Synthesis of Functionalized Diarylmethanes via Copper-Catalyzed Cross-Coupling of Arylmagnesium Reagents with Benzylic Phosphates

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Supporting Information

General considerations

Unless otherwise indicated, all reactions were carried out with magnetic stirring and in case of air- or moisture-sensitive compounds in flame-dried glassware under nitrogen. Syringes were used to transfer the reagents and the solvents were purged with nitrogen prior to use. Reactions were monitored by gas chromatography (GC and GC-MS) or thin layer chromatography.

Solutions of organomagnesium compounds were prepared, if not especially mentioned, by the reaction of Mg with aryl bromides in THF, titrated with a standard solution of I₂ in 0.5 M LiCl in THF and diluted with THF to the mentioned concentration.

Typical Procedures for the Preparation of Functionalized Diarylmethanes:

Typical Procedure 1 (TP 1).

In a flame dried Schlenk-tube under nitrogen the Grignard reagent (1.5 equiv.) in DME is cooled to -15 °C and CuCl (0.1 equiv.) is added. After 5 min at -15 °C triethylphosphite (0.2 equiv.) is added and the mixture again stirred for 5 min. Meanwhile a second flame dried schlenk tube is prepared, containing the benzylic phosphate (1.0 equiv.) in DME and tetrabutylammonium iodide (0.1 equiv.). This mixture is heated to 60 °C and then the mixture of the Grignard reagent, CuCl and triethylphosphite is added via canula over 30 min to the hot mixture of the benzylic phosphate and tetrabutylammonium iodide. The reaction mixture is stirred at 60 °C until the GC of a hydrolyzed aliquot shows completion of the reaction, then quenched with sat. NH₄Cl solution, extracted with ether, and the product is purified by column chromatography.

Typical Procedure 2 (TP 2).

In a flame dried Schlenk-tube under nitrogen an aromatic bromide or iodide (1.5. equiv.) is dissolved in DME and cooled to the mentioned temperature. Then *i*PrMgCl or *i*PrMgCl·LiCl (1.6 equiv.) is added dropwise via syringe. After completion of the exchange, the Grignard reagent (1.5 equiv.) in DME is cooled to -15 °C and CuCl (0.1 equiv.) is added. After 5 min at -15 °C triethylphosphite (0.2 equiv.) is added and the mixture again stirred for 5 min. Meanwhile a second flame dried schlenk tube is prepared, containing the benzylic phosphate (1.0 equiv.) in DME and tetrabutylammonium iodide (0.1 equiv.). This mixture is heated to 60 °C and then the mixture of the Grignard reagent, CuCl and triethylphosphite is added via canula over 30 min to the hot mixture of the benzylic phosphate and tetrabutylammonium iodide. The reaction mixture is stirred at 60 °C until the GC of a hydrolyzed aliquot shows completion of the reaction, then quenched with sat. NH₄Cl solution, extracted with ether, and the product is purified by column chromatography.

Ethyl 4-benzylbenzoate (**2a**)

Prepared according to the TP 2. To a solution of ethyl 4-iodobenzoate (207 mg, 0.75 mmol) in 0.5 mL DME, *i*PrMgCl (0.89 mL, 0.80 mmol, 0.9 M in THF) is added dropwise via syringe at -20 °C. The solution is stirred for 20 min, then CuCl (5.0 mg, 10 mol%) and P(OEt)₃ (17 mg, 20 mol%) is added. This mixture is added over 30 min via canula to a prewarmed mixture of benzyl diethyl phosphate (122 mg, 0.50 mmol) and TBAI (19 mg, 10 mol%). The reaction mixture is heated at 60 °C for 1h. The usual workup and purification by flash chromatography (pentane/ether 19:1) yielded **2a** as colourless liquid (96 mg, 80%).

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 7.87 (d, *J* = 8.4 Hz, 2H), 7.22-7.06 (m, 7H), 4.26 (q, *J* = 7.2 Hz, 2H), 3.92 (s, 2H), 1.28 (t, *J* = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 166.5, 146.3, 140.1, 129.7, 128.9, 128.5, 128.4, 126.3, 60.7, 41.9, 14.3.

IR (KBr): 2982 (w), 1711 (vs), 1610 (w), 1602 (w), 1495 (w), 1270 (vs), 1176 (m), 1098 (s), 1020 (m), 854 (w), 739 (m), 695 (m).

MS (70 eV, EI), *m/z* (%): 240 (60, M⁺), 195 (100), 167 (86), 152 (21), 128 (3), 91 (7), 82 (5).

HRMS *m/z*: calcd. for C₁₆H₁₆O₂: 240.1150; found: 240.1141.

Ethyl 4-benzylbenzoate (2a)

4 Apr 2006
1H

Acquisition Time (sec)	Comment	Date	Frequency (MHz)
9.0440	Ak Knochel	29/11/2005 15:38:12	300.13
Nucleus	Original Points Count	Points Count	Sweep Width (Hz)
¹ H	32768	32768	3623.19
	Temperature (grad C)		
	0.000

Ethyl 4-benzylbenzoate (2a)

4 Apr 2006
13C

Acquisition Time (sec)	Comment	Date	Frequency (MHz)
3.4079	Ak Knochel	29/11/2005 17:23:02	75.47
Nucleus	Original Points Count	Points Count	Sweep Width (Hz)
¹³ C	65536	65536	19230.77
	Temperature (grad C)		
	0.000

No.	Annotation	(ppm)
1	Chloroform-d	77.00

Ethyl 4-(4-methylbenzyl)benzoate (**2b**)

Prepared according to the TP 2. To a solution of ethyl 4-iodobenzoate (207 mg, 0.75 mmol) in 0.5 mL DME, *i*PrMgCl (0.89 mL, 0.80 mmol, 0.9 M in THF) is added dropwise via syringe at -20 °C. The solution is stirred for 20 min, then CuCl (5.0 mg, 10 mol%) and P(OEt)₃ (17 mg, 20 mol%) is added. This mixture is added over 30 min via canula to a prewarmed mixture of diethyl 4-methylbenzyl phosphate (129 mg, 0.50 mmol) and TBAI (19 mg, 10 mol%). The reaction mixture is heated at 60 °C for 1h. The usual workup and purification by flash chromatography (pentane/ether 19:1) yielded **2b** as colourless liquid (112 mg, 88%).

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 7.86 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 8.5 Hz, 2H), 7.01-6.94 (m, 4H), 4.25 (q, *J* = 7.2 Hz, 2H), 3.87 (s, 2H), 3.08 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 166.5, 146.6, 140.1, 137.1, 135.8, 129.7, 129.2, 128.8, 128.3, 60.7, 41.4, 20.9, 14.3.

IR (KBr): 2981 (w), 1713 (vs), 1609 (m), 1514 (w), 1366 (w), 1271 (vs), 1176 (m), 1103 (s), 1020 (m), 869 (w), 738 (m).

MS (70 eV, EI), *m/z* (%): 254 (90, M⁺), 239 (26), 209 (76), 181 (100), 165 (50), 105 (9), 77 (5).

HRMS *m/z*: calcd. for C₁₇H₁₈O₂: 254.1307; found: 254.1306.

Ethyl 4-(4-methylbenzyl)benzoate (2b)

4 Apr 2006
1H

Acquisition Time (sec)	Comment	Date	Frequency (MHz)
9.0440	Ak Knochel	16/12/2005 03:23:30	300.13
Nucleus	Original Points Count	Points Count	Sweep Width (Hz)
1H	32768	32768	3623.19
			Temperature (grad C)
			0.000

Ethyl 4-(4-methylbenzyl)benzoate (2b)

4 Apr 2006
13C

Acquisition Time (sec)	Comment	Date	Frequency (MHz)
3.4079	Ak Knochel	16/12/2005 04:23:38	75.47
Nucleus	Original Points Count	Points Count	Sweep Width (Hz)
13C	65536	65536	19230.77
			Temperature (grad C)
			0.000

No.	Annotation	(ppm)
1	Chloroform-d	77.00

Ethyl 4-(4-bromobenzyl)benzoate (**2c**)

Prepared according to the TP 2. To a solution of ethyl 4-iodobenzoate (207 mg, 0.75 mmol) in 0.5 mL DME, *i*PrMgCl (0.89 mL, 0.80 mmol, 0.9 M in THF) is added dropwise via syringe at -20 °C. The solution is stirred for 20 min, then CuCl (5.0 mg, 10 mol%) and P(OEt)₃ (17 mg, 20 mol%) is added. This mixture is added over 30 min via canula to a prewarmed mixture of 4-bromobenzyl diethyl phosphate (162 mg, 0.50 mmol) and TBAI (19 mg, 10 mol%). The reaction mixture is heated at 60 °C for 1h. The usual workup and purification by flash chromatography (pentane/ether 9:1) yielded **2c** as colourless liquid (115 mg, 72%).

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 7.83 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.12 (d, *J* = 8.2 Hz, 2H), 6.94 (d, *J* = 8.2 Hz, 2H), 4.27 (q, *J* = 7.1 Hz, 2H), 3.87 (s, 2H), 1.28 (t, *J* = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 166.4, 145.6, 139.1, 131.6, 130.6, 129.8, 128.8, 128.7, 120.2, 60.8, 41.2, 14.3.

IR (KBr): 2981 (w), 1712 (vs), 1610 (m), 1487 (m), 1403 (w), 1271 (vs), 1176 (m), 1102 (s), 1020 (m), 101 (s), 927 (w), 754 (m).

MS (70 eV, EI), *m/z* (%): 318 (74, M⁺), 290 (17), 275 (90), 245 (50), 211 (20), 165 (100), 97 (11), 82 (10).

HRMS *m/z*: calcd. for C₁₆H₁₅BrO₂: 318.0255; found: 318.0242.

Ethyl 4-(4-bromobenzyl)benzoate (2c)

5 Apr 2006
1H

Acquisition Time (sec)	9.0440	Comment	Ak Knochel	Date	16/12/2005 09:53:32	Frequency (MHz)	300.13
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3623.19
					Temperature (grad C)	0.000

Ethyl 4-(4-bromobenzyl)benzoate (2c)

5 Apr 2006
13C

Acquisition Time (sec)	3.4079	Comment	Ak Knochel	Date	16/12/2005 10:53:30	Frequency (MHz)	75.47
Nucleus	13C	Original Points Count	65536	Points Count	65536	Sweep Width (Hz)	19230.77
					Temperature (grad C)	0.000

No.	Annotation	(ppm)
1	Chloroform-d	77.00

Ethyl 4-(2-methoxybenzyl)benzoate (2d)

Prepared according to the TP 2. To a solution of ethyl 4-iodobenzoate (207 mg, 0.75 mmol) in 0.5 mL DME, *i*PrMgCl (0.89 mL, 0.80 mmol, 0.9 M in THF) is added dropwise via syringe at -20 °C. The solution is stirred for 20 min, then CuCl (5.0 mg, 10 mol%) and P(OEt)₃ (17 mg, 20 mol%) is added. This mixture is added over 30 min via canula to a prewarmed mixture of diethyl 2-methoxybenzyl phosphate (137 mg, 0.50 mmol) and TBAI (19 mg, 10 mol%). The reaction mixture is heated at 60 °C for 1h. The usual workup and purification by flash chromatography (pentane/ether 9:1) yielded **2d** as colourless liquid (109 mg, 81%).

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 7.85 (d, *J* = 8.3 Hz, 2H), 7.17-7.07 (m, 3H), 6.96 (d, *J* = 7.2 Hz, 1H), 6.80-6.74 (m, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.91 (s, 2H), 3.67 (s, 3H), 1.26 (t, *J* = 7.2 Hz, 3H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 166.6, 157.3, 146.5, 130.3, 129.5, 128.8, 128.6, 128.1, 127.7, 120.5, 110.4, 60.6, 55.2, 36.0, 14.3.

