Cyclization of Isothiosemicarbazones. Part 10.[1] A Novel Route to 2-Amino[1,2,4]triazolo[1,5-*a*]pyridine Derivatives

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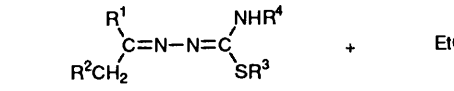
2-Alkylamino[1,2,4]triazolo[1,5-*a*]pyridine-8-carbonitrile and 8-carboxylate derivatives **3** are obtained directly in moderate yields by the reaction of ketone isothiosemicarbazones **1**, carrying a bulky alkyl group on the terminal nitrogen and at least one α-methylene group, with an active ethoxymethylene compound with elimination of a thiol. Butanone isothiosemicarbazone **1e** gives an isomeric pair of 5-ethyl- and 5,6-dimethyl-triazolopyridines **3e** and **3f** depending upon which of the α-carbons is incorporated into the ring system, with the 5,6-dimethyl compound being the major product. When the substituent on the terminal nitrogen is less bulky, the reaction gives both [1,2,4]triazolo[1,5-*a*]pyridines **3** and penta-substituted 2-triazolines **4** or the latter compounds only. A plausible reaction mechanism is proposed.

[1,2,4]Triazolo[1,5-*a*]pyridine derivatives have been prepared by the annulation of 1,2,4-triazole ring starting with amino-substituted pyridines by a multistep procedure.[2]

The present paper describes a novel route to 2-alkylamino[1,2,4]triazolo[1,5-*a*]pyridine derivatives by the one-step cyclization of isothiosemicarbazones substituted with a bulky group at the terminal nitrogen with ethoxymethylenemalononitrile **2a** or cyanoacetate **2b**.

In general, the reaction was performed by heating an equimolar mixture of **1** and **2** under reflux in chlorobenzene for 1–2 h, whereupon a highly darkened mixture resulted. Hot hexane-extraction followed by chromatographic separation gave the product **3** in moderate yield (Scheme 1). The reaction mixture from butanone isothiosemicarbazone **1e** contained two isomeric compounds **3e** and **3f** in the ratio **3e**:**3f** = *ca.* 1:10. When treated by the usual procedure, the dimethyl isomer **3f** deposited out of the cooled extract while the other isomer was retained in the solution and thus effective separation was achieved. Less reactive compound **2b** required a higher temperature and higher molar ratio of **1**:**2b** in order to obtain complete reaction. Attempts to prepare 5-unsubstituted or 2-anilino-triazolopyridine by the reaction of appropriately substituted **1** with **2a** resulted in the total recovery of the starting materials. Extensive efforts to improve the yield of triazolopyridines **3** were unsuccessful.

The structural assignment of triazolopyridines **3** was based on analytical and spectral data as well as comparison of the spectroscopic behaviour with a compound similarly produced from hexadeuterioacetone 4-*tert*-butyl-3-methylisothiosemicarbazone [$(CD_3)_2C$=N–N=C(SMe)NHBu^t]. Compound **3a** showed a nine-proton singlet (δ 1.48), a broad singlet (δ 4.84, exchangeable), a three-proton singlet (δ 2.74), and two characteristic AB-type doublets (δ 6.66 and 7.62, *J*/Hz 7.8 each). The first two singlets are easily assignable to the *tert*-butylamino structure. The deuteriated product **3b**,† however, showed no signals for the singlet at δ 2.74 and the upfield doublet. Furthermore, the downfield doublet of **3a** changed into a singlet of the same chemical shift value, but the signals arising from the *tert*-butylamino moiety remained unchanged in compound **3b**. Therefore, upon reaction with **2a**, one methyl group of the isopropylidene moiety of **1a** was retained as a substituent in the product while the other should be converted with the methine carbon of **2a** into a vinylene grouping. The methylthio group of **2a** might be lost in the course of the reaction probably in the form of methanethiol as indicated by the disagreeable odour. Consequently, it can be deduced that the reaction may be initiated by the attack of the α-methyl or methylene carbon of **1** onto the ethoxymethylene carbon of **2** to eliminate ethanol. Nucleophilic addition of the N-1 of **5** thus formed to the cyano triple bond to form **6**, followed by

