

Structural chemistry of oximes

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General experimental details

^1H NMR spectra were recorded on a Varian Unity plus 400 MHz spectrometer in CDCl_3 or d_6 -DMSO. Data is expressed in parts per million (ppm) downfield shift from tetramethylsilane or residual protiosolvent as internal reference and are reported as position (in ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constant (J in Hz) and integration (number of protons). Melting points were recorded on a Fisher-Johns melting point apparatus and are uncorrected. All the chemicals were purchased from Aldrich and used without further purification, unless otherwise noted.

Synthesis of 4-iodobenzaldehyde oxime, 1

In a mortar, 0.250 g (1.08 mmol) of 4-iodobenzaldehyde and 0.090 g (1.29 mmol) of hydroxylamine hydrochloride is ground together with a pestle. Then, 0.052 g (1.29 mmol) of crushed sodium hydroxide is added and the mixture is ground further with the addition of 0.1-0.2 mL methanol, for 2 minutes at room temperature. The reaction mixture is left for 5 minutes, after which it is ground for another 2 minutes with 0.1-0.2 mL methanol. At this stage the reaction is monitored by TLC. Upon completion of the reaction, a ^1H NMR spectrum of the crude mixture is taken in d_6 DMSO to confirm the formation of product. The crude mixture is washed with water to get rid of any inorganic salts and it is air dried. Colorless plate shaped crystals suitable for single-crystal X-ray diffraction were grown using slow evaporation from ethyl acetate under ambient conditions. Yield: 0.163 g (61%); mp 100-102°C (lit., 1 101-103°C); ^1H NMR (δ_{H} ; d_6 -DMSO, 400MHz): 7.38 (d, $J=1.00$ Hz, 2 H), 7.76 (d, $J=1.00$ Hz, 2 H), 8.10 (s, 1 H), 11.34 (s, 1 H).

Synthesis of 4-cyanoacetophenone oxime, 2

In a mortar, 0.250 g (1.72 mmol) of 4-acetylbenzonitrile and 0.144 g (2.07 mmol) of hydroxylamine hydrochloride is ground together with a pestle. Then, 0.083 g (2.07 mmol) of crushed sodium hydroxide is added and the mixture is ground further with the addition of 0.1-0.2 mL methanol, for 2 minutes at

room temperature. The reaction mixture is left for 5 minutes, after which it is ground for another 2 minutes with 0.1-0.2 mL methanol. At this stage the reaction is monitored by TLC. Upon completion of the reaction, a ^1H NMR spectrum of the crude mixture is taken in d_6 DMSO to confirm the formation of product. The crude mixture is washed with water to get rid of any inorganic salts and it is air dried. Colorless prism shaped crystals suitable for single-crystal X-ray diffraction were grown using slow evaporation from ethyl acetate under ambient conditions. Yield: 0.199 g (72%); mp 150-153°C (lit.,² 150-153°C); ^1H NMR (δ_{H} ; d_6 -DMSO, 400MHz): 2.17 (s, 3 H), 7.81-7.88 (m, 4 H), 11.67 (br. s., 1 H).

Synthesis of 4-bromoacetophenone oxime, 3

In a mortar, 0.250 g (1.26 mmol) of 4-bromoacetophenone and 0.105 g (1.51 mmol) of hydroxylamine hydrochloride is ground together with a pestle. Then, 0.060 g (1.51 mmol) of crushed sodium hydroxide is added and the mixture is ground further with the addition of 0.1-0.2 mL methanol, for 2 minutes at room temperature. The reaction mixture is left for 5 minutes, after which it is ground for another 2 minutes with 0.1-0.2 mL methanol. At this stage the reaction is monitored by TLC. Upon completion of the reaction, a ^1H NMR spectrum of the crude mixture is taken in d_6 DMSO to confirm the formation of product. The crude mixture is washed with water to get rid of any inorganic salts and it is air dried. Colorless plate shaped crystals suitable for single-crystal X-ray diffraction were grown using slow evaporation from methanol under ambient conditions. Yield: 0.226 g (84%); mp 126-129°C (lit.,³ 128-130°C); ^1H NMR (δ_{H} ; d_6 -DMSO, 400MHz): 2.14 (s, 3 H), 7.54-7.61 (m, 4 H), 11.32 (s, 1 H).

