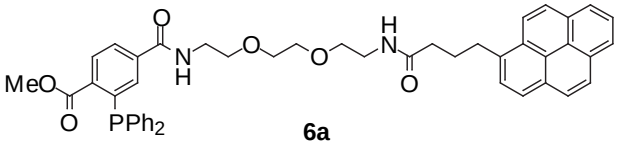
Conversion of Aryl Azides to O-Alkyl Imidates Via Modified Staudinger Ligation

José A. Restituyo, Lindsay R. Comstock, Scott G. Petersen, Thomas Stringfellow and Scott R. Rajski

General: All reactions were carried out under an inert atmosphere of argon unless indicated otherwise. All reagents were obtained from available commercial sources and used without additional purification unless otherwise noted. Anhydrous THF was from a J.T. Baker Cycle-Tainer product number 9446-Q1. NMR spectra were recorded on Varian Unity Inova 400 MHz and 500 MHz spectrometers using either TMS or solvent as the internal reference; the chemical shifts are reported in ppm, in δ units. High resolution mass spectral data were obtained using an IonSpec HiResMALDI FT-Mass Spectrometer with a 7 tesla superconducting magnet. HPLC mass spectral data were obtained using an Agilent 1100 HPLC-MSD SL quadrupole mass spectrometer. HPLC chromatograms disclosed were obtained using a Waters 600E 4-Solvent delivery system with 717 Plus autosampler with heater/cooler, 4 channel in-line degasser, and Millenium 3.2 (M32) software package. All solvents were 0.1% in TFA and HPLC grade quality. All reactions analyzed by HPLC were run in a 1:1 mixture of THF:H_2O at 30°C for the noted period of time and were ~1mM in both coupling components.

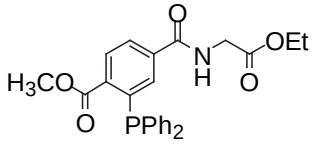


6a

2-Diphenylphosphanyl-N-(2-{2-[2-(4-pyren-1-yl-butyrylamino)-ethoxy]-ethoxy}-ethyl)-terephthalamic acid methyl ester (6a).

To 250mg of methyl 2-(diphenylphosphanyl) benzoic acid (0.687mmol) was added 3.4 mL of a 2:1:1 mixture of THF:DMF:H_2O along with 343μL distilled diisopropylethylamine (DIEA)(2 mmol). The solution was stirred at ambient temperature for 5 min followed by addition of 260mg (0.860mmol) O-(N-Succinimidyl)-N,N,N',N'-tetramethyluronium tetrafluoroborate (TSTU). The reaction was stirred 1 h at ambient temperature followed by dilution with 2.5mL anhydrous THF and transferred to a stirring solution of 1mL 2,2'-(Ethylenedioxy) diethylamine (6.8mmol) diluted in 3mL anhydrous THF. The reaction was stirred 2h at room temperature and then partitioned between saturated $NaHCO_3$ (pH = 9.5) and $CHCl_3$. The layers were separated and the aqueous fraction extracted twice with 20 mL $CHCl_3$. The organic layers were then combined and washed with saturated $NaHCO_3$ (3 x 30mL) which was sufficient for removal of excess diamine. 0.3mmol of this crude material was then coupled to the activated NHS ester of pyrenebutyric acid in the following manner. To 86.5mg (0.3mmol) pyrenebutyric acid was added 1.5mL of the THF:DMF:H_2O mixture noted above along with 150mL (.87mmol) DIEA. The solution of acid was stirred 5min at ambient temperature followed by addition of 113mg TSTU (0.37mmol). The NHS ester was formed over the course of 1h at room temperature and the activated ester diluted with 1mL THF. To the NHS ester was then added 0.3mmol of the phosphanyl amine diluted into 1.2mL anhydrous THF. The coupling was performed for 2h at room temperature, the reaction then partitioned between $CHCl_3$ and cold, saturated $NaHCO_3$. Layers were separated and then the $CHCl_3$ layer washed with saturated $NaHCO_3$ (2 x 30mL), 0.5N HCl (3 x 50mL), H_2O (2 x

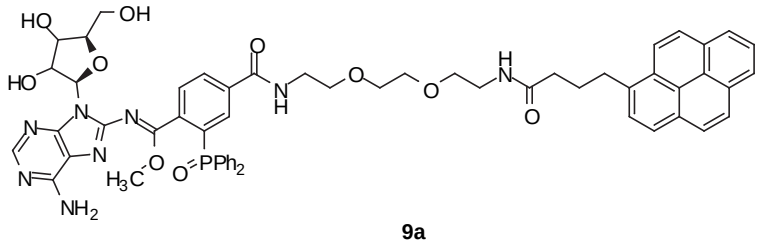
50mL), and brine (2 x 20mL). Finally the solution was dried over Na_2SO_4, solvents removed *in vacuo* and the coupled material subjected to 2 rounds of PTLC purification (5:5:3:1 Hex:CH_2Cl_2:EtOAc:MeOH) to afford 97.5mg **6a** (42.5% overall yield). ^{1}H NMR ($CDCl_3$) δ 8.30 (d, J= 9.2 Hz, 1H), 8.16 (d, J= 7.6 Hz, 2H), 8.10 (d, J= 9.2Hz, 2H), 8.05-7.96 (m, 4H), 7.85 (d, J= 7.6 Hz, 1H), 7.71 (dd, J= 8.0, 1.6 Hz, 1H), 7.39-7.25 (m, 10H), 6.34-6.26 (m, 1H), 5.96-5.88 (m, 1H), 3.77 (s,3H), 3.60-3.32 (m, 14H), 2.32-2.12 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 173.0, 166.9, 166.7, 141.9,141.6, 137.5, 137.4, 136.8, 136.1, 134.2, 134.0, 133.0, 131.6, 131.1, 131.0, 130.1, 129.2, 129.0, 128.8, 127.7, 127.6, 127.0, 126.8, 126.1, 125.2, 125.1, 125.0, 123.6, 70.4,70.3, 70.1, 69.7, 68.2, 52.4, 50.9, 40.0, 39.4,36.2, 33.0, 27.6, 25.8. HRMS (MALDI): calcd for $C_{47}H_{45}N_2O_6P$ [M+Na] = 787.2913, measured 787.2887.



6b

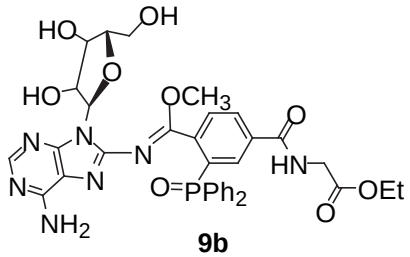
2-Diphenylphosphanyl-N-ethoxycarbonylmethyl-terephthalamic acid methyl ester (6b).

To 150mg. of methyl 2-(diphenylphosphanyl) benzoic acid (0.42mmol) was added 2 mL of a 2:1:1 mixture of THF:DMF:H_2O along with 206μL diisopropylethylamine (DIEA)(1.2 mmol). The solution was stirred at ambient temperature for 5 min followed by addition of 260mg (0.516mmol) O-(N-Succinimidyl)-N,N,N',N'-tetramethyluronium tetrafluoroborate (TSTU). The reaction was stirred 30min at ambient temperature followed addition of 430μL DIEA (2.52mmol) and 172.5mg (1.26mmol) glycine ethyl ester hydrochloride. The reaction was stirred 4h at room temperature and then partitioned between 20mL cold 1N HCl and $CHCl_3$ (30mL). Layers were separated and the organic fraction washed 3 more times with 20mL cold 1N HCl then 2 times with saturated $NaHCO_3$ (2 x 20mL) and brine. Solvent was dried over Na_2SO_4 followed by filtration of solids and removal of solvent *in vacuo*. Column chromatography (10:10:6:2:1, Hex:CH_2Cl_2:EtOAc:MeOH:Pet Et) afforded 79.4mg **6b** (43% yield) ^{1}H NMR ($CDCl_3$) δ 8.09 (dd, J= 8.1, 3.5 Hz, 1H), 7.81 (dd, J= 8.1, 1.5 Hz, 1H), 7.38-7.22 (m, 11H), 6.45-6.38 (m, 1H), 4.2 (q, J= 7.2 Hz, 2H), 4.08 (d, J= 5.2 Hz, 2H), 3.74 (s, 3H), 1.27 (t, J= 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 169.8, 166.8, 166.4, 142.1, 141.8, 137.2, 136.6, 134.2, 133.9, 132.7, 131.2, 129.3, 129.0, 128.9, 127.1, 61.9, 52.5, 42.1, 14.4. HRMS (MALDI): calcd for $C_{25}H_{24}NO_6P$ [M+Na] = 472.1290, measured 472.1296.



