Conformation and stereodynamics of 2,2′-disubstituted *N*,*N*′-diaryl ureas†

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Except in the most hindered of cases, *N*,*N*′-diaryl *N*,*N*′-dimethyl ureas adopt a conformation with the two aryl rings disposed *cis* to one another. Variable temperature NMR studies reveal the rate at which the Ar–N bonds rotate as well as the conformational preference of *ortho* disubstituted ureas in which more than one *cis* orientation is possible. In general, a conformation in which the aryl rings lie close in space but with their most bulky 2-substituents aligned *anti* is preferred, but with particularly bulky 2-substituents, conformations in which one of the aryl rings points away from the other may also be populated.

Introduction

Foldamers – oligomers which adopt a well-defined conformation over nanometre scales[1,2] – are a field of interest because of the potential use in materials or biological chemistry of such molecules. Many foldamers have been shown to adopt helical conformations, and in some cases those conformations have been controlled using side chain or terminal stereochemistry.[3,4] Foldamers made from polyamides or polyureas can be considered structurally analogous to helical peptides, and most foldamers of this type maintain their conformation through a network of hydrogen bonds.[2,4,5]

We are particularly interested in the potential of foldamers for transmission of stereochemical influences, and for that reason have sought to work with oligomers whose structure is compatible with a variety of potentially stereoselective reactions and which therefore do not contain acidic NH protons.[6] Governing conformation in such molecules is a challenge, but we have found that *dipole interactions* can be used to orientate a series of tertiary amide groups along a polyaromatic chain.[7] *π-Stacking interactions*[8] can also give rise to global conformational control: for example, extended stacked structures built from ureas of diamines have been reported to adopt helical conformations.[9]

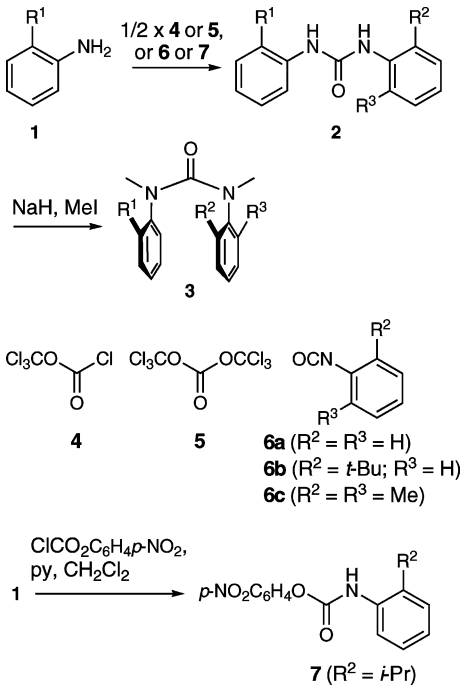
N-Methylation of aromatic amides and ureas has been proposed as a general strategy for control of conformation about the C–N bonds of such compounds, since it leads to structures in which close Ar–Ar contacts are prevalent.[10–13] However, little detailed work has been reported on the conformational preferences of simple mono-ureas, despite the fact that the helicity of an oligourea is dependent on the adoption by each individual urea linkage of a well-defined local conformation.

N,*N*′-Dimethyl-*N*,*N*′-diaryl ureas generally adopt a conformation about the two N–CO bonds that allows the aryl rings to lie *cis* to one another, presumably because of favourable π-stacking.[10,14–16] It has been suggested that a preference for π-stacking may be overcome, at least in the solid state, by electron-deficiency in the two aromatic rings.[15] In this paper we describe our kinetic and thermodynamic investigation of the conformation and stereodynamics of some simple ureas.[17]

Results and discussion

Synthesis of the ureas

Simple symmetrical ureas **3** ($R^1 = R^2$, $R^3 = H$, except **3k** which was made by the method used for unsymmetrical ureas described below) were made by condensing 2-substituted anilines **1** with diphosgene **4** or triphosgene **5**[18] and double methylation of the products **2** (Scheme 1; Table 1, entries 1–4 and 6). Condensation of *N*-methylanilines was slower, but avoided the methylation step and gave acceptable yields of products (entry 2).



