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Synthesis of *O*-Alkylbenzohydroximoyl Iodides and a Comparison of their Structures to other Oxime Derivatives

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Abstract The first general synthesis of (Z)-O-alkylbenzohydroximidoyl iodides [ArC(I)=NOR] is reported. X-ray crystallographic structures of two of these compounds confirm that they are in the Z-configuration: p-NO₂ArC(I)=NOCH₃ crystallizes in space group Pnma with lattice constants a = 12.682(2) Å, b = 6.5217(15) Å, and c = 11.755(2) Å, and p-ClArC(I)=NOCH₃ crystallizes in space group $P2_1/n$ with lattice constants a =15.670(4) Å, b = 5.742(4) Å, and c = 27.156(7) Å and beta angle 102.71(2). Their structures are compared to other *O*-alkylbenzohydroximoyl halides including p-NO₂ArC(F)=NOCH₃ which crystallizes in space group $P2_1/c$ with lattice constants a = 3.8475(10) Å, b =22.501(5) Å, and c = 10.088(2) Å and beta angle

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A. S. McKim Gaylord Chemical Company, L.L.C., Bogalusa, LA 70427, USA 91.130(11). The synthesis of two additional compounds containing the N-alkoxyimine moiety {methyl (Z)-Omethyl-4-nitrobenzothiohydroximate $[p-NO_2ArC(SCH_3)=$ NOCH₃] which crystallizes in space group P2₁/n with lattice constants a = 11.8046(15) Å, b = 7.0774(10) Å, and c = 12.2741(15) Å and beta angle 100.401(9) and (Z)-Omethyl-4-nitrobenzohydroximoyl azide $[p-NO_2ArC(N_3)=$ NOCH₃] which crystallizes in space group $P2_1/c$ with lattice constants a = 11.753(2) Å, b = 11.310(3) Å, and c = 7.351(2) Å and beta angle 103.805(15) are also reported. Their structures are compared to (Z)-ethyl benzohydroximate [PhC(OEt)=NOH] and (Z)-O-methyl-4nitrobenzohydroximoyl cyanide [p-NO₂ArC(CN)=NOCH₃] respectively. Characterizations include spectrometric identifications employing IR, ¹H-NMR, ¹³C-NMR and mass spectrometry.

Keywords Imidoyl iodide \cdot Imidoyl azide \cdot *N*-alkoxyimine \cdot *N*-alkoxyimidoyl halide \cdot Oxime thioether \cdot Thiohydroximate

Introduction

The use of the oxime ether or *N*-alkoxyimine moiety (C=N–OR) in pharmaceutical and agricultural compounds is becoming more widespread [1]. Current methods to incorporate this functional group often result in both geometric isomers of the oxime ether which then need to be identified and separated [1a,b,f, 2]. The differences in the ¹H- and ¹³C-NMR chemical shifts between the *Z* and *E* isomers of *N*-methoxyimines are small and assignment of configuration cannot be unambiguously made on the basis of spectroscopic measurements. Attempts to assign geometric configurations in *N*-methoxyimines using dipole

moment measurements have lead to incorrect assignments [3].

There is particular interest in developing new methods of incorporating the N-alkoxyimine moiety into molecules in a single, predictable E or Z configuration. We are currently working on techniques that begin with imidoyl halides (1Za-1Zn). Additionally, N-methoxyimines (C=N- OCH_3) that contain a leaving group attached to the carbon of the carbon-nitrogen double bond have high barriers to thermal Z/E isomerization and are therefore ideally suited for studies on the stereochemistry and mechanisms of nucleophilic substitution (Scheme 1) at the carbon-nitrogen double bond. Because both the synthetic method development and the mechanistic investigations require accurate knowledge of the configurations (Z or E) of compounds containing the N-alkoxyimine group, this paper examines the structure and geometry of the N-alkoxyimidoyl halides and the azide and thioether products produced from the imidoyl halides as determined by X-ray crystallography.

The syntheses of *O*-alkylbenzohydroximoyl chlorides and bromides have been known for some time. We have recently published the synthesis of the *O*-alkylbenzohydroximoyl fluorides (*N*-alkoxybenzenecarboximidoyl fluorides) like **1Za** (Scheme 2) [4]. The assignment of geometric configuration of the fluorides at that time was based on ¹H-NMR chemical shifts of the *N*-methoxy groups and by analogy with the previously prepared imidoyl chlorides. We now confirm that geometric assignment with an X-ray crystal structure of **1Za**.

A second product produced in the synthesis of the fluorides is a thioether **1Zo**. **1Zo** presumably arises from reaction of **1Za** with the solvent (DMSO). The isolation, characterization, and an alternate synthetic method of these



Scheme 1 Thermal stability of *N*-alkoxyimidoyl compounds and the potential stereochemistry of the products of nucleophilic substitution



Scheme 2 Synthesis of 1Za and 1Zo

compounds has been previously reported [5]. In the present work the structure 1Zo has been unambiguously determined by X-ray crystallography. Additionally, we have found that reaction of 1Zh with sodium azide ion results in *O*-methyl-4-nitrobenzohydroximoyl azide (1Zp). The X-ray structure of this compound too is discussed.