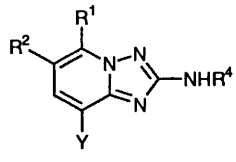


1 + **2**

1
a $R^1 = R^3 = Me$, $R^2 = H$, $R^4 = Bu^t$
b $R^1 = R^3 = Me$, $R^2 = H$, $R^4 = Pr^i$
c $R^1 = R^3 = Me$, $R^2 = H$, $R^4 = Et$
d $R^1 = R^3 = R^4 = Me$, $R^2 = H$
e $R^1 = R^2 = R^3 = Me$, $R^4 = Bu^t$
f $R^1 = Ph$, $R^2 = H$, $R^3 = Me$, $R^4 = Bu^t$
g R^1–$R^2 = -(CH_2)_3-$, $R^3 = Me$, $R^4 = Bu^t$
h R^1–$R^2 = -(CH_2)_4-$, $R^3 = Me$, $R^4 = Bu^t$

2
a Y = CN
b Y = CO_2Et

i, $-R^3SH$



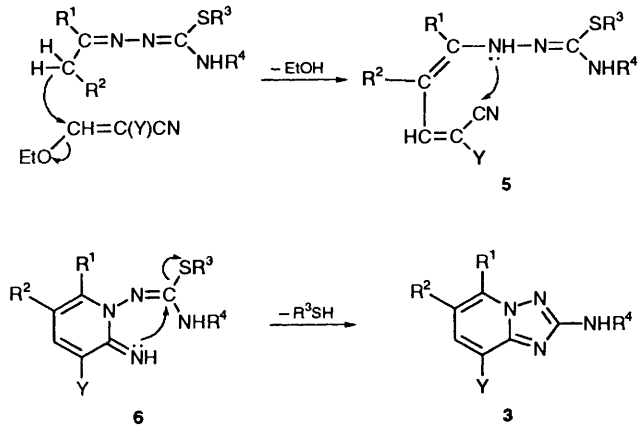
3

a $R^1 = Me$, $R^2 = H$, $R^4 = Bu^t$, Y = CN
b $R^1 = CD_3$, $R^2 = D$, $R^4 = Bu^t$, Y = CN
c $R^1 = Me$, $R^2 = H$, $R^4 = Pr^i$, Y = CN
d $R^1 = Me$, $R^2 = H$, $R^4 = Et$, Y = CN
e $R^1 = Et$, $R^2 = H$, $R^4 = Bu^t$, Y = CN
f $R^1 = R^2 = Me$, $R^4 = Bu^t$, Y = CN
g $R^1 = Ph$, $R^2 = H$, $R^4 = Bu^t$, Y = CN
h R^1–$R^2 = -(CH_2)_3-$, $R^4 = Bu^t$, $R^4 = CN$
i R^1–$R^2 = -(CH_2)_4-$, $R^4 = Bu^t$, $R^4 = CN$
j $R^1 = Me$, $R^2 = H$, $R^4 = Bu^t$, Y = CO_2Et

Scheme 1 *Reagents and conditions:* i, Chlorobenzene, 140 °C (bath temperature)

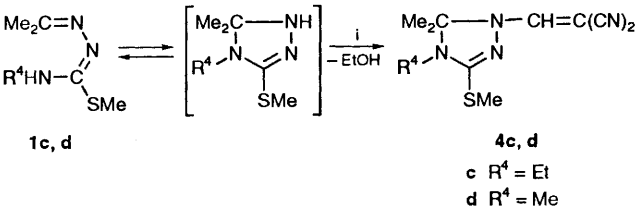
† It gave the molecular ion (*m*/*z* 233, 13%) greater than that of **3a** by 4 mass units.

intramolecular substitution to displace the thiol, probably through an addition–elimination process, can result in a [1,2,4]triazolo[1,5-*a*]pyridine ring system in which the cyanovinyl linkage of **2** is incorporated at the 1, 1a, 7 and 8 positions of the ring (Scheme 2). The reaction mechanism successfully



Scheme 2

explains the overwhelming formation of **3f** from the unsymmetrical ketone isothiosemicarbazone **1e** which should preferentially generate the highly substituted alkene **5** (R^1 = R^2 = Me) than the less substituted **5** (R^1 = Et, R^2 = H).