9a

(Z)-methyl N-6-amino-9-((2R,5S)-3,4-dihydroxy-5-(hydroxymethyl)-tetrahydro-furan-2-yl)-9H-purin-8-yl-2-(diphenylphosphoryl)-4-((2-(2-(2-(4-pyren-1-yl)butanamido)ethoxy)ethoxy)ethyl)carbamoyl)benzimidate (9a). To 8-azidoadenosine **7** (0.0123 g, 0.0400 mmol) in 1.0 mL 1:1 THF/H_2O was added pyrene phosphine **6a** (0.0306 g, 0.0400 mmol) in 1.0 mL 1:1 THF/H_2O. The reaction was incubated at 30 ˚C for 2h. The reaction mixture was extracted with ethyl acetate, washed with brine, and dried over Na_2SO_4. The solvent was removed and the resulting material purified by flash chromatography [3:2 EtOAc:Hex.] to yield **9a** as a light yellowish oil (34 mg, 82% yield). TLC and HPLC-MS revealed this material to be identical to that identified during the course of HPLC timetrial analyses. ^{1}H NMR ($CDCl_3$) δ 8.37 (d, J= 14.4 Hz, 1H), 8.24 (d, J= 9.6 Hz, 1H), 8.14-7.94 (m, 9H), 7.87-7.80 (m, 5H), 7.53-7.42 (m, 5H), 6.56 (d, J= 7.2 Hz, 1H), 5.01 (dd, J= 6.8, 5.2 Hz, 1H), 4.48 (d, J= 5.2 Hz, 1H), 4.30 (s, 1H), 3.96 (d, J= 12.8 Hz, 1H), 3.73-3.25 (m, 27H), 2.27-2.01 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 173.01, 167.75, 166.38, 154.75, 151.58, 148.67, 147.89, 135.70, 135.61, 132.72, 130.75, 130.66, 131.81, 128.95, 128.55, 126.68, 126.30, 125.68, 125.05, 124.63, 124.15, 120.62, 70.42, 70.36, 70.15, 69.79, 68.20, 52.44, 50.97, 40.01, 39.42, 36.22, 33.05, 27.66, 25.87. ^{31}P NMR ($CDCl_3$) δ 22.6. HRMS (MALDI): calcd for $C_{357}H_{57}N_8O_{10}P$ [M+Na] = 1067.3833, measured 1067.3420.

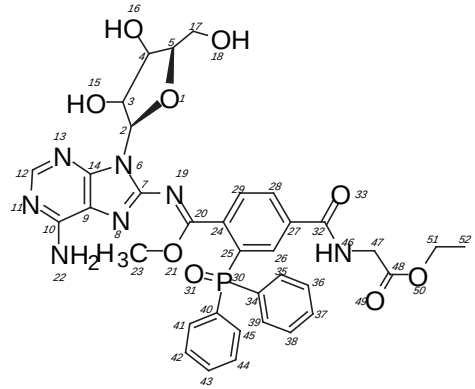


9b

[4-[6-Amino-9-(3,4-dihydroxy-5-hydroxymethyl-tetrahydro-furan-2-yl)-9H-purin-8-ylcarbamoyl]-3-(diphenyl-phosphinoyl)-benzoylamino]-acetic acid ethyl ester (9b). To 8-azidoadenosine **7** (0.0123 g, 0.0400 mmol) in 1.0 mL 1:1 THF/H_2O was added the glycine phosphine **6b** (0.0174 g, 0.0400 mmol) in 1.0 mL 1:1 THF/H_2O and reaction stirred at 30 ˚C for 2h. The reaction mixture was extracted with ethyl acetate, washed with brine, and dried over Na_2SO_4. The solvent was removed and the resulting material was purified by flash chromatography [3:2 EtOAc:Hex.] to yield **9b** as a yellowish oil (24 mg, 84% yield). As with **9a**, this material was identical in HPLC retention time and mass spectroscopic analysis to that material identified during HPLC timetrial analyses. The independently purified substances were also identical in R_f.

^{1}H NMR ($CDCl_3$) δ 8.28 (d, J= 14.4Hz, 1H), 8.04 (d, J= 8Hz, 1H), 7.87-7.77 (m, 5H), 7.73 (s, 1H), 7.52-7.39 (m, 7H), 6.43 (d, J= 7.6 Hz, 1H), 5.36 (s, 2H), 4.99-4.90 (m, 1H), 4.33 (d, J= 4.8 Hz, 1H), 4.21(s, 1H), 4.14 (q, J= 7.2 Hz, 2H), 4.06 (d, J= 5.6 Hz, 1H), 3.86 (d, J= 11.6 Hz, 1H), 3.65 (d, J= 11.6 Hz, 1H), 3.32 (s, 3H), 1.22 (t, J= 7.2 Hz, 3H).
^{13}C NMR ($CDCl_3$) δ 171.38, 170.15, 167.75, 166.33, 154.75, 151.45, 148.67, 147.89, 139.15, 136.37, 134.73, 132.74, 131.47, 130.78, 129.37, 128.90, 128.42, 128.34, 118.55, 88.29, 88.68, 73.18, 72.85, 68.16, 63.63, 61.73, 60.60, 52.75, 42.01, 25.80, 21.24, 14.39.
^{31}P NMR ($CDCl_3$) δ 19.8. HRMS (MALDI): calcd for $C_{35}H_{36}N_7O_9P$ [M+H] = 730.2390, measured 730.1780. [High resolution NMR experimental data follows]

Cumulative High Resolution NMR data for 9b.



9b

^{1}H NMR ($CDCl_3$, TMS Ref., 500 MHz):
δ 8.30 (d, $^{3}J(^{1}H,^{31}P)$ = 14.2 Hz, 1H, 26)
δ 8.07 (d, ^{3}J(28,29) = 8.0 Hz, 1H, 28)
δ 7.89 (d, ^{3}J(28,29) = 8.0 Hz, 1H, 29)
δ 7.78–7.88 (mm, 4H, 35,39,41,45)
δ 7.82 (s, 1H, 12)
δ 7.73 (t, ^{3}J(46,47) = 5.0 Hz, 1H, 46)
δ 7.54 (m, 2H, 37,43)
δ 7.45 (m, 4H, 36,38,42,44)
δ 7.30 (very broad)
δ 6.44 (d, ^{3}J(2,3) = 7.4 Hz, 1H, 2)
δ 5.17 (s, 2H, 22)
δ 4.98 (dd, ^{3}J(2,3) = 7.4 Hz, ^{3}J(3,4) = 5.0 Hz, 1H, 3)
δ 4.37 (d, ^{3}J(4,3) = 4.9 Hz, 1H, 4)
δ 4.24 (s (broad), 1H, 5)
δ 4.18 (q, ^{3}J(51,52) = 7.1 Hz, 2H, 51)
δ 4.10 (d, ^{3}J(46,47) = 5.4 Hz, 2H, 47)
δ 3.90 (d, ^{2}J(17,17') = 12.5 Hz, 1H, 17')
δ 3.69 (d, ^{2}J(17,17') = 12.5 Hz, 1H, 17)
δ 3.63 (m (broad, distorted), 1H, unassigned)
δ 3.33 (s, 3H, 23)
δ 1.25 (t, ^{3}J(51,52) = 7.2 Hz, 3H, 52)

Notes: The last number(s) within the parentheses gives the assignment according to the numbering scheme used in the molecular drawing. Assignments were made from ^{1}H 1D, gDQF-COSY and ROESY data.

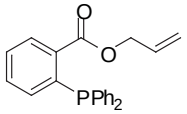
^{13}C NMR ($CDCl_3$, TMS Ref., 125 MHz):
δ 169.94 (48, gHMBC)
δ 167.53 (20, gHMBC)
δ 166.04 (32, gHMBC)
δ 154.52 and 154.48 (7, gHMBC)
δ 151.21 (unassigned)
δ 148.53 (14, gHMBC)
δ 147.86 (12, gHMBC)
δ 138.87 and 138.92 (d, $^2J(^{13}C,^{31}P)$ = 6.2 Hz, 24, gHMBC)
δ 136.15 and 136.25 (d, $^3J(^{13}C,^{31}P)$ = 11.6 Hz, 27, gHMBC)
δ 134.48 and 134.56 (d, $^2J(^{13}C,^{31}P)$ = 11.4 Hz, 26, gHMBC)
δ 132.72, 132.64, 132.59, 132.56, 132.50, 132.47 (35, 37, 39, 41, 43, 45, gHSQC)
δ 131.36 (28, gHSQC)
δ 130.65 and 130.57 (d, $^3J(^{13}C,^{31}P)$ = 8.4 Hz, 29, gHSQC)
δ 129.08 (unassigned)
δ 128.81, 128.71, 128.63 (36, 38, 42, 44, gHSQC)
δ 128.26 (unassigned)
δ 127.79 (unassigned)
δ 118.34 (10, gHMBC)
δ 88.25 (2, gHSQC)
δ 86.56 (5, gHSQC)
δ 73.21 (3, gHSQC)
δ 72.83 (4, gHSQC)
δ 63.46 (17, gHSQC)
δ 61.67 (51, gHSQC)
δ 52.60 (23, gHSQC)
δ 41.86 (47, gHSQC)
δ 14.12 (52, gHSQC)
δ 70 (impurity)
δ 29.70 (impurity)

Notes: The last number within the parentheses gives the assignment according to the numbering scheme used in the molecular drawing. A subsequent experiment code indicates the experiment that was used to make the assignment; gHSQC: gradient-selected hetero-nuclear single-quantum correlation, gHMBC: gradient-selected hetero-nuclear multiple-bond correlation.

General procedure for preparation of esters:

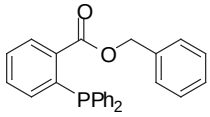
***Note**: 2-(diphenylphosphino) benzoic acid is available from Aldrich Chemical Corp. (cat. No. 45,488-5) and 2-diphenylphosphino-1-naphthoic acid was obtained from Alfa Aesar (cat. No. B22361).*

To PPh_3 (0.4898 mmol) in 2.3 mL anhydrous THF at 0ºC was added DIAD (0.4898 mmol). The reaction was stirred for 15 min., followed by the addition of alcohol (0.3265 mmol) in 1 mL anhydrous THF. After stirring for an additional 5 min., the carboxylic acid (0.3265 mmol) was added. The slurry was stirred for an additional 5 min. and warmed to room temperature – the mixture was stirred until the disappearance of the precipitate. The solvent was removed *in vacuo* and resulting material chromatographed over silica [9:1 Pet Ether/ (4:2:1 EtOAc/CH_2Cl_2/MeOH)] to yield the desired ester.



