The Reactions of Thiosemicarbazides and 5-Halovalerophenones

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5-Halovalerophenones reacted with substituted thiosemicarbazides affording two different heterocyclic ring systems. Reactions with 4-substituted thiosemicarbazides gave 3-aryl-4,5,6,7-tetrahydro-1*H*-1,2-diazepine-1-carbothioamides whereas reactions with 2,4-dimethylthiosemicarbazide gave hexahydro-1,3-dimethyl-8a-aryl[1,2,4]triazolo[1,5-*a*]pyridine-2(3*H*)-thiones.

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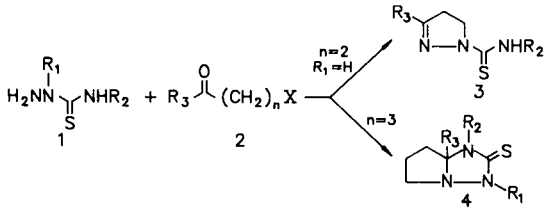
We have been investigating the reactions of thiosemicarbazides **1** and haloketones **2**. By varying the chain length between the carbonyl group and the electrophilic, halogen-bearing carbon of **2**, different heterocyclization reactions were observed. In this context, we have recently reported that the reactions of **1** and 3-halopropiophenones **2** (n = 2) afforded pyrazole derivatives **3** [1] whereas the reactions of **1** and 4-halobutyrophenones **2** (n = 3) gave derivatives of the pyrrolo[1,2-*b*]triazole ring system **4** [2] (Scheme I).

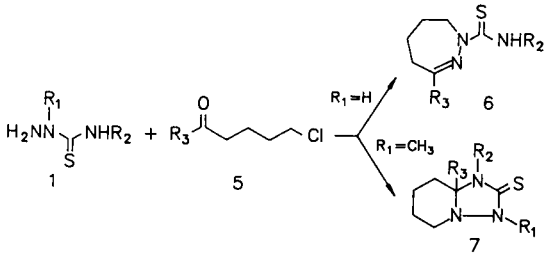
Scheme I



R_1=H,alkyl; R_2=alkyl; R_3=aryl; X=halogen

We have subsequently extended these studies and now wish to report that the reactions of thiosemicarbazides **1** and 5-halovalerophenones **5** [3] yield derivatives of either the tetrahydro-1,2-diazepine ring system **6** or the triazolo-[1,5-*a*]pyridine ring system **7** (Scheme II).

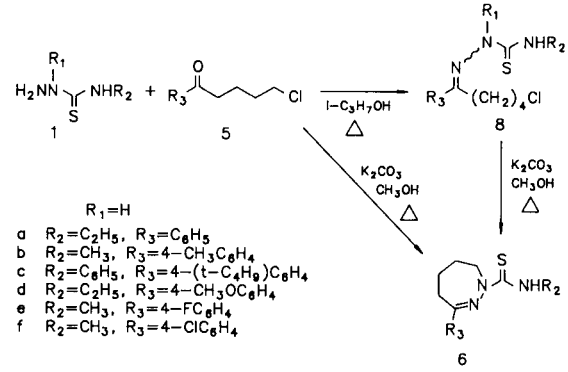
Scheme II



R_1=H,alkyl; R_2=alkyl,aryl; R_3=aryl

Reaction of 4-ethylthiosemicarbazide (**1**, R_1 = H, R_2 = C_2H_5) and 5-chlorovalerophenone (**5**, R_3 = C_6H_5) [4] in refluxing 2-propanol afforded no heterocyclic product and instead gave, in 77% yield, the thiosemicarbazone **8** (R_1 = H, R_2 = C_2H_5, R_3 = C_6H_5) as a mixture of *syn* and *anti* isomers. Refluxing **8** in methanol in the presence of potassium carbonate resulted in its cyclization to diazepine **6a** in 83% yield (Scheme III). As anticipated, the isolation and purification of the intermediate thiosemicarbazone could be avoided by simply refluxing **1** (R_1 = H, R_2 = C_2H_5), **5** (R_3 = C_6H_5), and potassium carbonate in methanol directly yielding **6a** in 61% yield.

