Synthesis and Configurations of O-Substituted Hydroximoyl Chlorides. Stereochemistry and Mechanism of Alkoxide Ion Substitution at the Carbon-Nitrogen Double Bond

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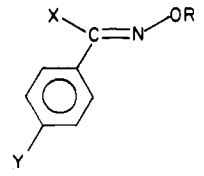
Received July 23, 1984

An X-ray crystallographic analysis of (*E*)-*O*-methyl-*p*-nitrobenzohydroximoyl chloride (**2b**) has been carried out to confirm the configuration of the compound. The dihedral angle between the benzene ring in **2b** and the hydroximoyl chloride functional group is 50°. This is considerably larger than the dihedral angle between the same two planes in the (*Z*)-hydroximoyl chloride (**1b**) and the *Z* and *E* isomers of ethyl benzohydroximate (**1g** and **2g**). Two new hydroximoyl chlorides, **5a** and **5b**, were synthesized by reaction of the corresponding hydroxamates **4a** and **4b** with thionyl chloride. The dipole moments of the *Z* and *E* isomers of *O*-methylbenzohydroximoyl chloride (**1a** and **2a**) were analyzed in terms of the conjugation within the hydroximoyl chloride functional group. A resonance correction term was calculated for each isomer. The configurations of **5a** and **5b** were determined to be *Z* by comparison of their experimental dipole moments to theoretical dipole moments. The theoretical dipole moment calculations of **5a** and **5b** and the corresponding *E* isomers included the resonance correction terms that were found for **1a** and **2a**. The (*Z*)-hydroximoyl chloride **5a** reacted with sodium ethoxide to give a substitution product (**7a**) with inverted configuration.

Sometime ago we reported the synthesis and separation of the *Z* and *E* isomers of *O*-methylbenzohydroximoyl chlorides (**1a–d** and **2a–d**).[1] Dipole moment measure-



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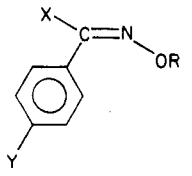


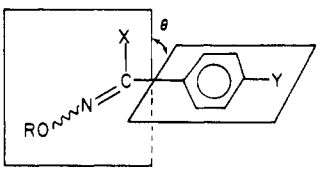
2

a, X = Cl; Y = H; R = CH_3
b, X = Cl; Y = NO_2; R = CH_3
c, X = Cl; Y = R = CH_3
d, X = Y = Cl; R = CH_3
e, X = OC_2H_5; Y = H; R = CH_3
f, X = OCH_3; Y = H; R = CH_3
g, X = OC_2H_5; Y = R = H
h, X = Cl; Y = R = H
i, X = Cl; Y = NO_2; R = H
j, X = Cl; Y = H; R = COC_6H_5

ments of these isomers indicated that the isomer obtained from the reaction of phosphorus pentachloride with a methyl benzohydroxamate had the *E* configuration. A subsequent X-ray crystallographic study[2] of **1b** showed that the configurational assignments based on dipole moment measurements were incorrect. Since the calculated values for the dipole moments of the (*E*)-*O*-methylbenzohydroximoyl chlorides are considerably different than the measured values, we decided to carry out an X-ray crystallographic analysis of **2b** in order to compare it to the previously reported X-ray analysis on the *Z* isomer **1b**. A comparison of certain structural features of these isomers is also of interest in regard to the mechanisms of nucleophilic substitution. We also report on the synthesis and configurations of two new hydroximoyl chlorides **5a** and **5b** and the stereochemistry of the ethoxide substitution reaction of one of them (**5a**).

Recent reports on the rates and stereochemistry of nucleophilic substitution on *O*-methylbenzohydroximoyl chlorides[3,4] (**1a–d** and **2a–d**) and ethyl *O*-methylbenzohydroximate[3] (**1e** and **2e**) have shown the configuration of the starting material plays an important role in the stereochemistry and the overall rates of the substitutions. The rates of reactions of the (*Z*) and the (*E*)-hydroximoyl chlroides **1a** and **2a** with methoxide ion in 90% dimethyl sulfoxide–10% methanol are essentially identical (k_{1a}/k_{2a} = 0.87 at 44.6 °C), but the rate of methoxide ion substitution with the (*Z*)-hydroximate **1e** is about 390 time faster than the rate of reaction of the *E* isomer **2e** with methoxide ion.[3] Compelling evidence has been offered by us that these reactions proceed by an addition–elimination mechanism.[3] One possible explanation for the large difference in the rates of nucleophilic substitution in the (*Z*)- and (*E*)-hydroximates (**1e** and **2e**) is that the rates of nucleophilic attack (the addition step) are vastly different in the two isomers. The (*E*)-hydroximate (**2e**) could be undergoing slower nucleophilic attack because the phenyl group is twisted from the O—C=N—O plane more in it

