as a dark gel suitable for the next step: NMR δ 1.38 (s, 9 H), 7.7–8.0 (m, 2 H), 8.30 (d, J = 1, 1 H).

4-*sec*-Butyl-2-nitrobenzenesulfenyl Chloride (5c). With the above procedure, **4c** (1.058 g) afforded crude **5c** (1.201 g, 98%) as a brown oil suitable for the next step: NMR δ 0.82 (t, J = 3, 3 H), 1.30 (d, J = 3, 3 H), 1.66 (pentet, J = 3, 2 H), 2.79 (sextet, J = 3, 1 H), 7.62 (dd, J = 4, 1, 1 H), 7.90 (d, J = 4, 1 H), 8.14 (d, J = 1, 1 H).

β-D-Glucopyranosyl 4-*tert*-Octyl-2-nitrophenyl Disulfide (6a). A mixture of **5a** (1.510 g, 5.01 mmol), β-D-thioglucose sodium salt (1.113 g, 5.10 mmol; Sigma Co.), and 15-crown-5 (1.106 g, 5.02 mmol) in dry acetonitrile (15 mL) was stirred at 25 °C for 10 min. The solvent was removed, and the residue was triturated with $CHCl_3$ and filtered. Chromatography over silica gel afforded, first, the orange diaryl disulfide ($CHCl_3$), second, 15-crown-5 (2% MeOH/$CHCl_3$), third, a brown unidentified oil (4% MeOH, $CHCl_3$), and finally disulfide **6a** (5% MeOH, $CHCl_3$), which crystallized upon removal of solvent. Recrystallization from ethyl acetate/hexane gave 1.233 g (54%) of **6a** as yellow crystals: mp 131–133 °C; NMR (acetone-d_6) δ 0.75 (s, 9 H), 1.43 (s, 6 H), 1.86 (s, 2 H), 2.7–4.7 (m, 12 H), 7.90 (dd, J = 4.5, 1, 1 H), 8.23 (d, J = 1, 1 H), 8.54 (d, J = 4.5, 1 H). Anal. Calcd for $C_{20}H_{31}NO_7S_2 \cdot {}^1/_2H_2O$: C, 51.04; H, 6.85; N, 2.98. Found: C, 51.27; H, 6.46; N, 2.65. The water solubility was 0.16 g/L.

β-D-Glucopyranosyl 4-*tert*-Butyl-2-nitrophenyl Disulfide (6b). With the above procedure, **5b** (70 mg) afforded **6b** (48 mg, 43%): mp 161–162 °C (acetone); NMR (CD_3OD) δ 1.40 (s, 9 H), 3.2–3.9 (m, 10 H), 4.4–4.6 (m, 1 H), 7.84 (dd, J = 4.5, 1, 1 H), 8.22 (d, J = 1, 1 H), 8.53 (d, J = 4.5, 1 H). Anal. Calcd for $C_{16}H_{23}NO_7S_2$: C, 47.39; H, 5.72; N, 3.45. Found: C, 47.21; H, 5.56; N, 3.16.

β-D-Glucopyranosyl 4-*sec*-Butyl-2-nitrophenyl Disulfide (6c). With the above procedure, **5c** (1.201 g) afforded **6c** (1.339 g, 67%): mp 125–126 °C (acetone); NMR (acetone-d_6) δ 0.84 (t, J = 3.5, 3 H), 1.28 (d, J = 3.5, 3 H), 1.63 (pentet, J = 3.5, 2 H), 2.6–2.9 (m, 2 H), 3.2–3.9 (m, 6 H), 4.2–4.8 (m, 4 H), 7.69 (dd, J = 4.5, 1, 1 H), 8.02 (d, J = 1, 1 H), 8.51 (d, J = 4.5, 1 H). Anal. Calcd for $C_{16}H_{23}NO_7S_2$: C, 47.39; H, 5.72; N, 3.45. Found: C, 47.06; H, 5.66; N, 3.11. The water solubility was 0.36 g/L.

β-D-Glucopyranosyl 2-Nitrophenyl Disulfide (6d). With the above procedure, 2-nitrophenylsulfenyl chloride (113 mg, Aldrich) afforded **6d** (122 mg, 60%): mp 77–79 °C (acetone); NMR (acetone-d_6) δ 2.80 (s, 2 H), 3.2–3.8 (m, 7 H), 4.1–5.0 (m, 3 H), 7.3–7.8 (m, 2 H), 8.05–8.2 (m, 1 H), 8.5–8.65 (m, 1 H). Anal. Calcd for $C_{12}H_{15}NO_7S \cdot {}^2/_3(CH_3)_2CO$: C, 43.32; H, 4.93; N, 3.61. Found: C, 43.18; H, 4.65; N, 3.22.