Scheme III

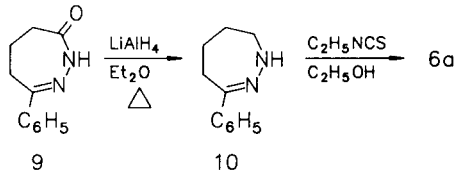


While both the mass spectrum and the elemental analysis of **6a** supported an empirical composition of $C_{14}H_{19}N_3S$, the structural assignment was based primarily upon consideration of the product's ^1H and ^{13}C nmr spectra. More specifically, in the ^1H nmr spectrum of **6a**, the methylene protons of the ethyl group appeared as a doublet of quartets centered at δ 3.69. Decoupling of the broad NH absorption centered at δ 7.25 caused this doublet of quartets to collapse to a single quartet thereby establishing the presence of the secondary ethyl amine group. In the ^{13}C nmr of **6a** both imine and thiocarbonyl resonances were observed at 164.0 and 179.9 ppm [5], respectively.

In order to verify the above structural assignment, we prepared **6a** by an alternate route. Thus, reduction of diazepin-3-one **9** [6] with lithium aluminum hydride in ether gave diazepine **10** [7] which without purification was immediately reacted with ethyl isothiocyanate resulting in a complex reaction mixture from which **6a** was isolated in low yield (Scheme IV). The poor yield of **6a** which was

realized by this procedure may reflect the reported instability of diazepine **10** [7].

Scheme IV

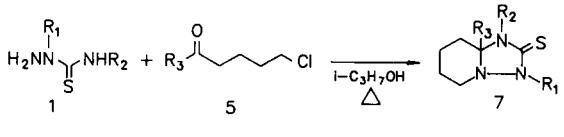


9 10

In order to establish the generality of this reaction as well as to provide additional examples for biological evaluation, several derivatives of this ring system were prepared (Scheme III).

Since diazepine formation clearly involved cyclization onto the 2-nitrogen of the thiosemicarbazide, we speculated that an alternate mode of ring closure might be observed if this nitrogen was substituted by an alkyl group. This proved to be the case as reaction of 2,4-dimethylthiosemicarbazide (**1**, $R_1 = R_2 = CH_3$) and 5-chlorovalerophenone (**5**, $R_3 = C_6H_5$) in refluxing 2-propanol afforded triazolo[1,5-*a*]pyridine **7a** in 67% yield (Scheme V).

Scheme V



1 5 7

$R_1 = R_2 = CH_3$

a $R_3 = C_6H_5$
b $R_3 = 4\text{-}CH_3C_6H_4$
c $R_3 = 4\text{-}(t\text{-}C_4H_9)C_6H_4$
d $R_3 = 4\text{-}CH_3OC_6H_4$
e $R_3 = 4\text{-}FC_6H_4$
f $R_3 = 4\text{-}ClC_6H_4$

The structural assignment was based largely upon consideration of the product's ^{13}C nmr spectrum which, in addition to verifying the presence of two methyl groups and four methylene groups, exhibited a quaternary carbon resonance at 83.1 ppm. The presence of the thiocarbonyl moiety was substantiated by an absorption at 178.4 ppm. The remaining spectral data, although less informative, were entirely consistent with the proposed structure. Additional examples of this ring system are presented in Scheme V.

EXPERIMENTAL

Melting points were determined in open capillaries on a Thomas Hoover apparatus and are uncorrected. Nuclear magnetic resonance spectra were recorded on Varian EM390 and XL300 spectrometers. The chemical shifts are given in parts per million from tetramethylsilane as the internal standard. Mass spectra were obtained on a Finnigan 4600 mass spectrometer.

General Procedure for the Preparation of 3-Aryl-4,5,6,7-tetrahydro-1*H*-1,2-diazepine-1-carbothioamides **6a-f**.

