Hydrogen bonding and structure of 2-hydroxy-*N*-acylanilines in the solid state and in solution

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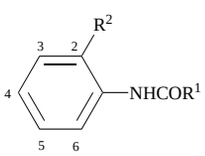
In crystals of 2-hydroxy-*N*-benzoylaniline and 2-hydroxy-*N*-trifluoroacetylaniline, ribbons of molecules are held by intermolecular hydrogen bonds between the hydroxy and carbonyl groups of adjacent molecules. The O · · · H · · · O bond lengths are 2.65 and 2.72 Å, respectively, indicating the hydrogen bonds are moderately strong. The alkyl and aryl groups on the carbonyl carbon and the amide nitrogen have the usual *trans* configuration. In solution in $CDCl_3$ and Me_2SO the ^1H NMR spectra of *N*-acetyl- and *N*-benzoyl-anilines with substituents H, CH_3 and OCH_3 at the 2-position show downfield shifts of *ca.* δ 0.2–1.5 for the proton in the 6-position of the aniline ring. This is compatible with a *trans* configuration for these amides and strong deshielding of the 6-H by the nearby carbonyl group. *N*-Acetyl- and *N*-benzoyl-anilines with a 2-hydroxy substituent behave similarly in Me_2SO but in $CDCl_3$ solution no downfield shift is observed and this is explained by the formation of an intramolecular hydrogen bond between the 2-hydroxy substituent and the amide carbonyl in this solvent.

Introduction

As part of our interest in the effect of hydrogen bonding on chemical properties[1] we report structural data for 2-hydroxy-*N*-acylanilines which have the potential for forming hydrogen bonds. X-Ray crystal structure determinations for 2-hydroxy-*N*-benzoylaniline and 2-hydroxy-*N*-trifluoroacetylaniline (**1** with



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R^1 = Ph and R^2 = OH and **1** with $R^1 = CF_3$ and R^2 = OH, respectively) have been obtained. Structural information in solution has been obtained from the ^1H NMR spectra of 2-hydroxy-*N*-acylanilines in $CDCl_3$ and in $[^2H_6]Me_2SO$. The ^1H NMR spectra of substituted *N*-acetyl-, *N*-benzoyl- and *N*-trifluoroacetyl-anilines (**1** with R^1 = Me, Ph and CF_3, respectively) each with substituents at the 2-position (**1** with R^2 = H, Me, OMe and OH) have been obtained and the chemical shift of the aromatic protons has been used to provide information about the configuration and conformation in solution.[2]

Experimental

Materials

Samples of *N*-benzoylaniline, *N*-acetylaniline and 2-hydroxy-*N*-acetylaniline were obtained from Aldrich and were used without purification. The remaining substrates were obtained by acylation of the commercially available substituted anilines with the acid chloride or the acid anhydride using a literature procedure.[3] Methods of purification and identification are described below.

***N*-Acetylaniline.** A commercial sample was used without purification; δ_H(400 MHz, $CDCl_3$) 8.26 (br s, 1 H, NH), 7.52–7.50 (d, 2 H, 6- and 2-H), 7.29–7.25 (t, 2 H, 3- and 5-H), 7.10–7.06 (t, 1 H, 4-H), 2.13 (s, 3 H, CH_3); δ_H(400 MHz, $[^2H_6]Me_2SO$) 9.94 (br s, 1 H, NH), 7.61–7.59 (d, 2 H, 6- and 2-H), 7.31–7.27 (t, 2 H, 3- and 5-H), 7.04–7.00 (t, 1 H, 4-H), 2.06 (s, 3 H, CH_3).

2-Methyl-*N*-acetylaniline. Recrystallisation from 1:1 ethanol–water gave white crystals with mp 113–114 °C (lit.[4] 114–115 °C); δ_H(360 MHz, $CDCl_3$) 7.29 (br s, 1 H, NH), 7.67–7.65 (d, 1 H, 6-H), 7.20–7.15 (m, 2 H, 3- and 5-H), 7.09–7.05 (t, 1 H, 4-H), 2.22 (s, 3 H, Ar–CH_3), 2.04 (s, 3 H, $COCH_3$); δ_H(400 MHz, $[^2H_6]Me_2SO$) 9.29 (br s, 1 H, NH), 7.40–7.38 (d, 1 H, 6-H), 7.19–7.18 (d, 1 H, 3-H), 7.16–7.12 (t, 1 H, 5-H), 7.07–7.03 (t, 1 H, 4-H), 2.19 (s, 3 H, Ar–CH_3), 2.05 (s, 3 H, $COCH_3$); δ_C(90.5 MHz, $CDCl_3$) 168.6 (CO), 135.6, 129.9 (quat. arom.), 130.5, 126.6. 125.4, 123.8 (CH), 24.1 ($COCH_3$), 17.8 (Ar–CH_3); δ_C(100.6 MHz, $[^2H_6]Me_2SO$) 168.5 (CO), 136.9, 131.9 (quat. arom.), 130.6, 126.2, 125.4, 125.3 (CH), 23.6 (COMe), 18.2 (Ar–CH_3); *m/z* (EI) 150.08 (8%, $M^+ + 1$), 149.09 (48%, M^+), 107.05 (100%, $M^+ + 1 - CH_3CO$), 106.04 (63%, $M^+ - CH_3CO$) (Found: M^+ 149.0854. $C_9H_{11}NO$ requires 149.0841).

2-Methoxy-*N*-acetylaniline. Recrystallisation from 1:2 EtOH–H_2O gave white needles (mp 87–88 °C, lit.[5] 86 °C); δ_H(400 MHz, $CDCl_3$) 8.36–8.34 (d, 1 H, 6-H), 7.78 (br s, 1 H, NH), 7.05–7.02 (m × 4, 1 H, 4-H), 6.97–6.93 (t, 1 H, 5-H), 6.88–6.86 (d, 1 H, 3-H), 3.88 (s, 3 H, OCH_3), 2.20 (s, 3 H, $COCH_3$); δ_H(400 MHz, $[^2H_6]Me_2SO$) 9.12 (br s, 1 H, NH), 7.93–7.91 (d, 1 H, 6-H), 7.07–7.00 (m × 9, 2 H, 3- and 4-H), 6.90–6.86 (m × 5, 1 H, 5-H), 3.82 (s, 3 H, OCH_3), 2.08 (s, 3 H, $COCH_3$); δ_C(100.6 MHz, $CDCl_3$) 168.2 (CO), 147.6, 127.7 (quat. arom.), 123.6, 121.1, 119.8, 109.8 (CH), 55.6 (OCH_3), 24.9 ($COCH_3$); δ_C(100.6 MHz, $[^2H_6]Me_2SO$) 168.3 (CO), 149.4, 127.3 (quat. arom.), 124.1, 121.9, 120.0, 110.9 (CH), 55.5 (OCH_3), 23.7 ($COCH_3$); *m/z* (EI) 165.08 (M^+, 100%), 123.07 ($M + 1^+ - CH_3CO$, 49%), 108.04 ($M + 1^+ - CH_3CO - CH_3$, 45%) (Found: M^+ 165.0798. $C_9H_{11}NO_2$ requires 165.0790).