Scheme 3 *Reagents and conditions:* i, **2a**, Chlorobenzene, 140 °C (bath temperature)

In the ^{13}C NMR spectra, the resonances of each ring carbon of **3** appeared at δ 148.44–150.78 (C-1a), 164.26–166.57 (C-2), 140.90–147.69 (C-5), 110.07–125.25 (C-6), 130.97–135.87 (C-7) and 93.37–95.15 (C-8*) with appropriate multiplicity. Taking into account the effect of substituents, these ^{13}C chemical shifts are substantially parallel to those values for the [1,2,4]triazolo[1,5-*a*]pyridine skeleton.[3]

When the substituent (R^4) on the terminal nitrogen of **1** is less bulky, the present reaction is somewhat complicated by the alternative mode of cyclization of the isothiosemicarbazones involved. Thus, when 4-ethylisothiosemicarbazone **1c** was subjected to the same cyclization conditions as described above for **1a**, the reaction mixture contained two cyclized products **3d** and **4c** in the molar ratio **3d**:**4c** = *ca.* 3:2 and a considerable amount of other unidentifiable materials. The 4-methyl compound **1d** did not produce the corresponding triazolopyridine, but gave the 2-triazoline derivative **4d** as the sole cyclized product (Scheme 3). The reaction between **1c** and **2b** resulted in only the impure triazoline and a trace of the corresponding **3**.

The ^{13}C NMR spectra of the 2-triazolines **4c** and **4d** showed that each compound has two equivalent methyl groups bonded to an sp^3 carbon (δ 27.09 and 25.67, respectively) and two non-equivalent cyano groups (δ 115.89–115.96 and δ 118.71–118.79), confirming the proposed structure in conjunction with other spectral data.

In general, thiosemicarbazones[4] and isothiosemicarbazones[5] tend to cyclize to five-membered compounds through intramolecular nucleophilic addition. The isothiosemicarbazones **1c** and **1d**, which carry a less bulky group on the terminal nitrogen, can cyclize to the corresponding 2-triazoline **4** by a similar intramolecular addition. However, when the substituent on the terminal nitrogen is bulkier beyond than ethyl, cyclization to the 2-triazoline is completely prevented and triazolopyridines **3** are the only observed product.

Experimental

Microanalyses were performed with a Perkin-Elmer 240D elemental analyser at the Microanalytical Laboratory of Kitasato University. IR, UV and mass spectra were recorded on Perkin-Elmer 983, JASCO UVIDEC 610 and JMS-DX100 instruments, respectively. ^1H and ^{13}C NMR spectra were obtained with a JNM EX-400 spectrometer operating at 400 and 100 MHz, respectively. Preparative high-performance liquid chromatography (HPLC) was carried out on a Kusano Kagaku KHLC-201 instrument with a 300 × 22 or a 300 × 15 mm glass column packed with silica gel.

3,4-*Disubstituted Isothiosemicarbazones* **1**.—These compounds were obtained by *S*-methylation of the corresponding 4-substituted thiosemicarbazones of the appropriate carbonyl compound and, in most cases, analysed as their hydriodides. In every case, isomeric mixtures consisting of *E*- and *Z*-forms about the N(2)=C bond in approximately 1:1 ratio were obtained upon neutralization of the hydriodide with aqueous sodium carbonate. The mixture was not separable into the components[6] and was used directly for further reactions.

General Procedure for the Reaction of Isothiosemicarbazones **1a**, **b** *and* **1e–h** *with Ethoxymethylenemalononitrile* **2a**.—A mixture of an isothiosemicarbazone and **2a** (1 mmol each) in chlorobenzene (1 cm^3) was heated at 140 °C (bath temperature) under a hood for 2 h and then evaporated under reduced pressure. The residue was extracted with boiling hexane to separate the desired product from the black resinous materials. Upon cooling, the deposited solids† were collected and subjected to chromatographic separation on silica gel (Wakogel C-300) with chloroform as the eluent to obtain fractions which showed blue fluorescence on a TLC sheet pre-coated with Kieselgel 60 F_{254} under ultraviolet light. Further purification by HPLC on silica gel with chloroform followed by crystallization from an appropriate solvent with active carbon gave an analytically pure compound.