Tetraacetyl-β-D-Glucopyranosyl 4-*tert*-Octyl-2-nitrophenyl Disulfide (7). Method A: A pyridine (5 mL) solution of **6a** (46.3 mg, 0.10 mmol) and acetic anhydride (170 mg, 1.7 mmol) was stirred at 25 °C for 1 h, and the solvent was removed. Recrystallization of the residue from ethyl acetate/hexane gave 39.1 mg (62%) of **7** as yellow crystals: mp 131.5 °C; NMR δ 0.69 (s, 9 H), 1.32 (s, 6 H), 1.81 (s, 2 H), 1.92, 1.98, and 2.06 (all s, 12 H), 3.45–3.7 (m, 1 H), 3.9–4.0 (m, 2 H), 4.5–5.2 (m, 4 H), 7.58 (dd, J = 4.5, 1, 1 H), 8.05–8.25 (m, 2 H). Anal. Calcd for $C_{28}H_{39}NO_{11}S_2$: C, 53.40; H, 6.24; N, 2.22. Found: C, 53.65; H, 6.10; N, 1.93.

Method B: A mixture of **5a** (45.5 mg, 0.151 mmol), β-D-thioglucose tetraacetate (55.2 mg, 0.152 mmol), and K_2CO_3 (70.9 mg, 0.525 mmol) in acetone (4 mL) was stirred at 25 °C for 50 min. Filtration followed by removal of solvent gave a yellow crystalline residue. Recrystallization from ethyl acetate/hexane gave 72.2 mg (72%) of **7** as yellow crystals, identical (melting point and NMR spectrum) with those obtained from method A (mmp 131–132 °C).

Acknowledgment. This research was supported by Public Health Service Research Grants GM 24951 and GM 27137 from the National Institute of General Medical Sciences.

Registry No. 1a, 46912-02-1; **1b**, 3279-07-0; **1c**, 3555-18-8; **2a**, 74752-31-1; **2b**, 74752-32-2; **2c**, 74752-33-3; **3a**, 74752-34-4; **3b**, 74752-35-5; **3c**, 74752-36-6; **4a**, 74752-37-7; **4b**, 74752-38-8; **4c**, 74752-39-9; **5a**, 74752-40-2; **5b**, 74752-41-3; **5c**, 74752-42-4; **6a**, 74752-43-5; **6b**, 74752-44-6; **6c**, 74752-45-7; **6d**, 74752-46-8; **7**, 19879-84-6; β-D-thioglucose sodium salt, 10593-29-0; dimethylthiocarbamoyl chloride, 16420-13-6.

A Novel Isothiocyanate Dimer

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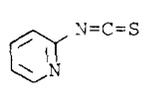
Received June 15, 1979

A novel type of formal isothiocyanate dimer, a 3-aryl-4-(arylimino)-1,3-thiazetidine-2-thione, has been isolated. The assignment of the structure **11** is based on physical chemical data, especially NMR and mass spectra, and is supported by an alternate synthesis.

Isothiocyanates are, in general, more stable and less reactive than isocyanates, and until 1960 no examples of dimers of isothiocyanates had been reported. At that time it was suggested[1] that the brick-red solid previously assumed[2] to be 2-pyridyl isothiocyanate (1) might be **2**. This



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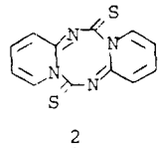

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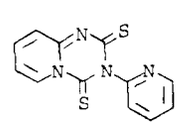
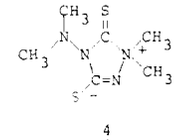


3

postulated structure was later shown[3,4] to be incorrect, and the correct structure for this dimer of **1** is in fact **3**. Similar dimers also involving atoms adjacent to the isothiocyanate group have been reported.[5-7] Another type of dimer involving adjacent atoms is the isolated[8] but unstable dimer, **4**, of (dimethylamino)isothiocyanate. Condensations of



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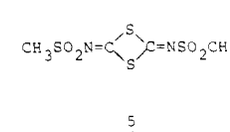

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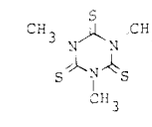

6

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(2) Fairfull, A. E. S.; Peak, D. A. *J. Chem. Soc.* **1955**, 796–802.
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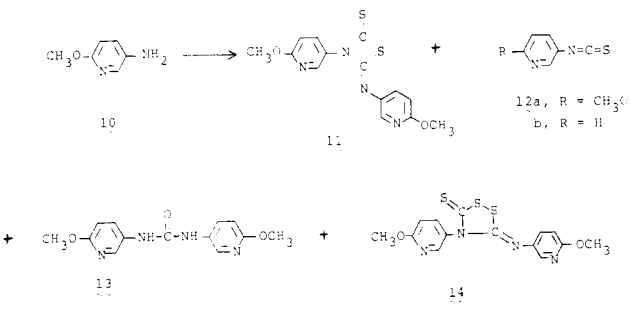
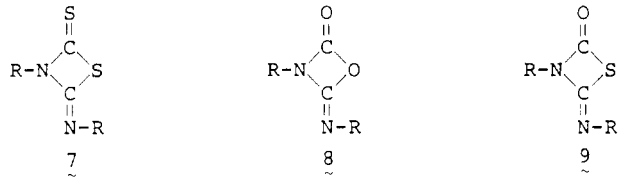
Scheme I



isothiocyanates involving only the NCS atoms have resulted in the formation of the dimer **5**[9] and the trimer **6**.[10,11]

