Reactions of 2-(pyrrol-1-yl)benzyl radicals and related species under flash vacuum pyrolysis conditions

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Supplementary Information

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The following pyrroles and related compounds were made by the method given in the main paper, unless stated otherwise:

**N-[2-(benzyloxy)phenyl]pyrrole 5aa**

Reaction of N-(2-hydroxyphenyl)pyrrole 4a (0.80 g, 50 mmol) with benzyl bromide (1.03 g, 55 mmol) as described in the main paper gave N-[2-(benzyloxy)phenyl]pyrrole 5aa (1.05 g, 85%), bp 160-165 °C (0.005 Torr) (Found C, 82.0; H, 6.2; N, 5.65; C₁₇H₁₅NO requires C, 81.9; H, 6.05; N, 5.6%); δH 7.42-7.05 (9H, m), 7.15 (2H, t, 3J and 4J 2.1), 6.42 (2H, t, 3J and 4J 2.1) and 5.13 (2H, s); δC 151.62 (quat), 136.54 (quat), 130.95 (quat), 128.38, 127.69, 127.18, 126.85, 125.69, 121.97, 121.46, 114.71, 108.70 and 70.81; m/z 249 (M+, 15%), 172 (20), 158 (42), 91 (100), 77 (23), 65 (28), 63 (12) and 51(22).

**N-[2-(Allylamino)phenyl]pyrrole 5b**

N-(2-Aminophenyl)pyrrole 4b (3.95 g, 25 mmol) was alkylated with allyl bromide (3.03 g, 25 mmol) as described in the main paper giving a mixture of starting material, mono- and di-allylated products. These were separated by chromatography on 6% deactivated alumina using hexane as eluent. The crude product was then purified by bulb to bulb distillation to give N-[2-(allylamino)phenyl]pyrrole 5b (2.11 g, 43%), bp 145-150 °C (0.1 Torr) (Found: M+ 198.1153. C₁₃H₁₄N₂ requires M+ 198.1157); δH 7.43-7.28 (2H, m), 6.98 (2H, t, 3J and 4J 2.0), 6.92-6.86 (2H, m), 6.53 (2H, t, 3J and 4J 2.0), 6.08-5.95 (1H, m), 5.41-5.26 (2H, m), 4.16 (1H, br) and 3.87 (2H, m); δC 143.56 (quat), 134.94, 128.88, 127.30 (quat), 127.13, 121.90, 116.64, 116.00, 111.46, 109.55 and 45.86; m/z 198 (M+, 100%), 197 (52), 183 (17), 171 (24), 169 (39), 157 (35), 156 (26), 155 (12), 131 (12), 130 (15), 118 (11), 77 (20) and 51(15).

**N-[2-(Allylthio)phenyl]pyrrole 5c**

Reaction of 2-aminothiophenol 3c (6.25 g, 50 mmol) with 2,5-dimethoxytetrahydrofuran (6.60 g, 50 mmol) as described in the main paper gave N-(2-mercaptophenyl)pyrrole 4c (6.28 g, 72%), bp 110-115 °C (0.05 Torr) [lit., 1119-121 °C (1.0 Torr)]; δH 7.41-7.20 (4H, m), 6.85 (2H, t, 3J and 4J 2.2), 6.39 (2H, t, 3J and 4J 2.2) and 3.41 (1H, s) spectrum compatible with that previously reported; m/z 175 (M+, 6%), 174 (9), 173 (17), and 40 (100).

Treatment of N-(2-mercaptophenyl)pyrrole 4c (2.00 g, 11.4 mmol) with allyl bromide under the conditions described in the main paper gave N-[2-(allylthio)phenyl]pyrrole 5c (2.46 g, 100%), bp 118-120 °C (0.03 Torr) (Found: C, 72.3; H, 6.2; N, 6.35. C₁₃H₁₄NS requires C, 72.5; H, 6.1; 6.5%); δH 7.47-7.26 (4H, m), 6.91 (2H, t, 3J and 4J 2.2), 6.36 (2H, t, 3J and 4J 2.2), 5.84-5.68 (1H, m), 5.17-5.03 (2H, m) and 3.35-3.30 (2H, m); δC 133.00, 132.78 (quat), 130.06, 127.50, 126.91, 126.53, 121.98, 117.87, 108.96, 108.80 (quat) and 35.86; m/z 215 (M+, 8%), 175 (16), 174 (100), 173 (20) and 45 (9).

