Supplementary Material (ESI) for Chemical Communications
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Microwave enhanced palladium catalysed coupling reactions: A diversity-oriented synthesis approach to functionalised flavones.

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Supplementary Information

General information

All reactions were carried out under an argon atmosphere in oven-dried vessels. All reagents were purchased from Aldrich or AlfaAesar and were used as received without further purification. 7-Hydroxyflavone was purchased from Apin Chemicals Ltd. SIMES.HCl (1,3-dimesitylimidazolinium chloride) was prepared using the procedure of Arduengo.[1] Microwave reactions were carried out on a CEM Discover (CEM Corp. USA). All reactions were monitored by thin-layer chromatography (TLC) on pre-coated silica gel plates (254μm). Flash column chromatography was carried out with Kiesegel 60M 0.04/0.063mm (200-400 mesh) silica gel. All yields quoted are isolated yields. ^{1}H NMR spectra were recorded at 300MHz and ^{13}C at 75MHz on a Bruker AMX 300 at ambient temperature in $CDCl_3$. The chemical shifts (δ) for ^{1}H and ^{13}C are quoted in ppm relative to residual signals of the solvent. Mass spectra were obtained on a VG70-SE mass spectrometer. Infrared spectra were obtained on a Shimadzu FTIR 8700 Spectrophotometer. Melting points were measured with a Gallenkamp apparatus and are uncorrected.

General procedure A - Synthesis of flavone scaffold

LHMDS (4 mmol, 1 M in THF) was added drop wise to a solution ketone (1 mmol) in THF (2 mL/mmol) at –78 ºC and the reaction was stirred a t –78 ºC for 30 min and at

–20 ºC for 2 h. The reaction was cooled to –78 ºC and acid chloride (1 mmol) in THF (2 mL/mmol) was added via cannula and the reaction was stirred at –78 ºC for 1 h and at RT for 2 h. The reaction was poured onto a mixture of ice and conc. HCl (2 mL/mmol) and extracted with $CHCl_3$ (x 3). The org phase was dried ($MgSO_4$) and the solvent was removed *in vacuo*. AcOH (2 mL/mmol) and conc. H_2SO_4 (2 mL/mmol) were added and the mixture stirred at reflux for 5 min. Ice was added and the solid filtered off, dissolved in 10% MeOH/DCM, dried ($MgSO_4$) and the solvent removed *in vacuo*. Purification by column chromatography (Et_2O/petrol) as appropriate yielded the desired flavone in as pale brown solids, which were recrystallised if required from MeOH/H_2O.

General procedure B – Triflation of hydroxyflavones

Hydroxyflavone (1 g, 4.2 mmol), Tf_2NPh (1.5 g, 4.2 mmol) and K_2CO_3 (1.74 g, 12.6 mmol) were stirred in THF at 120 ºC for 10 min (MW). Ethyl acetate was added and the solid filtered off. The solvents were removed *in vacuo* and purification by column chromatography (Et_2O/petrol) yielded desired triflated flavone.

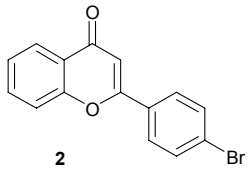
General procedure C – Suzuki reaction with POPd

Bromoflavone or flavone triflate (0.33 mmol), boronic acid (0.5 mmol), POPd (3 mol%) and CsF (0.66 mmol) were stirred in THF (6 mL/mmol) with either thermal or microwave heating as described in Table 1. Et_2O was added and the solid filtered off and the solvents were removed *in vacuo*. Purification was achieved by column chromatography (Et_2O/petrol) and/or recrystallisation as appropriate. Yield are given in Table 1

General procedure D – Buchwald-Hartwig reaction with $Pd_2(dba)_3$/BINAP

Bromoflavone (0.33 mmol,), $Pd_2(dba)_3$ (5 mol%), BINAP (7.5 mol%)and NaO^tBu (0.46 mmol) in MePh (2 mL/mmol) were cycled with Argon three time. *n*-Hexylamine (0.40 mmol) was added an the reaction was stirred at 110 ºC with either microwave or thermal heating as described in Table 2. Et_2O was added, the solid filtered off and the solvents were removed *in vacuo*. Purification was achieved by column chromatography (Et_2O/petrol) and/or recrystallisation from MeOH/H_2O as appropriate. Yields are given in Table 2.

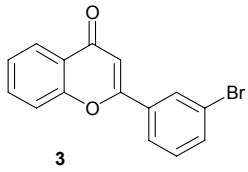
2-(4-Bromo-phenyl)-chromen-4-one 2.



2

Synthesised using general procedure A. mp = 166-169 °C; ν_{max}/cm^{-1} 3054, 1641, 1622, 1563 and 747; δ_H ($CDCl_3$, 300 MHz) 8.22 (1H, dd, *J* 6.3 and 1.6, 5-CH), 7.53-7.80 (5H, m, Ar), 7.55 (1H, d, *J* 7.8, Ar), 7.43 (1H, app t, *J* 7.1, Ar), 6.80 (1H, s, vinyl-H); δ_C ($CDCl_3$, 75 MHz) 178.3 (s), 162.3 (s), 156.2 (s), 134.0 (d), 132.4 (d), 130.7 (s), 127.7 (d), 126.4 (d), 125.8 (d), 125.4 (d), 123.9 (s), 118.1 (d), 107.7 (d); *m/z* (EI) 299.9778 (M+. $C_{15}H_9BrO_2$ requires 299.9780).

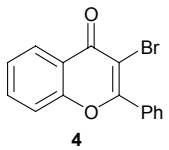
2-(3-Bromo-phenyl)-chromen-4-one 3.



3

Synthesised using general procedure A. mp = 106-108 °C; ν_{max}/cm^{-1} 3054, 1647, 1605 and 1561, 739; δ_H ($CDCl_3$, 300 MHz) 8.23 (1H, dd, *J* 6.4 and 1.4, C5-H), 8.09 (1H, app t, *J* 1.7, Ar), 7.84 (1H, d, *J* 6.4, Ar), 7.57-7.72 (2H, m, Ar), 7.55 (1H, d, *J* 8.1, Ar), 7.26-7.46 (2H, m, Ar), 6.80 (1H, s, vinyl-H); δ_C ($CDCl_3$, 75 MHz) 178.2 (s), 161.7 (s), 156.2 (s), 134.5 (d), 134.0 (d), 133.8 (s), 130.6 (d), 129.3 (d), 125.8 (d), 125.5 (d), 124.9 (d), 123.9 (s), 123.3 (s), 118.1 (d), 108.2 (d); *m/z* (EI) 299.9772 (M+. $C_{15}H_9BrO_2$ requires 299.9780).

