

# Aluminium chloride·2-isocyanatobenzoyl chloride complex: crystal structure and reactivity

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2-Amino-2'-hydroxybenzophenones **3** have been synthesized by acylation of phenols with 2-isocyanatobenzoyl chloride **2** in the presence of aluminium trichloride. The ring-chain tautomerism of the reagent **2** promoted by Lewis acid has been established on the basis of a crystal structure analysis of the 1:1 complex formed by **2** and aluminium trichloride.

As part of our study of the selective electrophilic aromatic substitution of phenolic substrates we investigated the *ortho*-acylation of metal phenolates<sup>1</sup> and the one-step *ortho*-bisacylation of aromatic rings.<sup>2</sup>

In addition, our observations, based on multinuclear NMR experiments<sup>2b</sup> and an X-ray crystal structure,<sup>2c</sup> on the ring-chain tautomerism involved in the complex between phthaloyl dichloride and aluminium trichloride, has prompted us to study both the structure and the reactivity of the complexes formed by 2-isocyanatobenzoyl chloride **2** with Lewis acids.

Reagent **2** when employed in Friedel-Crafts acylation of aromatic compounds<sup>3</sup> gave benzophenones at low temperatures but the corresponding 4,4-diarylbenzoxazin-2-ones at higher temperatures or with substrates more reactive than toluene.<sup>3a</sup>

Recently, 2-aminobenzophenones have received much attention as starting materials in the preparation of 1,4-benzodiazepines,<sup>4</sup> a well known class of drugs.

Here we describe the reactions of 2-isocyanatobenzoyl chloride and metal phenoxides in order to obtain 2-amino-2'-hydroxybenzophenones **3** and present new evidence for the ring-chain tautomerism<sup>5</sup> of reagent **2** promoted by aluminium trichloride.

## Results and discussion

Important information on the structure of the 2-isocyanatobenzoyl chloride·AlCl<sub>3</sub> complex has come from an X-ray analysis of crystals isolated from a 1:1 mixture of the acyl chloride and the Lewis acid in solution in 1,2-dichloroethane. The structure, reported in Fig. 1, throws light on the AlCl<sub>3</sub> promoted ring-chain tautomerism of the reagent **2**. Ring-chain tautomerism similar in nature occurs in the phthaloyl dichloride·AlCl<sub>3</sub> adduct (Fig. 2)<sup>2b,c</sup> (X = 3,4-dichloro) where the interaction of the carbonyl group with the metal [1.847(5) Å] is weaker and, consequently, the C=O bond length much shorter [1.214(8) Å] than in **I** [1.327(4) Å] (Scheme 1). The short Al–O bond distance [1.786(2) Å] indicates a strong interaction of AlCl<sub>3</sub> with the carbonyl group and is close to that observed for trichloro(ethyl benzoato-O)aluminium [1.761(3) Å].<sup>6</sup> The value of the bond angle Al–O(2)–C(1) is 150.4(3)° and is in accordance with a strong Al–O interaction as found in other trichloroaluminium adducts of R–C(X)=O (R = aryl, alkyl; X = Cl, O–R') and is far from the theoretical value of 120° for an sp<sup>2</sup> hybridized oxygen atom. A linear correlation between the Al–O bond distance and Al–O–C bond angle was found ( $r = -0.9558$ ,  $Y = 803.79 - 361.37X$ ) for seven similar complexes.<sup>2c,7</sup> The calculated Al–O–C bond angle for the observed Al–O bond