2-Hydroxy-*N*-acetylaniline. A commercial sample was used without purification. The ^1H NMR spectrum (400 MHz, $CDCl_3$) was run at two concentrations; at 3.3×10^{-4} mol dm^{-3} the spectrum showed peaks at δ 8.66 (s, 1 H, OH), 7.52 (br s, 1 H, NH), 7.17–7.12 (td, 1 H, 4-H), 7.04–7.02 (dd, 1 H, 3-H), 7.00–6.96 (dd, 1 H, 6-H), 6.89–6.85 (td, 1 H, 5-H), 2.29 (s, 3 H, CH_3) and at 3.3×10^{-5} mol dm^{-3} the shifts were δ 8.66 (s, 1 H, OH), NH not visible under $CHCl_3$, 7.13–7.12 (d, 1 H, 4-H, other peaks under $CHCl_3$), 7.04–7.02 (dd, 1 H, 3-H), 6.98–6.96 (dd, 1 H, 6-H), 6.89–6.85 (td, 1 H, 5-H), 2.29 (s, 3 H, CH_3); δ_H(400 MHz, $[^2H_6]Me_2SO$) 9.76 (br s, 1 H, OH), 9.32 (br s, 1 H, NH), 7.69–7.66 (dd, 1 H, 6-H), 6.95–6.90 (td, 1 H, 4-H), 6.87–6.84 (dd, 1 H, 3-H), 6.77–6.73 (td, 1 H, 5-H), 2.09 (s, 3 H, CH_3).

***N*-Benzoylaniline.** A commercial sample was used without purification; δ_H(400 MHz, $CDCl_3$) 8.05 (br s, 1 H, NH), 7.88–7.86 (d, 2 H, Ph), 7.67–7.65 (d, 2 H, 2- and 6-H), 7.54–7.45 (m, 3 H, Ph) 7.39–7.35 (t, 2 H, 3- and 5-H), 7.17–7.15 (t, 1 H, 4-H);

δ_H(360 MHz, [$^2H_6$]Me_2SO) 10.29 (br s, 1 H, NH), 7.99–7.97 (d, 2 H, Ph), 7.83–7.81 (d, 2 H, 2- and 6-H), 7.60–7.54 (m, 3 H, Ph), 7.39–7.35 (t, 2 H, 3- and 5-H), 7.13–7.09 (t, 1 H, 4-H).

2-Methyl-*N*-benzoylaniline. Recrystallisation from 1:1 ethanol–water gave white crystals with mp 144–145 °C (lit.[6] 147 °C); δ_H(360 MHz, $CDCl_3$) 7.91–7.86 (m × 5, 2 H, Ph), 7.89–7.88 (d, 1 H, 6-H), 7.75 (br s, 1 H, NH), 7.57–7.53 (m × 9, 1 H, Ph), 7.50–7.45 (m × 8, 2 H, Ph), 7.25–7.22 (m × 5, 2 H, 3- and 5-H), 7.14–7.09 (td, 1 H, 4-H), 2.32 (s, 3 H, CH_3); δ_H(400 MHz, [$^2H_6$]Me_2SO) 9.90 (br s, 1 H, NH), 8.00–7.98 (d, 2 H, Ph), 7.61–7.51 (m × 8, 3 H, Ph), 7.36–7.34 (d, 1 H, 6-H), 7.29–7.27 (d, 1 H, 3-H), 7.24–7.20 (m × 5, 1 H, 5-H), 7.19–7.15 (m × 4, 1 H, 4-H), 2.24 (s, 3 H, CH_3); δ_C(90.6 MHz, $CDCl_3$) 165.7 (CO), 135.8, 135.0, 129.4 (quat. arom.) 131.8, 130.6, 128.8, 127.1, 126.9, 125.4, 123.2 (CH), 17.9 (CH_3); δ_C(100.6 MHz, [$^2H_6$]-Me_2SO) 165.16 (CO), 136.3, 134.4, 133.6, (quat. arom.), 131.4, 130.2, 128.3, 127.5, 126.5, 125.9 (CH), 17.8 (CH_3); *m/z* (EI) 212.11 (M + 1^+, 25%), 211.11 (M^+, 100%), 105.03 ($PhCO^+$, 81%), 77.04 (Ph^+, 23%) (Found: M^+ 211.1050). $C_{14}H_{13}NO$ requires 211.0997.

2-Methoxy-*N*-benzoylaniline. A literature procedure[7] involving benzoylation with benzoyl chloride in dichloromethane in the presence of triethylamine was used. Recrystallisation from ethanol gave an off-white solid with mp 68–69 °C (lit.[8] 59.5 °C); δ_H(360 MHz, $CDCl_3$) 8.56 (br s, 1 H, NH), 8.55–8.53 (dd, 1 H, 6-H), 7.91–7.88 (m, 2 H, Ph), 7.57–7.46 (m, 3 H, Ph), 7.10–7.06 (td, 1 H, 4-H), 7.04–6.99 (td, 1 H, 5-H), 6.93–6.90 (dd, 1 H, 3-H), 3.92 (s, 3 H, CH_3); δ_H(360 MHz, [$^2H_6$]Me_2SO) 9.44 (br s, 1 H, NH), 7.99–7.97 (m, 2 H, Ph), 7.82–7.79 (dd, 1 H, 6-H), 7.62–7.50 (m, 3 H, Ph), 7.21–7.16 (td, 1 H, 4-H), 7.11–7.08 (dd, 1 H, 3-H), 7.00–6.96 (td, 1 H, 5-H), 3.84 (s, 3 H, CH_3); δ_C(90.6 MHz, $CDCl_3$) 165.2 (CO), 148.1, 135.3, 127.8 (quat. arom.), 131.7, 128.7, 127.0 123.9, 121.2, 119.8, 109.9 (CH), 55.8 (CH_3); δ_C(90.6 MHz, [$^2H_6$]Me_2SO) 164.9 (CO), 151.4, 134.4, 126.8 (quat. arom.), 131.5, 128.4, 127.4, 125.6, 124.2, 120.1, 111.3 (CH), 55.6 (CH_3); *m/z* (EI) 228.11 (M + 1^+, 36%), 227.11 (M^+, 100%), 105.03 ($PhCO^+$, 100%), 77.04 (Ph^+, 35%) (Found: M^+ 227.1143. $C_{14}H_{13}NO_2$ requires 227.0946).