We now report a basically different type of isothiocyanate dimer represented by the imino-1,3-thiazetidine-2-thione structure **7**. Analogous imino-1,3-oxazetidin-2-

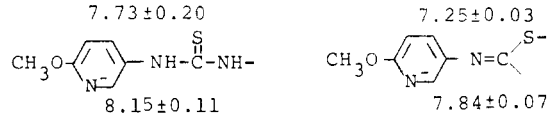


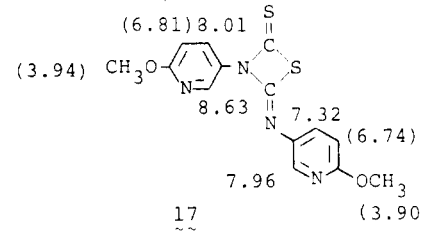
ones **8** have been suggested[12] as the dimers of isocyanates and, in particular, have been postulated[13,14] as unstable intermediates in the formation of carbodiimides from isocyanates. However, as yet, no stable examples of **8** have been unambiguously characterized. The reaction of phosgene with thioureas has been reported[15,16] to give imino-1,3-thiazetidin-2-ones **9**. However, no examples of the imino-1,3-thiazetidine-2-thione structure **7**, either as examples of isothiocyanate dimers or as synthesized from other precursors, could be found in the literature.

When **10** was treated with 1 equiv of thiophosgene and 1 equiv of $NaHCO_3$ in an aqueous–organic medium by a reported isothiocyanate synthesis procedure,[17] the stable crystalline dimer **11** was isolated (Scheme I). Surprisingly, no evidence for the presence of the monomer **12a** was found in the organic mother liquors of **11** even though the unsubstituted analogue **12b** was reported[2] as a stable liquid. The aqueous layer from the preparation of **11** deposited crystals of the hydrochloride of the symmetrical urea **13**. This reaction was then repeated with 2 equiv of $NaHCO_3$; in this case, in addition to the dimer **11**, a 49% yield of the monomer **12a** *was* isolated. A similar reaction using 2 equiv of triethylamine produced no dimer but did give some of the monomer, and also the dithiazolidine **14** was isolated.

Attempts were made to obtain crystals of **11** suitable for a single-crystal X-ray structure determination. However, recrystallization of **11** from a variety of solvents, including hexane, ether, dichloromethane, toluene, diglyme, acetone, and *tert*-pentanol, gave only very fine needles. Similar crystals were obtained from a variety of mixed solvents by using the apparatus of Brown and Trefonas.[18]

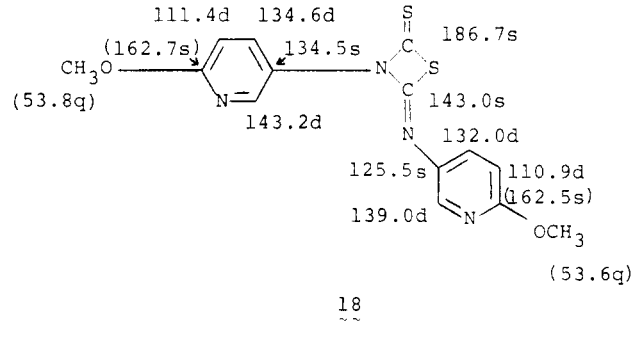
The assignment of structure **11** is based primarily on spectral properties. In particular, the NMR spectrum clearly contains signals associated with two different 2,5-disubstituted pyridine rings. The differences between the signals for the two α-protons (0.67 ppm) and for the two γ-protons (0.69 ppm) are too large to be due simply to geometric syn–anti stereoisomers around a C–N bond possessing double bond character. Differently substituted pyridyl rings are therefore present. The only likely structure which fits this criterion is that of **11**. In connection with other studies in these laboratories, we had occasion to observe the NMR spectra of a number of (6-methoxy-3-pyridyl)amine derivatives. A variety of compounds with partial structure as in **15** showed average





chemical shifts (δ) as indicated for this nonconjugated ring. The spectra of a number of compounds containing the conjugated ring of **16** showed signals at higher field as indicated. Therefore, the signals occurring at higher field were assigned to the pyridylimine group of **11** while the lower field signals were assigned to the pyridylamine group as in **17**. The pairs of assigned signals in parentheses are more conjectural and may well be reversed.

The proton-decoupled ^{13}C spectrum contains the expected 14 discrete signals in positions consistent with the assigned structure. In addition, the single-frequency, off-resonance, ^{13}C spectrum has the expected multiplicities for each signal as shown in **18**.



