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REACTION OF 1-METHYLTHIO-3,4-DIHYDROISOQUINOLINES WITH AMINES

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A study was carried out on the reaction of 1-methylthio-3,4-dihydroisoquinolines with aromatic and aliphatic amines, thiourea, semicarbazide, and thiosemicarbazide. The reactions with anthranilic acid and 2-amino-3-carboethoxy-4,5-dimeurylthiophene give 6,6-dimethyl-5,6-dihydro-8H-isoquino[1,2-b]quinazolin-8-one and6,6,9,10-tetramethyl-5,6-dihydro-8H-benzo[i]thieno[2,3-b]quinolizin-8-one, respectively. 1-Semicarbazido- and 1-thiosemicarbazido-3,4-dihydroisoquinolines were shown to undergo thermal elimination of ammonia to give substituted 1,2,4-triazolo[3,4-a]isoquinolin-3-ones and 1,2,4-triazolo[3,4-a]isoquinoline-3-thiones.

Thiolactimic esters are commonly used for introducing functional groups into the side-chains of heterocyclic compounds [1] and construction of fused polycyclic systems [2]. We have already studied the reactions of substituted 1-methylthio-3,4-dihydroisoquinolines with CH-acids and carboxylic acid hydrazides [3, 4]. In the present work, we describe the reaction of thioethers Ia-Ic with aromatic and aliphatic amines, thiourea, semicarbazide, and thiosemicarbazide (see Scheme 1).

The reactions with amines were carried out either by heating the reagents in acetic acid at reflux (method A) or their fusion at 150°C (method B). Our results show that the nature of the amine has a definite effect on the reaction course. Aromatic amines, in which the NH_2 group is sterically available, such as aniline, *o*-toluidine, *o*-bromoaniline, *p*-nitroaniline, and *p*-carboethoxyaniline, react smoothly with sulfides Ia-Ic by methods A and B to give products of the replacement of the SMe group (IIa-IIg) in approximately equal yields by the two methods. Under the same conditions, 2,6-xylidine, 2,6-dichloroaniline, N-methylaniline, and 1-aminoadamantane do not react with Ia-Ic but rather are converted under the conditions of method A into substituted 3,4-dihydroisocarbostyryls (IIIa-IIIc). There is probably competition between nucleophilic substitution and solvolysis of the SMe group by the action of the acetate ion formed from the amine salts in acetic acid. Indeed, the addition of a tertiary amine such as triethylamine, N-methylpiperidine, or pyridine to a solution of sulfide Ia in acetic acid at reflux leads to the rapid evolution of methyl mercaptan and formation of 3,3-dimethyl-3,4-dihydroisocarbostyryl IIIa. In the general case, the reaction of acetate anion with 1-methylthio derivative I leads to the corresponding 1-acetoxy derivative, whose hydrolysis under the reaction conditions gives rise to product III.

^{13}C NMR spectroscopy showed that isocarbostyryl IIIa has nonplanar structure with distorted conformation of the azacyclohexane fragment as indicated by the different chemical shifts of the axial (19.23 ppm) and equatorial methyl groups (25.48 ppm).

Benzylamine reacts smoothly with sulfide Ia under conditions of methods A and B to give IIh isolated as its hydrochloride salt. Morpholine and ethanolamine do not react with Ia in acetic acid at reflux (method A) but facilitate its conversion to IIIa. The same nucleophilic substitution product (IIi) is formed from sulfide Ia upon its heating in morpholine at reflux or maintenance with ethanolamine under conditions of method B. In the latter case, product formation is clearly accompanied by dehydration.

