EXPERIMENTAL

Melting points were determined on a capillary point apparatus equipped with a digital thermometer and are uncorrected.

The NMR spectra were recorded on a Varian Inova instrument, operating at 500 MHz for ^{1}H, 125 MHz for ^{13}C and 50 MHz for ^{15}N, equipped with a three channel, 5 mm, indirect detection probe, with z-axis gradients. The solvent was DMSO-d_6, and the temperature was 25 °C, unless specified otherwise. The chemical shifts for ^{1}H and ^{13}C were referenced to the residual solvent signal, 2.50 ppm for ^{1}H and 39.5 ppm for ^{13}C, on the tetramethylsilane scale. The chemical shifts for ^{15}N were referenced to Ξ = 10.1328898, corresponding to 0 for neat ammonia. On the Ξ scale the frequency of protons in tetramethylsilane is 100.0000000 MHz. For conversion to the neat nitromethane scale, subtract 381.7 ppm.

^{1}H spectra were acquired in one transient, with a 90 ° pulse, no relaxation delay and an acquisition time of 5 s, over a spectral window from 16 to -2 ppm. The FID was zero-filled to 131072 points prior to Fourier transform.

Typically, ^{1}H-^{13}C gHMBC spectra were acquired in 4096 points in *f2*, on a spectral window from 1.5 to 11 ppm, and 1 s relaxation delay. In *f1*, 512 increments were acquired in 1 transient over a spectral window from 170 to 10 ppm, then the corresponding FID's were zero-filled twice prior to the second Fourier transform.

^{1}H-^{15}N CIGAR-gHMBC spectra were acquired with a pulse sequence optimized for ^{15}N, as decribed in ref. [03MRC307]. 2048 points were acquired in *f2*, over a spectral window typically from 1.5 to 11 ppm, with 1 s relaxation delay. 1024 increments were acquired in *f1*, on a spectral window from 0 to 400 ppm, and the corresponding FID was zero-filled twice prior to Fourier transform. The accordion delay was optimized for a value of ^{1}H-^{15}N coupling constants between 3 and 10 Hz. The number of transients per increment was between 4 and 64, depending on the concentration of the sample. Total experiment time was in most cases, *ca*. 2 hrs.

Activation parameters for rotation have been measured in toluene-d8 by line-shape analysis using gNMR, in the temperature range 40 to 75 °C for compound **1**, 50 to 75 °C for compound **2**, and 0 to 45 °C for compound **3**. The temperature was raised on automation in steps of 5 °C, and 20 minutes were allowed for temperature equilibration before shimming at each temperature. For compound **4**, the measurements were done in DMSO-*d6* in the temperature range 115 to 150 °C. Because the sample decomposes at higher temperature, presumably by oxidation to the nitro compound, only 5 minutes were allowed for equilibration after a temperature change. The reading of the thermocouple was corrected according to the ethylene glycol standard.

2,3-Dimethyl-1-nitrosoindolizine (1)

A solution of sodium nitrite (0.67 g, 9.7 mmol) in water (10 mL) was slowly added at 0-5° C to a stirred solution of 2,3-dimethylindolizine (1.67 g, 9.6 mmol) in 5N HCl (30 mL). After 1 hr of stirring, 2N NaOH was added to make the solution slightly basic, and the reaction mixture was extracted with $CHCl_3$ (3 X 30 mL). The organic extracts were combined and dried over anhydrous $MgSO_4$. The solvent was then evaporated to dryness under reduced pressure to give a mixture of 2,3-dimethyl-1-nitrosoindolizine **1** as green microcrystals (83 %); m.p. 147.0 - 149.0° C. HRMS calc. for $[C_{10}H_{10}N_2O+H]^+$, 175.0866; Found: 175.0862.

Methyl 2-methyl-1-nitrosoindolizine-3-carboxylate (2)

A solution of sodium nitrite (2.2 g, 31.90 mmol) in water (10 mL) was slowly added at 0 - 5° C to a stirred solution of 2-methyl-indolizine-3-carboxylic acid methyl ester (3.9 g, 20.61 mmol) in glacial acetic acid (50 mL). After 30 min stirring at room temperature, the resulting brown solution was poured into water, and green microcrystals were collected. The obtained green microcrystals was washed with water and dried under vacuum to give methyl 2-methyl-1-nitrosoindolizine-3-carboxylate **2** (82 %); m.p. 131.0-132.0° C [Lit. m.p. 132.0-133.0° C][72JCS(P1)2954]