The mass spectra of **11** are also interesting and supportive of the assigned structure. Under usual conditions, the spectrum shows peaks at m/z 76, 78, 96, 137, 166, 227, 256, and 332 with no peaks between 256 and 332. More interesting, however, are the spectra determined under conditions more prone to thermal decomposition. In that case, an early scan shows no peak at m/z 332 but a base

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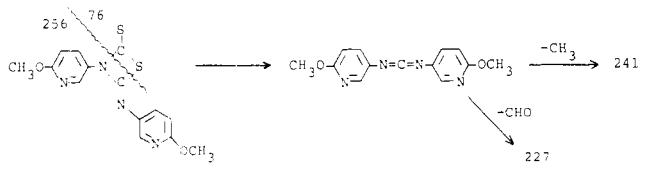
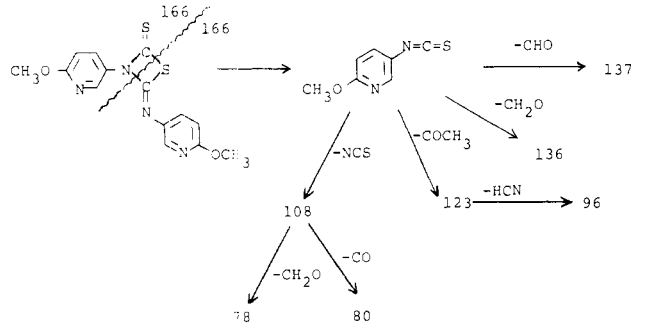
Scheme II



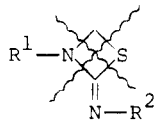
Scheme III



peak at m/z 256 with other peaks at m/z (relative intensity) 241 (3), 227 (16), 166 (12), 137 (4), 136 (5), 123 (2), 108 (4), 96 (5), 80 (19), 78 (8), and 76 (55). These are interpreted as occurring via the cleavages shown in Scheme II (and also via cleavages shown later). Later scans show a weak parent ion at m/z (relative intensity) 332 (6), a base peak at 166, and other peaks at 256 (35), 241 (2), 227 (9), 137 (24), 136 (18), 123 (6), 108 (3), 96 (13), 80 (13), 78 (11), and 76 (14), occurring via the above cleavages and via those shown in Scheme III.

In addition, a high-resolution mass spectrum indicated that the fragments at m/z 332, 256, 241, 227, 166, 137, 136, 96, and 78 had the empirical formulas required for the above fragmentations.

This dual mode of cleavage of the four-membered ring of **11** is analogous to that recently reported[19] for the 1,3-thiazetidine structure **19**.



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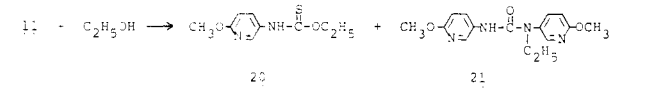
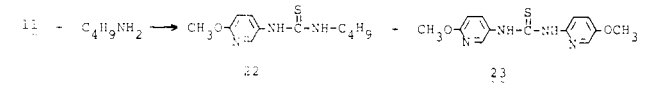
The structure of **11** is also supported by some of its reactions. An attempt to recrystallize **11** from ethanol gave instead another material, **20**. When this reaction was





repeated quantitatively, 1.22 mol of **20**/mol of **11** was isolated. The mother liquor of this reaction yielded **21** which *may* have arisen via the corresponding carbodiimide and *o*-ethylisourea. Reaction of **11** with butylamine at room temperature readily gave, in a yield of 1.34 mol/mol of **11**, the unsymmetrical thiourea **22** and smaller amounts of the symmetrical thiourea **23**. The unsymmetrical compound was also prepared from **10** and butyl isothiocyanate. The symmetrical thiourea was also prepared by the procedure of Fry and Farquhar.[20] It may have arisen in the reaction of **11** and butylamine via dissociation of **22** to butyl isothiocyanate and **10** followed by reaction of **10** with **11** or **22**.

The formation of **20** and **22** can readily be rationalized by nucleophilic attack of the alcohol or amine on either the thione or the isothiourea carbons. The resulting intermediates could then collapse to product and 1 equiv of **12a** which could then react with further reagent to give more product. Alternatively, the intermediates themselves could be attacked by further reagent. The formation of **20** and **22** probably does *not* arise via prior dissociation of **11** to **12a**. These latter two compounds can coexist in solution, and heating **11** in various unreactive solvents does not cause any dissociation into **12a**.

The mechanism of formation of **11** is not completely understood. It is not simply dimerization of **12a** since heating a toluene solution of **12a** under reflux for 18 h gave no TLC evidence for the formation of **11**. Under the conditions of formation of **11**, thiophosgene may attack some intermediate or some preformed thiourea, i.e., **23**. Indeed, reaction of thiophosgene and **23** in toluene or ether at room temperature readily gave the dimer **11**. This last reaction is added support for the structure of this product.[21]

Experimental Section

Melting points were taken in open capillary tubes by using a Thomas-Hoover melting point apparatus and are corrected. Organic solutions were dried with anhydrous Na_2SO_4. Ultraviolet spectra were recorded on a Cary UV spectrophotometer, Model 14M. Infrared spectra were recorded on a Beckman Model IR-9 spectrophotometer. Proton and carbon-13 nuclear magnetic resonance spectra were recorded on a Varian XL-100 instrument. Low-resolution mass spectra were taken with either a CEC 21-110 or a Varian MAT CH5 instrument, and high-resolution mass spectra were taken with the CEC 21-110 instrument and recorded on photoplates.

