Supporting Information

Palladium-Catalyzed Couplings of Pyrid-4-yl Nonaflates with Methyl Diazoacetate

Christian Eidamshaus, Paul Hommes, Hans-Ulrich Reissig*

Institut für Chemie und Biochemie, Freie Universität Berlin
Takustr. 3, D-14195 Berlin, Germany

hreissig@chemie.fu-berlin.de

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1) General Methods

Reactions were performed under argon in sealed tubes. Solvents and liquid reagents were added by syringe. CH$_3$CN was purchased from Sigma-Aldrich (Chromasolv$^\text{®}$ plus, for HPLC, ≥99.9%) and used without further purification. Pd(PPh$_3$)$_4$ was purchased from Acros Organics and used as received. NEt$_3$ was distilled from CaH$_2$ and stored over KOH under argon. Methyl diazoacetate was prepared from glycine methyl ester hydrochloride following a literature procedure.$^{[1]}$ Thin layer chromatography (TLC) analyses were performed on TLC plates purchased from Merck (silica gel 60, fluorescence indicator F254, 0.25 mm layer thickness). Products were purified by flash chromatography on silica gel 60 (230–400 mesh, Machery-Nagel). NMR spectra were recorded with Bruker (AC 500, AVIII 700) and JOEL (Eclipse 500) instruments. Chemical shifts are reported relative to solvent residual peaks or TMS [$^1$H: $\delta = 0.00$ ppm (TMS), $\delta = 7.26$ ppm (CDCl$_3$); $^{13}$C: $\delta = 77.0$ ppm (CDCl$_3$)]. Integrals are in accordance with assignments, and coupling constants are given in Hz. All $^{13}$C NMR spectra are proton-decoupled. For detailed peak assignments 2D spectra were measured (COSY, HMQC, HMBC). IR spectra were measured with a Jasco FT/IR-4100 spectrometer. HRMS analyses were performed with a Varian Ionspec QFT-7 (ESI-FT ICRMS) instrument. Elemental analyses were carried out with CHN-Analyzer Vario EL or Vario EL III instruments. Melting points were measured with a Reichert apparatus (Thermovar) and are uncorrected.
2) Experimental Procedures

Methyl 2-diazo-2-(2-methyl-6-phenylpyridin-4-yl)acetate (14b): Following the typical procedure, a solution of pyridyl nonaflate 13b[2] (932 mg, 1.99 mmol), methyl diazoacetate (299 mg, 2.99 mmol), Pd(PPh3)4 (115 mg, 0.10 mmol) and triethylamine (0.42 mL, 2.99 mmol) in CH3CN (20 mL) was stirred at 45 °C for 1.5 h. The formed precipitate was filtered off, washed with cold CH3CN and hexane (5 mL each) and afterwards dried in vacuo to give 217 mg (41%) of pure 14b as a yellow solid. The filtrate was concentrated in vacuo and redissolved in EtOAc (30 mL), washed with water (3x30 mL), dried with Na2SO4, filtered and concentrated to dryness. The crude product was purified by flash column chromatography on silica gel (hexane:EtOAc 40:1; 15:1) to provide 18 mg (2%) of reisolated starting material 13b and additional 228 mg (43%) of 14b.