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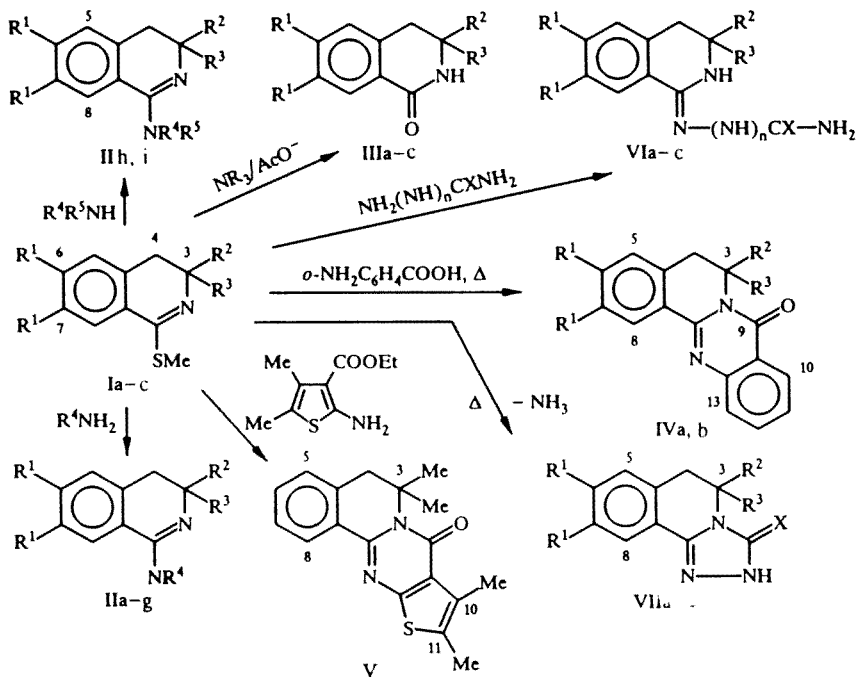
Scheme*



I, III, IV a $R^1 = H$, $R^2 = R^3 = Me$, b $R^1 = OMe$, $R^2 = R^3 = Me$, c $R^1 = H$, $R^2 = Me$, $R^3 = Et$; II a $R^1 = H$, $R^2 = R^3 = Me$, $R^4 = Ph$, b $R^1 = H$, $R^2 = R^3 = Me$, $R^4 = o\text{-}MeC_6H_4$, c $R^1 = H$, $R^2 = R^3 = Me$, $R^4 = o\text{-}BrC_6H_4$, d $R^1 = OMe$, $R^2 = R^3 = Me$, $R^4 = Ph$, e $R^1 = OMe$, $R^2 = R^3 = Me$, $R^4 = o\text{-}BrC_6H_4$, f $R^1 = H$, $R^2 = R^3 = Me$, $R^4 = p\text{-}NO_2C_6H_4$, g $R^1 = H$, $R^2 = R^3 = Me$, $R^4 = p\text{-}EtOOCC_6H_4$, h $R^1 = R^4 = H$, $R^2 = R^3 = Me$, $R^5 = CH_2Ph$, i $R^1 = H$, $R^2 = R^3 = Me$, $R^4R^5 =$ morpholyl; VI a $R^1 = H$, $R^2 = R^3 = Me$, X = S, n = 0, b $R^1 = H$, $R^2 = Me$, $R^3 = Et$, X = S, n = 0, c $R^1 = H$, $R^2 = R^3 = Me$, X = O, n = 1; VII a $R^1 = H$, $R^2 = R^3 = Me$, X = O, b $R^1 = H$, $R^2 = R^3 = Me$, X = S, c $R^1 = OMe$, $R^2 = R^3 = Me$, X = S

The reaction of Ia and Ib with anthranilic acid by both methods leads to 6,6-dimethyl-5,6-dihydro-8H-isoquino-[1,2-*b*]quinazolin-8-one IVa and IVb. In the case of sulfide Ia and 2-amino-4,5-dimethylthiophene-3-carboxylic acid under conditions of method B, the reaction mixture is completely converted into a tar. However, the ethyl ester of this acid gives 6,6,10,11-tetramethyl-5,6-dihydro-8H-benzo[*i*]thieno[2,3-*b*]quinazolin-8-one (V) in good yield through method A. Kametani [5] has reported a less convenient preparation of analogous systems by the reaction of 3,4-dihydroisoquinoline with the adduct of anthranilic acid and thionyl chloride.

