Microwave-assisted Nucleophilic Cleavage of 5,7-Dimethyl-2-phenyl-1-oxo-1*H*-pyrazolo[1,2-*a*]pyrazol-4-ylium-3-olate to α-Phenylmalonamides

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Three α-phenylmalonamides have been prepared by the selective nucleophilic cleavage of 5,7-dimethyl-2-phenyl-1-oxo-1*H*-pyrazolo[1,2-*a*]pyrazol-4-ylium-3-olate in solventless microwave syntheses. The three weak nucleophiles employed were aniline, *p*-chloroaniline and *m*-toluidine. The α-phenylmalonamides of these three aniline derivatives could not be prepared using the previously reported solvent syntheses *via* 3-oxopyrazolo[1,2-*a*]pyrazol-8-ylium-1-olates. All products were characterised using, infrared spectroscopy, ^{1}H nmr and electrospray mass spectrometry. The single crystal X-ray structures of the starting pyrazolo-[1,2-*a*]pyrazole and α-phenylmalon-*m*-toluidide are also reported.

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Introduction.

In 1980 K.T. Potts *et al.* [1] investigated the reaction of the strong bielectrophile, (chlorocarbonyl)phenylketene (**1a**), with pyrazole (**2a**), which led to the formation of a new type of heterocyclic zwitterion, anhydro-1-hydroxy-3-oxo-2-phenylpyrazolo[1,2-*a*]pyrazolium hydroxide (**3a**) (Figure 1). Compound (**3a**) could also be produced by the reaction of malonaldehyde diethyl acetal and 3,5-dihydroxy-4-phenylpyrazole when the reaction was catalysed by H_2SO_4. Phenyl-, methyl- and methylthio-substituted pyrazoles and benzopyrazole derivatives gave substituted derivatives of **3**. A concurrent paper in 1980 by W. Friedrichsen [2] reported five derivatives of **3**, which he called 1-oxo-1*H*-pyrazolo[1,2-*a*]pyrazol-4-ium-3-olates; prepared by the reaction of malonyldichlorides (**1b**) and substituted pyrazoles. In 1982, Zvilichovsky and David [3] formed more substituted derivatives of **3** by the condensation of 1,3-dicarbonyl compounds with 3,5-dihydroxy-4-phenylpyrazole and its analogues. It was in this paper that compounds of **3** were found to decompose under the influence of bases and amines and the kinetics of decomposition with morpholine were studied. Two main breakdown routes, and the subsequent formation of the breakdown products, were dependant on several factors

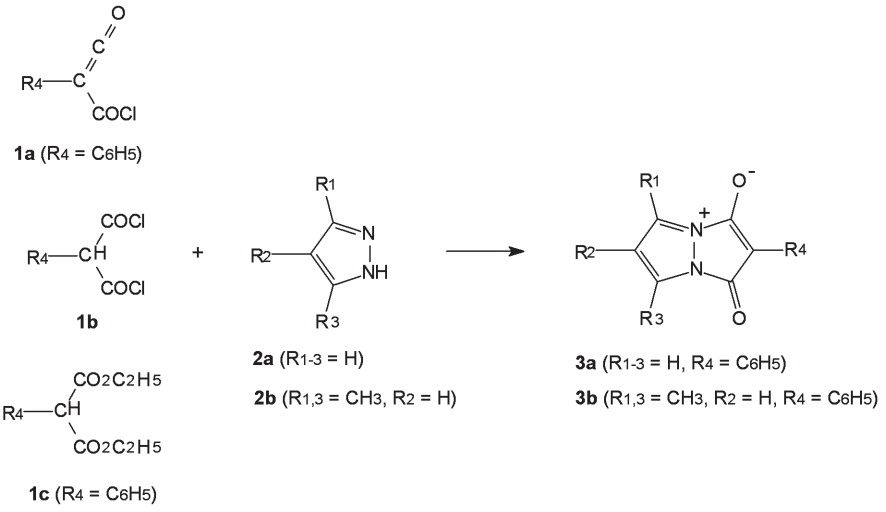

Figure 1. Selected synthetic routes to 3-oxopyrazolo[1,2-a]pyrazol-8-ylium-1-olates.