The imidoyl fluorides were initially made in the interest of further understanding the mechanism of nucleophilic substitution at the carbon atom of the C=N bond of an *N*-alkoxyimine. It was found that the fluorides react much faster than the bromide (**1Zc-h** and **1Ec-h**) or chloride (**1Zb** or **1Eb**) analogue in these reactions and result exclusively in retained stereochemistry about the C=N bond [6]. These findings have opened up synthetic opportunities involving nucleophilic substitution by carbon nucleophiles at the C=N bond of *N*-alkoxyimidoyl halides which are currently being explored [7].

To complete the series of N-alkoxyimidoyl halides, we now report the first general synthesis of O-alkylbenzohydroximoyl iodides (N-methoxybenzocarboxyimidoyl iodides). The synthesis of N-hydroxyimidoyl iodides has been reported by the reaction of an organometallic reagent with a β -nitrostyrene to generate the nitronate for subsequent reaction with hydroiodic acid [8]. Only one iodide compound (2,2-diphenylpropanohydroximoyl iodide) was synthesized by this method as other attempts yielded compounds too unstable to characterize. N-alkylimidoyl iodides have also been reported to be generated in situ by reaction of an acylated oxime with trimethylsilyl iodide or diethylaluminum iodide [9]. Generation of these iodide compounds was inferred from NMR studies and subsequent reaction with nucleophiles, but the compounds were not isolated. The synthesis of N-(benzyloxy)-2,2,2-trifluoroacetimidoyl iodide has been reported [10], but to our knowledge this is the only incident of an N-alkoxyimidoyl iodide having been synthesized. The synthesis of N-aryltrifluoroacetimidoyl

iodides have also been reported [11]. These compounds were made by the reaction of the corresponding chloride compound with sodium iodide in acetone. We have found this procedure to be ineffective in the synthesis of N-alkoxyimidoyl iodides. This paper reports a modification to this procedure whereby N-alkoxyimidoyl iodides (1Zi-1Zn) are synthesized from the corresponding N-alkoxyimidoyl bromide (1Zc-1Zh). These compounds prove to be stable enough for purification and isolation. X-ray crystal structure determination has been performed on two of the Z-imidoyl iodides (1Zm and 1Zn), and these structures are compared to those of the other imidoyl halides. The structures of all the N-alkoxyimidoyl halides, thioether, and azide will be compared to one another and to other compounds containing the N-alkoxyimine or N-hydroxyimine group, paying special attention to the planarity of these molecules (Table 1).

Experimental Data

General Methods

¹H-NMR spectra were acquired at 300.13 MHz, and the ¹³C-NMR spectra at 75.47 MHz using a Bruker AC 300 spectrometer in (²H) chloroform. Low resolution GC-MS data was collected on a Hewlett-Packard 5890 Series II GC with a HP-1 crosslinked methyl silicone gum column (12 m × 0.2 mm × 0.33 µm film thickness) and a Hewlett-Packard 5971 series mass selective detector. Ultraviolet spectral data were recorded with 95% ethanol as a solvent on a Shimadzu UV-2101PC Spectrometer. Infrared spectral data were recorded on a Perkin-Elmer 16 PC FTIR or a Nicolet Magna 560 FTIR over the frequency range of 4000–600 cm⁻¹. New compounds gave a single peak in the GC-MS and showed the required number of carbons in the

Table 1N-alkoxyimines



Compounds 1Z and 1E	Х	Y	R
1Za & 1Ea	F	NO ₂	CH ₃
b	Cl	NO_2	CH ₃
c	Br	Н	CH ₃
d	Br	CH ₃	CH ₃
e	Br	OCH ₃	CH ₃
f	Br	Cl	CH ₃
g	Br	Cl	<i>i</i> -Pr
h	Br	NO_2	CH ₃
i	Ι	Н	CH ₃
j	Ι	CH ₃	CH ₃
k	Ι	OCH ₃	CH ₃
1	Ι	Cl	CH ₃
m	Ι	Cl	<i>i</i> -Pr
n	Ι	NO_2	CH ₃
0	SCH ₃	NO_2	CH ₃
р	N ₃	NO_2	CH ₃
q	CN	NO_2	CH ₃

¹³C-NMR spectrum. The iodo compounds were further characterized from their high-resolution mass spectra. Exact masses were obtained by the Central Science Laboratory at the University of Tasmania. Elemental analyses were performed by Midwest Microlabs, LLC, in Indianapolis, IN.