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\text{Me}_2\text{C}_\text{N}_2\text{N}=\text{O}_2
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M.p.: 137-138 °C. 1H NMR (500 MHz, CDCl3): δ = 2.62 (s, 3 H, Me), 3.90 (s, 3 H, OMe), 7.19 (d, J = 1.2 Hz, 1 H, 5-H), 7.39-7.42 (m, 1 H, Ph), 7.44-7.47 (m, 2 H, Ph), 7.69 (d, J = 1.2 Hz, 1 H, 3-H), 7.96-7.98 (m, 2 H, Ph) ppm. 13C NMR (126 MHz, CDCl3): δ = 24.9 (q, Me), 52.2 (q, OMe), 63.8 (s, C=N2), 111.6 (d, C-3), 114.9 (d, C-5), 127.1, 128.6, 128.9 (3 d, Ph), 136.1 (s, C-4), 139.5 (s, Ph), 157.4 (s, C-6), 158.6 (s, C-2), 164.3 (s, CO) ppm. IR (ATR): ν = 3065-3005 (C-H), 2950, 2915 (C-H), 2095 (CN2), 1710 (C=O), 1595, 1540 (C=C, C=N), 1440, 1360, 1280, 1150 cm⁻¹. HRMS (ESI-TOF): m/z calcd. for C15H14N3O2 [M+H]+: 268.1081; found: 268.1102. Anal. calcd. for C15H13N3O2 (267.3): C 67.40, H 4.90, N 15.72; found: C 67.44, H 4.88, N 15.65.
Methyl 2-diazo-2-(6-methyl-2,2'-bipyridin-4-yl)acetate (14c): Following the typical procedure, a solution of pyridyl nonaflate 13c [2] (713 mg, 1.52 mmol), methyl diazoacetate (228 mg, 2.28 mmol), Pd(PPh₃)₄ (122 mg, 0.11 mmol) and triethylamine (0.32 mL, 2.28 mmol) in CH₃CN (15 mL) was stirred at 45 °C for 1.5 h. The formed precipitate was filtered off, washed with little amounts of cold CH₃CN and hexane and afterwards dried in vacuo to give 268 mg (66%) of pure 14c as a yellow solid. The filtrate was concentrated in vacuo and re-dissolved in EtOAc (30 mL), washed with water (3×30 mL), dried with Na₂SO₄, filtered and concentrated to dryness. The crude product was purified by flash column chromatography on silica gel (hexane:EtOAc 2:1) to provide additional 85 mg (21%) of 14c.

M.p.: 155-160 °C. ¹H NMR (500 MHz, CDCl₃): δ = 2.62 (s, 3 H, Me), 3.90 (s, 3 H, OMe), 7.28 (ddd, J = 7.7, 4.8, 1.0 Hz, 1 H, 5'-H), 7.57 (d, J = 1.6 Hz, 1 H, 5-H), 7.79 (td, J = 7.7, 1.7 Hz, 1 H, 4'-H), 8.10 (d, J = 1.6 Hz, 1 H, 3-H), 8.39 (d, J = 7.7 Hz, 1 H, 3'-H), 8.65 (ddd, J = 4.8, 1.7, 1.0 Hz, 1 H, 6'-H) ppm. ¹³C NMR (126 MHz, CDCl₃): δ = 24.8 (q, Me), 52.2 (q, OMe), 64.1 (s, C=N₂), 111.3 (d, C-3), 117.1 (d, C-5), 121.2 (d, C-3'), 123.7 (d, C-5'), 136.4 (s, C-4), 136.8 (d, C-4'), 149.1 (d, C-6'), 155.8, 156.0 (2 s, C-2, C-2'), 158.4 (s, C-6), 164.3 (s, CO) ppm. IR (ATR): ν = 3060 (=C-H), 2950, 2925 (C-H), 2105 (CN₂), 1715 (C=O), 1600-1545 (C=C, C=N), 1440-1360, 1280-1260 cm⁻¹. HRMS (ESI-TOF): m/z calcd. for C₁₄H₁₂N₄O₂ [M+H⁺]: 269.1033; found: 269.1037. Anal. calcd. for C₁₄H₁₂N₄O₂ (268.3): C 62.68, H 4.51, N 20.88; found: C 62.67, H 4.56, N 20.85.

4,4''-Bis(1-diazo-2-methoxy-2-oxoethyl)-6,6''-dimethyl-2,2'-6',2''-terpyridine (14d): Following the typical procedure, a mixture of pyridyl nonaflate 13d [2] (614 mg, 0.72 mmol), methyl diazoacetate (215 mg, 2.15 mmol), Pd(PPh₃)₄ (83 mg, 0.072 mmol) and triethylamine (0.30 mL, 2.15 mmol) in CH₃CN (7 mL) was stirred at 45 °C. (Note: Initially 13d was only partially dissolved). After 1 h the
precipitate was filtered off, washed with little amounts of cold CH$_3$CN and hexane and afterwards dried in vacuo to give 303 mg (93%) of pure 14d as a yellow solid.