2-tert-*Butylamino*-5-*methyl*[1,2,4]*triazolo*[1,5-a]*pyridine*-8-*carbonitrile* **3a**. (50%); m.p. 141–142 °C (from benzene) (Found: C, 62.6; H, 6.6; N, 30.6. $C_{12}H_{15}N_5$ requires C, 62.9; H, 6.6; N, 30.55%); $\nu_{max}(CCl_4)/cm^{-1}$ 3442 (NH) and 2235 (CN); λ_{max}(EtOH)/nm 207 (ε/dm^3 mol^{-1} cm^{-1} 23 700), 246 (27 900), 293 (6000) and 345 (7100); $\delta_H(CDCl_3)$ 1.48 (9 H, s, CMe_3), 2.74 (3 H, s, 5-Me), 4.84 (1 H, br s, NH), 6.66 (1 H, d, *J* 7.8, 6-H) and 7.62 (1 H, d, *J* 7.8, 7-H); $\delta_C(CDCl_3)$ 18.17 (qd, $^1J_{CH}$ 130.8 and $^3J_{CH}$ 3.3, 5-Me), 28.91 (qq, $^1J_{CH}$ 125.9 and $^3J_{CH}$ 4.4, CMe_3), 51.48 (m, CMe_3), 94.34 (d, $^3J_{CH}$ 10.0, C-8), 110.07 (dq, $^1J_{CH}$ 169.1 and $^3J_{CH}$ 4.6, C-6), 115.12 (d, $^3J_{CH}$ 6.0, CN), 133.84 (d, $^1J_{CH}$ 167.2, C-7), 142.71 (m, C-5), 149.81 (d, $^3J_{CH}$ 8.2, C-1a) and 165.21 (s, C-2); *m*/*z* 229 (M^+, 18%), 214 (M^+ − 15, 100) and 173 (31).

2-*Isopropylamino*-5-*methyl*[1,2,4]*triazolo*[1,5-a]*pyridine*-8-*carbonitrile* **3c**. (25%); m.p. 111 °C (from Pr^iOH) (Found: C, 61.4; H, 6.0; N, 32.6. $C_{11}H_{13}N_5$ requires C, 61.4; H, 6.1;

* 8-Carboxylate compound **3j** exhibited the resonance for C-8 at δ 112.80.

† Compound **3e** was obtained from the supernatant liquid in this procedure.

N, 32.5%); $\nu_{max}(CCl_4)/cm^{-1}$ 3444 (NH) and 2235 (CN); λ_{max}(EtOH)/nm 206 (24 400), 245 (28 500), 293 (6300) and 347 (7900); $\delta_H(CDCl_3)$ 1.30 (6 H, d, *J* 6.5, CMe_2), 2.73 (3 H, s, 5-Me), 4.05 (1 H, quin, *J* 6.5, $CHMe_2$), 4.67 (1 H, br s, NH), 6.65 (1 H, d, *J* 7.8, 6-H) and 7.62 (1 H, d, *J* 7.8, 7-H); $\delta_C(CDCl_3)$ 18.13 (qd, $^1J_{CH}$ 130.9 and $^3J_{CH}$ 3.3, 5-Me), 23.11 (q,* $^1J_{CH}$ 125.9, CMe_2), 45.07 (dquin, $^1J_{CH}$ 139.1 and $^2J_{CH}$ 4.4, CMe_2), 94.59 (d, $^3J_{CH}$ 9.3, C-8), 110.30 (dq, $^1J_{CH}$ 166.0 and $^3J_{CH}$ 4.4, C-6), 115.09 (d, $^3J_{CH}$ 6.0, CN), 133.92 (dd, $^1J_{CH}$ 168.8 and $^2J_{CH}$ 3.3, C-7), 142.80 (m, C-5), 150.49 (d, $^3J_{CH}$ 8.8, C-1a) and 166.04 (d, $^2J_{CH}$ 2.2, C-2); *m/z* 215 (M^+, 16%) and 200 ($M^+ - 15$, 100).

