Supporting Information for

An Efficient Method for the Synthesis of Unsymmetrical 2,2’-Bis(pyrrolyl)alkanes.

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Table of contents

General procedure for the synthesis of N-benzylhydroxylamines SI2 – SI4

Copies of $^1$H and $^{13}$C NMR Spectra for compounds 1c, 1ca, 1f, 1fa, 1g, 1h, 1ha, 3a, 3b, 3c, 3d, 3e, 3f, 3g, 3h, 3i, 3j, 3k, 3l, 3m, 6a, 6b, 6c, 6d, 4a, 4b, 4c, 4d SI5-SI32
Nitrones A, B, C were prepared using Dondoni\textsuperscript{1} procedure for the preparation of N-benzyl nitrones. Nitrone D was prepared using the Murahashi\textsuperscript{2} method by oxidation of \(N,N\)-dibenzyamine.

![Nitrones A, B, C, D](image)

Typical procedure for the synthesis of \(N\)-benzylhydroxylamines.

Freshly distilled acetyl chloride (1 equiv) was added dropwise to anhydrous methanol at 0 °C and the mixture was stirred for 15 min. The appropriate nitrore (1.2 or 2 equiv) was added and the mixture was cooled at –78 °C before the addition of the pyrrole derivate (1 equiv). The media was then warmed to the appropriate temperature and stirred for the appropriate time. The mixture was treated with saturated aqueous NaHCO\textsubscript{3} solution and allowed to warm to room temperature. The pH value was then 8-9. The aqueous layer was extracted three times with CH\textsubscript{2}Cl\textsubscript{2}. The combined organic layers were washed with brine, dried over anhydrous MgSO\textsubscript{4} and concentrated. The obtained \(N\)-benzylhydroxylamine was purified by flash chromatography on silica gel pretreated with 3% of triethylamine (v/v).

\(N\)-Benzy-\(N\)-((4-ethyl-3,5-dimethyl-1\textsuperscript{H}-pyrrol-2-yl)(4-methoxyphenyl)methyl)hydroxylamine 1c. Prepared according to the above general procedure from nitrore A (588 mg, 2.44 mmol) in 12 mL of MeOH, acetyl chloride (96 mg, 1.22 mmol) and 2,4-dimethyl-3-ethylpyrrole 2c (150 mg, 1.22 mmol). The mixture was stirred at –78 °C for 1 hour. Purification (eluent: pentane/EtOAc, 7/3 to 4/6) afforded \(N\)-benzylhydroxylamine 1c (280 mg, 0.77 mmol, 63%) as a brown foam and the symmetrical 2,2′-bis(pyrrolyl)alkane 1ca as a yellow foam (60 mg, 0.16 mmol, 27%); mp 60-61 °C; \(v\)\textsubscript{max}/\textsubscript{cm} \(^{−1}\) 3450, 2960, 2925, 2850, 1690, 1506, 1250 and 1033; \(\delta\) (400 MHz; CDCl\textsubscript{3}) 9.4 (CH\textsubscript{N}), 3.44 (br, NH), 3.40, 2960, 2920, 2850, 1690, 1506, 1250 and 1033; \(\delta\) (400 MHz; CDCl\textsubscript{3}; Me\textsubscript{2}Si) 1.07 (3H, t, \(J = 7.5\) Hz, CH\textsubscript{3}), 1.94 (3H, s, CH\textsubscript{3}), 2.15 (3H, s, CH\textsubscript{3}), 2.39 (2H, q, \(J = 7.5\) Hz, CH\textsubscript{3}), 3.78-3.84 (4H, m, OCH\textsubscript{3}) and 1H of CH\textsubscript{2}Ph, 3.89 (1H, d, J = 13.5 Hz, 1H of CH\textsubscript{2}Ph), 4.59 (1H, br s, OH), 4.95 (1H, s, CHN), 6.86 (2H, d, J = 8.8 Hz, 2H\textsubscript{Ar}), 7.24-7.35 (7H, m, 7H\textsubscript{Ar}), 7.93 (1H, br s, NH); \(\delta\) (75 MHz; CDCl\textsubscript{3}) 9.4 (CH\textsubscript{N}), 11.4 (CH\textsubscript{3}), 15.9 (CH\textsubscript{3}), 17.8 (CH\textsubscript{3}), 55.4 (OCH\textsubscript{3}), 61.4 (CH\textsubscript{2}Ph), 65.5 (CH\textsubscript{N}), 113.9 (2CH\textsubscript{2}), 120.1 (C\textsubscript{O}), 122.5 (C\textsubscript{O}), 127.2 (CH\textsubscript{2}), 128.3 (2CH\textsubscript{2}), 128.9 (2CH\textsubscript{2}), 129.3 (2CH\textsubscript{2}), 134.2 (C\textsubscript{O}), 138.5 (C\textsubscript{O}), 158.7 (C-OCH\textsubscript{3}); MS (ESI\textsuperscript{+}) \(m/z\) 242 ([M+Na\textsuperscript{+}], 100); Elemental analysis, cald (%) for C\textsubscript{27}H\textsubscript{32}N\textsubscript{2}O\textsubscript{3}; C, 75.80; H, 7.75; N, 7.69. Found: C, 76.11; H, 7.94; N, 7.45.