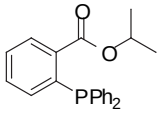
10a

2-Diphenylphosphanyl-benzoic acid allyl ester (10a):
Reaction was carried out with allyl alcohol; yield (0.099 g, 87.5 %). ^{1}H NMR ($CDCl_3$) δ 8.09-8.06 (m, 1H), 7.37-7.24 (m, 12H), 6.99-6.96 (m, 1H), 5.84 (ddt, J= 17.2, 10.4, 5.6 Hz, 1H), 5.32 (dd, J= 17.2, 1.2 Hz, 1H), 5.22 (dd, J= 10.4, 1.2 Hz, 1H), 4.64 (d, J= 5.6 Hz, 1H); ^{31}P NMR ($CDCl_3$) δ -3.35; ^{13}C NMR ($CDCl_3$) δ 166.5, 140.8, 140.5, 138.1, 138.0, 134.5, 134.4, 134.3, 134.2, 133.9, 132.1, 130.8, 130.8, 128.7, 128.6, 128.5, 128.3, 118.5, 65.9. HRMALDI: calcd for $C_{22}H_{19}O_2P$ ($M + H^+$) 347.11, obsd 347.123.



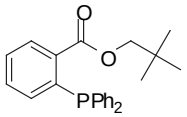
10b

2-Diphenylphosphanyl-benzoic acid benzyl ester (10b):
Reaction was carried out with benzyl alcohol; yield (0.116 g, 89.6 %). ^{1}H NMR ($CDCl_3$) δ 8.09-8.06 (m, 1H), 7.37-7.24 (m, 17H), 6.95-6.92 (m, 1H), 5.19 (s, 2H); ^{31}P NMR ($CDCl_3$) δ -3.44; ^{13}C NMR ($CDCl_3$) δ 166.7, 140.9, 140.7, 138.4, 138.1, 138.0, 135.9, 135.3, 134.5, 134.4, 134.2, 134.2, 134.0, 132.2, 131.0, 130.9, 128.8, 128.7, 128.6, 128.6, 128.5, 128.4, 128.3, 67.0. HRMALDI: calcd for $C_{26}H_{21}O_2P$ ($M + H^+$) 397.13, obsd 397.140.



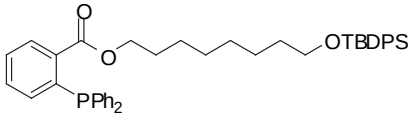
10c

2-Diphenylphosphanyl-benzoic acid isopropyl ester (10c):
Reaction was carried out with isopropyl alcohol; yield (0.105 g, 92.1 %). ^{1}H NMR ($CDCl_3$) δ 8.08-8.06 (m, 1H), 7.37-7.24 (m, 12H), 6.95-6.92 (m, 1H), 5.11 (sept, J= 6.4 Hz, 1H), 1.17 (s, 6H); ^{31}P NMR ($CDCl_3$) δ -3.69; ^{13}C NMR ($CDCl_3$) δ 166.6, 140.2, 139.9, 138.4, 138.3, 135.4, 135.3, 134.4, 134.2, 133.9, 133.8, 131.8, 130.7, 130.6, 128.9, 128.7, 128.6, 128.5, 128.3, 69.1, 21,9. HRMALDI: calcd for $C_{22}H_{21}O_2P$ ($M + H^+$) 349.13, obsd 349.139.



10d

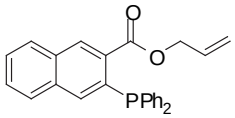
2-Diphenylphosphanyl-benzoic acid 2,2-dimethyl-propyl ester (10d):
Reaction was carried out with neopentyl alcohol; yield (0.102 g, 83.0%). ^{1}H NMR ($CDCl_3$) δ 8.10-8.07 (m, 1H), 7.40-7.25 (m, 12H), 6.96-6.93 (m, 1H), 3.89 (s, 2H), 0.94 (s, 9H); ^{31}P NMR ($CDCl_3$) δ -3.73; ^{13}C NMR ($CDCl_3$) δ 166.8, 141.0, 140.8, 138.2, 138.1, 134.7, 134.5, 134.1, 133.9,133.8, 132.0, 130.5, 130.5, 128.8, 128.7, 128.6, 128.6, 128.5, 128.3, 74.6, 31.6, 26.7. HRMALDI: calcd for $C_{24}H_{25}O_2P$ ($M + H^+$) 377.16, obsd 377.170.



10e

2-Diphenylphosphanyl-benzoic acid 8-(tert-butyldiphenylsilanyloxy)-octyl ester (10e):

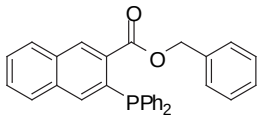
Reaction was carried out with 8-(tert-Butyl-diphenyl-silanyloxy)-octan-1-ol; yield (0.169 g, 76.7 %). ^{1}H NMR ($CDCl_3$) δ 8.06-8.03 (m, 1H), 7.69-7.66 (m, 4H), 7.42-7.24 (m, 18H), 6.94-6.90 (m, 1H), 4.14 (t, J= 6.8 Hz, 2H), 3.65 (t, J= 6.8 Hz, 2H), 1.58-1.52 (m, 4H), 1.34-1.24 (m, 8H), 1.05 (s, 9H); ^{31}P NMR ($CDCl_3$) δ -3.63; ^{13}C NMR ($CDCl_3$) δ 167.2, 140.5, 140.2, 138.3, 138.2, 135.7, 135.4, 135.1, 134.9, 134.5, 134.4, 134.3, 134.2, 134.0, 133.9, 133.8, 132.1, 132.0, 130.7, 129.7, 128.8, 128.7, 128.7, 128.6, 128.6, 128.6, 128.4, 127.8, 65.6, 64.1, 32.7, 29.4, 28.6, 27.1, 26.1, 25.9, 19.4. HRMALDI: calcd for $C_{43}H_{49}O_3PSi$ ($M + H^+$) 673.32, obsd 673.336.



11a

3-Diphenylphosphanyl-naphthalene-2-carboxylic acid allyl ester (11a)

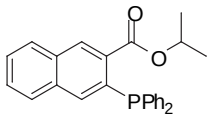
^{1}H NMR ($CDCl_3$) δ 7.93-7.91 (m, 1H), 7.77-7.772 (m, 2H), 7.51-7.47 (m, 2H), 7.32-7.26 (m, 10H), 7.15(dd, J= 8.4, 3.2, 1H), 5.84 (ddt, J= 17.0, 10.4, 6.0 Hz, 1H), 5.26 (dd, J= 2.8., 1.6 Hz, 1H), 5.22 (dd, J= 2.8, 1.6 Hz, 1H), 4.82 (dt, J= 6.0, 1.2 Hz, 2H); ^{31}P NMR ($CDCl_3$) δ -8.14; ^{13}C NMR ($CDCl_3$) δ 169.0, 139.2, 138.9, 137.1, 136.9,134.1, 133.9, 133.7, 133.6, 133.4, 133.2, 131.9,130.1, 130.0, 129.8, 129.0, 128.9, 128.8, 128.7, 128.4, 127.7, 127.5, 125.5, 119.2, 70.2. HRMALDI: calcd for $C_{26}H_{21}O_2P$ ($M + H^+$): 397.135, measured: 397.120.



11b

3-Diphenylphosphanyl-naphthalene-2-carboxylic acid benzyl ester (11b)

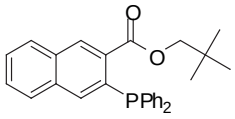
^{1}H NMR ($CDCl_3$) δ 7.90-7.85 (m, 1H), 7.80-7.72 (m, 2H), 7.52-7.47 (m, 2H), 7.32-7.26 (m, 10H), 7.21-7.25(m, 5H), 7.20 (dd, J= 8.4, 3.2, 1H), 5.40 (s, 2H); ^{31}P NMR ($CDCl_3$) δ -8.31; ^{13}C NMR ($CDCl_3$) δ 169.3, 139.5, 139.2, 137.1, 137.0, 135.5,134.1, 133.9, 133.7, 133.6, 133.2, 133.0, 130.1, 130.0, 129.9, 129.0, 128.9, 128.4, 127.7, 127.6, 125.5, 70.3. HRMALDI: calcd for $C_{26}H_{21}O_2P$ ($M + H^+$): 447.151, measured: 447.148.