X-ray Data Collection and Structure Determination¹

Intensity data were collected using graphite monochromated MoK α radiation ($\lambda = 0.71073$ Å) on a Nonius KappaCCD diffractometer fitted with an Oxford Cryostream cooler. Data reduction included absorption corrections by the multi-scan method for **1Zn** and **1Zo**. Crystal data and experimental details are given in Table 2. Structures were solved by direct methods and refined by full-matrix least squares, using SHELXL97 [12]. Hydrogen atoms were treated as riding in idealized positions, with a torsional parameter refined for each methyl group.

For 1Zm, X-ray data were collected on an ENRAF-Nonius CAD-4 diffractometer with monochromated MoK α radiation ($\lambda = 0.71073$ Å). Crystals were mounted by epoxy on glass fibers. Data were collected using a θ -2 θ technique. Data reduction included absorption corrections by the ψ -scan method. Crystal data and experimental details are also given in Table 2. Structures were solved by direct methods and refined by full-matrix least squares, using NRC386 (PC version of NRCVAX) [13]. Hydrogen atoms were treated as riding in idealized positions, with map positions for each methyl group that were subsequently idealized.

General Procedure for the Preparation of *N*-Alkoxyimidoyl Bromides (**1Zc-1Zh**)

The procedure for the synthesis of these compounds is as that described by Johnson et al. [14] in their synthesis of (Z)-O-methyl-4-nitrobenzohydroximoyl bromide (**1Zh**).

O-Isopropyl-4-chlorobenzohydroximoyl Bromide (1Zg)

Following the above general procedure, using *O*-isopropyl-4-chlorobenzohydroxamate (17.218 g, 0806 mol) a yellow semi-solid material was obtained which was recrystallized in methanol. The first recrystallization yielded light tan crystals (16.177 g, 73%). A second recrystallization in methanol yielded white crystals (12.210 g, 55%), mp 37.0–37.5 °C, $R_{\rm f}$ (hexane, alumina) = 0.88. FT-IR (nujol mull) 829, 996, 1092, 1465, 1583, 1592 cm⁻¹. ¹H-NMR (300 MHz, CDCl₃) δ 1.39 (d, $J_{\rm HH}$ = 6.4 Hz, 6H, CH₃), 4.61 (m, $J_{\rm HH}$ = 6.2, 1H, OCH), 7.36 (d, $J_{\rm HH}$ = 8.6 Hz, 2H, ArH), 7.79 (d, $J_{\rm HH}$ = 8.6 Hz, 2H, ArH); ¹³C-NMR (75 MHz, CDCl₃) δ 21.6, 77.8, 127.9, 128.5, 129.3, 132.8, 136.3. GC-MS: m/z 277 (18%), 275 (M, 13), 235 (11), 233 (9), 198 (4), 196 (14), 156 (32), 154 (100), 139 (11), 137 (35), 125 (11), 123 (20), 113 (9), 111 (29), 102 (23), 75 (18). Anal. Calcd. For C₁₀H₁₁ClBrNO (%): C, 43.43; H, 4.01; Br, 28.89; Cl, 12.82; N, 5.06; Found: C, 43.22; H, 4.02; Br, 28.51; Cl, 12.66; N, 4.96.

General Procedure for the Preparation of *N*-Alkoxyimidoyl Iodides (**1Zi-1Zn**)

The corresponding *N*-alkoxyimidoyl bromide (**1Zc-1Zh**) (~2 mmol) and sodium iodide (~20 mmol) in sulfolane (12 mL) were heated between approximately 95 and 105 °C for 2–4 days under nitrogen purge. On cooling, this mixture was poured into 100 mL of saturated sodium thiosulfate solution. This was extracted with hexane (5 × 100 mL). The hexane extract was dried with anhydrous magnesium sulfate, filtered, and the solvent was removed by rotary evaporation. Samples were purified by preparative GLC for spectral analysis and characterization.

(Z)-O-Methylbenzohydroximoyl Iodide (1Zi)

This compound was obtained as a viscous liquid by the above procedure with the temperature being maintained at 105 °C for approximately two days (yield ~51%). No other compound was seen by GC-MS after work-up. FT-IR (neat): 942, 1046, 1249, 1444, 1556, 1584, 2817, 2896, 2936, 2975, 3057 cm⁻¹. ¹H-NMR (300 MHz, CDCl₃) δ 4.21 (s, 3H, OCH₃), 7.38 (m, 3H, ArH), 7.78 (d, *J* 6.1 Hz, 2H, ArH). ¹³C-NMR (75 MHz, CDCl₃) δ 62.58, 116.78, 128.26, 129.36, 130.29, 136.13. GC-MS: *m/z* 261 (M, 7.9%), 134 (100), 127 (23.4), 119 (80.8), 103 (72.1), 91 (13.0), 76 (37.3). (Found: M⁺⁺, 260.96506. C₈H₈INO requires 260.96506).