3-Bromo-2-phenyl-chromen-4-one 4.

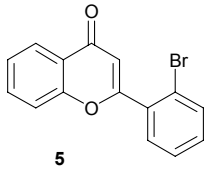


4

Synthesised using general procedure A. mp = 115-118 °C; ν_{max}/cm^{-1} 1647, 1616 and 1558; δ_H ($CDCl_3$, 300 MHz) 8.30 (1 H, dd, *J* 8.0, 1.6. C5-H), 7.89-7.82 (2 H, m, C6, H and C8-H), 7.72 (1 H, ddd, *J* 8.6, 7.1, 1.6, C7-H), 7.61-7.41 (5 C, m, Ph); δ_C ($CDCl_3$, 75 MHz) 173.2 (s), 162.1 (s), 155.7 (s), 134.2 (d), 132.9 (s), 131.2 (d), 129.3

(d), 128.4 (d), 126.6 (d), 125.8 (d), 121.8 (s), 117.9 (d), 109.3 (s); *m/z* (CI) 300.9857 (M+H. $C_{15}H_{10}BrO_2$ requires 300.9864).

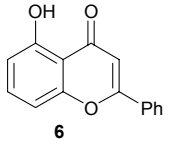
2-(2-Bromo-phenyl)-chromen-4-one 5.



5

Synthesised using general procedure A. mp = 122-124 °C; ν_{max}/cm^{-1} 3053, 1651, 1608 and 1574, 1221 and 739; δ_H ($CDCl_3$, 300 MHz) 8.26 (1H, dd, *J* 6.3 and 1.7, C5-H), 7.70-7.74 (2H, m, Ar), 7.53-7.57 (1H, m, Ar), 7.35-7.56 (4H, m, Ar), 6.59 (1H, s, vinyl-H); δ_C ($CDCl_3$, 75 MHz) 178.2 (s), 164.0 (s), 156.6 (s), 134.1 (s), 134.0 (d), 134.0 (d), 131.9 (d), 130.9 (d), 127.7 (d), 125.8 (d), 125.4 (d), 123.9 (s), 121.9 (s), 118.3 (d), 112.9 (d); *m/z* (EI) 299.9788 (M+. $C_{15}H_9BrO_2$ requires 299.9780).

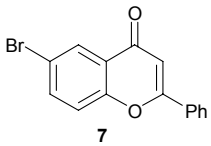
5-Hydroxy-2-phenyl-chromen-4-one 6.



6

Synthesised using general procedure A. mp = 230-233 °C;; ν_{max}/cm^{-1} 3260, 1628, 1594, 1580 and 1574; δ_H (90% DMSO-d_6/$CDCl_3$, 300 MHz) 7.99-7.91 (2 H, m, Ar), 7.56-7.49 (4 H, m, Ar), 7.43 (1 H, d, *J* 3.0, Ar), 7.25 (1 H, dd, *J* 9.0, 3.0, Ar), 6.79 (1 H, s, C3-H); δ_C (90% DMSO-d_6/$CDCl_3$, 75 MHz) 180.9 (s), 165.6 (s), 156.5 (s), 151.9 (s), 133.1 (d), 132.9 (s), 130.3 (d), 127.6 (d), 125.6 (s), 125.0 (d), 120.9 (d), 109.2 (d), 107.1 (d); *m/z* (FAB) 223 (M-OH+H).

6-Bromo-2-phenyl-chromen-4-one 7.

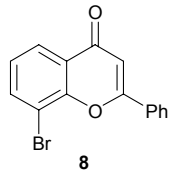


7

Synthesised using general procedure A. mp = 191 °C; ν_{max}/cm^{-1} 3054, 1648, 1614, 1599 and 1495; δ_H ($CDCl_3$, 300 MHz) 8.36 (1H, d, J = 2.4 Hz, C5-H), 7.92 (2H, dd, *J* 4.7 and 2.1, Ar), 7.79 (1H, dd, *J* 4.7 and 2.4, Ar), 7.42-7.59 (4H, m, Ar), 6.84 (s, 1H, vinyl-H); δ_C ($CDCl_3$, 75 MHz) 177.1 (s), 163.7 (s), 155.0 (s), 136.8 (d), 131.9 (d),

131.4 (s), 129.1 (d), 128.4 (d), 123.4 (d), 125.3 (s), 120.1 (d), 118.7 (s), 107.6 (d); *m/z* (EI) 299.9789 (M+. $C_{15}H_9BrO_2$ requires 299.9780).

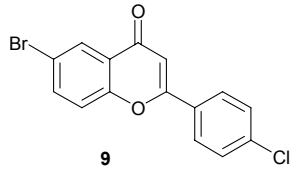
8-Bromo-2-phenyl-chromen-4-one 8.



8

Synthesised using general procedure A. mp = 165-168 °C; ν_{max}/cm^{-1} 1649 and 1556; δ_H ($CDCl_3$, 300 MHz) 8.17 (1 H, dd, *J* 7.9 and 1.6, C5-H), 8.00-8.05 (2 H, m, Ph), 7.92 (1 H, dd, *J* 7.9 and 1.6, C7-H), 7.59-7.50 (3 H, m, Ph), 7.30 (1 H, app t, *J* 7.9, C6-H), 6.87 (1 H, s, C3-H); δ_C ($CDCl_3$, 75 MHz) 177.8 (s), 163.4 (s), 152.7 (s), 137.1 (d), 131.9 (d), 131.2 (s), 129.2 (d), 126.5 (d), 125.8 (d), 125.3 (s), 125.1 (d), 112.0 (s), 107.2 (d); *m/z* (FAB) 300.9866 (M+H. $C_{15}H_{10}BrO_2$ requires 300.9864).

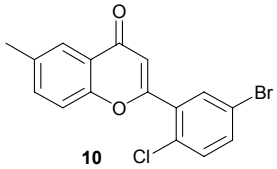
6-Bromo-2-(4-chloro-phenyl)-chromen-4-one 9.