11c

3-Diphenylphosphanyl-naphthalene-2-carboxylic acid isopropyl ester (11c)

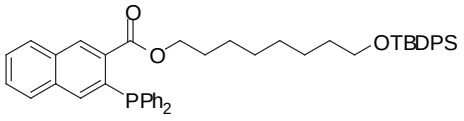
^{1}H NMR ($CDCl_3$) δ 8.00 (dd, J= 8.8, 1.2 Hz, 1H), 7.85-7.80 (m, 2H), 7.62-7.54 (m, 2H), 7.35-7.38 (m, 10H), 7.20 (dd, J= 8.4, 3.2, 1H), 5.45 (sept, J=6 Hz, 1H), 1.33 (d, J= 6.4Hz, 6H); ^{31}P NMR ($CDCl_3$) δ -9.39; ^{13}C NMR ($CDCl_3$) δ 168.9, 137.2, 137.1, 134.1, 133.9, 133.7, 133.6, 132.4, 132.2, 130.0, 129.9, 129.8, 128.8, 128.7, 128.4, 127.6, 127.4, 125.5, 70.01, 21.9. HRMALDI: calcd for $C_{26}H_{23}O_2P$ (M + H^+): 399.151, measured: 399.145



11d

3-Diphenylphosphanyl-naphthalene-2-carboxylic acid 2,2-dimethyl-propyl ester (11d)

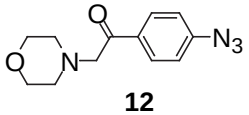
^{1}H NMR ($CDCl_3$) δ 7.98-7.90 (m, 1H), 7.83-776(m, 2H), 7.57-7.49 (m, 2H), 7.37-7.29 (m, 10H), 7.23-7.15 (m, 1H), 4.18 (s, 2H) 0.90 (s, 9H); ^{31}P NMR ($CDCl_3$) δ -8.71; ^{13}C NMR ($CDCl_3$) δ 169.8, 137.9, 137.1, 137.0, 133.9, 133.8, 133.7, 133.6, 132.7, 132.5, 130.1, 129.9, 129.8, 129.0, 128.8, 128.7, 128.3, 127.9, 127.6, 127.5, 125.6, 75.1, 31.4, 26.7. HRMALDI: calcd for $C_{28}H_{27}O_2P$ (M + H^+): 427.182, measured: 427.165



11e

3-Diphenylphosphanyl-naphthalene-2-carboxylic acid 8-(tert-butryl-diphenyl-silanyloxy)-octyl ester (11e)

^{1}H NMR ($CDCl_3$) δ 7.97-7.94 (m, 1H), 7.80-7.34 (m, 2H), 7.68-765 (m, 4H), 7.55-7.48 (m, 2H), 7.39-7.28 (m, 16H), 7.18-7.15 (m, 1H), 4.36 (t, J= 6.4 Hz, 2H), 3.64 (t, J= 6.4 Hz, 2H), 1.57-1.49(m, 4H), 1.32-1.18 (m, 8H),1.04 (s, 9H); ^{31}P NMR ($CDCl_3$) δ -8.35; ^{13}C NMR ($CDCl_3$) δ 169.5, 142.2, 140.0, 139.6, 137.3, 137.2,135.9, 134.4, 133.8, 133.7, 133.6, 133.0, 132.9, 130.1, 130.0, 129.9, 129.8, 129.0, 128.9, 128.8, 128.7, 128.4, 127.9, 127.7, 127.5, 125.6, 66.0, 64.2, 32.8, 29.4, 28.7, 27.2, 26.2, 19.5, 14.5. HRMALDI: calcd for $C_{47}H_{51}O_4PSi$ (M + H^+): 739.337, measured: 739.330.

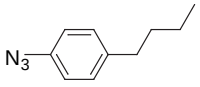


12

1-(4-Azido-phenyl)-2-morpholin-4-yl-ethanone (12).

To 37.7mg of tetrahydro-1,4-oxazine (0.43mmol) was added 2mL anhydrous THF along with 62.4μL distilled triethylamine (0.45mmol). The solution was chilled to 0^{o}C for 5 min followed by the addition of 51.8mg 4-azidophenacyl bromide (0.22mmol). The

solution was stirred and sheltered from light at 0°C for 2h after which time TLC (7:3:2:0.5 Hex:EtOAc:CH_2Cl_2:MeOH) revealed complete consumption of the 4-azidophenacyl bromide and generation of a new UV-active spot with $R_f \sim 0.25$. The solid triethylamine hydrochloride was filtered from the solution and the THF removed *in vacuo*. PTLC using the TLC conditions noted above afforded 46mg of aryl azide **12** in 85% yield. ^{1}H NMR ($CDCl_3$) δ 8.05-8.04 (m, 1H), 8.03-8.02 (m, 1H), 7.10-7.09 (m, 1H), 7.08-7.07 (m, 1H), 3.78-3.75 (m, 6H), 2.61-2.59 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 194.85, 145.35, 132.75, 130.40, 119.17, 66.97, 64.94, 54.03. LRMS (ESI) calcd for $C_{12}H_{14}N_4O_2$ [M+H] = 247.12, measured 247.0. *HR mass spectral data not attainable due to azide lability.*

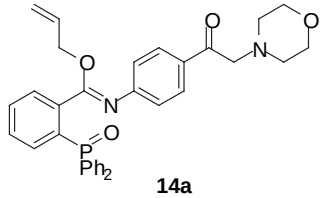


13

1-Azido-4-butyl-benzene (13)
^{1}H NMR ($CDCl_3$) δ 7.19 (d, J= 8.4Hz, 2H), 7.97 (d, J= 8.4 Hz, 2H), 2.62 (t, J= 7.6 Hz, 2H), 1.67-1.57 (m, 2H), 1.412-1.35 (m, 2H), 0.965 (t, J= 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 140.0, 137.5, 130.0, 119.1, 35.2, 33.9, 22.5, 14.2. ESI: calcd for $C_{10}H_{13}N_3$ ($M + H^+$): 176.11, measured: 176.10. *HR mass spectral data not attainable due to azide lability*

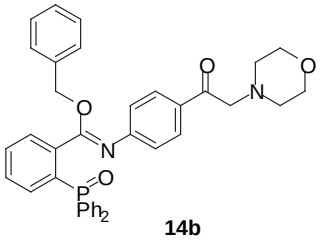
General Procedure for Staudinger Ligations (for phosphines **10a-e**, **11a-e**):

To the aryl azide (0.0124 g, 0.0505 mmol) in 252.5 µL 1:1 THF/H_2O was added the phosphine (0.0200 g, 0.0505 mmol) in 252.5 µL 1:1 THF/H_2O. The reaction was incubated at RT for 1.5 h. The product was extracted into EtOAc, washed with brine, and dried over Na_2SO_4. The solvent was removed *in vacuo* and the resulting material was chromatographed [9:1 Pet Ether/ (4:2:1 EtOAc/CH_2Cl_2/MeOH] to yield the desired conjugate as a light yellow oil.



14a

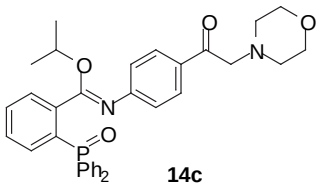
2-(Diphenyl-phosphinoyl)-N-[4-(2-morpholin-4-yl-acetyl)-phenyl]-benzimidic acid allyl ester (14a) :
Reaction was carried out with 2-Diphenylphosphanyl-benzoic acid allyl ester and 1-(4-Azido-phenyl)-2-morpholin-4-yl-ethanone; yield (0.0210 g, 64.4 %). ^{1}H NMR ($CDCl_3$) δ 7.88-7.85 (m, 1H), 7.70-7.61 (m, 7H), 7.57-7.52 (m, 4H), 7.47 (td, J= 7.6, 2.8 Hz, 4H), 6.63 (d, J= 8.8 Hz, 2H), 5.51 (ddt, J= 17.2, 10.4, 6.4 Hz, 1H), 5.04 (dd, J= 17.6, 1.2 Hz, 1H), 5.02 (dd, J= 10.4, 1.2 Hz, 1H), 4.35 (d, J= 6.0 Hz, 2H), 3.77-3.75 (m, 4H), 3.69 (s, 2H), 2.57-2.54 (m, 4H); ^{31}P NMR ($CDCl_3$) δ 9.13; ^{13}C NMR ($CDCl_3$) δ 194.2, 167.4, 137.1, 137.1, 134.7, 134.6, 132.5, 132.4, 132.3, 132.2, 132.1, 132.1, 131.6, 131.3, 131.1, 131.0, 130.7, 130.7, 138.4, 130.3, 129.8, 129.0, 128.9, 125.4, 122.6, 122.4, 118.7, 67.1, 66.5, 64.2, 54.2. HRMALDI: calcd for $C_{34}H_{33}N_2O_4P$ ($M + H^+$) 565.22, obsd 565.216.



14b

2-(Diphenyl-phosphinoyl)-N-[4-(2-morpholin-4-yl-acetyl)-phenyl]-benzimidic acid benzyl ester (14b):

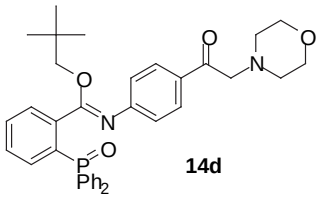
Reaction was carried out with 2-Diphenylphosphanyl-benzoic acid benzyl ester and 1-(4-Azido-phenyl)-2-morpholin-4-yl-ethanone; yield (0.0164 g, 52.9 %). ^{1}H NMR ($CDCl_3$) δ 7.86 (dd, J= 7.2, 3.6 Hz, 1H), 7.69-7.63 (m, 7H), 7.54-7.51 (m, 4H), 7.42 (td, J= 7.6, 2.8 Hz, 4H), 7.26-7.17 (m, 3H), 6.98 (d, J= 8.8 Hz, 2H), 6.66 (d, J= 8.8 Hz, 2H), 4.91 (s, 2H), 3.77-3.75 (m, 4H), 3.68 (s, 2H), 2.57-2.54 (m, 4H); ^{31}P NMR ($CDCl_3$) δ 9.05; ^{13}C NMR ($CDCl_3$) δ 194.2, 167.6, 137.1, 137.1, 135.3, 134.7, 134.6, 132.5, 132.4, 132.3, 132.2, 132.1, 132.1, 131.2, 131,1, 130.9, 130.8, 130.7, 130.2, 129.8, 129.8, 128.9, 128.8, 128.5, 128.4, 128.2, 125.5, 122.6, 122.4, 67.4, 67.0, 64.2, 54.2. HRMALDI: calcd for $C_{38}H_{35}N_2O_4P$ ($M + H^+$) 615.23, obsd 615.231.