(Z)-O-Methyl-4-methylbenzohydroximoyl Iodide (1Zj)

This compound was obtained as a viscous liquid by the above procedure with temperature being maintained at 97 °C for approximately three days. GC-MS revealed this to be 98.6% **1Zj** and 1.4% starting material **1Zb**. (Yield of

¹ Supplementary crystallographic data for this paper in CIF format can be obtained, free of charge, via http://www.ccdc.cam.ac.uk/conts/ retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K. (Fax: 44–1223–336033 or e-mail: deposit@ccdc.cam.ac.uk)

Table 2	Crystal	data,	data	collection	and	refinement	parameters
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Compound	1Zm	1Zn	1Za	1Zo	1Zp
CCDC deposition #	CCDC 646439	CCDC 645654	CCDC 645655	CCDC 645656	CCDC 645657
Formula	C ₁₀ H ₁₁ NOCII	$C_8H_7N_2O_3I$	$C_8H_7N_2O_3F$	$C_9H_{10}N_2O_3S$	C ₈ H ₇ N ₅ O ₃
Color/shape	Colorless slice	Colorless needle	Colorless needle	Colorless fragment	Colorless fragment
Formula weight	323.6	306.1	198.2	226.3	221.2
Crystal system	Monoclinic	Orthorhombic	Monoclinic	Monoclinic	Monoclinic
Space group	P2 ₁ /n	Pnma	P2 ₁ /c	P2 ₁ /n	P2 ₁ /c
Temp., K	293	110	110	110	115
Cell constants					
<i>a</i> , Å	15.670(4)	12.682(2)	3.8475(10)	11.8046(15)	11.753(2)
<i>b</i> , Å	5.742(4)	6.5217(15)	22.501(5)	7.0774(10)	11.310(3)
<i>c</i> , Å	27.156(7)	11.755(2)	10.088(2)	12.2741(15)	7.351(2)
β , deg.	102.71(2)	-	91.130(11)	100.401(9)	103.805(15)
Cell volume, Å ³	2383.5(19)	972.2(3)	873.2(3)	1008.6(2)	948.9(4)
Formula units/cell	8	4	4	4	4
$D_{\rm calc}, {\rm g/cm}^{-3}$	1.803	2.091	1.507	1.490	1.548
$\mu_{\rm calc}, {\rm mm}^{-1}$	2.85	3.276	0.130	0.309	0.123
Transm. coeff.	0.701-0.997	0.639-0.695	-	0.913-0.941	-
Diffractometer/scan	Enraf-Nonius CAD4/0-20	Nonius KappaCCD/ ω	Nonius KappaCCD/w	Nonius KappaCCD/ ω	Nonius KappaCCD/ ω
Radiation	MoK α ($\lambda = 0.71073$ Å)				
Crystal size, mm	$0.2\times0.4\times0.5$	$0.12\times0.13\times0.15$	$0.08 \times 0.12 \times 0.27$	$0.20 \times 0.25 \times 0.30$	$0.17 \times 0.30 \times 0.42$
Reflections measured	4449	12,477	10,870	20,423	11,399
R _{int}	0.085	0.022	0.022	0.019	0.022
Independent reflections	2226	2383	1777	3431	2165
θ range, deg	$2 < \theta < 20$	$3.2 < \theta < 35.6$	$2.5 < \theta < 26.4$	$2.5 < \theta < 32.6$	$2.5 < \theta < 27.5$
Range of h, k, l	±15, 0-5, 0-26	±20, ±10, ±18	±4, ±27, ±12	±17, ±10, ±18	±15, ±14, ±9
Reflections observed	1638	1905	1392	2790	1695
Criterion for observed	$I > 2.5\sigma$ (I)	$I > 2\sigma$ (I)	$I > 2\sigma$ (I)	$I > 2\sigma$ (I)	$I > 2\sigma$ (I)
Data/parameters	2226/253	2383/91	1777/128	3431/138	2165/147
R (obs)	0.053	0.028	0.040	0.038	0.035
$R_{\rm w}, F^2$ (all data)	0.084	0.068	0.107	0.099	0.096
GOF	1.53	1.068	1.054	1.059	1.031
Max resid. Peaks (eÅ-3)	0.89, -1.22	1.04, -1.30	0.24, -0.27	0.41, -0.39	0.25, -0.23

1Zj ~81%) FT-IR (neat): 817, 875, 943, 1019, 1046, 1180, 1247, 1578, 2936 cm⁻¹. ¹H-NMR δ 2.39 (s, 3H, CH₃), 4.19, (s, 3H, OCH₃), 7.17 (d, *J* 8.5 Hz, 2H, ArH), 7.66 (d, *J* 8.5 Hz, 2H, ArH). ¹³C-NMR δ 21.30, 62.52, 116.98, 128.98, 129.31, 133.50, 140.65. GC-MS: 275 (M, 8.2%), 148 (100), 133 (60.2), 117 (89.4), 104 (8.0), 89 (14.2). (Found: M⁺⁺, 274.98160. C₉H₁₀INO requires 274.98072).