IR (KBr): 2981 (w), 1172 (vs), 1610 (m), 1492 (m), 1415 (w), 1271 (vs), 1242 (vs), 1176 (m), 1103 (s), 1020 (s), 928 (w), 747 (s), 701 (w).

MS (70 eV, EI), *m/z* (%): 270 (100, M⁺), 225 (45), 197 (77), 165 (25), 152 (11), 91 (39).

HRMS *m/z*: calcd. for C₁₇H₁₈O₃: 270.1256; found: 270.1257.

Ethyl 4-(2-methoxybenzyl)benzoate (2d)

5 Apr 2006
1H

Acquisition Time (sec)	9.0440	Comment	Ak Knochel	Date	16/12/2005 05:53:30	Frequency (MHz)	300.13
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3623.19
						Temperature (grad C)	0.000

Ethyl 4-(2-methoxybenzyl)benzoate (2d)

5 Apr 2006
13C

Acquisition Time (sec)	3.4079	Comment	Ak Knochel	Date	16/12/2005 06:53:28	Frequency (MHz)	75.47
Nucleus	13C	Original Points Count	65536	Points Count	65536	Sweep Width (Hz)	19230.77
						Temperature (grad C)	0.000

No.	Annotation	(ppm)
1	Chloroform-d	77.00

1-Benzyl-4-methoxybenzene (2e)

Prepared according to the TP 1. To a solution of 4-methoxyphenylmagnesium bromide (0.87 mL, 0.75 mmol, 0.86 M in THF) in 0.5 mL DME, CuCl (5.0 mg, 10 mol%) and P(OEt)₃ (17 mg, 20 mol%) is added. This mixture is added over 30 min via canula to a prewarmed mixture of benzyl diethyl phosphate (122 mg, 0.50 mmol) and TBAI (19 mg, 10 mol%). The reaction mixture is heated at 60 °C for 1h. The usual workup and purification by flash chromatography (pentane) yielded **2e** as colourless liquid (72 mg, 73%).

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 7.21-6.99 (m, 7H), 6.73 (d, *J*= 8.7 Hz, 2H), 3.83 (s, 2H), 3.67 (s, 3H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 158.0, 141.6, 133.2, 129.8, 128.8, 128.4, 125.9, 133.9, 55.2, 41.0.

IR (KBr): 3062 (w), 3027 (w), 1610 (m), 1510 (vs), 1494 (m), 1440 (m), 1300 (w), 1243 (vs), 1175 (m), 1034 (m), 836 (w), 768 (w), 723 (m), 696 (m).

MS (70 eV, EI), *m/z* (%): 198 (100, M⁺), 167 (30), 121 (22), 91 (8), 51 (4).

HRMS *m/z*: calcd. for C₁₄H₁₄O: 198.1045; found: 198.1033.

1-Benzyl-4-methoxybenzene (2e)

5 Apr 2006
1H

Acquisition Time (sec)	9.0440	Comment	Ak Knochel	Date	21/12/2005 11:08:46	Frequency (MHz)	300.13
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3623.19
						Temperature (grad C)	0.000

1-Benzyl-4-methoxybenzene (2e)

5 Apr 2006
13C

Acquisition Time (sec)	3.4079	Comment	Ak Knochel	Date	21/12/2005 12:09:00	Frequency (MHz)	75.47
Nucleus	13C	Original Points Count	65536	Points Count	65536	Sweep Width (Hz)	19230.77
						Temperature (grad C)	0.000

No.	Annotation	(ppm)
1	Chloroform-d	77.00

1-Methoxy-4-(4-methylbenzyl)benzene (**2f**)

Prepared according to the TP 1. To a solution of 4-methoxyphenylmagnesium bromide (0.87 mL, 0.75 mmol, 0.86 M in THF) in 0.5 mL DME, CuCl (5.0 mg, 10 mol%) and P(OEt)₃ (17 mg, 20 mol%) is added. This mixture is added over 30 min via canula to a prewarmed mixture of diethyl 4-methylbenzyl phosphate (129 mg, 0.50 mmol) and TBAI (19 mg, 10 mol%). The reaction mixture is heated at 60 °C for 1h. The usual workup and purification by flash chromatography (pentane) yielded **2f** as colourless liquid (85 mg, 80%).

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 7.02-6.96 (m, 6H), 6.74 (d, J = 8.6 Hz, 2H), 3.80 (s, 2H), 3.69 (s, 3H), 2.23 (s, 3H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 157.9, 138.5, 135.4, 133.5, 129.8, 129.1, 128.7, 133.8, 55.2, 40.6, 21.0.

IR (KBr): 3002 (w), 2909 (w), 1610 (w), 1508 (vs), 1462 (m), 1301 (w), 1242 (vs), 1175 (m), 1106 (w), 1036 (m), 848 (w), 804 (m).

MS (70 eV, EI), m/z (%): 212 (100, M⁺), 197 (76), 181 (20), 165 (15), 121 (14), 105 (8), 77 (6).

HRMS m/z : calcd. for C₁₅H₁₆O: 212.1201; found: 212.1215.

1-Methoxy-4-(4-methylbenzyl)benzene (2f)

5 Apr 2006
1H

Acquisition Time (sec)	9.0440	Comment	Ak Knochel	Date	16/12/2005 04:53:30	Frequency (MHz)	300.13
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3623.19
					Temperature (grad C)	0.000

1-Methoxy-4-(4-methylbenzyl)benzene (2f)

5 Apr 2006
13C

Acquisition Time (sec)	3.4079	Comment	Ak Knochel	Date	16/12/2005 05:53:30	Frequency (MHz)	75.47
Nucleus	13C	Original Points Count	65536	Points Count	65536	Sweep Width (Hz)	19230.77
					Temperature (grad C)	0.000

No.	Annotation	(ppm)
1	Chloroform-d	77.00

4-(4-Methoxybenzyl)benzonitrile (**2g**)

Prepared according to the TP 2. To a solution of 4-bromobenzonitrile (137 mg, 0.75 mmol) in 0.5 mL DME, *i*PrMgCl·LiCl (0.73 mL, 0.80 mmol, 1.1 M in THF) is added dropwise via syringe at 0 °C. The solution is stirred for 3 h, then CuCl (5.0 mg, 10 mol%) and P(OEt)₃ (17 mg, 20 mol%) is added. This mixture is added over 30 min via canula to a prewarmed mixture of diethyl 4-methoxybenzyl phosphate (137 mg, 0.50 mmol) and TBAI (19 mg, 10 mol%). The reaction mixture is heated at 60 °C for 1h. The usual workup and purification by flash chromatography (pentane/ether 9:1) yielded **2g** as colourless liquid (80 mg, 72%).

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 7.45 (d, *J*= 8.5 Hz, 2H), 7.17 (d, *J*= 8.5 Hz, 2H), 6.98 (d, *J*= 8.7 Hz, 2H), 6.76 (d, *J*= 8.7 Hz, 2H), 3.87 (s, 2H), 3.69 (s, 3H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 158.3, 147.2, 132.2, 131.3, 129.9, 129.4, 118.9, 114.1, 109.8, 55.2, 41.0.

IR (KBr): 2933 (w), 2226 (m), 1609 (m), 1510 (vs), 1462 (m), 1440 (m), 1301 (m), 1244 (vs), 1176 (s), 1110 (m), 1032 (s), 917 (w), 861 (m), 809 (s), 761 (m).

MS (70 eV, EI), *m/z* (%): 223 (100, M⁺), 208 (23), 192 (13), 180 (12), 121 (27), 77(6).

HRMS *m/z*: calcd. for C₁₅H₁₃NO: 223.0997; found: 223.0981.

4-(4-Methoxybenzyl)benzonitrile (2g)

9 Apr 2006
1H

Acquisition Time (sec)	9.0440	Comment	Ak Knochel	Date	29/11/2005 13:53:12	Frequency (MHz)	300.13
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3623.19
						Temperature (grad C)	0.000

4-(4-Methoxybenzyl)benzonitrile (2g)

9 Apr 2006
13C

Acquisition Time (sec)	3.4079	Comment	Ak Knochel	Date	29/11/2005 14:23:00	Frequency (MHz)	75.47
Nucleus	13C	Original Points Count	65536	Points Count	65536	Sweep Width (Hz)	19230.77
						Temperature (grad C)	0.000

No.	Annotation	(ppm)
1	Chloroform-d	77.00

4-(Furan-3-ylmethyl)benzonitrile (**2h**)

Prepared according to the TP 2. To a solution of 4-bromobenzonitrile (137 mg, 0.75 mmol) in 0.5 mL DME, *i*PrMgCl·LiCl (0.73 mL, 0.80 mmol, 1.1 M in THF) is added dropwise via syringe at 0 °C. The solution is stirred for 3 h, then CuCl (5.0 mg, 10 mol%) and P(OEt)₃ (17 mg, 20 mol%) is added. This mixture is added over 30 min via canula to a prewarmed mixture of diethyl furan-3-ylmethyl phosphate (117 mg, 0.50 mmol) and TBAI (19 mg, 10 mol%). The reaction mixture is heated at 60 °C for 1h. The usual workup and purification by flash chromatography (pentane/ether 49:1) yielded **2h** as colourless liquid (60 mg, 63%).

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 7.60 (d, *J* = 8.1 Hz, 2H), 7.40 (s br, 1H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.26 (s br, 1H), 6.22 (s br, 1H), 3.85 (s, 2H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 145.9, 143.4, 139.8, 132.2, 129.3, 122.6, 118.9, 110.9, 110.1, 31.2.

IR (KBr): 2920 (w), 2228 (s), 1767 (w), 1712 (w), 1607 (m), 1501 (m), 1416 (m), 1383 (w), 1278 (w), 1175 (m), 1066 (s), 1020 (vs), 975 (s), 915 (m), 873 (s), 786 (vs), 749 (s), 679 (m).

MS (70 eV, EI), *m/z* (%): 183 (100, M⁺), 154 (57), 127 (27), 115 (10), 51 (5).

HRMS *m/z*: calcd. for C₁₂H₉NO: 183.0684; found: 183.0696.

4-(Furan-3-ylmethyl)benzonitrile (2h)

9 Apr 2006
1H

Acquisition Time (sec)	4.1943	Comment	Christiane Kofink, AK Knochel	Date	Mar 14 2006	Frequency (MHz)	300.10
Nucleus	1H	Number of Transients	8	Original Points Count	16384	Points Count	16384
Temperature (grad C)	27.	Solvent	cdcl3	Sweep Width (Hz)	3906.25

4-(Furan-3-ylmethyl)benzonitrile (2h)

9 Apr 2006
13C

Acquisition Time (sec)	1.6010	Comment	Christiane Kofink, AK Knochel	Date	Mar 14 2006
Frequency (MHz)	75.47	Nucleus	13C	Number of Transients	1024
Solvent	cdcl3	Sweep Width (Hz)	18115.94	Original Points Count	29004
Temperature (grad C)	27.000	Points Count	32768

No.	Annotation	(ppm)
1	Chloroform-d	77.00

2-(Furan-3-ylmethyl)benzonitrile (**2i**)

Prepared according to the TP 2. To a solution of 2-bromobenzonitrile (137 mg, 0.75 mmol) in 0.5 mL DME, *i*PrMgCl·LiCl (0.73 mL, 0.80 mmol, 1.1 M in THF) is added dropwise via syringe at 0 °C. The solution is stirred for 3 h, then CuCl (5.0 mg, 10 mol%) and P(OEt)₃ (17 mg, 20 mol%) is added. This mixture is added over 30 min via canula to a prewarmed mixture of diethyl furan-3-ylmethyl phosphate (117 mg, 0.50 mmol) and TBAI (19 mg, 10 mol%). The reaction mixture is heated at 60 °C for 1h. The usual workup and purification by flash chromatography (pentane/ether 49:1) yielded **2i** as colourless liquid (60 mg, 63%).