Scheme 1 Synthesis of ureas.

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Table 1 Symmetric and unsymmetrical ureas

Entry	Reagent	R^1	R^2	R^3	Yield **2**	Product	Yield **3**
1	**4**	F	F	H	90	**3a**	98
2	**4**	Cl	Cl	H	70	**3b**	95
3	**5**	Br	Br	H	65	**3c**	70[a]; 65[b]
4	**4**	Me	Me	H	94	**3d**	95
5	**4**	Et	Et	H	96	**3e**	93
6	**7a**	Et	*i*-Pr	H	95	**3f**	81
7	**4**	*i*-Pr	*i*-Pr	H	97	**3g**	88
8	**6a**	Me	*t*-Bu	H	98	**3h**	96
9	**6a**	Et	*t*-Bu	H	97	**3i**	95
10	**4**	*i*-Pr	*t*-Bu	H	—	**3j**	79[c]
11	**6a**	*t*-Bu	*t*-Bu	H	98	**3k**	95
12	**6b**	F	Me	Me	80	**3l**	97
13	**6b**	Cl	Me	Me	93	**3m**	96
14	**6b**	Br	Me	Me	78	**3n**	98
15	**6b**	I	Me	Me	86	**3o**	77
16	**6b**	Me	Me	Me	86	**3p**	95
17	**6b**	Et	Me	Me	97	**3q**	97
18	**6b**	*i*-Pr	Me	Me	98	**3r**	94
19	**6b**	*t*-Bu	Me	Me	98	**3s**	90
20	**6b**	OMe	Me	Me	96	**3t**	66
21	**6b**	OCF_3	Me	Me	33	**3u**	95
22	**6c**	*t*-Bu	H	H	90[d]	**3v**	70[d]

[a] From **2** using dimethyl sulfate; [b] From **5** using *N*-methyl-2-bromoaniline; [c] Yield from **1**. [d] See references.[19,20]

Unsymmetrical ureas were made by one of two methods. When an appropriate isocyanate **6** was available, an aniline **1** was added to an isocyanate **6** and the product was methylated (Table 1, entries 8–21). With some relatively unhindered isocyanates, however, significant amounts of symmetrical ureas derived from the isocyanate component of the mixture were also formed, presumably by *in situ* hydrolysis of the isocyanate to an aniline. Replacing the isocyanate with an *O*-phenyl or *O*-*p*-nitrophenyl carbamate **7** (formed by addition of the aniline to phenyl or *p*-nitrophenyl chloroformate) solved this problem (entry 6). The "homocoupling" problem was much less significant when the isocyanate **6** was 2,6-disubstituted. Activated carbamates were also convenient alternatives when the appropriate isocyanates were not readily available commercially. Yields of the additions and methylations were good except in the cases with deactivated anilines (entry 21).

Conformation and stereodynamics

Many of the ureas **3** displayed exchange-broadened ^{1}H NMR spectra at room temperature. In most cases, however, the exchanging peaks decoalesced and were sharp at temperatures below −50 °C in toluene. At such temperatures, ureas **3l–u** show only one set of peaks, which includes (in most cases) a pair of diastereotopic methyl groups. Results described below show that urea N–CO bonds rotate slowly on the NMR timescale below −50 °C, so the simplicity of these spectra suggests that only a single N–CO–N conformer is populated in solution. Previous reports of conformational preference in *N*,*N*′-diaryl-*N*,*N*′-dialkyl ureas have concluded that the conformation in which both aryl rings lie close to one another (the *cis*,*cis* or *endo* conformation shown in Fig. 1) is generally preferred.[10,14–16] *Exo* conformers (see Fig. 3) of *N*,*N*′-diaryl-*N*,*N*′-dimethyl ureas are generally not observed: the only known example of such a urea favouring the *exo* conformation (in the solid state) is *N*,*N*′-dimethyl-*N*,*N*′-bis(2,4-dinitrophenyl)urea.[15]

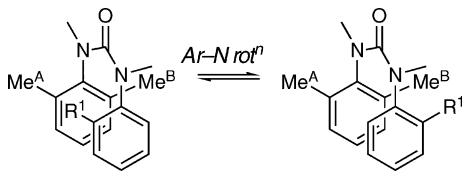

Fig. 1 Conformation and Ar–N rotation in **3l–u**.

