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Ultrasound effect on the synthesis of 4-alkyl-(aryl)aminobenzaldehydes

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Abstract—The sonochemical nucleophilic aromatic substitutions on 4-fluorobenzaldehyde with different azacycloalkanes and azoles have been studied. A beneficial ultrasound effect was observed, reactions were clean and high yields of the products were isolated after 15 min sonication. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

The synthesis of 4-alkylaminoacetophenones via the S_NAr reaction of 4-fluoroacetophenone with appropriate amines under potassium carbonate catalysis was described by Bader et al.[1] and Gale et al.[2] Cozzi et al.[3] claimed that S_NAr reactions on the haloarenes having mild electron-withdrawing groups such as the formyl group needs rather harsh conditions.

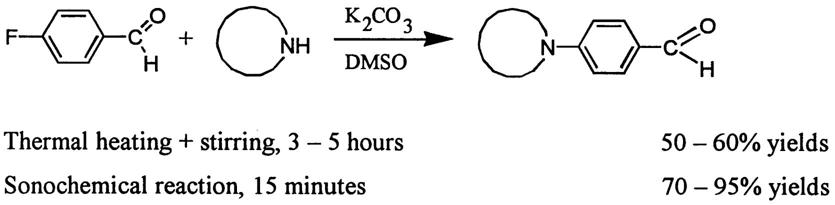
On the other hand Smith et al.[4] described the ultrasound acceleration of Ullmann diarylether synthesis, Hanoun et al.[5] described the ultrasound acceleration of Ullmann–Goldberg synthesis of *N*-arylanthranilic acids and Cerrada et al.[6] described ultrasound acceleration of the S_NAr reaction of 4-nitrofluorobenzene with a range of azoles.

The main aim of this work was to examine the possible beneficial ultrasound effect on the S_NAr reactions of 4-fluorobenzaldehyde with different alicyclic as well as aromatic amines.

2. Results and discussion

At the beginning of our work we checked the procedure described by Cozzi et al.,[3] using dimethylsulfoxide (DMSO) as the solvent and potassium carbonate as the base. We found out that a long reaction time is necessary to achieve reasonable yields, and the reaction resulted in rather impure products which were difficult to purify. Exchange of potassium carbonate for dimethylaniline as the base did not improve the achieved results. We therefore decided to perform the sonochemical S_NAr reactions of 4-fluorobenzaldehyde with different azacycloalkanes and azoles. Dimethylsulfoxide was used as the solvent and potassium carbonate as the base (Scheme 1). Control experiments with some amines under thermal heating were also performed. For all sonochemical experiments it was characteristic that the temperature of the reaction mixture rose very sharply up to 100–140°C during the first 5–8 min of sonication. Prolonging the sonication did not cause further temperature rise, and in some cases even a drop in reaction temperature was observed. From this observation it follows that an exothermic reaction was started by sonication and further, that the reaction was, possibly, completed after 8–10 min of sonication.

Application of ultrasound shortened the reaction time from 5 h under classical conditions to 15 min, and the yields of the products were 15–30% higher than in the experiments with 5 h thermal heating of the reaction mixture at 100°C.



Scheme 1. Thermal heating plus stirring, 3–5 h 50–60% yields; sonochemical reaction, 15 min 70–95% yields.

Keywords: ultrasound; 4-dialkylaminobezaldehydes; nucleophilic aromatic substitutions.

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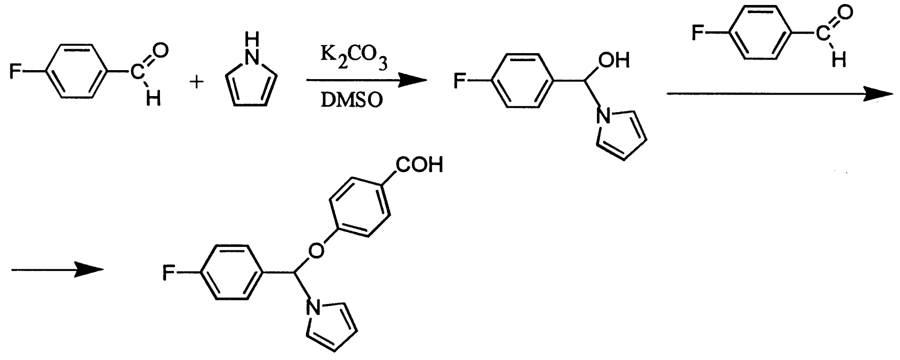
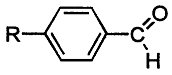


Scheme 2.