**bis-[2-(Pyrrol-1-yl)benzyl] oxalate 5d**

A mixture of methyl 2-aminobenzoate 3da (3.02 g, 20 mmol), 2,5-dimethoxytetrahydrofuran (1.98 g, 20 mmol) and glacial acetic acid (15 cm³) in dioxane (30 cm³) was heated under reflux for 2 h. The volatiles were then removed on a rotary evaporator and the residue azeotroped with xylene to remove any remaining acetic acid to give N-[2-(carbomethoxy) phenyl]pyrrole 4da (3.65 g, 91%), which was then reduced to the hydroxymethyl compound.

A solution of N-[2-(carbomethoxy) phenyl]pyrrole 4da (6.00 g, 30 mmol) in dry ether (100 cm³) was added dropwise to an ice-cold suspension of lithium aluminium hydride (1.26 g, 33 mmol) in dry ether (100 cm³). The mixture was then heated under reflux for 2 h. Wet ether (50 cm³) then water (50 cm³) were added followed by aqueous sodium tartrate (1 M, 50 cm³). The solution was filtered and the ether layer was separated. The aqueous layer was extracted with ether (2 x 50 cm³) and the combined organic extracts
washed with water (3 × 50 cm³) and dried (MgSO₄). The solvent was removed to yield the crude product, which was purified by bulb to bulb distillation to yield \(N\)-[2-(hydroxymethyl)phenyl]pyrrole 4d (4.38 g, 85%), bp 155-160 °C (0.4 Torr) [lit., 212 120 °C (0.2 Torr)] (Found: M⁺, 173.0846 C₁₁H₁₁NO requires M⁺, 173.0840); \(\delta^H\) 7.57-7.53 (1H, m), 7.43-7.27 (3H, m), 6.86 (2H, t, \(^3J\) and \(^4J\) 2.1), 6.34 (2H, t, \(^3J\) and \(^4J\) 2.1), 4.53 (2H, s) and 2.07 (1H, br); spectrum compatible with literature data; m/z 173 (M⁺, 100%), 155 (16), 154 (32), 144 (41), 115 (35), 105 (25), 89 (10), 77 (50), 51 (24) and 50 (14).

A solution of \(N\)-[2-(hydroxymethyl)phenyl]pyrrole 4d (4.00 g, 23 mmol) and triethylamine (3.03 g, 30 mmol) in dry ether (200 cm³) was cooled in ice and a solution of oxalyl chloride (1.51 g, 11.5 mmol) in dry ether (20 cm³) was added dropwise. The mixture was stirred for 2 h. Water (100 cm³) was added and the mixture was extracted with dichloromethane (3 × 50 cm³). The combined extracts were dried (MgSO₄) and the solvent was removed to provide crude product which was recrystallised to yield bis-[2-(pyrrol-1-yl)benzyl] oxalate 5d (3.51 g, 75%), mp 153-155 °C (from ethanol) (Found: C, 71.8; H, 4.95; N, 7.0. C₂₄H₂₀N₂O₄ requires C, 72.0; H, 5.05; N, 7.0%); \(\delta^H\) 7.57-7.31 (8H, m), 6.84 (4H, t, \(^3J\) and \(^4J\) 2.1), 6.30 (4H, t, \(^3J\) and \(^4J\) 2.1) and 5.15 (4H, s); \(\delta^C\) 184.31 (quat), 156.83 (quat), 140.90 (quat), 130.70, 129.78, 127.77, 126.92, 122.43, 109.50 and 64.44; m/z 400 (M⁺, 7%), 399 (20), 172 (22), 157 (16), 156 (100), 155 (55), 154 (35), 129 (11) and 128 (12).

1-(2-Benzylaminophenyl)pyrazole 7
A solution of 1-(2-aminophenyl)pyrazole 6 (2.04 g, 13 mmol) 3 and re-distilled benzaldehyde (1.3 g, 13 mmol) in ethanol (20 cm³) was kept for ca. 48 h in the presence of 4A molecular sieves. Removal of the solvent under reduced pressure gave crude 1-(2-N-benzyliminophenyl)pyrazole as an oil, which was freed from unchanged amine by bulb-to-bulb distillation at 120-123 °C (0.02 Torr) (2.56 g, 80%) (Found M⁺, 247.1120. C₁₆H₁₃N₃ requires M⁺ 247.1109); \(\delta^H\) 8.47 (1H, s), 8.1-7.1 (11H, m) and 6.40 (1H, t, \(^3J\) 2.1); \(\delta^C\) 161.08, 143.45 (quat), 140.21, 135.82 (quat), 133.89 (quat), 132.12, 131.67, 128.93, 128.77, 127.52, 126.61, 124.30, 119.34 and 106.28; m/z 247 (M⁺, 31%), 219 (15), 170 (70), 145 (11), 144 (100), 143 (13), 118 (11), 117 (19), 90 (19), 89 (18) and 77 (26).