The diastereotopicity of the 2,6-dimethyl groups furthermore indicates that both Ar–N bonds rotate slowly on the NMR timescale. Raising the temperature at which the ^{1}H NMR spectrum was acquired led to coalescence of the methyl signals. Rotation about either Ar–N bond interconverts these diastereotopic signals Me^A and Me^B (Fig. 1), and dynamic NMR techniques (modelling line broadening at increasing temperature in toluene using commercial software gNMR to quantify exchange rates) and Eyring analysis of the exchange rates obtained[21] allowed us to extract the associated free energies of activation $\Delta G^{\ddagger}$. These values can be interpreted as rates for Ar–N bond rotation about the less hindered of the two Ar–B bonds (though an alternative mechanism of interconversion, in which Ar–N rotation is not rate determining, is discussed below), and their values at temperatures close to the coalescence point are reported in Table 2. For purposes of comparison, estimates of the half life for interconversion of the conformers extrapolated to 298 K are also given in Table 2. No coalescence was observed in the case of **3s** – this compound is discussed further below.

Half-lives for conformational interconversion are consistent with those published for related compounds,[19] and increase slightly with increasing steric hindrance, though the steric effect is relatively small (except when R^1 = *t*-Bu), presumably either because the R^1 substituent moves away from the other ring during conformer interconversion about the Ar–N bond or because Ar–N rotation is not in fact rate determining in most cases (see below). Electron-withdrawing substituents have a lowering effect on the barrier height, perhaps by weakening the urea conjugation and allowing greater N–CO flexibility or by stabilizing the coplanar arrangement the ring, and the urea must pass through at the transition state for rotation. Only **3s** has a barrier high enough to suggest resolvability into atropisomers[22] – the estimated minimum barrier to enantiomerisation in this compound suggests a room

Table 2 Activation parameters associated with bond rotation in **3l–u**

Entry	Urea	R^1	$\Delta G^{\ddagger}$/kJ mol^{-1}	T/K[a]	$t_{1/2}$/ms (298 K)[b]
1	**3l**	F	38.0 ± 1.0	193	0.02
2	**3m**	Cl	50.9 ± 1.5	233	2.4
3	**3n**	Br	56.3 ± 1.5	263	5.0
4	**3o**	I	62.6 ± 1.5	288	15.6
5	**3p**	Me	52.9 ± 1.0	253	2.6
6	**3q**	Et	56.8 ± 1.5	273	5.2
7	**3r**	*i*-Pr	61.7 ± 1.5	298	7.5
8	**3s**	*t*-Bu	>84[c]	383	>5800
9	**3t**	OMe	48.9 ± 1.5	233	2.2
10	**3u**	OCF_3	39.4 ± 1.0	183	0.59

[a] Temperature for which $\Delta G^{\ddagger}$ is reported. [b] Estimated by extrapolation of the Eyring plot to 298 K. [c] Estimated minimum value: no coalescence at 110 °C.