9

Synthesised using general procedure A. mp = 217-220 °C; ν_{max}/cm^{-1} 3056, 1654 and 1468; δ_H ($CDCl_3$, 300 MHz) 8.34 (1H, d, J 2.4, C5- H), 7.77-7.86 (3H, m), 7.45-7.52 (3H, m), 6.79 (1H, s, C3-H); δ_C ($CDCl_3$, 75 MHz) 176.9 (s), 162.5 (s), 154.9 (s), 138.2 (s), 136.9 (d), 129.9 (s), 129.4 (d), 128.5 (d), 127.6 (d), 125.2 (s), 120.0 (d), 118.9 (s), 107.7 (d); *m/z* (EI) 333.9388 (M+. $C_{15}H_8O_2ClBr$ requires 333.9391).

2-(5-Bromo-2-chloro-phenyl)-6-methyl-chromen-4-one 10.

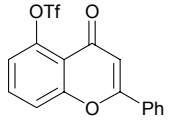


10

Synthesised using general procedure A. mp = 153-156 °C; ν_{max}/cm^{-1} 1651-1615; δ_H ($CDCl_3$, 300 MHz) 8.02 (1 H, br, C5-H), 7.78 (1 H, d, *J* 2.4, C2'-H), 7.56 (1 H, dd, *J* 8.6 and 2.4, C4'-H), 7.52 (1 H, dd, *J* 8.5 and 2.2, C7-H), 7.42 (1 C, d, *J* 8.5, C8-H), 7.40 (1 H, d, *J* 8.6, C3'-H), 6.65 (1 H, s, C3-H), 2.47 (3 H, s, CH_3); δ_C ($CDCl_3$, 75 MHz) 177.9 (s), 160.7 (s), 154.8 (s), 135.6 (s), 135.3 (s), 134.5 (d), 133.5 (d), 133.2

(d), 132.2 (d), 131.9 (s), 125.1 (d), 123.4 (s), 120.6 (s), 117.9 (d), 113.1 (d), 21.0 (q); *m/z* (CI) 348.9624 (M+H. $C_{16}H_{11}BrClO_2$ requires 348.9631).

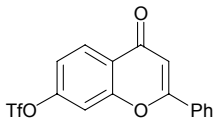
Trifluoro-methanesulfonic acid 4-oxo-2-phenyl-4H-chromen-5-yl ester 11.



11

Synthesised using general procedure b. mp = 122-123 °C; ν_{max}/cm^{-1} 1651, 1626 and 1574; δ_H ($CDCl_3$, 300 MHz) 8.12 (1 H, d, *J* 2.9, Ar), 7.89-7.94 (2 H, m, Ar), 7.69 (1 H, d, *J* 9.1, Ar), 7.61 (1 H, dd, *J* 9.1 and 2.9, Ar), 7.51-7.59 (3 H, m, Ar), 6.85 (1 H, s, C3-H); δ_C ($CDCl_3$, 75 MHz) 176.7 (s), 164.1 (s), 154.9 (s), 146.1 (s), 132.1 (d), 131.1 (s), 129.2 (d), 127.0 (s), 126.4 (d), 125.1 (s), 120.7 (d), 118.3 (d), 118.7 (q, *J* 320.8) 107.4 (d); *m/z* (FAB) 371.0204 ($M+H^+$. $C_{16}H_{10}F_3O_5S$ requires 371.0201).

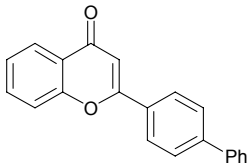
Trifluoro-methanesulfonic acid 4-oxo-2-phenyl-4H-chromen-7-yl ester 13.



13

Synthesised using general procedure B. mp = 133-135 °C; ν_{max}/cm^{-1} 1654 and 1614; δ_H ($CDCl_3$, 300 MHz) 8.34 (1 H, d, *J* 8.8, C5-H), 7.87-7.96 (2 H, m), 7.50-7.60 (4 H, m), 7.34 (1 H, dd, *J* 8.8 and 2.3, C6-H), 6.85 (1 H, s, C3-H); δ_C ($CDCl_3$, 75 MHz) 176.8 (s), 164.2 (s), 156.4 (s), 152.2 (s), 132.1 (d), 131.0 (s), 129.2 (d), 128.4 (d), 126.3 (d), 123.7 (s), 118.7 (q, *J* 322), 118.6 (d), 111.5 (d), 107.9 (d); *m/z* (FAB) 371.0194 ($M+H^+$. $C_{16}H_{10}F_3O_5S$ requires 371.0201).

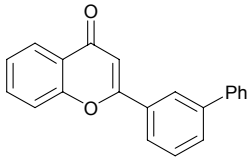
2-Biphenyl-4-yl-chromen-4-one.



Synthesised using general procedure C. mp = 151-155 °C; ν_{max}/cm^{-1} 3054, 1644, 1622 and 1563; δ_H ($CDCl_3$, 300 MHz) 8.26 (1H, dd, *J* 6.0 and 1.7, C5-H), 8.03 (1H, dt, *J* 8.9 and 2, Ar), 7.60-7.78 (6H, m, Ar), 7.39-7.52 (4H, m, Ar), 6.90 (1H, s, vinyl-H); δ_C ($CDCl_3$, 75 MHz) 178.3 (s), 163.2 (s), 156.3 (s), 144.4 (s), 139.8 (s), 133.8 (d), 130.5

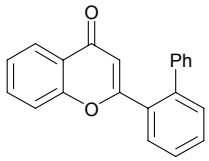
(s), 129.0 (d), 128.2 (d), 127.7 (d), 127.2 (d), 126.8 (d), 125.8 (d), 125.3 (d), 124.0 (s), 118.1 (d), 107.5 (d); *m/z* (EI) 298.0983 (M+. $C_{21}H_{14}O_2$ requires 298.0988).

2-Biphenyl-3-yl-chromen-4-one.



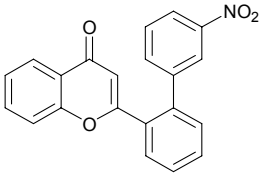
Synthesised using general procedure C. mp = 120-123 °C; ν_{max}/cm^{-1} 1645 and 1609; δ_H ($CDCl_3$, 300 MHz) 8.24 (1 H, t, *J* 7.9 and 1.6, C5-H), 8.11 (1 H, t, *J* 1.7, Ar), 7.87 (1 H, ddd, *J* 7.8, 1.9 and 1.2, Ar), 7.73 (1 H, ddd, 8.4, 1.5 and 1.3, Ar), 7.37-7.69(9 H, m, Ar), 6.89 (1 H, s, C3-H); δ_C ($CDCl_3$, 75 MHz) 178.3 (s), 163.2 (s), 156.2 (s), 142.1 (s), 140.0 (s), 133.7 (d), 132.2 (s), 130.3 (d), 129.4 (d), 128.9 (d), 127.9 (d), 127.1 (d), 125.6 (d), 125.2 (d), 125.0 (d), 123.9 (s), 118.1 (d), 107.7 (d) ; *m/z* (FAB) 299.1066 ($M+H^+$. $C_{21}H_{15}O_2$ requires 299.1072).