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 7.51-7.35 (m, 5H), 7.22 (s br, 1H), 6.19 (s br, 1H), 3.79 (s, 2H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 143.5, 141.8, 139.8, 133.1, 132.0, 130.0, 129.2, 122.7, 112.5, 110.9, 104.7, 30.7.

IR (KBr): 2917 (w), 2229 (s), 17770 (w), 1582 (w), 1430 (w), 1154 (w), 1066 (m), 1022 (s), 976 (m), 873 (s), 782 (s), 734 (s), 710 (m).

MS (70 eV, EI), *m/z* (%): 183 (100, M⁺), 154 (63), 127 (26), 115 (9), 81 (11), 51 (6).

HRMS *m/z*: calcd. for C₁₂H₉NO: 183.0684; found: 183.0689.

2-(Furan-3-ylmethyl)benzonitrile (2i)

21 Apr 2006
1H

Acquisition Time (sec)	4.1943	Comment	Christiane Kofink, AK Knochel	Date	Mar 14 2006	Frequency (MHz)	300.10
Nucleus	1H	Number of Transients	8	Original Points Count	16384	Points Count	16384
Temperature (grad C)	27.000	Solvent	cdcl3	Sweep Width (Hz)	3906.25

2-(Furan-3-ylmethyl)benzonitrile (2i)

21 Apr 2006
13C

Acquisition Time (sec)	1.6010	Comment	Christiane Kofink, AK Knochel	Date	Mar 14 2006
Frequency (MHz)	75.47	Nucleus	13C	Number of Transients	1024
Solvent	cdcl3	Sweep Width (Hz)	18115.94	Original Points Count	29004
		Temperature (grad C)	27.000	Points Count	32768

Ethyl 4-(furan-3-ylmethyl)benzoate (**2j**)

Prepared according to the TP 2. To a solution of ethyl 4-iodobenzoate (207 mg, 0.75 mmol) in 0.5 mL DME, *i*PrMgCl (0.89 mL, 0.80 mmol, 0.9 M in THF) is added dropwise via syringe at -20 °C. The solution is stirred for 20 min, then CuCl (5.0 mg, 10 mol%) and P(OEt)₃ (17 mg, 20 mol%) is added. This mixture is added over 30 min via canula to a prewarmed mixture of diethyl furan-3-ylmethyl phosphate (117 mg, 0.50 mmol) and TBAI (19 mg, 10 mol%). The reaction mixture is heated at 60 °C for 1h. The usual workup and purification by flash chromatography (pentane/ether 19:1) yielded **2j** as colourless liquid (82 mg, 71%).

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 8.00 (d, *J* = 8.3 Hz, 2H), 7.39 (s br, 1H), 7.30 (d, *J* = 8.3 Hz, 2H), 7.24 (s br, 1H), 6.24 (s br, 1H), 4.39 (q, *J* = 7.2 Hz, 2H), 3.84 (s, 2H), 1.41 (t, *J* = 7.2 Hz, 3H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 166.5, 145.6, 143.2, 139.7, 129.8, 128.6, 128.5, 123.4, 111.1, 60.8, 31.2, 14.3.

IR (KBr): 2982 (w), 1710 (vs), 1611 (m), 1416 (w), 1367 (w), 1272 (vs), 1177 (m), 1101 (s), 1020 (s), 873 (m), 772 (w), 719 (m).

MS (70 eV, EI), *m/z* (%): 230 (85, M⁺), 185 (100), 157 (61), 128 (33), 81 (4).

HRMS *m/z*: calcd. for C₁₄H₁₄O₃: 230.0943; found: 230.0939.

Ethyl 4-(furan-3-ylmethyl)benzoate (2j)

5 Apr 2006
1H

Acquisition Time (sec)	4.0000	Comment	Christiane Kofink, AK Knochel	Date	Mar 7 2006	Frequency (MHz)	300.10
Nucleus	1H	Number of Transients	32	Original Points Count	15625	Points Count	16384
Temperature (grad C)	27.000			Solvent	cdcl3	Sweep Width (Hz)	3906.25

Ethyl 4-(furan-3-ylmethyl)benzoate (2j)

5 Apr 2006
13C

Acquisition Time (sec)	1.6010	Comment	Christiane Kofink, AK Knochel	Date	Mar 7 2006	Frequency (MHz)	75.47
Nucleus	13C	Number of Transients	1024	Original Points Count	29004	Points Count	32768
Solvent	cdcl3	Sweep Width (Hz)	18115.94	Temperature (grad C)	27.000

Ethyl 2-(thiophen-2-ylmethyl)benzoate (**2k**)

Prepared according to the TP 2. To a solution of ethyl 2-iodobenzoate (207 mg, 0.75 mmol) in 0.5 mL DME, *i*PrMgCl (0.89 mL, 0.80 mmol, 0.9 M in THF) is added dropwise via syringe at $-20\text{ }^{\circ}\text{C}$. The solution is stirred for 3 h, then CuCl (5.0 mg, 10 mol%) and P(OEt)₃ (17 mg, 20 mol%) is added. This mixture is added over 30 min via canula to a prewarmed mixture of diethyl thiophen-2-ylmethyl phosphate (125 mg, 0.50 mmol) and TBAI (19 mg, 10 mol%). The reaction mixture is heated at $60\text{ }^{\circ}\text{C}$ for 1 h. The usual workup and purification by flash chromatography (pentane/ether 19:1) yielded **2k** as colourless liquid (75 mg, 61%).

¹H-NMR (CDCl₃, 300 MHz, 25 $^{\circ}\text{C}$): δ = 7.95 (d, J = 7.6 Hz, 1H), 7.76 (m, 1H), 7.32 (d, J = 7.6 Hz, 2H), 7.14 (d, J = 5.1 Hz, 1H), 6.91 (s br, 1H), 6.79 (s br, 1H), 4.59 (s, 2H), 4.36 (q, J = 7.1 Hz, 2H), 1.37 (t, J = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 75 MHz, 25 $^{\circ}\text{C}$): δ = 167.4, 143.8, 141.6, 132.0, 131.0, 130.7, 129.7, 126.6, 125.1, 123.7, 60.9, 34.0, 29.6, 14.2.

IR (KBr): 3070 (w), 2980 (w), 1712 (vs), 1601 (w), 1577 (w), 1440 (w), 1366 (w), 1292 (m), 1259 (s), 1171 (w), 1109 (m), 1073 (s), 1047 (w), 850 (w), 740 (w), 692 (m).

MS (70 eV, EI), m/z (%): 246 (5, M⁺), 200 (100), 171 (23), 133 (28), 128 (4), 77 (2).

HRMS m/z : calcd. for C₁₄H₁₄O₂S: 246.0715; found: 246.0711.

Ethyl 2-(thiophen-2-ylmethyl)benzoate (2k)

9 Apr 2006
1H

Acquisition Time (sec)	4.0000	Comment	Christiane Kofink, AK Knochel	Date	Mar 28 2006	Frequency (MHz)	399.94
Nucleus	¹ H	Number of Transients	16	Original Points Count	25596	Points Count	32768
Temperature (grad C)				Solvent	cdcl3	Sweep Width (Hz)	6398.98

Ethyl 2-(thiophen-2-ylmethyl)benzoate (2k)

9 Apr 2006
13C

Acquisition Time (sec)	1.6000	Comment	Christiane Kofink, AK Knochel	Date	Mar 28 2006
Frequency (MHz)	100.58	Nucleus	¹³ C	Number of Transients	1024
Solvent	cdcl3	Sweep Width (Hz)	24132.73	Original Points Count	38612
		Temperature (grad C)	30.000	Points Count	65536

Ethyl 2-(thiophen-3-ylmethyl)benzoate (**2l**)

Prepared according to the TP 2. To a solution of ethyl 2-iodobenzoate (207 mg, 0.75 mmol) in 0.5 mL DME, *i*PrMgCl (0.89 mL, 0.80 mmol, 0.9 M in THF) is added dropwise via syringe at $-20\text{ }^{\circ}\text{C}$. The solution is stirred for 3 h, then CuCl (5.0 mg, 10 mol%) and $\text{P}(\text{OEt})_3$ (17 mg, 20 mol%) is added. This mixture is added over 30 min via canula to a prewarmed mixture of diethyl thiophen-3-ylmethyl phosphate (125 mg, 0.50 mmol) and TBAI (19 mg, 10 mol%). The reaction mixture is heated at $60\text{ }^{\circ}\text{C}$ for 1 h. The usual workup and purification by flash chromatography (pentane/ether 19:1) yielded **2l** as colourless liquid (101 mg, 82%).

$^1\text{H-NMR}$ (CDCl_3 , 300 MHz, $25\text{ }^{\circ}\text{C}$): δ = 7.93 (d, J = 7.8 Hz, 1H), 7.45 (t, J = 7.4 Hz, 1H), 7.28 (m, 3H), 6.95 (d, J = 4.9 Hz, 1H), 6.89 (s br, 1H), 4.40 (s, 2H), 4.33 (q, J = 7.1 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H).

$^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz, $25\text{ }^{\circ}\text{C}$): δ = 167.5, 141.7, 141.2, 131.8, 131.0, 130.5, 130.0, 128.4, 126.2, 125.1, 121.1, 60.8, 34.5, 14.1.

IR (KBr): 2980 (w), 1712 (vs), 1601 (w), 1576 (w), 1487 (w), 1445 (w), 1365 (w), 1255 (s), 1126 (m), 1073 (s), 1126 (m), 1073 (s), 1047 (w), 940 (w), 756 (m), 714 (m).

MS (70 eV, EI), m/z (%): 246 (23, M^+), 200 (100), 171 (46), 133 (52), 105 (4), 77 (3).

HRMS m/z : calcd. for $\text{C}_{14}\text{H}_{14}\text{O}_2\text{S}$: 246.0715; found: 246.0721.

Ethyl 2-(thiophen-3-ylmethyl)benzoate (2l)

9 Apr 2006
1H

Acquisition Time (sec)	4.0000	Comment	Christiane Kofink, AK Knochel	Date	Mar 28 2006	Frequency (MHz)	399.94
Nucleus	1H	Number of Transients	16	Original Points Count	25596	Points Count	32768
Temperature (grad C)	30.000	Solvent	cdcl3	Sweep Width (Hz)	6398.98

Ethyl 2-(thiophen-3-ylmethyl)benzoate (2l)

9 Apr 2006
13C

Acquisition Time (sec)	1.6000	Comment	Christiane Kofink, AK Knochel	Date	Mar 28 2006	Frequency (MHz)	100.58
Nucleus	13C	Number of Transients	1024	Original Points Count	38612	Points Count	65536
Solvent	cdcl3	Sweep Width (Hz)	24132.73	Temperature (grad C)	30.000

No.	Annotation	(ppm)
1	Chloroform-d	77.00

Methyl 4-((2-methyl-1-tosyl-1H-indol-3-yl)methyl)benzoate (2m)

Prepared according to the TP 2. To a solution of 3-iodo-2-methyl-1-tosyl-1H-indole (308 mg, 0.75 mmol) in 0.5 mL DME, *i*PrMgCl (0.89 mL, 0.80 mmol, 0.9 M in THF) is added dropwise via syringe at -20°C . The solution is stirred for 3 h, then CuCl (5.0 mg, 10 mol%) and $\text{P}(\text{OEt})_3$ (17 mg, 20 mol%) is added. This mixture is added over 30 min via canula to a prewarmed mixture of methyl 4-((diethoxyphosphoryloxy)methyl)benzoate (151 mg, 0.50 mmol) and TBAI (19 mg, 10 mol%). The reaction mixture is heated at 60°C for 1h. The usual workup and purification by flash chromatography (pentane/ether 9:1) yielded **2m** as colourless solid (151 mg, 70%).