3-(6-Methoxy-3-pyridinyl)-4-[(6-methoxy-3-pyridinyl)imino]-1,3-thiazetidine-2-thione (11). A. From 10. A solution of 26.5 mL (40.0 g, 0.35 mol) of $CSCl_2$ in 250 mL of ether was added over 20 min to a rapidly stirred mixture of 37.2 g (0.30 mol) of 6-methoxy-3-pyridinamine (**10**), 30.0 g (0.36 mol) of $NaHCO_3$, and 250 mL of H_2O; a vigorous evolution of CO_2 occurred during the first half of the addition. After the mixture was stirred at ambient temperature for 1.5 h, the color of the $CSCl_2$ had essentially disappeared. The mixture was filtered, and the solids were washed with ether. The filtrate was separated into an aqueous layer (see the isolation of **13**) and an ether layer (which contained only a minimal amount of material). The original filter cake was extracted several times with CH_2Cl_2. The extracts were dried and concentrated with the addition of ether to give 14.15 g (28%) of **11** as fine yellow needles: mp 147.5–148.5 °C; UV max (C_2H_5OH) 230 nm (infl, ϵ 17 200), 253 (20 000), 280 (15 600), 302 (infl, 12 600), 333 (11 820); IR ($CHCl_3$) 1730, 1705 cm^{-1}; for NMR and mass spectra, see Discussion. Anal. Calcd for $C_{14}H_{12}N_4O_2S_2$: C, 50.58; H, 3.64; N, 16.86; S, 19.29. Found: C, 50.45; H, 3.42; N, 16.75; S, 19.26.

B. From 23. A slurry of 581 mg (2 mmol) of **23** and 0.4 mL (0.60 g, 5.2 mmol) of $CSCl_2$ in 15 mL of toluene was stirred at room temperature for 18 h. The reaction remained heterogeneous, and TLC analysis indicated that the only material in solution was **11**. The solid (salts and starting material) was removed by filtration, and the filtrate was concentrated under vacuum. The

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(21) Part of this work was presented at the 178th Meeting of the American Chemical Society, Washington, DC, Sept 10–14, 1979; Abstract ORGN 48.

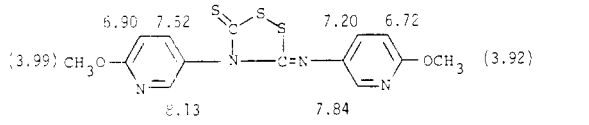
residue was recrystallized from CH_2Cl_2–ether to give 221 mg (33%) of **11**, mp 146.5–148 °C, undepressed on mixture with a sample of **11** prepared in A.

***N,N'*-Bis(6-methoxy-3-pyridinyl)urea Hydrochloride.** On standing at room temperature, the aqueous layer from the preparation of **11** gradually deposited crystals. After 4 days, these were collected and recrystallized from CH_3OH to give 3.50 g (13%) of the hydrochloride of **13** as colorless crystals: mp 178–180 °C dec; compatible IR, UV, NMR, and mass spectra. Anal. Calcd for $C_{13}H_{14}N_4O_3$·HCl: C, 50.25; N, 4.87; Cl, 11.41; N, 18.03. Found: C, 50.22; H, 5.00; Cl, 11.27; N, 18.05.

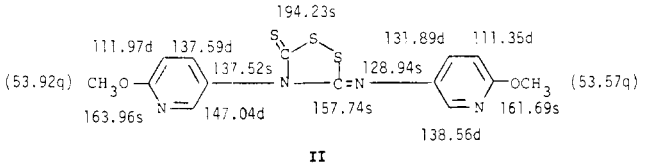
***N,N'*-Bis(6-methoxy-3-pyridinyl)urea (13).** To a slurry of **13**·HCl in H_2O was added a slight excess of NaOH. The reaction mixture, which was heterogeneous throughout, was stirred for 15 min and filtered. Recrystallization of the solid from CH_3OH gave a 75% yield of **13** as colorless crystals: mp 232.5–235 °C; compatible IR, UV, NMR, and mass spectra. Anal. Calcd for $C_{13}H_{14}N_4O_3$: C, 56.93; H, 5.14; N, 20.43. Found: C, 56.98; H, 5.11; N, 20.73.

5-Isothiocyanato-2-methoxypyridine (12a). A mixture of 12.40 g (0.10 mol) of **10**, 20.0 g (0.24 mol) of $NaHCO_3$, and 80 mL of H_2O was treated with a solution of 8.83 mL (13.3 g, 0.12 mol) of $CSCl_2$ under the conditions reported for the preparation of **11**. Workup as before gave 3.40 g (20%) of **11** as pale yellow crystals, mp 146–148.5 °C. The original filtrate was diluted with some ether, and the organic layer was separated, dried, and passed over a plug of silica gel. The eluate was concentrated, and the residue was crystallized from hexane to give 8.08 g (49%) of **12a** as colorless crystals: mp 56.5–57.5 °C; UV max (hexane) 228 nm (ϵ 27 800), 260 (infl, 9600), 274 (14 750), 285 (infl, 12 850), 307 (infl, 4700); IR ($CHCl_3$) 2110 cm^{-1} (s, br, N=C=S); NMR ($CDCl_3$) δ 8.09 (d, 1, J = 2.5 Hz, 6-H), 7.42 (dd, 1, J = 2.5, 9 Hz, 4-H), 6.71 (d, 1, J = 9 Hz, 3-H), 3.93 (s, 3, OCH_3); mass spectrum, m/z (relative intensity) 166 (100), 165 (56), 137 (46), 136 (29), 96 (23), 78 (27). Anal. Calcd for $C_7H_6N_2OS$: C, 50.58; H, 3.64; N, 16.86; S, 19.29. Found: C, 50.83; H, 3.46; N, 16.74; S, 19.16.

