d, J = 13.1 Hz, 4-H_α), 3.50 (1H, d, J = 14.6 Hz, 2-H_α), 3.31 (1H, d, J = 14.6 Hz, 2-H_β), 3.09 (3H, s, NCH_3), 2.69 (1H, d, J = 13.1 Hz, 4-H_β); δ_C (CD_2Cl_2, −65 °C): 203.5 and 201.4 (2 × C═O), 151.5 (Ar-C_1), 140.8 and 140.2 (indanone-C_2), 136.0 (indanone-C_2), 135.3, 134.4, 127.2, 126.7, 125.9, 125.4, 125.2 (Ar-C_7), 123.2 and 123.0 (indanone-C_2), 119.6, 108.5 (Ar-C_2), 59.2 (3-C), 58.8 (2-C), 40.6 (N-CH_3), 39.0 (4-C); ν_{max}: 2919, 2866, 1736, 1698, 1580, 1511, 1467, 1440, 1391, 1342, 1330, 1278, 1232, 1213, 1195, 1149, 1104, 1088, 1023, 972, 923, 915, 826, 816, 803, 783, 747, 725, 756, 712, 686, 642, 593, 563; *HRMS*: (LTQ Orbitrap XL, DCM/MeOH/NH_4OAc) found: 328.1336 $[M + H]^+$; $C_{22}H_{17}NO_2 + H^+$ requires 328.1332.

X-ray crystallography

X-ray single-crystal diffraction measurements were made either on a Bruker Nonius diffractometer located at the window of a Nonius FR591 rotating-anode X-ray generator (Mo-Kα) equipped with a Roper CCD or/and APEX II detector (for **7**, **8**, **9**, **10**, **12**, **22** and **23**), or an Oxford Diffraction Xcalibur diffractometer (Mo-Kα) equipped with a Sapphire3 detector (for **13**, **14**, **24** and **25**). Structures were solved and refined with the SHELXS and SHELXL suites[21] using the XSEED[22] interface. Molecular illustrations were made with Mercury.[23]

Crystal data for 7·trifluoroacetate. $C_{13}H_{14}NO^+ \cdot C_2F_3O_2^-$, M_r = 313.27, triclinic, a = 8.6837(3), b = 12.8490(4), c = 13.8588(5) Å, α = 103.171(2) β = 93.108(2), γ = 106.795(2)°, V = 1429.42(8) Å^3, Z = 4, $P\bar{1}$, D_c = 1.46 g cm^{-3}, μ = 0.127 mm^{-1}, T = 120 K, 5017 unique reflections, 4621 with $F^2 > 2\sigma$, $R(F, F^2 > 2\sigma)$ = 0.0704, $R_w(F^2$, all data) = 0.163. Crystals from acetonitrile. The crystal of (**9b**) was a non-merohedral twin with the two domains related by 180° about the reciprocal vector [100]. The crystal structure was refined using data in HKLF 5 in SHELXL. The refined percentage ratio of the twin domains was 60 : 40. Additionally, in the crystal structure one –CF_3 group of trifluoroacetate shows positional disorder, which has been modelled as three different orientations.

Crystal data for 7·Cl. $C_{13}H_{14}NO^+ \cdot Cl^-$, M_r = 235.70, orthorhombic, a = 9.9646(4) b = 11.9986(5), c = 19.3145(7) Å, V = 2309.27(16) Å^3, Z = 8, $Pbca$, D_c = 1.36 g cm^{-3}, μ = 0.308 mm^{-1}, T = 150 K, 2708 unique reflections (R_{int} = 0.0274), 2301 with $F^2 > 2\sigma$, $R(F, F^2 > 2\sigma)$ = 0.045, $R_w(F^2$, all data) = 0.098. Crystals from methanol.

Crystal data for 8. $C_{18}H_{17}NO_2 \cdot H_2O$, M_r = 297.34, monoclinic, a = 18.5849(7), b = 9.1076(3), c = 19.5453(8) Å, β = 112.680(2)°, V = 3052.5(2) Å^3, Z = 8, $P2_1/c$, D_c = 1.29 g cm^{-3}, μ = 0.088 mm^{-1}, T = 120 K, 6982 unique reflections (R_{int} = 0.0588), 5042 with $F^2 > 2\sigma$, $R(F, F^2 > 2\sigma)$ = 0.050, $R_w(F^2$, all data) = 0.127. Crystals from acetonitrile.

Crystal data for 9. $C_{19}H_{19}NO_2 \cdot H_2O$, M_r = 311.37, triclinic, a = 8.4223(2), b = 9.4076(3), c = 10.8996(3) Å, α = 85.508(2), β = 73.336(2), γ = 68.462(2)°, V = 769.22(4) Å^3, Z = 2, $P\bar{1}$, D_c = 1.34 g cm^{-3}, μ = 0.091 mm^{-1}, T = 120 K, 3522 unique reflections (R_{int} = 0.0463), 2834 with $F^2 > 2\sigma$, $R(F, F^2 > 2\sigma)$ = 0.043, $R_w(F^2$, all data) = 0.114. Crystals from methanol/ether.