2-Biphenyl-2-yl-chromen-4-one.



Synthesised using general procedure C. mp = 110-111 °C; ν_{max}/cm^{-1} 3054, 1644, 1622 and 1563; δ_H ($CDCl_3$, 300 MHz) 8.23 (1 H, app t, *J* 7.2), 7.93-7.88 (1 H, m, Ar), 7.76-7.68 (2 H, m, Ar), 7.58-7.23 (10 H, m, Ar**)**, 6.82 (1 H, s, C3-H); δ_C ($CDCl_3$, 75 MHz) 178.2, 163.4, 156.3, 134.0, 131.9, 131.6, 130.9, 128.4, 127.7, 126.3, 125.8, 125.4, 121.9, 112.9, 107.6; *m/z* (FAB) 298.0983 ($M+H^+$. $C_{21}H_{14}O_2$ requires 298.0988).

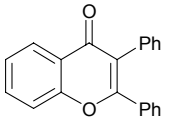
2-(3'-Nitro-biphenyl-2-yl)-chromen-4-one.



Synthesised using general procedure C. mp = 107-109 °C (from $MeOH/H_2O$); ν_{max}/cm^{-1} 1647, 1608 and 1533; δ_H ($CDCl_3$, 300 MHz) 8.27-8.31(1 H, m, C5-H), 8.15 (2 H, m), 7.74 (1 H, dd, *J* 7.5 and 1.1), 7.48-7.69 (5 H, m), 7.44 (1 H, t, *J* 7.9*),* 7.35 (1

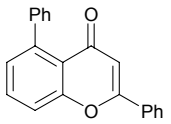
H, ddd, *J* 7.3, 1.0 and 0.7), 6.93 (1 H, d, *J* 8.4, C8-H), 6.45 (1 H, s, C3-H); δ_C ($CDCl_3$, 75 MHz) 177.8 (s), 164.7 (s), 155.9 (s), 148.2 (s), 142.4 (s), 138.8 (s), 134.4 (d), 133.9 (d), 131.7 (d), 131.3 (d), 130.9 (d), 130.0 (d), 129.3 (d), 128.8 (d), 125.6 (d), 125.3 (d), 123.6 (s), 123.4 (d), 122.3 (d), 117.4 (d), 112.4 (d); *m/z* (FAB) 344.0924 ($M+H^+$. $C_{21}H_{14}NO_4$ requires 344.0923).

2,3-Diphenyl-chromen-4-one.



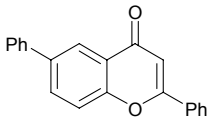
$Pd(PPh_3)_4$ (12 mg, 0.01 mmol) was added to a mixture of 3-Bromo-2-phenyl-chromen-4-one (100 mg, 0.33 mmol), $PhB(OH)_2$ (121 mg, 0.99 mmol) and K_3PO_4 (420 mg, 1.98 mmol) in THF (3 mL). The reaction was stirred at 85 ºC for 30 min and at 120 ºC for 1 h (microwave) then Et_2O was added and the solid filtered off. The solvents were removed *in vacuo* and purification by column chromatography (40-70% Et_2O/petrol) yielded a white solid (84 mg, 0.28 mmol, 85%). mp = 122-125 °C; ν_{max}/cm^{-1} 1639, 1622, 1609 and 1558; δ_H ($CDCl_3$, 300 MHz) 8.31 (1 H, dd, *J* 8.0 and 1.6, C5-H), 7.71 (1 H, ddd, *J* 8.5, 7.1 and 1.6, C7-H), 7.54 (1 H, d, *J* 8.5, C8-H), 7.48-7.36 (3 H, m), 7.36-7.19 (9 H, m); δ_C ($CDCl_3$, 75 MHz) 177.3 (s), 161.5 (s), 156.0 (s), 133.6 (d), 133.3 (s), 132.8 (s), 131.2 (d), 130.0 (d), 129.5 (d), 128.2 (d), 128.0 (d), 127.6 (d), 126.4 (d), 125.0 (d), 123.5 (s), 122.9 (s), 117.9 (d); *m/z* (CI) 299.1074 (M+H. $C_{21}H_{15}O_2$ requires 299.1072).

2,5-Diphenyl-chromen-4-one.



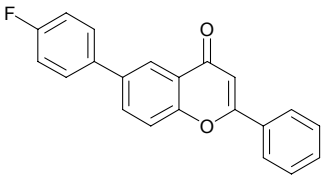
Synthesised using general procedure C. mp = 152-154 °C; ν_{max}/cm^{-1} 1645, 1618 and 1568; δ_H ($CDCl_3$, 300 MHz) 8.45 (1 H, t, *J* 1.9,), 7.91-7.98 (3 H, m), 7.60-7.72 (3 H, m), 7.34-7.59 (6 H, m), 6.86 (1 H, s,C5-H); δ_C ($CDCl_3$, 75 MHz) 178.4 (s), 163.4 (s), 155.6 (s), 139.2 (s), 138.3 (s), 132.6 (d), 131.7 (s), 131.6 (d), 129.0 (d), 129.0 (d), 127.8 (d), 127.1 (d), 126.3 (d), 124.1 (s), 123.5 (d), 118.6 (d), 107.5 (d); *m/z* (FAB) 299.1069 ($M+H^+$. $C_{21}H_{15}O_2$ requires 299.1072).

2,6-Diphenyl-chromen-4-one.



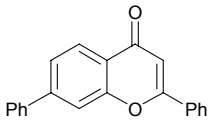
Synthesised using general procedure C. mp = 149-152 °C (from MeOH/H_2O); ν_{max}/cm^{-1} 1635, 1566 and 1495; δ_H ($CDCl_3$, 300 MHz) 8.46 (1 H, d, *J* 2.3, 5C-H), 7.89-8.02 (3 H, m), 7.61-7.74 (3 H, m), 7.34-7.59 (6 H, m), 6.87 (1 H, s, C3-H); δ_C ($CDCl_3$, 75 MHz) 178.5 (s), 163.4 (s), 155.7 (s), 139.3 (s), 138.4 (s), 132.6 (d), 131.8 (s), 131.6 (d), 129.1 (d), 129.0 (d), 127.8 (d), 127.2 (d), 126.3 (d), 124.1 (s), 123.5 (d), 118.6 (d), 107.6 (d); *m/z* (FAB) 299.1069 ($M+H^+$. $C_{21}H_{15}O_2$ requires 299.1072).

