Reactions of Alkyl Isothiocyanates with Dianions of Cyclic Thioureas

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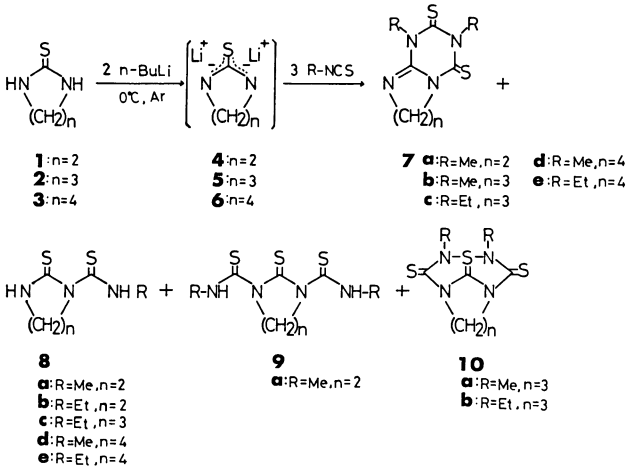
Synopsis. The reactions of methyl (or ethyl) isothiocyanate with dianions (**4**, **5**, and **6**), which are readily derived from available cyclic thioureas (**1**, **2**, and **3**) with butyllithium, gave ring fused 1,3-disubstituted 1,3,5-triazine-2,4(1*H*,3*H*)-dithiones (**7**) and/or thiocarbamoyl derivative (**8**) as major products.

Recently we have reported that the bromomagnesium thioureide acts effectively as a carbon dioxide carrier in the carboxylation of active methylene compounds under mild conditions.[1] In our continuing investigation on the properties of the dianions, which are readily derived from available cyclic thioureas with butyllithium, we have found the formation of 7,8-dihydro-1,3-dimethyl-6*H*-pyrimido[1,2-*a*][1,3,5]-triazine-2,4(1*H*,3*H*)-dithione (**7b**) and 3,4-dimethyl-1,6-propano-1*H*,6*H*-**3a**-thia(S^{IV})-1,3,4,6-tetraazapentalene-2,5(3*H*,4*H*)-dithione (**10a**) by the reaction of methyl isothiocyanate with dianion (**5**). The reaction behavior of dianions of cyclic thioureas has not been well investigated so far.[2] This paper reports the reaction of alkyl isothiocyanates with dianions (**4**, **5**, and **6**). The reactions were carried out in tetrahydrofuran (THF) at room temperature for 24 h under argon. When the RNCS:dianion molar ratio was 3:1, **7** was obtained in relatively good yield. The outline of the reaction pathway is shown in Scheme 1.

Reactions of alkyl isothiocyanates with dianions **4**, **5**, and **6** gave ring fused 1,3-disubstituted 1,3,5-triazine-2,4(1*H*,3*H*)-dithione (**7**), thiocarbamoyl de-

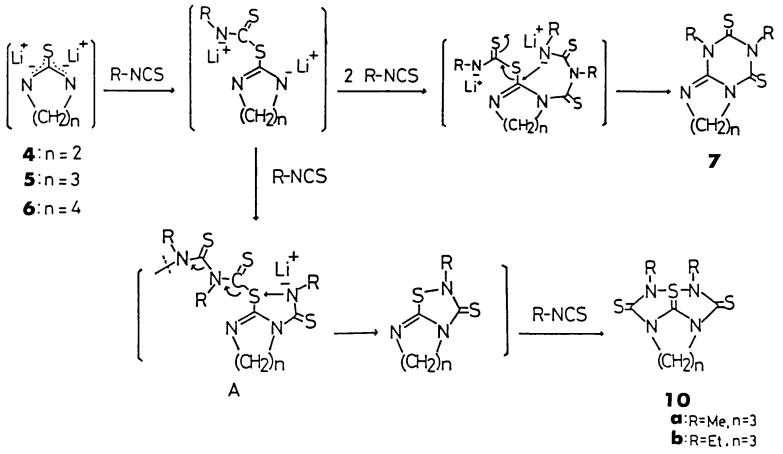


Scheme 1.