Lower yields of the products in experiments with aziridine or 1-methylaziridine (24%) were due to the low stability of the three-membered ring. Indirect proof of this was the formation of tarry material. Lower yields in the case of *N*-monoalkylpiperazines can be caused by the fact that products are oils and an extraction procedure has to be implemented for their isolation.

Ultrasound had also another positive effect—the products were very pure. Usual work-up of the reaction mixture with water afforded, in many cases, analytically pure materials. Chromatographic separation of the product was necessary just in the case of the reactions with aziridine or 1-methylaziridine and 1,2,3-benzotriazole, when a 3:1 mixture of positional isomers is formed. Unsuccessful experiments of S_NAr substitution with indole and pyrrole were also obtained. No substitution product was detected by ^{1}H NMR spectroscopy in the experiments with indole and just approximately 10% of the product was isolated in the reaction with pyrrole. The potential intermediate of this reaction (aminoalcohol) underwent reaction with a second molecule of 4-fluorobenzaldehyde and gave 10% of 4-(4-fluoro-α-pyrrol-1-ylbenzyloxy)benzaldehyde. This reaction route is depicted in Scheme 2.

Table 1. 4-Alkyl-(aryl)aminobenzaldehydes



Entry	R	Yield (%)
1	Aziridin-1-yl	24
2	Azetidin-1-yl	81
3	2-Methylaziridin-1-yl	24
4	Pyrrolidin-1-yl	92 (62[a])
5	Piperidin-1-yl	85 (48[a])
6	Hexamethylenimin-1-yl	95 (58[a], 78[b])
7	Morpholin-4-yl	60 (60[a])
8	Thiomorpholin-4-yl	45
9	4-Methylpiperazin-1-yl	73 (57[a])
10	4-Heptylpiperazin-1-yl	64
11	4-Octylpiperazin-1-yl	51
12	4-Ethoxycarbonylpiperazin-1-yl	39 (70[a])
13	7,15-Diazadispiro[5.1.5.3]hexadecane-15-yl	72 (31[a])
14	Pyrrol-1-yl	10
15	Imidazol-1-yl	75
16	1,2,4-Triazol-1-yl	49
17	5-Methylsulfanyltetrazol-1-yl	2
18	3,5-Bis-methylsulfanyl-1,2,4-triazol-1-yl	2
19	Benzimidazol-1-yl	80
20	Benzotriazol-1-yl	17
21	Benzotriazol-2-yl	55

[a] Yields of classical S_NAr reactions.

[b] Reaction performed under classical conditions (heating at 100°C, magnetic stirring for 15 min) with sonochemically activated K_2CO_3 (K_2CO_3 was sonicated 15 min in DMSO).

Our results (Table 1) indicate that ultrasound considerably enhances the S_NAr substitution of the fluorine on 4-fluorobenzaldehyde with different alicyclic as well as aromatic amines, catalyzed by potassium carbonate. One can assume that catalysis is caused by very powerful micro-streaming, which accompanies implosions of micro-bubbles and provides effective mass transfer. Potassium carbonate particles are disrupted and its active surface is therefore considerably enlarged, which means that the catalytic activity of potassium carbonate is also enhanced. This hypothesis is confirmed by the experiment when potassium carbonate was sonicated 15 min in DMSO, then 4-fluorobenzaldehyde and azetidine were added and the reaction was performed under heating at 100°C and magnetic stirring for 15 min. The yield of this reaction was 78% instead of 95% (the yield of the sonochemical reaction). The yield of the silent reaction without ultrasonic activation of potassium carbonate was 58% after 5 h. If this is the case then a similar effect should be observed if the reaction is performed in UltraTurax, as foreseen by Reisse.[7]

3. Conclusion

Application of ultrasonic irradiation in the nucleophilic aromatic substitutions of 4-fluorobenzaldehyde with different azacycloalkanes and azoles allows (i) a shortening of the reaction time from 5 h to 15 min, (ii) increased yields and (iii) simplification of work-up of the reaction mixtures after the reactions.