Table 3 Activation parameters and ratios associated with conformer interconversion in **3**

Entry	Urea	R^1	R^4	Ratio of conformers *anti*-**3**:*syn*-**3**[a] (T/°C)[b]	$t_{1/2}$/ms (298 K)	$\Delta G^{\ddagger}_{min-maj}$/kJ mol^{-1} (298 K)	$\Delta G^{\ddagger}_{maj-min}$/kJ mol^{-1} (298 K)
1	**3a**	F	F	Broad (all)	—	—	—
2	**3b**	Cl	Cl	57 : 43 (−90)	0.15	51.9 ± 1.8	52.4 ± 1.8
3	**3c**	Br	Br	70 : 30 (−75)	5.0	60.2 ± 1.5	61.5 ± 1.5
4	**3d**	Me	Me	50 : 50 (−70)	0.11	51.4 ± 3.2	51.4 ± 3.2
5	**3e**	Et	Et	50 : 50 (−80)	3.4	59.8 ± 1.2	59.8 ± 1.2
6	**3f**	Et	*i*-Pr	60 : 40 (−50)	4.0	59.8 ± 1.5	60.6 ± 1.5
7	**3g**	*i*-Pr	*i*-Pr	70 : 30 (−30)	13.3	62.5 ± 1.5	64.2 ± 1.5
8	**3h**	Me	*t*-Bu	35 : 35 : 15 : 15 (−90)	1.8[d]	58.2 ± 1.3[d]	58.2 ± 1.3[d]
				70 : 30 (−20)	5.9[e]	60.5 ± 1.0[e]	62.1 ± 1.0[e]
9	**3i**	Et	*t*-Bu	35 : 35 : 15 : 15 (−90)	3.1[d]	59.6 ± 1.0[d]	59.6 ± 1.0[d]
				70 : 30 (−50)	7.0[e]	60.9 ± 1.0[e]	62.5 ± 1.0[e]
10	**3j**	*i*-Pr	*t*-Bu	Mixture (−90)	6.1[d]	—	—
				73 : 27 (−50)	26[e]	64.1 ± 1.5[e]	65.9 ± 1.5[e]
11	**3k**	*t*-Bu	*t*-Bu	Mixture (−90)	31[d]	—	—
				60 : 40 (+100)	—	—	—
12	**3v**	*t*-Bu	H	60 : 40 (−90)[c]	2.6	58.9 ± 0.9	59.5 ± 0.9

[a] Arbitrary assignment of *anti* stereochemistry to major conformer. [b] In d_8-toluene unless otherwise stated. [c] In CD_3OD. [d] Faster of two rotational processes. [e] Slower of two rotational processes.

temperature half-life of racemisation of at least minutes. The corresponding half-life for the other compounds is of the order of milliseconds.

In contrast with ureas **3l–u**, ureas **3a–g** showed two sets of peaks in their ^{1}H NMR spectra, corresponding to two conformers, at the slow exchange limit. As shown in Table 3, ratios of the conformers varied from 1 : 1 to 4 : 1, depending on the sizes of R^1 or R^2, and we assign them the structures *syn*-**3** and *anti*-**3** illustrated in Fig. 3. The paired signals coalesce on raising the temperature. Fig. 2 shows an example of the typical set of ^{1}H NMR spectra obtained for **3g**, illustrating paired signals at low temperature and the coalescences as the temperature rises. In this case, signals assigned to the two conformers coalesce between −10 and +20 °C, according to peak separation. A related study of an *N*,*N*′-dimethyl-bis(1-naphthyl)urea reported observation of an "uninformative" mixture of conformers.[16]

Given the known preference of similar ureas for *cis*,*cis* (*endo*) conformations, we assume the conformational interconversion observed by NMR is that between *anti*- and *syn*-**3a–g**, as illustrated in Fig. 3. We assume that the major conformer has the less sterically hindered *anti* stereochemistry.[23] We discount an alternative possibility, that one of the conformers results from isomerisation about the N–CO bond (the *exo* conformers in Fig. 3), since such conformers would then likewise have been observed in **3l–u**. Moreover, both conformers display ^{1}H NMR signals in the region δ 7.0–6.0, suggestive of a close Ar–Ar interaction.[10,12]