14c

2-(Diphenyl-phosphinoyl)-N-[4-(2-morpholin-4-yl-acetyl)-phenyl]-benzimidic acid isopropyl ester (14c):

Reaction was carried out with 2-Diphenylphosphanyl-benzoic acid isopropyl ester and 1-(4-Azido-phenyl)-2-morpholin-4-yl-ethanone; yield (0.0213 g, 65.5 %). ^{1}H NMR ($CDCl_3$) δ 7.90-7.85 (m, 1H), 7.71-7.61 (m, 8H), 7.56-7.52 (m, 3H), 7.46 (td, J= 7.6, 3.2 Hz, 4H), 6.62 (d, J= 8.8 Hz, 2H), 4.78 (sept, J= 6.4 Hz, 1H), 3.77-3.75 (m, 4H), 3.68 (s, 2H), 2.57-2.54 (m, 4H), 0.97 (d, J= 6.4 Hz, 6H); ^{31}P NMR ($CDCl_3$) δ 9.73; ^{13}C NMR ($CDCl_3$) δ 194.2, 166.7, 137.3, 137.3, 135.2, 135.1, 132.6, 132.5, 132.3, 132.0, 132.0, 131.2, 131.1, 131.0, 130.9, 129.8, 128.9, 128.8, 125.4, 122.6, 122.4, 67.1, 66.1, 64.2, 54.2, 21.5. HRMALDI: calcd for $C_{34}H_{35}N_2O_4P$ ($M + H^+$) 567.23, obsd 567.228.

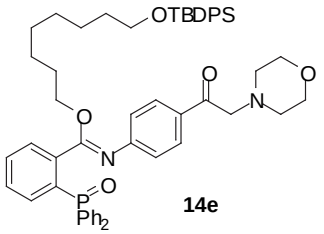


14d

2-(Diphenyl-phosphinoyl)-N-[4-(2-morpholin-4-yl-acetyl)-phenyl]-benzimidic acid (2,2-dimethyl-propyl) ester (14d):

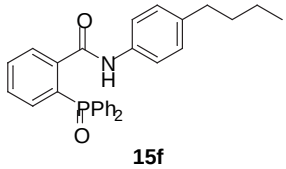
Reaction was carried out with 2-Diphenylphosphanyl-benzoic acid 2,2-dimethyl-propyl ester and 1-(4-Azido-phenyl)-2-morpholin-4-yl-ethanone; yield (0.0211 g, 66.8 %). ^{1}H NMR ($CDCl_3$) δ 7.90-7.85 (m, 1H), 7.71-7.61 (m, 8H), 7.59-7.52 (m, 3H), 7.47-7.43 (m,

4H), 6.63 (d, J= 8.8 Hz, 2H), 3.77-3.75 (m, 4H), 3.68 (s, 2H), 3.58 (s, 2H), 2.57-2.254 (m, 4H), 0.77 (s, 9H); ^{31}P NMR ($CDCl_3$) δ 9.38; ^{13}C NMR ($CDCl_3$) δ 194.1, 167.3, 137.1, 137.0, 135.2, 135.1, 132.5, 132.4, 132.3, 132.0, 132.0, 131.2, 131.1, 130.5, 130.4, 129.8, 129.7, 128.9, 128.8, 125.4, 122.6, 122.4, 74.8, 67.1, 64.2, 54.2, 31.4, 26.5. HRMALDI: calcd for $C_{36}H_{39}N_2O_4P$ ($M + H^+$) 595.26, obsd 595.244.



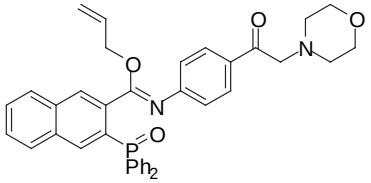
14e

2-(Diphenyl-phosphinoyl)-N-[4-(2-morpholin-4-yl-acetyl)-phenyl]-benzimidic acid [8-(tert-Butyl-diphenyl-silanyloxy)-octyl] ester (14e):
Reaction was carried out with 2-Diphenylphosphanyl-benzoic acid 8-(tert-butyl-diphenyl-silanyloxy)-octyl ester and 1-(4-Azido-phenyl)-2-morpholin-4-yl-ethanone; yield (0.0347 g, 65.6 %). ^{1}H NMR ($CDCl_3$) δ 7.87-7.84 (m, 1H), 7.70-7.64 (m, 11H), 7.55-7.51 (m, 4H), 7.40-7.34 (m, 10H), 6.63 (d, J= 8.8 Hz, 2H), 3.82 (t, J= 6.8 Hz, 2H), 3.77-3.75 (m, 4H), 3.68 (s, 2H), 3.64 (t, J= 6.8 Hz, 2H), 2.57-2.52 (m, 4H), 1.59-1.49 (m, 2H), 1.35-1.20 (m, 4H), 1.17-1.09 (m, 6H), 1.04 (s, 9H); ^{31}P NMR ($CDCl_3$) δ 9.18; ^{13}C NMR ($CDCl_3$) δ 194.1, 167.7, 137.4, 137.3, 135.7, 134.9, 134.8, 134.3, 132.5, 132.4, 132.3, 132.2, 132.1, 132.0, 131.0, 130.9, 130.7, 130.7, 130.4, 129.8, 129.7, 129.7, 129.1, 128.9, 128.8, 128.5, 128.4, 127.7, 125.4, 122.5, 122.4, 119.1, 67.0, 67.0, 66.0, 64.1, 54.2, 32.7, 29.3, 29.3, 28.1, 27.0, 25.9, 25.8, 19.4. HRMALDI: calcd for $C_{55}H_{63}N_2O_5PSi$ ($M + H^+$) 891.42, obsd 891.331.



15f

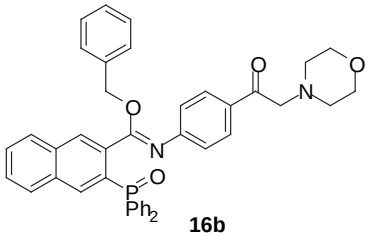
***N*-(4-butylphenyl)-2-(diphenylphosphoryl)benzamide (15f):**
^{1}H NMR ($CDCl_3$) δ 10.54 (bs, 1H), 8.09-8.06 (m, 1H), 7.70-7.63 (m, 5H), 7.53-7.49 (m, 2H), 7.44-7.39 (m, 5H), 7.32-7.30 (m, 2H), 7.15-7.09 (m, 1H), 7.01 (d, J= 8.4 Hz, 2H), 2.54 (t, J= 7.6 Hz, 2H), 1.59-1.52 (m, 2H), 1.37-1.28 (m, 2H), 0.92 (t, J= 7.6 Hz, 3H); ^{31}P NMR ($CDCl_3$) δ 36.36; ^{13}C NMR ($CDCl_3$) δ 165.4, 141.7, 141.6, 139.0, 135.7, 133.5, 133,4, 133.06, 132.97, 132.6, 132.55, 132.49, 132.4, 131.8, 131.7, 131.3, 130.32, 130.28, 130.23, 131.17, 129.3, 129.0, 128.8, 128.6, 120.3, 35.3, 33.9, 22.4, 14.2. HRMALDI: calcd for $C_{29}H_{28}NO_2P$ ($M + H^+$) 454.19, obsd 454.181.



16a

3-(Diphenyl-phosphinoyl)-N-[4-(2-morpholin-4-yl-acetyl)-phenyl]-naphthalene-2-carboximidic acid allyl ester (16a).

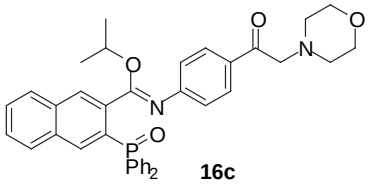
^{1}H NMR ($CDCl_3$) δ 9.17 (s, 1H), 8.31 (d, J= 8Hz, 1H), 7.87-784 (m, 2H), 7.77-7.69 (m, 4H), 7.64-7.35 (m, 6H), 7.31 (d, J= 8.4 Hz, 2H), 7.24 (dd, J= 12.0, 8.0 Hz, 2H), 7.05 (d, J= 8.4 Hz, 2H), 5.78 (ddt, J= 17.0, 10.4, 6.0 Hz, 1H), 5.21 (dd, J= 17.2, 1.2 Hz, 1H), 5.12 (dd, J= 10.4, 1.2 Hz, 1H), 4.73 (d, J= 6.4 Hz, 2H), 3.77-3.75 (m, 4H), 3.69 (s, 2H), 2.57-2.52 (m, 4H); ^{31}P NMR ($CDCl_3$) δ 33.32; ^{13}C NMR ($CDCl_3$) δ 195.0, 166.9, 151.2, 137.9, 137.5, 136.7, 135.0,134.2, 133.0, 131.8, 131.5, 130.4, 129.6, 128.7, 128.0, 127.1, 125.9, 121.8, 115.1, 67.1, 66.5, 64.2, 54.2. HRMALDI: calcd for $C_{38}H_{35}N_2O_4P$ ($M + H^+$): 615.241, measured: 615.225



16b

3-(Diphenyl-phophinoyl-Np[4-2-morpholin-4-yl-acetyl)-phenyl]-naphthalene-2-carboximidic acid benzyl ester (16b)

^{1}H NMR ($CDCl_3$) δ 9.20 (s, 1H), 8.30 (d, J= 8Hz, 1H), 7.87-783 (m, 2H), 7.75-7.70 (m, 4H), 7.63-7.22 (m, 15H), 7.04 (d, J= 8.8 Hz, 2H), 4.65 (s, 2H), 3.77-3.75 (m, 4H), 3.68 (s, 2H), 2.57-2.52 (m, 4H); ^{31}P NMR ($CDCl_3$) δ 33.26; ^{13}C NMR ($CDCl_3$) δ 195.0, 166.2, 150.4, 140.6, 137.9, 136.6, 135.1, 134.2, 132.9, 131.5, 130.4, 129.6, 128.7, 128.6, 128.0, 127.3, 127.1, 125.9, 121.8, 67.9, 67.0, 64.2, 54.2. HRMALDI: calcd for $C_{42}H_{37}N_2O_4P$ ($M + H^+$): 665.256, measured: 665.241