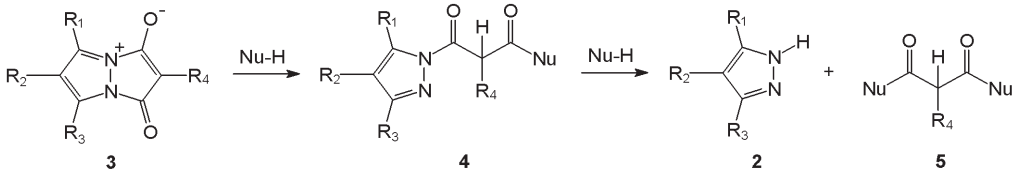

Figure 2. Suggested breakdown pathway for the decomposition of **3** with nucleophiles.

including the presence of water in the reaction solution and the substituents on **3**. Continuing work by Potts *et al.* [4] altered the naming scheme of **3** to 3-oxopyrazolo[1,2-*a*]pyrazol-8-ylium-1-olate, similar to that of Friedrichsen. In Potts *et al*.'s final major work on **3** [4d], decomposition with nucleophiles (primarily morpholine, aniline or water) was studied in more detail and a breakdown pathway suggested (Figure 2). This current work covers the development of methods to improve the general preparation of malonamide derivatives from the nucleophilic cleavage of **3**, thus microwave driven decomposition was investigated.

et al. [4d] found that **3b** decomposed by nucleophilic cleavage over several days at 25 ˚C, compared to a few seconds for the unsubstituted derivative. For this current study, three weak nucleophiles (aniline, *p*-chloroaniline and *m*-toluidine) where chosen because it was not possible to prepare the three aniline derivatives, to the same level of quality as the heterocyclic amines, using the boiling solvent and precipitation methods previously employed by Potts *et al*. [4d]. With the anilines, minimal product was formed after 5 – 6 days of reflux in THF. In this current study, all compounds were characterised using infrared

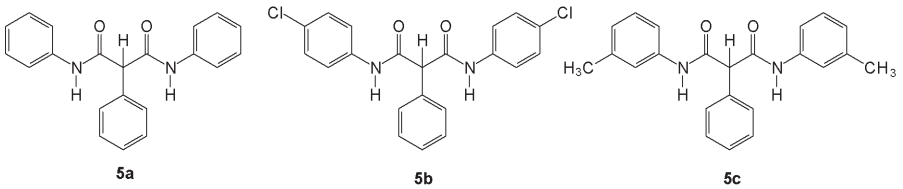

Figure 3. Chemical diagrams of the α-phenylmalonamides prepared in this study.

Vast reductions in both reaction times and thermal decomposition products are the two main advantages of microwave synthesis. In recent years interest into the suitability of microwave irradiation for the synthesis of organic compounds has greatly increased [5]. For example, Veverkova *et al*. [5d] synthesised 9-sustituted acridine derivatives in a 120 W microwave shortening the reaction time from 20-40 hours for the conventional method to 3-8 minutes, with yields between 60 – 80 %. Aniyappan *et al*. [6] synthesised derivatives of 1,4-dihydropyridines in a domestic microwave with reaction times of 0.75 – 3 minutes (pulsed every 15 seconds) and produced very high yields. Furthermore, Karale *et al*. [7] successfully prepared derivatives of 3-methyl-4-[(chromon-3-yl)-methylene]-1-phenylprazolin-5-(4*H*)-one without solvent or the required catalysts using a domestic microwave, taking only 2 – 5 minutes and in good yields. Massicot *et al*. [8] also prepared tartramides in a solvent-free synthesis using microwave activation while selective peptide bond cleavage in acid solutions has been achieved by Wu *et al*. [9] through the use of microwave techniques. Many microwave syntheses have been performed using polar solvents, such as alcohol, DMF and water as these mediums efficiently transfer absorbed energy to the reaction. Solvent free synthesis has the advantage of saving on materials and time, as there is no solvent to remove after completion of the reaction, thus increasing overall reaction efficiency.