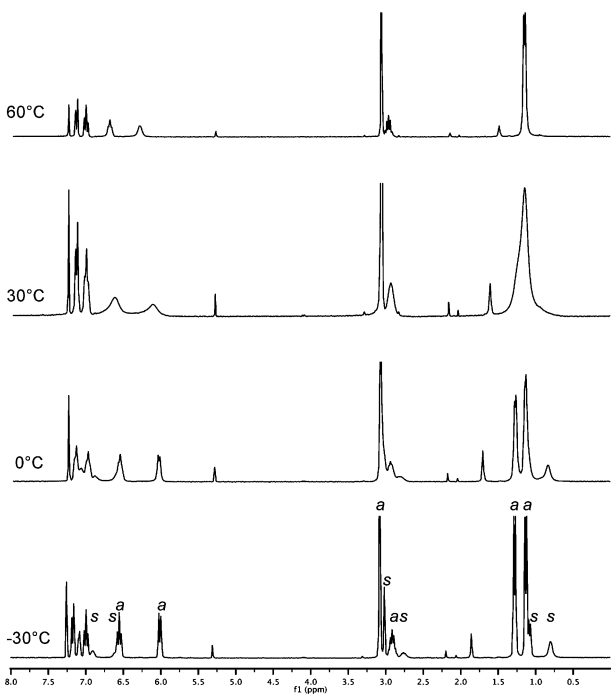

Fig. 2 VT NMR study of monourea **3g**. Signals labelled *a* correspond to *anti*-**3g**; signals labelled *s* correspond to *syn*-**3g**.

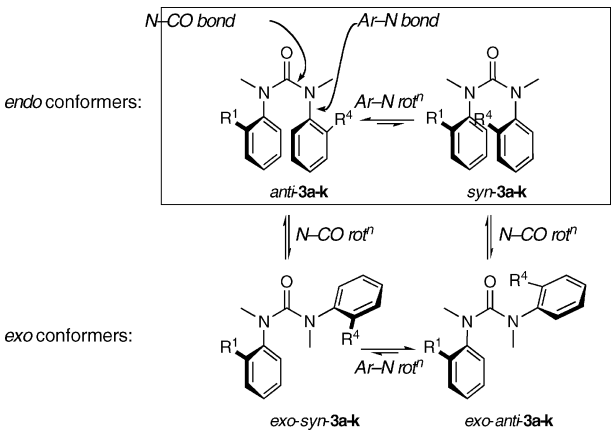

Fig. 3 Interconverting conformers of ureas **3a–k**.

Using the same dynamic NMR techniques as for **3l–u**[21] gave exchange rates associated with the interconversion of these conformers. As in Table 2, we associate these values with the rate of Ar–N bond rotation, though a possible alternative interpretation is that interconversion takes place *via exo* conformers with rate-determining N–CO rotation. Fig. 4 illustrates the lineshapes modelled at a series of temperatures around T_c, the coalescence temperature, for the *ortho* protons of **3e**. The ratios of the two conformers observed at the slow exchange limit are

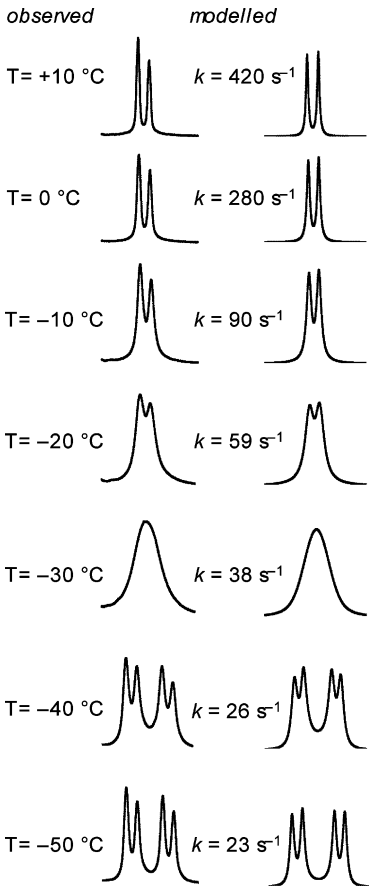

Fig. 4 Modelling lineshape in **3e** (*ortho* protons).