Under conditions of method B, thiourea reacts with sulfides I to give thioureas VIa and VIb, while the reaction of semicarbazide and thiosemicarbazide with I gives products of cyclization with the loss of ammonia, namely, triazolo[3,4-*a*]isoquinolines VIIa-VIIc. Linear products VI are also formed from semicarbazide and thiosemicarbazide under milder conditions upon heating in methanol at reflux. These products may be converted into VII by heating in DMF at reflux or by heating at 170-180°C for 5-10 min. Product VIb exists in two enantiomeric forms and the signal of the ring amino group proton is seen as two broad singlets with overall intensity of 1H.

Cyclic amidines IIa-IIg, similar to VIa-VIc, may exist in two tautomeric forms. The exocyclic position of the azomethine bond is the most probable. The downfield shift of the signal for 8-H due to the deshielding effect of the C=N bond supports this hypothesis: the multiplet for 8-H for amidines IIa-IIg is found at 7.28-8.29, while it is seen at 8.03-8.18 ppm in VI. On the other hand, the 8-H signal is found at 6.65 ppm for 1-morpholino derivative IIi, in which the azomethine bond is fixed in the ring, and almost overlaps with the multiplet of the aromatic protons at $C_{(5)}$, $C_{(6)}$, and $C_{(7)}$.

*The numbering of the atoms in this scheme has been used for describing their NMR spectra. The names of all the compounds are in accord with IUPAC rules.

TABLE 1. Indices of Products I-VII

Compound	Chemical formula	Found, % / Calculated, % C	H	N	mp, °C	Crystallization solvent	Yield, %
Ic	$C_{13}H_{17}NS$	70.85 71,19	8.11 7,81	6.83 6,39	*	—	80
IIa	$C_{17}H_{18}N_2$	80.99 81,56	7.94 7,25	11.27 11,19	43...45	Hexane–propanol-2	85
IIb	$C_{18}H_{20}N_2$	81.22 81,78	7.65 7,63	10.44 10,60	79...80	Hexane–propanol-2	72
IIc	$C_{17}H_{17}BrN_2$	61.66 62,02	5.91 5,20	8.37 8,51	107...108	Ethanol	54
IId	$C_{19}H_{22}N_2O_2$	73.20 73,52	7.05 7,14	8.90 9,03	121...123	Hexane	53
IIe	$C_{19}H_{21}BrN_2O_2$	58.24 58,62	5.47 5,44	6.77 7,20	131...134	Hexane	59
IIf	$C_{17}H_{17}N_3O_2$	68.95 69,14	6.09 5,80	14.18 14,23	115...119	Hexane	79
IIg	$C_{20}H_{22}N_2O_2$	74.28 74,51	7.17 6,88	8.93 8,69	118...119	Ethanol	68
IIh · HCl	$C_{18}H_{20}N_2 \cdot HCl$	71.05 71,87	6.98 7,04	9.28 9,31	243...245	Ethanol	83
IIi	$C_{15}H_{20}N_2O$	68.91 69,20	7.52 7,74	11.01 10,76	85...87	Hexane	78
IIIa	$C_{11}H_{13}NO$	75.59 75,40	7.53 7,48	8.05 7,99	146...147	Hexane	78
IIIb	$C_{13}H_{17}NO_3$	66.80 66,36	7.48 7,28	5.44 5,95	228...230	Methanol–water	71
IIIc	$C_{12}H_{15}NO$	75.95 76,16	8.23 7,99	7.28 7,40	155...157	Hexane–propanol-2	80
IVa	$C_{18}H_{16}N_2O$	77.99 78,24	5.70 5,84	9.98 10,14	68...70	Hexane	78
IVb	$C_{20}H_{20}N_2O_3$	71.14 71,41	5.75 5,99	8.13 8,33	148...150	Ethanol	77
V	$C_{18}H_{18}N_2OS$	70.66 69,73	6.03 5,84	8.28 9,04	149...151	Hexane	53
VIa	$C_{12}H_{15}N_3S$	61.17 61,77	6.85 6,48	18.33 18,01	92...94	Ethanol	42
VIb	$C_{13}H_{17}N_3S$	62.90 63,12	7.07 6,93	16.95 16,99	74...76	Toluene	65
VIc	$C_{12}H_{16}N_4O$	61.91 62,05	6.71 6,94	24.59 24,12	170...171	Ethylacetate–hexane	54
VIIa	$C_{12}H_{13}N_3O$	66.77 66,96	6.34 6,09	19.91 19,52	221...223	Ethanol	58
VIIb	$C_{12}H_{13}N_3S$	62.30 62,31	5.80 5,66	18.22 18,17	204...205	Ethanol	57
VIIc	$C_{14}H_{17}N_3O_2S$	57.92 57,71	6.02 5,88	14.58 14,42	235...237	Ethanol	68