Reported here are the results of how the use of microwave synthesis was employed to significantly improve the breakdown reaction rate of **3b**. This specific analogue was chosen because of its very low rate constant in reactions with morpholine, a strong nucleophile. Potts

spectroscopy, ^{1}H NMR and electrospray mass spectrometry. The single crystal X-ray structures of **3b** and α-phenylmalon-*m*-toluidide **5c** (Figure 3) are also reported.

Results and Discussion.

Preparation and Structure for **3b**.

The synthesis of **3b** was adopted from the method of Kappe and Kos [10] where derivatives of **3** were prepared by the reaction of substituted diethyl malonates with substituted pyrazoles in a 2:1 ratio. Compound **3b** was prepared from **1c** and **2b** with the loss of two molar equivalence of ethanol. Diphenyl ether was used as the solvent because of its high boiling point (bp 258 – 260 ˚C), which took the reaction over 200 ˚C, instead of relying on the boiling point of the malonate (bp 201 ˚C). The use of this particular solvent meant that the reactant ratios could be made more equivalent although the ethanol produced had to be irreversibly removed because its presence in the reaction solution lowered the boiling point of the solvent and dramatically reduced the formation of product. Furthermore, the ease of sublimation of **2b** meant that some of this reactant was lost in the open system although use of a distillation head allowed most of the sublimed material to be recollected. Yield using this procedure (as opposed to that outlined in reference [10]) was also improved by adding the thermally unstable malonate only when the solvent containing **2b** had begun to boil.

The infrared, ^{1}H nmr and melting point data for **3b** have been previously reported by three separate groups [2,4d,10] but the electrospray mass spectroscopy (es-ms) results have not. In the es-ms spectrum a dominant molecular ion ($M+H^+$) peak at m/z 241 is observed as well as lesser ($M+Na^+$) (m/z 263) and ($2M+Na^+$) (m/z 503) peaks.

Es-ms experiments for **3b** were conducted analogous to those done for a series of squaraine dyes where self-assembled superstructures of doubly charged (xM+2Na$^+$) ions of up to x = 10 were formed [11]. Compounds such as **3** and squaraines share similar molecular characteristics such as resonant C–O$^-$ moieties which are suspected to create a coordination sphere around the Na$^+$ ions. Experimentally, collection of the es-ms spectra required the use of dry injection solvents. Langley *et al*. [11], observed that the presence of water in the injection solvent hindered the self-assembly process, leaving only a molecular ion peak and possibly a 2M species.

The X-ray crystal structure of **3a** has been previously published [12] and the bond distances have generated significant discussion about the resonant nature of these compounds. The structure of **3a** comprises an essentially flat molecule with a 7.3º dihedral angle between the fused pyrazole rings and the phenyl ring. The structure of **3a** resides on a two-fold axis thus only half of the molecule is unique. The structure of **3b** (Figure 4) comprises a full molecule with a dihedral angle of 16.61(5)º. Table 1 lists

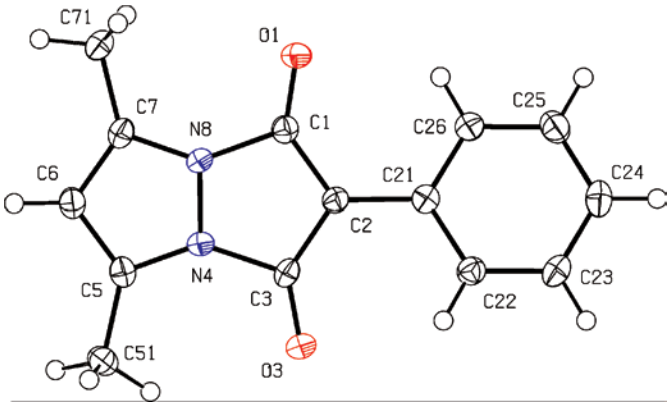

Figure 4. Molecular configuration and atom numbering scheme for **3b**, showing 50% probability ellipsoids.