Sodium borohydride (0.72 g, 19 mmol) was added to a solution of 1-(2-N-benzyliminophenyl)pyrazole (1.12 g, 4.5 mmol) in methanol (20 cm³) and the resulting solution was heated under reflux for a further 15 min. The reaction mixture was added to water (30 cm³) and then extracted with dichloromethane (2 × 30 cm³). The extracts were dried (MgSO₄) and the solvents were removed under reduced pressure to yield 1-(2-benzylaminophenyl)pyrazole 7 (0.76 g, 67%) as an oil which crystallised, mp 76-77 °C (from n-hexane) (Found: C, 77.05; H, 6.1; N 17.0. C₁₆H₁₅N₃ requires C, 77.1; H, 6.0; N, 16.85%); \(\delta^H\) 7.29-6.99 (12H, m), 6.55 (2H, s), 3.14 (1H, s) and 2.29 (6H, s); \(\delta^C\) 141.84 (quat), 140.25, 138.75 (quat), 129.85, 128.46, 128.25, 126.61, 124.30, 119.34 and 106.28; m/z 249 (M⁺, 100%), 248 (19), 195 (18), 180 (29), 172 (28), 170 (14), 145 (34), 144 (17), 131 (20), 130 (15), 106 (17), 104 (13), 92 (10), 91 (83), 89 (12), 78 (15) and 77 (37).

The following 2,5-diarylpyrroles were made by the general method described in the main paper:

2,5-Di-p-toly1-N-(2-mercaptophenyl)pyrrole 25b
2-Aminothiophenol 3c (1.32 g, 10.5 mmol) and 4′,4′-dimethyldiphenacyl 4 (2.73 g, 10.3 mmol) gave 2,5-di-p-toly1-N-(2-mercaptophenyl)pyrrole 25b (55%), mp 114-117 °C; (Found: C, 79.5; H, 5.9; N, 3.85. C₂₄H₂₁NS.0.33H₂O requires C, 79.75; H, 6.0; N 3.9%); (Found: M⁺, 355.1387. C₂₄H₂₁NS requires M⁺ 355.1395); \(\delta^H\) 7.29-6.99 (12H, m), 6.55 (2H, s), 3.14 (1H, s) and 2.29 (6H, s); \(\delta^C\) 136.70 (quat), 136.02 (quat), 135.33 (quat),
133.54 (quat), 130.80, 129.81 (quat), 129.13, 128.61, 128.54, 127.88, 125.59, 109.64 and 20.99; m/z 355 (M+, 100%), 354 (45), 264 (37) and 91 (42).

2,5-Di-(thien-2-yl)-N-(2-mercaptophenyl)pyrrole 25c
A slightly different method was used to make 25c. A solution of 1,4-di(thien-2-yl)-1,4-butanedione5 (1.25 g, 5 mmol), 2-aminothiophenol 3c (0.63 g, 5 mmol) and p-toluenesulfonic acid (80 mg, 0.46 mmol) in toluene (15 cm³) was heated under reflux with stirring for 24 h under nitrogen. The toluene was evaporated and the residue was worked up as described above to give 2,5-di-(thien-2-yl)-N-(2-mercaptophenyl)pyrrole 25c (0.47 g, 28%); mp 132-135 °C (from propan-2-ol); (Found: C, 62.3; H, 3.75; N, 4.0. C₁₈H₁₃NS₃·0.5H₂O requires C, 62.05; H, 4.0; N, 4.0%); δH 7.38 (3H, m), 7.22 (1H, m), 7.06 (2H, dd, 3J 5.1, 4J 1.2), 6.83 (2H, dd, 3J 3.7, 5.1), 6.64 (2H, s), 6.63 (2H, dd, 3J 3.7, 4J 1.2) and 3.11 (1H, s, SH); δC 135.52 (quat), 134.92 (quat), 133.95 (2 quat), 131.10, 129.87, 129.37, 128.94 (2 quat), 126.80 (2 CH), 126.06, 123.80 (2 CH), 123.48 (2 CH) and 109.96 (2 CH); m/z 339 (M+, 100%), 306 (29), 217 (48), 218 (20), 195 (29), 194 (28), 150 (26) and 111 (32).