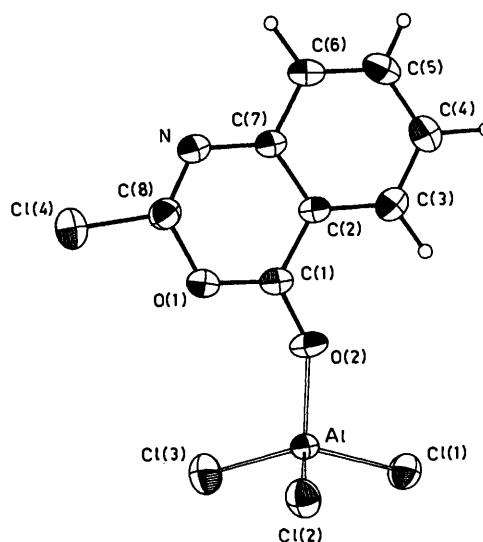


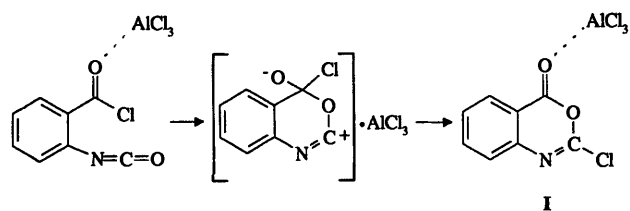
Fig. 1 Perspective view of the complex **I**. The thermal ellipsoids are drawn at the 30% probability level.

distance is 158.4°, and is in agreement with the experimental value.

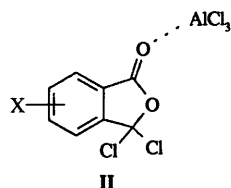
For an angle value of 180° the corresponding calculated bond distance result of 1.726 Å is very close to the Al–O bond distance of 1.733(4) Å found in Ph<sub>3</sub>PO·AlCl<sub>3</sub>,<sup>8</sup> where the oxygen atom is linearly coordinated. The linear coordinative bonding mode at oxygen may be interpreted as a double bond at the metal and the wide range of angular values found in this class of compounds, all greater than 120°, indicates that the bond order may be > 1.

The crystal structure indicates that the addition of AlCl<sub>3</sub> across the isocyanate group, as previously reported in the literature,<sup>3b,9</sup> is not, indeed, established, the N–C(8) bond distance [1.258(5) Å] being, in fact, in accord with N=C double bond retention. Moreover, the cyclic structure, promoted by 1 equivalent of AlCl<sub>3</sub>, is different from that hypothesized by Rao *et al.* as a consequence of initial addition of AlCl<sub>3</sub> to the isocyanate group and intramolecular rearrangement due to a second equivalent of the Lewis acid.<sup>9</sup>

We propose that the COCl group of **2** by coordination with AlCl<sub>3</sub> increases its reactivity toward nucleophilic intramolecular addition. Subsequent rearrangement gives the complex **I** that reacts with the aromatic substrate affording the reaction products.



Scheme 1



Scheme 2

In fact, the reaction of 2-isocyanatobenzoyl chloride and phenols in the presence of aluminium chloride gave hydroxylated 2-aminobenzophenones **3** (Scheme 2).

2-Aminobenzophenones, an important class of compounds for the synthesis of a wide variety of heterocyclic systems,<sup>10</sup> are of specific interest for the preparation of new 1,4-benzodiazepines by a variety of different routes.<sup>11</sup> Many of these are ineffective for substrates containing acidic hydrogen and few syntheses of hydroxylated 2-aminobenzophenones have been reported.<sup>12</sup>

We have investigated the synthesis of 2-amino-2'-hydroxybenzophenones of general structure **3** starting from 2-isocyanatobenzoyl chloride **2** and phenols **1** (Scheme 2). Exploratory experiments, carried out with 2-methylphenol and **2** in the presence of different Lewis acids (e.g. EtAlCl<sub>2</sub>, EtMgBr, TiCl<sub>4</sub>, SnCl<sub>4</sub>) in CH<sub>2</sub>Cl<sub>2</sub> at room temperature for 2 h, gave unsatisfactory results.

Variable amounts of AlCl<sub>3</sub> gave 2-amino-4'-hydroxy-3'-methylbenzophenone (20–29% yield) along with products from phenolic oxygen attack.