selected bond distances for the structures of both **3a** and **3b**. The bond lengths obtained for **3b** are highly consistent with those for **3a**, with the only molecular difference between the two compounds being the inclusion of the two methyl groups in **3b** on C5 and C7. The resonant C–O$^-$ bonds in both compounds are slightly longer than the average C=O bond length of 1.200(12) Å [13], being between 1.215(3) - 1.219(2) Å. The N–N bond lengths for **3a** and **3b** are slightly shorter than the average N–N single bond of 1.366(19) Å [13]. There is no difference between the C1–C2 and C2–C3 bond lengths in both compounds [1.409(2) – 1.422(2) Å] and the similar bond lengths in pyrazole [av. 1.412(16) Å] [13]. Bond lengths for C1–N8 and C3–N4 are close to C–N single bonds [av. 1.498(18) Å] [13] but the C5–N4 and C7–N8 bonds are much shorter,

Table 1
Selected bonds distances (Å) for **3a** [12] and **3b**.

	3a	**3b**
C1–O1	1.215(3)	1.219(2)
C1–C2	1.410(4)	1.409(2)
C1–N8	1.491(3)	1.478(2)
C2–C3	1.411(3)[a]	1.422(2)
C3–O3	1.216(3)[a]	1.219(2)
C3–N4	1.492(4)[a]	1.481(2)
N4–C5	1.336(4)[a]	1.352(2)
N4–N8	1.340(3)	1.352(2)
C5–C6	1.372(5)[a]	1.387(2)
C6–C7	1.386(5)	1.389(2)
C7–N8	1.335(4)	1.352(2)

[a] generated distances.

being between expected pyrazole C–N bonds [av. 1.359(12) Å] [13] and C=N bonds [av. 1.331(14) Å] [13]. All bond lengths in both compounds are consistent with the charge delocalisation over the molecule with the negative charge across the β-diketone enolate and phenyl ring and the positive charge over the pyrazolium ring. This charge delocalisation explains the shorter C–N bond lengths in the pyrazolium ring, where the positive charge is delocalised over the whole pyrazolium ring making the bonds in this part of the molecule very strained and shorter. In the other ring, where the negative charge is mostly delocalised through the O–C–C–C–O moiety, the C–N bonds are correspondingly longer.

Nucleophilic Cleavage and Structure for **5**.

The microwave preparation of the α-phenylmalonamides, one of the breakdown products of **3b**, required the heating of **3b** and a nucleophile in a high-walled sealed vessel in a microwave for 3 minutes. Most of the produced pyrazole sublimed up the sides of the reaction vessel, hence the use of the high walls, so extraction of the malonamide using minimal THF, precipitation and subsequent washing with a **2b** miscible solvent (such as ethanol) yielded high purity products. The microwave synthesis method developed for the aniline-based compounds in this study was extremely efficient and gave very high yields for the three malonanilides. One specific advantage in these reactions, and the predominant reason for their high reaction efficiency, is the production of a by-product with a high sublimation rate thus **2b** could be separated from the malonamides as the reaction proceeded. The use of a sealed high-walled vessel allowed the pyrazole to condense and crystallise in an area of the container away from the malonamide. The optimal reaction time of 3 minutes was determined by carrying out small-scale reactions using **3b** and morpholine at different times from 30 seconds to 12 minutes (pulsed every 30 seconds) and then running a thin layer chromatography plate using ethyl acetate as the solvent.

From these experiments it was found that up to 2.5 minutes, **3b** was still present but after 3.5 minutes the reactants started to char/decompose and the malonamide could not be recovered. Visually, 3 minutes was when all of the red colouration from **3b** disappeared. No solvent was required for any of the reactions in the microwave because the first two nucleophiles used are all liquids at room temperature and *p*-chloroaniline although a solid, has a melting point 69 – 72 °C, and quickly turned to liquid upon irradiation in the microwave. Interestingly, when the morpholine microwave experiments were scaled up the resultant α-phenylmalonamide could not be obtained in high yield. In summary, these results show that the stronger nucleophiles, but weaker acids, are best suited to a solvent reflux reaction whereas the weaker nucleophiles, but stronger acids, react well using microwave techniques. The corresponding pK_a values for each of the nucleophiles are 8.33 (morpholine), 4.63 (aniline), 4.15 (*p*-chloroaniline) and 4.73 (*m*-toluidine) showing a significant difference between the heterocyclic amine and the anilines. Further studies are planned to investigate the performance in the microwave of nucleophiles with pK_a values between 5 – 8.