Table 1. Reactions of Alkyl Isothiocyanates with Dianions[a]

Dianion	R-NCS R	Product yield/%[b] 7	8	9	10
4	Me	10 (**7a**)[c]	38 (**8a**)	48 (**9a**)	—
4	Et	—	53 (**8b**)	—	—
5	Me	61 (**7b**)	—	—	15 (**10a**)
5	Et	36 (**7c**)	19 (**8c**)	—	10 (**10b**)
6	Me	22 (**7d**)	48 (**8d**)	—	—
6	Et	13 (**7e**)	40 (**8e**)	—	—

a) All reactions were carried out at room temperature for 24 h. b) Isolated yields. c) Isolated products are designated in parentheses.

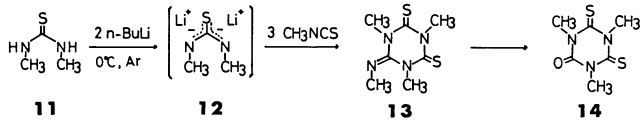


Scheme 2.

rivative (**8**), bis(thiocarbamoyl) derivative (**9**), and heteropentalene derivative (**10**). The yields are summarized in Table 1. The yields of products depended on the ring size of cyclic thiourea, the alkyl group of alkyl isothiocyanate, and reaction conditions. The dianions, **5**, and **6**, reacted with alkyl isothiocyanate to give the ring fused compound **7** in good yields, whereas the dianion **4** to give **7** in poor yields. A possible mechanism for the formation of **7** is given in Scheme 2.

The reaction of methyl (or ethyl) isothiocyanate with dianion **5** at room temperature for 24 h under argon afforded heteropentalene derivative **10** as a minor product together with ring fused compound **7**. The compound **10**, **3a**-thia(S^{IV})pentalene system containing π-hypervalent sulfur, is of interest from the structural point of view. The structure of **10** was determined by IR, Mass, ^{1}H NMR, ^{13}C NMR, and elemental analysis. Our mechanistic interpretation for the formation of **10** is outlined in Scheme 2. When the dianions **4** and **6** were used, heteropentalene derivatives were not obtained. For these results there are two possible explanations. One is that the intermediates A derived from the dianions **4** and **6** have unfavorable configurations for the attack of N atom to S atom compared with the intermediate A derived from the dianion **5**. The other is that the strain of heteropentalene derivative with five- or seven-membered ring is larger than that of **10**.

Next, we have examined the reaction of alkyl isothiocyanate with the dianion of acyclic thiourea.



11 **12** **13** **14**

When the reaction of methyl isothiocyanate with dianion (**12**), which is derived from *N,N'*-dimethylthiourea (**11**) with butyllithium, was carried out at room temperature for 24 h under argon, 5,6-dihydro-1,3,5-trimethyl-6-methylimino-1,3,5-triazine-2,4-(1*H*,3*H*)-dithione (**13**) was obtained as a crude product in 84% yield. The structure of **13** was determined by the following spectral data: IR (KBr) 1682 cm^{-1} (C=N); MS (70 eV) *m/z*, 216 (M$^+$); ^{1}H NMR ($CDCl_3$) δ=3.25 (s, 3H), 3.60 (s, 6H), and 3.90 (s, 3H). When the crude product **13** was chromatographed on preparative TLC (silica gel using dichloromethane as an eluent), it was converted into the 3,4,5,6-tetrahydro-1,3,5-trimethyl-4,6-dithioxo-1,3,5-triazin-2(1*H*)-one (**14**) in quantitative yield.

Experimental

Melting points were determined on a Yanagimoto melting point apparatus and were uncorrected. Proton magnetic resonance (^{1}H NMR) spectra were obtained using a Hitachi Perkin-Elmer R-24 spectrometer (60 MHz), JEOL FX-90Q (90 MHz), and JEOL JNM-GX270 (270 MHz). ^{13}C NMR spectra were obtained using a JEOL FX-90Q and JEOL JNM-GX270. Chemical shifts are reported in ppm form TMS as an internal standard and are given in δ units. The IR spectra were determined on a Hitachi 215 Grating infrared spectrometer. Mass spectra were obtained with a SHIMADZU-LKB 9000 instrument equipped with a solid injector; the ionizing voltage was 70 eV.