2-Hydroxy-*N*-benzoylaniline. Recrystallisation from ethanol gave off-white crystals with mp 169–172 °C (lit.[9] 167.5–168.5 °C). The ^1H NMR spectrum in $CDCl_3$ was run at a concentration of 0.047 mol dm^{-3} and the chemical shift values were δ_H(400 MHz) 8.63 (s, 1 H, OH), 8.13 (br s, 1 H, NH), 7.93–7.50 (m, 5 H, Ph), 7.22–7.19 (td, 1 H, 4-H), 7.17–7.15 (dd, 1 H, 6-H), 7.09–7.06 (dd, 1 H, 3-H), 6.95–6.90 (td, 1 H, 5-H). At a concentration of 4.7×10^{-4} mol dm^{-3} the values were δ_H(400 MHz) 8.63 (s, 1 H, OH), 8.08 (br s, 1 H, NH), 7.93–7.51 (m, 5 H, Ph), 7.18–7.16 (td, 1 H, 4-H), 7.18–7.16 (dd, 1 H, 6-H), 7.10–7.08 (dd, 1 H, 3-H), 6.95–6.91 (td, 1 H, 5-H); δ_H(360 MHz, [$^2H_6$]Me_2SO) 9.79 (br s, 1 H, OH), 9.53 (s, 1 H, NH), 7.99–7.51 (m, 5 H, Ph), 7.70–7.67 (dd, 1 H, 6-H), 7.07–7.02 (td, 1 H, 4-H), 6.94–6.92 (dd, 1 H, 3-H), 6.86–6.81 (td, 1 H, 5-H); δ_C(100.6 MHz, $CDCl_3$) 166.9 (CO), 148.5, 133.6, 126.04 (quat. arom.) 132.2, 128.9, 127.5, 126.7, 122.2, 120.6, 119.0 (CH); δ_C(90.5 MHz, [$^2H_6$]Me_2SO) 165.1 (CO), 149.3, 134.3, 125.8 (quat. arom.), 131.6, 128.4, 127.4, 125.6, 124.0, 118.9, 115.9 (CH); *m/z* (EI) 213.08 (68%, M^+), 105.03 (100%, $PhCO^+$), 77.04 (20%, Ph^+) (Found: M^+ 213.0817. $C_{13}H_{11}NO_2$ requires 213.0790).

***N*-Trifluoroacetylaniline.** Recrystallisation from 1:1 ethanol–water gave a white powder with mp 91.5–92.5 °C (lit.[10] 87.5–88.5 °C); δ_H(360 MHz, $CDCl_3$) 7.92 (br s, 1 H, NH), 7.58–7.56 (dt, 2 H, 2- and 6-H), 7.42–7.38 (td, 2 H, 3- and 5-H), 7.27–7.23 (td, 1 H, 4-H); δ_H(400 MHz, [$^2H_6$]Me_2SO) 11.26 (br s, 1 H, NH), 7.68–7.65 (dt, 2 H, 2- and 6-H), 7.44–7.39 (td, 2 H, 3- and 5-H), 7.25–7.21 (td, 1 H, 4-H); δ_C(90.5 MHz, $CDCl_3$) 155.1 and 154.7 (d, CO), 135.1 (quat. arom.), 129.4, 126.4, 120.6 (CH), 117.3, 114.1 (d, CF_3); δ_C(100.6 MHz, [$^2H_6$]Me_2SO) 154.6 and 154.2 (d, CO), 136.3 (quat. arom.), 128.9, 125.5, 121.0 (CH), 117.2 (CF_3); δ_F(338.9 MHz, $CDCl_3$) −76.2205 and −76.2243 (d, *J* 1.29, CF_3); δ_F(376.5 MHz, [$^2H_6$]Me_2SO) −73.43 (s, CF_3); *m/z* (EI) 189.04 (100%, M^+), 120.04 (32%, $M^+ - CF_3$), 77.04 (26%, Ph^+) (Found: M^+ 189.0409. $C_8H_6NOF_3$ requires 189.0401).

2-Methyl-*N*-trifluoroacetylaniline. Recrystallisation from ethanol gave white needles with mp 81–82 °C (lit.[11] 78–79 °C); δ_H(360 MHz, $CDCl_3$) 7.79–7.76 (d, 1 H, 6-H), 7.73 (br s, 1 H, NH), 7.30–7.18 (m, 3 H, 3-, 4- and 5-H), 2.30 (s, 3 H, CH_3); δ_H(360 MHz, [$^2H_6$]Me_2SO) 10.99 (br s, 1 H, NH), 7.34–7.24 (m, 4 H, 3-, 5- and 6-H), 2.18 (s, 3 H, CH_3); δ_C(90.5 MHz, $CDCl_3$) 155.4 and 155.0 (d, CO), 132.8, 130.3 (quat. arom.), 130.9, 127.2, 127.1, 123.5 (CH), 117.5 and 114.4 (d, CF_3), 17.4 (CH_3); δ_F(90.5 MHz, [$^2H_6$]Me_2SO) 155.2 and 154.8 (d, CO), 133.9, 133.2 (quat. arom.), 130.6, 127.5, 126.6, 126.4 (CH), 117.6 and 114.5 (d, CF_3), 17.3 (CH_3); δ_F(338.9 MHz, $CDCl_3$) −76.1376 and −76.1417 (d, *J* 1.39, CF_3); δ_F(338.9 MHz, [$^2H_6$]Me_2SO) −69.69 (s, CF_3); *m/z* (EI) 203.05 (100%, M^+), 134.06 (44%, $M^+ - CF_3$), 106.08 (26%, $M^+ - CF_3CO$) (Found: M^+ 203.0549. $C_9H_8NOF_3$ requires 203.0558).