Two characteristic bands are commonly observed in the infrared spectra of amides, these are the carbonyl stretching vibration between 1690 – 1650 cm^{-1} and the N-H stretching absorption around 3300 cm^{-1}. The frequency of the carbonyl vibration is lower for amide C=O than for esters or ketones and can be reduced by as much as 20 – 60 cm^{-1} [14,15]. The carbonyl peaks for the secondary amides **5a** – **5c** have an expectedly higher range of 1679 – 1641 cm^{-1}. The larger than expected reduction in C=O position for these types of amides may be due to the constraining effects of hydrogen-bonding associations to the carbonyl oxygen atoms, observed in the crystal structure of **5c**. Interestingly, each of the carbonyl peaks are split with differences of 20 – 45 cm^{-1} between the separate peaks, which is not uncommon for amide C=O peaks [14]. The infrared spectra of the secondary amides **5a** – **5c** also show N–H stretching frequencies 3310 – 3258 cm^{-1}. Standard ^1H nmr spectra was obtained for all of the malonamides. In terms of es-ms analysis, self-assembly with Na^+ ions was also a possibility with the presence of the two carbonyl oxygens per malonamide thus each of the spectra were run analogous to the Langley *et al.* [11] experiments. All spectra show ($M+H^+$), ($M+Na^+$) and ($2M+Na^+$) peaks except for **5b** and **5c** that do not show ($M+H^+$). However, the interesting aspect of the behaviour of these compounds in es-ms analysis is the increased occurrence of the ($xM+Na^+$) species, which in all spectra are significantly stronger than the ($M+H^+$) species. The X-ray crystal structure of **5c** is shown in Figure 5 while a packing diagram of **5c** showing the N–H—O hydrogen-bonding interactions is given in Figure 6. Direct syntheses and varying chemical data for **5b** [16] and **5c** [17] have been previously published but the only previously reported structures similar to the **5** series of molecules are α-phenylmalonamide [18], α-phenylmalonpiperadide and α-phenylmalonmorpholide [19].

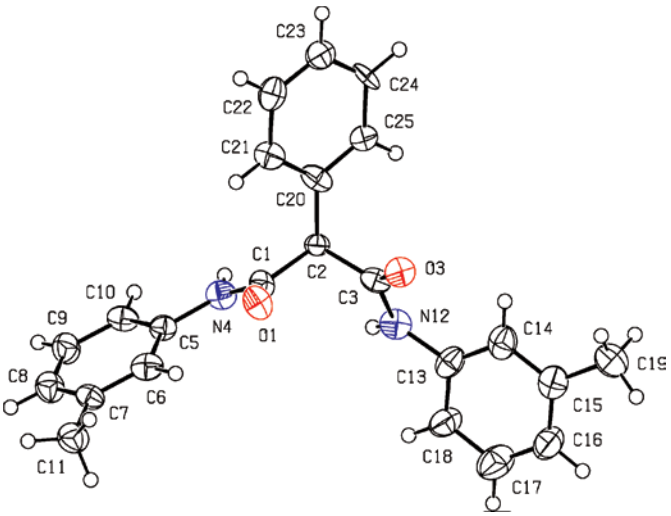

Figure 5. Molecular configuration and atom numbering scheme for **5c**, showing 50% probability ellipsoids.