2,5-Di-(thien-2-yl)-N-(2-hydroxyphenyl)pyrrole 25e
Using the method described above for 25c using 1,4-di(thien-2-yl)-1,4-butanedione 5 (1.25 g, 5 mmol), 2-aminophenol 3a (0.55 g, 5 mmol) and p-toluenesulfonic acid (80 mg, 0.46 mmol) in toluene (15 cm³) 2,5-di-(thien-2-yl)-N-(2-hydroxyphenyl)pyrrole 25e (1.09 g, 68%) was obtained mp 95-98 °C; (Found M+, 323.04367. C₁₈H₁₃NOS₂ requires M 323.04331) δH 7.40 (1H, m), 7.21 (1H, dd, 3J 7.8, 4J 1.7), 6.95-7.05 (4H, m), 6.81 (2H, dd, 3J 3.7, 5.1), 6.64 (2H, dd, 3J 3.7, 4J 1.1), 6.63 (2H, s) and 5.25 (1H, br s, OH); δC 153.46 (quat), 133.76 (2 quat), 132.18, 130.72, 130.07 (2 quat), 127.02 (2 CH), 124.86 (quat), 124.15 (2 CH), 123.72 (2 CH), 121.04, 116.62 (CH) and 110.43 (2 CH); m/z 323 (M+, 100%), 282 (34), 217 (30), 195 (15), 194 (10), 150 (23) and 111 (32).

The following allyl and related derivatives were made by the general method described in the main paper, unless stated otherwise:

2,5-Di-p-tolyl-N-(2-allylthio)phenyl)pyrrole 26b
2,5-Di-p-tolyl-N-(2-mercaptophenyl)pyrrole 25b (1.00 g, 2.80 mmol) gave 2,5-di-p-tolyl-N-(2-allylthio)phenyl)pyrrole 26b (1.09 g, 98%) mp 124-126 °C; (Found: M+, 395.1719. C₂₇H₂₅NS requires M 395.1708); δH 7.20-6.84 (12H, m), 6.40 (2H, s), 5.47 (1H, m), 4.91-4.82 (2H, m), 3.23-3.19 (2H, m) and 2.16 (6H, s); δC 153.46 (quat), 133.76 (2 quat), 132.18, 130.72, 130.07 (2 quat), 127.02 (2 CH), 124.86 (quat), 124.15 (2 CH), 123.72 (2 CH), 121.04, 116.62 (CH) and 110.43 (2 CH); m/z 323 (M+, 100%), 282 (34), 217 (30), 195 (15), 194 (10), 150 (23) and 111 (31).
123.60 (2 CH), 123.53 (2 CH), 117.92, 109.55 (2 CH) and 34.77; m/z 379 (M+, 100%), 337 (44), 303 (29), 217 (93), 203 (36), 162 (43), 111 (60) and 84 (64).

2,5-Diphenyl-N-[2-(allyloxy)phenyl]pyrrole 26d
2,5-Diphenyl-N-(2-hydroxyphenyl)pyrrole 25d (3.11 g, 0.01 mol) gave 2,5-diphenyl-N-[2-(allyloxy)phenyl]pyrrole 26d (3.23 g, 95%), mp 106-108 °C (from ethanol) (Found: C, 85.0; H, 6.0; N, 3.95. C_{25}H_{21}NO requires C, 85.45; H, 6.0; N, 4.0%)

δ_H 7.52-7.03 (12H, m), 6.87-6.77 (2H, m), 6.50 (2H, s), 5.51 (1H, m), 5.01 (2H, m) and 4.16 (2H, m); δ_C 154.37 (quat), 136.10 (quat), 133.51 (quat), 132.70, 130.69, 128.92, 128.47 (quat), 127.99, 127.58, 125.93, 120.48, 116.72, 113.17, 109.10 and 68.64; m/z 351 (M+, 100%), 310 (12) and 191 (21).

2,5-Di-(thien-2-yl)-N-[2-(allyloxy)phenyl]pyrrole 26e
2,5-Di-(thien-2-yl)-N-(2-hydroxyphenyl)pyrrole 25e (0.549 g, 1.70 mmol) gave 2,5-di-(thien-2-yl)-N-[2-(allyloxy)phenyl]pyrrole 26e (0.58 g, 95%) mp 61-64 °C; (Found M+, 363.07313. C_{21}H_{17}NOS_{2} requires M 363.07461)

δ_H 7.42 (1H, m), 7.28 (1H, dd, J= 3.7, 5.1), 7.01-6.90 (4H, m), 6.79 (2H, dd, J= 3.7, J= 5.1), 6.60 (2H, dd, J= 3.7, J= 1.7), 6.57 (2H, s), 6.57 (2H, s), 5.65 (1H, m), 5.08-5.00 (2H, m) and 4.38 (2H, m); δ_C 155.98 (quat), 135.01 (quat), 132.49 (2 quat), 131.55 (2 quat), 130.48, 130.04, 126.65 (2 CH), 123.50 (4 CH), 120.76, 116.73, 113.56, 109.37 (2 CH) and 68.81 (one CH signal overlapping); m/z 363 (M+, 100%), 322 (25), 289 (14), 214 (14), 203 (22), 152 (16), 79 (53) and 65 (98).