Mp.: 121°C .

$^1\text{H-NMR}$ (CDCl_3 , 300 MHz, 25°C): δ = 8.25 (d, J = 8.5 Hz, 1H), 7.89 (d, J = 8.2 Hz, 2H), 7.65 (d, J = 8.2 Hz, 2H), 7.32-7.09 (m, 7H), 4.03 (s, 2H), 3.90 (s, 3H), 2.59 (s, 3H), 2.38 (s, 3H).

$^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz, 25°C): δ = 166.8, 144.9, 144.7, 136.6, 136.1, 133.9, 130.3, 129.8, 129.7, 128.1, 127.9, 126.2, 124.1, 123.5, 188.5, 118.34, 114.8, 51.9, 29.9, 21.5, 12.9.

IR (KBr): 1716 (s), 1610 (m), 1453 (m), 1361 (s), 1277 (vs), 1236 (m), 1171 (vs), 1106 (s), 1089 (s), 988 (m), 938 (m), 877 (w), 811 (m), 744 (vs), 704 (m), 686 (m).

MS (70 eV, EI), m/z (%): 433 (41, M^+), 278 (100), 218 (10), 178 (6), 91 (8).

HRMS m/z : calcd. for $\text{C}_{25}\text{H}_{23}\text{NO}_4\text{S}$: 433.1348; found: 433.1327.

Indole derivative 2m

9 Apr 2006
1H

Acquisition Time (sec)	2.0486	Comment	Christiane Kofink, AK Knochel	Date	Feb 22 2006	Frequency (MHz)	300.10
Nucleus	1H	Number of Transients	8	Original Points Count	9849	Points Count	16384
Temperature (grad C)	27.000	Solvent	cdcl3	Sweep Width (Hz)	4807.69

Indole derivative 2m

9 Apr 2006
13C

Acquisition Time (sec)	1.3005	Comment	Christiane Kofink, AK Knochel	Date	Feb 22 2006	Frequency (MHz)	75.47
Nucleus	13C	Number of Transients	2000	Original Points Count	23560	Points Count	32768
Solvent	cdcl3	Sweep Width (Hz)	18115.94	Temperature (grad C)	27.000

Methyl 4-((1-benzyl-2-methyl-1H-indol-3-yl)methyl)benzoate (2n)

Prepared according to the TP 2. To a solution of 1-benzyl-3-iodo-2-methyl-1H-indole (260 mg, 0.75 mmol) in 0.5 mL DME, *i*PrMgCl (0.89 mL, 0.80 mmol, 0.9 M in THF) is added dropwise via syringe at -20°C . The solution is stirred for 3 h, then CuCl (5.0 mg, 10 mol%) and $\text{P}(\text{OEt})_3$ (17 mg, 20 mol%) is added. This mixture is added over 30 min via canula to a prewarmed mixture of methyl 4-((diethoxyphosphoryloxy)methyl)benzoate (151 mg, 0.50 mmol) and TBAI (19 mg, 10 mol%). The reaction mixture is heated at 60°C for 1h. The usual workup and purification by flash chromatography (pentane/ether 9:1) yielded **2n** as colourless solid (143 mg, 77%).

Mp.: 115°C .

$^1\text{H-NMR}$ (CDCl_3 , 300 MHz, 25°C): δ = 7.98 (d, J = 7.9 Hz, 2H), 7.48 (d, J = 7.3 Hz, 1H), 7.36-7.27 (m, 6H), 7.20-7.07 (m, 2H), 7.04-7.01 (m, 2H), 5.38 (s, 2H), 4.23 (s, 2H), 3.93 (s, 3H), 2.35 (s, 3H).

$^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz, 25°C): δ = 167.1, 147.3, 137.9, 136.6, 133.6, 129.6, 128.7, 128.2, 128.0, 127.7, 127.2, 125.9, 121.0, 119.3, 118.2, 109.6, 109.0, 51.9, 46.6, 30.5, 10.4.

IR (KBr): 3030 (w), 2919 (w), 1721 (s), 1608 (m), 1468 (m), 1430 (m), 1279 (vs), 1194 (m), 1172 (s), 1101 (s), 1020 (m), 923 (w), 8118 (w), 755 (m), 737 (vs), 715 (s), 696 (s).

MS (70 eV, EI, m/z (%): 369 (100, M^+), 354 (14), 338 (4), 278 (10), 234 (22), 218 (7), 91 (77), 65 (4).

HRMS m/z : calcd. for $\text{C}_{25}\text{H}_{23}\text{NO}_2$: 369.1729; found: 369.1737.

Indole derivative 2n

12 Apr 2006
1H

Acquisition Time (sec)	2.0486	Comment	Christiane Kofink, AK Knochel	Date	Feb 23 2006	Frequency (MHz)	300.10
Nucleus	1H	Number of Transients	8	Original Points Count	9849	Points Count	16384
Temperature (grad C)	27.000	Solvent	cdcl3	Sweep Width (Hz)			4807.69

Indole derivative 2n

12 Apr 2006
13C

Acquisition Time (sec)	1.3005	Comment	Christiane Kofink, AK Knochel	Date	Feb 23 2006
Frequency (MHz)	75.47	Nucleus	13C	Number of Transients	4096
Solvent	cdcl3	Sweep Width (Hz)	18115.94	Original Points Count	23560
		Temperature (grad C)	27.000	Points Count	32768

1-Benzyl-3-(2-bromobenzyl)-2-methyl-1H-indole (**2o**)

Prepared according to the TP 2. To a solution of 1-benzyl-3-iodo-2-methyl-1H-indole (260 mg, 0.75 mmol) in 0.5 mL DME, *i*PrMgCl (0.89 mL, 0.80 mmol, 0.9 M in THF) is added dropwise via syringe at -20°C . The solution is stirred for 3 h, then CuCl (5.0 mg, 10 mol%) and P(OEt)₃ (17 mg, 20 mol%) is added. This mixture is added over 30 min via canula to a prewarmed mixture of methyl 2-bromobenzyl diethyl phosphate (162 mg, 0.50 mmol) and TBAI (19 mg, 10 mol%). The reaction mixture is heated at 60°C for 1h. The usual workup and purification by flash chromatography (pentane/ether 19:1) yielded **2o** as colourless solid (163 mg, 85%).

Mp.: 122°C .

¹H-NMR (CDCl₃, 300 MHz, 25°C): δ = 7.68 (d, J = 9.3 Hz, 1H), 7.51 (d, J = 9.3 Hz, 1H), 7.39-7.05 (m, 11H), 5.43 (s, 2H), 4.31 (s, 2H), 2.37 (s, 3H).

¹³C-NMR (CDCl₃, 75 MHz, 25°C): δ = 140.4, 137.9, 136.6, 134.1, 132.4, 129.9, 128.7, 128.2, 127.4, 127.3, 127.2, 125.9, 124.5, 121.0, 119.2, 118.4, 109.0, 108.9, 46.6, 30.7, 10.4.

IR (KBr): 3028 (w), 1564 (w), 1494 (m), 1468 (m), 1452 (m), 1416 (m), 1368 (m), 1263 (w), 1178 (w), 1019 (m), 928 (w), 834 (w), 748 (s), 732 (vs), 722 (s), 691 (m).

MS (70 eV, EI), m/z (%): 389 (100, M^+), 376 (13), 298 (11), 234 (31), 218 (22), 178 (10), 91 (99), 65 (6).

HRMS m/z : calcd. for C₂₃H₂₀BrN: 389.0779; found: 389.0762.

Indole derivative 2o

21 Apr 2006
1H

Acquisition Time (sec)	4.0000	Comment	Christiane Kofink, AK Knochel	Date	Mar 4 2006	Frequency (MHz)	300.10
Nucleus	1H	Number of Transients	32	Original Points Count	15625	Points Count	16384
Temperature (grad C)	27.000			Solvent	cdcl3	Sweep Width (Hz)	3906.25

Indole derivative 2o

21 Apr 2006
13C

Acquisition Time (sec)	1.6010	Comment	Christiane Kofink, AK Knochel	Date	Mar 4 2006
Frequency (MHz)	75.47	Nucleus	13C	Number of Transients	2048
Solvent	cdcl3	Sweep Width (Hz)	18115.94	Original Points Count	29004
		Temperature (grad C)	27.000	Points Count	32768

2-Methyl-3-(thiophen-3-ylmethyl)-1-tosyl-1H-indole (**2p**)

Prepared according to the TP 2. To a solution of 3-iodo-2-methyl-1-tosyl-1H-indole (308 mg, 0.75 mmol) in 0.5 mL DME, *i*PrMgCl (0.89 mL, 0.80 mmol, 0.9 M in THF) is added dropwise via syringe at $-20\text{ }^{\circ}\text{C}$. The solution is stirred for 3 h, then CuCl (5.0 mg, 10 mol%) and $\text{P}(\text{OEt})_3$ (17 mg, 20 mol%) is added. This mixture is added over 30 min via canula to a prewarmed mixture of diethyl thiophen-3-ylmethyl phosphate (125 mg, 0.50 mmol) and TBAI (19 mg, 10 mol%). The reaction mixture is heated at $60\text{ }^{\circ}\text{C}$ for 1h. The usual workup and purification by flash chromatography (pentane/ether 19:1) yielded **2p** as colourless solid (156 mg, 82%).

Mp: $113\text{ }^{\circ}\text{C}$.

$^1\text{H-NMR}$ (CDCl_3 , 300 MHz, $25\text{ }^{\circ}\text{C}$): δ = 8.24 (d, J = 8.3 Hz, 1H), 7.65 (d, J = 8.3 Hz, 2H), 7.30-7.20 (m, 6H), 6.83 (d, J = 4.8 Hz, 1H), 6.67 (s br, 1H), 3.96 (s, 2H), 2.58 (s, 3H), 2.37 (s, 3H),

$^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz, $25\text{ }^{\circ}\text{C}$): δ = 144.6, 139.9, 136.6, 136.2, 133.4, 130.5, 129.8, 127.8, 126.2, 125.6, 124.0, 123.4, 120.6, 119.1, 118.6, 114.8, 24.9, 21.5, 12.9.

IR (KBr): 3093 (w), 2918 (w), 1594 (w), 1452 (m), 1353 (s), 1294 (w), 1221 (m), 1168 (vs), 1150 (s), 1086 (s), 1016 (m), 974 (s), 940 (m), 867 (w), 811 (m), 767 (s), 746 (vs), 659 (s).

MS (70 eV, EI), m/z (%): 381 (38, M^+), 226 (100), 184 (10), 91 (6), 65 (2).

HRMS m/z : calcd. for $\text{C}_{21}\text{H}_{19}\text{NO}_2\text{S}_2$: 381.0857; found: 381.0834.