(Z)-O-Methyl-4-chlorobenzohydroximoyl Iodide (1Zl)

This compound was obtained as a viscous liquid by the above procedure with the temperature being maintained at 93 °C for approximately three days. GC-MS revealed this to be 93.5% **1Zl** and 6.5% starting material **1Zd**. (Yield of **1Zl** ~77%.) FT-IR (neat): 828, 873, 949, 1013, 1047, 1094, 1242, 1483, 1574, 2937. ¹H-NMR δ 4.20 (s, 3H,

OCH₃), 7.34 (d, J 8.5 Hz, 2H, ArH), 7.72 (d, J 8.5 Hz, 2H, ArH). ¹³C-NMR δ 62.73, 115.30, 128.45, 130.55, 134.59, 136.50. GC-MS: 297 (3.7%), 295 (M, 11.1), 170 (31.1), 168 (94.3), 155 (24.8), 153 (75.1), 139 (33.1), 137 (100), 127 (23.6), 102 (31.4), 75 (16.0). (Found: M⁺, 294.92659. C₈H₇ClINO requires 294.92609).

(Z)-O-Methyl-4-nitrobenzohydroximoyl Iodide (1Zn)

This compound was obtained as a crystalline solid by the above procedure with the temperature being maintained between 95 and 97 °C for approximately four days. GC-MS revealed this to be 94.8% **1Zn**, 3.6% **1Zh** and 1.6% 4-nitrobenzonitrile. (Yield of **1Zn** ~95%, m.p. 94.2–95.2 °C) FT-IR (Nujol mull): 955, 1039, 1343, 1456, 1514, 1543 cm⁻¹. ¹H-NMR δ 4.25 (s, 3H, OCH₃), 7.97 (d, *J* 8.5 Hz, 2H, ArH). ⁸C-NMR δ

63.19, 113.82, 123.41, 130.21, 141.65, 148.63. GC-MS: 306 (M, 4.9%), 179 (100), 164 (7.9), 134 (17.5), 102 (13.7), 90 (5.7), 75 (4.2). (Found: M^+ , 305.95018. $C_8H_7IN_2O_3$ requires 305.95014).

(Z)-O-Methyl-4-methoxybenzohydroximoyl Iodide (1Zk)

This compound was obtained as a viscous liquid by the above procedure with the temperature being maintained at 95 °C for approximately two days. GC-MS revealed this to be 100% **1Zk**. (Yield of **1Zk** ~ 87%) FT-IR (neat): 1034, 1050, 1173, 1246, 1257, 2854, 2924 cm⁻¹. ¹H-NMR δ 3.85 (s, 3H, OCH₃), 4.17 (s, 3H, OCH₃), 6.88 (d, *J* 8.5 Hz, 2H, ArH), 7.72 (d, *J* 8.5 Hz, 2H, ArH). ¹³C-NMR δ 55.42, 62.45, 113.60, 116.60, 128.73, 130.85, 161.28. GC-MS: 291 (M, 6.9%), 164 (52.7), 133 (100), 103 (15.4), 90 (20.4). (Found: M⁺⁺, 290.97561. C₉H₁₀INO₂ requires 290.97563).

(Z)-N-Isopropoxy-4-chlorobenzenecarboximidoyl Iodide (**1Zm**)

This compound was obtained as light tan, feathery crystals by the above procedure with the temperature being maintained at 105 °C for approximately two days. GC-MS revealed this to be 93.5% **1Zm** and 6.5% **1Zg**. (Yield of **1ZM** ~ 64%, m.p. 46.9–47.5 °C.) FT-IR (nujol mull): 987, 1461, 828, 1377 cm⁻¹. ¹H-NMR δ 1.41 (d, *J* 6.3 Hz, 6H, CH₃), 4.69 (m, *J* 6.3, 1H, OCH), 7.33 (d, *J* 8.6 Hz, 2H, ArH), 7.72 (d, *J* 8.6 Hz, 2H, ArH). ¹³C-NMR δ 21.81, 77.57, 114.48, 128.39, 130.58, 135.06, 136.21. GC-MS 323 (M, 4.7%), 198 (16.5), 196 (48.9), 156 (32.4), 154 (100), 139 (14.5), 137 (44.2), 127 (8.1), 113 (6.5), 111 (19.5), 102 (21.4), 90 (6.7), 75 (9.9). (Found: M⁺⁺, 322.95738. C₉H₁₀INO₂ requires 322.95739).