General Procedure for the Reaction of Alkyl Isothiocyanate with Dianions, (4, 5, and 6). To a cooled THF solution (0 °C) of 3,4,5,6-tetrahydro-2(1*H*)-pyrimidinethione (**2**, 2.0 mmol) was added a hexane solution of butyllithium (4.4 mmol) with stirring at 0 °C under argon, and the mixture was stirred for 1 h under same conditions. To the resulting dianion (**5**) was added dropwise a THF solution of methyl isothiocyanate (6.0 mmol). The solution immediately became orange, and the mixture was stirred for 24 h under argon. After THF was evaporated, the residue was poured into an aqueous ammonium chloride. The solution was extracted with chloroform, and the extract was washed with water, dried over Na_2SO_4, and condensed under reduced pressure. The residue was chromatographed on a silica-gel column or preparative TLC (dichloromethane as an eluent) to give products, **7b** (61%) and **10a** (15%). All compounds were recrystallized from hexane–chloroform to give colorless solid.

6,7,8,8a-Tetrahydro-1,3-dimethylimidazo[1,2-*a*][1,3,5]triazine-2,4(1*H*,3*H*)-dithione (7a). Mp 128—129 °C; IR (KBr) 1677 (C=N) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.68 (s, 3H, CH_3), 4.03 (s, 3H, CH_3), and 3.7—4.4 (m, 4H, NCH_2CH_2N); MS *m/z* 214 (M$^+$). Found: C, 39.47; H, 4.78; N, 26.21%. Calcd for $C_7H_{10}N_4S_2$: C, 39.23; H, 4.70; N, 26.42%.

7,8-Dihydro-1,3-dimethyl-6*H*-pyrimido[1,2-*a*][1,3,5]triazine-2,4(1*H*,3*H*)-dithione (7b). Mp 143—145 °C (lit,[3] 141—142 °C).

7,8-Dihydro-1,3-diethyl-6*H*-pyrimido[1,2-*a*][1,3,5]triazine-2,4(1*H*,3*H*)dithione (7c). Mp 92—94 °C; IR (KBr) 1600 (C=N) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.22 (t, 3H, *J*=7.0 Hz, CH_2CH_3), 1.32 (t, 3H, *J*=7.0 Hz, CH_2CH_3), 1.90 (m, 2H, $NCH_2CH_2CH_2N$), 3.50 (t, 2H, *J*=6.0 Hz, $C=NCH_2$), 4.15 (t, 2H, *J*=6.0 Hz, NCH_2), 4.50 (q, 2H, *J*=7.0 Hz, CH_2CH_3), and 4.96 (q, 2H, *J*=7.0 Hz, CH_2CH_3); MS *m/z* 256 (M$^+$). Found: C, 47.08; H, 6.34; N, 21.80%. Calcd for $C_{10}H_{16}N_4S_2$: C, 46.85; H, 6.29; N, 21.85%.

6,7,8,9-Tetrahydro-1,3-dimethyl-1,3,5-triazino[1,2-*a*][1,3]diazepine-2,4(1*H*,3*H*)-dithione (7d). Mp 97—98 °C; IR (KBr) 1682 (C=N) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.00 (m, 4H, $NCH_2CH_2CH_2CH_2N$), 3.65 (s, 3H, CH_3), 3.75 (t, 2H, *J*=7.0 Hz, $C=NCH_2$), 4.00 (s, 3H, CH_3), and 4.35 (t, 2H, *J*=7.0 Hz, NCH_2); ^{13}C NMR ($CDCl_3$) δ=22.56, 24.46, 38.49, 43.31, 137.74, and 175.82; MS *m/z* 242 (M$^+$). Found: C, 44.35; H, 5.78; N, 22.84%. Calcd for $C_9H_{14}N_4S_2$: C, 44.60; H, 5.82; N, 23.12%.