Indole derivative 2p

12 Apr 2006
1H

Acquisition Time (sec)	4.1943	Comment	Christiane Kofink, AK Knochel	Date	Mar 17 2006	Frequency (MHz)	300.10
Nucleus	1H	Final Points Count	16384	Points Count	16384	Solvent	cdcl3
Temperature (grad C)	27.000					Sweep Width (Hz)	3906.25

Indole derivative 2p

12 Apr 2006
13C

Acquisition Time (sec)	1.8010	Comment	Christiane Kofink, AK Knochel	Date	Mar 17 2006
Frequency (MHz)	75.47	Nucleus	13C	Number of Transients	2048
Solvent	cdcl3	Sweep Width (Hz)	18115.94	Original Points Count	29004
		Temperature (grad C)	27.000	Points Count	32768

No.	Annotation	(ppm)
1	Chloroform-d	77.00

1-Benzyl-2-methyl-3-(thiophen-3-ylmethyl)-1H-indole (2q)

Prepared according to the TP 2. To a solution of 1-benzyl-3-iodo-2-methyl-1H-indole (260 mg, 0.75 mmol) in 0.5 mL DME, *i*PrMgCl (0.89 mL, 0.80 mmol, 0.9 M in THF) is added dropwise via syringe at -20°C . The solution is stirred for 3 h, then CuCl (5.0 mg, 10 mol%) and P(OEt)₃ (17 mg, 20 mol%) is added. This mixture is added over 30 min via canula to a prewarmed mixture of diethyl thiophen-3-ylmethyl phosphate (125 mg, 0.50 mmol) and TBAI (19 mg, 10 mol%). The reaction mixture is heated at 60°C for 1h. The usual workup and purification by flash chromatography (pentane) yielded **2q** as colourless solid (137 mg, 86%).

Mp.: 68°C .

¹H-NMR (CDCl₃, 600 MHz, 25°C): δ = 7.51-7.47 (m, 1H), 7.28-7.21 (m, 5H), 7.13-7.05 (m, 2H), 6.99-6.97 (m, 3H), 6.88 (s br, 1H), 5.33 (s, 2H), 4.11 (s, 2H), 2.31 (s, 3H).

¹³C-NMR (CDCl₃, 150 MHz, 25°C): δ = 142.4, 138.1, 136.6, 133.1, 128.8, 128.2, 128.0, 127.2, 126.0, 125.3, 120.9, 120.3, 119.2, 118.3, 110.4, 109.0, 104.8, 46.6, 25.3, 10.3.

IR (KBr): 3854 (w), 3745 (w), 3108 (m), 3026 (m), 2908 (m), 1653 (w), 1560 (w), 1494 (m), 1468 (vs), 1454 (s), 1418 (m), 1350 (m), 1336 (s), 1259 (w), 1178 (w), 1020 (w), 759 (m), 741 (s), 713 (m), 700 (m).

MS (70 eV, EI, m/z (%): 317 (100, M⁺), 302 (33), 234 (10), 226 (16), 184 (8), 91 (82), 65 (6).

HRMS m/z : calcd. for C₂₁H₁₉NS: 317.1238; found: 317.1214.

Indole derivative 2q

12 Apr 2006
1H

Acquisition Time (sec)	4.0000	Comment	Christiane Kofink, AK Knochel	Date	Mar 17 2006	Frequency (MHz)	599.71
Nucleus	1H	Number of Transients	8	Original Points Count	31250	Points Count	32768
Temperature (grad C)	27.000			Solvent	cdcl3	Sweep Width (Hz)	7812.50

Indole derivative 2q

12 Apr 2006
13C

Acquisition Time (sec)	1.6000	Comment	Christiane Kofink, AK Knochel	Date	Mar 17 2006
Frequency (MHz)	150.81	Nucleus	13C	Number of Transients	4096
Solvent	cdcl3	Sweep Width (Hz)	36764.71	Original Points Count	58824
		Temperature (grad C)	27.000	Points Count	65536

Ethyl 1-benzyl-3-(furan-3-ylmethyl)-1H-indole-2-carboxylate (2r)

Prepared according to the TP 2. To a solution of ethyl 1-benzyl-3-iodo-1H-indole-2-carboxylate (304 mg, 0.75 mmol) in 0.5 mL DME, *i*PrMgCl (0.89 mL, 0.80 mmol, 0.9 M in THF) is added dropwise via syringe at -20°C . The solution is stirred for 3 h, then CuCl (5.0 mg, 10 mol%) and P(OEt)₃ (17 mg, 20 mol%) is added. This mixture is added over 30 min via canula to a prewarmed mixture of diethyl furan-3-ylmethyl phosphate (117 mg, 0.50 mmol) and TBAI (19 mg, 10 mol%). The reaction mixture is heated at 60°C for 1h. The usual workup and purification by flash chromatography (pentane/ether 49:1) yielded **2r** as colourless solid (165 mg, 92%).

Mp.: 63°C .

¹H-NMR (CDCl₃, 600 MHz, 25°C): δ = 7.71 (d, J = 8.1 Hz, 1H), 7.33-7.13 (m, 8H), 7.01 (d, J = 7.4 Hz, 2H), 6.29 (s, 1H), 5.78 (s, 2H), 4.33-4.29 (m, 4H), 1.28 (t, J = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 150 MHz, 25°C): δ = 162.4, 142.6, 139.2, 138.8, 138.6, 128.5, 127.0, 126.7, 126.1, 125.6, 124.5, 123.3, 120.9, 120.4, 111.2, 110.7, 60.61, 48.3, 21.1, 14.2.

IR (KBr): 3063 (w), 2983 (w), 1685(vs), 1522 (m), 1498 (m), 1452 (m), 1372 (m), 1263 (s), 1248 (s), 1192 (m), 1137 (s), 1124 (s), 1025 (m), 1012 (m), 872 (m), 735 (s); 697 (m).

MS (70 eV, EI), m/z (%): 359 (77, M⁺), 330 (9), 286 (12), 268 (92), 222 (36), 194 (6), 166 (10), 91 (100), 65 (7).

HRMS m/z : calcd. for C₂₃H₂₁NO₃ : 359.1521; found: 359.1500.

Indole derivative 2r

12 Apr 2006
1H

Acquisition Time (sec)	4.0000	Comment	Christiane Kofink, AK Knochel	Date	Mar 6 2006	Frequency (MHz)	599.71
Nucleus	1H	Number of Transients	8	Original Points Count	31250	Points Count	32768
Temperature (grad C)	27.000					Solvent	cdcl3
						Sweep Width (Hz)	7812.50

Indole derivative 2r

12 Apr 2006
13C

Acquisition Time (sec)	1.6000	Comment	Christiane Kofink, AK Knochel	Date	Mar 6 2006
Frequency (MHz)	150.81	Nucleus	13C	Number of Transients	4096
Solvent	cdcl3	Sweep Width (Hz)	36764.71	Original Points Count	58624
		Temperature (grad C)	27.000	Points Count	65536

Typical Procedure for the Preparation of Functionalized Phosphates:

Typical Procedure 3 (TP 3).

In a round bottom flask with magnetic stirring and a septum, the corresponding benzylic alcohol (1.0 equiv.), DMAP (0.1 equiv.) and NEt_3 (1.1 equiv.) are dissolved in THF (10 mL/mmol). Then diethyl chlorophosphate (1.1 equiv.) is added slowly via syringe. During the addition a white precipitate forms. The reaction mixture is stirred at rt until the GC of an aliquot shows completion of the reaction, then quenched with sat. NH_4Cl solution, extracted with ether, and the product is purified by column chromatography.

Benzyl diethyl phosphate **4a**

Prepared according to TP 3. Phenylmethanol (15.0 mmol, 1.62 g), NEt₃ (22.5 mmol, 3.16 mL) and DMAP (1.50 mmol, 183 mg), are dissolved in THF. This mixture is treated with diethyl chlorophosphate (16.5 mmol, 2.85 g) and stirred at rt for 4h. Standard work up and purification yielded **4a** (3.20 g, 88%) as colourless liquid.

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 7.30-7.21 (m, 5H), 4.96 (d, J = 8.3 Hz, 2H), 4.02-3.92 (m, 4H), 1.19 (t, J = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 135.70 (d, J (C,P)= 6.8 Hz), 128.1, 128.0, 127.4, 68.59 (d, J (C,P)= 5.6 Hz), 63.36 (d, J (C,P)= 5.9 Hz), 15.65 (d, J (C,P)= 6.8 Hz).

³¹P-NMR (CDCl₃, 200 MHz, 25 °C): δ = 0.084.

IR (KBr): 2980 (w), 1518 (w), 1260 (s), 1025 (vs), 1009 (vs), 801 (m), 751 (w).

MS (70 eV, EI, m/z (%): 244 (51, M⁺), 215 (25), 187 (32), 138 (17), 107 (95), 91 (100), 65 (17).

HRMS m/z : calcd. for C₁₁H₁₇O₄P: 244.0864; found: 244.0879.

Benzyl diethyl phosphate 4a

21 Apr 2006
1H

Acquisition Time (sec)	Comment	Date	Frequency (MHz)
9.0440	Ak Knochel	14/11/2005 14:37:42	300.13
Nucleus	Original Points Count	Points Count	Sweep Width (Hz)
1H	32768	32768	3623.19
			Temperature (grad C)
			0.000

Benzyl diethyl phosphate 4a

21 Apr 2006
13C

Acquisition Time (sec)	Comment	Date	Frequency (MHz)
3.4079	Ak Knochel	14/11/2005 14:52:40	75.47
Nucleus	Original Points Count	Points Count	Sweep Width (Hz)
13C	65536	65536	19230.77
			Temperature (grad C)
			0.000

No.	Annotation	(ppm)
1	Chloroform-d	77.00

Diethyl 4-methylbenzyl phosphate **4b**

Prepared according to TP 3. *p*-Tolylmethanol (5.00 mmol, 611 mg), NEt₃ (5.5 mmol, 0.77 mL) and DMAP (0.10 mmol, 61 mg), are dissolved in THF. This mixture is treated with diethyl chlorophosphate (5.50 mmol, 949 mg) and stirred at rt for 4h. Standard work up and purification yielded **4b** (1.07 g, 83%) as colourless liquid.

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 7.20 (d, *J*= 8.1 Hz, 2H), 7.09 (d, *J*= 8.0 Hz, 2H), 4.94 (d, *J*= 8.1 Hz, 2H), 4.05-3.94 (m, 4H), 2.27 (s, 3H), 1.22 (t, *J*= 7.1 Hz, 6H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 138.2, 132.8 (d, *J*(C,P)= 6.8 Hz), 129.1, 127.9, 68.83 (d, *J*(C,P)= 5.6 Hz), 63.57 (d, *J*(C,P)= 5.9 Hz), 21.03, 15.92 (d, *J*(C,P)= 6.8 Hz).

³¹P-NMR (CDCl₃, 200 MHz, 25 °C): δ = 0.159.

IR (KBr): 2983 (w), 1518 (w), 1262 (s), 1025 (vs), 1009 (vs), 801 (m), 753 (w).

MS (70 eV, EI), *m/z* (%): 258 (45, M⁺), 229 (44), 132 (21), 121 (80), 105 (100), 77 (22).

HRMS *m/z*: calcd. for C₁₂H₁₉O₄P: 258.1021; found: 258.1001.

Diethyl 4-methylbenzyl phosphate 4b

21 Apr 2006
1H

Acquisition Time (sec)	9.0440	Comment	Ak Knochel	Date	13/12/2005 20:23:24	Frequency (MHz)	300.13
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3623.19
					Temperature (grad C)	0.000

Diethyl 4-methylbenzyl phosphate 4b

21 Apr 2006
13C

Acquisition Time (sec)	3.4079	Comment	Ak Knochel	Date	13/12/2005 22:23:40	Frequency (MHz)	75.47
Nucleus	13C	Original Points Count	65536	Points Count	65536	Sweep Width (Hz)	19230.77
					Temperature (grad C)	0.000

No.	Annotation	(ppm)
1	Chloroform-d	77.00

4-Bromobenzyl diethyl phosphate **4c**

Prepared according to TP 3. (4-Bromophenyl)methanol (5.00 mmol, 935 mg), NEt₃ (5.5 mmol, 0.77 mL) and DMAP (0.10 mmol, 61 mg), are dissolved in THF. This mixture is treated with diethyl chlorophosphate (5.50 mmol, 949 mg) and stirred at rt for 4h. Standard work up and purification yielded **4c** (1.27 g, 78%) as colourless liquid.