Table I. Dihedral Angle between the Aryl Plane and the RON=CX Plane in Hydroximoyl Chlorides and Hydroximates



X	Y	R	isomer	dihedral angle (θ), deg	ref
Cl	NO_2	CH_3	*Z*	17	2
Cl	NO_2	CH_3	*E*	50	this work
OEt	H	H	*Z*	29	5
OEt	H	H	*E*	39	5

(1) Johnson, J. E.; Nalley, E. A.; Kunz, Y. K.; Springfield, J. R. *J. Org. Chem.* **1976**, *41*, 252–259.
(2) Bertolasi, V.; Sacerdoti, M.; Tassi, D. *Cryst. Struct. Commun.* **1977**, *6*, 335–341.
(3) Johnson, J. E.; Nalley, E. A.; Weidig, C.; Arfan, M. *J. Org. Chem.* **1981**, *46*, 3623–3629.
(4) Johnson, J. E.; Cornell, S. C. *J. Org. Chem.* **1980**, *45*, 4144–4148.

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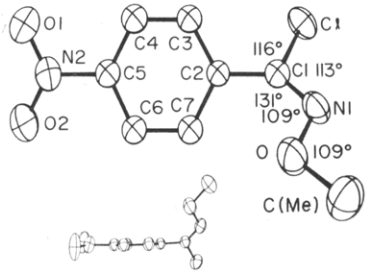
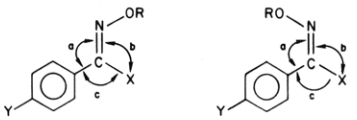


Figure 1. ORTEP drawing of (*E*)-*O*-methyl-*p*-nitrobenzohydroximoyl chloride showing selected bond angles. Inset: View parallel to the plane of the nitrobenzene ring.

Table II. Bond Angles around the Trigonal Carbon in Some Compounds Containing a Carbon–Nitrogen Double Bond



			angle, deg				angle, deg			
X	Y	R	a	b	c	ref	a	b	c	ref
Cl	NO_2	CH_3	119	122	118	2	131	113	116	this work
OEt	H	H	117	130	113	5	130	120	111	5
H	Cl	H	121			6	132			6

than in the *Z* isomer. A twisted phenyl group in **2e** could partially block nucleophilic attack perpendicular to the O—C=N—O plane and decrease its rate of reaction. This sort of explanation would require the corresponding dihedral angles in the hydroximoyl chlorides **1a** and **2a** to be similar since they react at almost the same rate with methoxide ion. We have now completed an X-ray crystallographic analysis of **2b** which shows that the dihedral angle between the benzene ring and the hydroximoyl chloride functional group is 50° (Table I). This is considerably larger than the dihedral angle of 17° between the same two planes in the *Z* isomer. A perspective view of **2b** showing the large dihedral angle is given in Figure 1. Table I also contains the dihedral angles reported[5] for the *Z* and *E* isomers of ethyl benzohydroximate (**1g** and **2g**) which should serve as models for the *O*-methyl derivatives of these isomers (**1e** and **2e**). The dihedral angle for the (*E*)-hydroximate (39°) is larger than in the *Z* isomer (29°), but the difference between the two isomers is not nearly as large as in the case of the (*Z*)-and (*E*)-hydroximoyl chlorides **1b** and **2b**. If the conformations of these isomers in solution are similar in a general way to those found in the solid state, we suggest that a difference in the rates of nucleophilic attack resulting from conformational differences is not a major contributor to the large difference in the overall rates of methoxide substitution on **1e** and **2e**.

Another noteworthy feature of the **2b** structure is the N=C—Ar bond angle (131°) which is considerably larger than the corresponding angle in the *Z* isomer **1b** (119°). This difference fits a general pattern (Table II) which has been reported previously for benzohydroximates[5] and benzaldoximes.[6] It should also be pointed out that the methoxy group in **2b** is in the *s-trans* conformation as is the methoxy group in the *Z* isomer **1b**.