A mixture of the 5-chlorovalerophenone (20.3 mmoles), the 4-substituted thiosemicarbazide (20.3 mmoles), potassium carbonate (2.81 g, 20.3 mmoles), and methanol (100 ml) was stirred and heated to reflux. After being refluxed for 24 hours, the solvent was evaporated at reduced pressure and the concentrate was dissolved in a two phase mixture of ethyl acetate and water. This two phase mixture was transferred to a separatory funnel where the two phases were thoroughly mixed. The ethyl acetate layer was separated and the aqueous layer was extracted three times with ethyl acetate. The ethyl acetate layers were combined, washed with saturated aqueous sodium chloride, and dried over anhydrous sodium sulfate. The drying agent was removed by filtration and the filtrate was evaporated at reduced pressure leaving the crude product which was purified by a combination of flash chromatography [8] and crystallization.

3-Phenyl-4,5,6,7-tetrahydro-*N*-ethyl-1*H*-1,2-diazepine-1-carbothioamide (**6a**).

Following flash chromatography (dichloromethane) and crystallization from 2-propanol, this compound was obtained in 61% yield as pale yellow spars, mp 93-95°; ^1H nmr (deuteriochloroform): δ 1.24 (t, 3H, J = 7.2 Hz), 1.79 (m, 2H), 1.96 (m, 2H), 2.96 (m, 2H), 3.69 (dq, 2H, J = 5.5 and 7.2 Hz), 4.40 (m, 2H), 7.25 (broad s, 1H), 7.39-7.50 (m, 3H), 7.72-7.78 (m, 2H); ^{13}C nmr (deuteriochloroform): 14.4, 21.3, 26.6, 31.2, 40.0, 52.0, 126.7, 128.2, 130.1, 137.1, 164.0, 179.9 ppm; ms: 261 (M^+, 100).

Anal. Calcd. for $C_{14}H_{19}N_3S$: C, 64.33; H, 7.33; N, 16.08. Found: C, 64.40; H, 7.35; N, 16.23.

3-(4-Methylphenyl)-4,5,6,7-tetrahydro-*N*-methyl-1*H*-1,2-diazepine-1-carbothioamide (**6b**).

Following flash chromatography (1.5% ethyl acetate/dichloromethane) and crystallization from 2-propanol, this compound was isolated in 62% yield as pale yellow crystals, mp 87-89°; ^1H nmr (deuteriochloroform): δ 1.76 (m, 2H), 1.96 (m, 2H), 2.40 (s, 3H), 2.93 (m, 2H), 3.17 (d, 3H, J = 4.9 Hz), 4.39 (m, 2H), 7.23 (d, 3H, J = 8.0 Hz), 7.65 (d, 2H, J = 8.0 Hz); ^{13}C nmr (deuteriochloroform): 21.3, 21.4, 26.9, 31.2, 32.0, 52.3, 127.0, 129.2, 134.5, 140.9, 165.3, 181.4 ppm; ms: 261 (M^+, 79).

Anal. Calcd. for $C_{14}H_{19}N_3S$: C, 64.33; H, 7.33; N, 16.08. Found: C, 64.09; H, 7.43; N, 16.11.

3-[4-(1,1-Dimethylethyl)phenyl]-4,5,6,7-tetrahydro-*N*-phenyl-1*H*-1,2-diazepine-1-carbothioamide (**6c**).

Following flash chromatography (25% hexane/dichloromethane) and crystallization from 2-propanol, this compound was obtained in 44% yield as pale yellow crystals, mp 82-84°; ^1H nmr (deuteriochloroform): δ 1.35 (s, 9H), 1.83 (m, 2H), 2.01 (m, 2H), 3.01 (m, 2H), 4.47 (m, 2H), 7.13-7.79 (m, 9H), 9.05 (broad s, 1H); ^{13}C nmr (deuteriochloroform): 21.5, 26.5, 31.1, 31.2, 34.8, 52.0, 124.7, 125.4, 125.5, 126.8, 128.3, 134.0, 138.9, 164.1, 165.0, 178.6 ppm; ms: 365 (M^+, 100).

Anal. Calcd. for $C_{22}H_{27}N_3S$: C, 72.29; H, 7.44; N, 11.50. Found: C, 72.18; H, 7.47; N, 11.55.