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 7.41 (d, J = 8.5 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 4.93 (d, J = 8.3 Hz, 2H), 4.06-3.96 (m, 4H), 1.23 (t, J = 7.1 Hz, 6H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 134.95 (d, J (C,P)= 6.8 Hz), 131.5, 129.3, 122.2, 67.91 (d, J (C,P)= 5.3 Hz), 63.68 (d, J (C,P)= 5.9 Hz), 15.83 (d, J (C,P)= 6.8 Hz).

³¹P-NMR (CDCl₃, 200 MHz, 25 °C): δ = 0.107.

IR (KBr): 2983 (w), 1595 (w), 1489 (m), 1262 (s), 1020 (vs), 1002 (vs), 973 (s), 852 (w), 798 (m).

MS (70 eV, EI), m/z (%): 321 (51, M⁺), 293 (40), 265 (46), 185 (100), 171 (96), 125 (45), 89 (70), 63 (16).

HRMS m/z : calcd. for C₁₁H₁₆BrO₄P: 321.9970; found: 321.9947.

4-Bromobenzyl diethyl phosphate 4c

21 Apr 2006
1H

Acquisition Time (sec)	Comment	Date	Frequency (MHz)
9.0440	Ak Knochel	16/12/2005 08:38:32	300.13
Nucleus	Original Points Count	Points Count	Sweep Width (Hz)
1H	32768	32768	3623.19
			Temperature (grad C)
			0.000

4-Bromobenzyl diethyl phosphate 4c

21 Apr 2006
13C

Acquisition Time (sec)	Comment	Date	Frequency (MHz)
3.4079	Ak Knochel	16/12/2005 09:38:48	75.47
Nucleus	Original Points Count	Points Count	Sweep Width (Hz)
13C	65536	65536	19230.77
			Temperature (grad C)
			0.000

No.	Annotation	(ppm)
1	Chloroform-d	77.00

Diethyl 2-methoxybenzyl phosphate **4d**

Prepared according to TP 3. (2-Methoxyphenyl)methanol (5.00 mmol, 691 mg), NEt_3 (5.5 mmol, 0.77 mL) and DMAP (0.10 mmol, 61 mg), are dissolved in THF. This mixture is treated with diethyl chlorophosphate (5.50 mmol, 949 mg) and stirred at rt for 4h. Standard work up and purification yielded **4d** (1.96 g, 80%) as colourless liquid.

$^1\text{H-NMR}$ (CDCl_3 , 300 MHz, 25 °C): δ = 7.33 (d, J = 7.5 Hz, 1H), 7.20-7.05 (m, 1H), 6.90-6.78 (m, 2H), 5.05 (d, J = 7.2 Hz, 2H), 4.07-3.98 (m, 4H), 3.75 (s, 3H), 1.23 (t, J = 7.1 Hz, 6H).

$^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz, 25 °C): δ = 156.9, 129.5, 129.0, 124.39 (d, $J(\text{C,P})$ = 7.6 Hz), 120.3, 110.1, 64.31 (d, $J(\text{C,P})$ = 5.0 Hz), 63.53 (d, $J(\text{C,P})$ = 5.9 Hz), 55. 2, 15.93 (d, $J(\text{C,P})$ = 6.8 Hz).

$^{31}\text{P-NMR}$ (CDCl_3 , 200 MHz, 25 °C): δ = 0.264.

IR (KBr): 2983 (w), 1595 (w), 1605 (w), 1495 (m), 1441 (w), 1246 (s), 1021 (vs), 1000 (vs), 964 (s), 880 (w), 752 (m).

MS (70 eV, EI), m/z (%): 274 (10, M^+), 245 (7), 185 (5), 137 (34), 120 (100), 91 (65), 65 (9).

HRMS m/z : calcd. for $\text{C}_{12}\text{H}_{19}\text{O}_5\text{P}$: 274.097; found: 274.0985.

Diethyl 2-methoxybenzyl phosphate 4d

21 Apr 2006
1H

Acquisition Time (sec)	Comment	Date	Frequency (MHz)
9.0440	Ak Knochel	16/12/2005 07:23:30	300.13
Nucleus	Original Points Count	Points Count	Sweep Width (Hz)
1H	32768	32768	3623.19
			Temperature (grad C)
			0.000

Diethyl 2-methoxybenzyl phosphate 4d

21 Apr 2006
13C

Acquisition Time (sec)	Comment	Date	Frequency (MHz)
3.4079	Ak Knochel	16/12/2005 08:23:40	75.47
Nucleus	Original Points Count	Points Count	Sweep Width (Hz)
13C	65536	65536	19230.77
			Temperature (grad C)
			0.000

No.	Annotation	(ppm)
1	Chloroform-d	77.00

Diethyl 4-methoxybenzyl phosphate **4e**

Prepared according to TP 3. (4-Methoxyphenyl)methanol (15.0 mmol, 2.07 g), NEt₃ (22.5 mmol, 3.16 mL) and DMAP (1.50 mmol, 183 mg), are dissolved in THF. This mixture is treated with diethyl chlorophosphate (16.5 mmol, 2.83 g) and stirred at rt for 4h. Standard work up and purification yielded **4e** (2.88 g, 70%) as colourless liquid.

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 7.22 (d, J = 8.7 Hz, 2H), 6.78 (d, J = 8.7 Hz, 2H), 4.88 (d, J = 8.4 Hz, 2H), 3.99-3.90 (m, 4H), 3.67 (s, 3H), 1.18 (t, J = 7.1 Hz, 6H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 159.5, 129.4, 127.76 (d, J (C,P)= 6.5 Hz), 113.5, 68.51 (d, J (C,P)= 5.9 Hz), 63.26 (d, J (C,P)= 5.9 Hz), 54.8, 15.61 (d, J (C,P)= 6.8 Hz).

³¹P-NMR (CDCl₃, 200 MHz, 25 °C): δ = 0.264.

IR (KBr): 2983 (w), 1595 (w), 1605 (w), 1495 (m), 1441 (w), 1246 (s), 1021 (vs), 1000 (vs), 964 (s), 880 (w), 752 (m).

MS (70 eV, EI), m/z (%): 274 (10, M⁺), 245 (7), 185 (5), 137 (34), 120 (100), 91 (65), 65 (9).

HRMS m/z : calcd. for C₁₂H₁₉O₅P: 274.097; found: 274.0985.

Diethyl 4-methoxybenzyl phosphate 4e

23 Apr 2006

Acquisition Time (sec)	9.0440	Comment	Ak Knochel	Date	14/11/2005 07:53:22	Frequency (MHz)	300.13
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3623.19
						Temperature (grad C)	0.000

Diethyl 4-methoxybenzyl phosphate 4e

23 Apr 2006

Acquisition Time (sec)	3.4079	Comment	Ak Knochel	Date	14/11/2005 08:23:20	Frequency (MHz)	75.47
Nucleus	13C	Original Points Count	65536	Points Count	65536	Sweep Width (Hz)	19230.77
						Temperature (grad C)	0.000

No.	Annotation	(ppm)
1	Chloroform-d	77.00

Diethyl furan-3-ylmethyl phosphate **4f**

Prepared according to TP 3. Furan-3-ylmethanol (20.0 mmol, 1.96 g), NEt₃ (21.0 mmol, 2.95 mL) and DMAP (2.00 mmol, 244 mg), are dissolved in THF. This mixture is treated with diethyl chlorophosphate (21.0 mmol, 3.62 g) and stirred at rt for 8h. Standard work up and purification yielded **4f** (3.69 g, 79%) as colourless liquid.

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 7.49 (s br, 1H), 7.40 (s br, 1H), 6.48 (s br, 1H), 4.96 (d, *J*= 8.8 Hz, 2H), 4.13-4.03 (m, 4H), 1.31 (t, *J*= 7.1 Hz, 6H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 143.5, 141.3, 120.89 (d, *J*(C,P)= 6.1 Hz), 110.2, 63.68 (d, *J*(C,P)= 5.5 Hz), 60.63 (d, *J*(C,P)= 5.5 Hz), 15.99 (d, *J*(C,P)= 6.6 Hz).

³¹P-NMR (CDCl₃, 200 MHz, 25 °C): δ = 0.253.

IR (KBr): 2984 (w), 1505 (w), 1444 (w), 1259 (s), 1160 (m), 1021 (vs), 972 (vs), 873 (s), 798 (s), 739 (m).

MS (70 eV, EI), *m/z* (%): 234 (36, M⁺), 206 (18), 109 (27), 97 (67), 81 (100), 53 (19).

HRMS *m/z*: calcd. for C₉H₁₅O₅P: 234.0657; found: 234.0661.

Diethyl furan-3-ylmethyl phosphate 4f

23 Apr 2006

Acquisition Time (sec)	4.0000	Comment	Christiane Kofink, AK Knochel	Date	Mar 3 2006	Frequency (MHz)	300.10
Nucleus	¹ H	Number of Transients	32	Original Points Count	15625	Points Count	16384
Temperature (grad C)	27.000	Solvent	cdcl3	Sweep Width (Hz)	3906.25

Diethyl furan-3-ylmethyl phosphate 4f

23 Apr 2006

Acquisition Time (sec)	1.6010	Comment	Christiane Kofink, AK Knochel	Date	Mar 3 2006
Frequency (MHz)	75.47	Nucleus	¹³ C	Number of Transients	2000
Solvent	cdcl3	Sweep Width (Hz)	18115.94	Original Points Count	29004
		Temperature (grad C)	27.000	Points Count	32768

No.	Annotation	(ppm)
1	Chloroform-d	77.00

Diethyl thiophen-2-ylmethyl phosphate **4g**

Prepared according to TP 3. Thiophen-2-ylmethanol (20.0 mmol, 2.88 g), NEt₃ (21.0 mmol, 2.95 mL) and DMAP (2.00 mmol, 244 mg), are dissolved in THF. This mixture is treated with diethyl chlorophosphate (21.0 mmol, 3.62 g) and stirred at rt for 8h. Standard work up and purification yielded **4g** (2.68 g, 54%) as colourless liquid.

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 7.29 (s br, 1H), 7.07 (s br, 1H), 6.95 (s br, 1H), 5.18 (d, *J*= 8.8 Hz, 2H), 4.09-4.00 (m, 4H), 1.26 (t, *J*= 7.1 Hz, 6H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 138.04 (d, *J*(C,P)= 6.6 Hz), 127.9, 126.9, 126.7, 63.64 (d, *J*(C,P)= 5.5 Hz), 63.19 (d, *J*(C,P)= 5.5 Hz), 15.85 (d, *J*(C,P)= 6.6 Hz).

³¹P-NMR (CDCl₃, 200 MHz, 25 °C): δ = -0.222.

IR (KBr): 2983 (w), 1505 (w), 1442 (w), 1259 (s), 1167 (m), 994 (vs), 851 (s), 828 (s), 704 (s).

MS (70 eV, EI, *m/z* (%): 250 (49, M⁺), 221 (35), 193 (32), 113 (53), 97 (100), 81 (9), 45 (11).

HRMS *m/z*: calcd. for C₉H₁₅O₄PS : 250.0429; found: 250.0424.