presented in Table 3, along with half-lives for interconversion of the conformers obtained by extrapolating (for purposes of comparison) the Eyring plots to 298 K. The rates are consistent with those previously determined for simpler analogues of **3**,[16,19] and (like the conformational ratios) are only weakly dependent on steric hindrance, presumably either because R^1 or R^4 moves away from the other ring during the rotation or because the interconversion does indeed proceed through rate-determining N–CO rotation. Conformational exchange in **3a** was too fast at accessible temperatures to determine kinetic parameters by VT NMR.

t-Butyl substituted ureas **3h–k** display different conformational behaviour. At low temperature (−90 °C in toluene or MeOH), *four* sets of peaks become apparent, presumably a result of appreciable population of conformers represented in Fig. 3 as *exo-anti*-**3** and *exo-syn*-**3**. Two of the conformers are similar to those seen in **3d–g** in that they display aromatic signals in the δ 6.6–6.0 ppm region, and we assume that these are *endo* conformers. The other two conformers have aromatic signals lying around δ 7.0 ppm, and we assume these are *exo* conformers, populated because of the greater steric hindrance experienced in these heavily substituted ureas. Although difficult to quantify precisely because of exchange broadening, the population of the *exo* conformers increases with increasing steric hindrance, and in **3k** the upfield *endo* signals form only perhaps 10% of the total aromatic signals. Evidence that the additional pairing of signals arises from the presence of *exo* conformers (which are reported to be favoured in bis(2,4-dinitrophenyl)ureas[15]) is provided by **3v**.[20] The symmetry of one of the rings precludes the existence of *syn* and *anti* isomers, but this compound nonetheless exhibits two clean sets of peaks in its ^{1}H NMR spectrum in a 60 : 40 ratio at −90 °C which coalesce at around −20 °C. One (the less abundant) of these sets of peaks clearly lacks the shielded aromatic ^{1}H NMR signals characteristic of the π-stacked ureas,[16] as expected for an *exo* conformer. We speculate that once the combined steric bulk carried by the two rings reaches a certain point, steric repulsion begins to counteract π-stacking interactions: a *t*-butyl group on either ring is sufficient to provide such a degree of repulsion.

On warming to around −50 to −20 °C, the signals in **3h–k** coalesce in pairs to give two sets of peaks in the ratios shown in Table 3. At higher temperatures, coalescence of the resulting pairs of signals takes place for **3h–j**, as observed for **3b–g**. Table 3 shows that the barriers to both bond rotations are similar in magnitude. The complexity of the signals arising from the interconverting mixture of four conformers at low temperature makes further detailed analysis impossible. The second coalescence does not take place for **3k**, whose ^{1}H NMR spectrum displays two conformers (in a ratio of about 60 : 40) at least up to 100 °C.

The conformational mixtures observed in ureas **3a–k** suggest that further extension of these compounds into oligoureas should serve only to compound the complexity of the conformational mixtures. This is clearly at odds with the reported well-defined helical conformations of more extended oligoureas.[9] Further work aimed at understanding the origin of the conformation of helical oligoureas is under way.

Experimental

Full experimental data is given in the supporting information. Typical procedures are listed below. Details of instrumentation *etc.* have been reported before.[13]