3-(4-Methoxyphenyl)-4,5,6,7-tetrahydro-*N*-ethyl-1*H*-1,2-diazepine-1-carbothioamide (**6d**).

Following flash chromatography (dichloromethane) and crystallization from 2-propanol, this compound was obtained in 67% yield as pale yellow crystals, mp 76-78°; ^1H nmr (deuteriochloroform): δ 1.24 (t, 3H, J = 7.2 Hz), 1.75 (m, 2H), 1.95 (m, 2H), 2.91 (m, 2H), 3.69 (dq, 2H, J = 5.5 and 7.2 Hz), 3.86 (s, 3H), 4.35 (m, 2H), 6.95 (d, 2H, J = 8.9 Hz), 7.12 (broad s, 1H), 7.74 (d, 2H, J = 8.9 Hz); ^{13}C nmr (deuteriochloroform): 14.5, 21.4, 26.9, 30.9, 40.1, 52.1, 55.3, 113.7, 128.5, 129.3, 161.4, 165.2, 179.8 ppm; ms: 291 (M^+, 100).

Anal. Calcd. for $C_{15}H_{21}N_3OS$: C, 61.82; H, 7.26; N, 14.42. Found: C, 61.73; H, 7.24; N, 14.35.

3-(4-Fluorophenyl)-4,5,6,7-tetrahydro-*N*-methyl-1*H*-1,2-diazepine-1-carbothioamide (**6e**).

Following flash chromatography (2% ethyl acetate/dichloromethane) and crystallization from 2-propanol, this compound was obtained in 63%

yield as pale yellow crystals, mp 109-111°; ^{1}H nmr (deuteriochloroform): δ 1.79 (m, 2H), 1.97 (m, 2H), 2.94 (m, 2H), 3.18 (d, 3H, J = 4.8 Hz), 4.41 (m, 2H), 7.08-7.14 (m, 2H), 7.25 (broad s, 1H), 7.73-7.79 (m, 2H); ^{13}C nmr (deuteriochloroform): 21.4, 26.7, 31.3, 32.1, 52.3, 115.4, 115.7, 129.0, 129.1, 133.5, 133.6, 162.4, 163.4, 165.8, 181.5 ppm; ms: 265 (M^+, 88).

Anal. Calcd. for $C_{13}H_{16}FN_3S$: C, 58.84; H, 6.08; N, 15.84. Found: C, 58.96; H, 6.13; N, 15.69.

3-(4-Chlorophenyl)-4,5,6,7-tetrahydro-*N*-methyl-1*H*-1,2-diazepine-1-carbothioamide (**6f**).

Following flash chromatography (dichloromethane) and crystallization from 2-propanol, this compound was obtained in 62% yield as pale yellow crystals, mp 119-121°; ^{1}H nmr (deuteriochloroform): δ 1.79 (m, 2H), 1.96 (m, 2H), 2.93 (m, 2H), 3.18 (d, 3H, J = 4.8 Hz), 4.42 (m, 2H), 7.29 (broad s, 1H), 7.38 (d, 2H, J = 8.6 Hz), 7.69 (d, 2H, J = 8.6 Hz); ^{13}C nmr (deuteriochloroform): 21.4, 26.6, 31.2, 32.0, 52.3, 128.2, 128.6, 136.0, 136.4, 162.3, 181.7 ppm; ms: 281 (M^+, 100), 283 (37).

Anal. Calcd. for $C_{13}H_{16}ClN_3S$: C, 55.41; H, 5.72; N, 14.91. Found: C, 55.29; H, 5.77; N, 14.88.

2-(5-Chloro-1-phenylpentylidene)-*N*-ethylhydrazinecarbothioamide (**8**).