Diethyl thiophen-2-ylmethyl phosphate 4g

23 Apr 2006

Acquisition Time (sec)	4.1943	Comment	Christiane Kofink, AK Knochel	Date	Mar 14 2006	Frequency (MHz)	300.10
Nucleus	¹ H	Number of Transients	8	Original Points Count	16384	Points Count	16384
Temperature (grad C)	27.000	Solvent	cdcl3	Sweep Width (Hz)	3906.25

Diethyl thiophen-2-ylmethyl phosphate 4g

23 Apr 2006

Acquisition Time (sec)	1.6010	Comment	Christiane Kofink, AK Knochel	Date	Mar 14 2006	Frequency (MHz)	125.76
Nucleus	¹³ C	Number of Transients	1024	Original Points Count	29004	Points Count	32768
Solvent	cdcl3	Sweep Width (Hz)	18115.94	Temperature (grad C)	27.000

Diethyl thiophen-3-ylmethyl phosphate **4h**

Prepared according to TP 3. Thiophen-3-ylmethanol (20.0 mmol, 2.88 g), NEt₃ (21.0 mmol, 2.95 mL) and DMAP (2.00 mmol, 244 mg), are dissolved in THF. This mixture is treated with diethyl chlorophosphate (21.0 mmol, 3.62 g) and stirred at rt for 8h. Standard work up and purification yielded **4h** (2.29 g, 49%) as colourless liquid.

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 7.30-7.27 (m, 2H), 7.11 (s br, 1H), 5.05 (d, J = 8.6 Hz, 2H), 4.09-3.99 (m, 4H), 1.27 (t, J = 7.2 Hz, 6H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 136.98 (d, J (C,P)= 6.6 Hz), 127.1, 126.2, 124.1, 63.97 (d, J (C,P)= 5.5 Hz), 63.59 (d, J (C,P)= 5.5 Hz), 15.90 (d, J (C,P)= 7.2 Hz).

³¹P-NMR (CDCl₃, 200 MHz, 25 °C): δ = 0.160.

IR (KBr): 2983 (w), 1505 (w), 1442 (w), 1260 (s), 1162 (m), 1011 (vs), 967 (vs), 859 (m), 785 (s), 750 (m), 689 (m).

MS (70 eV, EI, m/z (%): 250 (66, M⁺), 221 (28), 193 (36), 113 (76), 97 (100), 81 (11), 45 (16).

HRMS m/z : calcd. for C₉H₁₅O₄PS : 250.0429; found: 250.0426.

Diethyl thiophen-3-ylmethyl phosphate 4h

23 Apr 2006

Acquisition Time (sec)	4.1943	Comment	Christiane Kofink, AK Knochel	Date	Mar 15 2006	Frequency (MHz)	300.10
Nucleus	¹ H	Number of Transients	8	Original Points Count	16384	Points Count	16384
Temperature (grad C)	27.000	Solvent	cdcl3	Sweep Width (Hz)	3906.25

Diethyl thiophen-3-ylmethyl phosphate 4h

23 Apr 2006

Acquisition Time (sec)	1.6010	Comment	Christiane Kofink, AK Knochel	Date	Mar 14 2006	Frequency (MHz)	75.47
Nucleus	¹³ C	Number of Transients	1024	Original Points Count	29004	Points Count	32768
Solvent	cdcl3	Sweep Width (Hz)	18115.94	Temperature (grad C)	27.000

No.	Annotation	(ppm)
1	Chloroform-d	77.00

2-Bromobenzyl diethyl phosphate **4i**

Prepared according to TP 3. (2-Bromophenyl)methanol (5.00 mmol, 935 mg), NEt₃ (5.5 mmol, 0.77 mL) and DMAP (0.10 mmol, 61 mg), are dissolved in THF. This mixture is treated with diethyl chlorophosphate (5.50 mmol, 949 mg) and stirred at rt for 4h. Standard work up and purification yielded **4i** (1.26 g, 75%) as colourless liquid.

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 7.49-7.43 (m, 2H), 7.29-7.24 (m, 1H), 7.14-7.09 (m, 1H), 5.07 (d, *J*= 7.2 Hz, 2H), 4.11-4.01 (m, 4H), 1.25 (t, *J*= 7.1 Hz, 6H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 135.38 (d, *J*(C,P)= 7.9 Hz), 132.5, 129.6, 129.1, 127.5, 122.3, 68.11 (d, *J*(C,P)= 5.0 Hz), 63.85 (d, *J*(C,P)= 5.9 Hz), 15.99 (d, *J*(C,P)= 6.5 Hz).

³¹P-NMR (CDCl₃, 200 MHz, 25 °C): δ = -0.043.

IR (KBr): 2983 (w), 1595 (w), 1442 (m), 1264 (s), 1164 (w), 1019 (vs), 976 (vs), 882 (m), 750 (m), 659 (m).

MS (70 eV, EI), *m/z* (%): 321 (51, M⁺), 293 (45), 265 (43), 185 (100), 171 (20), 125 (45), 89 (16), 63 (5).

HRMS *m/z*: calcd. for C₁₁H₁₆BrO₄P: 321.9970; found: 321.9940.

2-Bromobenzyl diethyl phosphate 4i

23 Apr 2006

Acquisition Time (sec)	9.0440	Comment	Ak Knochel	Date	14/12/2005 01:23:24	Frequency (MHz)	300.13
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3623.19
						Temperature (grad C)	0.000

2-Bromobenzyl diethyl phosphate 4i

23 Apr 2006

Acquisition Time (sec)	3.4079	Comment	Ak Knochel	Date	14/12/2005 03:23:34	Frequency (MHz)	75.47
Nucleus	13C	Original Points Count	65536	Points Count	65536	Sweep Width (Hz)	19230.77
						Temperature (grad C)	0.000

No.	Annotation	(ppm)
1	Chloroform-d	77.00

Methyl 4-((diethoxyphosphoryloxy)methyl)benzoate **4j**

Prepared according to TP 3. Methyl 4-(hydroxymethyl)benzoate (9.50 mmol, 1.58 g), NEt₃ (10.0 mmol, 1.50 mL) and DMAP (1.00 mmol, 122 mg), are dissolved in THF. This mixture is treated with diethyl chlorophosphate (10.0 mmol, 1.78 g) and stirred at rt for 8h. Standard work up and purification yielded **4j** (2.27 g, 79%) as colourless liquid.

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 7.89-7.87 (m, 2H), 7.32-7.30 (m, 2H), 4.97-4.95 (m, 2H), 3.96 (s br, 4H), 3.75 (s, 3H), 1.15 (s, 6H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 166.2, 140.77 (d, *J*(C,P)= 6.7 Hz), 129.7, 129.4, 126.9, 67.75 (d, *J*(C,P)= 5.1 Hz), 63.57 (d, *J*(C,P)= 5.6 Hz), 51.7, 15.71 (d, *J*(C,P)= 6.7 Hz).

³¹P-NMR (CDCl₃, 200 MHz, 25 °C): δ = 0.104.

IR (KBr): 2985 (w), 1720 (s), 1616 (w), 1436 (m), 1272 (vs), 1178 (m), 1107 (m), 1010 (vs), 964 (vs), 872 (m), 841 (m), 754 (s), 700 (m).

MS (70 eV, EI), *m/z* (%): 302 (59, M⁺), 273 (20), 245 (35), 231 (16), 165 (100), 149 (54), 125 (17), 89 (14).

HRMS *m/z*: calcd. for C₁₃H₁₉O₆P: 302.0919; found: 302.0934.

Phosphate 4j

23 Apr 2006

Acquisition Time (sec)	4.0000	Comment	Christiane Kofink, AK Knochel	Date	Feb 18 2006	Frequency (MHz)	599.71
Nucleus	¹ H	Number of Transients	8	Original Points Count	38462	Points Count	65536
Temperature (grad C)	27.000	Solvent	cdcl3	Sweep Width (Hz)			9615.38

Phosphate 4j

23 Apr 2006

Acquisition Time (sec)	1.6000	Comment	Christiane Kofink, AK Knochel	Date	Feb 18 2006
Frequency (MHz)	150.81	Nucleus	¹³ C	Number of Transients	2048
Solvent	cdcl3	Sweep Width (Hz)	36764.71	Original Points Count	58824
		Temperature (grad C)	27.000	Points Count	65536

Synthesis of Trimethoprim 1:

5-Bromo-2,4-di-*tert*-butoxypyrimidine 5

5-Bromo-2,4-dichloropyrimidine (10.0 mmol, 2.28 g) is dissolved in dry THF (50 mL). Then a solution of sodium *tert*-butoxide (25.0 mmol, 2.40 g) in THF (100 mL) is added dropwise at rt and the reaction mixture stirred for 5 h. The reaction is quenched with water (50 mL) and extracted with EtOAc (3 x 50 mL). Purification by flash chromatography yielded the desired product **5** as colorless solid (2.79 g, 92%).

Mp.: 61 °C.

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 8.25 (s, 1H), 1.65 (s, 9H), 1.60 (s, 9H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 165.6, 162.9, 158.9, 99.5, 83.2, 80.7, 28.3.

IR (KBr): 2974 (w), 2930 (w), 1567 (s), 1538 (s), 1438 (m), 1389 (vs), 1361 (vs), 1287 (m), 1228 (m), 1151 (vs), 1088 (vs), 1014 (s), 938 (m), 900 (s), 846 (s), 782 (s), 750 (m), 681 (m).

MS (70 eV, EI), *m/z* (%): 302 (2100, M⁺), 246 (8), 191 (100), 147 (16), 57 (54).

HRMS *m/z*: calcd. for C₁₂H₁₉BrN₂O₂: 302.0630; found: 302.0643.

5-Bromo-2,4-di-tert-butoxypyrimidine 5

24 Jul 2006

Acquisition Time (sec)	2.0486	Comment	Christiane Kofink, AK Knochel	Date	May 29 2006	Frequency (MHz)	300.10
Nucleus	¹ H	Number of Transients	8	Original Points Count	9278	Points Count	16384
Temperature (grad C)	27.000	Solvent	cdcl3	Sweep Width (Hz)	4528.99

5-Bromo-2,4-di-tert-butoxypyrimidine 5

24 Jul 2006

Acquisition Time (sec)	1.6010	Comment	Christiane Kofink, AK Knochel	Date	May 29 2006	Frequency (MHz)	75.47
Nucleus	¹³ C	Number of Transients	2048	Original Points Count	29004	Points Count	32768
Solvent	cdcl3	Sweep Width (Hz)	18115.94	Temperature (grad C)	27.000

No.	Annotation	(ppm)
1	Chloroform-d	77.00

Diethyl 3,4,5-trimethoxybenzyl phosphate **6**

Prepared according to TP 3. (3,4,5-Trimethoxyphenyl)methanol (15.0 mmol, 2.97 g), NEt₃ (16.0 mmol, 2.24 mL) and DMAP (1.50 mmol, 183 mg), are dissolved in THF. This mixture is treated with diethyl chlorophosphate (16.0 mmol, 2.76 g) and stirred at rt for 4 h. Standard work up and purification yielded **6** (4.17 g, 83%) as colourless liquid.

¹H-NMR (CDCl₃, 300 MHz, 25 °C): δ = 6.58-6.55 (m, 2H), 4.96-4.91 (m, 2H), 4.07-4.01 (m, 4H), 3.82-3.76 (m, 9H), 1.27-1.24 (m, 6H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 153.1, 137.8, 131.45 (d, *J*(C,P)= 6.6 Hz), 104.8, 69.05 (d, *J*(C,P)= 5.5 Hz), 63.63 (d, *J*(C,P)= 5.9 Hz), 60.6, 55.9, 15.92 (d, *J*(C,P)= 6.6 Hz).

³¹P-NMR (CDCl₃, 200 MHz, 25 °C): δ = 0.230.

IR (KBr): 2983 (w), 1593 (m), 1508 (m), 1462 (m), 1334 (m), 1261 (s), 1249 (s), 1227 (vs), 1022 (vs), 969 (vs), 822 (w).