6-(4-Fluoro-phenyl)-2-phenyl-chromen-4-one.



Synthesised using general procedure C. mp = 164-165 °C; ν_{max}/cm^{-1} 3053, 1645, 1618 and 1570; δ_H ($CDCl_3$, 300 MHz) 8.38 (1 H, d, *J* 2.3, C5-H), 7.91-7.97 (2 H, m, Ph), 7.88 (1 H, dd, *J* 8.7 and 2.3, C7-H), 7.63 (2 H, d, *J* 8.6, *meta*F-H), 7.62 (1 H, d, *J* 8.7, C8-H), 7.55 (2 H, dd, *J* 5.3 and 1.9, Ph), 7.15 (2 H, app t, *J* 8.6, *ortho*F-H), 6.85 (1 H, s, C3-H); δ_C ($CDCl_3$, 75 MHz) 178.3 (s), 163.4 (s), 162.7 (d, *J* 247); 155.6 (s), 137.4 (s), 135.4 (d, *J* 3), 132.4 (d), 131.7 (d), 129.1 (d), 128.8 (d), 128.7 (d), 126.3 (d), 124.1 (s), 123.4 (d), 118.7 (d), 116.0 (d), 115.7 (d), 107.5 (d); *m/z* (FAB) 317.0979 (M+. $C_{21}H_{14}FO_2$ requires 317.0978).

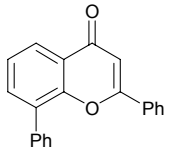
2,7-Diphenyl-chromen-4-one.



Synthesised using general procedure C. mp = 144-146 °C; ν_{max}/cm^{-1} 1643, 1625 and 1608; δ_H ($CDCl_3$, 300 MHz) 8.28 (1 H, d, *J* 8.3) 7.93-7.97 (2 H, m), 7.78 (1 H, d, *J* 1.5), 7.62-7.73 (3 H, m), 7.58-7.40 (4 H, m), 6.84 (1 H, s); δ_C ($CDCl_3$, 75 MHz) 178.2 (s), 163.5 (s), 156.6 (s), 146.9 (s), 139.1 (s), 131.8 (s), 131.6 (d), 129.0 (d), 128.6 (d),

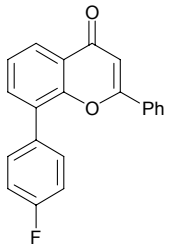
127.3 (d), 126.3 (d), 126.1 (d), 124.3 (d), 122.7 (s), 116.1 (d), 107.7 (d),; *m/z* (FAB) 29.1074 (M^+. $C_{21}H_{15}O_2$ requires 299.1072).

2,8-Diphenyl-chromen-4-one.



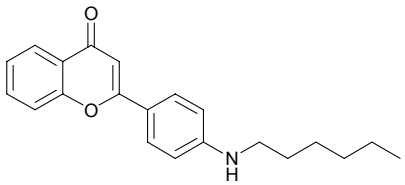
Synthesised using general procedure C. mp = 124-127 °C; ν_{max}/cm^{-1} 1643; δ_H ($CDCl_3$, 300 MHz) 8.26 (1 H, dd, *J* 7.9 and 1.6), 7.69-7.81 (3 C, m), 7.63-7.67 (2 H, m), 7.59-7.38 (7 H, m), 6.89 (1 h, s, C3-H); δ_C ($CDCl_3$, 75 MHz) 178.6 (s), 163.2 (s), 153.1 (s), 136.2 (s), 134.7 (d), 132.0 (s), 131.7 (s), 131.6 (d), 129.7 (d), 129.1 (d), 128.5 (d), 128.2 (d), 126.3 (d), 125.2 (d), 125.1 (d), 124.5 (s) 107.1 (d); *m/z* (FAB) 299.1074 (M+H. $C_{21}H_{15}O_2$ requires 299.1072).

8-(4-Fluoro-phenyl)-2-phenyl-chromen-4-one.



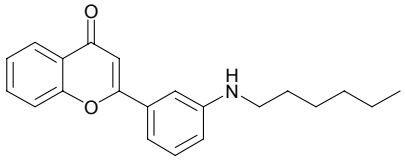
Synthesised using general procedure C. mp = 147-150 °C (from $MeOH/H_2O$); ν_{max}/cm^{-1} 1643, 1602 and 1576; δ_H ($CDCl_3$, 300 MHz) 8.26 (1 H, dd, *J*7.9 and 1.6, C5-H), 7.78-7.66 (3 C, m), 7.66-7.57 (2 C, m), 7.55-7.41 (4 h, m), 7.30-7.17 (2 H, m), 6.88 (1 H, s, C3-H); δ_C ($CDCl_3$, 75 MHz) 178.4 (s), 163.1 (s), 162.6 (s, J_{C-F} 248), 161.1 (s), 153.0 (s), 134.6 (d), 132.1 (s, J_{C-F} 3), 131.6 (d), 131.5 (s), 131.40 (d), 131.3 (d), 130.9 (s), 129.1 (d), 126.3 (d), 126.2 (d), 125.1 (d, J_{C-F} 4), 124.4 (s), 115.5 (d, J_{C-F} 22), 107.1 (d); *m/z* (FAB) 317.0981 ($M+H^+$. $C_{21}H_{14}FO_2$ requires 317.0978).

2-(4-Hexylamino-phenyl)-chromen-4-one.