2-tert-*Butylamino*-5-*ethyl*[1,2,4]*triazolo*[1,5-a]*pyridine*-8-*carbonitrile* **3e**. (3%) m.p. 119 °C (from Pr^i_2O) (Found: C, 64.4; H, 7.0; N, 28.6. $C_{13}H_{17}N_5$ requires C, 64.2; H, 7.0; N, 28.8%); $\nu_{max}(CCl_4)/cm^{-1}$ 3442 (NH) and 2235 (CN); λ_{max}(EtOH)/nm 207 (25 200), 246 (28 000), 295 (6400) and 348 (7800); $\delta_H(CDCl_3)$ 1.42 (3 H, t, *J* 7.3, CH_2Me), 1.47 (9 H, s, CMe_3), 3.14 (2 H, q, *J* 7.3, CH_2Me), 4.90 (1 H, br s, NH), 6.68 (1 H, d, *J* 7.3, 6-H) and 7.65 (1 H, d, *J* 7.3, 7-H); $\delta_C(CDCl_3)$ 10.46 (qt, $^1J_{CH}$ 128.7 and $^2J_{CH}$ 5.5, CH_2Me), 24.96 (tq, $^1J_{CH}$ 130.5 and $^2J_{CH}$ 3.7, CH_2Me), 28.91 (q, $^1J_{CH}$ 126.7, CMe_3), 51.44 (m, CMe_3) 94.33 (d, $^3J_{CH}$ 9.2, C-8), 108.16 (dt, $^1J_{CH}$ 169.2 and $^3J_{CH}$ 3.7, C-6), 115.18 (d, $^3J_{CH}$ 5.5, CN), 134.07 (d, $^1J_{CH}$ 169.1, C-7), 147.69 (m, C-5), 149.83 (d, $^3J_{CH}$ 9.2, C-1a) and 165.14 (s, C-2); *m/z* 243 (M^+, 19%), 228 ($M^+ - 15$, 100) and 187 (24).

2-tert-*Butylamino*-5,6-*dimethyl*[1,2,4]*triazolo*[1,5-a]*pyridine*-8-*carbonitrile* **3f**. (23%); m.p. 169–170 °C (from EtOH) (Found: C, 64.0; H, 7.1; N, 29.0. $C_{13}H_{17}N_5$ requires C, 64.2; H, 7.0; N, 28.8%); $\nu_{max}(CCl_4)/cm^{-1}$ 3441 (NH) and 2234 (CN); λ_{max}(EtOH)/nm 210 (21 900), 247 (28 800), 297 (6000) and 353 (7500); $\delta_H(CDCl_3)$ 1.47 (9 H, s, CMe_3), 2.35 (3 H, s, 6-Me), 2.72 (3 H, s, 5-Me), 4.77 (1 H, br s, NH) and 7.52 (1 H, s, 7-H); $\delta_C(CDCl_3)$ 15.00 (q, $^1J_{CH}$ 130.5, 5-Me), 17.50 (dq, $^1J_{CH}$ 128.7 and $^3J_{CH}$ 4.6, 6-Me), 28.98 (q, $^1J_{CH}$ 125.9, CMe_3), 51.43 (m, CMe_3), 93.37 (s, C-8), 115.23 (d, $^3J_{CH}$ 5.5, CN), 117.92 (m, C-6), 135.87 (dq, $^1J_{CH}$ 165.5 and $^3J_{CH}$ 4.6, C-7), 140.90 (m, C-5), 148.63 (d, $^3J_{CH}$ 8.3, C-1a) and 165.11 (s, C-2); *m/z* 243 (M^+, 25%), 228 ($M^+ - 15$, 100) and 187 (13).

2-tert-*Butylamino*-5-*phenyl*[1,2,4]*triazolo*[1,5-a]*pyridine*-8-*carbonitrile* **3g**. (39%); m.p. 217–218 °C (from acetonitrile) (Found: C, 69.8; H, 6.0; N, 23.95. $C_{17}H_{17}N_5$ requires C, 70.1; H, 5.9; N, 24.0%); $\nu_{max}(CCl_4)/cm^{-1}$ 3440 (NH) and 2235 (CN); λ_{max}(EtOH)/nm 205 (19 700), 245 (15 500), 261 (11 700), 324 (11 000) and 368 (6700); $\delta_H(CDCl_3)$ 1.44 (9 H, s, CMe_3), 4.87 (1 H, br s, NH), 6.94 (1 H, d, *J* 7.8, 6-H), 7.54 (3 H, m, Ph), 7.75 (1 H, d, *J* 7.8, 7-H) and 8.02 (2 H, m, Ph); $\delta_C(CDCl_3)$ 29.01 (qq, $^1J_{CH}$ 126.9 and $^3J_{CH}$ 3.6, CMe_3), 51.52 (m, CMe_3), 95.15 (d, $^3J_{CH}$ 9.2, C-8), 110.53 (d, $^1J_{CH}$ 171.0, C-6), 115.18 (d, $^3J_{CH}$ 7.3, CN), 128.53, 129.22, 130.92 and 131.47 (m, Ph), 134.01 (d, $^1J_{CH}$ 167.3, C-7), 143.36 (m, C-5), 150.78 (d, $^3J_{CH}$ 7.3, C-1a) and 165.31 (s, C-2); *m/z* 291 (M^+, 23%) and 276 ($M^+ - 15$, 100).