3-Ethyl-5-((4-ethyl-5-methyl-1\textsuperscript{H}-pyrrol-2-yl)(4-methoxyphenyl)methyl)-2,4-dimethyl-1\textsuperscript{H}-pyrrole 1ca; mp 88-89 °C; \(v\)\textsubscript{max}/\textsubscript{cm} \(^{−1}\) 3444 (br, NH), 3401, 2960, 2920, 2850, 1690, 1506, 1250 and 1033; \(\delta\) (400 MHz; CDCl\textsubscript{3}; Me\textsubscript{2}Si) 1.05 (6H, t, \(J = 7.5\) Hz, 2CH\textsubscript{3}), 1.77 (6H, s, 2CH\textsubscript{3}), 2.09 (6H, s, 2CH\textsubscript{3}), 2.36 (4H, q, \(J = 7.5\) Hz, 2CH\textsubscript{2}), 3.79 (3H, s, OCH\textsubscript{3}), 5.37 (1H, s, CH), 6.83 (2H, d, J = 8.8 Hz, 2H\textsubscript{Ar}), 7.01 (2H, br s, 2NH), 7.07 (2H, d, J = 8.8 Hz, 2H\textsubscript{Ar}), \(\delta\) (75 MHz; CDCl\textsubscript{3}) 9.3 (2CH\textsubscript{2}), 11.2 (2CH\textsubscript{2}), 15.8 (2CH\textsubscript{2}), 17.9 (2CH\textsubscript{2}), 40.1 (CH\textsubscript{3}), 55.3 (OCH\textsubscript{3}), 113.6 (C), 114.0 (2CH\textsubscript{2}, 120.7 (2C), 121.3 (2C), 125.4 (2C), 129.5 (2CH\textsubscript{2}), 134.8 (2C), 158.2 (C). MS (ESI\textsuperscript{+}) \(m/z\) 387 ([M+Na\textsuperscript{+}], 100); HRMS (ESI\textsuperscript{+}) C\textsubscript{26}H\textsubscript{32}N\textsubscript{2}O\textsubscript{3} [M–H\textsuperscript{−}] requires 363.2430 found 363.2429.