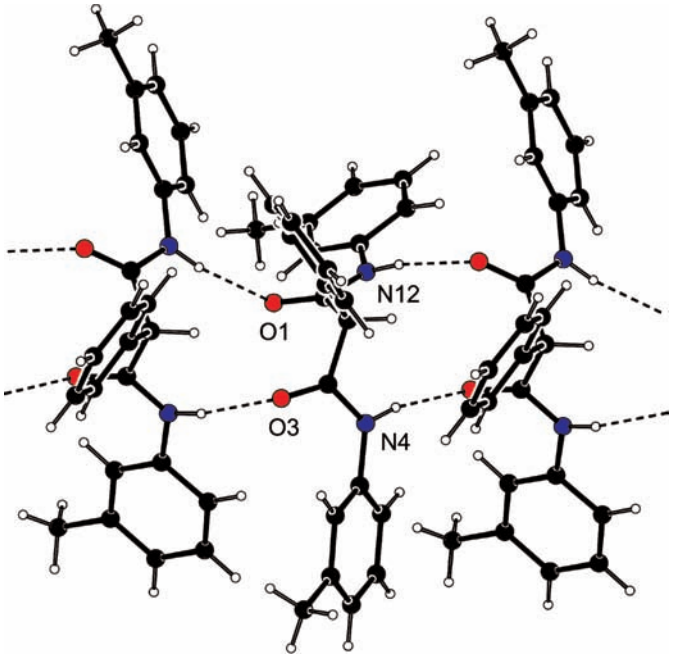

Figure 6. Molecular packing for **5f**. Hydrogen-bonding interactions are shown as dotted lines; N4–H—-O3 2.927(8) Å (x, -y + $1^1/_2$, z + $^1/_2$) and N12–H—-O1 2.891(8) Å (x, -y + $1^1/_2$, z + $^1/_2$).

EXPERIMENTAL

3,5-Dimethylpyrazole, diethyl phenylmalonate, diphenyl ether**,** aniline, *p*-chloroaniline and *m*-toluidine were obtained

Table 2

Crystallographic details for **3b** and **5c**.

	3b	**5c**
CCDC reference	204756	204759
Formula	$C_{14}H_{12}N_2O_2$	$C_{23}H_{22}N_2O_2$
M_r	240.26	358.43
Crystal class	monoclinic	monoclinic
Space group	$P2_1/c$	$P2_1/c$
a (Å)	7.3624(3)	8.9449(6)
b (Å)	11.4935(4)	24.068(2)
c (Å)	13.9255(7)	9.1160(8)
? (?)	94.287(1)	109.095(5)
V(Å^3)	1175.08(9)	1854.6(3)
D_c (g cm^{-3})	1.358	1.284
Z	4	4
μ(Mo-K_α) (mm^{-1})	0.93	0.82
T_{min}, T_{max}	0.982, 0.991	0.988, 0.998
Colour	red	colourless
Crystal size (mm)	0.20 x 0.10 x 0.10	0.15 x 0.05 x 0.02
Total data	8861	9295
Unique data	2689	3532
R_{int}	0.063	0.316
N [I>2.0σ(I)]	1944	877
R1	0.046	0.092
wR2	0.106	0.147
S	1.01	0.88
A[a]	0.0649	0.0436

[a] $w = [\sigma^2(F_o^2) + (AP)^2]^{-1}$ [where $P = (F_o^2 + 2F_c^2)/3$]

from Key Organics Ltd. Aniline and *m*-toluidine were distilled before use and *p*-chloroaniline was re-crystallised from ethanol. Infrared spectra were recorded as pressed KBr discs on a Nicolet 205 FT-IR spectrometer. ^{1}H NMR data were recorded on a Bruker Spectrospin 400 NMR spectrometer. Electrospray mass spectra were recorded in positive ion mode on a Micromass Platform mass spectrometer (Southampton University).

5,7-Dimethyl-2-phenyl-1-oxo-1*H*-pyrazolo[1,2-*a*]pyrazol-4-ylium-3-olate (**3b**).

Diethyl phenylmalonate (**1c**) (39.7 g, 0.18 mol) was dropwise added to a boiling solution of 3,5-dimethylpyrazole (**2b**) (13.4 g, 0.14 mol) in diphenyl ether (80 mL) and boiled for a further 30 minutes. A distillation head was fitted to the top of the reaction vessel to allow for the removal of ethanol as well as the recollection of **2b** and any solvent vapour lost during the reaction. Upon cooling the product precipitated and was collected *in vacuo* and washed with light petroleum (40 – 60 °C), yielding intensely coloured red crystals, 5.93 g (18%); ir (KBr): 1672 (C–O$^-$); ^{1}H nmr (400 MHz, d-DMSO, Me_4Si): δ 2.65 (s, 6 H, CH_3), 6.65 (s, 1 H), 7.05 - 7.35 (m, 3 H, ArH), 7.95 - 8.00 (m, 2 H, ArH); es-ms: m/z 241 (12) (M+H$^+$), 263 (100) (M+Na$^+$), 503 (28) (2M+Na$^+$).