Electrophilic attack at the more electron-rich oxygen- and *para*-positions indicated that the reaction does not occur *via* a template process. It may be explained, however, by noting that in complex **I** (Scheme 1) the group in the *ortho* position to the reacting carbonyl function has a mesomeric donor effect even larger than that of the isocyanate, while in the corresponding phthaloyl dichloride complex **II** (Fig. 2) it has an electron-withdrawing inductive effect.<sup>13</sup>

In fact, coordinated *ortho*-bisacylation with phthaloyl dichlorides gave anthraquinones.<sup>2</sup> Such a result agrees with those reported for the aliphatic acyl chloride series, when reaction occurred *via* a metal-template process when an electron-withdrawing  $\alpha$ -substituent was present.<sup>1</sup>

We examined next the reaction of 4-methylphenol **1a** with the reagent **2** in CH<sub>2</sub>Cl<sub>2</sub> at room temperature for 2 h in the presence of AlCl<sub>3</sub> as metal promoter (Scheme 2; R<sup>2</sup> = Me and R<sup>1</sup>, R<sup>3</sup> = H). This gave the *ortho*-hydroxylated benzophenone **3a** (12%) and oxygen-attack products **4a** + **5a**<sup>14</sup> (20%). An increase in the amount of AlCl<sub>3</sub> (2 or 3 equiv.) increased the yield of **3a** (22 and 30% respectively).

Under these conditions the reactivity of **2** is very high and

Table 1 Synthesis of 2-amino-2'-hydroxybenzophenones **3**

Phenol <b>1</b>	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	Product <b>3</b>	Yield (%)
<b>1a</b>	H	Me	H	<b>3a</b>	30
<b>1b</b>	H	Bu <sup>t</sup>	H	<b>3b</b>	27
<b>1c</b>		-OCH <sub>2</sub> O-	H	<b>3c</b>	38*
<b>1d</b>	H		-(CH=CH)-	<b>3d</b>	33

\* Et<sub>2</sub>AlCl was employed instead of AlCl<sub>3</sub>.

its reaction with the products just formed,<sup>15</sup> giving **7a**, **8a**<sup>14</sup> and higher molecular weight compounds, explains the lack of selectivity, that is *ca.* 40%. Moreover **6a** was isolated<sup>14</sup> showing that the amino ketone **3** can react with itself. The reaction was extended to variously substituted phenols (see Table 1).

In spite of the low product yields, the reported reaction is attractive since it represents a straightforward route to 2-amino-2'-hydroxybenzophenones, compounds previously synthesized in lower yields by photorearrangements of phenyl anthranilates<sup>12b</sup> or salicylanilide.<sup>12a</sup>

In conclusion, we have shown in our work that AlCl<sub>3</sub> coordinates the carbonyl group coming from the parent chloroformyl function of **2**, in contrast with the data reported in the literature.<sup>9</sup> Also we have described the reaction of 2-isocyanatobenzoyl chloride with *para*-substituted phenolic substrates in the presence of AlCl<sub>3</sub> to afford, by direct acylation, 2-amino-2'-hydroxybenzophenones **3**. Such products may be transformed into heterocyclic compounds with potential biological activity as well as into polydentate ligands.

## Experimental

Mps were obtained on an Electrothermal melting-point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 298 spectrophotometer. <sup>1</sup>H NMR spectra were recorded on a Bruker AC 100 spectrometer at 100 MHz and on a Bruker AMX400 spectrometer at 400 MHz.

Chemical shifts are expressed in ppm relative to tetramethylsilane as internal standard and *J* values are expressed in Hz. Mass spectra were recorded on a Finnigan SSQ 710 instrument in CI mode. Microanalyses were carried out by Dipartimento di Chimica Generale ed Inorganica, Chimica Analitica, Chimica Fisica dell'Università di Parma. TLC analyses and chromatography were performed on Merck PF<sub>254</sub> silica gel using hexane-ethyl acetate mixtures or dichloromethane. All the phenolates were prepared as previously described.<sup>14</sup> All reagents were of commercial quality from freshly opened containers. 2-Isocyanatobenzoyl chloride was prepared as reported in the literature<sup>16</sup> and was distilled twice before use.

### X-Ray structure analysis of 3-chloro-2,4-benzoxazin-1-one-AlCl<sub>3</sub> **I**

Crystals of complex **I** suitable for the X-ray structural analysis were obtained by crystallisation from 1,2-dichloroethane and sealed under liquid paraffin in Lindemann capillaries.