5-Chlorovalerophenone (3.94 g, 20.0 mmoles) and 4-ethylthiosemicarbazide (2.39 g, 20.0 mmoles) were stirred and heated to reflux in 2-propanol (100 ml). After being refluxed 41 hours, the 2-propanol was evaporated at reduced pressure leaving a viscous oil which was purified by flash chromatography (dichloromethane). The purified oil was dissolved in ether and the ethereal solution was filtered. The filtrate was evaporated at reduced pressure and any residual solvent was removed at high vacuum affording 4.6 g (77%) of **8** as a viscous, pale yellow oil [9,10]; ^{1}H nmr (deuteriochloroform): δ 1.29, 130 (overlapping t, 3H, J = 7.1 and 7.1 Hz), 1.63-1.93 (m, 4H), 2.59 (t, 0.9H, J = 7.3 Hz), 2.73 (t, 1.1H, J = 8.0 Hz), 3.55 (t, 2H, J = 6.3 Hz), 3.67-3.82 (m, 2H), 7.18-7.72 (m, 6H), 8.49 (broad s, 0.45H), 8.84 (broad s, 0.55H); ^{13}C nmr (deuteriochloroform): 14.4, 14.5, 23.1, 23.2, 26.1, 31.7, 31.9, 37.1, 39.2, 39.4, 44.1, 44.7, 126.1, 126.5, 128.5, 129.5, 129.6, 129.7, 132.7, 136.3, 149.5, 151.8, 177.1, 177.5 ppm; ms: 297 (M^+, 5), 299 (2).

Anal. Calcd. for $C_{14}H_{20}ClN_3S$: C, 56.46; H, 6.77; N, 14.10. Found: C, 56.61; H, 7.04; N, 13.90.

Preparation of 3-Phenyl-4,5,6,7-tetrahydro-*N*-ethyl-1*H*-1,2-diazepine-1-carbothioamide (**6a**) from Thiosemicarbazone **8**.

A mixture of thiosemicarbazone **8** (0.69 g, 2.3 mmoles), potassium carbonate (0.33 g, 2.4 mmoles), and methanol (11 ml) was stirred and heated to reflux. After being refluxed 24 hours, the methanol was evaporated at reduced pressure and the concentrate was dissolved in a two phase mixture of ethyl acetate and water. This two phase mixture was transferred to a separatory funnel where the two phases were thoroughly mixed. The ethyl acetate layer was separated and the aqueous layer was extracted two times with ethyl acetate. The ethyl acetate layers were combined, washed with saturated aqueous sodium chloride, and dried over anhydrous sodium sulfate. The drying agent was removed by filtration and the filtrate was evaporated at reduced pressure leaving a solid which was purified by flash chromatography (dichloromethane). Crystallization from 2-propanol gave 0.50 g (83%) of **6a** as pale yellow spars, mp 93-95°. This material was identical in all respects with an authentic sample prepared as described previously.

Alternate Synthesis of 3-Phenyl-4,5,6,7-tetrahydro-*N*-ethyl-1*H*-1,2-diazepine-1-carbothioamide (**6a**).

To a stirred suspension of lithium aluminum hydride (0.57 g, 15 mmoles) and dry ether (11 ml) was added portionwise 2,4,5,6-tetrahydro-7-phenyl-1,2-diazepin-3-one (0.94 g, 5.0 mmoles). The resulting mixture was heated to reflux. After being refluxed for 22 hours, the reaction was cooled in an ice bath where it was quenched by the sequential addition of water (0.57 ml), 15% aqueous sodium hydroxide (0.57 ml), and water (1.7 ml). The colorless precipitate was removed by filtration and it was washed with several portions of ether. The filtrate was evaporated at reduced pressure leaving an oil which was dissolved in ethanol (12 ml). To this solution was added ethyl isothiocyanate (0.44 ml, 5.0 mmoles) and the reaction was heated to reflux. After being refluxed for 7 hours, the ethanol was evaporated at reduced pressure and the resulting oil was purified by flash chromatography (dichloromethane). Crystallization from 2-propanol gave 0.12 g (9%) of **6a** as pale yellow spars, mp 92-94°. This material was spectroscopically identical with an authentic sample prepared as described previously.

General Procedure for the Preparation of Hexahydro-1,3-dimethyl-8a-aryl[1,2,4]triazolo[1,5-*a*]pyridine-2(3*H*)-thiones **7a-f**.