N^1,*N*^{3},2-Triphenylmalonamide (**5a**), *N*^{1},*N*^{3}-Bis(4-chlorophenyl)-2-phenylmalonamide (**5b**), 2-Phenyl-*N*^{1},*N*^{3}-di-*m*-tolylmalonamide (**5c**).

For **5a**, 2:1 molar amounts of aniline (0.39 g, 4.17 mmol) and **3b** (0.50 g, 2.08 mmol) were heated in a sealed 10 mL glass sample vial in a 800 W Daewoo microwave for 3 minutes. Upon cooling the crude product was dissolved in minimal THF and pipetted into 100 mL of cool deionised water. Collection *in vacuo* followed by washing with minimal amounts of cool ethanol yielded a white powder, 0.58 g (84%), mp 196 – 198°; ir (KBr): 3310 (NH), 3026 (CH), 1677, 1650 (CO); ^{1}H nmr (400 MHz, d-DMSO, Me_4Si): δ 4.90 (s, 1 H), 7.04 - 7.65 (m, 15 H, ArH), 10.25 (s, 2 H, NH); es-ms: m/z 331 (94) (M+H$^+$), 353 (100) (M+Na$^+$), 683 (86) (2M+Na$^+$).

Anal. Calcd. for $C_{21}H_{18}N_2O_2$: C, 76.33; H, 5.49; N, 8.48. Found: C, 76.23; H, 5.48; N, 8.40.

Compound **5b** was produced analogous to **5a** using *p*-chloroaniline (0.53 g, 4.17 mmol) and **3b** (0.50 g, 2.08 mmol). The final product was collected *in vacuo* as an off-white solid, 0.60 g (72%), mp 219 – 221°; ir (KBr): 3258 (NH), 3057 (CH), 1679, 1641 (CO); ^{1}H nmr (400 MHz, d-DMSO, Me_4Si): δ 4.90 (s, 1 H), 7.28 - 7.68 (br m, 13 H, ArH), 10.36 (s, 2 H, NH); es-ms: m/z 421 (100) (M+Na$^+$), 423 (70) (M+Na$^+$), 821 (59) (2M+Na$^+$).

Anal. Calcd. for $C_{21}H_{16}Cl_2N_2O_2$: C, 63.31; H, 4.05; N, 7.04. Found: C, 63.30; H, 4.02; N, 7.10.

Compound **5c** was produced analogous to **5a** using *m*-toluidine (0.45 g, 4.17 mmol) and **3b** (0.50 g, 2.08 mmol). The final product was collected *in vacuo* as an off-white solid, 0.50 g (68%), mp 180 – 182°; ir (KBr): 3260 (NH), 3063, 2920 (CH), 1675, 1655 (CO); ^{1}H nmr (400 MHz, d-DMSO, Me_4Si): δ 2.25 (s, 6 H, CH_3), 4.90 (s, 1 H), 6.80 - 7.90 (m, 13 H, ArH), 10.15 (s, 2 H, NH); es-ms: m/z 381 (46) (M+Na$^+$), 739 (100) (2M+Na$^+$).

Anal. Calcd. for $C_{23}H_{22}N_2O_2$: C, 77.06; H, 6.19; N, 7.82. Found: C, 77.08; H, 6.20; N, 7.78.

X-ray Structure Analysis.

General crystallographic details for compounds **3b** and **5c** are listed in Table 2. All crystals were grown from chloroform solutions. Crystallographic data was collected on a Bruker Nonius Kappa CCD area diffractometer using monochromatised Mo-Kα X-ray radiation (λ = 0.71073Å) equipped with an Oxford Cryosystems low temperature device (Southampton University). Lattice parameters were calculated using 4997 **3b** and 6197 **5c** reflections with $2.91° < \theta < 27.48°$. Intensity data were collected at a temperature of 120 K using φ-ω scans to a maximum 2θ value of 55°. Multi-scan absorption corrections were applied to all data sets using the program SORTAV [20]. Structures were solved by direct methods and refined using the SHELX-97 package [21]. All hydrogen atoms not involved in the strong hydrogen-bonding associations were included in the refinement at calculated positions as riding models with C-H set to 0.95 Å (Ar-H), 0.98 Å (CH_3) and 1.00 Å (CH). The NH hydrogen atoms in **5c** were located by difference methods and both positional and thermal parameters were refined. For **5c**, a high R_{int} value was the result of weak high angle data.