**Crystal data.** C<sub>8</sub>H<sub>4</sub>AlCl<sub>4</sub>NO<sub>2</sub>, *M* = 314.92, triclinic, *a* = 6.865(3), *b* = 9.891(4), *c* = 10.512(4) Å,  $\alpha$  = 88.76(2),  $\beta$  = 73.12(2),  $\gamma$  = 71.51(2)°, *V* = 645.8(5) Å<sup>3</sup>, (from the  $\theta$  values of 30 carefully centred reflections, having 21.03 <  $\theta$  < 37.00°,  $\lambda$  = 1.541 838 Å), space group *P* $\bar{1}$ , *Z* = 2, *D*<sub>x</sub> = 1.619 g cm<sup>-3</sup>. White, air-sensitive prisms; crystal dimensions 0.28 × 0.35 × 0.45 mm,  $\mu$ (Cu-K $\alpha$ ) = 88.83 cm<sup>-1</sup>.

**Data collection and processing.** Siemens AED diffractometer,  $\theta/2\theta$  mode with  $\theta$  scan width (°) = 1.20 + 0.142 tan  $\theta$ ,  $\theta$  scan speed 3–12° min<sup>-1</sup>, Nickel-filtered Cu-K $\alpha$  radiation; 2456 unique reflections measured (3 <  $\theta$  < 70°,  $\pm h$ ,  $\pm k$ , *l*), 1726 with *I* > 2 $\sigma$ (*I*) [absorption correction (max., min. transmission factors = 1.000, 0.792)].<sup>17</sup> No decay was observed during processing.

**Structure analysis and refinement.** Heavy-atom methods (Al and Cl atoms) followed by normal heavy-atom procedures. Full-matrix least-squares refinement with all non-hydrogen atoms anisotropic and the hydrogen atoms isotropic. The weighting scheme  $w = 1.0000/[\sigma^2(F_o) + 0.00261F_o^2]$  gave satisfactory agreement analyses. Final  $R$  and  $R_w$  values are 0.0414, 0.0524. The system of computer programs SHELXS86,<sup>18a</sup> SHELXS76,<sup>18b</sup> PARST<sup>18c</sup> and ORTEP<sup>18d</sup> and sources of scattering factor data are given in ref. 19. All calculations were carried out on the GOULD POWERNODE and ENCORE 91 of the Centro di Studio per la Strutturistica Diffraattometrica del C.N.R. Parma, Italy.

Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, 1996, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/29.

### 2-Amino-2'-hydroxy-5'-methylbenzophenone 3a

**General procedure.** A solution of 4-methylphenol (0.54 g, 5 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (10  $\text{cm}^3$ ) was added, under nitrogen, to a stirred suspension of  $\text{AlCl}_3$  (1.99 g, 15 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (10  $\text{cm}^3$ ). After 15 min a solution of 2-isocyanatobenzoyl chloride 2 (0.91 g, 5 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (10  $\text{cm}^3$ ) was added in 10 min to give a deep-green colour. Stirring was continued at room temperature for 2 h after which the reaction was quenched by the addition of ice and water (30  $\text{cm}^3$ ) to the mixture followed by aq. NaOH (4 mol  $\text{dm}^{-3}$ ; 50  $\text{cm}^3$ ). After the mixture had been stirred for 30 min the organic phase was separated and the basic extraction with 4 mol  $\text{dm}^{-3}$  aq. NaOH (2  $\times$  50  $\text{cm}^3$ ) was repeated with vigorous stirring. The organic layer was dried and evaporated and the residue was subjected to preparative TLC with hexane-ethyl acetate (80:20) to give compounds 4a, 5a, 6a and 7a. The combined aqueous phases were acidified with aqueous HCl to pH  $\sim$ 6 and extracted with  $\text{CH}_2\text{Cl}_2$  (3  $\times$  40  $\text{cm}^3$ ). The combined extracts were dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated under reduced pressure and the residue was flash-chromatographed. Compound 3a (0.34 g, 30%) was eluted with hexane-ethyl acetate (80:20); with an increase in the eluent polarity (60:40) compound 8a (0.17 g, 9% yield) was isolated.