2-tert-*Butylaminodihydrocyclopenta*[1′,2′:5,6][1,2,4]*triazolo*[1,5-a]*pyridine*-8-*carbonitrile* **3h**. (36%); m.p. 168–169 °C (from acetonitrile) (Found: C, 65.7; H, 6.8; N, 27.6. $C_{14}H_{17}N_5$ requires C, 65.9; H, 6.7; N, 27.4%); $\nu_{max}(CCl_4)/cm^{-1}$ 3441 (NH) and 2234 (CN); λ_{max}(EtOH)/nm 212 (17 700), 249 (29 400), 298 (6400) and 355 (7100); $\delta_H(CDCl_3)$ 1.47 (9 H, s, CMe_3), 2.34 (2 H, quin, *J* 7.3, 4′-CH_2), 3.04 (2 H, t, *J* 7.3, 3′-CH_2), 3.30 (2 H, t, *J* 7.8, 5′-CH_2), 4.80 (1 H, br s, NH) and 7.58 (1 H, s, 7-H); $\delta_C(CDCl_3)$ 23.20 (t, $^1J_{CH}$ 132.3, C-4′), 29.12 (q, $^1J_{CH}$ 126.9, CMe_3), 30.40 and 30.62 (each t, $^1J_{CH}$ 134.2, C-3′ and C-5′), 51.60 (m, CMe_3), 93.90 (s, C-8), 115.74 (d, $^3J_{CH}$ 5.5, CN), 125.25 (m, C-6), 130.97 (d, $^1J_{CH}$ 165.4, C-7), 146.57 (m, C-5), 150.41 (d, $^3J_{CH}$ 9.2, C-1a) and 166.12 (s, C-2); *m/z* 255 (M^+, 14%) and 240 ($M^+ - 15$, 100).

* Each component split into a multiplet.

2-tert-*Butylaminotetrahydrobenzo*[1′,2′:5,6][1,2,4]*triazolo*[1,5-a]*pyridine*-8-*carbonitrile* **3i**. (41%); m.p. 170–172 °C (from acetonitrile) (Found: C, 67.0; H, 7.1; N, 25.7. $C_{15}H_{19}N_5$ requires C, 66.9; H, 7.1; N, 26.0%); $\nu_{max}(CCl_4)/cm^{-1}$ 3441 (NH) and 2234 (CN); λ_{max}(EtOH)/nm 211 (20 900), 248 (29 200), 296 (6700) and 352 (7000); $\delta_H(CDCl_3)$ 1.46 (9 H, s, CMe_3), 1.86 (2 H, m, 4′-CH_2), 1.98 (2 H, m, 5′-CH_2), 2.78 (2 H, t, *J* 6.0, 3′-CH_2), 3.09 (2 H, t, *J* 6.5, 6′-CH_2), 4.76 (1 H, br s, NH) and 7.46 (1 H, s, 7-H); $\delta_C(CDCl_3)$ 21.23 and 22.09 (each t, $^1J_{CH}$ 128.7, C-4′ and C-5′), 25.46 and 27.05 (each t, $^1J_{CH}$ 128.7, C-3′ and C-6′), 28.99 (q, $^1J_{CH}$ 126.9, CMe_3), 51.41 (m, CMe_3), 93.71 (s, C-8), 115.27 (d, $^3J_{CH}$ 5.5, CN), 119.59 (m, C-6), 135.13 (d, $^1J_{CH}$ 165.4, C-7), 141.57 (m, C-5), 148.44 (d, $^3J_{CH}$ 7.3, C-1a) and 165.05 (s, C-2); *m/z* 269 (M^+, 13%) and 254 ($M^+ - 15$, 100).