4-(6-Methoxy-3-pyridinyl)-5-[(6-methoxy-3-pyridinyl)imino]-1,2,4-dithiazolidine-3-thione (14). A solution of 9.50 mL (14.33 g, 0.125 mol) of $CSCl_2$ in 40 mL of ether was added over 20 min to a rapidly stirred mixture of 12.40 g (0.10 mol) of **10**, 35.7 mL (25.9 g, 0.256 mol) of triethylamine, 80 mL of H_2O, and 80 mL of ether. Spontaneous refluxing of the ether occurred during the addition. A precipitate formed immediately which redissolved when the addition was about three-fourths complete to give two clear layers. After the addition was complete, the mixture was stirred at ambient temperature for 1 h. TLC analysis showed the absence of **11**, the presence of **12a**, and several other spots. The layers were separated, and the organic layer was washed with water, dried, and concentrated. The residue was chromatographed over silica gel. Elution with 60–90% CH_2Cl_2 in hexane gave crude **12a** which was crystallized to give 1.60 g (10%) as colorless crystals, mp 56–57.5 °C. Further elution with 1–20% ethyl acetate in CH_2Cl_2 gave some crude **14**. The remainder of the material then crystallized in the column. A portion of this was removed and shown by mixture melting point to be **13**. The crude **14** was then purified on thick-layer plates developed in 10% ethyl acetate in toluene to give **14** as an orange gum: UV max ($CHCl_3$) 290 nm (ϵ 10 650), 322 (infl, 5370), 385 (infl, 460); IR ($CHCl_3$) 1632 cm^{-1}; NMR ($CDCl_3$) as shown in structures I and II with the expected proton and ^{13}C SFORD multiplicities as indicated;



I



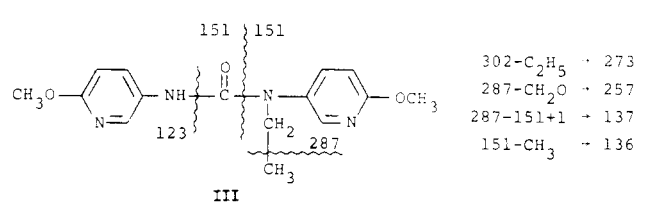
II

mass spectrum, m/z (relative intensity) 364 (73), 198 (100), 166 (58), 165 (44), 137 (36), 134 (100), 133 (52), 105 (36), 96 (28). Anal. Calcd for $C_{14}H_{12}N_4O_2S_3$: C, 46.13; H, 3.32; N, 15.37; S, 26.39. Found: C, 46.49; H, 3.37; N, 15.44; S, 25.78.

The purified **14** gradually crystallized when the mixture was allowed to stand. It was recrystallized from CH_2Cl_2/ether to give crystals suitable for a single-crystal X-ray analysis; mp 138–141 °C. The unit cell contains two independent molecules of **14** differing by 180° in their conformations about the pyridyl–imine bond. The crystal data are as follows: space group, $P2_1a$; a, 26.713 (5) Å; b, 9.854 (2) Å; c, 12.239 (2) Å; β, 91.28 (1)°; Z, 8; d_{calcd}, 1.502 g cm^{-3}; μ (Cu Kα), 41.8 cm^{-1}. The intensity data were measured on a Hilger-Watts diffractometer (Ni-filtered Cu Kα radiation, θ–2θ scans, pulse-height discrimination). The size of the crystal used for data collection was approximately 0.10 × 0.15 × 0.4 mm; the data were corrected for absorption. Of the 3024 independent reflections for $\theta < 48°$, 2518 were considered to be observed [$I > 2.5\sigma(I)$]. The structure was solved by a multiple-solution procedure[22] and was refined by full-matrix least-squares methods. In the final refinement, anisotropic thermal parameters were used for the heavier atoms and isotropic temperature factors were used for the hydrogen atoms. The hydrogen atoms were included in the structure factor calculations, but their parameters were not refined. The final discrepancy indices are R = 0.038 and R_w = 0.045 for the 2518 observed reflections. The final difference map has no peaks greater than ±0.3 eA^{-3}.