In connection with this work we have synthesized two new hydroximoyl chlorides (**5a** and **5b**) in which the carbon atom attached to the hydroximoyl chloride moiety is

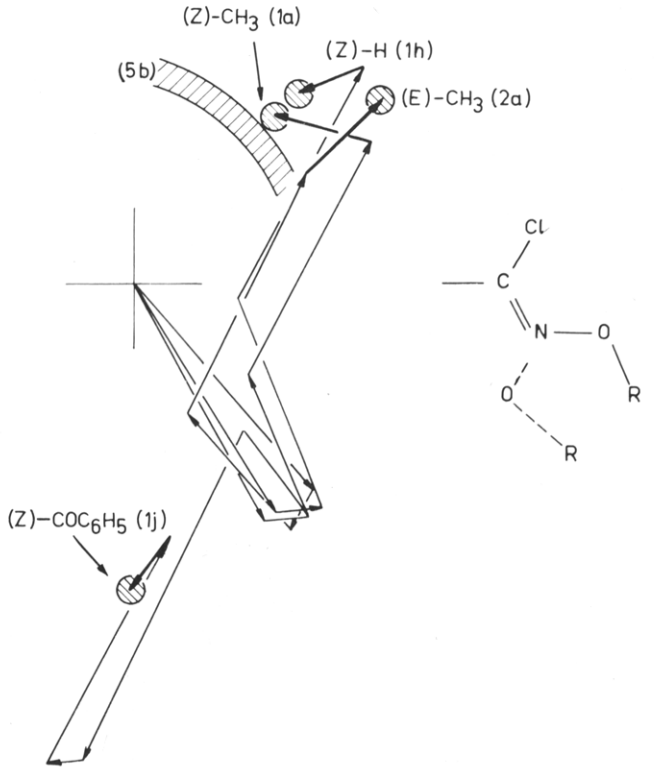
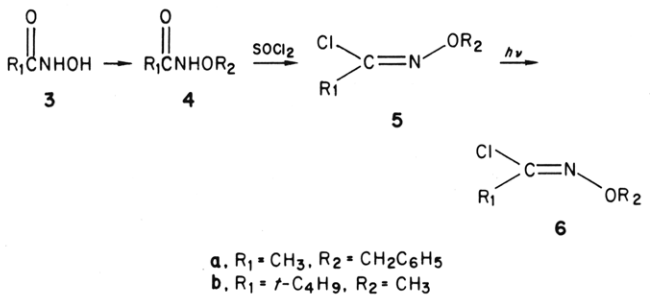


Figure 2. Vector analysis of dipole moments of hydroximoyl chloride derivatives. The end points of experimental vectors are shown by shadowed areas, theoretical dipole moments are constructed from bond moments (light arrows), and the difference vector between theory and experiment is the resonance moment (heavy arrows).

Scheme I



a, $R_1 = CH_3$, $R_2 = CH_2C_6H_5$
b, $R_1 = t\text{-}C_4H_9$, $R_2 = CH_3$

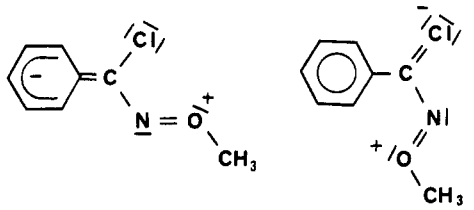
saturated. Reaction of the hydroxamates **4a** and **4b** with thionyl chloride gave the corresponding hydroximoyl chlorides **5a** and **5b** in moderate yields (Scheme I). The ^1H NMR spectra of the crude samples of **5a** and **5b** indicated that only one isomer was formed in these reactions.

Now that the X-ray structures of **1b** and **2b** have been determined, and the configurations of these compounds are known unambiguously, we are in a position to analyze the dipole moments[7] of these isomers in terms of the conjugation within the hydroximoyl chloride functional group. The results of these calculations are shown in Figure 2 along with the previous calculations on other derivatives.[8,9] The experimental dipole moments are shown as vectors from the origin of coordinates toward the

(5) Larsen, I. K. *Acta Chem. Scand.* **1971**, *25*, 2409–2420.
(6) Jensen, K. G. *Acta Crystallogr., Sect. A* **1969**, *A25*, sl48–sl49.
(7) Exner, O.; Waisser, K. *Collect. Czech. Chem. Commun.* **1982**, *47*, 828–837.
(8) Exner, O.; Jehlicka, V.; Barbaro, G.; Dondondi, A. *Collect. Czech. Chem. Commun.* **1977**, *42*, 833–842.
(9) Smolikova, J.; Exner, O.; Barbaro, G.; Macciantelli, D.; Dondondi, A. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1051–1056.
(10) Significant resonance dipole moments have also been determined by using this approach for simpler functional groups with n–π conjugation, such as amides and thioamides (see ref 7).