2-Methoxy-*N*-trifluoroacetylaniline. Recrystallisation from 1:1 ethanol–water gave white crystals with mp 52.5–53.5 °C (lit.[11] 50.0–50.5 °C); δ_H(360 MHz, $CDCl_3$) 8.58 (br s, 1 H, NH), 8.33–8.30 (dd, 1 H, 6-H), 7.20–7.15 (td, 1 H, 4-H), 7.04–6.99 (td, 1 H, 5-H), 6.95–6.92 (dd, 1 H, 3-H), 3.93 (s, 3 H, CH_3); δ_H(360 MHz, [$^2H_6$]Me_2SO) 10.70 (br s, 1 H, NH), 7.41–7.38 (dd, 1 H, 6-H), 7.34–7.29 (td, 1 H, 4-H), 7.14–7.12 (dd, 1 H, 3-H), 7.01–6.97 (td, 1 H, 5-H), 3.81 (s, 3 H, CH_3); δ_C(90.5 MHz, $CDCl_3$) 155.0 and 154.0 (d, CO), 148.3, 125.0 (quat. arom.), 126.0, 121.2, 120.2, 110.2 (CH), 117.5 and 114.2 (d, CF_3), 55.9 (CH_3); δ_C(90.5 MHz, [$^2H_6$]Me_2SO) 155.5, 155.1 and 154.7 (t, CO), 153.0, 123.3 (quat. arom.), 128.3, 126.4, 120.2, 112.0 (CH), 120.7, 117.5, 114.3 (t, CF_3), 55.9 (CH_3); δ_F(338.9 MHz, $CDCl_3$) −76.3000 and −76.3035 (d, *J* 1.19, CF_3); δ_F(338.9 MHz, [$^2H_6$]Me_2SO) −69.61 (s, CF_3); *m/z* (EI) 219.05 (100%, M^+), 150.05 (30%, $M^+ - CF_3$), 122.06 (7%, $M^+ - CF_3CO$) (Found: M^+ 219.0499. $C_9H_8NO_2F_3$ requires 219.0507).

2-Hydroxy-*N*-trifluoroacetylaniline. Recrystallisation from 1:1 methanol–water gave an off-white powder with mp 164–168 °C (lit.[3] 166.0–166.5 °C); δ_H(360 MHz, $CDCl_3$) 8.42 (br s, 1 H, NH), 7.98–7.95 (dd, 1 H, 6-H), 7.16–7.11 (td, 1 H, 4-H), 7.03–6.98 (td, 1 H, 5-H), 6.95–6.92 (dd, 1 H, 3-H), 5.92 (br s, 1 H, OH); δ_H(360 MHz, [$^2H_6$]Me_2SO) 10.23 (br s, 1.5 H, OH and NH), 7.33–7.30 (dd, 1 H, 6-H), 7.16–7.11 (dqd, 1 H, 4-H), 6.99–6.95 (dd, 1 H, 3-H), 6.85–6.80 (td, 1 H, 5-H); δ_C(100.6 MHz, $CDCl_3$) 155.0 and 154.5 (d, CO), 145.7, 123.8 (quat. arom.), 126.9, 121.7, 121.5, 116.5 (CH), 117.0 and 114.0 (d, CF_3); δ_C(90.5 MHz, [$^2H_6$]Me_2SO) 155.1, 154.7 and 154.4 (t, CO), 151.2, 122.2 (quat. arom.), 127.9, 126.4, 118.8, 116.0 (CH), 120.7, 117.5 and 114.4 (t, CF_3); δ_F(338.9 MHz, $CDCl_3$) −75.9645 and −75.9686 (d, *J* 1.39); δ_F(338.9 MHz, [$^2H_6$]Me_2SO) −73.34 (s, CF_3); *m/z* (EI) 205.03 (100%, M^+), 136.04 (38%, $M^+ - CF_3$), 108.05 (26%, $M^+ - CF_3CO$) (Found: M^+ 205.0331. $C_8H_6NO_2F_3$ requires 205.0351).

X-Ray crystal structure analyses

For structure determination, crystals of 2-hydroxy-*N*-benzoylaniline were obtained by recrystallisation from ethanol. For 2-hydroxy-N-trifluoroacetylaniline a sample obtained by recrystallisation from 1:1 methanol–water was dissolved in hot toluene to give a saturated solution which was allowed to cool and suitable crystals were formed after several days. Structural analyses were carried out at room temperature on an automated Picker four circle diffractometer using Ni-filtered Cu-Kα radiation with pulse height analysis. Data were reduced and the structures solved using the NRCVAX package of programmes.[12] Scanning was in θ–2θ scan mode.

The solution to the structure of 2-hydroxy-*N*-benzoylaniline was obtained by direct and Fourier difference methods. The positions of the non-hydrogen atoms were refined by a full-matrix anisotropic least squares method with unit weighting of the *F* values. The hydrogen atoms attached to carbon were

Table 1 Crystal data for 2-hydroxy-*N*-benzoylaniline and 2-hydroxy-*N*-trifluoroacetylaniline

	2-Hydroxy-*N*-benzoylaniline	2-Hydroxy-*N*-trifluoroacetylaniline
Formula	$C_{13}H_{11}NO_2$	$C_8H_5NO_2F_3$
M_r	213.23	204.06
Crystal size/mm	0.25 × 0.20 × 0.03	0.7 × 0.5 × 0.025
Habit	Platy	Platy
Crystal system	Monoclinic	Orthorhombic
Space group	$P2_1/c$	$P2_12_12_1$
a/Å	10.970(5)	5.297(4)
b/Å	7.060(2)	30.567(10)
c/Å	14.205(11)	5.256(2)
β/°	89.23(5)	—
V/Å^3	1100.1(1.0)	851.0(1.0)
d_c/Mg m^{-3}	1.288	1.601
Z	4	4
μ/cm^{-1}	6.7	13.8
$F(000)$	449.38	417.87
Measured reflections	887	567
Reflns with $I > 2.5\sigma(I)$	817	410
No. of l.s. parameters	152	120
R	0.049	0.061
R_w	0.050	0.060
G. of f.	8.65	3.88
Index ranges, h	−10, +10	0, 5
k	0, 6	0, 30
l	0, 13	0, 5
$\Delta\rho$ (min., max.) e/Å^3	−0.23, 0.34	−0.20, 0.21