N-Benzyl-N-((4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)(4-iodophenyl)methyl)hydroxylamine 1f. To anhydrous CH$_2$Cl$_2$ (2 mL) at -40 °C was added nitromethane B (122 mg, 0.36 mmol) followed by the addition of HCl (90 μL, 2.0 N in Et$_2$O, 0.18 mmol) and 3-acetyl-2,4-dimethylpyrrole 2b (25 mg, 0.18 mmol). The mixture was stirred at -40 °C for 24 hours and then treated with a saturated aqueous NaHCO$_3$ solution. The pH value was 8-9. The aqueous layer was extracted three times with CH$_2$Cl$_2$. The combined organic layers were washed with brine, dried over anhydrous MgSO$_4$ and concentrated. The crude product was purified by flash chromatography on silica gel (eluent: pentane/EtOAc, 1/1 to 1/4) to afford N-benzylhydroxylamine 1f (45 mg, 95 μmol, 52%) as a white solid and a mixture of the symmetrical bispyrrolylalkane and BnNH$_2$. The latter mixture was washed twice with aqueous HCl 0.1N to afford the symmetrical 2,2’-bis(pyrrolyl)alkane 1fa as a pink powder (4 mg, 8 μmol, 9%); mp 99-100 °C; $\nu_{max}$/cm$^{-1}$ 3409 (br, NH), 3323, 3028, 2938, 2869, 1615 (CO), 1484, 1349, 1406, 1251 and 1009; $\delta$ (400 MHz; CDCl$_3$; Me$_2$Si) 2.15 (3H, s, CH$_3$), 2.44 (3H, s, CH$_3$), 2.51 (3H, s, CH$_3$), 3.89 (2H, q, $AB$-J$_{AB} = 13.2$ Hz, CH$_2$Ph), 4.98 (2H, s, CHN and OH), 7.06 (2H, d, $J = 8$ Hz, 2H$_{Ar}$), 7.29-7.30 (5H, m, 5H$_{Ar}$), 7.63 (2H, d, $J = 8$ Hz, 2H$_{Ar}$), 8.70 (1H, br s, NH). $\delta$: 75 MHz; CDCl$_3$) 12.0 (CH$_3$), 15.6 (CH$_3$), 31.16 (CH$_3$), 61.8 (CH$_3$), 63.2 (CHN), 92.8 (C-I), 120.3 (C), 121.15 (C), 123.4 (C), 127.7 (2CH$_3$), 129.3 (2CH$_2$Ph), 129.4 (2CH$_2$Ph), 135.2 (C), 137.4 (C), 137.7 (2CH$_2$Ph), 140.7 (C), 195.5 (CO); MS (ESI$^+$/m/z 971 ([M+Na]$^+$), 50), 497 ([M+Na]$^+$), 50; Elemental Analysis, cald (%) for C$_{22}$H$_{23}$N$_2$O: C, 55.71; H, 4.89; N, 5.91. Found: C, 55.61; H, 4.80; N, 5.78.

1-(5-((4-acetyl-3,5-dimethyl-1H-pyrrol-2-yl)(4-iodophenyl)methyl)-2-methyl-1H-pyrrol-3-yl)ethanone 1fa; mp 160-161 °C; $\nu_{max}$/cm$^{-1}$ 3436 (br, NH), 3280, 2960, 2924, 2850, 1623 (CO), 1475, 1453, 1406 and 1002; $\delta$ (300 MHz; CDCl$_3$; Me$_2$Si) 2.11 (6H, s, 2CH$_3$), 2.33 (6H, s, 2CH$_3$), 2.37 (6H, s, 2CH$_3$), 5.49 (1H, s, CH), 6.80 (2H, d, $J = 8.4$ Hz, 2H$_{Ar}$), 7.57 (2H, d, $J = 8.4$ Hz, 2H$_{Ar}$), 8.54 (2H, br s, 2NH); $\delta$: 75 MHz; CDCl$_3$) 12.0 (2CH$_3$), 15.3 (2CH$_3$), 31.0 (2CH$_3$), 38.1 (CH), 92.6 (C-I), 117.0 (C), 121.8 (C), 125.6 (2C), 130.3 (2CH$_2$Ar), 134.8 (2C), 137.9 (2CH$_2$Ar), 140.7 (C), 196.1 (CO); MS (ESI$^+$/m/z 511 ([M+Na]$^+$), 23), 489 ([M+H]$^+$), 77; HRMS (ESI$^-$) C$_{27}$H$_{25}$O$_2$N$_2$INa ([M+Na]$^-$) requires 511.0852 found 511.0852.