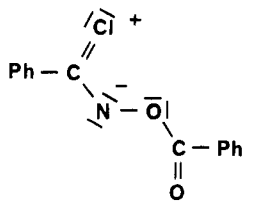
shadowed area which represents the experimental uncertainty. The direction of the vectors was determined by comparison with a para-substituted derivative (construction of a triangle). Only in the case of the aliphatic derivatives **5a** and **5b** does the direction of the vector remain unknown. The theoretical dipole moments were calculated as vector sums of bond moments (light arrows), using bond angles obtained from the X-ray structures of the appropriate derivatives. The vector difference between the calculated and experimental dipole moments (heavy arrows) is the resonance correction term, representing electron delocalization with respect to the classical structure. This quantity is relatively small and therefore is sensitive to errors in both the experimental determination and the theoretical calculation. Nevertheless, the differences between individual derivatives and between stereoisomers are obvious and in our opinion represent real differences.

The resonance moment of (*Z*)-*O*-methylbenzohydroximoyl chloride (**1a**) corresponds in its direction to a transfer from oxygen to the benzene ring according to resonance structure I. In (*E*)-*O*-methylbenzohydroximoyl



I II

chloride (**2a**) some of the negative charge seems to be transferred to the chlorine via d–π acceptor resonance[11] (resonance structure II). We suggest that the differences in direction of the resonance moments in **1a** and **2a** are due to stereoelectronic effects.[12] The antiperiplanar arrangement of the Cl—C=N—O orbitals in the *E* isomer favors the d–π resonance contribution which results in a resonance moment pointing toward the chlorine atom. In the *Z* isomer the antiperiplanar arrangement of the C_6H_5—C=N—O orbitals favors delocalization of a nonbonded electron pair on oxygen into the benzene ring. In the parent hydroximoyl chlorides (**1h** and **1i**) and particularly in their *O*-benzoyl derivatives (**1j**) the direction of the resonance moments points to more contribution from resonance structure III. The change in direction of the



III

resonance moment in **1j** is consistent with our interpretation since in **1j** the oximino oxygen unbonded pairs should be also delocalized into the benzoyl group making these electrons less available for delocalization into the hydroximoyl chloride functional group.

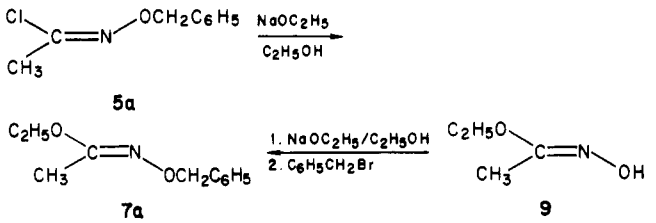
The changes in direction of the resonance vectors of these compounds clearly show the difficulty in determining configurations from dipole moments in oximino compounds. The resonance moments (heavy arrows in Figure 2), however, can serve as ad hoc corrections in calculating the dipole moments anticipated for closely related compounds. For example, we can calculate the anticipated dipole moments of the aliphatic *O*-alkylhydroximoyl chlorides **5a** and **5b**, using the corrections derived from the aromatic derivatives **1a** and **2a**. For the *Z* configuration we obtain 1.64 and 1.66 D, respectively, while the *E* configuration with the appropriate correction gave 2.33 and 2.30 D (Table III). On the basis of the similarity of the experimental dipole moments of **5a** and **5b** to the calculated values for the *Z* configuration, we conclude that both **5a** and **5b** have the *Z* configuration.

Table III. Dipole Moment Data for Hydroximoyl Chlorides and Hydroximates

compd	theor dipole moment,[a] D	exptl dipole moment,[b] D	ref
1a	1.83 (1.45)	1.38 ± 0.02	1
2a	1.32 (2.04)	2.00 ± 0.04	1
1b	2.87 (3.53)	3.58 ± 0.03	1
2b	3.25 (2.93)	2.91 ± 0.04	1
1c	2.09 (1.66)	1.73 ± 0.03	1
2c	1.58 (2.30)	2.36 ± 0.04	1
1d	0.93 (1.29)	1.22 ± 0.03	1
2d	0.85 (1.21)	1.21 ± 0.05	1
5a	(1.64)	1.26 ± 0.05	this work
6a	(2.33)		
5b	(1.66)	1.46 ± 0.01	this work
6b	(2.30)		
7a		0.88 ± 0.01	this work
9		0.91 ± 0.03	this work
1g		2.52	11
2g		1.41	11

[a] Calculated by using the following bond (or group) moments: CH_3—O, 1.04 D; N—O, 0.3 D; C =N, 1.8 D; C—Cl, 1.75 D; NO_2, 4.3D; Ar—CH_3, 0.3 D; Ar—Cl, 1.6 D. The bond angles used in the calculations were those found by X-ray crystallographic analysis of **1b** (ref 2) and **2b** (this work). Numbers in parentheses are the theoretical dipole moments calculated by using an ad hoc correction for conjugation. [b] The experimental dipole moments were measured in benzene at 25 °C.