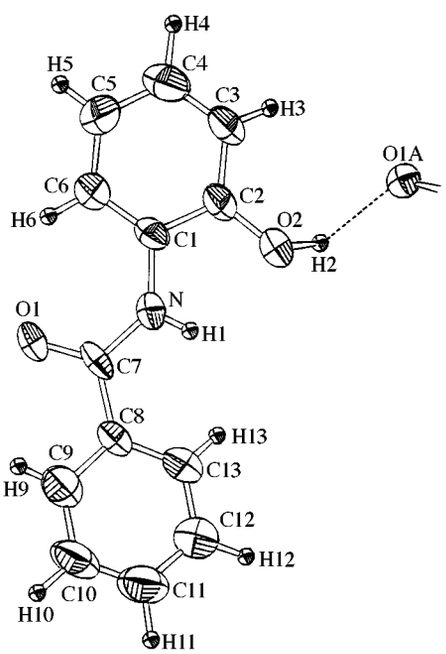


Fig. 1 Molecular structure of 2-hydroxy-*N*-benzoylaniline with atomic numbering (ORTEP,[13] 50% probability ellipsoids for non-hydrogen atoms; arbitrary radii for hydrogen atoms)

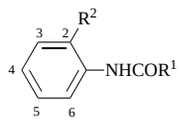
placed in calculated positions with isotropic temperature factors, and these were fixed during refinement. The OH and NH hydrogen atoms were located in the difference map and their positions refined with fixed isotropic temperature factors. The resulting hydrogen (H1) position for the NH group indicates that C1, C7, H1 and N are coplanar within experimental error, but the position of H2 gives an unrealistically short O2–H2 distance (see Fig. 1 for numbering). If the temperature factor of H2 was allowed to vary during the refinement, it became unreasonably large. We conclude from this that X-ray data do not give an accurate value for the position of H2 which is probably disordered. Structural details for 2-hydroxy-*N*-benzoylaniline are given in Tables 1 and 2 and in the ORTEP[13] diagram (Fig. 1).

Table 2 Interatomic distances and interbond angles for 2-hydroxy-*N*-benzoylaniline and 2-hydroxy-*N*-trifluoroacetylaniline

Bond	2-Hydroxy-*N*-benzoylaniline	2-Hydroxy-*N*-trifluoroacetylaniline
	Bond length/Å	Bond length/Å
C1–C2	1.399(7)	1.368(15)
C2–C3	1.398(7)	1.40(2)
C3–C4	1.381(9)	1.39(2)
C4–C5	1.382(8)	1.37(2)
C5–C6	1.401(7)	1.41(2)
C6–C1	1.372(7)	1.39(2)
C1–N	1.430(6)	1.416(14)
C7–N	1.347(6)	1.319(15)
C2–O2	1.361(7)	1.358(14)
C7–O1	1.246(6)	1.214(15)
C7–C8	1.489(7)	—
C7–C81	—	1.554(11)
C7–C82	—	1.560(10)
C8–C9	1.380(7)	—
C9–C10	1.396(8)	—
C10–C11	1.389(10)	—
C11–C12	1.372(9)	—
C12–C13	1.396(8)	—
C13–C8	1.398(8)	—
C81–F1	—	1.365(15)
C81–F2	—	1.367(15)
C81–F3	—	1.349(14)
C82–F4	—	1.297(14)
C82–F5	—	1.250(15)
C82–F6	—	1.281(12)
O2–O1A	2.648(5)	2.723(11)
O2–H2	see text	1.145(8)
H2–O1A	see text	1.751(8)
	Bond angle/deg	Bond angle/deg
C1–C2–O2	115.9(4)	117(1)
C3–C2–O2	123.2(4)	122(1)
C1–N–C7	129.7(4)	127(1)
N–C7–O1	121.4(4)	127(1)
C8–C7–O1	121.8(4)	—
C81–C7–O2	—	120(1)
C82–C7–O2	—	116(1)
O2–H2–O1A	—	139.1(5)

The crystal structure analysis of 2-hydroxy-*N*-trifluoroacetylaniline was less straightforward. On crystallization from toluene, the crystals formed in extensive very thin sheets. Remarkably, these crystals are extremely flexible when wet, being capable of bending to arcs of 5 mm radius or less without damage. When dry however, the crystals are brittle. This interesting observation could be the result of a phase transition on drying or to desolvation and is the subject of a continuing investigation. Crystals used for structural analysis were originally wet and had been allowed to dry. One crystal, cut from an extended sheet was mounted on the diffractometer, but during data collection a standard intensity fell by 30% in 24 h and the crystal was clearly eroded. This is not due primarily to crystal volatility since crystals left in open vessels remained unchanged for weeks. After several other attempts at data collection the final solution was to seal the crystal in a 1.5 mm diameter capilliary (*ex* Pantak) and (this may have been crucial) to move the Ni filter from the detector to the beam side of the crystal. Two octants of reciprocal space were scanned without significant loss in standard intensity. The peak profiles were of irregular, serrated form, implying that the sample was not a single crystal but a stack of closely aligned platelets. Thus the experimental data were not of ideal form for accurate structure analysis and this is borne out by the relatively large esds of the final atomic coordinates. A Gaussian absorption correction was applied after data reduction. Crystal data are set out in Tables 1 and 2.[14] The 0k0 reflections were clearly absent for k odd; both the odd h00s and odd 00ls were weak, but because

Table 3 ^{1}H NMR chemical shifts for substituted *N*-acylanilines[a]