1,3-Bis(2-isopropylphenyl)urea, 2g

2-Isopropylaniline (1.35 g, 1.42 cm^3, 10 mmol), was dissolved in CH_2Cl_2 (20 cm^3) at 0 °C and triethylamine (2.2 g, 3.1 cm^3, 22 mmol) added in one portion. Diphosgene (0.99 g, 0.60 cm^3, 5.0 mmol) was added dropwise and the reaction mixture allowed to warm to room temperature over 18 h. The white precipitate was isolated and recrystallised from EtOAc–pentane to give *1,3-bis(2-isopropylphenyl)urea* **2g** (2.87 g, 97%), as white plates, m.p. 188–190 °C (from EtOAc–pentane); R_f (EtOAc–pentane, 3 : 7) 0.50; υ_{max} (film)/cm^{-1} 3318 and 3302 (N–H) and 1647 (C=O); δ_H (400 MHz; d_6-DMSO) 8.63 [2 H, s, (NH) × 2], 7.57 (2 H, dd, *J* 8.0 and 2.0, CH-d), 7.24 (2 H, dd, *J* 8.0 and 2.0, CH-a), 7.10 (2 H, td, *J* 8.0 and 2.0, CH-c), 7.03 (2 H, td, *J* 8.0 and 2.0, CH-b), 3.31 [2 H, hept, *J* 7.0, (CH) × 2] and 1.20 [12 H, d, *J* 7.0 (CH_3) × 4]; δ_C (100 MHz; d_6-DMSO) 154.9 (C=O), 140.6 (C), 136.7 (C), 126.2 (CH), 125.8 (CH), 124.8 (CH), 124.4 (CH), 27.5 (CH) and 23.9 (CH_3); *m/z* (CI) 297 (100%, M + H$^+$); (Found: M + H$^+$, 297.1959, $C_{19}H_{24}N_2O$ requires M + H, 297.1962).

1-(2-Isopropylphenyl)-3-(2,6-dimethylphenyl)urea, 2r

2-Isopropylaniline (0.68 g, 0.71 cm^3, 5.0 mmol), was dissolved in CH_2Cl_2 (10 cm^3) at room temperature. 2,6-Dimethylphenyl isocyanate (0.74 g, 0.70 cm^3, 5.0 mmol) added dropwise and

stirred for 20 h. The solvent was removed under reduced pressure and the residue recrystallised from EtOAc–petrol to give *1-(2-isopropylphenyl)-3-(2,6-dimethylphenyl)urea* **2r** (1.5 g, 98%), as white cubes, m.p. 255–257 °C (from EtOAc–pentane); R_f (EtOAc–pentane, 1 : 4) 0.29; υ_{max} (film)/cm^{-1} 1631 (C=O); δ_H (400 MHz; d_6-DMSO) 7.92 [1 H, s, $(NH)_A$], 7.89 [1 H, br., $(NH)_B$], 7.58 (1 H, dd, *J* 8.0 and 2.0, CH-d), 7.24 (1 H, dd, *J* 8.0 and 2.0, CH-a), 7.10 (1 H, td, *J* 8.0 and 2.0, CH-c), 7.07–6.98 (4 H, m, CH-b, CH-e and CH-f), 3.18 [1 H, hept, *J* 7.0, (CH)], 2.21 [6 H, s, $(CH_3) \times 2$] 1.20 [3 H, s, $(CH_3)_A$] and 1.18 [3 H, s, $(CH_3)_B$]; δ_C (100 MHz; d_6-DMSO) 154.2 (C=O), 140.2 (C), 136.8 (C), 136.3 (C), 136.2 (C), 128.4 (CH), 126.5 (CH), 126.4 (CH), 125.8 (CH), 124.5 (CH), 124.4 (CH), 125.4 (CH), 27.6 (CH), 23.7 (CH_3) and 18.9 (CH_3); *m/z* (ESI$^+$) 283 (100%, M + H$^+$); (Found: M + H$^+$, 283.1804, $C_{18}H_{22}N_2O$ requires M + H, 283.1810).