Scheme II



5a **7a** **9**

When a hexane solution of **5a** was irradiated with ultraviolet light, a small amount of the *E* isomer **6a** (ca. 17%) was formed as indicated by the ^1H NMR spectrum of the irradiated sample. The ^1H NMR spectrum of the irradiated sample showed the methyl singlet for the original isomer **5a** at 2.01 ppm and another methyl singlet further downfield at 2.09 ppm. The signals for the methylene hydrogens in the benzyl group were very close to each other in **5a** and **6a**, but it could be determined on an expanded scale that the singlet for the methylene hydrogens in **6a** was slightly upfield from the methylene singlet in **5a**. The relative positions of the $NOCH_2$ ^1H NMR signals for **5a** and **6a** are consistent with the correlations established for the *Z* and *E* isomers of benzohydroximoyl chlorides[1] (**1a–d**) and benzohydroximates[13] (**1e** and **1f**); i.e., the $NOCH_2$

(11) Ferguson, L. N. "The Modern Structural Theory of Organic Chemistry"; Prentice-Hall: Englewoods Cliffs, NJ, 1963; p 396.
(12) Deslongchamps, P. "Stereoelectronic Effects in Organic Chemistry"; Pergamon Press: Elmford, NY, 1983.
(13) Johnson, J. E.; Springfield, J. R.; Hwang, J. S.; Hayes, L. J.; Cunningham, W. C.; McClaugherty, D. L. *J. Org. Chem.* **1971**, *36*, 284–294.

signals are further downfield in the *Z* isomer than in the *E* isomer. Unfortunately, we were not able to separate **6a** from the mixture of **5a** and **6a** by prepartive GLC.

The (*Z*)-hydroximoyl chloride **5a** reacted with sodium ethoxide in absolute ethanol to give ethyl (*E*)-*O*-benzylacetohydroximate (**7a**) which was prepared independently by alkylation of ethyl (*E*)-acetohydroximate[14,15] (**9**) with benzyl bromide (Scheme II). The configuration of **7a** was determined to be *E* by comparison of its dipole moment to the dipole moment of **9** and the dipole moments of similar compounds (**1g** and **2g**)[5,16] of known configuration (Table III). It is possible the inversion of configuration observed during the conversion of **5a** to **7a** is due to the stereomutation of the tetrahedral intermediate initially formed by attack of ethoxide ion on **5a**. The mechanism of this reaction is under investigation and the results will be reported in due course.

Experimental Section

General Methods. Infrared spectra (IR) were recorded with a Perkin-Elmer Model 225 spectrophotometer. ^{1}H NMR spectra were determined in $CDCl_3$ solutions on a Varian A-60A spectrometer, and the chemical shifts are expressed as δ values in parts per million from Me_2Si as an internal standard. The GLC (analytical and preparative) were carried out with a column (30 ft × 0.375 in.) consisting of 20% silicone gum rubber (SE-30) on 45–60 mesh Chromosorb W. The dipole moments were determined by using a procedure described previously.[1] Microanalysis were carried out at Atlantic Microlab. Atlanta, GA.

X-ray Structural Determination of (*E*)-*O*-Methyl-*p*-nitrobenzohydroximoyl Chloride (2b). The synthesis of **2b** has been reported previously.[1] Single crystals of **2b** were obtained by slow evaporation of a methanol–water solution. X-ray data collection was carried out with an Enraf-Nonius CAD-4 automated diffractometer using graphite-monochromated Mo Kα X-rays (λ = 0.71073 Å) at ambient temperatures. The $C_8H_7N_2O_3Cl$ molecules (fw = 214.6) crystallized in the orthorhombic space group $Pna2_1$ with a = 19.735 (5) Å, b = 3.827 (5) Å, c = 12.302 (5) Å, Z = 4, and D_{calcd} = 1.53 g cm^{-3}. At total of 1653 reflections were scanned in the θ–2θ mode over the range (1.0 + 0.35 tan θ)° at speeds of 2–20° min^{-1} for 2θ values up to 60°. Of these reflections only 636 had $I > 3\sigma(I)$; this data set had the largest number of observed reflections of three data sets obtained from three different crystals.