Crystal data for 10. $C_{21}H_{23}NO_2$, M_r = 321.40, monoclinic, a = 9.6118(4), b = 10.0248(6), c = 18.7717(10) Å, β = 103.180

(3)°, V = 1761.13(16) Å^3, Z = 4, $P2_1/n$, D_c = 1.21 g cm^{-3}, μ = 0.077 mm^{-1}, T = 100 K, 3103 unique reflections (R_{int} = 0.1218), 1967 with $F^2 > 2\sigma$, $R(F, F^2 > 2\sigma)$ = 0.060, $R_w(F^2$, all data) = 0.158. Crystals from acetone.

Crystal data for 12. $C_{19}H_{19}N_3O_3$, M_r = 337.37, triclinic, a = 8.3360(4), b = 8.7036(3), c = 12.1220(6) Å, α = 89.456(3), β = 85.190(2), γ = 65.248(3) °, V = 795.56(6) Å^3, Z = 2, $P\bar{1}$, D_c = 1.41 g cm^{-3}, μ = 0.097 mm^{-1}, T = 120 K, 3656 unique reflections (R_{int} = 0.0420), 2967 with $F^2 > 2\sigma$, $R(F, F^2 > 2\sigma)$ = 0.049, $R_w(F^2$, all data) = 0.135. Crystals from methanol. Mátyus *et al.* have made a preliminary report of this structure.[15]

Crystal data for 13. $C_{22}H_{17}NO_2$, M_r = 327.37, monoclinic, a = 8.8717(3), b = 11.5384(3), c = 15.6190(5) Å, β = 95.980(3)°, V = 1590.14(8) Å^3, Z = 4, $P2_1/c$, D_c = 1.37 g cm^{-3}, μ = 0.088 mm^{-1}, T = 150 K, 3648 unique reflections (R_{int} = 0.0185), 2836 with $F^2 > 2\sigma$, $R(F, F^2 > 2\sigma)$ = 0.039, $R_w(F^2$, all data) = 0.097. Crystals from acetone.

Crystal data for 14. $C_{21}H_{23}NO_4$, M_r = 353.40, monoclinic, a = 10.1338(3), b = 16.0686(5), c = 10.9554(4) Å, β = 95.661(3)°, V = 1775.23(10)Å^3, Z = 4, $P2_1/n$, D_c = 1.32 g cm^{-3}, μ = 0.091 mm^{-1}, T = 150 K, 4116 unique reflections (R_{int} = 0.0188), 3047 with $F^2 > 2\sigma$, $R(F, F^2 > 2\sigma)$ = 0.038, $R_w(F^2$, all data) = 0.094. Crystals from acetone.

Crystal data for 22. $C_{18}H_{19}NO_2$, M_r = 281.34, triclinic, a = 6.8270(4), b = 8.7630(5), c = 13.1899(7) Å, α = 102.408(4), β = 98.689(4), γ = 94.696(3)°, V = 756.45(7) Å^3, Z = 2, $P\bar{1}$, D_c = 1.24 g cm^{-3}, μ = 0.080 mm^{-1}, T = 120 K, 3453 unique reflections (R_{int} = 0.0666), 2384 with $F^2 > 2\sigma$, $R(F, F^2 > 2\sigma)$ = 0.057, $R_w(F^2$, all data) = 0.139. Crystals from methanol/ether.

Crystal data for 23. $C_{21}H_{23}NO_4$, M_r = 353.40, monoclinic, a = 31.2818(6), b = 7.09570(10), c = 16.7814(3) Å, β = 107.3740(10)°, V = 3554.96(11) Å^3, Z = 8, $C2/c$, D_c = 1.32 g cm^{-3}, μ = 0.091 mm^{-1}, T = 120 K, 4070 unique reflections (R_{int} = 0.0329), 3462 with $F^2 > 2\sigma$, $R(F, F^2 > 2\sigma)$ = 0.045, $R_w(F^2$, all data) = 0.120. Crystals from DCM/ether.

Crystal data for 24. $C_{18}H_{17}N_3$, M_r = 275.35, monoclinic, a = 15.0771(5), b = 6.6633(2), c = 15.5200(6) Å, β = 109.378(4)°, V = 1470.86(9) Å^3, Z = 4, $P2_1/n$, D_c = 1.24 g cm^{-3}, μ = 0.076 mm^{-1}, T = 150 K, 3365 unique reflections (R_{int} = 0.0157), 2690 with $F^2 > 2\sigma$, $R(F, F^2 > 2\sigma)$ = 0.038, $R_w(F^2$, all data) = 0.098. Crystals from acetone.