4. Experimental

The ^{1}H NMR spectra were recorded at 300 MHz on a Varian Gemini spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard. The ^{13}C NMR spectra were recorded at 75 MHz in $CDCl_3$. The IR spectra were recorded on a Perkin–Elmer 1600 FT-IR instrument as 2% solutions in chloroform and the elemental analyses were recorded on a Carlo-Erba instrument. Melting points were determined on a Kofler hot stage and uncorrected. All sonochemical experiments were carried out in a glass reactor fitted to an ultrasonic horn ULTRAGEN (20 kHz, 300 W) for 15 min under an air atmosphere.

Starting materials were either commercially available or prepared according to literature procedures. Aziridine and 1-methylaziridine were prepared according to Ref. 8, azetidine according to Ref. 9 and *N*-ethoxycarbonylpiperazine according to Ref. 10. *N*-Alkylpiperazines were prepared by the following procedure.

4.1. Synthesis of *N*-alkylpiperazines

The appropriate iodoalkane (0.1 mol) was added dropwise over 10 min to a solution of anhydrous piperazine (21.5 g, 0.25 mol) in anhydrous methanol (60 mL). The reaction mixture was left for one day at room temperature and the solid piperazine hydrogeniodide was filtered off and the filtrate was concentrated under reduced pressure. The residual oil was dissolved in diethyl ether (150 mL) and washed twice with aqueous 3 M sodium hydroxide (100 mL). The ether solution was dried over Na_2SO_4, and ether evaporated on a rotary vacuum evaporator, with the residue being distilled bulb to bulb on a Buchi instrument at 8 mmHg pressure.

4.2. The general procedure for classical S_NAr reactions on 4-fluorobenzaldehyde

Potassium carbonate (3.04 g; 0.022 mol) was added to the solution of appropriate secondary cyclic amine (0.02 mol) and 4-fluorobenzaldehyde (2.48 g; 0.22 mol) in DMSO (20 mL). The reaction mixture was heated at 100°C for 3–5 h. The reaction mixture was then poured into water (400 mL) and the emulsion formed was extracted three times into diethyl ether (75 mL). The ether solution was washed with water, dried over anhydrous Na_2SO_4, ether was distilled off on a rotary vacuum evaporator and the crude product was chromatographed on silica using isohexane:ethyl acetate 9:1–2:1 as the eluent.

4.3. The general procedure for sonochemical S_NAr reactions on 4-fluorobenzaldehyde

Potassium carbonate (3.04 g; 0.022 mol) was added to the solution of appropriate secondary cyclic amine (0.02 mol) and 4-fluorobenzaldehyde (2.48 g; 0.022 mol) in DMSO (20 mL). The reaction mixture was sonicated for 15 min. The temperature of the reaction mixture attained 150°C at the end of sonication. The reaction mixture was cooled down to 60°C and then poured into distilled water (400 mL). The emulsion formed was extracted three times into diethyl ether (75 mL). The ether solution was washed with water, dried over anhydrous Na_2SO_4, ether was distilled off on a rotary vacuum evaporator and the product was collected by filtration with suction. In the case where the product was an oil or not pure enough (TLC) it was purified by chromatography on silica using isohexane:ethyl acetate 9:1–2:1 as the eluent. The results are given in the Table 1.

4.4. Synthesis of 4-(benzotriazol-1-yl)benzaldehyde and 4-(benzotriazol-2-yl)benzaldehyde

Potassium carbonate (4.42 g; 0.032 mol) was added to the solution of 1,2,3-benzotriazole (3.57 g; 0.03 mol) and 4-fluorobenzaldehyde (3.72 g; 0.03 mol) in DMSO (20 mL). The reaction mixture was sonicated for 10 min and then cooled to room temperature. The solid reaction mixture was suspended in distilled water (200 mL) and the crude product (5.9 g; mp 138–148°C) was filtered off with suction. This product was purified by chromatography on silica using isohexane:ethyl acetate 1:1, and later with pure chloroform as the eluent.