1,3-Bis(2-isopropylphenyl)-1,3-dimethylurea, 3g

1,3-Bis(2-isopropylphenyl)urea **2g** (1.72 g, 5.8 mmol) was dissolved in THF (50 cm^3) and cooled to 0 °C. Sodium hydride (0.58 g, 14.5 mmol) was added portionwise and stirred at room temperature for 1 h. Methyl iodide (1.1 cm^3, 17.4 mmol) was added and stirred at room temperature for 18 h. Water (40 cm^3) was added and extracted with EtOAc (3 × 40 cm^3). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2; 10% EtOAc in pentane) to give *1,3-bis(2-isopropylphenyl)-1,3-dimethylurea* **3g** (1.65 g, 88%), as white prisms, m.p. 195–197 °C (from EtOAc–pentane); R_f (EtOAc–pentane, 3 : 7) 0.61; υ_{max} (film)/cm^{-1} 1646 (C=O); δ_H (400 MHz; $CDCl_3$) 7.05 (2 H, d, *J* 7.0, CH-d), 6.91 (2 H, t, *J* 7.0, CH-c), 6.55 (2 H, br., CH-a), 6.07 (2 H, br., CH-b), 2.97 [6 H, s, $(NCH_3) \times 2$], 2.86 [2 H, br., (CH) × 2] and 1.05 (12 H, br., $(CH_3) \times 4$]; δ_C (100 MHz; $CDCl_3$) 162.9 (C=O), 146.0 (C), 142.9 (C), 128.3 (CH), 126.9 (CH), 126.6 (CH), 126.3 (CH), 40.2 (NCH_3), 27.3 (CH), 25.9 (CH_3) and 23.5 (CH_3); *m/z* (ESI$^+$) 325 (100%, M + H$^+$); (Found: M + H$^+$, 325.2274. $C_{21}H_{29}N_2O$ requires M + H, 325.2270). Elem. Anal. for $C_{21}H_{28}N_2O$: calcd: C, 77.74%; H, 8.70%; N, 8.63%; found: C, 77.68%; H, 8.79%; N, 8.63%.

1-(2-Isopropylphenyl)-1,3-dimethyl-3-(2,6-dimethylphenyl)urea, 3r

1-(2-Isopropylphenyl)-3-(2,6-dimethylphenyl)urea **2r** (1.20 g, 4.2 mmol) was dissolved in THF (30 cm^3) and cooled to 0 °C. Sodium hydride (0.42 g, 11.5 mmol) was added portionwise and stirred at room temperature for 1 h. Methyl iodide (0.86 cm^3, 12.6 mmol) was added and stirred at room temperature for 18 h. Water (40 cm^3) was added and extracted with EtOAc (3 × 30 cm^3). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2; 10% EtOAc in pentane) to give *1-(2-isopropylphenyl)-1,3-dimethyl-3-(2,6-dimethylphenyl)urea* **3r** (1.24 g, 94%), as off-white blocks, m.p. 90–92 °C (from EtOAc–pentane); R_f (EtOAc–pentane, 1 : 4) 0.73; υ_{max} (film)/cm^{-1} 1632 (C=O); δ_H (400 MHz; $CDCl_3$) 7.12 (1 H, d, *J* 7.0, CH-d), 7.05 (1 H, d, *J* 7.0, CH-a), 6.90 (2 H, br., CH-b and CH-c), 6.71 (2 H, br., CH-e^1 and CH-e^2), 6.19 (1 H, br., CH-f), 3.07 [3 H, s, $(NCH_3)_A$], 3.02–2.90 [4 H, br., (CH) and $(NCH_3)_B$], 2.08 [3 H, s, $(CH_3)_A$], 1.63 [3 H, s, $(CH_3)_B$] and 1.11 [6 H, s, 2 × (CH_3)]; δ_C (100 MHz; $CDCl_3$) 164.4 (C=O), 146.6 (C), 143.0 (C), 142.3 (C), 136.8 (C), 136.4 (C), 128.8 (CH), 128.7 (CH), 128.6 (CH), 127.2 (CH), 126.8 (CH), 126.6 (CH), 126.2 (CH), 40.4 $(NCH_3)_A$, 37.4 $(NCH_3)_B$, 27.4 (CH), 25.6 $(CH_3)_A$, 23.4 $(CH_3)_B$, 18.0 $(CH_3)_C$ and 17.9 $(CH_3)_D$; *m/z* (ESI$^+$) 311 (100%, M + H$^+$); (Found: M + H$^+$, 311.2098, $C_{20}H_{26}N_2O$ requires M + H, 311.2118). Purity was established by LC–MS analysis.

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