**2-Amino-2'-hydroxy-5'-methylbenzophenone 3a.** Yellow solid, mp 64–65 °C (Found: C, 74.1; H, 5.6; N, 6.3.  $\text{C}_{14}\text{H}_{13}\text{NO}_2$  requires C, 74.0; H, 5.8; N, 6.2%);  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$  3460, 3360 and 1610;  $\delta_{\text{H}}(400 \text{ MHz}; \text{CDCl}_3)$  2.26 (3 H, s,  $\text{CH}_3$ ), 5.2 (2 H, br s,  $\text{NH}_2$ ), 6.72 (1 H, ddd,  $J$  7.9, 7.3 and 1.0, 5-H), 6.76 (1 H, dd,  $J$  8.2 and 1.0, 3-H), 6.96 (1 H, d,  $J$  8.4, 3'-H), 7.28 (1 H, dd,  $J$  8.4 and 1.9, 4'-H), 7.31 (1 H, ddd,  $J$  8.2, 7.3 and 1.5, 4-H), 7.34 (1 H, d,  $J$  1.9, 6'-H), 7.40 (1 H, dd,  $J$  7.9 and 1.5, 6-H) and 11.33 (1 H, s, OH); a long-range correlation was observed between  $\text{CH}_3$  and 4'-H as well as 6'-H;  $\delta_{\text{C}}(25 \text{ MHz}; \text{CDCl}_3)$  20.04 ( $\text{CH}_3$ ), 115.94, 117.17, 117.91, 119.63 (C), 120.25 (C), 127.58 (C), 132.78, 133.03, 133.41, 136.37, 149.05 (C), 160.23 (C) and 201.80 (C) (assignments were made by DEPT);  $m/z$  228 ( $\text{M}^+ + 1$ , 84%), 227 ( $\text{M}^+$ , 58), 163 (30), 135 (66), 120 (100) and 109 (18).

**2-Amino-2'-hydroxy-5'-tert-butylbenzophenone 3b.** Yellow solid (decomp. before melting) (Found: C, 76.0; H, 7.2; N, 6.9.  $\text{C}_{17}\text{H}_{19}\text{NO}_2$  requires C, 75.8; H, 7.1; N, 5.2%);  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$  3490, 3384 and 1618;  $\delta_{\text{H}}(400 \text{ MHz}; \text{CDCl}_3)$  1.25 [9 H, s, ( $\text{CH}_3$ )<sub>3</sub>C], 5.3 (2 H, br s,  $\text{NH}_2$ ), 6.70 (1 H, ddd,  $J$  7.9, 7.1 and 0.9, 5-H), 6.76 (1 H, dd,  $J$  8.3 and 0.9, 3-H), 6.99 (1 H, d,  $J$  8.5, 3'-H), 7.29 (1 H, ddd,  $J$  8.3, 7.1 and 1.2, 4-H), 7.39 (1 H, dd,  $J$  7.9 and 1.2, 6-H), 7.51 (1 H, dd,  $J$  8.5 and 2.4, 4'-H), 7.55 (1 H, d,  $J$  2.4, 6'-H) and 11.30 (1 H, s, OH);  $m/z$  270 ( $\text{M}^+ + 1$ , 100%), 214 (16), 177 (15) and 120 (73).

**2-Amino-2'-hydroxy-4',5'-methylenedioxybenzophenone 3c.** Yellow solid, mp 160–162 °C (Found: C, 65.6; H, 4.4; N, 5.4.

$\text{C}_{14}\text{H}_{11}\text{NO}_4$  requires C, 65.4; H, 4.3; N, 5.4%);  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$  3472, 3380 and 1627;  $\delta_{\text{H}}(400 \text{ MHz}; \text{CDCl}_3)$  4.8 (2 H, br s,  $\text{NH}_2$ ), 5.97 (2 H, s,  $\text{OCH}_2\text{O}$ ), 6.53 (1 H, s, 3'-H), 6.72 (1 H, td,  $J$  7.8 and 0.9, 5-H), 6.75 (1 H, dd,  $J$  8.2 and 0.9, 3-H), 6.96 (1 H, s, 6'-H), 7.26 (1 H, td,  $J$  8.2 and 1.5, 4-H), 7.31 (1 H, dd,  $J$  7.8 and 1.5, 6-H) and 12.79 (1 H, s, OH);  $m/z$  258 ( $\text{M}^+ + 1$ , 10%), 120 (100) and 93 (25).