Synthesis of 4-iodoacetophenone oxime, 4

In a mortar, 0.250 g (1.02 mmol) of 4-iodoacetophenone and 0.085 g (1.22 mmol) of hydroxylamine hydrochloride is ground together with a pestle. Then, 0.049 g (1.22 mmol) of crushed sodium hydroxide is added and the mixture is ground further with the addition of 0.1-0.2 mL methanol, for 2 minutes at room temperature. The reaction mixture is left for 5 minutes, after which it is ground for another 2

minutes with 0.1-0.2 mL methanol. At this stage the reaction is monitored by TLC. Upon completion of the reaction, a ^1H NMR spectrum of the crude mixture is taken in d_6 DMSO to confirm the formation of product. The crude mixture is washed with water to get rid of any inorganic salts and it is air dried. Yellow prism shaped crystals suitable for single-crystal X-ray diffraction were grown using slow evaporation from ethyl acetate under ambient conditions. Yield: 0.207 g (78%); mp 156-160°C (lit.,⁴ 156-158°C); ^1H NMR (δ_{H} ; d_6 -DMSO, 400MHz): 2.12 (s, 3 H), 7.44 (d, J = 8.6 Hz, 2 H), 7.75 (d, J = 8.6 Hz, 2 H), 11.30 (s, 1 H).

Synthesis of (z)-2-(4-bromophenyl)-N'-hydroxyacetimidamide, 5

In a round-bottom flask, 4-bromophenylacetonitrile (0.200g, 1.02 mmol) was dissolved in 50 ml of methanol. Hydroxylamine hydrogen chloride (0.142 g, 2.04 mmol) and a solution of NaOH (0.082g, 2.04 mmol) in 15 ml of water was added to the round-bottom flask. The mixture was then refluxed for 24 hours. Once the absence of starting material was confirmed via TLC, methanol was removed under reduced pressure, and the obtained solid was washed with water, and recrystallized in methanol to yield colorless prisms. Yield: 0.117 g (50%); mp 120-124°C (lit.,⁵ 133-135°C); ^1H NMR (δ_{H} ; d_6 -DMSO, 400MHz): 3.22 (s, 2 H), 5.44 (s, 2 H), 7.22 (d, J =8.4 Hz, 2 H), 7.47 (d, J =8.4 Hz, 2 H), 8.92 (s, 1 H).

Synthesis of 1,4-bis(cyanooximinomethyl)benzene, 6

In an Erlenmeyer flask, 1,4-phenylenediacetonitrile (0.400 g, 2.56 mmol) was dissolved in 2-propanol, and was added to a solution of Na metal (0.250 g, 10.87 mmol) in 2-propanol (540 mL). The solution immediately turned blue. A separate 500-mL three-necked flask was equipped with a stir bar, 10.0 g of NaNO_2 , 100 mL of distilled H_2O , and 50 mL of methanol. The NaNO_2 was allowed to dissolve with stirring. A greased septum was introduced into one neck, and a greased one-hole rubber stopper was placed firmly into the central neck. A dropper funnel (125 mL) was greased and attached to the third neck with a Keck clip. A solution of 2:1 $\text{H}_2\text{O}/\text{H}_2\text{SO}_4$ (50 mL) was prepared and kept in an ice bath ($\sim 4^\circ\text{C}$).

After a glass U-tube apparatus was assembled between the *i*-PrONa/acetonitrile solution in the Erlenmeyer flask and the NaNO₂/H₂O/MeOH solution in the three-necked flask, the acid/water solution was placed into the dropper funnel, and the acid/water solution was added dropwise to the NaNO₂/H₂O/MeOH solution inside the flask. Small bubbles of the evolving CH₃ONO gas were immediately seen upon the reaction of the acid with the sodium nitrite. Methyl nitrite gas flowed into the Erlenmeyer flask as observed by gas bubbles under the surface of *i*-PrONa/acetonitrile solution. The solution changed color from blue to green to yellow, and the solution turned cloudy thereafter. The acid/water mixture was slowly added to the NaNO₂/H₂O/MeOH solution in small aliquots until all was added (about 1 h). The U-tube apparatus was dismantled, and the now cloudy *i*-PrONa/acetonitrile/CH₃ONO solution was placed under an N₂ atmosphere. The solution was left to stir for 3 days, after which the solid was filtered off. It was then dissolved in water and upon acidification to ~pH 2 a white precipitate emerged. The remaining 2-propanol was removed from the filtrate to leave behind an orange solid. The solid was dissolved in water and acidified with 1M HCl to form a pale yellow solid, which was then recrystallized from water to yield colorless plates. Yield: 0.451 g (87%); mp 240-247°C (dec.); ¹H NMR (δ_H; d₆-DMSO, 400MHz):⁶ 7.87 (s, 4 H), 14.05 (s, 2 H).