2,5-Di-p-tolyl-N-[2-(benzylamino)phenyl]pyrrole 26f
Benzylamine (10.72 g, 0.1 mol) was added over 30 min to a stirred, ice-cooled suspension of 2-fluoronitrobenzene 27 (10 g, 0.071 mol), and anhydrous potassium carbonate (13.8 g, 0.1 mol) in DMSO (100 cm^3). After 1 h water (50 cm^3) was added and the product extracted with dichloromethane (3 × 50 cm^3). The combined organic extracts were dried (MgSO_4) and the solvent evaporated to give N-benzyl-2-nitroaniline 28 an orange solid. (14.5 g, 89%) mp 69-72 °C (lit., 77 °C);

δ_H 8.46 (1H, br s, NH), 8.16 (1H, dd, J= 8.6, J= 1.6), 7.35-7.20 (6H, m), 6.77 (1H, d, J= 8.6), 6.60 (1H, dt, J= 8.3, J= 1.3) and 4.55 (2H, d, J= 5.7);

δ_C 145.13 (quat), 137.23 (quat), 136.09, 132.29 (quat), 128.81 (1H, d, J= 8.6), 6.60 (1H, dt, J= 8.3, J= 1.3) and 4.55 (2H, d, J= 5.7); δ_C 145.13 (quat), 137.23 (quat), 136.09, 132.29 (quat), 128.81 (2 CH), 127.58, 126.92 (2 CH), 126.75, 115.60, 114.07 and 65 (98).

A solution of N-benzyl-2-nitroaniline 28 (8.0 g, 0.035 mol) in methanol was hydrogenated over 5% Pd/C (20 mg) at 20 bar for 24 h. The product was dissolved in hexane, filtered and the filtrate concentrated to give N-benzyl-o-phenylenediamine 29 as an oil. (6.80 g, 98%) which was sufficiently pure for the next stage;

δ_H 8.46 (1H, br s, NH), 8.16 (1H, dd, J= 8.6, J= 1.6), 7.35-7.20 (6H, m), 6.77 (1H, d, J= 8.6), 6.60 (1H, dt, J= 8.3, J= 1.3) and 4.55 (2H, d, J= 5.7); δ_C 145.13 (quat), 137.23 (quat), 136.09, 132.29 (quat), 128.81 (2 CH), 127.58, 126.92 (2 CH), 126.75, 115.60, 114.07 and 65 (98).

Using the method described for 25c, a solution of 4,4′-dimethylphenacyl 4 (4.00 g, 15 mmol), N-benzyl-o-phenylenediamine 29 (6.00 g, 30 mmol) and PTSA (80 mg, 0.46 mmol) in toluene (50 cm^3) gave 2,5-di-p-tolyl-N-[2-(benzylamino)phenyl]pyrrole 26f (1.66 g, 25%) as a white solid mp 163-165 °C (from toluene) (Found: C, 86.55; H, 6.55; N, 6.55. C_{12}H_{14}N_2 requires C, 86.9; H, 6.55; N, 6.55 %). δ_H 7.15-7.00 (13H, m), 6.74 (2H, dd, J= 7.9, J= 2.1), 6.58 (1H, td, J= 7.5, J= 1.3), 6.53 (2H, s), 6.40 (1H, dd, J= 8.2, J= 1.2), 4.08 (2H, s) and 2.23 (4H, s); δ_C 144.36 (quat), 138.57 (quat), 135.70 (quat), 135.15 (quat), 129.89 (quat), 129.82, 128.46 (4 CH), 127.99 (2 CH), 127.48 (4 CH), 126.42, 126.25 (2 CH), 124.33 (quat), 116.34, 110.94, 109.26 (2 CH), 46.61 and 20.83; m/z 428 (M+, 100%), 351 (9), 337 (27), 247 (12), 219 (13) and 91 (47).
NOE results:

Fig. 1 NOE enhancements for 19-22.

Fig. 2 NOE enhancements for 32a, 33a, 34a and 36a.
Fig. 3 NOE enhancements for 32b and 33b; NOESY correlations for 34b.

References