**2-Amino-2'-hydroxynaphthophenone 3d.** Yellow solid, mp 188–189 °C (Found: C, 77.8; H, 5.0; N, 5.4.  $\text{C}_{17}\text{H}_{13}\text{NO}_2$  requires C, 77.6; H, 5.0; N, 5.3%);  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$  3480, 3355 and 1618;  $\delta_{\text{H}}(400 \text{ MHz}; \text{CDCl}_3)$  6.2 (2 H, br s,  $\text{NH}_2$ ), 6.43 (1 H, td,  $J$  8.0 and 0.9, 5-H), 6.77 (1 H, dd,  $J$  8.5 and 0.9, 3-H), 7.11 (1 H, dd,  $J$  8.0 and 1.5, 6-H), 7.21 (1 H, d,  $J$  9.0, 3'-H or 4'-H), 7.2–7.4 (3 H, m, 4-H, 6'-H and 7'-H), 7.49 (1 H, dd,  $J$  7.6 and 1.7, 5'-H or 8'-H), 7.76 (1 H, dd,  $J$  7.5 and 1.9, 8'-H or 5'-H), 7.87 (1 H, d,  $J$  9.0, 4'-H or 3'-H) and 8.7 (1 H, br s, OH);  $\delta_{\text{C}}(25 \text{ MHz}; [\text{H}_6]\text{DMSO})$  114.26, 116.62, 117.78 (C), 118.08, 120.78 (C), 122.80, 123.16, 126.70, 127.34 (C), 127.94, 129.78, 131.47 (C), 133.78, 134.48, 150.94 (C), 151.58 (C) and 198.92 (C), (assignments were made by DEPT);  $m/z$  264 ( $\text{M}^+ + 1$ , 40%), 263 ( $\text{M}^+$ , 35) and 120 (100).

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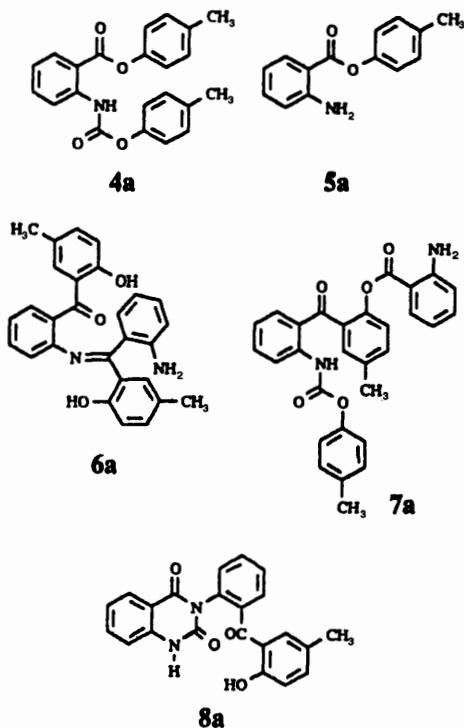
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**4a**:  $\delta_{\text{H}}$ (400 MHz;  $\text{CDCl}_3$ ) 2.34 (3 H, s,  $\text{CH}_3$ ), 2.38 (3 H, s,  $\text{CH}_3$ ), 6.8–7.8 (10 H, m, H-arom), 8.30 (1 H, dd,  $J$  8.0 and 1.7, H-arom), 8.52 (1 H, d,  $J$  7.8, H-arom) and 10.8 (1 H, br s, NH);  $m/z$  362 ( $\text{M}^+ + 1$ , 44%), 282 (33), 254 (78), 146 (49), 137 (33) and 108 (100).

**5a**:  $\delta_{\text{H}}$ (400 MHz;  $\text{CDCl}_3$ ) 2.37 (3 H, s,  $\text{CH}_3$ ), 5.8 (2 H, br s,  $\text{NH}_2$ ), 6.69 (1 H, d,  $J$  8.4, H-arom), 6.71 (1 H, td,  $J$  8.0, 7.1 and 1.0, H-

arom), 7.06 (2 H, d,  $J$  8.3, H-arom), 7.21 (2 H, d,  $J$  8.3, H-arom), 7.33 (1 H, ddd,  $J$  8.4, 7.1 and 1.6, H-arom) and 8.08 (1 H, dd,  $J$  8.0 and 1.6, H-arom);  $m/z$  228 ( $\text{M}^+ + 1$ , 100%), 183 (17) and 121 (38).