4.4.1. 4-(Aziridin-1-yl)benzaldehyde. Pale yellow solid, 0.71 g, 24%, mp 31–32°C; [Found: C, 73.2; H, 6.1; N, 9.6. C_9H_9NO requires C, 73.45; H, 6.16; N, 9.52%]; R_f (ethyl acetate) 0.49; ν_{max} ($CHCl_3$) 2998, 2739, 1694, 1665, 1602, 1574, 1508, 1335, 1305, 1153, 907, 843 cm^{-1}; δ_H (300 MHz $CDCl_3$) 9.88 (1H, s, CHO), 7.77 (2H, d, J=8.7 Hz, Ar—H), 7.11 (2H, d, J=8.7 Hz, Ar—H), 2.22 (4H, s, 2×CH$_2$ aziridin); δ_C (75 MHz, $CDCl_3$) 191.3, 161.3, 131.5, 121.5, 27.9.

4.4.2. 4-(Azetidin-1-yl)benzaldehyde. Yellow solid, 2.61 g, 81%, mp 33–34°C; [Found: C, 74.4; H, 6.7; N, 8.8. $C_{10}H_{11}NO$ requires C, 74.51; H, 6.88; N, 8.69%]; R_f (ethyl acetate) 0.6; ν_{max} ($CHCl_3$) 2865, 2745, 1678, 1598, 1557, 1528, 1481, 1391, 1305, 1159, 834, 823 cm^{-1}; δ_H (300 MHz $CDCl_3$) 9.72 (1H, s, CHO), 7.70 (2H, d, J=8.7 Hz, Ar—H), 6.38 (2H, d, J=8.7 Hz, Ar—H), 4.03 (4H, t, J=7.5 Hz, 2×CH$_2$ azetidin), 2.44 (2H, m, CH$_2$ azetidin); δ_C (75 MHz, $CDCl_3$) 190.4, 155.1, 132.0, 125.7, 109.7, 51.4, 16.5.

4.4.3. 4-(2-Methylaziridin-1-yl)benzaldehyde. Colourless oil, 0.77 g, 24%; [Found: C, 74.3; H, 6.9; N, 8.7. $C_{10}H_{11}NO$ requires C, 74.51; H, 6.88; N, 8.69%]; R_f (ethyl acetate) 0.59; ν_{max} ($CHCl_3$) 2978, 2799, 1700, 1605, 1587, 1513, 1410, 1308, 1245, 1162, 846 cm^{-1}; δ_H (300 MHz $CDCl_3$) 9.86 (1H, s, CHO), 7.76 (2H, d, J=8.4 Hz, Ar—H), 7.07 (2H, d, J=8.4 Hz, Ar—H), 2.29 (1H, m, CH$_3$*CH* methylaziridin), 2.18 (1H, d, J=6.0 Hz, NC*Ha*Hb, methylaziridin), 2.13 (1H, d, J=3.3 Hz, NCHa*Hb*, methylaziridin), 1.40 (3H, d, J=5.7 Hz, CHC*H*$_3$); δ_C (75 MHz, $CDCl_3$) 190.8, 160.7, 131.2, 121.0, 35.4, 34.9, 18.1.

4.4.4. 4-(Pyrrolidin-1-yl)benzaldehyde. White solid, 3.22 g, 92%, mp 79–82°C, lit.[11] 84–85°C; [Found: C, 75.5; H, 7.6; N, 8.1. $C_{11}H_{13}NO$ requires C, 75.39; H, 7.48; N, 8.00%]; R_f (ethyl acetate) 0.62; ν_{max} ($CHCl_3$) 2978, 2856, 2739, 1675, 1597, 1553, 1530, 1485, 1393, 1351, 1187, 1168 cm^{-1}; δ_H (300 MHz $CDCl_3$) 9.72 (1H, s, CHO), 7.73 (2H, d, J=8.7 Hz, Ar—H), 6.57 (2H, d, J=8.7 Hz, Ar—H), 3.39 (4H, m, 2×H2, 2×H5 pyrrolidin), 2.05 (4H, m, 2×H3, 2×H4 pyrrolidin); δ_C (75 MHz, $CDCl_3$) 190.3, 152.0, 132.2, 124.8, 111.2, 47.7, 25.4.