		δ_H (splitting pattern)		
Substituents	Solvent	δ(4-H)	δ(6-H)	δ(6-H) − δ(4-H)
R^1 = Me, R^2 = H	$CDCl_3$	7.10–7.06 (t)	7.52–7.50 (d)	0.43
	Me_2SO	7.04–7.00 (t)	7.61–7.59 (d)	0.58
R^1 = Me, R^2 = Me	$CDCl_3$	7.09–7.05 (t)	7.67–7.65 (d)	0.59
	Me_2SO	7.07–7.03 (t)	7.40–7.38 (d)	0.34
R^1 = Me, R^2 = OMe	$CDCl_3$	7.05–7.02 (m × 4)	8.36–8.34 (d)	1.32
	Me_2SO	7.07–7.00 (m)	7.93–7.91 (d)	0.88
R^1 = Me, R^2 = OH	$CDCl_3$[b]	7.17–7.12 (td)	7.00–6.96 (dd)	−0.17
	$CDCl_3$[c]	7.13–7.12 (td)	6.98–6.96 (dd)	−0.16
	Me_2SO	6.95–6.90 (td)	7.69–7.66 (dd)	0.75
R^1 = Ph, R^2 = H	$CDCl_3$	7.17–7.14 (t)	7.67–7.65 (d)	0.50
	Me_2SO	7.13–7.09 (t)	7.83–7.81 (d)	0.71
R^1 = Ph, R^2 = Me	$CDCl_3$	7.14–7.09 (td)	7.89–7.88 (d)	0.77
	Me_2SO	7.19–7.15 (m × 4)	7.36–7.34 (d)	0.18
R^1 = Ph, R^2 = OMe	$CDCl_3$	7.10–7.06 (td)	8.55–8.53 (dd)	1.46
	Me_2SO	7.21–7.16 (td)	7.82–7.79 (dd)	0.62
R^1 = Ph, R^2 = OH	$CDCl_3$[d]	7.22–7.19 (td)	7.17–7.15 (dd)	−0.05
	$CDCl_3$[e]	7.18–7.16 (td)	7.18–7.16 (dd)	0.00
	Me_2SO	7.07–7.02 (td)	7.70–7.67 (dd)	0.64
R^1 = CF_3, R^2 = H	$CDCl_3$	7.27–7.23 (td)	7.58–7.56 (dt)	0.32
	Me_2SO	7.25–7.21 (td)	7.68–7.65 (dt)	0.44
R^1 = CF_3, R^2 = Me	$CDCl_3$	7.30–7.18 (m)	7.79–7.76 (d)	0.54
	Me_2SO	7.34–7.24 (m)	7.34–7.24 (m)	0.00
R^1 = CF_3, R^2 = OMe	$CDCl_3$	7.20–7.15 (td)	8.33–8.30 (dd)	1.14
	Me_2SO	7.34–7.29 (td)	7.41–7.38 (dd)	0.08
R^1 = CF_3, R^2 = OH	$CDCl_3$	7.16–7.11 (td)	7.98–7.95 (dd)	0.83
	Me_2SO	7.16–7.11 (d,q,d)	7.33–7.30 (dd)	0.18

[a] Concentrations of *N*-acylanilines were usually in the range *ca.* 0.01–0.1 mol dm^{-3}. Concentrations were [b] 3.3 × 10^{-4}, [c] 3.3 × 10^{-5}, [d] 0.047 and [e] 4.7 × 10^{-4} mol dm^{-3}.

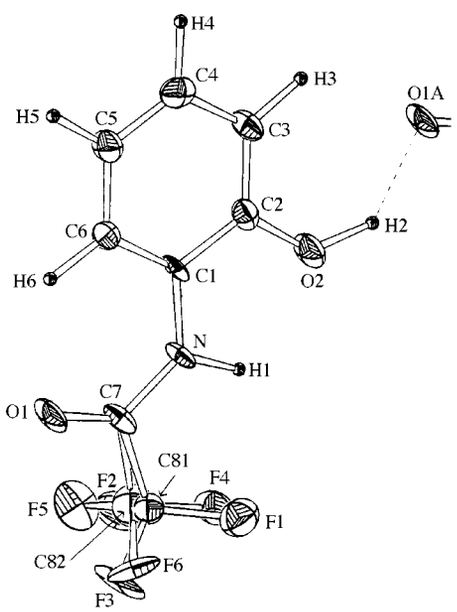


Fig. 2 Molecular structure of 2-hydroxy-*N*-trifluoroacetylaniline with atomic numbering (ORTEP,[13] 50% probability ellipsoids for non-hydrogen atoms; arbitrary radii for hydrogen atoms)

of the small *a* and *b* cell parameters there were too few to be certain that these were systematically absent. This means the space group is any of the four $P*2_1*$, where * is either 2 or 2_1. All combinations of 2 and 2_1 were tried but none gave a tractable result by direct methods except $P2_12_12_1$. Because the *B* face of the unit cell is so small, the four molecules must be packed in extended form in the *y*-direction. In any space group other than $P2_12_12_1$ the ends of the molecules would have to be related by diad axes and for molecular packing reasons this is virtually unknown. Solution by direct methods using SOLVER in $P2_12_12_1$ was not straightforward. Not until the ninth phase set in order of merit was reached could a refinable molecular fragment be recognised on the E map. Full matrix anisotropic least squares refinement showed that the fluorine atoms are disordered in six half-occupied positions. They have unacceptable bond lengths with C8 unless this atom is given two half-occupied positions. Most hydrogen positions were revealed on the final F map. These were given theoretical positions except for H2 where there is an intermolecular hydrogen bond from atom O1 to atom O2. An ORTEP plot for 2-hydroxy-*N*-trifluoroacetylaniline showing this is given in Fig. 2. Refinement details are given in Table 1 and bond length and interbond angles of interest are given in Table 2. In the structure there are substantial differences in C–F bond lengths ranging from *ca.* 1.29 to *ca.* 1.36 Å. Discrepancies in C–F bond lengths in trifluoromethyl groups have been found previously.[15]

NMR studies

^{1}H, ^{13}C and where appropriate ^{19}F NMR spectra were run in $CDCl_3$ and [$^2H_6$]Me_2SO with concentrations of *N*-acylanilines usually in the range *ca.* 0.01–0.1 mol dm^{-3} using either Bruker AMX400 or Bruker AM360 instruments. In the case of 2-hydroxy-*N*-benzoylaniline the ^{1}H NMR spectrum in $CDCl_3$ was run at concentrations of 0.047 and 4.7 × 10^{-4} mol dm^{-3} and for 2-hydroxy-*N*-acetylaniline in $CDCl_3$ the spectrum was run at concentrations of 3.3 × 10^{-4} and 3.3 × 10^{-5} mol dm^{-3}. The effects of a change in concentration on the spectra were extremely small and the results are given in the Experimental section and in Table 3. TMS was used as the internal standard for ^{1}H and ^{13}C NMR spectra. In some cases the assignment of

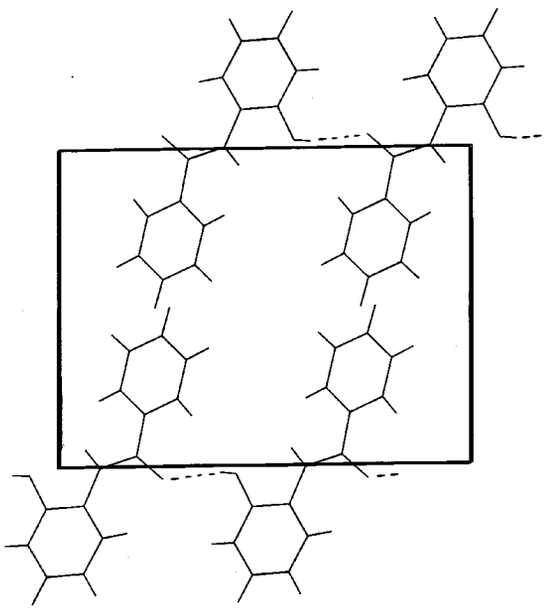


Fig. 3 Packing diagram for 2-hydroxy-*N*-benzoylaniline in *y*-projection

signals was assisted by the use of decoupling, NOE and COSY techniques.