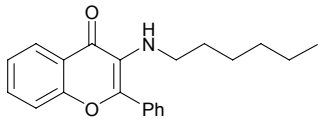
Synthesised using general procedure D. mp = 121-123 °C; ν_{max}/cm^{-1} 3400 and 1636; δ_H ($CDCl_3$, 300 MHz) 8.15 (1 H, ddd, J 7.9, 1.7 and 0.5, C5-H), 7.71 (2 H, d, *J* 8.8, C2'-H), 7.60 (1 C, ddd, *J* 8.5, 7.4 and 1.7, C7-H), 7.48 (1 H, ddd, *J* 8.5, 1.1 and 0.5, C8-H), 7.32 (1 H, ddd, *J* 7.9, 7.4 and 1.1, C6-H), 6.6 (1 H, s, C3-H), 6.6 (2 H, d, *J* 8.8, C3'-H), 4.4 (1 H, t, *J* 5.3, NH), 3.1 (2 C, dt, *J* 5.3 and 7.0), 1.74-1.58 (2 C, m), 1.49-1.21 (6 H, m), 0.9 (3 H, t, *J* 6.6); δ_C ($CDCl_3$, 75 MHz) 178.1 (s), 164.2 (s), 156.0 (s), 151.3 (s), 133.0 (d), 127.8 (d), 125.3 (d), 124.6 (d), 123.9 (s), 118.8 (s), 117.7 (d), 112.1 (d), 104.1 (d), 43.3 (t), 31.5 (t), 29.2 (t), 26.7 (t), 22.5 (t), 13.9 (q); *m/z* (EI)321.1735 (M^+. $C_{21}H_{23}O_2N$ requires 321.1729).

2-(3-Hexylamino-phenyl)-chromen-4-one.



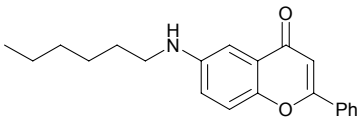
Synthesised using general procedure D. mp = 109-110 °C; ν_{max}/cm^{-1} 2930, 2858, 1643, 1609 and 1572; δ_H ($CDCl_3$, 300 MHz) 8.22 (1 H, dd, *J* 7.1 and 1.1, C5-H), 7.68 (1 H, ddd, *J* 8.0, 7.6 and 1.1, C7-H), 7.55 (1 H, dd, *J* 7.6 and 0.7, C8-H), 7.40 (1 H, ddd, *J* 8.0, 7.1 and 0.7, C6-H), 7.25 (2 H, m, Ar), 7.09 (1 H, app t, *J* 2.3, Ar), 6.79 (1 C, s, C3-H), 6.74 (1 H, ddd, *J* 7.8, 2.3 and 1.1, Ar), 3.89 (1 H, br, NH), 3.16 (2 H, t, *J* 7.1, NHC*H*$_2$), 1.70-1.60 (2 C, m, CH_2), 1.48-1.29 (6 H, m, 3 x CH_2), 0.91 (3 H, t, *J* 6.9, CH_3); δ_C ($CDCl_3$, 75 MHz) 178.5 (s), 164.1 (s), 156.2 (s), 148.9 (s), 133.6 (d), 132.6 (s), 129.8 (d), 125.6 (d), 125.0 (d), 124.0 (s), 118.0 (d), 115.8 (d), 115.0 (d), 109.7 (d), 107.5 (d), 43.8 (t), 31.6 (t), 29.4 (t), 26.8 (t), 22.6 (t), 14.0 (q); *m/z* (FAB) 322.1803 (M+H. $C_{21}H_{24}NO_{2y}$ requires 322.1807).

3-Hexylamino-2-phenyl-chromen-4-one.



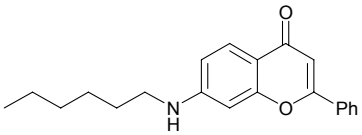
BINAP (3 mg, 3.3 μmol) was dissolved in MePh (400 μL) at 40 ºC then allowed to cool to RT and $Pd(OAc)_2$ (750 μg, 3.3 μmol) was added. The reaction stirred for 1 min and 3-bromo-2-phenyl-chromen-4-one 4 (100 mg, 0.33 mmol) followed by n-hexylamine (44uL, 0.33 mmol) were added and the reaction stirred for 2 min. NaO^tBu (44 mg, 0.4 mmol) was added and the reaction stirred at 110 ºC (MW) for 2 x 15 min. petroleum ether (40/60) was added and the mixture filtered through celite twice. The solvent was removed *in vacuo* to yield the title compound as a brown oil (36 mg, 0.12 mmol, 34%). ν_{max}/cm^{-1} 2930, 2858, 1643 and 1570; δ_H ($CDCl_3$, 300 MHz) 10.00 (1 H, s, NH), 7.87-7.81 (1 H, ddd, *J* 7.7, 1.3 and 0.6, C5-H), 7.48-7.56 (5 H, m, Ph), 7.43 (1 H, ddd, *J* 9.1, 7.0 and 1.3, C7-H), 7.12-7.17 (2 H, m, Ar), 3.22 (2 H, t, *J* 6.8, NHCH_2), 1.58 (2 C, app quin, *J* 7.5, $NHCH_2CH_2$), 1.16-1.40 (6 H, m, 3 x CH_2), 0.85 (3 H, t, *J* 6.9, CH_3); δ_C ($CDCl_3$, 75 MHz) 161.0 (s), 152.0 (s), 132.1 (d), 130.2 (d), 129.9 (s), 129.1 (d), 128.7 (d), 124.8 (s), 122.9 (d), 121.3 (d), 112.6 (d), 44.5 (t), 31.4 (t), 30.8 (t), 26.3 (t), 22.5 (t), 14.0 (q); *m/z* (CI) 3221815 (M+H. $C_{21}H_{24}NO_2$ requires 322.1807).

6-Hexylamino-2-phenyl-chromen-4-one.



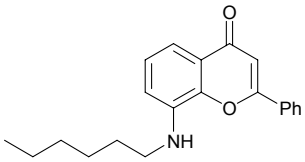
Synthesised using general procedure D. mp = 112-114 °C; ν_{max}/cm^{-1} 2932, 2860, 1643, 1610 and 1572; δ_H ($CDCl_3$, 300 MHz) 7.85-7.89 (2 H, m, Ar), 7.44-7.54 (3 H, m, Ar), 7.37 (1 H, d, *J* 9.0, C8-H), 7.22 (1 H, d, *J* 2.9, C5-H), 6.97 (1 H, dd, *J* 9.0 and 2.9, C7-H), 6.76 (1 H, s, C3-H), 3.90 (1 H, br, NH), 3.16 (2 H, t, *J* 7.1, CH_2NH), 1.63 (2 H, app quin, *J* 7.1, CH_2CH_2NH), 1.17-1.48 (6 H, m, 3 x CH_2), 0.89 (3 C, t, *J* 6.7, CH_3); δ_C ($CDCl_3$, 75 MHz) 178.6 (s), 162.5 (s), 149.2 (s), 146.1 (s), 132.1 (s), 131.1 (d), 128.9 (d), 126.0 (d), 124.8 (s), 121.1 (d), 118.8 (d), 106.5 (d), 103.5 (d), 44.2 (t), 31.5 (t), 29.2 (t), 26.8 (t), 22.5 (t), 14.0 (q); *m/z* (FAB) 322.1807 (M+H. $C_{21}H_{24}NO_2$ requires 322.1800)..