2-(Methylamino)-1-nitrosoindolizine-3-carboxylate (3)

A solution of sodium nitrite (1.7 g, 24.0 mmol) in water (10 mL) was slowly added at 0 -5˚ C to a stirred solution of 2-methyl-indolizine-3-carboxylic acid ethyl ester (4.45 g, 20.4 mmol) in glacial acetic acid (50 mL). The reaction was stirred for 3 hr at 0˚ C and then 2M NaOH was added dropwise to pH 7-8. The reaction mixture was extracted with DCM (3 X 0 mL) and the combined organic extracts were collected and dried over anhydrous MgSO4 and concentrated under reduced pressure. The residue was purified by column chromatography using EtOAC/hexanes as an eluent (1:1 to 4:1) to give 2-(Methylamino)-1-nitrosoindolizine-3-carboxylate **3** as green microcrystals (77 %), m.p. 156.0-157.0˚ C. Anal. Calc. for $C_{12}H_{13}N_3O_3$ (247.26): C, 58.29; H, 5.30; N, 16.99. Found: C, 57.96; H, 5.194; N, 17.36.

2-Methyl-3-nitrosoindolizine (4)

This compound was prepared according to literature [46JCS1075]. M. p. 99.0-100.0˚ C [lit. m.p. 103.5-106˚ C] [46JCS1075]. Anal. Calc. for $C_9H_8N_2O$ (160.18): C, 67.49; H, 5.03; N, 17.48. Found: C, 67.17; H, 5.13; N, 17.48.

2,6,7-Trimethyl-5-nitrosopyrrolo[1,2-b]pyridazine (5)

A solution of sodium nitrite (2.2 g, 30 mmol) in water (10 mL) was slowly added at 16-20˚ C to a stirred solution of 2,6,7-Trimethylpyrrolo[1,2-b]pyridazine (4.8 g , 30 mmol) in glacial acetic acid (20 mL). After 30 min of stirring, the resulting brown solution was poured into water (100 mL), neutralized with $NaHCO_3$, and extracted with dichloromethane. The extract was dried over $MgSO_4$, distilled under vacuum, and the residue was crystallized from methanol to give green crystals of 2,6,7-trimethyl-5-nitrosopyrrolo[1,2-b]pyridazine (97%), m.p. 132-133˚C. Anal. Calc. for $C_{10}H_{11}N_3O$ (189.22): C, 63.48; H, 5.86; N, 22.21. Found: C, 63.82; H, 5.94; N, 22.17. HRMS (ESI) Calc. For $[C_{10}H_{11}N_3O+H]^+$: 190.0975. Found: 190.0967.

4-Methoxy-3-nitrosopyrazolo[1,5-a]pyridine (6)

A solution of sodium nitrite (0.44 g, 4.6 mmol) in water (2 mL) was slowly added at 0^{o}C to a stirred solution 4-methoxypyrazolo[1,5-a]pyridine (0.5 g , 3.4 mmol) in glacial acetic acid (4 mL). After 1h green solid precipitate, filtered, washed with water and dried in vacuum to give 4-methoxy-3-nitrosopyrazolo[1,5-a]pyridine **7** (32%), m.p. 216.0-218.0˚ C. HRMS (ESI) calc. for $[C_8H_7N_3O_2+H]^+$, 178.0611; Found: 178.0615.

2-Methylindolizine (10)

This compound was prepared according to literature method [46JCS1069]. M. p. 60.0-61.0˚ C [lit. m.p. 57.0-59.0˚ C] [46JCS1069].

2,6,7-trimethylpyrrolo[1,2-b]pyridazin-5-yl)acetamide (11)

2,6,7-Trimethylpyrrolo[1,2-b]pyridazin-5-amine (1.75 g, 10 mmol) was dissolved in a mixture of toluene (20 mL) and acetic anhydride (2.02 g, 20 mmol) at room temperature. The reaction mixture was stirred for extra 1 hr and the yellow precipitate was filtered and washed with diethyl ether (50 mL) to give 2,6,7-trimethylpyrrolo[1,2-b]pyridazin-5-yl)acetamide **3** (92 %), m.p. 239-240˚ C. Anal. Calc. for $C_{12}H_{15}N_3O$ (217.27): C, 66.34; H, 6.96; N, 19.34. Found: C, 65.65; H, 7.02; N, 19.07.

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