Results and discussion

Crystal structures of 2-hydroxy-*N*-benzoylaniline and 2-hydroxy-*N*-trifluoroacetylaniline

Structural details for 2-hydroxy-*N*-benzoylaniline are given in Tables 1 and 2 and in the ORTEP[13] diagram Fig. 1. The structure consists of infinite ribbons of molecules of 2-hydroxy-*N*-benzoylaniline connected by intermolecular hydrogen bonds between the hydroxy and carbonyl groups of adjacent molecules as shown in Fig. 3. The O···H···O bond length of 2.65 Å identifies the bond as moderately strong.[1,16] There are no short intermolecular contacts involving the electronegative atoms other than this O2···H2···O1A contact. The shortest contact to the nitrogen atom is the intramolecular distance to H13 (2.60 Å) which is too long to be significant.

Structure details for 2-hydroxy-*N*-trifluoroacetylaniline are given in Tables 1 and 2 and in the ORTEP diagram Fig. 2. As for 2-hydroxy-*N*-benzoylaniline, the structure of 2-hydroxy-*N*-trifluoroacetylaniline consists of infinite ribbons of molecules connected by intermolecular hydrogen bonds involving the hydroxy and carbonyl groups of adjacent molecules. For 2-hydroxy-*N*-trifluoroacetylaniline the O···H···O hydrogen bond length is 2.72 Å somewhat longer and therefore weaker than that found for 2-hydroxy-*N*-benzoylaniline. No other short intermolecular contacts were found for either oxygen or nitrogen atoms. The shortest contact is that between disordered F3 and H2. The intermolecular hydrogen bonding is such as to give rise to similar molecular packing in the two crystal structures Figs. 3 and 4. In 2-hydroxy-*N*-benzoylaniline the ribbons extend along the *z*-axis, alternate molecules being related by the *c* glide. In 2-hydroxy-*N*-trifluoroacetylaniline the ribbons extend along the *x*-axis. All these molecules have identical orientation, being related solely by the *a* cell parameter. In 2-hydroxy-*N*-benzoylalaniline the ribbons are stacked two to a cell, whereas in 2-hydroxy-*N*-trifluoroacetylaniline there are four to a cell so that layers of (disordered) fluorine atoms abut.

A similar crystal structure[17] with intermolecular hydrogen bonds between hydroxy and carbonyl groups has been found for 3-hydroxy-2-(acetylamino)fluorene (**2**). The O···H···O bond length is 2.68 Å, intermediate between the bond lengths found for 2-hydroxy-*N*-benzoylaniline and 2-hydroxy-*N*-trifluoroacetylaniline. By contrast 1-hydroxy-2-(acetylamino)-

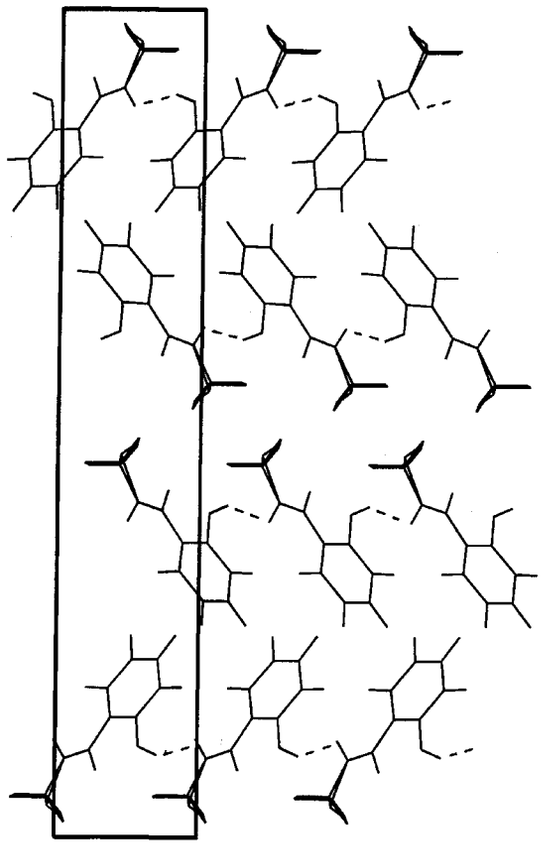
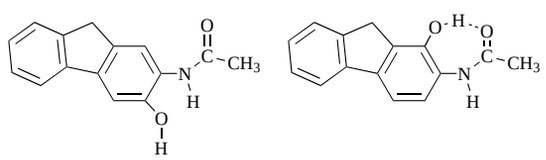


Fig. 4 Packing diagram for 2-hydroxy-*N*-trifluoroacetylaniline in *z*-projection



2 **3**

fluorene (**3**) has a strong intramolecular O···H···O hydrogen bond of length 2.51 Å but a very weak intermolecular hydrogen bond.