MS (70 eV, EI), *m/z* (%): 334 (100, M⁺), 305 (17), 277 (8), 181 (69), 165 (40), 137 (5).

HRMS *m/z*: calcd. for C₁₄H₂₃O₇P: 334.1181; found: 334.1164.

Diethyl 3,4,5-trimethoxybenzyl phosphate 6

6 Jun 2006

Acquisition Time (sec)	4.0000	Comment	Christiane Kofink, AK Knochel	Date	Apr 26 2006	Frequency (MHz)	399.94
Nucleus	¹ H	Number of Transients	16	Original Points Count	32768	Solvent	cdcl3
Temperature (grad C)	30.000

Diethyl 3,4,5-trimethoxybenzyl phosphate 6

7 Jun 2006

Acquisition Time (sec)	1.6000	Comment	Christiane Kofink, AK Knochel	Date	Apr 26 2006	Frequency (MHz)	100.58
Nucleus	¹³ C	Number of Transients	2048	Original Points Count	38612	Points Count	65536
Solvent	cdcl3	Sweep Width (Hz)	24132.73	Temperature (grad C)	30.000

No.	Annotation	(ppm)
1	Chloroform-d	77.00

2,4-Di-*tert*-butoxy-5-(3,4,5-trimethoxybenzyl)pyrimidine **7**

Prepared according to the TP 2. To a solution of 5-bromo-2,4-di-*tert*-butoxypyrimidine (2.20 g, 7.25 mmol) in 5.0 mL DME, *i*PrMgCl · LiCl (5.95 mL, 7.73 mmol, 1.3 M in THF) is added dropwise via syringe at 0 °C. The solution is stirred for 4 h, then CuBr (69 mg, 10 mol%) and P(OEt)₃ (160 mg, 20 mol%) is added. This mixture is added over 30 min via canula to a prewarmed mixture of diethyl 3,4,5-trimethoxybenzyl phosphate (1.62 g, 4.83 mmol) and TBAI (177 mg, 10 mol%). The reaction mixture is heated at 60 °C for 1h. The usual workup and purification by flash chromatography (pentane/ether 1:1) yielded **7** as colourless solid (1.56 g, 81%).

Mp.: 78 °C.

¹H-NMR (CDCl₃, 600 MHz, 25 °C): δ = 7.97 (s, 1H), 6.40 (s, 2H), 3.81 (s, 9H), 3.64 (s, 2H), 1.60 (s, 9H), 1.56 (s, 9H).

¹³C-NMR (CDCl₃, 75 MHz, 25 °C): δ = 168.1, 163.0, 157.4, 153.1, 135.7, 115.2, 105.7, 81.3, 80.0, 60.9, 56.1, 33.7, 28.4.

IR (KBr): 2975 (w), 2932 (w), 1591 (s), 1554 (s), 1506 (m), 1456 (m), 1405 (vs), 1363 (s), 1332 (m), 1236 (m), 1150 (s), 1123 (vs), 1053 (s), 1011 (s), 936 (m), 805 (m).

MS (70 eV, EI), *m/z* (%): 404 (36, M⁺), 348 (26), 292 (100), 261 (46), 41 (14).

HRMS *m/z*: calcd. for C₂₂H₃₂N₂O₅: 404.2311; found: 404.2321.

Diarylmethane 7

6 Jun 2006

Acquisition Time (sec)	4.0000	Comment	Christiane Kofink, AK Knochel	Date	May 29 2006	Frequency (MHz)	599.70
Nucleus	¹ H	Number of Transients	8	Original Points Count	36232	Points Count	65536
Temperature (grad C)	27.000	Solvent	cdcl3	Sweep Width (Hz)	9057.97

Diarylmethane 7

6 Jun 2006

Acquisition Time (sec)	1.6000	Comment	Christiane Kofink, AK Knochel	Date	May 29 2006
Frequency (MHz)	150.81	Nucleus	¹³ C	Number of Transients	2048
Solvent	cdcl3	Sweep Width (Hz)	36764.71	Original Points Count	58824
		Temperature (grad C)	27.000	Points Count	65536

5-(3,4,5-Trimethoxybenzyl)pyrimidine-2,4(1H,3H)-dione

2,4-Di-tert-butoxy-5-(3,4,5-trimethoxybenzyl)pyrimidine **6** was dissolved in MeOH (5.0 mL). Then conc. HCl (2.0 mL) was added dropwise and immediately a precipitate was formed. The reaction mixture was stirred 15 min at rt, then the precipitate was filtered off and washed with cold MeOH and dried *in vacuo* to yield the desired product as colourless solid (87%, 1.04 g). The compound was used for the next step to prepare 2,4-Dichloro-5-(3,4,5-trimethoxybenzyl)pyrimidine **7** without further purification.

Mp.: 216 °C.

¹H-NMR (DMSO-*d*⁶, 400 MHz, 25 °C): δ = 11.01 (s br, 1H), 11.63 (s br, 1H), 7.17 (d, *J* = 5.9 Hz, 1H), 6.51 (s, 2H), 3.69 (s, 6H), 3.58 (s, 3H), 3.39 (s, 2H).

¹³C-NMR (DMSO-*d*⁶, 100 MHz, 25 °C): δ = 164.3, 152.7, 151.3, 138.7, 135.8, 135.6, 111.8, 105.9, 59.9, 55.8, 31.9.

IR (KBr): 3130 (w), 1712 (m), 1667 (vs), 1585 (s), 1508 (m), 1422 (vs), 1241 (s), 1224 (s); 1129 (vs), 993 (m), 844 (m), 761 (m), 686 (m).

MS (70 eV, EI), *m/z* (%): 292 (100, M⁺), 261 (32), 234 (8), 191 (6), 146 (4), 77 (3).

HRMS *m/z*: calcd. for C₁₄H₁₆N₂O₅: : 292.1059; found: 292.1048.

Uracilderivative to compound 8

6 Jun 2006

Acquisition Time (sec)	4.0000	Comment	Christiane Kofink, AK Knochel	Date	May 29 2006	Frequency (MHz)	399.92
Nucleus	¹ H	Number of Transients	64	Original Points Count	25641	Points Count	32768
Temperature (grad C)	27.000	Solvent	dmsO	Sweep Width (Hz)	6410.26

Uracil derivative to compound 8

7 Jun 2006

Acquisition Time (sec)	1.6000	Comment	Christiane Kofink, AK Knochel	Date	May 29 2006	Frequency (MHz)	100.57
Nucleus	¹³ C	Number of Transients	2048	Original Points Count	39216	Points Count	65536
Solvent	dmsO	Sweep Width (Hz)	24509.80	Temperature (grad C)	27.000

2,4-Dichloro-5-(3,4,5-trimethoxybenzyl)pyrimidine **8**

To a stirred mixture of POCl₃ (1.02 g, 8.75 mmol) and *N,N*-dimethylbenzenamine (640 mg, 5.25 mmol) in a 25 mL schlenk flask with reflux condenser the 5-(3,4,5-trimethoxybenzyl)pyrimidine-2,4(1H,3H)-dione was added portion wise over 30 min. Then the reaction mixture was refluxed for 1 h at 110 °C. Afterwards the reaction mixture was pured on ice, extracted with diethyl ether, and the organic layer dried over Na₂SO₄. Purification by flash chromatography (ether) yielded **8** as colourless solid (990 mg, 86%).

Mp: 131 °C.

¹H-NMR (CDCl₃, 600 MHz, 25 °C): δ = 8.27 (s, 1H), 6.37 (s, 2H), 3.96 (s, 2H), 3.82 (s, 3H), 3.81 (s, 6H).

¹³C-NMR (CDCl₃, 150 MHz, 25 °C): δ = 162.0, 160.2, 158.4, 153.6, 137.3, 131.8, 131.5, 105.9, 60.8, 56.1, 35.8.

IR (KBr): 2961 (w), 2940 (w), 2840 (w), 1593 (w), 15008 (m), 1456 (m), 1421 (m), 1388 (m), 1338 (m), 1293 (w), 1251 (m), 1175 (m), 1125 (vs), 1080 (m), 1005 (s), 855 (s), 836 (s), 737 (m), 686 (m).

MS (70 eV, EI), *m/z* (%): 328 (100, M⁺), 313 (66), 249 (6), 234 (15), 161 (9), 124 (6).

HRMS *m/z*: calcd. for C₁₄H₁₄Cl₂N₂O₃ : 328.0381; found: 328.0383.

Compound 8

6 Jun 2006

Acquisition Time (sec)	4.0000	Comment	Christiane Kofink, AK Knochel	Date	May 29 2006	Frequency (MHz)	599.70
Nucleus	¹ H	Number of Transients	8	Original Points Count	36232	Points Count	65536
Temperature (grad C)	27.000	Solvent	cdcl3	Sweep Width (Hz)	9057.97

Compound 8

6 Jun 2006

Acquisition Time (sec)	1.6000	Comment	Christiane Kofink, AK Knochel	Date	May 29 2006
Frequency (MHz)	150.81	Nucleus	¹³ C	Number of Transients	2048
Solvent	cdcl3	Sweep Width (Hz)	36764.71	Original Points Count	58824
		Temperature (grad C)	27.000	Points Count	65536

5-(3,4,5-Trimethoxybenzyl)pyrimidine-2,4-diamine 1 (Trimethoprim)

2,4-Dichloro-5-(3,4,5-trimethoxybenzyl)pyrimidine **7** was suspended in a solution of NH_3 in MeOH (10 mL, 7 N) in an autoclave and heated in the oven at 175 °C for 6h. Then the solvent is removed *in vacuo*. Recrystallization in MeOH, yielded the desired product **1** as a colourless solid (85%, 369 mg).

Mp: 285 °C (decomp.).

$^1\text{H-NMR}$ (DMSO-*d*₆, 400 MHz, 25 °C): δ = 7.96 (s br, 2H), 7.59 (s br, 2H), 7.49 (s, 1H), 6.62 (s, 2H), 3.73 (s, 6H), 3.62 (s, 3H), 3.59 (s, 2H).

$^{13}\text{C-NMR}$ (DMSO-*d*₆, 100 MHz, 25 °C): δ = 163.9, 154.5, 152.8, 139.8, 136.1, 133.1, 108.8, 106.3, 59.9, 55.9, 32.1.

IR (KBr): 3162 (w), 2724 (w), 1670 (m), 1640 (s), 1590 (m), 1499 (m), 1418 (m), 1341 (m), 1321 (m), 1238 (vs), 1129 (vs), 993 (m), 884 (m), 765 (m), 630 (m).

MS (70 eV, EI), *m/z* (%): 290 (100, M^+), 259 (21), 243 (10), 200 (4), 123 (5), 81 (2).

HRMS *m/z*: calcd. for $\text{C}_{14}\text{H}_{18}\text{N}_4\text{O}_3$: 290.1379; found: 290.1359.

Trimethoprim 1

6 Jun 2006

Acquisition Time (sec)	4.0000	Comment	Christiane Kofink, AK Knochel	Date	May 29 2006	Frequency (MHz)	399.92
Nucleus	¹ H	Number of Transients	64	Original Points Count	25641	Points Count	32768
Temperature (grad C)	27.000	Solvent	cdcl3	Sweep Width (Hz)	6410.26

Trimethoprim 1

6 Jun 2006

Acquisition Time (sec)	1.6000	Comment	Christiane Kofink, AK Knochel	Date	May 29 2006
Frequency (MHz)	100.57	Nucleus	¹³ C	Number of Transients	2048
Solvent	cdcl3	Sweep Width (Hz)	24509.80	Original Points Count	39216
		Temperature (grad C)	27.000	Points Count	65536