*mp 105-110°C (4 mm Hg).

The conformation with *trans* arrangement of the aromatic fragments relative to the exocyclic azomethine bond is most likely for IIa-IIg. This proposal finds support using the ALCHEMY II molecular model program.

EXPERIMENTAL

The IR spectra were taken on a UR-20 spectrometer for samples in vaseline mull. The ^1H and ^{13}C NMR spectra were taken on a Tesla BS-587A spectrometer at 80 and 20.59 MHz, respectively, in $CDCl_3$ and DMSO-d_6 (for VIa-VIc, VIIa, and VIIb) with HMDS as the internal standard. The mass spectra were taken on a Hitachi M-80 mass spectrometer with direct sample inlet into the ion source. The ionizing voltage was 70 eV. The reaction course and purity of the products were monitored using thin-layer chromatography on Silufol UV-254 plates with 9:1 chloroform—acetone as the eluent. The spots were developed with 1% chloranil in benzene.

The physical indices of the products and their elemental analysis data are given in Table 1, while the spectral indices of these products are given in Table 2.

TABLE 2. Spectral Indices of I-VII

Compound	IR spectrum, ν, cm^{-1}	PMR spectrum, δ, ppm				
		R^2, R^3	4-CH_2, s	arom		additional protons
				8-H	other	
1	2	3	4	5	6	7
Ic	1620 (C=N), 1320 (MeS)	1,01 c (Me), 0,90 t ($CH_2\underline{CH_3}$), 1,50 q ($\underline{CH_2}CH_3$)	2,59	7,50 m	6,86...7,28 m (5-, 6-, 7-H)	2,33 s (S-Me)
IIa	1620 (C=N), 3385 (N–H)	1,10 s (–Me_2)	2,79	8,25 m	6,84...7,28 m (5-, 6-, 7-H)	4,63 br.s (NH)
IIb	1630 (C=N), 3380 (N–H)	1,07 s (–Me_2)	2,78	8,30 m	6,60...7,35 m (5-, 6-, 7-H and $4H_{Ar}$)	2,08 s (Me in Ar), 4,36 br.s (NH)
IIc	1628 (C=N), 3396 (N–H)	1,14 s (–Me_2)	2,82	8,29 m	6,84...7,85 m (5-, 6-, 7-H and $4H_{Ar}$)	4,35 br.s (NH)
IId	1628 (C=N), 3378 (N–H)	1,13 s (–Me_2)	2,74	7,78 s	6,55 s (5-H), 6,84...7,29 m ($5H_{Ph}$)	3,88 c (6- and 7-OMe), 4,53 br.s (NH)
IIe	1634 (C=N), 3390 (N–H)	1,15 s (–Me_2)	2,75	7,81 s	6,56 s (5-H), 6,94...7,20 m ($4H_{Ar}$)	3,88 c (6- and 7-OMe), 4,27 br.s (NH)
IIf	1688, 1632 (C=N), 1616 (C=C), 1330, 3340 (N–H)	1,32 s (–Me_2)	2,94	7,99 m	6,95...7,08 d (2'-, 6'-H_{Ar}), 7,14...7,40 m (5-, 6-, 7-H), 8,03...8,20 d (3'-, 5'-H_{Ar})	5,90 br.s (NH)
IIg	1670 (C=O), 1605, 1565, 3300 (N–H)	1,01 s (–Me_2)	2,55	7,28 m	6,18 d (2'-,6'-H_{Ar}), 6,31...6,65 m (5-, 6-, 7-H), 7,11 d (3'-, 5'-H_{Ar})	1,23 t ($OCH_2\underline{CH_3}$), 3,88 q ($O\underline{CH_2}CH_3$), 4,11 br.s (NH)
IIh · HCl	1660 (C=N), 1590 (C=C), 3100, 3200 (N–H)	1,19 s (–Me_2)	2,87	6,90...7,32 m (5-, 6-, 7-, 8-H and $5H_{Ph}$)		5,51 s ($\underline{CH_2}Ph$), 8,87 br.s (NH)
IIi	1600 (C=C), 1565 (C=N), 1300, 1265, 1250, 1120	0,89 s (–Me_2)	2,27	6,26...6,68 m (5-, 6-, 7-, 8-H)		2,78 t ($(CH_2)_2N$), 3,38 t ($(CH_2)_2O$)
IIIa	1660 (C=O), 1595 (C=C), 3170 (N–H)	1,25 s (–Me_2)	2,85	7,95 m	7,32...7,48 m (5-, 6-, 7-H)	6,44 br.s (NH)