Analysis of the Patterson map provided the positions of the chlorine atom, and the other non-hydrogen atoms were located by direct methods. All hydrogen atoms were observed on a difference map. The methyl hydrogen atoms are disordered: the difference map indicated two staggered sets forming a planar hexagon of half-occupied hydrogen atom positions. All hydrogen atoms were constrained to idealized (C–H = 0.95 Å) positions with isotropic temperature factors of B = 5.0 Å^2 for the least-squares refinement. Because of the paucity of observed data, all carbon atoms except the methyl carbon atom were refined with isotropic thermal factors. The final full-matrix least-squares refinement included 91 parameters for a parameter-to-reflection ratio of 1:7 and gave R = 0.052 and R_w = 0.051. The largest shift was 0.01σ, the gof was 1.04, and the final difference map had a maximum peak value of 0.3 eÅ^{-3}. The atom numbering scheme and intramolecular bond angles of interest are shown in Figure 1.

(*Z*)-*O*-Benzylacetohydroximoyl Chloride (5a). Benzyl acetohydroxamate[17] (21.2 g, 0.128 mol) and thionyl chloride were mixed together in a 100-mL round-bottomed flask that was immersed in an ice bath. The flask was heated in an oil bath for 4 h at 98 °C, the remaining thionyl chloride was removed from the reaction solution using a rotary evaporator, and the residual oil was distilled, bp 62–71 °C (0.04–0.05 torr), to give a colorless oil (11.5 g, 56%). GLC analysis of this oil showed that it was mainly one component. Removal of traces of inorganic chloride was accomplished by dissolving the oil in ether and washing the ether with water and a 3 N sodium hydroxide solution. After drying the ether solution and evaporation of the ether, the oil was distilled to give the analytical sample of **5a**: bp 51–54 °C (0.03 torr); IR (neat) 1615 (m, C=N); NMR δ 2.01 (s, 3, CH_3) 5.07 (s, 2, CH_2), 7.29 (s, 5, C_6H_5).

Anal. Calcd for $C_9H_{10}NOCl$: C, 58.87; H, 5.49; N, 7.63; Cl, 19.31. Found: C, 58.95; H, 5.52; N, 7.55; Cl, 19.24.

A 0.1 M hexane solution of **5a** was irradiated for 4 h with ultraviolet light using a 200-W, medium-pressure mercury lamp in a quartz apparatus (Ace Glass Inc.). The hexane solution was shaken with solid, anhydrous sodium carbonate, and the hexane was removed by evaporation at aspirator pressure. The ^{1}H NMR spectrum of the residual oil showed two methyl singlets, one at 2.01 ppm due to **5a** and another at 2.09 ppm which was assigned to **6a** (ratio of signals at 2.01 and 2.09 ppm ≃ 83:17). On a sweep width of 50 ppm the irradiated sample also showed two methylene singlets with the new singlet appearing slightly upfield from the methylene singlet in **5a**. Attempted separation of **5a** and **6a** by preparative GLC was unsuccessful.

Trimethylacetohydroxamic Acid (3b). Hydroxylamine hydrochloride (35.6 g, 0.513 mol) was thoroughly mixed with anhydrous potassium carbonate (70.9 g, 0.513 mol) in a morter. The mixture was placed in a 1-L Erlenmeyer flask equipped with standard tapered joint and a condenser (to prevent overflow of the reaction mixture caused by evolution of carbon dioxide). Trimethylacetyl chloride (61.9 g, 0.513 mol) dissolved in ether (300 mL) was added to the flask. Water (75 mL) was carefully added over a 2-h period through the condenser into the Erlenmeyer flask. The condenser was then removed and more water (150 mL) was carefully poured down the side of the flask. The water layer was separated and saved for extraction, and crystals of **3b** (36.8 g) were obtained after evaporation of the ether. The aqueous portion was extracted with ether until it no longer gave a purple color with ferric chloride. The ether extracts were dried over anhydrous magnesium sulfate and the ether was evaporated to give additional **3b** (5.2 g). The combined **3b** (42.0 g, 70%) had a melting point of 154–156 °C (sub); reported[18] mp 160–161 °C (sub); IR (Nujol) 3280 (m, br, NH and OH), 1640 (s, C=O); NMR δ 1.20 (s, *t*-C_4H_9).