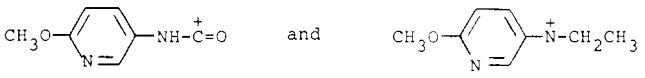
***O*-Ethyl (6-Methoxy-3-pyridinyl)carbamothioate (20).** A mixture of 1.662 g (10 mmol) of **11** and 15 mL (hardly enough to wet all the solid) of absolute ethanol was heated on a steam bath under reflux. Two hours later, it looked as if little if any solution had taken place, and TLC analysis indicated that no reaction had occurred. Heating was continued over the weekend. TLC analysis then indicated that the starting material was gone and that two products had formed. The ethanol was evaporated under vacuum, and the residue was chromatographed over silica gel with 25% ethyl acetate in hexane. The more mobile spot was collected and recrystallized from ether–hexane to give 1.298 g (1.22 mol/mol of **11**) as colorless crystals: mp 90–91.5 °C; UV max (C_2H_5OH) 223 nm (ϵ 8800), 276 (13 020); NMR ($CDCl_3$) δ 8.75 (br, 1, NH), 8.19 (d, 1, J = 2.5 Hz, 2-H), 7.68 (dd, 1, J = 2.5, 8.5 Hz, 4-H), 6.77 (d, 1, J = 8.5 Hz, 5-H), 4.63 (q, 2, J = 7 Hz, OCH_2CH_3), 3.95 (s, 3, OCH_3), 1.38 (t, 3, J = 7 Hz, OCH_2CH_3); mass spectrum, m/z 212. Anal. Calcd for $C_9H_{12}N_2O_2S$: C, 50.93; H, 5.70; N, 13.20; S, 15.10. Found: C, 50.96; H, 5.76; N, 13.27; S, 14.87.

***N*-Ethyl-*N,N'*-bis(6-methoxy-3-pyridinyl)urea (21).** The less mobile spot from the above reaction was collected and isolated as a colorless oil (0.5 g, 15%) which was solvated with 0.25 molar ether: UV max (C_2H_5OH) 236 nm (infl, ϵ 13 900), 246 (14 720), 290 (infl, 6540); IR ($CHCl_3$) 3415 (NH), 1655 cm^{-1} (urea), no C–O–C band of a pseudourea;[23] NMR ($CDCl_3$) δ 7.85 (m, 2, 2-H), 7.31 (m, 2, 4-H), 6.68 (d, 2, J = 9 Hz, 5-H), 6.10 (br, 1, NH), 4.37 (q, 2, J = 7 Hz, NCH_2CH_3), 3.87 (s, 6, OCH_3), 1.36 (t, 3 J = 7 Hz, NCH_2CH_3); mass spectrum indicates the cleavages shown in structure III.



III

A high-resolution mass spectrum confirms the composition of the m/z 302, 273, 137, and 123 peaks. Although the expected doublet at m/z 151 was not fully resolved, the ^{13}C isotope peaks at m/z 152 were resolved and confirmed the expected compositions:



Anal. Calcd for $C_{15}H_{18}N_4O_3$·0.25$C_4H_{10}O$: C, 59.89; H, 6.44; N,

(22) Germain, G.; Main, P.; Woolfson, M. M. *Acta Crystallogr., Sect. A* **1971**, *A27*, 368–376.

(23) Forman, S. E.; Erickson, C. A.; Adelman, H. *J. Org. Chem.* **1963**, *28*, 2653–2658.

17.46; S, 0. Found: C, 59.82; H, 6.53; N, 17.21; S, <0.07.

N-Butyl-N'-(6-methoxy-3-pyridinyl)thiourea (22). A. From 10. A solution of 12.1 g (0.097 mol) of **10** and 11.5 g (0.10 mol) of butyl isothiocyanate in 100 mL of benzene was allowed to stand at room temperature overnight and then evaporated under vacuum. The residue was recrystallized from CH_2Cl_2–ether to give 12.5 g (54%) of **14b** as colorless crystals: mp 87.5–89.5 °C; UV (C_2H_5OH) 243 nm (ϵ 20 000), 270 (infl, 1000), 300 (infl, 3200); NMR ($CDCl_3$) δ 8.34 (s, 1, NH), 8.20 (d, 1, J = 2.5 Hz, 2-H), 7.63 (dd, 1, J = 2.5, 8.5 Hz, 4-H), 6.87 (d, 1, J = 8.5 Hz, 5-H), 6.10 (m, 1, NH), 4.00 (s, 3, OCH_3), 3.64 (m, 2, NCH_2C), 1.45 (m, 4, $NCH_2CH_2CH_2CH_3$), 0.92 (t, 3, J = 7 Hz, CCH_3); mass spectrum, m/z 239. Anal. Calcd for $C_{11}H_{17}N_3OS$: C, 55.22; H, 7.16; N, 17.56; S, 13.38. Found: C, 55.30; H, 7.12; N, 17.72; S, 13.47.

B. From 11. A 1.662-g (10 mmol) sample of **11** was dissolved in 15 mL of CH_2Cl_2 with some heat. Butylamine (1.10 mL, 0.81 g, 11 mmol) was added, and the reaction was allowed to stand at ambient temperature for 2 h and then concentrated under vacuum. The residue was chromatographed over silica gel. Elution with CH_2Cl_2 followed by crystallization from ether gave 1.598 g (1.34 mol/mol of **11**) as colorless crystals, mp 87.5–89 °C, undepressed on mixture with material prepared in A.

N,N'-Bis(6-methoxy-3-pyridinyl)thiourea (23). A. From 11. Further elution of the silica gel column from the isolation of **22** from **11** with 5% methanol in $CHCl_3$ followed by crystallization from $CHCl_3$ gave 158 mg (5%) of **23** as colorless crystals: mp 174–175 °C; compatible IR, UV, NMR, and mass spectra. Anal. Calcd for $C_{13}H_{14}N_4O_2S$: C, 53.77; H, 4.86; N, 19.30; S, 11.04. Found: C, 53.57; H, 4.86; N, 19.02; S, 11.14.