7-Hexylamino-2-phenyl-chromen-4-one.



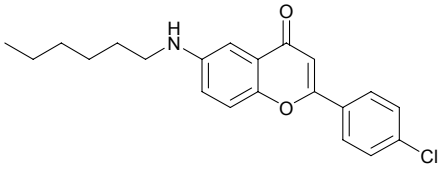
Synthesised using general procedure D. mp = 127-130 °C; ν_{max}/cm^{-1} 3055, 2931, 2860, 1632, 1603 and 1593; δ_H ($CDCl_3$, 300 MHz) 7.96 (1 H, d, *J* 8.8, C5-H), 7.85-7.92 (2 H, m, C2'-H), 7.43-7.52 (3 H, m, Ar), 6.69 (1 H, s, C3-H), 6.61 (1 H, dd, *J* 8.8 and 2.2, C6-H), 6.51 (1 H, d, J = 2.2, C8-H); δ_C ($CDCl_3$, 75 MHz) 177.7 (s), 162.1 (s), 158.8 (s), 153.1 (s), 132.2 (s), 131.0 (d), 128.8 (d), 126.6 (d), 126.0 (d), 114.4 (s), 112.9 (d), 107.3 (d), 96.3 (d), 43.5 (t), 31.5 (t), 29.0 (t), 26.7 (t), 22.5 (t), 14.0 (t); *m/z* (FAB) 322.1803 ($M+H^+$. $C_{21}H_{24}NO_2$ requires 322.1807).

8-Hexylamino-2-phenyl-chromen-4-one.



Synthesised using general procedure D. mp = 100-102 °C; ν_{max}/cm^{-1} 2932, 2860, 1639, 1589, 1576 and 1506; δ_H ($CDCl_3$, 300 MHz) 7.86-7.79 (2 H, m, Ar), 7.56-7.49 (3 H, m, Ar), 7.47 (1 H, dd, *J* 7.9 and 1.4, C5-H), 7.24 (1 H, app t, *J* 7.9, C6-H), 6.88 (1 H, dd, *J* 7.9 and 1.3, C7-H), 6.76 (1 H, s, C3-H), 4.46 (1 H, br, NH), 3.19-3.32 (2 H, m, C*H*$_2$NH), 1.75 (2 H, app quin, *J* 7.1, C*H*$_2$CH$_2$NH), 1.25-1.54 (6 H, m, 3 x CH_2), 0.92 (3 H, t, *J* 7.0, CH_3); δ_C ($CDCl_3$, 75 MHz) 178.8 (s), 162.3 (s), 144.8 (s), 138.1 (s), 132.2 (s), 131.3 (d), 129.1 (d), 126.1 (d), 125.5 (d), 123.8 (s), 112.8 (d), 111.6 (d), 107.8 (d), 43.7 (t), 31.5 (t), 29.2 (t), 26.8 (t), 22.6 (t), 14.0 (q); *m/z* (FAB) 322.1808 ($M+H^+$. $C_{21}H_{24}NO_2$ requires 322.1807).

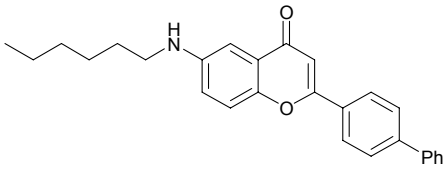
2-(4-Chloro-phenyl)-6-hexylamino-chromen-4-one 14.



Synthesised using general procedure D with n-hexylamine (0.33 mmol). mp = 123-125 °C; ν_{max}/cm^{-1} 2929, 2858, 1643, 1608, 1572 and 1512; δ_H ($CDCl_3$, 300 MHz) 7.81 (2 H, d, *J* 7.9, C2'-H), 7.46 (2 H, d, *J* 7.9, C3'-H), 7.37 (1 H, br d, *J* 7.7, C7-H), 7.21

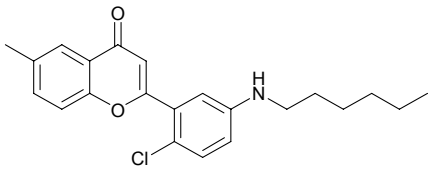
(1 H, br s, C5-H), 6.97 (1 H, d, *J* 7.7, C8-H), 6.72 (1 H, s, C3-H), 3.17 (2 H, t, *J* 6.4, NHC*H*$_2$), 1.71-1.57 (2 H, m, NHCH$_2$C*H*$_2$), 1.50-1.15 (6 H, m, 3 x CH$_2$), 0.89 (3 H, t, *J* 7.0); δ_C ($CDCl_3$, 75 MHz) 178.5 (s), 161.5 (s), 149.2 (s), 146.2 (s), 137.4 (s), 130.7 (s), 129.3 (d), 127.4 (d), 124.8 (s), 121.3 (d), 118.9 (d), 106.7 (d), 103.6 (d), 44.3 (t), 31.6 (t), 29.3 (t), 26.8 (t), 22.6 (t), 14.1 (q); *m/z* (CI) 356.1423 (M+H. $C_{21}H_{22}ClNO_2$ requires 356.1417).

2-(3-Hexylamino-phenyl)-6-phenyl-chromen-4-one 15.