The 5-chlorovalerophenone (20.0 mmoles) and 2,4-dimethylthiosemicarbazide (4.78 g, 40.1 mmoles) were stirred and heated to reflux in 2-propanol (95 ml). After being refluxed for between 48-72 hours, the 2-propanol was evaporated at reduced pressure. The concentrate was dissolved in a two phase mixture of ethyl acetate and saturated aqueous sodium bicarbonate. This two phase mixture was transferred to a separatory funnel where the two layers were thoroughly mixed. The ethyl acetate layer was separated, washed with saturated aqueous sodium chloride, and dried over anhydrous sodium sulfate. The drying agent was removed by filtration and the filtrate was evaporated at reduced pressure leaving the crude product which was purified by a combination of flash chromatography and crystallization.

Hexahydro-1,3-dimethyl-8a-phenyl[1,2,4]triazolo[1,5-*a*]pyridine-2(3*H*)-thione (**7a**).

Following flash chromatography (dichloromethane) and crystallization from 2-propanol, this compound was obtained in 67% yield as colorless crystals, mp 85-87°; ^{1}H nmr (deuteriochloroform): δ 1.32-1.84 (m, 4H), 2.07-2.33 (m, 2H), 2.52 (dt, 1H, J = 3.1 and 10.8 Hz), 3.17 (s, 3H), 3.28 (m, 4H), 7.22-7.37 (m, 5H); ^{13}C nmr (deuteriochloroform): 19.8, 21.7, 30.4, 31.0, 33.2, 48.1, 83.1 (C_{8a}), 125.5, 127.7, 127.9, 141.7, 178.4 ppm; ms: 261 (M^+, 100).

Anal. Calcd. for $C_{14}H_{19}N_3S$: C, 64.33; H, 7.33; N, 16.07. Found: C, 64.30; H, 7.41; N, 15.94.

Hexahydro-1,3-dimethyl-8a-(4-methylphenyl)[1,2,4]triazolo[1,5-*a*]-pyridine-2(3*H*)-thione (**7b**).

Following flash chromatography (dichloromethane) and crystallization from 2-propanol, this compound was obtained in 84% yield as colorless spars, mp 139-141°; ^{1}H nmr (deuteriochloroform): δ 1.36-1.84 (m, 4H), 2.08-2.30 (m, 2H), 2.32 (s, 3H), 2.55 (dt, 1H, J = 3.2 and 10.8 Hz), 3.19 (s, 3H), 3.24 (m, 4H), 7.13 (d, 2H, J = 8.1 Hz), 7.23 (d, 2H, J = 8.1 Hz); ^{13}C nmr (deuteriochloroform): 18.9, 20.9, 21.6, 30.2, 30.9, 33.4, 48.0, 83.2 (C_{8a}), 125.8, 128.8, 137.8, 138.7, 178.8 ppm; ms: 275 (M^+, 100).

Anal. Calcd. for $C_{15}H_{21}N_3S$: C, 65.41; H, 7.68; N, 15.26. Found: C, 65.30; H, 7.75; N, 15.13.

Hexahydro-1,3-dimethyl-8a-[4-(1,1-dimethylethyl)phenyl][1,2,4]triazolo-[1,5-*a*]pyridine-2(3*H*)-thione (**7c**).

Following flash chromatography (1% ethyl acetate/dichloromethane) and crystallization from 2-propanol, this compound was obtained in 77% yield as colorless irregular prisms, mp 110-112°; ^{1}H nmr (deuteriochloroform): δ 1.29 (s, 9H), 1.38-1.85 (m, 4H), 2.10-2.33 (m, 2H), 2.55 (dt, 1H, J = 2.9 and 10.8 Hz), 3.21 (s, 3H), 3.25 (m, 4H), 7.25 (d, 2H, J = 8.4 Hz), 7.33 (d, 2H, J = 8.4 Hz); ^{13}C nmr (deuteriochloroform): 19.9, 21.7, 30.2, 31.0, 31.2, 33.4, 34.4, 48.2, 83.2 (C_{8a}), 125.1, 126.5, 138.6, 150.8, 178.8 ppm; ms: 317 (M^+, 63).