Reaction of Acetone 4-tert-*Butyl*-3-*methylisothiosemicarbazone* **1a** *with Ethyl Ethoxymethylenecyanoacetate* **2b**.—A solution of **1a** (0.45 g, 2.2 mmol) and **2b** (0.26 g, 1.5 mmol) in DMF (0.9 cm^3) was heated above 150 °C for 1 h and evaporated under reduced pressure. The residue was repeatedly triturated with water to remove the residual solvent and then dried by azeotropic evaporation with benzene. Chromatographic separation on silica gel with chloroform as the eluent gave the desired product as a reddish yellow crystals (0.16 g, 39%). Further purification by means of HPLC on silica gel followed by crystallization yielded ethyl 2-*tert*-butylamino-5-methyl[1,2,4]triazolo[1,5-*a*]pyridine-8-carboxylate **3j** as long prisms, m.p. 103–104 °C (from Pr^iOH) (Found: C, 58.9; H, 7.4; N, 19.9. $C_{14}H_{20}N_4O_2 \cdot \frac{1}{2}H_2O$ requires C, 58.9; H, 7.4; N, 19.6%); $\nu_{max}(CCl_4)/cm^{-1}$ 3441 (NH) and 1712 (C=O); λ_{max}(EtOH)/nm 205 (21 300), 245 (26 800), 295 (6200) and 344 (7500); $\delta_H(CDCl_3)$ 1.42 (3 H, t, *J* 7.1, CH_2Me), 1.47 (9 H, s, CMe_3), 2.73 (3 H, s, 5-Me), 4.45 (2 H, q, *J* 7.1, OCH_2), 4.84 (1 H, br s, NH), 6.64 (1 H, d, *J* 7.3, 6-H) and 8.01 (1 H, d, *J* 7.3, 7-H); $\delta_C(CDCl_3)$ 14.39 (qt, $^1J_{CH}$ 127.0 and $^2J_{CH}$ 2.7, CH_2Me), 18.27 (qd, $^1J_{CH}$ 130.5 and $^3J_{CH}$ 3.7, 5-Me), 28.99 (q, $^1J_{CH}$ 126.5, CMe_3), 51.21 (m, CMe_3), 61.27 (tq, $^1J_{CH}$ 147.3 and $^2J_{CH}$ 4.4, OCH_2), 109.56 (dq, $^1J_{CH}$ 167.3 and $^3J_{CH}$ 3.7, C-6), 112.80 (d, $^3J_{CH}$ 9.2, C-8), 132.13 (d, $^1J_{CH}$ 167.3, C-7), 142.17 (m, C-5), 149.14 (d, $^3J_{CH}$ 8.8, C-1a), 164.26 (dt, $^3J_{CH}$ 4.9 and 3.3, C=O) and 165.36 (s, C-2); *m/z* 276 (M^+, 26%), 261 ($M^+ - 15$, 100) and 215 (77).