N-benzyl-N-(1-(5-methyl-1H-pyrrol-2-yl)propyl)hydroxylamine 1g. Prepared according to the above general procedure from nitroene C (1.00 g, 6.13 mmol) in 25 mL of anhydrous MeOH, acetyl chloride (442 mg, 5.62 mmol) and 2-methylpyrrole 2a (425 mg, 5.24 mmol). The mixture was stirred at -40 °C during 2.5 hours. Purification (eluent: CH$_2$Cl$_2$/EtOAc, 95/5) afforded N-benzylhydroxylamine 1g (985 mg, 4.03 mmol, 77%) as a beige solid; mp 82-83 °C; $\nu_{max}$/cm$^{-1}$ 3444 (br, NH), 3219, 2967, 2863, 1579, 1493, 1450; $\delta$ (400 MHz; CDCl$_3$; Me$_2$Si) 0.82 (3H, t, $J = 7.5$ Hz, CH), 1.66-1.73 (1H, m, 1H of CH$_3$), 1.87-1.79 (1H, m, 1H of CH$_3$), 2.36 (3H, s, CH$_3$), 3.45-3.48 (2H, m, CHN and 1H of CH$_2$Ph), 3.63 (1H, d, $J = 13.5$ Hz, 1H of CH$_2$Ph), 5.77 (1H, br s, H$_{Ar}$), 5.87-5.85 (1H, s, H$_{Ar}$), 6.47 (1H, br s, OH), 7.21-7.29 (5H, m, 5H$_{Ar}$), 8.26 (1H, br s, NH). $\delta$: 100 MHz; CDCl$_3$) 11.6 (CH$_3$), 13.3 (CH$_3$), 25.5 (CH$_3$), 64.1 (CH$_3$), 65.7 (CHN), 104.9 (CH$_2$Ar), 108.6 (CH$_2$Ar), 127.3 (CH$_2$Ar), 127.7 (C), 128.3 (C), 128.3 (C), 129.8 (2CH$_2$Ar), 138.1 (C); MS (ESI$^-$) m/z 122 ([M+H$_2$N$^-$]$, 100); Elemental Analysis, cald (%) for C$_{13}$H$_{19}$N$_2$: C, 73.74; H, 8.26; N, 11.47. Found: C, 73.71; H, 8.27; N, 11.29.

N-benzyl-N-((5-methyl-1H-pyrrol-2-yl)(phenyl)methyl)hydroxylamine 1h. Prepared according to the above general procedure from nitromethane D (170 mg, 0.80 mmol) in 2.5 mL of anhydrous MeOH, acetyl chloride (32 mg, 0.40 mmol) and 2-methylpyrrole 2a (32 mg, 0.40 mmol). The mixture was stirred at -78 °C during 1.5 hour. Purification (eluent:
pentane/CH₂Cl₂ 20/80) afforded N-benzylhydroxylamine 1h (38 mg, 0.13 mmol, 32%) as a yellow solid and the symmetrical 2,2'-bis(pyrrolyl)alkane 1ha (10 mg, 40 µmol, 20%) as a yellow solid; mp 45-46 °C; ν max/cm⁻¹ 3516 (br, NH), 3431, 3024, 2920, 2902, 2850, 1488 and 1449; δH (400 MHz; CDCl₃; Me₄Si) 2.19 (3H, s, CH₃), 3.76 (2H, s, CH₂Ph), 4.71 (1H, br s, OH), 4.86 (1H, s, CH), 5.76 (1H, m, H₂Py), 5.88-5.90 (1H, m, H₂Py), 7.16-7.36 (10H, m, 10H Ar), 8.25 (1H, br s, NH); δC (75 MHz; CDCl₃) 13.3 (CH₃), 61.6 (CH₂), 68.4 (CHN), 105.5 (CH₂Py), 109.8 (CH₂Py), 127.3 (2CH₃), 127.4 (2CH₃), 128.3 (2CH₃), 129.3 (2CH₃), 138.3 (2C), 141.0 (2C); MS (ESI) m/z 170 ([MH-C₈H₁₃N]+, 100); Elemental analysis, cald (%) for C₁₉H₂₀N₂O: C, 78.06; H, 6.90; N, 9.59. Found: C, 77.96; H, 7.01; N, 9.45.

5,5'-(Phenylmethylene)bis(2-methyl-1H-pyrrole) 1ha: ν max/cm⁻¹ 3427 (br, NH), 3362, 2915, 2850, 1592, 1440 and 1410; δH (400 MHz; CDCl₃; Me₂Si) 2.21 (6H, s, 2CH₃), 5.36 (1H, s, CH), 5.75-5.77 (2H, m, 2HPy), 5.80 (2H, br s, 2HPy), 7.24-7.26 (3H, m, 3Hₐ), 7.30-7.32 (2H, m, 2Hₐ), 7.63 (2H, br s, 2NH); δC (100 MHz; CDCl₃) 13.1 (2CH₃), 44.2 (CH), 105.9 (2CH₂Py), 107.3 (2CHₐ), 126.9 (CHₐ), 127.3 (2Cₚy), 128.5 (2CH₃), 128.6 (2CH₃), 131.3 (2Cₚy), 142.5 (Cₚy); MS (DCI) m/z 251 ([M+H]+, 100).