4.4.5. 4-(Piperidin-1-yl)benzaldehyde. White solid, 3.22 g, 85%, mp 60–61°C, lit.[11] 62–64°C; [Found: C, 76.2; H, 8.1; N, 7.3. $C_{12}H_{15}NO$ requires C, 76.14; H, 7.99; N, 7.40%]; R_f (ethyl acetate) 0.64; ν_{max} ($CHCl_3$) 2939, 2928, 2741, 1664, 1592, 1560, 1518, 1436, 1393, 1361, 1172, 1127, 1024, 919 cm^{-1}; ^{1}H NMR data consistent with lit.;[12] δ_C (75 MHz, $CDCl_3$) 190.4, 155.2, 132.0, 126.1, 113.3, 48.4, 25.4, 24.4.

4.4.6. 4-(Hexamethylenimin-1-yl)benzaldehyde. Yellow solid, 3.86 g, 95%, mp 35°C; [Found: C, 76.7; H, 8.4; N, 6.7. $C_{13}H_{17}NO$ requires C, 76.80; H, 8.43; N, 6.89%]; R_f (ethyl acetate) 0.65; IR data constistent with lit.;[13] ^{1}H NMR data consistent with lit.;[12] δ_C (75 MHz, $CDCl_3$) 190.2, 155.2, 131.9, 126.1, 113.0, 48.3, 27.7, 26.0.

4.4.7. 4-(Morpholin-4-yl)benzaldehyde. White solid, 2.29 g, 60%, mp 62–64°C, lit.[11] 61–63°C; [Found: C, 69.2; H, 6.9; N, 7.2. $C_{11}H_{13}NO_2$ requires C, 69.08; H, 6.86; N, 7.33%]; R_f (ethyl acetate) 0.52; ν_{max} ($CHCl_3$) 2839, 2750, 1690, 1666, 1600, 1566, 1519, 1450, 1382, 1173, 1122, 929 cm^{-1}; ^{1}H NMR data consistent with lit.;[2] δ_C (75 MHz, $CDCl_3$) 190.5, 155.2, 131.8, 127.7, 113.5, 66.5, 47.3.

4.4.8. 4-(Thiomorpholin-4-yl)benzaldehyde. Yellow solid, 1.87 g, 45%, mp 35–40°C; [Found: C, 63.6; H, 6.1; N, 6.6; S, 15.3. $C_{11}H_{13}NOS$ requires C, 63.75; H, 6.33; N, 6.76; S, 15.44%]; R_f (ethyl acetate) 0.64; ν_{max} ($CHCl_3$) 2741, 1688, 1666, 1598, 1561, 1519, 1433, 1393, 1359, 1170, 954 cm^{-1}; δ_H (300 MHz $CDCl_3$) 9.78 (1H, s, CHO), 7.75 (2H, d, J=9.0 Hz, Ar—H), 6.87 (2H, d, J=9.0 Hz, Ar—H), 3.84 (4H, m, CH_2—S—CH_2), 2.71 (4H, m, CH_2—N—CH_2); δ_C (75 MHz, $CDCl_3$) 190.3, 153.8, 132.1, 126.4, 113.7, 50.3, 25.8.

4.4.9. 4-(4-Methylpiperazin-1-yl)benzaldehyde. Yellow solid, 2.98 g, 73%, mp 57–60°C; [Found: C, 70.4; H, 8.0; N, 13.6. $C_{12}H_{16}N_2O$ requires C, 70.56; H, 7.89; N, 13.71%]; R_f (ethyl acetate) 0.09; ν_{max} ($CHCl_3$) 2945, 2808, 2751, 1687, 1666, 1599, 1563, 1519, 1450, 1393, 1381, 1292, 1173, 1143, 1007, 923 cm^{-1}; ^{1}H NMR data consistent with lit.;[14] δ_C (75 MHz, $CDCl_3$) 190.4, 155.0, 131.9, 127.1, 113.5, 54.7, 47.1, 46.1.