Reaction of Acetone 4-*Ethyl*-3-*methylisothiosemicarbazone* **1c** *with* **2a**.—A mixture of **1c** (1.52 g, 8.8 mmol) and **2a** (1.07 g, 8.8 mmol) in chlorobenzene (5 cm^3) was heated at 140 °C for 1 h and evaporated under reduced pressure. The residue was subjected to chromatographic separation on silica gel (Wakogel C-300, 100 g) with chloroform to give two fractions I and II in the eluting order. Fraction I gave **4c** as a crystalline solid (0.17 g, 8%) which was recrystallized from ethanol to yield a pure sample of **4c** as fine prisms, m.p. 220 °C (Found: C, 52.9; H, 6.1; N, 28.0. $C_{11}H_{15}N_5S$ requires C, 53.0; H, 6.1; N, 28.1%); ν_{max}(KBr)/cm^{-1} 2207 and 2190 (CN) and 1646 (C=C); $\delta_H(CDCl_3)$ 1.25 (3 H, t, *J* 7.2, CH_2Me), 1.58 (6 H, s, 5,5-Me_2), 2.62 (3 H, s, SMe), 3.27 (2 H, q, *J* 7.2, NCH_2) and 6.86 (1 H, s, CH=C); $\delta_C(CDCl_3)$ 13.86 (q, $^1J_{CH}$ 144.0, SMe), 16.08 (qt, $^1J_{CH}$ 128.1 and $^2J_{CH}$ 2.2, CH_2Me), 27.09 (qq, $^1J_{CH}$ 128.7 and $^3J_{CH}$ 2.7, 5,5-Me_2), 37.07 (tq, $^1J_{CH}$ 136.9 and $^2J_{CH}$ 4.4, CH_2Me), 48.73 (d, $^3J_{CH}$ 3.3, C-5), 86.61 (m, CH=*C*) and 115.96 (d, $^3J_{CH}$ 9.9, CN), 118.79 (d, $^3J_{CH}$ 5.5, CN), 140.19 (d, $^1J_{CH}$ 171.0, *C*H=C) and 160.11 (m, C-3); *m/z* 249 (M^+, 26%), and 234 ($M^+ - 15$, 100). Fraction II gave **3d** (0.21 g, 12%) as fine crystals, m.p. 166 °C (from ethanol) (Found: C, 59.4; H, 5.5; N, 34.7. $C_{10}H_{11}N_5$ requires C, 59.7; H, 5.5; N, 34.8%); $\nu_{max}(CCl_4)/cm^{-1}$ 3447 (NH) and 2235 (CN); λ_{max}(EtOH)/nm 206 (22 300), 245 (27 700), 293 (5600) and 347 (7200); $\delta_H(CDCl_3)$ 1.30 (3 H, t, *J* 7.2, CH_2Me), 2.74 (3 H, s, 5-Me), 3.52 (2 H, q, *J* 7.2, NCH_2), 4.85 (1 H, br s,

NH), 6.69 (1 H, d, *J* 7.7, 6-H) and 7.64 (1 H, d, *J* 7.7, 7-H); $\delta_C(CDCl_3)$ 15.23 (qt, $^1J_{CH}$ 126.5 and $^3J_{CH}$ 3.3, CH_2Me), 18.16 (dq, $^1J_{CH}$ 130.9 and $^3J_{CH}$ 3.3, 5-Me), 38.09 (qt, $^1J_{CH}$ 138.0 and $^2J_{CH}$ 4.4, NCH_2), 94.46 (d, $^3J_{CH}$ 9.3, C-8), 110.30 (dq, $^1J_{CH}$ 174.8 and $^3J_{CH}$ 4.4, C-6), 115.06 (d, $^3J_{CH}$ 6.0, CN), 133.95 (dd, $^1J_{CH}$ 168.8 and $^2J_{CH}$ 4.4, C-7), 142.83 (m, C-5), 150.52 (d, $^3J_{CH}$ 8.2, C-1a) and 166.57 (t, $^3J_{CH}$ 3.3, C-2); *m/z* 201 (M^+, 69%), 186 (100) and 173 (31).

1-(2,2-*Dicyanovinyl*)-3-*methylthio*-4,5,5-*trimethyl*[1,2,4]-*triazoline* **4d**. (11%); m.p. 217–218 °C (from ethanol) (Found: C, 51.2; H, 5.6; N, 29.5. $C_{10}H_{13}N_5S$ requires C, 51.0; H, 5.6; N, 29.8%); $\nu_{max}(CCl_4)/cm^{-1}$ 2208 and 2187 (CN) and 1638 (C=C); $\delta_H(CDCl_3)$ 1.56 (6 H, s, 5,5-Me_2), 2.62 (3 H, s, SMe), 2.87 (3 H, s, 4-Me) and 6.83 (1 H, s, CH=C); $\delta_C(CDCl_3)$ 13.83 (q, $^1J_{CH}$ 144.0, SMe), 25.67 (qq, $^1J_{CH}$ 129.2 and $^3J_{CH}$ 2.7, 5,5-Me_2), 27.99 (q, $^1J_{CH}$ 139.1, 4-Me), 86.36 (m, CH=*C*), 115.89 (d, $^3J_{CH}$ 9.9, CN), 118.71 (d, $^3J_{CH}$ 5.5, CN), 140.54 (d, $^1J_{CH}$ 171.0, *C*H=C) and 160.83 (m, C-3); *m/z* 235 (M^+, 18%), 220 ($M^+ - 15$, 75) and 149 (100).

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