Methyl Trimethylacetohydroxamate (4b). Trimethylacetohydroxamic acid (15.0 g, 0.128 mol) was dissolved in a solution of potassium hydroxide (14.4 g, 0.256 mol) and water (100 mL) and the solution was cooled in an ice bath. Ice (20 g) was added to the solution, followed by addition of dimethyl sulfate (16.1 g, 0.128 mol). More ice was added until the volume of the reaction mixture reached 275 mL. The reaction solution was kept for 2 days at ambient temperature, after which time it gave a negative ferric chloride test. The solution was continuously extracted with ether for 3 days using a liquid–liquid extractor. The ether extract was dried over magnesium sulfate, the ether was evaporated, and the residual oil was distilled to give **4b** as a clear, viscous oil (10.4 g, 64%), bp 70–73 °C (0.8 torr). Redistillation of the oil gave the analytical sample of **4b**: bp 72–74 °C (0.8 torr); IR (neat) 3250 (s, br, NH), 1625 (s, br, C=O); NMR δ 1.20 (s, 9, *t*-C_4H_9), 3.75 (s, CH_3). Anal. Calcd for $C_6H_{13}NO_2$: C, 54.94; H, 9.99; N, 10.68. Found: C, 54.75; H, 10.00; N, 10.49.

(*Z*)-*O*-Methyltrimethylacetohydroximoyl Chloride (5b). Thionyl chloride (11.2 g, 0.094 mol) was added to a solution of methyl trimethylacetohydroxamate (10.0 g, 0.076 mol) in anhydrous ether (200 mL). The solution was heated with an oil bath at 72 °C for 4 h. The unreacted thionyl chloride was removed by distillation and ether (100 mL) was added to the residual oil. The ether solution was washed alternatively with water and 10% sodium bicarbonate solution (2 × 30 mL each). The ether solution was dried over magnesium sulfate, the ether was removed by using a rotary evaporator, and the resulting oil was distilled at atmospheric pressure by using a Perkin-Elmer annular spinning band distillation apparatus to give **5b** (7.66 g, 67%); bp 123.0–124.5 °C. Preparative GLC of the oil gave the analytical sample of **5b**:

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IR (neat) 1595 (s, C=N); NMR δ 1.23 (s, 9, t-C_4H_9), 3.93 (s, 3, CH_3).

Anal. Calcd for $C_6H_{12}NOCl$: C, 48.17; H, 8.08; N, 9.36; Cl, 23.70. Found: C, 48.07; H, 8.06; N, 9.37; Cl, 23.61.

Ethyl (*E*)-Acetohydroximate (9). Ethyl (*E*)-acetohydroximate (**9**) was prepared according to the procedure of Houben and Schmidt,[19] bp 69–71 °C (13 torr); NMR δ 1.29 (t, 3, *J* = 7 Hz, $COCH_2CH_3$), 1.99 (s, 3, CH_3C), 4.01 (q, 2, *J* = 7 Hz, $COCH_2CH_3$); lit. bp 59.0–59.5 °C (14 torr[8]); lit. NMR[7] δ 2.00 (CH_3CN), 3.99 ($COCH_3$).

Ethyl (*E*)-*O*-Benzylacetohydroximate (7a). A solution of sodium ethoxide was prepared by adding sodium (4.75 g, 0.207 mol) to anhydrous ethanol (100 mL) in a 250-mL round-bottomed flask fitted with a condensor and a drying tube. The reaction flask was immersed in an ice bath, and ethyl (*E*)-acetohydroximate (**9**, 150 g, 0.122 mol) was added followed by the slow addition of benzyl bromide (20.6 g, 0.122 mol). The reaction solution was heated with an oil bath at 50–60 °C for 62 h after which time the ethanol was removed by using a rotary evaporator. The residue was carefully acidified with cold, dilute hydrochloric acid, inorganic salts were removed by filtration, and the filter pad was washed with ether (645 mL). The ether layer was separated from the filtrate and the aqueous layer was extracted with ether (2 × 20 mL). The combined ether extracts were washed with 10% sodium bicarbonate solution (2 × 20 mL) and water (2 × 20 mL). The ether extract was dried over magnesium sulfate, the ether was evaporated, and the residue was distilled to give **7a** as a colorless oil (15.6 g, 60%); bp 65–68 °C (0.08 torr). Redistillation gave the analytical sample of **7a**: bp 91–92.5 °C/0.95 torr; IR (neat) 1640 (s, C=N); NMR δ 1.23 (t, *J* = 7 Hz, 3, OCH_2CH_3), 1.92 (s, 3, CH_3), 4.01 (q, *J* = 7 Hz, 2, OCH_2CH_3), 4.93 (s, $CH_2C_6H_5$), 7.33 (s, 5, C_6H_5).

Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.51; H, 7.82; N, 7.23.

Reaction of (*Z*)-*O*-Benzylacetohydroximoyl Chloride (5a) with Sodium Ethoxide. (*Z*)-*O*-Benzylacetohydroximoyl chloride (**5a**, 4.00 g, 0.0218 mol) was added to a solution of sodium ethoxide (from 1.84 g of sodium) in ethanol (50 mL) and the solution was heated at 66–70 °C. The progress of the reaction was followed by removing 150-μL aliquots of the reaction solution and analyzing them by using the Beilstein test and GLC. After heating the reaction solution for 72 min, a negative Beilstein test was obtained and the hydroximoyl chloride **5a** was no longer detectable by GLC analysis. The GLC analysis indicated that the reaction product was almost entirely ethyl (*Z*)-*O*-benzylacetohydroximate (**7a**). The reaction mixture was filtered to remove precipitated sodium chloride, and the ethanol was evaporated from the filtrate at reduced pressure. The oily residue was filtered to remove inorganic salts and the filtered salts were washed with ethanol. The filtrate was poured into a beaker containing a mixed bed resin consisting of approximately 50% cation-exchange resin (Dowex 50-W-X2, 5.2 mequiv/dry gram) and 50% anion-exchange resin (Dowex 1-X2, 3.5 mequiv/dry gram). The resin was removed by filtration and the ethanol was evaporated in vacuo to give a clear, brownish oil (2.53 g, 52.3%). The oil was purified by preparative GLC and the major component was identified as the hydroximate **7a** by comparison of its ^1H NMR spectrum to the spectrum of an authentic sample of **7a** which had been prepared by the reaction of ethyl (*E*)-acetohydroximate with benzyl bromide. A minor product collected by preparative GLC was determined to be benzyl alcohol.

Acknowledgment. We gratefully acknowledgement support of this research by an Institutional Research Grant from the Texas Woman's University (J.E.J.) and the Robert A. Welch Foundation (J.E.J.).

Registry No. **2b**, 41071-36-7; **3b**, 29740-67-8; **4b**, 64214-63-7; **5a**, 95017-93-9; **5b**, 95017-94-0; **6a**, 95017-95-1; **7**, 95017-96-2; **7a**, 86208-93-7; **9**, 20703-41-7; benzyl acetohydroxamate, 4797-81-3; trimethylacetyl chloride, 3282-30-2.

Supplementary Material Available: Listings of final atomic positional parameters, anisotropic temperature factors, and intramolecular distances and angles (Tables IV–VI) (3 pages). Ordering information is given on any current masthead page.

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Tetrahydropyridines from 3-Picoline 1-Oxide and *tert*-Butyl and 1-Adamantyl Mercaptans in Acetic Anhydride. Structural Elucidation by Long-Range 2D *J*(C-H) Resolved NMR Spectroscopy[1]

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Received November 29, 1983

The reaction of 3-picoline 1-oxide with either *tert*-butyl or 1-adamantyl mercaptan in acetic anhydride yielded a mixture of 2-(alkylthio)-3-picolines, 2- and 3-(alkylthio)-5-picolines, and *trans,trans*-1-acetyl-2-(alkylthio)-3,4-diacetoxy-1,2,3,4-tetrahydropyridines **5**. When triethylamine was included in such reactions, the same picolyl sulfides (albeit in different yields) were obtained together with 1-acetyl-2-(alkylthio)-3-hydroxy-3-methyl-4-acetoxy-1,2,3,4-tetrahydropyridines **6**. The structure of **6d** was determined from an analysis of the long-range proton–carbon-13 spin coupling constants obtained from heteronuclear 2D *J* resolved experiments. The sulfide and alcohol of **6d** were found to be trans and the alcohol and acetoxy group cis.

The reaction of 3-picoline 1-oxide (**1**) with *tert*-butyl mercaptan in acetic anhydride produced the three isomeric sulfides **2–4** (R = t-C_4H_9)[2] together with the tetrahydropyridine **5a**.[3] However, it was found that the inclusion of triethylamine in such a reaction produced, besides the picolyl sulfides, the new tetrahydropyridine **6a**. When 1-adamantyl mercaptan (1-AdmSH) was used instead of *tert*-butyl mercaptan, the corresponding 1-adamantyl sulfides were isolated.

Pyridyl Sulfides, 2–4. When *tert*-butyl mercaptan was used, it was possible to separate the aromatic sulfides from tetrahydropyridines initially by high vacuum distillation, keeping the pot temperature between 100–120 °C. The

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