Crystal data for 25. $C_{22}H_{17}NO_2$, M_r = 327.37, orthorhombic, a = 15.9448(12), b = 7.7430(6), c = 26.4365(18) Å, V = 3263.9(4) Å^3, Z = 8, $Pbca$, D_c = 1.33 g cm^{-3}, μ = 0.086 mm^{-1}, T = 150 K, 3842 unique reflections (R_{int} = 0.0201), 2281 with $F^2 > 2\sigma$, $R(F, F^2 > 2\sigma)$ = 0.047, $R_w(F^2$, all data) = 0.119. Crystals from acetone.

Solid state NMR and DFT calculations

Cross-polarisation, magic-angle-spinning (CPMAS) ^{1}H–^{13}C and ^{1}H–^{15}N NMR measurements in the solid state were undertaken at 11.7 T using a Bruker Avance III-500 spectrometer producing ^{1}H, ^{13}C and ^{15}N Larmor frequencies of 500.10, 125.76 and 50.68 MHz, respectively. A Bruker 4 mm HXY probe in dual channel mode was utilised to enable MAS frequencies of 700, 900 and 12 000 Hz. All ^{13}C CPMAS data were acquired with an initial ^{1}H $\pi/2$ pulse time of 2.5 µs, a ^{1}H-^{13}C contact time of 1 ms and a recycle time of 8 s. These ^{13}C data were indirectly referenced to neat TMS (δ_{iso} 0 ppm) *via* a secondary solid reference of ^{13}C labelled alanine which provided three distinct resonances for the methyl, backbone and carboxyl carbons at isotropic shifts of δ_{iso} 20.5, 50.5 and 178 ppm, respectively.[24] All ^{15}N CPMAS data were acquired with an initial ^{1}H $\pi/2$ pulse time of 2.5 µs, a ^{1}H–^{13}C contact time of 1.5 ms and a recycle time of 8 s. Similarly, all ^{15}N data were indirectly referenced to $MeNO_2$ in $CHCl_3$ (δ_{iso} 0 ppm) *via* a secondary reference of histidine which provided three distinct resonances at −333.1, −204.3 and −191.0 ppm.[25] Spinning sideband analyses of these data were completed using the commercial Bruker TOPSPIN 2.1 sola program.

Theoretical density functional theory (DFT) studies were undertaken on compound **7** (using the crystal coordinate file generated from diffraction studies) involved programs from Accelrys Software which were implemented from the Materials Studio 5.5 suite.[26] The correlation generalized gradient approximation (GGA) was applied in the manner originally suggested by Perdew–Burke–Ernzerhof (PBE functional).[27] The necessary energy minimisation and geometry optimisation performed on **7** in its native periodic lattice using a plane–wave/pseudopotential approach were achieved using the CASTEP code[13] which was implemented with unmodified ultrasoft pseudopotentials generated directly from the Materials Studio package. Typical convergence criteria applied during the geometry optimization were 2.72×10^{-4} eV for energy and 0.054 eV Å^{-1} for force. A basis set convergence to 0.003 mH (or 1.10×10^{-4} eV) per atom was achieved with a plane–wave cut-off energy of 840 eV and a sampling of 8 k-points within the 1st Brillouin zone. GIPAW-DFT calculations[28,29] were used to compute the ^{13}C and ^{15}N NMR shielding parameters which are calculated with respect to the bare atom. To translate these results into isotropic shifts (δ_{iso}, eqn (1)), a conversion is required where a shielding (σ_{cal}, eqn (2)) is generated to calibrate against the bare atoms' calculated shielding (σ_{DFT}). This is achieved by taking the mean ($\bar{x}$) of the experimental and adding it to the mean of the calculated shielding (σ_{DFT}). The σ_{cal} for ^{13}C is always approximately 168 ppm and the σ_{cal} for ^{15}N is always approximately −160 ppm. All plane–wave CASTEP DFT computation was performed using the HECToR national high-performance computing cluster.

$$\delta_{iso} = \sigma_{cal} - \sigma_{DFT} \quad (1)$$

$$\sigma_{cal} = \bar{x}(\delta_{iso\ experimental}) + \bar{x}(\sigma_{DFT}) \quad (2)$$

Acknowledgements

We thank the EPSRC for grant EP/E018203/1 from the Physical Organic Chemistry Initiative, the EPSRC Mass Spectrometry Service for data, and the Chemical Database Service[30] for access to the Cambridge Structural Database.[8] We thank Nottingham Trent University for support for diffraction facilities and EPSRC

for funding the National Crystallography Service at Southampton University. JVH thanks EPSRC and the University of Warwick for partial funding of the solid state NMR infrastructure at Warwick, and acknowledges additional support for this infrastructure obtained through Birmingham Science City: Innovative Uses for Advanced Materials in the Modern World (West Midlands Centre for Advanced Materials Project 2), with support from Advantage West Midlands (AWM) and partial funding by the European Regional Development Fund (ERDF). JVH acknowledges the facilities of HECToR, the UK's national high-performance computing service, which is provided by UoE HPCx Ltd at the University of Edinburgh, Cray Inc. and NAG Ltd, and funded by the Office of Science and Technology through EPSRC's High End Computing Programme.

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