Anal. Calcd. for $C_{18}H_{27}N_3S$: C, 68.09; H, 8.57; N, 13.24. Found: C, 68.10; H, 8.63; N, 13.26.

Hexahydro-1,3-dimethyl-8a-(4-methoxyphenyl)[1,2,4]triazolo[1,5-*a*]pyridine-2(3*H*)-thione (**7d**).

Following flash chromatography (2% ethyl acetate/dichloromethane) and crystallization from 2-propanol, this compound was obtained in 81% yield as small colorless plates, mp 129-131°; ^{1}H nmr (deuteriochloroform): δ 1.37-1.84 (m, 4H), 2.10-2.29 (m, 2H), 2.53-2.64 (m,

1H), 3.20 (s, 7H), 3.79 (s, 3H), 6.85 (d, 2H, J = 8.9 Hz), 7.28 (d, 2H, J = 8.9 Hz); ^{13}C nmr (deuteriochloroform): 20.0, 21.6, 30.0, 30.9, 33.6, 47.9, 55.2, 83.0 (C_{8a}), 113.5, 127.2, 133.3, 159.4, 178.6 ppm; ms: 291 (M^+, 100).

Anal. Calcd. for $C_{15}H_{21}N_3OS$: C, 61.82; H, 7.26; N, 14.42. Found: C, 61.81; H, 7.37; N, 14.16.

Hexahydro-1,3-dimethyl-8a-(4-fluorophenyl)[1,2,4]triazolo[1,5-*a*]pyridine-2(3*H*)-thione (**7e**).

Following flash chromatography (dichloromethane) and crystallization from 2-propanol, this compound was obtained in 68% yield as colorless crystals, mp 101-103°; ^{1}H nmr (deuteriochloroform): δ 1.35-1.86 (m, 4H), 2.04-2.17 (m, 1H), 2.23-2.34 (m, 1H), 2.52 (dt, 1H, J = 3.3 and 11.0 Hz), 3.19 (s, 3H), 3.27 (m, 4H), 6.95-7.04 (m, 2H), 7.29-7.37 (m, 2H); ^{13}C nmr (deuteriochloroform): 19.8, 21.6, 30.5, 30.9, 33.2, 48.1, 82.9 (C_{8a}), 114.8, 115.1, 127.6, 127.7, 137.8, 137.9, 160.6, 163.9, 178.9 ppm; ms: 279 (M^+, 53).

Anal. Calcd. for $C_{14}H_{18}FN_3S$: C, 60.19; H, 6.49; N, 15.04. Found: C, 60.03; H, 6.59; N, 14.98.

Hexahydro-1,3-dimethyl-8a-(4-chlorophenyl)[1,2,4]triazolo[1,5-*a*]pyridine-2(3*H*)-thione (**7f**).

Following flash chromatography (dichloromethane) and crystallization from 2-propanol, this compound was obtained in 61% yield as colorless plates, mp 145-147°; ^{1}H nmr (deuteriochloroform): δ 1.34-1.86 (m, 4H), 2.02-2.14 (m, 1H), 2.24-2.33 (m, 1H), 2.49 (dt, 1H, J = 3.2 and 11.1 Hz), 3.18 (s, 3H), 3.28 (m, 4H), 7.28 (s, 4H); ^{13}C nmr (deuteriochloroform): 19.9, 21.9, 30.7, 31.1, 33.2, 48.3, 83.0 (C_{8a}), 127.3, 128.3, 133.8, 140.9, 178.8 ppm; ms: 295 (M^+, 100), 297 (39).

Anal. Calcd. for $C_{14}H_{18}ClN_3S$: C, 56.84; H, 6.13; N, 14.20. Found: C, 56.84; H, 6.14; N, 14.22.

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[9] Thiosemicarbazone **8** decomposed upon both attempted distillation and attempted boiling point determination.

[10] After standing in the refrigerator for over a month, thiosemicarbazone **8** crystallized giving pale yellow crystals, mp 69-72°.