B. From 10. A solution of 12.41 g (0.10 mol) of **10** and 15.8 mL (15.5 g, 0.20 mol) of pyridine in 50 mL of CS_2 was heated under reflux while a solution of 12.7 g (0.05 mol) of I_2 in 125 mL of CS_2 was added over 15 min. The mixture was stirred an additional 30 min at ambient temperature. The precipitate of pyridine hydriodide was removed by filtration and washed with CH_2Cl_2. The filtrate was concentrated under vacuum, and the residue was heated with xylene on the steam bath. The insoluble solid was collected and heated with $CHCl_3$. The solution was treated with charcoal and concentrated. Recrystallization of the resulting solid from $CHCl_3$ gave 1.60 g (11%) of **23** as pale pink crystals, mp 173–174 °C, undepressed on mixture with a sample from A.

Acknowledgment. We thank our Physical Chemistry Department, under the direction of Dr. R. P. W. Scott, for microanalyses and IR and UV spectra.

Registry No. 10, 6628-77-9; **11**, 74763-57-8; **12a**, 52023-93-5; **13**, 74763-58-9; **13**·HCl, 74763-59-0; **14**, 74763-60-3; **20**, 74763-61-4; **21**, 74763-62-5; **22**, 74763-63-6; **23**, 74763-64-7.

Notes

Configuration of Arylchloromethaniminoxy Radicals. A Reassignment

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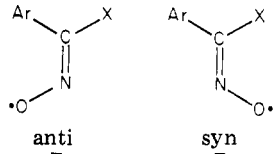
Received June 6, 1980

In a previous article some of us[1] reported that iminoxy radicals **1** obtained by oxidation of benzohydroxymoyl chlorides with lead tetraacetate in benzene solution exist in only one of the two possible configurations which, on the basis of the ESR spectral parameters, was assigned to be anti (*E*).[2] In a more recent study on the stereochemistry of a variety of iminoxyls,[3] we have found that in aprotic solvents the preferred geometry of the radicals derived from ortho-unsubstituted benzaldoximes is anti (*Z*), viz., that the aryl group and the oxygen are on the same side of the plane defined by the C=N bond, while substitution of the ortho positions of the aryl ring leads to a stabilization of the syn isomer. Stabilization of the syn configuration is also observed by substitution of the azomethine proton by an XR_n group (X = Si, Sn, and Ge; R_n are alkyls or aryls), the effect being that the larger the atomic number of X the greater the stabilization. In contradiction with these new findings, it appeared to be the assignment previously made for arylchloromethaniminoxyls. We therefore collected further experimental data on these radicals and on related iminoxyls with the aim of establishing on more firm grounds their preferred geometry.



	anti	syn
1; X = Cl	*E*	*Z*
2; X = Me	*Z*	*E*
3; X = H	*Z*	*E*
4; X = CH_2OH	*E*	*Z*
5; X = *t*-Bu	*Z*	*E*

The assignment of the anti configuration to arylchloromethaniminoxyls (**1**) was based[1] on the following arguments: (i) the magnitude of the hyperfine splitting at the chlorine atom (ca. 1.7 G) in radicals **1** appeared to be small for the syn configuration in comparison with a value of ca. 27 G which was reported for the coupling at the azomethine hydrogen in the syn isomeric radical (*E*)-**3** (Ar = Ph) from benzaldoxime;[4] (ii) the splittings to the halogen of the phenyl ring in iminoxyls **1** containing a chlorine or a bromine atom in one of the ortho positions (a_{Cl} = 2.15 G, a_{Br} = 9.8 G) were *large* and *similar* to the values reported by Norman and Gilbert[4] for the radicals from *o*-chloro- and *o*-bromoacetophenone oximes **2** which were assigned the anti configuration (**Z**).

We now have several indications that neither the magnitude of the hyperfine splitting at the azomethine chlorine

(1) A. Dondoni, G. F. Pedulli, and G. Barbaro, *J. Org. Chem.*, 37, 3564 (1972).

(2) Due to the variable priority order between the groups Ar and X (X = H, alkyl, Cl, CH_2OH) on the iminoxy radicals **1–5**, the *E* and *Z* notation may indicate opposite stereochemistry. This may be misleading for the objectives of the present work and clarity of the discussion. Therefore, in order to keep a uniform notation, we used the classical term syn to indicate compounds where X and O are on the *same* side with respect to the plane defined by the C=N double bond and the term anti for compounds where X and O are on *opposite* sides.

(3) A. Alberti, G. Barbaro, A. Battaglia, M. Guerra, F. Bernardi, A. Dondoni, and G. F. Pedulli, submitted for publication in *J. Org. Chem.*

(4) R. O. C. Norman and B. C. Gilbert, *J. Phys. Chem.*, 71, 14 (1967); B. C. Gilbert and R. O. C. Norman, *J. Chem. Soc B*, 981 (1967).

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