![Chemical structure of 14d]

M.p.: >200 °C (decomposition). $^1$H NMR (CDCl$_3$:CD$_3$OD:CF$_3$CO$_2$H (7:1:1), 500 MHz): $\delta$ = 2.79 (s, 6 H, Me), 3.81 (s, 6 H, OMe), 7.71 (s br, 2 H, 5-H), 8.16 (t, $J \approx$ 8 Hz, 1 H, 4'-H), 8.28 (d, $J \approx$ 8 Hz, 2 H, 3'-H), 8.47 (s br, 2 H, 3-H) ppm. $^{13}$C NMR (CDCl$_3$:CD$_3$OD:CF$_3$CO$_2$H (7:1:1), 126 MHz): $\delta$ = 19.4 (q, Me), 52.7 (q, OMe), 67.8 (s, C=N$_2$), 113.9 (d, C-3), 118.1 (d, C-5), 124.8 (d, C-3'), 140.6 (d, C-4'), 146.6 (s, C-4), 147.8, 147.9 (2 s, C-2, C-2'), 154.3 (s, C-6), 162.0 (s, CO) ppm. IR (ATR): $\nu$ = 3060 (=C-H), 2955, 2930-2905 (C-H), 2100 (CN$_2$), 1710 (C=O), 1605, 1575, 1545 (C=C, C=N), 1440, 1405, 1295-1230 cm$^{-1}$. HRMS (ESI-TOF): $m/z$ calcd. for C$_{23}$H$_{20}$N$_7$O$_4$ [M+H]$^+$: 458.1571; found: 458.1581.

Anal. calcd. for C$_{23}$H$_{19}$N$_7$O$_4$ (457.4): C 60.39, H 4.19, N 21.43; found: C 59.99, H 4.27, N 21.15.

2,5-Bis[4-(1-diazo-2-methoxy-2-oxoethyl)-6-methylpyrid-2-yl]thiophene (14e): Following the typical procedure, a mixture of pyridyl nonaflate 13e [21] (395 mg, 0.46 mmol), methyl diazoacetate (137 mg, 1.37 mmol), Pd(PPh$_3$)$_4$ (53 mg, 0.05 mmol) and triethylamine (0.19 mL, 1.37 mmol) in CH$_3$CN (4.5 mL) was stirred at 45 °C. (Note: Initially 13e was only partially dissolved). After 1 h the precipitate was filtered off, washed with little amounts of cold CH$_3$CN and hexane and afterwards dried in vacuo to give 164 mg (77%) of pure 14e as a yellow solid.

![Chemical structure of 14e]

M.p.: 156-157 °C. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 2.56 (s, 6 H, Me), 3.89 (s, 6 H, OMe), 7.08 (s br, 2 H, 5'-H), 7.59 (s, 2 H, 2-H), 7.65 (s br, 2 H, 3'-H) ppm. $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ = 24.7 (q, Me),
Methyl 2-diazo-2-[3-methoxy-2,6-di(thiophen-2-yl)pyridin-4-yl]acetate (14f): Following the typical procedure, a solution of pyridyl nonaflate 13f\(^3\) (114 mg, 0.20 mmol), methyl diazoacetate (30 mg, 0.30 mmol), Pd(PPh\(_3\))\(_4\) (23 mg, 0.02 mmol) and triethylamine (41 µL, 0.30 mmol) in CH\(_3\)CN (2 mL) was stirred at 45 °C for 3 d. After work-up, the obtained crude product was purified by flash column chromatography on silica gel (hexane:EtOAc 9:1 to 8:2) to provide 21 mg (28%, 53% brsm) of 14f as a yellow oil and 53 mg of re-isolated starting material 13f. Excess methyl diazoacetate was removed under high vacuum at 50 °C.