X-ray crystallography

Table 1. Crystallographic data for 1-6

	1	2	3	4	5	6
Systematic name	4-iodobenzaldehyde oxime	4-cyanoacetophenone oxime	4-bromoacetophenone oxime	4-iodoacetophenone oxime	(z)-2-(4-bromophenyl)-N'-hydroxyacetimidamide	1,4-bis(cyanooximinomethyl) benzene
Formula moiety	C ₇ H ₆ INO	C ₉ H ₈ N ₂ O	C ₈ H ₈ BrNO	C ₈ H ₈ INO	C ₈ H ₉ BrN ₂ O	C ₁₀ H ₆ N ₄ O ₂
Empirical formula	C ₇ H ₆ INO	C ₉ H ₈ N ₂ O	C ₈ H ₈ BrNO	C ₈ H ₈ INO	C ₈ H ₉ BrN ₂ O	C ₁₀ H ₆ N ₄ O ₂
Molecular weight	247.03	160.17	214.06	261.05	229.08	214.19
Color, Habit	colourless plate	colourless prism	colourless plate	yellow prism	colourless prism	colourless plate
Crystal system	Triclinic	Monoclinic	Triclinic	Triclinic	Monoclinic	Orthorhombic
Space group, Z	P-1, 2	P2 ₁ /c, 4	P-1, 4	P-1, 4	P2 ₁ , 2	Pbca, 4
a, Å	7.2039(6)	7.8002(6)	9.3167(10)	9.4291(11)	7.5420(13)	5.1610(6)
b, Å	7.3949(6)	7.5923(6)	9.4251(10)	9.8004(12)	5.2358(10)	11.1506(12)
c, Å	7.7816(7)	13.8966(10)	10.9584(12)	11.1290(12)	10.9174(18)	16.0413(18)
α , °	107.835(3)	90.00	100.324(5)	101.367(3)	90.00	90.00
β , °	100.821(3)	90.298(3)	102.635(5)	101.044(3)	90.495(5)	90.00
γ , °	90.778(3)	90.00	112.088(4)	113.824(3)	90.00	90.00
V, Å ³	386.48(6)	822.97(11)	832.88(16)	879.16(18)	431.09(13)	923.15(18)
X-ray wavelength	0.71073	0.71073	0.71073	0.71073	0.71073	0.71073
μ , mm ⁻¹	4.071	0.088	4.874	3.585	4.718	0.114
Absorption corr	multi-scan	multi-scan	multi-scan	multi-scan	multi-scan	none
T min / max	0.338 / 0.792	0.971 / 0.988	0.442 / 0.528	0.534 / 0.615	0.397 / 0.484	N/A
Reflections						
collected	9716	10135	18378	26665	6535	13112
independent	2515	2834	5858	5705	2356	1443
observed	2395	2082	4872	5082	2237	1190
Threshold expression	>2 σ (I)	>2 σ (I)	>2 σ (I)	>2 σ (I)	>2 σ (I)	>2 σ (I)
R ₁ (observed)	0.0194	0.0644	0.0247	0.0260	0.0267	0.0437
wR ₂ (all)	0.0507	0.2202	0.0641	0.0765	0.0632	0.1418
S	0.962	1.527	1.038	1.077	1.052	1.365
$\Delta\rho$ max / min	0.741 / -0.554	0.544 / -0.291	0.479 / -0.387	0.606 / -1.474	0.562 / -0.761	0.348 / -0.266

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