4.4.10. 4-(4-Heptylpiperazin-1-yl)benzaldehyde. Pale yellow solid, 3.69 g, 64%, mp 27–30°C; [Found: C, 75.1; H, 9.7; N, 9.6. $C_{18}H_{28}N_2O$ requires C, 74.96; H, 9.78; N, 9.71%]; R_f (ethyl acetate) 0.45; ν_{max} ($CHCl_3$) 2931, 2855, 1690, 1667, 1599, 1563, 1519, 1453, 1390, 1312, 1173, 1129, 1005; ^{1}H NMR data consistent with the lit.;[15] δ_C (75 MHz, $CDCl_3$) 190.4, 155.1, 131.9, 127.0, 113.4, 58.7, 52.9, 47.1, 31.8, 29.3, 27.5, 26.9, 22.7, 14.1.

4.4.11. 4-(4-Octylpiperazin-1-yl)benzaldehyde. Yellow solid, 3.09 g, 51%, mp 22–25°C; [Found: C, 75.3; H, 9.9; N, 9.4. $C_{19}H_{30}N_2O$ requires C, 75.45; H, 10.00; N, 9.26%]; R_f (ethyl acetate) 0.46; ν_{max} ($CHCl_3$) 2929, 2856, 1683, 1668, 1600, 1563, 1519, 1455, 1389, 1292, 1173, 1129, 1006; ^{1}H NMR data consistent with lit.;[15] δ_C (75 MHz, $CDCl_3$) 190.4, 155.1, 131.9, 127.0, 113.4, 58.7, 52.9, 47.1, 31.9, 29.5, 29.3, 27.6, 26.9, 22.7, 14.1.

4.4.12. 4-(Ethoxycarbonylpiperazin-1-yl)benzaldehyde. White solid, 2.05 g, 39%, mp 49–51°C; [Found: 64.2; H, 6.8; N, 10.6. $C_{14}H_{18}N_2O_3$ requires C, 64.11; H, 6.92; N, 10.68%]; R_f (ethyl acetate) 0.52; ν_{max} ($CHCl_3$) 2747, 1689, 1600, 1565, 1518, 1433, 1386, 1287, 1172, 1127, 1080, 1002 cm^{-1}; δ_H (300 MHz $CDCl_3$) 9.82 (1H, s, CHO), 7.79 (2H, d, J=8.5 Hz, Ar—H), 6.93 (2H, d, J=8.5 Hz, Ar—H), 4.19 (2H, q, J=7.2 Hz, CH_2CH_3), 3.66 (4H, m, 2×CH_2 piperazin), 3.41 (4H, m, 2×CH_2 piperazin), 1.29 (3H, t, J=7.2 Hz, CH_2CH_3); δ_C(75 MHz, $CDCl_3$) 190.5, 155.4, 154.8, 131.9, 127.6, 113.9, 61.7, 47.1, 43.1, 14.7.

4.4.13. 4-(7,15-Diazodispiro[5.1.5.3]hexadecan-15-yl)-benzaldehyde. Yellow solid, 4.70 g, 72%, mp 85–86°C; [Found: C, 77.4; H, 9.4; N, 8.6. $C_{21}H_{30}N_2O$ requires C, 77.26; H, 9.26; N, 8.58%]; R_f (ethyl acetate) 0.32; ν_{max} ($CHCl_3$) 2930, 2857, 1602, 1508, 1477, 1444, 1425, 1047, 929 cm^{-1}; δ_H (300 MHz $CDCl_3$) 9.72 (1H, s, CHO), 7.72 (2H, d, J=9.1 Hz, Ar—H), 6.83 (2H, d, J=9.1 Hz, Ar—H), 3.28 (4H, s, NCH_2C), 1.50 (20H, sb, 5×CH_2 cykl); δ_C (75 MHz, $CDCl_3$) 190.0, 149.8, 131.0, 125.9, 110.5, 58.9, 48.9, 32.6, 25.3, 21.7.