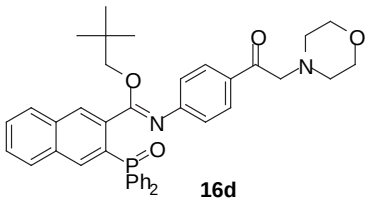


16c

3-(Diphenyl-phosphinoyl)-N-[4-(2-morpholin-4-yl-acetyl)-phenyl]-naphthalene-2-carboximidic acid isopropyl ester (16c)

^{1}H NMR ($CDCl_3$) δ 9.20 (s, 1H), 8.29 (d, J= 8Hz, 1H), 7.86-784 (m, 2H), 7.75-7.71 (m, 4H), 7.64-7.33 (m, 6H), 7.30 (d, J= 8.4 Hz, 2H), 7.25 (dd, J= 12.0, 8.0 Hz, 2H), 7.05 (d, J= 8.4 Hz, 2H), 5.05 (sept, J= 6.4 Hz, 1H), 3.77-3.75 (m, 4H), 3.68 (s, 2H), 2.57-2.54 (m, 4H), 1.16 (d, J= 6.4 Hz, 6H); ^{31}P NMR ($CDCl_3$) δ 33.26; ^{13}C NMR ($CDCl_3$) δ 195.0, 166.7, 150.2, 137.9, 136.7, 136.0, 135.2, 133.0, 131.8, 129.7, 128.5, 127.9, 127.1, 126.0,

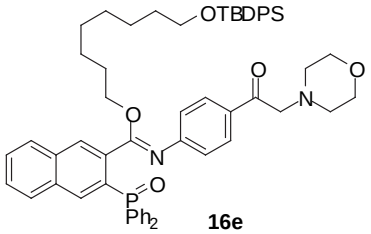
122.0, 66.9, 66.1, 64.2, 54.2, 21.5. HRMALDI: calcd for $C_{38}H_{37}N_2O_4P$ (M + H^+): 617.256, measured: 617.252.



16d

3-(Diphenyl-phosphinoyl)-N-[4-(2-morpholin-4-yl-acetyl)-phenyl]-naphthalene-2-carboximidic acid 2,2-dimethyl-propyl ester (16d)

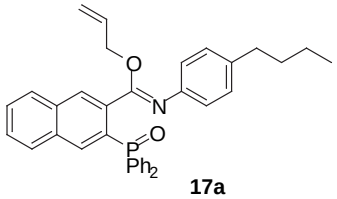
^{1}H NMR ($CDCl_3$) δ 9.21 (s, 1H), 8.30 (d, J= 8Hz, 1H), 7.86-784 (m, 2H), 7.76-7.70 (m, 4H), 7.64-7.32 (m, 6H), 7.31 (d, J= 8.4 Hz, 2H), 7.24 (dd, J= 12.0, 8.0 Hz, 2H), 7.05 (d, J= 8.4 Hz, 2H), 3.77-3.75 (m, 4H), 3.60 (s, 2H), 3.58 (s, 2H), 2.57-2.52 (m, 4H), 0.79 (s, 9H); ^{31}P NMR ($CDCl_3$) δ 33.18; ^{13}C NMR ($CDCl_3$) δ 195.0,166.5, 150.3, 137.9, 136.7, 136.0, 135.0, 132.9, 131.5, 129.6, 128.6, 128.0, 125.6, 121.8, 75.0, 67.1, 64.2, 54.2, 31.4, 26.5. HRMALDI: calcd for $C_{40}H_{41}N_2O_4P$ (M + H^+): 645.288, measured: 645.281.



16e

3-(Diphenyl-phosphinoyl)-N-[4-(2-morpholin-4-yl-acetyl)-phenyl]-naphthalene-2-carboximidic acid 8-(tert-butyl-diphenyl-silanyoxy)-octyl ester (16e)

^{1}H NMR ($CDCl_3$) δ 9.20 (s, 1H), 8.30 (d, J= 8Hz, 1H), 7.86-784 (m, 2H), 7.76-7.70 (m, 4H), 7.64-7.32 (m, 16H), 7.31 (d, J= 8.4 Hz, 2H), 7.24 (dd, J= 12.0, 8.0 Hz, 2H), 7.05 (d, J= 8.4 Hz, 2H), 3.80 (t, J= 6.8 Hz, 2H), 3.77-3.75 (m, 4H), 3.68 (s, 2H), 3.62 (t, J= 6.8 Hz, 2H), 2.57-2.54 (m, 4H), 1.59-1.49 (m, 2H), 1.35-1.20 (m, 4H), 1.17-1.09 (m,6H), 1.02 (s, 9H); ^{31}P NMR ($CDCl_3$) δ 33.23; ^{13}C NMR ($CDCl_3$) δ 166.5, 150.3, 137.9, 136.7, 136.0, 135.0, 132.9, 131.5, 129.6, 128.6, 128.0, 125.6, 121.8, 75.0, 35.5, 31.5, 34.6, 26.5, 22.7, 14.0. HRMALDI: calcd for $C_{59}H_{65}N_2O_5PSi$ (M + H^+): 941.447, measured: 941.432.

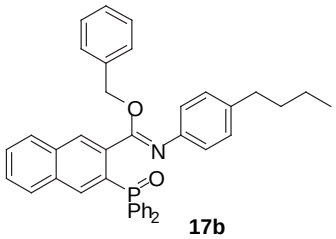


17a

N-(4-Butyl-phenyl)-2-(diphenyl-phosphinoyl)-naphthalene-1-carboximidic acid allyl ester (17a)

^{1}H NMR ($CDCl_3$) δ 9.17 (s, 1H), 8.31 (d, J= 8Hz, 1H), 7.87-784 (m, 2H), 7.77-7.69 (m, 4H), 7.64-7.35 (m, 6H), 7.31 (d, J= 8.4 Hz, 2H), 7.24 (dd, J= 12.0, 8.0 Hz, 2H), 7.05 (d, J= 8.4 Hz, 2H), 5.78 (ddt, J= 17.0, 10.4, 6.0 Hz, 1H), 5.21 (dd, J= 17.2, 1.2 Hz, 1H), 5.12 (dd, J= 10.4, 1.2 Hz, 1H), 4.73 (d, J= 6.4 Hz, 2H), 2.55 (t, J= 7.6 Hz, 2H), 1.62-1.58

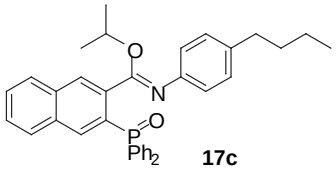
(m, 2H), 1.38-1.31 (m, 2H), 0.94 (t, J= 7.4 3H); ^{31}P NMR ($CDCl_3$) δ 33.32; ^{13}C NMR ($CDCl_3$) δ 166.9, 151.2, 137.9, 137.5, 136.7, 135.0,134.2, 133.0, 131.8, 131.5, 130.4, 129.6, 128.7, 128.0, 127.1, 125.9, 121.8, 115.1, 67.2, 35.5, 34.6, 22.7, 14.0. HRMALDI: calcd for $C_{36}H_{34}NO_2P$ (M + H^+): 544.240, measured: 544.235



17b

N-(4-Butyl-phenyl)-2-(diphenyl-phosphinoyl)-naphthalene-1-carboximidic acid benzyl ester (17b).

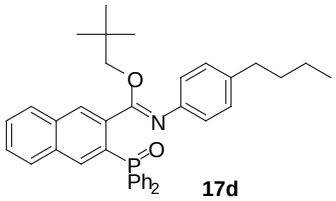
^{1}H NMR ($CDCl_3$) δ 9.20 (s, 1H), 8.30 (d, J= 8Hz, 1H), 7.87-783 (m, 2H), 7.75-7.70 (m, 4H), 7.63-7.22 (m, 15H), 7.04 (d, J= 8.8 Hz, 2H), 4.65 (s, 2H), 2.57 (t, J= 7.6 Hz, 2H), 1.60-1.55 (m, 2H), 1.40-1.32 (m, 2H), 0.94 (t, J= 7.4 3H); ^{31}P NMR ($CDCl_3$) δ 33.22; ^{13}C NMR ($CDCl_3$) δ 166.2, 150.4, 140.6, 137.9, 136.6, 135.1, 134.2, 132.9, 131.5, 130.4, 129.6, 128.7, 128.6, 128.0, 127.3, 127.1, 125.9, 121.8, 67.9, 34.6, 33.5, 21.8, 13.8. HRMALDI: calcd for $C_{40}H_{36}NO_2P$ (M + H^+): 594.256, measured: 594.251



17c

N-(4-Butyl-phenyl)-3-(diphenyl-phosphinoyl)-naphthalene-2-carboximidic acid isopropyl ester (17c)

^{1}H NMR ($CDCl_3$) δ 9.20 (s, 1H), 8.29 (d, J= 8Hz, 1H), 7.86-784 (m, 2H), 7.75-7.71 (m, 4H), 7.64-7.33 (m, 6H), 7.30 (d, J= 8.4 Hz, 2H), 7.25 (dd, J= 12.0, 8.0 Hz, 2H), 7.05 (d, J= 8.4 Hz, 2H), 5.05 (sept, J= 6.4 Hz, 1H), 2.55 (t, J= 7.6 Hz, 2H), 1.62-1.58 (m, 2H), 1.38-1.31 (m, 2H), 1.16 (d, J= 6.4 Hz, 6H), 0.94 (t, J= 7.4 3H); ^{31}P NMR ($CDCl_3$) δ 33.26; ^{13}C NMR ($CDCl_3$) δ 166.7, 150.2, 137.9, 136.7, 136.0, 135.2, 133.0, 131.8, 129.7, 128.5, 127.9, 127.1, 126.0, 122.0, 66.9, 35.5, 34.6, 22.7, 21.5, 14.0. HRMALDI: calcd for $C_{36}H_{36}NO_2P$ (M + H^+): 546.256, measured: 546.249.