TABLE 2. (Continued)

Compound	IR spectrum, ν, cm^{-1}	PMR spectrum, δ, ppm				
		R^2, R^3	4-CH_2, s	arom		additional protons
				8-H	other	
1	2	3	4	5	6	7
IIIb	1650 (C=O), 1595 (C=C), 3195 (N–H)	1,25 s (–Me_2)	2,79	7,57 s	6,51 (5-H)	3,86 s (6- and 7-OMe), 5,67 br.s (NH)
IIIc	1652 (C=O), 1600 (C=C), 3294 (N–H)	1,25 s (Me), 0,88 t ($CH_2\underline{CH_3}$), 1,46 q ($\underline{CH_2}CH_3$)	2,80	8,23 m	6,91...7,65 m (5-, 6-, 7-H)	6,54 br.s (NH)
IVa	1658 (C=O), 1586 (C=N), 1550, 1325, 1145	1,84 s (–Me_2)	3,08	7,18...8,33 m (5-, 6-, 7-, 8-, 10-, 11-, 12-, 13-H)		–
IVb	1660 (C=O), 1630 (C=N), 1590, 1500 (C=C), 1260 (ν_{as} OMe), 1050 (ν_s OMe)	1,71 s (–Me_2)	2,89	8,09 s	6,59 s (5-H), 7,32...7,67 m (10-, 11-, 12-H), 2,77 s (13-H)	3,88 s and 3,93 s (6- and 7-OMe)
V	1675 (C=O), 1610 (C=N), 1530 (C=C)	1,68 s (– Me_2)	3,01	8,07 s	7,16...7,39 m (5-, 6-, 7-H)	2,31 s (10-Me), 2,37 s (11-Me)
VIa	1665 (C=N), 1600 (C=C), 3170, 3260, 3350 (NH)	1,35 s (–Me_2)	2,89	8,03 m	7,05...7,38 m (5-, 6-, 7-H)	7,50 br.s (NH), 8,51 br.s and 9,23 br. s (NH_2)
VIb	1660 (C=N), 1600 (C=C), 3165, 3240, 3250 (sh, N–H)	0,94 t ($CH_2\underline{CH_3}$), 1,29 s (Me), 1,69 q ($\underline{CH_2}CH_3$)	2,92	8,18 m	7,09...7,54 m (5-, 6-, 7-H)	6,56 br.s and 7,87 br.s (NH), 8,58 br.s and 9,11 br.s (NH_2)
VIc	1680 (C=O), 3360, 3400 (sh, N–H)	1,13 s (–Me_2)	2,71	8,06	7,07...7,26 (5-, 6-, 7-H)	6,21 br.s (NH), 6,30 br.s (NH_2), 8,75 br.s (NH)
VIIa	1690 (C=O), 1595, 1570, 3360 (N–H)	1,65 s (–Me_2)	2,99	7,88 m	7,25...7,40 m (5-, 6-, 7-H)	9,93 br.s (NH)
VIIb	1605 (C=N), 1590, 1570, 3220 (N–H)	1,83 s (–Me_2)	3,02	7,83 m	7,01...7,50 m (5-, 6-, 7-H)	11,96 br.s (NH)
VIIc	1604 (C=N), 1496, 3260 (N–H)	1,83 s (–Me_2)	2,95	7,31 m	6,62 s (5-H)	3,86 s (6- and 7-OMe), 11,34 br.s (NH)

*Numbering of atoms given in Scheme.