Preparation of Methyl (*Z*)-*O*-Methyl-4nitrobenzothiohydroximate (**1Zo**)

(*Z*)-*N*-methoxy-4-nitrobenzenecarboximidoyl bromide (**1Zh**, 1.0 g, 3.9 mmol) and spray dried potassium fluoride (0.75 g, 13 mmol) in dry DMSO (12 mL) were heated and stirred at 115 °C for 4 h and then at 140 °C for 68 h. On cooling, saturated sodium chloride solution (30 mL) was added and the organic products were extracted into ether (3×20 mL). The ether solution was washed with 5% sodium hydroxide solution (2×15 mL), dried (MgSO₄) and the solvent removed by evaporation to give 0.32 g of crude product containing both **1Za** and **1Zo**. The products were separated by dry column chromatography on silica using dichloromethane/hexane (2:1) as the eluting solvent. Recrystallization from hexane gave the desired product (1Zo, 0.20 g, 23%) as a slightly creamy crystalline solid, m.p. 113–114 °C. Anal. Calcd. for C₉H₁₀N₂O₃S: C, 47.78; H, 4.46; N, 12.38; S, 14.17. Found C, 47.66; H, 4.50; N, 12.06; S, 14.05. FT-IR (Nujol, cm⁻¹): 1598 m (C=N), 1558 m, 1519 vs, 1346 vs, 1309 s, 1272 s, 1049 s, 1015 s, 997 s, 967 s, 856 s, 847 s. UV: one λ_{max} at 248 nm (log $\varepsilon = 4.02$) and two inflections at 260 nm (log $\varepsilon = 4.00$) and 314 nm (log ε = 3.72) were determined. GC-MS: 226 (M, 35%), 225 (91), 209 (81), 195 (21), 179 (84), 164 (54), 149 (63), 134 (100), 120 (20), 118 (21), 103 (33), 102 (56), 90 (50), 76 (46), 75 (55), 63 (23), 51(35), 50 (40). ¹H-NMR (δ , ppm): 2.07 (s, 3H, SCH₃), 4.01 (s, 3H, OCH₃), 7.61 (d, 2H, J = 8.6 Hz, aromatic H), 8.21 (d, 2H, J = 8.6 Hz, aromatic H). 13 C-NMR (δ , ppm): 15.27 (SCH₃), 62.99 (OCH₃), 123.72, 129.62 (aromatic CH), 139.12 and 148.17 (aromatic C), 152.62 (C=N).

Preparation of (*Z*)-*N*-Methoxy-4nitrobenzenecarboximidoyl Azide (**1Zp**)

In a 40 mL screw top vial were combined anhydrous DMSO (35 mL), hydroximoyl bromide 1Zh (0.689 g, 2.71 mmol), and sodium azide (0.8827 g, 13.6 mmol). The mixture was stirred magnetically for 4 days at room temperature, until the starting material was consumed (as monitored using HPLC). The reaction mixture was slowly poured onto ice water (120 g), which caused the crude product to precipitate as a solid. The solid was isolated by suction filtration and was recrystallized to provide 1Zp as an off-white crystalline solid (521 mg, 87%), m.p. 70.0-70.9 °C. IR (Nujol): 2156, 2097, 1599, 1565, 1520, 1321, 1261, 1045, 861 cm⁻¹. ¹H-NMR (300 MHz, CDCl₃): δ 4.06 (s, 3 H, OCH₃); 7.94 (d, J 8.9 Hz, 2H, ArH); 8.20 (d, J 8.9 Hz, 2H, ArH). ¹³C-NMR (CDCl₃): δ 63.24, 123.35, 126.73, 136.41, 140.81, 148.49. Anal. Calcd. for C₈H₇N₅O₃: C, 43.44; H, 3.19; N, 31.66; Found: C, 43.32; H, 3.30; N, 31.40.

Results and Discussion

O-Alkylbenzohydroximoyl iodides (**1Zi-1Zn**) were prepared in acceptable to excellent yields (51–95%) by reacting the corresponding *O*-alkylbenzohydroximoyl bromide (**1Zc-1Zh**) compound with sodium iodide in sulfolane (Scheme 3). These reactions prove to be highly sensitive to temperature. At low temperatures the reaction takes an exorbitant length of time; at higher temperatures an elimination reaction to form a nitrile prevails. It was found that temperature ranges between 95 and 105 °C



Scheme 3 Synthesis of N-alkoxyimidoyl iodides

provided the best conversion to the iodide while minimizing the formation of the nitrile.

While conversion of the *N*-alkoxyimidoyl bromide to the *N*-alkoxyimidoyl iodide appeared to proceed almost quantitatively by these conditions in most instances, small amounts of the bromide starting material (between 1.4%and 6.5% in most cases) remained unreacted. The isolation of pure *N*-alkoxyimidoyl iodide, therefore, proved to be almost an intractable problem due to the very similar polarity of the *N*-alkoxyimidoyl bromide starting material and the lability of the C–I bond in the product. Attempts at fractional vacuum distillation failed because of the partial decomposition of the iodide compound with the heating necessary to accomplish distillation. Analytical samples were therefore produced by low temperature preparative GLC (at temperatures lower than 105 °C to prevent formation of the nitrile).