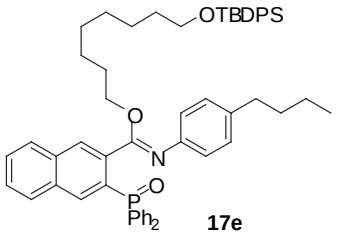


17d

N-(4-Butyl-phenyl)-3-(diphenyl-phosphinoyl)-naphthalene-2-carboximidic acid 2,2-dimethyl-propyl ester (17d)

^{1}H NMR ($CDCl_3$) δ 9.21 (s, 1H), 8.30 (d, J= 8Hz, 1H), 7.86-784 (m, 2H), 7.76-7.70 (m, 4H), 7.64-7.32 (m, 6H), 7.31 (d, J= 8.4 Hz, 2H), 7.24 (dd, J= 12.0, 8.0 Hz, 2H), 7.05 (d, J= 8.4 Hz, 2H), 3.60 (s, 2H), 2.55 (t, J= 7.6 Hz, 2H), 1.62-1.58 (m, 2H), 1.38-1.31 (m,

2H), 0.94 (t, J= 7.4 3H), 0.79 (s, 9H); ^{31}P NMR ($CDCl_3$) δ 33.18; ^{13}C NMR ($CDCl_3$) δ 166.5, 150.3, 137.9, 136.7, 136.0, 135.0, 132.9, 131.5, 129.6, 128.6, 128.0, 125.6, 121.8, 75.0, 35.5, 31.5, 34.6, 26.5, 22.7, 14.0. HRMALDI: calcd for $C_{38}H_{40}NO_2P$ (M + H^+): 574.287, measured: 574.265.

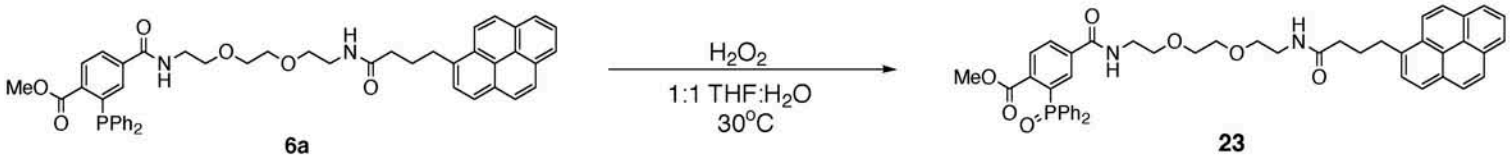


17e

N-(4-Butyl-phenyl)-3-(diphenyl-phosphinoyl)-naphthalene-2-carboximidic acid 8-(ter-butyl-diphenyl-silanyloxy)-octyl ester (17e)

^{1}H NMR ($CDCl_3$) δ 9.20 (s, 1H), 8.30 (d, J= 8Hz, 1H), 7.86-784 (m, 2H), 7.76-7.70 (m, 4H), 7.64-7.32 (m, 16H), 7.31 (d, J= 8.4 Hz, 2H), 7.24 (dd, J= 12.0, 8.0 Hz, 2H), 7.05 (d, J= 8.4 Hz, 2H), 3.80 (t, J= 6.8 Hz, 2H), 3.62 (t, J= 6.8 Hz, 2H), 2.55 (t, J= 7.6 Hz, 2H), 1.62-1.28 (m, 10H),1.17-1.09 (m,6H), 1.02 (s, 9H), 0.94 (t, J= 7.4, 3H); ^{31}P NMR ($CDCl_3$) δ 33.23; ^{13}C NMR ($CDCl_3$) δ 166.5, 150.3, 137.9, 136.7, 136.0, 135.0, 132.9, 131.5, 129.6, 128.6, 128.0, 125.6, 121.8, 75.0, 35.5, 31.5, 34.6, 26.5, 22.7, 14.0. HRMALDI: calcd for $C_{57}H_{64}NO_3PSi$ (M + H^+): 870.447, measured: 870.443.

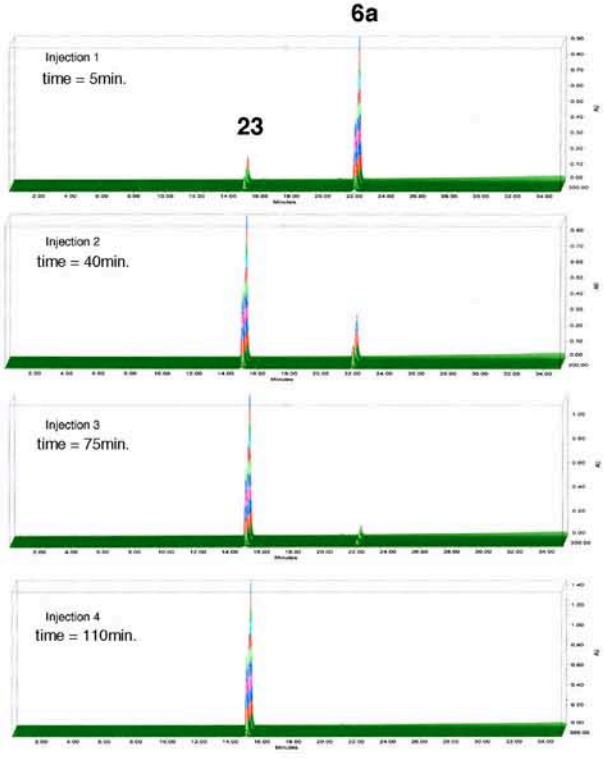
INDEX OF HPLC TRACES



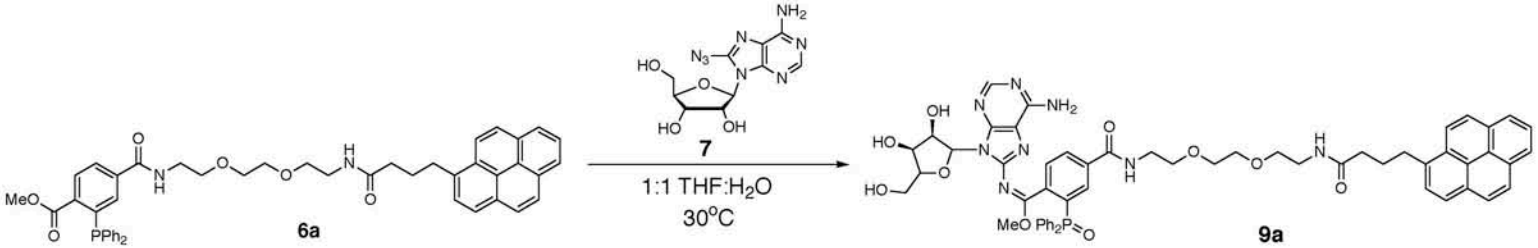
Flow rate: 1.5 mL/min.
Gradient:

time	%H_2O (0.1% TFA)	%CH_3CN (0.1%TFA)
1.0	65	35
30	10	90
35	65	35

Photodiode array detection 240nm - 380nm
Column: Phenomenex Luna 5u C8
150 x 4.60mm 5 micron



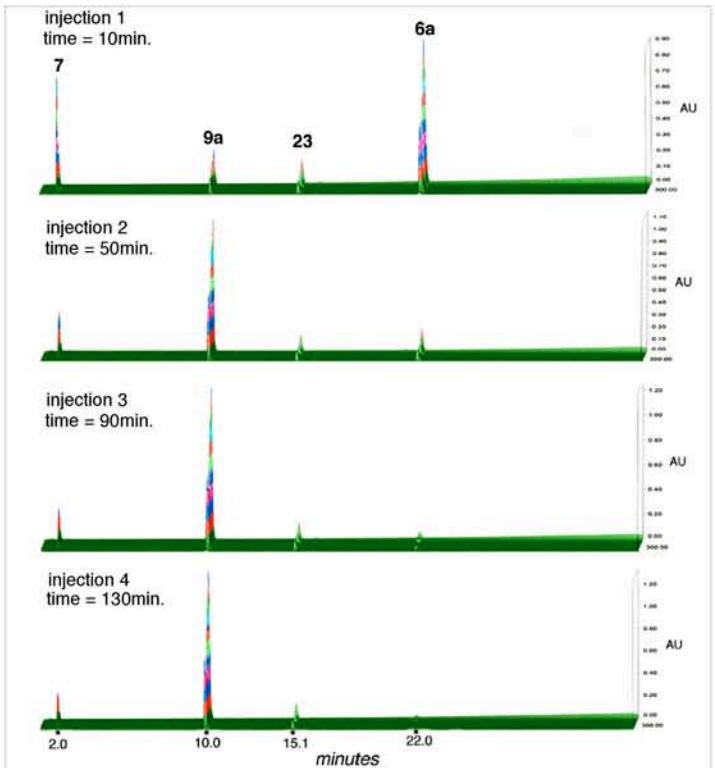
HPLC 1



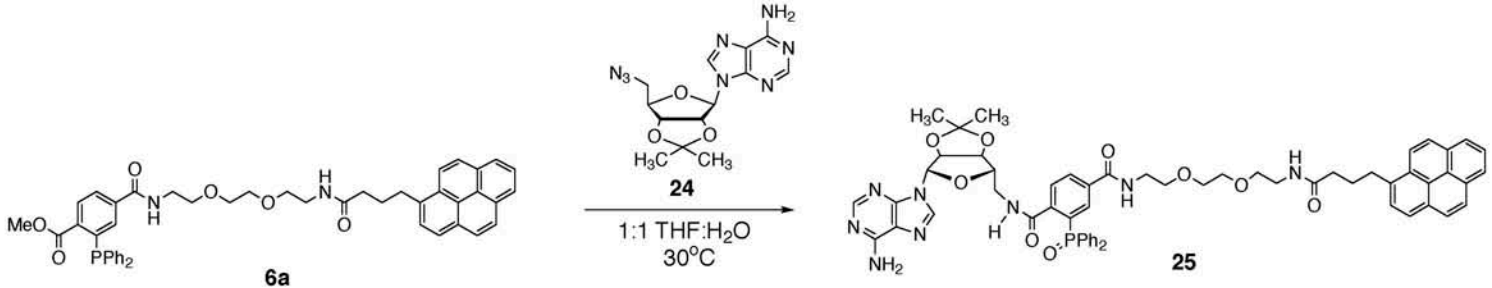
Flow rate: 1.5 mL/min.
Gradient:

time	%H_2O (0.1% TFA)	%CH_3CN (0.1%TFA)
1.0	65	35
30	10	90
35	65	35

Photodiode array detection 240nm - 380nm
Column: Phenomenex Luna 5u C8
150 x 4.60mm 5 micron



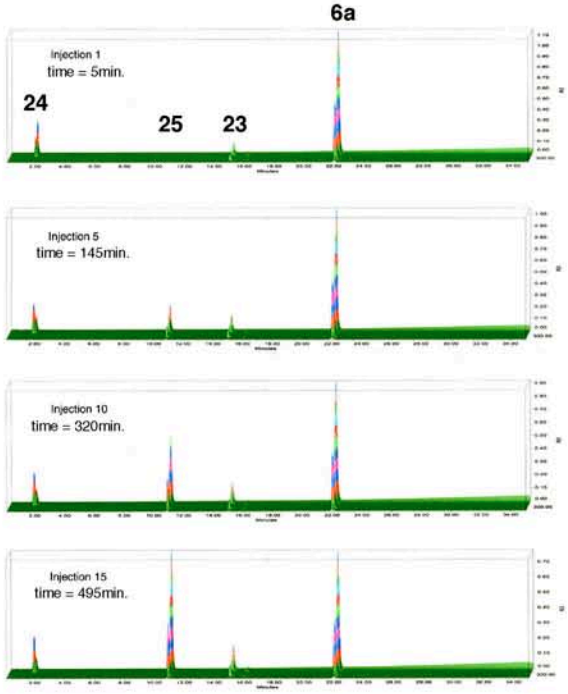
HPLC 2



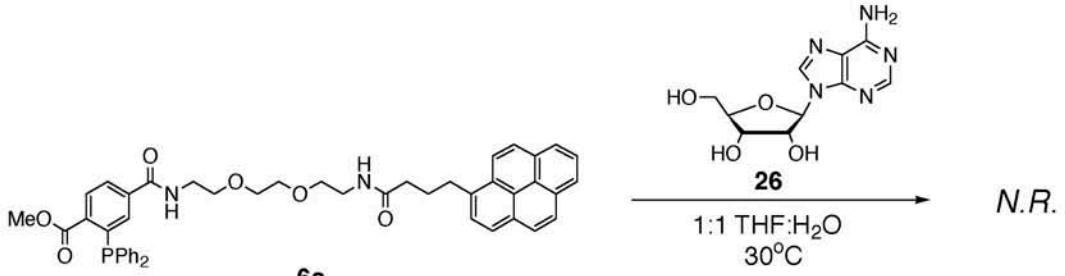
Flow rate: 1.5 mL/min.
Gradient:

time	%H_2O (0.1% TFA)	%CH_3CN (0.1%TFA)
1.0	65	35
30	10	90
35	65	35

Photodiode array detection 240nm - 380nm
Column: Phenomenex Luna 5u C8
150 x 4.60mm 5 micron



HPLC 3

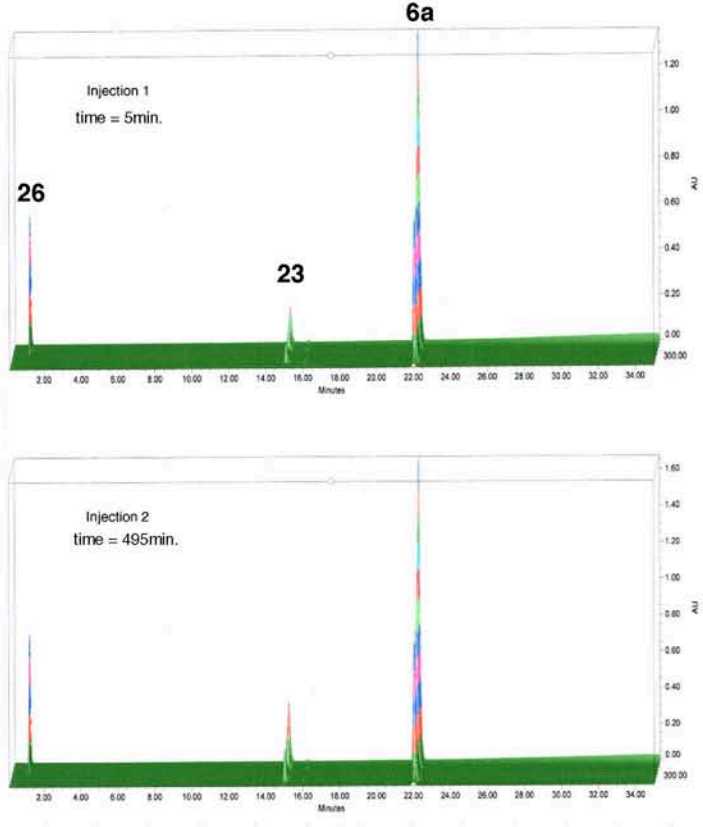


6a

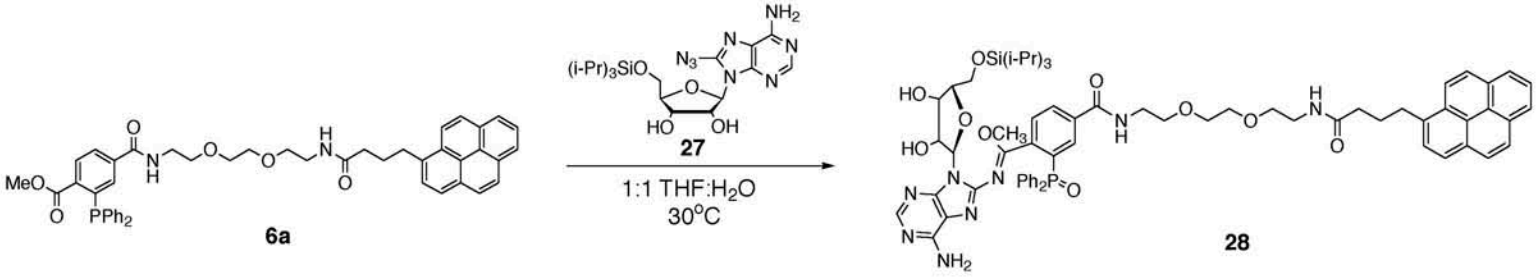
Flow rate: 1.5 mL/min.
Gradient:

time	%H_2O (0.1% TFA)	%CH_3CN (0.1%TFA)
1.0	65	35
30	10	90
35	65	35

Photodiode array detection 240nm - 380nm
Column: Phenomenex Luna 5u C8
150 x 4.60mm 5 micron



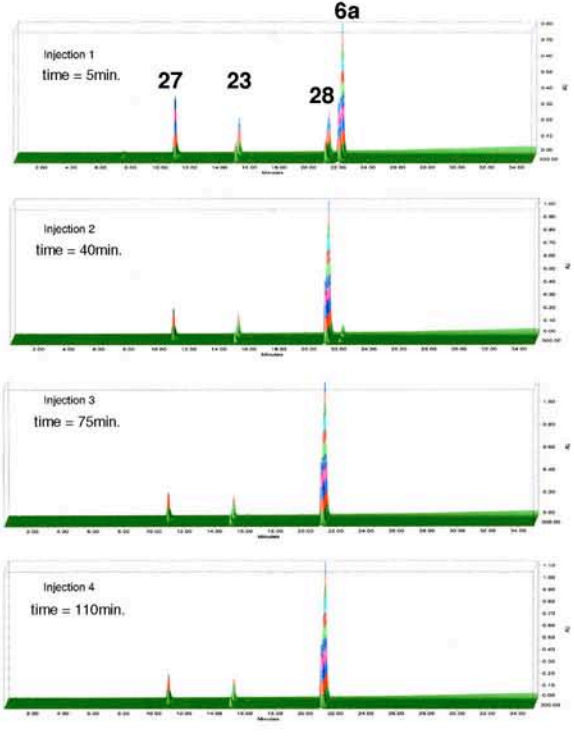
HPLC 4



Flow rate: 1.5 mL/min.
Gradient:

time	%H_2O (0.1% TFA)	%CH_3CN (0.1%TFA)
1.0	65	35
30	10	90
35	65	35

Photodiode array detection 240nm - 380nm
Column: Phenomenex Luna 5u C8
150 x 4.60mm 5 micron



HPLC 5