Products Ia [4] and Ib [3] were described in our previous work, while 3-methyl-1-methylthio-3-ethyldihydroisoquinoline Ic were obtained according to a reported procedure [4].

3,3-Dialkyl-1-arylamino-1,2,3,4-tetrahydroisoquinolines (IIa-IIg). A. A mixture of 10 mmoles sulfide I, 11 mmoles amine, and 20 ml 98% acetic acid was heated at reflux until sulfide I disappeared, as indicated by thin-layer chromatography (1-4 h). The cooled reaction solution was poured into 100 ml water and traces of III were filtered off. The solution was brought to pH 8 by adding ammonia and extracted with chloroform. The extract was dried and the solvent was evaporated or distilled off. The residue was crystallized to give product II.

B. A mixture of 10 mmoles sulfide I and 11 mmoles amine was maintained on a metal bath at 150°C until the starting sulfide completely disappeared, as indicated by thin-layer chromatography (1-3 h). The melt was poured into 50 ml petroleum ether (bp 70-100°C). Product II separated and was purified when necessary with activated charcoal and crystallized.

Hydrochloride Salt of 1-Benzylamino-3,3-dimethyl-3,4-dihydroisoquinoline (IIh·HCl). The crude product obtained from benzylamine and sulfide Ia under conditions of methods A and B was dissolved in ether and a stream of dry HCl was passed through the solution. The hydrochloride salt formed was crystallized from ethanol.

3,3-Dimethyl-1-morpholino-3,4-dihydroisoquinoline (IIi). A mixture of 2.08 g (10 mmoles) sulfide Ia and 10 ml morpholine was heated at reflux for 6 h, cooled, poured into 100 ml water, and stirred for 12 h. Product IIi was then filtered off, dried, and crystallized.

Substituted 3,4-Dihydroisocarbostyryls (IIIa-IIIc). A mixture of 5 mmoles sulfide Ia-Ic, 20 mmole of tertiary amine (triethylamine or N-methylpiperidine) or pyridine, and 10 ml acetic acid was heated at reflux for 2 h, poured into 50 ml water, and brought to pH 8 by adding aqueous ammonia. Product IIIa-IIIc was filtered off, dried, and crystallized. ^{13}C NMR spectrum ($CDCl_3$): 174.50 (s, $C_{(1)}$), 136.76, 130.29, 128.98, 128.07 (d, $C_{(5)}$-$C_{(8)}$), 136.57, (s, $C_{(4a)}$), 124.86 (s, $C_{(8)}$), 55.19 (s, $C_{(3)}$), 37.98 (t, $C_{(4)}$), 25.48 (q, $3Me_e$), 19.23 q ($3\text{-}Me_a$).

6,6-Dimethyl-5,6-dihydro-8H-isoquino[1,2-*b*]quinazolin-8-one (IVa) was obtained from sulfide Ia and anthranilic acid under conditions of methods A and B with approximately the same yield. Mass spectrum, *m/z* (*I*, %): M^+ 276 (80), [M^+ − Me] 261 (100), [M^+ − 2Me] 246 (10), [$M^{+\cdot}$] 157 (25).

6,6-Dimethyl-2,3-dimethoxy-5,6-dihydro-8H-isoquino[1,2-*b*]quinazolin-8-one (IVb) was obtained according to method B from sulfide Ib and anthranilic acid. ^{13}C NMR spectrum ($CDCl_3$): 162.67 (s, $C_{(9)}$), 152.84 (s, $C_{(6)}$), 150.37 (s, $C_{(7)}$), 148.69 (s, $C_{(13a)}$), 145.63 (s, $C_{(9a)}$), 134.17 (s, $C_{(4a)}$), 128.83 (s, $C_{(8a)}$), 126.59, 125.46, 121.86 (d, $C_{(10)}$—$C_{(13)}$), 120.69 (s, $C_{(1)}$), 110.91 (d, $C_{(8)}$), 109.71 (d, $C_{(5)}$), 60.04 (s, $C_{(3)}$), 56.24 and 56.09 (q, 6- and 7-OMe), 43.81 (t, $C_{(4)}$), 25.97 ppm (q, 3-Me).