6,7,8,9-Tetrahydro-1,3-diethyl-1,3,5-triazino[1,2-*a*][1,3]diazepine-2,4(1*H*,3*H*)-dithione (7e). Mp 67—70 °C; IR (KBr) 1650 (C=N) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.22 (t, 3H, *J*=7.0 H, CH_2CH_3), 1.35 (t, 3H, *J*=7.0 Hz, CH_2CH_3), 1.9 (m, 4H, $NCH_2CH_2CH_2CH_2N$), 3.7 (t, 2H, *J*=5.5 Hz, $C=NCH_2$), 4.23 (t, 2H, *J*=5.5 Hz, NCH_2), 4.4 (q, 2H, *J*=7.0 Hz, CH_2CH_3), and 4.8 (q, 2H, *J*=7.0 Hz, CH_2CH_3); MS *m/z* 270 (M$^+$). Found: C, 48.90; H, 6.89; N, 20.55%. Calcd for $C_{11}H_{18}N_4S_2$: C, 48.86; H, 6.71; N, 20.72%.

1-(Methylthiocarbamoyl)-2-imidazolidinethione (8a). Mp 205—206 °C; IR (KBr) 3170 (NH) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.16 (d, 3H, *J*=4.3 Hz, CH_3), 3.60 (d, of t, 2H, *J*=1.2 and 8.9 Hz, $HNCH_2$), 4.67 (t, 2H, *J*=8.9 Hz, NCH_2), 6.5 (br, 1H, NH), and 11.9 (br, 1H, NH); ^{13}C NMR ($CDCl_3$) δ=32.63, 40.12, 52.25, 179.24, and 180.70; MS *m/z* 175 (M$^+$). Found: C, 34.09; H, 5.23; N, 23.80%. Calcd for $C_5H_9N_3S_2$: C, 34.26; H, 5.18; N, 23.97%.

1-(Ethylthiocarbamoyl)-2-imidazolidinethione (8b). Mp 171—172 °C; IR (KBr) 3250 (NH) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.31 (t, 3H, *J*=7.3 Hz, CH_2CH_3), 3.59 (d of t, 2H, *J*=0.8

and 9.1 Hz, $HNC\underline{H}_2$), 3.67 (d of q, 2H, J=5.0 and 7.3 Hz, $C\underline{H}_2CH_3$), 4.66 (t, 2H, J=9.1 Hz, NCH_2), 6.6 (br, 1H, NH), and 11.9 (br, 1H, NH); MS m/z 189 (M^+). Found: C, 38.21; H, 5.94; N, 22.28%. Calcd for $C_6H_{11}N_3S_2$: C, 38.07; H, 5.86; N, 22.20%.

1-(Ethylthiocarbamoyl)perhydropyrimidine-2-thione (8c). Mp 152—154 °C; IR (KBr) 3180 (NH) cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.33 (t, 3H, J=7.3 Hz, $CH_2C\underline{H}_3$), 2.11 (m, 2H, $NCH_2C\underline{H}_2CH_2N$), 3.35 (d of t, 2H, J=2.4 and 6.4 Hz, $HNC\underline{H}_2$), 3.70 (d and q, 2H, J=4.9 and 7.3 Hz, $C\underline{H}_2CH_3$), 4.40 (t, 2H, J=5.5 Hz, NCH_2), 7.3 (br, 1H, NH), and 11.2 (br, 1H, NH); MS m/z 203 (M^+). Found: C, 41.15; H, 6.44; N, 20.50%. Calcd for $C_7H_{13}N_3S_2$: C, 41.35; H, 6.44; N, 20.67%.

1-(Methylthiocarbamoyl)perhydro-1,3-diazepine-2-thione (8d). Mp 138—140 °C; IR (KBr) 3170 (NH) cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.5—2.2 (m, 4H, $NCH_2C\underline{H}_2C\underline{H}_2CH_2N$), 3.15 (d, 3H, J=5.0 Hz, CH_3), 3.35 (d of t, 2H, J=6.0 and 7.0 Hz, $HNC\underline{H}_2$), 4.25 (t, 2H, J=7.0 Hz, NCH_2), 8.25 (br, 1H, NH), and 8.95 (br, 1H, NH); ^{13}C NMR ($CDCl_3$) δ=25.11, 26.30, 32.53, 47.54, 53.17, 182.43, and 189.10; MS m/z 203 (M^+). Found: C, 41.07; H, 6.61; N, 20.48%. Calcd for $C_7H_{13}N_3S_2$: C, 41.35; H, 6.44; N, 20.67%.