These reactions were also found to form a single geometric isomer. X-ray crystallographic studies have demonstrated that this is the Z-isomer in the case of 1Zmand 1Zn. It is presumed therefore that all these reactions proceed with retention of the stereochemistry about the C=N bond.

The structure of **1Zm** is shown in Fig. 1. There are two molecules arranged in the asymmetric unit in a manner that mimics mirror plane symmetry. The bond distances, bond

angles, and torsional angles of the two molecules agree to within 2σ except for those angles involving the C–O bond in the isoproxy moiety. The molecules are not planar; the central carbon and one terminal carbon of each isopropoxy group are at least 1 Å out of the phenyl plane. The mean C=N distance is 1.280(19) Å, and the mean C–I distance is 2.090(13) Å. The C–I bonds form a mean dihedral angle of 29.5° with the phenyl plane. Intermolecular interactions shorter than the sum of van der Waals radii were not observed.

The structure of **1Zn** is shown in Fig. 2. The molecule lies on a mirror plane in the crystal, thus it is perfectly planar, except for methyl H atoms. The C=N distance is 1.286(3) Å, and the C–I distance is 2.096(2) Å.

Attempts at producing the *E*-isomer under the irradiation conditions used to produce the *E* isomer of the *N*-alkoxy-imidoyl bromide [15], chloride [16], and fluoride [4] compounds have failed with the *N*-alkoxyimidoyl iodides. Irradiation of a benzene solution of **1Zm** under conditions for the preparation of either an (*E*)-*O*-alkylbenzohydroximoyl chloride, fluoride or bromide led to rapid decomposition of **1Zm** to 4-chlorobenzonitrile.

Comparison of the crystal structures of the (Z)-Omethyl-4-nitrobenzohydroximoyl halides (1Za, 1Zb, and 1Zn) reveals that the planarity of the molecule is impacted by the halogen atom. The assignment of the Z configuration to 1Za had previously been made based upon comparison of NMR and reactivity data of 1Za to that of 1Zb. The X-ray structure substantiates that the stereochemistry of 1Za had been previously appropriately assigned [4].

The structure of 1Za is shown in Fig. 3. The molecule deviates slightly from planarity, with all atoms but methyl C8 exhibiting mean deviation 0.045 Å, and C8 lying





Fig. 2 X-ray crystal structure for 1Zn (ellipsoid probabilities are 50%)

0.267(2) Å from that plane. The nitro group is twisted slightly out of the phenyl plane, with torsion angle $-5.1(2)^{\circ}$ about C5-N2. The oxime plane is also twisted slightly out of the phenyl plane, with torsion angle $7.9(2)^{\circ}$ about C1-C2. The C=N distance is 1.266(2) Å, and the C–F distance is 1.346(2) Å. While (Z)-*N*-methoxy-4-nitrobenzenecarboximidoyl bromide (**1Zh**) is also crystalline, crystal quality was sufficient only to confirm the identity of the compound, and the structure is not included here.



Fig. 3 X-ray crystal structure of 1Za (ellipsoid probabilities are 50%)

As seen in Table 3, the halogen atom affects the magnitude of the dihedral angle θ . As the van der Waals radius of the halogen increases from fluorine to chlorine to iodine, the C–X bond lengthens from 1.3462 Å (**1Za**) to 1.731 Å in compound (**1Zb**) [17] and to 2.090 Å in compound (**1Zm**). Additionally, the angle θ increases from 7° (**1Za**) to 17° (**1Zb**) to 27° (**1Zm**).

Surprisingly, the angle θ in the iodide-containing molecule (**1Zn**) is 0°. This is unusual when compared to both **1Zm** and to 1-phenyl-1-iodoethylene (PhC(I)=CHR) compounds. Both the *cis* and *trans* geometric isomers of 1-phenyl-1-iodoethylenes display a twist to the aromatic ring relative to the plane defined by the I–C=C bonds [21]. The planarity of **1Zn** could be caused by intermolecular interactions ("packing forces"). This planarity allows the molecules to stack with perpendicular distance of b/2 = 3.26 Å. Also, there is a C–H…I intermolecular interaction which might be relevant. Such contacts are expected to be quite weak, but this one is nearly linear (C–H…I angle 174°) with C3–H3…I1 (at *x*–1/2, 1/2–*y*, 1/2–*z*), C…I 3.976 Å, and H…I 3.03 Å.

Substitution reactions using *N*-methoxyimidoyl halides as starting materials are of interest because of the potential to produce a single geometric isomer of the product [4]. Again, whether the stereochemistry about the C=N bond in the product is *E* or *Z* has been difficult to unambiguously ascertain by NMR and dipole measurements. X-ray crystallography has been performed on two of the substitution products (**1Zo** and **1Zp**) derived from *N*-methoxyimidoyl halides which happen to be crystalline substances, and both have been found to be in the *Z*-configuration.