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REFERENCES AND NOTES

[1] K. T. Potts, S. Kanemasa and G. Zvilichovsky, *J. Am. Chem. Soc.*, **102**, 3971 (1980).

[2] W. Friedrichsen, *Naturforsch. Teil. B*., **35**, 1002 (1980).

[3] G. Zivilichovsky and M. David, *J. Org. Chem*., **47**, 295 (1982).

[4a] K. T. Potts and W. R. Kuehnling, *J. Org. Chem*., **49**, 3672 (1984); [b] K. T. Potts and P. Murphy, *J. Chem. Soc*., *Chem. Commun*., 144 (1986); [c] K. T. Potts, P. Murphy and M. R. DeLuca, *J. Org. Chem*., **53**, 2889 (1988); [d] K. T. Potts, P. Murphy, M. R. DeLuca and W. R. Kuehnling, *J. Org. Chem*., **53**, 2898 (1988).

[5a] Y. Xu and Q. –X. Guo, *Heterocycles*, **63**, 903 (2004); [b] C. O. Kappe, *Angew. Chem., Int. Ed.*, **43**, 6250 (2004); [c] A. de la Hoz, Á. Díaz-Ortiz and A. Moreno, *Chem. Soc. Rev*., **34**, 164 (2005); [d] E. Vervakova, M. Noskova and S. Toma, *Syn. Comm*., **32**, 729 (2002).

[6] M. Aniyappan, D. Muralihara and P. T. Permal, *Syn. Comm*., **32**, 650 (2002).

[7] B. K. Karale, V. P. Chovan, A. S. Mane, R. V. Hangarge, C. H. Gill and M. S. Shingare, *Syn. Comm*., **32**, 497 (2002).

[8] F. Massicot, R. Plantier-Royon, C. Portella, D. Saleur and A.V.R.L. Sudha, *Synthesis*, 2441 (2001).

[9] C. -Y.Wu, S. -T. Chen, S. -H. Chiou and K. -T. Wang, *J. Protein Chem.*, **11**, 45 (1992).

[10] T. Kappe and C. Kos, *Synthesis*, 629 (1989).

[11] G. J. Langley, E. Hecquet, I. P. Morris and D. G. Hamilton, *Rapid Commun. Mass Spectrosc*., **11**, 165 (1997).

[12] C. L. Raston and A. H. White, *Aust. J. Chem*., **37**, 2577 (1984).

[13] F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen and R. Taylor, *J. Chem. Soc., Perkin Trans 2*, S1 (1987).

[14] E. J. Forbes, K. T. Morgan and J. Newton, *J. Chem. Soc*., 835 (1963).

[15] W. O. George and P. S. McIntyre, Infrared Spectroscopy, Wiley, New York, 1987, p 296.

[16] W. Stadlbauer, R. Laschober, H. Lutschounig, G. Schlinder and T. Kappe, *Monatsh. Chem*., **123**, 617 (1992).

[17] E. S. A. M. Badawey, A. M. M. Hassan and F. S. G. Goliman, *Monatsh. Chem*., **121**, 665 (1990).

[18] J. Sakamoto, T. Nakagawa, N. Kanehisa, Y. Kai, M. Katsura, *Acta Cryst*., C**56**, e485 (2000).

[19] D. E. Lynch, G. E. Spicer and I. McClenaghan, *Acta Cryst*., C**59**, o715 (2003).

[20a] R. H. Blessing, *Acta Cryst*., A**51**, 33 (1995); [b] R. H. Blessing, *J. Appl. Cryst*., **30**, 421 (1997).

[21] G. M. Sheldrick, SHELX-97, University of Göttingen, Germany, 1997.