**6a**:  $\delta_{\text{H}}$ (400 MHz;  $\text{CDCl}_3$ ) 2.15 (3 H, s,  $\text{CH}_3$ ), 2.22 (3 H, s,  $\text{CH}_3$ ), 4.0 (2 H, br s,  $\text{NH}_2$ ), 6.52 (1 H, d,  $J$  8.1, H-arom), 6.69 (1 H, t,  $J$  7.4, H-arom), 6.83 (1 H, d,  $J$  7.9, H-arom), 6.87 (1 H, d,  $J$  8.4, H-arom), 6.92 (1 H, d,  $J$  1.6, H-arom), 6.94 (1 H, d,  $J$  8.5, H-arom), 7.01 (1 H, dd,  $J$  7.4 and 1.5, H-arom), 7.1–7.2 (4 H, m, H-arom), 7.24 (1 H, td,  $J$  7.9 and 1.8, H-arom), 7.31 (1 H, dd,  $J$  7.2 and 1.8, H-arom), 7.32 (1 H, dd,  $J$  8.5 and 1.9, H-arom), 11.78 (1 H, s, OH) and 13.3 (1 H, br s, OH);  $m/z$  473 ( $\text{M}^+ + 1$ , 100%) and 436 ( $\text{M}^+$ , 41).

**7a**:  $\delta_{\text{H}}$ (400 MHz;  $\text{CDCl}_3$ ) 2.37 (6 H, s, 2  $\text{CH}_3$ ), 6.1 (2 H, br s,  $\text{NH}_2$ ), 6.51 (1 H, ddd,  $J$  8.1, 7.1 and 0.9, H-arom), 6.55 (1 H, dd,  $J$  8.4 and 0.9, H-arom), 7.05 (2 H, d,  $J$  8.3, H-arom), 7.10 (1 H, ddd,  $J$  8.0, 7.4 and 1.0, H-arom), 7.13 (1 H, d,  $J$  8.2, H-arom), 7.15 (1 H, ddd,  $J$  8.4, 7.1 and 1.5, H-arom), 7.22 (2 H, d,  $J$  8.3, H-arom), 7.22 (1 H, d,  $J$  2.0, H-arom), 7.28 (1 H, dd,  $J$  8.2 and 2.0, H-arom), 7.32 (1 H, dd,  $J$  8.1 and 1.5, H-arom), 7.55 (1 H, ddd,  $J$  8.6, 7.4 and 1.5, H-arom), 8.21 (1 H, dd,  $J$  8.0 and 1.5, H-arom), 8.38 (1 H, d,  $J$  8.6, H-arom) and 10.38 (1 H, s, NH);  $m/z$  481 ( $\text{M}^+ + 1$ , 9%), 373 (9), 254 (47), 228 (51), 146 (100) and 120 (39).

**8a**:  $\delta_{\text{H}}$ (400 MHz;  $\text{CDCl}_3$ ) 2.18 (3 H, s,  $\text{CH}_3$ ), 6.82 (1 H, d,  $J$  8.4, H-arom), 6.89 (1 H, d,  $J$  8.0, H-arom), 7.18 (1 H, t,  $J$  7.9, H-arom), 7.19 (1 H, dd,  $J$  8.4 and 2.2, H-arom), 7.33 (1 H, d,  $J$  2.2, H-arom), 7.47 (1 H, d,  $J$  7.5, H-arom), 7.53 (1 H, td,  $J$  7.9 and 1.3, H-arom), 7.59 (1 H, t,  $J$  7.7, H-arom), 7.64 (1 H, dd,  $J$  7.7 and 1.9, H-arom), 7.72 (1 H, td,  $J$  7.5 and 1.9, H-arom), 8.07 (1 H, d,  $J$  7.9, H-arom), 9.7 (1 H, br s, NH) and 11.33 (1 H, s, OH);  $m/z$  373 ( $\text{M}^+ + 1$ , 100%), 265 (36), 237 (26) and 146 (15).

15 Similar reactivity of **2** during quenching procedure was reported (ref. 3).

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