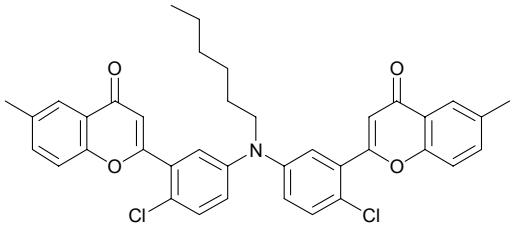
Synthesised using general procedure C. mp = 144-146 °C; ν_{max}/cm^{-1} 2930, 2858, 1644, 1620 and 1578 ; δ_H ($CDCl_3$, 300 MHz) 7.99 (2 H, d, *J* 8.6, C2'-H), 7.74 (2 H, d, *J* 8.6, C3'-H), 7.65 (2 H, dd, *J* 8.2, 1.2, Ar), 7.53-7.37 (4 H, m, Ar), 7.26 (1 H, s, C5-H), 6.99 (1 H, dd, *J* 9.0, 2.9, C7-H), 6.83 (1 H, s, C3-H), 3.20 (2 H, t, *J* 7.1, NHC*H*$_2$), 1.66 (2 H, app quin, *J* 7.2, NHCH$_2$C*H*$_2$), 1.49-1.27 (6 H, m, 3 x CH$_2$), 0.91 (3 H, t, *J* 6.9, CH$_3$); δ_C ($CDCl_3$, 75 MHz) 178.7 (s), 162.5 (s), 149.4 (s), 146.1 (s), 144.0 (s), 139.9 (s), 130.98, 129.00, 128.13, 127.59, 127.16, 126.64, 124.91, 121.23, 118.93, 106.5 (d), 103.8 (d), 44.4 (t), 31.6 (t), 29.4 (t), 26.9 (t), 22.7 (t), 14.1 (q); *m/z* (FAB) 398.2110 (M+H. $C_{27}H_{28}NO_2$ requires 398.2120).

2-(2-Chloro-5-hexylamino-phenyl)-6-methyl-chromen-4-one 16.



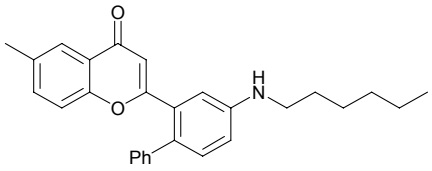
Synthesised using general procedure D with n-hexylamine (0.33 mmol). mp = 95-98 °C; ν_{max}/cm^{-1} 2930, 2858, 1647, 1618, 1601 and 1578; δ_H ($CDCl_3$, 300 MHz) 8.00 (1 H, br s, C5-H), 7.46 (1 H, dd, *J* 8.6, 1.8, C7-H), 7.37 (1 H, d, *J* 8.6, C8-H), 7.22 (1 H, d, *J* 8.8, C3'-H), 6.77 (1 H, d, *J* 2.8, C2'-H), 6.62 (1 H, dd, *J* 8.8, 2.8, C4'-H), 6.59 (1 H, s, C3-H), 4.02 (1 H, br, NH), 3.08 (2 H, app t, *J* 7.1, NHC*H*$_2$), 2.43 (3 H, s, ArC*H*$_3$), 1.68-1.52 (2 H, m, NHCH$_2$C*H*$_2$), 1.46-1.18 (6 H, m, 3 x CH$_2$), 0.87 (3 H, t, *J* 6.5, CH$_2$C*H*$_3$); δ_C ($CDCl_3$, 75 MHz) 178.4 (s), 163.4 (s), 154.9 (s), 147.4 (s), 135.2

(s), 135.0 (d), 132.2 (s), 131.2 (d), 125.0 (d), 123.5 (s), 119.4 (s), 118.0 (d), 115.7 (d), 113.8 (d), 112.5 (d), 43.9 (t), 31.6 (t), 29.3 (t), 26.8 (t), 22.6 (t), 21.0 (q), 14.1 (q); *m/z* (FAB) 370.1588 (M+H. $C_{22}H_{25}ClNO_2$ requires 370.1574).



mp = 98-100 °C; ν_{max}/cm^{-1} 2929, 2860, 1647, 1616, 1575; δ_H ($CDCl_3$, 300 M) 8.02 (2 H, s, C5-H), 7.50 (2 H, dd, *J* 8.5, 1.8, C7-H), 7.42 (2 H, d, *J* 7.1), 7.44-7.35 (4 H, m, C8-H and C3'-H), 7.26 (2 H, d, *J* 2.3, C2'-H), 7.09 (1 H, dd, *J* 8.7, 2.8 C4'-H), 6.61 (1 H, s, C3-H), 3.74 (2 H, d, *J* 7.3, NCH_2), 2.47 (6 H, s, $ArCH_3$), 1.78-1.60 (2 H, m, NCH_2CH_2), 1.41-1.21 (6 H, m, 3 x CH_2), 0.87 (3 H, t, *J* 6.3, CH_2CH_3); δ_C ($CDCl_3$, 75 M) 178.2 (s), 162.3 (s), 154.8 (s), 146.2 (s), 135.5 (s), 135.2 (d), 133.0 (s), 131.8 (d), 125.3 (s), 125.1 (d), 124.0 (d), 123.5 (s), 122.56 (d), 118.0 (d), 112.8 (d), 52.7 (t), 31.5 (t), 27.3 (t), 26.7 (t), 22.6 (t), 21.0 (q), 14.0 (q); *m/z* (FAB) 638.1875 (M+H. $C_{38}H_{34}Cl_2NO_4$ requires 638.1865)..

2-(4-Hexylamino-biphenyl-2-yl)-6-methyl-chromen-4-one 17.



Synthesised using general procedure C. mp = 120-123 °C; ν_{max}/cm^{-1} 2930, 2858, 1643, 1614 and 1574; δ_H ($CDCl_3$, 300 MHz) 7.94 (1 H, d, *J* 0.9, C5-H), 7.35-7.16 (7 H, m, Ar), 6.89-6.73 (3 H, m, Ar), 6.44 (1 H, s, C3-H), 3.91 (1 H, br s, NH), 3.18 (1 H, app t, *J* 7.0, NHC*H*$_2$), 2.41 (3 H, s ArCH_3), 1.66 (1 H, app quin, *J* 7.1, $NHCH_2CH_2$), 1.50-1.24 (6 H, m, 3 x CH_2), 0.92 (3 H, t, *J* 5.8, CH_2CH_3); δ_C (**, 75 MHz) 178.5 (s), 166.6 (s), 154.5 (s), 147.8 (s), 141.1 (s), 134.9 (s), 134.7 (d), 132.4 (s), 132.0 (d), 130.2 (s), 128.5 (d), 128.2 (d), 126.4 (d), 124.8 (d), 123.4 (s), 117.6 (d), 115.1 (d), 113.1 (d), 111.7 (d), 44.0 (t), 31.6 (t), 29.4 (t), 26.9 (t), 22.7 (t), 20.9 (q), 14.1 (t); *m/z* (FAB) 412.2286 (M+H. $C_{28}H_{30}NO_2$ requires 412.2276).

1. I. Arduengo, Anthony J., R. Krafczyk, R. Schmutzler, H. A. Craig, J. R. Goerlich, W. J. Marshall and M. Unverzagt, *Tetrahedron*, 1999, **55**, 14523-14534.