4.4.14. 4-(Pyrrol-1-yl)benzaldehyde. White solid, 0.34 g, 10%, mp 92–94°C, lit.[16] 94–95°C; [Found: C, 77.0; H, 5.2; N, 8.3. $C_{11}H_9NO$ requires C, 77.17; H, 5.30; N, 8.18%]; R_f (ethyl acetate) 0.15; IR data consistent with lit.;[14] ^{1}H NMR data consistent with lit.;[14] δ_C (75 MHz, $CDCl_3$) 190.9, 145.3, 133.3, 131.6, 120.0, 119.1, 112.0.

4.4.15. 4-(Imidazol-1-yl)benzaldehyde. White solid, 2.58 g, 75%, mp 150°C, lit.[17] 146–147°C, lit.[18] 149–150°C; [Found: C, 69.5; H, 4.8; N, 16.1. $C_{10}H_8N_2O$ requires C, 69.76; H, 4.68; N, 16.27%]; R_f (ethyl acetate) 0.14; ν_{max} ($CHCl_3$) 2988, 2737, 1704, 1607, 1585, 1519, 1485, 1302, 1170, 1110, 1054, 835 cm^{-1}; ^{1}H NMR data consistent with lit.;[14] δ_C (75 MHz, $CDCl_3$) 191.0, 142.0, 135.7, 135.3, 131.9, 131.6, 121.4, 117.9.

4.4.16. 4-(1,2,4-Triazol-1-yl)benzaldehyde. White solid, 1.70 g, 49%, mp 146–148C, lit.[19] 148–149°C; [Found: C, 62.3; H, 3.9; N, 24.1. $C_9H_7N_3O$ requires C, 64.42; H, 4.07; N, 24.26%]; R_f (ethyl acetate) 0.33; ν_{max} ($CHCl_3$) 2744, 1705, 1607, 1590, 1519, 1501, 1408, 1303, 1281, 1168, 1142, 1048, 980, 953, 835 cm^{-1}; ^{1}H NMR data consistent with lit.;[14] δ_C (75 MHz, $CDCl_3$) 190.3, 152.8, 140.8, 1407, 135.1, 131.0, 119.5.

4.4.17. 4-(5-Methylsulfanyltetrazol-1-yl)benzaldehyde. White solid, 90 mg, 2%, mp 96–97°C; [Found: C, 49.0; H, 3.5; N, 25.3; S, 14.4. $C_9H_8N_4OS$ requires C, 49.08; H, 3.66; N, 25.44, S, 14.56%]; R_f (hexane/ethyl acetate 3:1) 0.26; ν_{max} ($CHCl_3$) 2962, 2932, 2860, 2742, 1706, 1605, 1510, 1413, 1399, 1285, 1164, 1130, 1075, 1040, 991, 837 cm^{-1}; δ_H (300 MHz $CDCl_3$) 10.10 (1H, s, CHO), 8.31 (2H, d, J=8.9 Hz, Ar—H), 8.09 (2H, d, J=8.9 Hz, Ar—H), 2.78 (3H, s, SCH_3); δ_C (75 MHz, $CDCl_3$) 191.0, 142.6, 141.0, 133.8, 131.0, 130.4, 17.0.

4.4.18. 4-(3,5-Bis-methylsulfanyl-1,2,4-triazol-1-yl)benzaldehyde. White solid, 0.11 g, 2%, mp 84–85°C; [Found: C, 49.9; H, 4.0; N, 16.00; S, 24.0. $C_{11}H_{11}N_3OS_2$ requires C, 49.79; H, 4.18; N, 15.84; S, 24.16%]; R_f (hexane/ethyl acetate 3:1) 0.20; ν_{max} ($CHCl_3$) 2934, 2740, 1704, 1604, 1512, 1454, 1434, 1363, 1302, 1275, 1168, 1009, 841 cm^{-1}; δ_H (300 MHz $CDCl_3$) 10.06 (1H, s, CHO), 8.01 (2H, d, J=8.7 Hz, Ar—H), 7.83 (2H, d, J=8.7 Hz, Ar—H), 2.76 (3H, s, SCH_3), 2.65 (3H, s, $S—CH_3$); δ_C (75 MHz, $CDCl_3$) 191.1, 163.1, 155.4, 142.0, 135.5, 131.1, 123.1, 16.0, 14.4.