1-(Ethylthiocarbamoyl)perhydro-1,3-diazepine-2-thione (8e). Mp 102—104 °C; IR (KBr) 3170 (NH) cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.26 (t, 3H, J=7.3 Hz, $CH_2C\underline{H}_3$), 1.64—2.06 (m, 4H, $NCH_2C\underline{H}_2C\underline{H}_2CH_2N$), 3.35 (d of t, 2H, J=4.8 and 5.6 Hz, $HNC\underline{H}_2$), 3.65 (d of q, 2H, J=4.8 and 7.3 Hz, $C\underline{H}_2CH_3$), 4.22 (t, 2H, J=6.0 Hz, NCH_2), 7.8 (br, 1H, NH), and 9.1 (br, 1H, NH); MS m/z 277 (M^+). Found: C, 43.98; H, 7.05; N, 19.50%. Calcd for $C_8H_{15}N_3S_2$: C, 44.21; H, 6.96; N, 19.33%.

1,3-Bis(methylthiocarbamoyl)-2-imidazolidinethione (9a). Mp 152—154 °C; IR (KBr) 3150 (NH) cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.28 (d, 6H, J=5.0 Hz, 2×CH_3), 4.4 (s, 4H, NCH_2CH_2N), and 11.1 (br, 2H, 2×NH); ^{13}C NMR ($CDCl_3$) δ=33.04, 48.38, 174.23, and 180.91; MS m/z 248 (M^+). Found: C, 33.70; H, 4.94; N, 22.48%. Calcd for $C_7H_{12}N_4S_3$: C, 33.85; H, 4.87; N, 22.56%.

3,4-Dimethyl-1,6-propano-1*H*,6*H*-3a-thia(S^{IV})-1,3,4,6-tetraazapentalene-2,5(3*H*,4*H*)-dithione (10a). Mp 201—203 °C (decomp); IR (KBr) 2920, 1580, 1540, 1500, 1245, 1195, and 1120 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.36 (m, 2H, $NCH_2C\underline{H}_2CH_2N$), 3.24 (s, 6H, 2×$CH_3$), and 4.4 (t, 4H, J=6.0 Hz, 2×NCH_2); ^{13}C NMR ($CDCl_3$) δ=19.91, 30.91, 44.72, 155.78, and 169.48; MS m/z 187 (M^+-CH_3NCS). Found: C, 36.44; H, 4.43; N, 21.18%. Calcd for $C_8H_{12}N_4S_3$: C, 36.90; H, 4.64; N, 21.52%.

3,4-Diethyl-1,6-propano-1*H*,6*H*-3a-thia(S^{IV})-1,3,4,6-tetraazapentalene-2,5(3*H*,4*H*)-dithione (10b). Mp 217—220 °C (decomp); IR (KBr) 2960, 2910, 1570, 1530, 1490, 1230, 1180, and 1120 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.33 (t, 6H, J=7.0 Hz, 2×$CH_2C\underline{H}_3$), 2.36 (m, 2H, $NCH_2C\underline{H}_2CH_2N$), 3.78 (q, 4H, J=7.0 Hz, 2×$C\underline{H}_2CH_3$), and 4.41 (t, 4H, J=6.0 Hz, 2×NCH_2); ^{13}C NMR ($CDCl_3$) δ=13.82, 20.01, 39.93, 44.61, 156.11, and 168.65; MS m/z 201 ($M^+-CH_3CH_2NCS$). Found: C, 41.52; H, 5.56; N, 19.55%. Calcd for $C_{10}H_{16}N_4S_3$: C, 41.64; H, 5.59; N, 19.42%.

3,4,5,6-Tetrahydro-1,3,5-trimethyl-4,6-dithioxo-1,3,5-triazin-2(1*H*)-one (14). Mp 112—113 °C; IR (KBr) 1720 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.7 (s, 6H, 2×CH_3) and 4.2 (s, 3H, CH_3); MS m/z 203 (M^+). Found: C, 35.61; H, 4.55; N, 20.74%. Calcd for $C_6H_9N_3OS_2$: C, 35.45; H, 4.46; N, 20.67%.

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