\(^1\)H NMR (700 MHz, CDCl\(_3\)): \(\delta = 3.79, 3.95 \ (2 \text{ s, } 3 \text{ H each, OMe, CO}_2\text{Me}), 7.10 \ (dd, \ J = 3.6, 5.0 \text{ Hz, } 1 \text{ H, Thio}), \ 7.13-7.19 \ (m, 1 \text{ H, Thio}), \ 7.38 \ (dd, \ J = 1.1, 5.0 \text{ Hz, } 1 \text{ H, Thio}), \ 7.43-7.50 \ (m, 1 \text{ H, Thio}), \ 7.59 \ (dd, \ J = 1.1, 3.6 \text{ Hz, } 1 \text{ H, Thio}), \ 7.98 \ (dd, \ J = 1.1, 3.6 \text{ Hz, } 1 \text{ H, Thio}) \ 8.05 \ (s, 1 \text{ H, 5-H}) \text{ ppm.} \ ^{13}\text{C NMR (176 MHz, CDCl}_3\): \(\delta = 52.4 \ (q, \text{ OMe}), 60.3 \ (q, \text{ CO}_2\text{Me}), 115.1 \ (d, \text{ C-5}), 124.7, 127.7, 127.9, 128.0, 128.2, 128.5 \ (6 \text{ d, Thio}), 130.3, 140.7, 144.5, 145.4, 145.8, 148.0 \ (6 \text{ s, Thio, C-2/C-3/C-4/C-6}), 165.1 \ (s, \text{ CO}) \text{ ppm; the signal for the CN}_2-\text{group could not be detected. HRMS (ESI-TOF): } m/z \text{ calcd. for C}_{17}\text{H}_{14}\text{N}_3\text{O}_5\text{S}_2 [M+H]^+: 372.0471; \text{ found: 372.0460.}
Methyl 2-(5-benzyl-6-methyl-2,2'-bipyridin-4-yl)-2-diazoacetate (14g): Following the typical procedure, a solution of pyridyl nonaflate 13g[2] (284 mg, 0.51 mmol), methyl diazoacetate (76 mg, 0.76 mmol), Pd(PPh₃)₄ (41 mg, 0.04 mmol) and triethylamine (0.11 mL, 0.79 mmol) in CH₃CN (5 mL) was stirred at 45 °C for 4 d. The crude product was purified by flash column chromatography on silica gel (hexane:EtOAc 10:1; 2:1) to provide 152 mg of re-isolated starting material 13g and 68 mg of 14g (37%, 81% brsm) as a yellow oil.

![Chemical structure of 14g]

¹H NMR (500 MHz, CDCl₃): δ = 2.56 (s, 3 H, Me), 3.74 (s, 3 H, OMe), 4.14 (s, 2 H, CH₂), 6.98-7.00 (m, 2 H, Ph), 7.17-7.20 (m, 1 H, Ph), 7.23-7.26 (m, 2 H, Ph), 7.30 (ddd, J = 7.7, 4.8, 1.0 Hz, 1 H, 5'-H), 7.80 (td, J = 7.7, 1.8 Hz, 1 H, 4'-H), 8.30 (s, 1 H, 3-H), 8.41 (m, J = 7.7 Hz, 1 H, 3'-H), 8.66 (ddd, J = 4.8, 1.8, 1.0 Hz, 1 H, 6'-H) ppm. ¹³C NMR (126 MHz, CDCl₃): δ = 23.5 (q, Me), 35.5 (t, CH₂), 52.3 (q, OMe), 60.4 (s, C=N₂), 120.7 (d, C-3), 121.0 (d, C-3’), 123.6 (d, C-5’), 126.4, 127.7, 128.5 (3 d, Ph), 132.8 (s, C-5), 135.1 (s, C-4), 136.9 (d, C-4’), 138.2 (s, Ph), 149.2 (d, C-6’), 154.0, 155.7 (2 s, C-2, C-2’), 159.0 (s, C-6), 165.6 (s, CO) ppm. IR (ATR): ν = 3085-3000 (C-H), 2950, 2845 (C-H), 2090 (CN₂), 1705(C=O), 1580, 1540 (C=C, C=N), 1440, 1285 cm⁻¹. HRMS (ESI-TOF): m/z calcd. for C₂₁H₁₉N₄O₂ [M+H]⁺: 359.1515; found: 359.1503.

References


[2] For the preparation of pyrid-4-yl nonaflate 13b see: Dash, J.; Reissig, H.-U. *Chem. - Eur. J.* 2009, 15, 6811-6814; pyrid-4-yl nonaflates 13c, 13d, 13e and 13g were synthesized analogously.

3) $^1$H- and $^{13}$C-NMR Spectra of compound 14c