4.4.19. 4-(Benzimidazol-1-yl)benzaldehyde. White solid, 3.56 g, 80%, mp 106–108°C, lit.[20] 100–101°C; [Found: C, 75.5; H, 4.4; N, 12.6. $C_{14}H_{10}N_2O$ requires C, 75.66; H, 4.54; N, 12.60%]; R_f (ethyl acetate) 0.32; ν_{max} ($CHCl_3$) 2966, 2741, 1705, 1603, 1578, 1516, 1494, 1455, 1377, 1292, 1169, 976, 835 cm^{-1}; δ_H (300 MHz $CDCl_3$) 10.12 (1H, s, CHO), 8.21 (1H, s, H2 benzimidazol), 8.13 (2H, d, J=8.4 Hz, Ar—H), 7.92 (1H, m, H4 benzimidazol), 7.75 (2H, d, J=8.4 Hz, Ar—H), 7.64 (1H, m, H benzimidazol), 7.40 (2H, m, H5, H6 benzimidazol); δ_C (75 MHz, $CDCl_3$) 190.7, 141.8, 135.3, 131.7, 123.7, 124.3, 123.5, 121.1, 110.5, 144.4, 133.0.

4.4.20. 4-(Benzotriazol-1-yl)benzaldehyde. White solid, 3.69 g, 55%, mp 159–160°C, lit.[19] 156–158°C; [Found: C, 70.0; H, 4.1; N, 18.6. $C_{13}H_9N_3O$ requires C, 69.95; H, 4.06; N, 18.82%]; R_f (chloroform) 0.17; ν_{max} ($CHCl_3$) 2743, 1705, 1604, 1515, 1453, 1395, 1293, 1284, 1165, 1059, 1009, 837 cm^{-1}; ^1H NMR data consistent with lit.;[2] δ_C (75 MHz, $CDCl_3$) 190.8, 146.9, 141.7, 135.7, 131.9, 131.4, 129.0, 124.9, 122.5, 120.8, 110.4.

4.4.21. 4-(Benzotriazol-2-yl)benzaldehyde. White solid, 1.14 g, 17%, mp 189–191°C, lit.[19] 193–195°C; [Found: C, 70.1; H, 4.0; N, 18.6. $C_{13}H_9N_3O$ requires C, 69.95; H, 4.06; N, 18.82%]; R_f (chloroform) 0.36; IR data consistent with lit.;[2] ^1H NMR data consistent with lit.;[2] δ_C (75 MHz, $CDCl_3$) 191.0, 145.4, 144.2, 136.1, 131.0, 128.0, 120.9, 118.6.

4.4.22. 4-(4-Fluoro-α-pyrrol-1-ylbenzyloxy)benzaldehyde. White solid, 0.24 g, 10%; mp 126–127°C (from cyclohexane) [Found: C, 73.3; H, 4.7; N, 4.8; F, 6.5. $C_{18}H_{14}FNO_2$ requires C, 73.16; H, 4.75; N, 4.75; F, 6.44%]; R_f (hexane/ethyl acetate 3:1) 0.27; ν_{max} ($CHCl_3$) 2742, 1697, 1599, 1582, 1511, 1305, 1159, 1083, 1015, 833; δ_H (300 MHz $CDCl_3$) 9.90 (1H, s, CHO), 7.82 (2H, d, J=8.7 Hz, Ar—H), 7.36 (2H, d, J=9.0 Hz, Ar—H), 7.14 (2H, d, J=8.7 Hz, Ar—H), 7.09 (2H, d, J=9.0 Hz, Ar—H), 6.93 (1H, s, NCHO), 6.83 (2H, t, J=2.4 Hz, H2, H5 pyrrol), 6.25 (2H, t, J=2.4 Hz, H3, H4 pyrrol); δ_C (75 MHz, $CDCl_3$) 191.0, 163.5, 161.7, 133.6, 132.2, 128.4, 119.7, 117.1, 116.1, 110.2, 86.9; δ_F (282 MHz, $CDCl_3$) −111.8.

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