6,6,9,10-Tetramethyl-5,6-dihydro-8H-benzo[*i*]thieno[2,3-*b*]quinolizin-8-one (V). A solution of 1.99 g (10 mmoles) 2-amino-3-carboethoxy-4,5-dimethylthiophene and 2.05 g (10 mmoles) thioether Ia in acetic acid was heated at reflux for 16 h, cooled, poured into 200 ml water, and brought to pH 8 by adding aqueous ammonia. Product V was filtered off, dried, and crystallized. Mass spectrum, *m/z* (*I*, %): M^+ 310 (100), [M^+ − Me] 295 (80), [$M]^{+\cdot}$ 157 (100).

Substituted 1-(N-aminothiocarbonyl)imino-3,4-dihydroisoquinolines (VIa and VIb). A mixture of sulfide Ia or Ib with thiourea was heated at 150°C for 2-3 h. The reaction mixture was then poured into water. Product VIa or VIb was dried and crystallized.

3,3-Dimethyl-1-semicarbazido-3,4-dihydroisoquinoline (VIc). A mixture of 4.08 g (20 mmoles) sulfide Ia, 2.22 g (20 mmoles) semicarbazide hydrochloride, and 3.03 g (30 mmoles) triethylamine in 30 ml methanol was heated at reflux for 4 h and poured into 100 ml water. Then, water was removed by decantation from the tarry precipitate, which was triturated with ether and crystallized from aqueous 2-propanol to give 1.4 g of a 1:1 solvate of IVc and 2-propanol, mp 163-165°C. PMR spectrum ($CDCl_3$): 1.07 (6H, d, $\underline{CH}_3$—CH), 1.16 (6H, s, 3,3-Me_2), 2.92 (2H, s, 4-CH_2), 3.26 (1H, br.s, OH), 4.01 (1H, m, $\underline{CH}$—CH_3), 6.21 (1H, br.s, 2-NH), 6.30 (2H, br.s, NH_2), 7.10-7.28 (3H, m, 5,6,7-H), 8.06 (1H, d, 8-H), 8.62 ppm (1H, s, NH). Found: C, 60.88; H, 8.53; N, 18.92%. Calculated for $C_{12}H_{16}N_4O\cdot(CH_3)_2CHOH$: C, 61.62; H, 8.27; N, 19.16%. Crystallization of the solvate from ethyl acetate—hexane gave pure VIc.

5,5-Dimethyl-2,3,5,6-tetrahydro-1,2,4-triazolo[3,4-*a*]isoquinolin-3-one (VIIa). A mixture of 2.4 g (11.8 mmoles) sulfide Ia, 1.11 g (10 mmoles) semicarbazide hydrochloride, and 1.0 g anhydrous sodium acetate in 6 ml DMF was heated at reflux for 3 h and cooled. Product VIIa was filtered off and crystallized. Mass spectrum, *m/z* (*I*, %): M^+ 215 (35), [M^+ − Me] 200 (100), 166 (19), 156 (15), 142 (8), 130 (12). Product VIIa was also obtained by heating VIc in DMF at reflux for 1 h. The reaction mixture was then poured into water and the precipitate was crystallized.

5,5-Dimethyl-2,3,5,6-tetrahydro-1,2,4-triazolo[3,4-*a*]isoquinoline-3-thione (VIIb). A mixture of 10 mmoles sulfide Ia and 11 mmoles thiosemicarbazide in 8 ml DMF was heated at reflux for 3 h. The reaction mixture was then poured into water and the precipitate was crystallized. Product VIIc was obtained analogously from sulfide Ib.

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