The structure of **1Zo** is shown in Fig. 4. The C=N distance is 1.286(2) Å, and the C–S distance is 1.7552(12) Å. The S–Me bond is essentially anti to C=N (torsion angle about C1–S1 18.29(11)°), and the phenyl group is twisted out of the oxime plane, with torsion angle $62.13(15)^{\circ}$ about C1–C2. The nitro group is nearly coplanar with the phenyl group, having torsion angle $5.1(2)^{\circ}$ about C5–N2.

A Comparison of the Methyl (*Z*)-*O*-methyl-4-nitrobenzothiohydroximate (**1Zo**) to the (*Z*)-ethyl benzohydroximate (**1Zr**) shows that both of these compounds twist the aromatic ring out of the plane to avoid a steric interaction with the "X" substituent (Table 3). Here the thiomethyl group causes a large dihedral angle between these two planes of 61°, presumably because of the atomic radius of the sulfur atom.

The structure of **1Zp** is shown in Fig. 5. Azide **1Zp** has C=N distance 1.285(2) Å and C1–N3 distance 1.402(2) Å. The azide substituent is slightly nonlinear, with angle 167.49(13)° about N4. The molecule is roughly planar, with all atoms other than methyl C8 having mean deviation 0.039 Å from a common plane, and C8 0.279(1) Å out of that plane. The molecule is slightly bowed, with all phenyl

Table 3 Dihedral angle between the aryl plane and the N=C–X plane



Compound	Х	Y	R	Isomer	Dihedral angle (θ), deg	Reference
1Zm	Ι	Cl	<i>i</i> -Pr	Ζ	27	This work
1Zn	Ι	NO_2	CH ₃	Ζ	0	This work
1Zb	Cl	NO_2	CH ₃	Ζ	17	[17]
1Eb	Cl	NO_2	CH ₃	Ε	50	[3]
1Za	F	NO_2	CH ₃	Ζ	7	This work
1Zo	SCH ₃	NO_2	CH ₃	Ζ	61	This work
1Zr	OCH ₂ CH ₃	Н	Н	Ζ	29	[18]
1Er	OCH ₂ CH ₃	Н	Н	Ε	39	[18]
1Zp	N ₃	NO_2	CH ₃	Ζ	1.5	This work
1Zq	CN	NO_2	CH ₃	Ζ	9.1	[19]
1Eq	CN	NO_2	CH ₃	E	4.7	[20]





Fig. 4 X-ray crystal structure of 1Zo (ellipsoid probabilities are 50%)

Fig. 5 X-ray crystal structure of 1Zp (ellipsoid probabilities are 50%)

C atoms lying on one side of the best plane, and the nitro group and oxime substituent lying on the opposite side.

The final comparison is between substituents in which the atoms of the group can also have π -bond overlap with the C=N bond (**1Zp**) and (**1Zq**). As seen, this additional conjugation, along with a lack of steric crowding, appears to favor the molecule adopting an almost planar geometry.

Information about the geometry of N-methoxyimines could prove valuable in further studies of the reactivities of these molecules. The dihedral angle (Table 3) of the aromatic ring relative to the C=N bond has been considered as a possible contributor to the large differences in methoxide substitution reaction rates with the O-methyl derivative of **1Er** where θ is 39° reacting slower $(k_z/k_E = 300)$ [22] than the *O*-methyl derivative of **1Zr** where θ is 29°. This factor, however, was thought to have little effect in the rate of nucleophilic substitution of compounds similar to 1Zb (θ of 17°) and **1Eb** (θ of 50°). In compounds that differ from **1Zb** and **1Eb** only in the fact that there is no substituent on the aromatic ring, both the Z and E isomers undergo substitution by methoxide at similar rates [3]. It is reasonable to expect that N-methoxyimine molecules in which the C=N bond and the aromatic ring are co-planar would exhibit a greater-than-expected stability due to resonance effects.

Conclusion

A general synthesis of O-alkylbenzohydroximoyl iodides has been developed. The geometric stereochemistry of two of these compounds has been determined by X-ray crystallography to be in the Z configuration. Comparison of the structure of these compounds to other O-alkylbenzohydroximoyl halides reveals that the planarity of the molecule is impacted both by the halogen atom and by the substituent present on the aromatic ring. The structures of two compounds produced by substitution of the halogen of an O-methyl-4-nitrobenzohydroximoyl halide (O-methyl-4nitrobenzohydroximoyl azide and methyl O-methyl-4nitrobenzothiohydroximate) have also been determined by X-ray crystallography. They too have been found to be in the Z configuration. It is found that the azide compound is almost planar due to extended conjugation and lack of steric crowding. The thiohydroximate is found to have the largest deviation from planarity of all these molecules due to the bulkiness of the thiomethyl group.

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