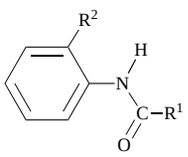
^{1}H NMR spectra of substituted *N*-acylanilines in $CDCl_3$ and $[^2H_6]Me_2SO$

It has been known for many years[2,18] that the chemical shift of the protons in the 2-and 6-positions of *N*-acylanilines is displaced downfield by *ca*. 1 ppm compared with the proton in the 4-position. The effect is caused by the magnetic anisotropy of the carbonyl group of the amide. The barrier to rotation about the Ph–N bond is low, whereas the barrier to rotation about the C–N bond within the amide group[19] is 60–80 kJ mol^{-1}, and the most stable conformation of an amide has a *trans* arrangement of the substituents on the carbonyl group and nitrogen. Generally when one of the *ortho*-positions is occupied by a substituent (2-position), the remaining *ortho* proton (6-position) continues to show the downfield shift, because the comparatively free rotation about the Ph–N bond still allows the *ortho* proton to be influenced by the carbonyl group. We have now found that if the 2-position is occupied by a hydroxy group, the proton at the 6-position no longer shows a downfield shift when the spectrum is recorded in $CDCl_3$ and the chemical shift is comparable to that for the proton in the *para* position. Thus a hydroxy substituent at the 2-position in *N*-acylanilines leads to anomalous behaviour compared with other substituents and experiments were carried out to provide an explanation.

The ^{1}H NMR spectra were taken in $CDCl_3$ and $[^2H_6]Me_2SO$ for substituted *N*-acetyl-, *N*-benzoyl- and *N*-trifluoroacetyl-

anilines each with H, Me, OMe and OH substituents in the 2-position. Details of the ^{1}H NMR spectra are given in the Experimental section and the values of the chemical shift differences of the protons at the 4- and 6-positions are given in Table 3. The results for the *N*-acetyl- and *N*-benzoyl-anilines are similar and are discussed together. The results for *N*-trifluoroacetylanilines are discussed separately.

For the *N*-acetylanilines and *N*-benzoylanilines (**1** with R^1 = Me and Ph, respectively) with substituents R^2 = H, Me and OMe at the 2-position, the difference in chemical shifts of protons at the 4- and 6-positions range from δ(6-H) − δ(4-H) 0.43 to 1.46 in $CDCl_3$ and from 0.18 to 0.88 in [$^2H_6$]Me_2SO. The results for these *N*-acylanilines in solution in $CDCl_3$ and [$^2H_6$]Me_2SO identify the structure shown in **4** which accounts for the strong deshielding of the 6-H by the nearby carbonyl group. The range of values for δ(6-H) − δ(4-H) with differently substituted *N*-acylanilines is expected [2] and reflects the effect of



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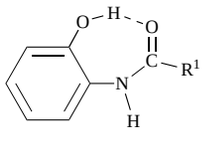

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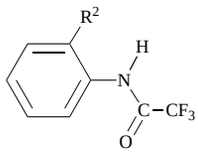
the substituent at the 2-position on the precise angle and distance between the carbonyl group and 6-H. However what is unexpected are the values δ(6-H) − δ(4-H) of −0.17 and −0.05 found in $CDCl_3$ for 2-hydroxy-*N*-acetylaniline and 2-hydroxy-*N*-benzoylaniline, respectively. We can account for this by assuming that for 2-hydroxy-*N*-acetylaniline and 2-hydroxy-*N*-benzoylaniline in $CDCl_3$ an intramolecular hydrogen bond is formed between the hydroxy and amide carbonyl as in **5**. In this conformation the deshielding effect of the carbonyl group on the 6-H atom is absent. Further, the hydroxy resonance in the NMR spectrum is extremely sharp which supports the existence of a hydrogen bond. The intramolecular hydrogen bond found [20] for 1-hydroxy-2-(acetylamino)fluorene (**3**) in the solid state and referred to above provides evidence that the structural requirements for formation of an intramolecular hydrogen bond in **5** which will include some loss of planarity between the amide group and the aromatic ring can be satisfied. The O···H···O bond length is short (2.51 Å) indicative of a strong hydrogen bond. We prefer to explain the low values of δ(6-H) − δ(4-H) for 2-hydroxy-*N*-acetylaniline and 2-hydroxy-*N*-benzoylanaline in $CDCl_3$ in terms of intramolecular hydrogen bonding rather than intermolecular hydrogen bonding because dilution has no effect on the values of δ(6-H) − δ(4-H) nor on other parts of the spectrum and because a similar intramolecular hydrogen bond is found for **3** in the solid state. The values of δ(6-H) − δ(4-H) are not compatible with a *cis* configuration of the alkyl and aryl substituents about the amide bond. It is interesting that for 2-hydroxy-*N*-acetylaniline and 2-hydroxy-*N*-benzoylaniline in [$^2H_6$]Me_2SO the values δ(6-H) − δ(4-H) 0.75 and 0.64, respectively, are found within the expected range for structure **4**. We assume that in [$^2H_6$]Me_2SO a strong intermolecular hydrogen bond is formed between the hydroxy group and the strongly hydrogen-bonding solvent [18] and the intramolecular hydrogen bond is disrupted thus favouring structure **4**.

The results for substituted *N*-trifluoroacetylanilines are different from those for *N*-acetylanilines and *N*-benzoylanilines. In $CDCl_3$, values of δ(6-H) − δ(4-H) ranging from 0.32 to 1.14 are found with substituents R^2 = H, Me, OMe and OH. Thus the structure in **6** is preferred. For 2-hydroxy-*N*-trifluoroacetylaniline the intramolecular hydrogen bond will be weakened compared with that in 2-hydroxy-*N*-acetylaniline and 2-hydroxy-*N*-benzoylanilines because of the lower basicity of the carbonyl oxygen. In [$^2H_6$]Me_2SO for *N*-trifluoroacetylaniline the result δ(6-H) − δ(4-H) = 0.44 is observed and indicates that structure **6** is preferred. However for 2-substituted *N*-trifluoroacetylanilines with R^2 = Me, OMe and OH the values of δ(6-H) − δ(4-H) in [$^2H_6$]Me_2SO are close to zero and hence a low energy conformation **7** with the carbonyl group located



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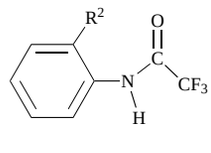

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away from the 6-H position is more important. In this case the acidity of the amide proton in *N*-trifluoroacetylanilines is high and a stabilising interaction with the solvent may be important in [$^2H_6$]Me_2SO. With substituents at the 2-position (R^2 = Me, OMe and OH) such an interaction with the solvent may be disrupted by steric hindrance in structure **6** and conformation **7** may therefore be preferred, whereas for 2-trifluoroacetylaniline (R^2 = H) structure **6** can be adopted. It is less likely that the low values of δ(6-H) − δ(4-H) for 2-substituted-trifluoroacetylanilines in [$^2H_6$]Me_2SO indicate that a *cis* configuration of the substituents about the amide bond is the preferred configuration although this cannot be ruled out.

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