Recrystallization from ether afforded 10.5 g of the pure product as a colorless solid: mp 85–88 °C; IR (KBr) 3480, 3250, 2980, 1320, 1290, 1140, 1015 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.4 (s, 9 H), 4.85 (br s, 1 H), 6.9 (d, 1 H, J = 15 Hz), 7.3–7.7 (m, 4 H), 7.95 (d, 1 H, J = 15 Hz).

A mixture of **15** (R = Cl) (1.5 g, 5.5 mmol) and 300 mg of *p*-toluenesulfonic acid monohydrate in 18 mL of xylenes was heated at reflux temperature for 4 h. As the reaction solution cooled to room temperature, a precipitate formed. This solid was filtered, washed with hexane, and dried. The yield of pure **16** was 1.1 g (96%) as a colorless solid: mp 125–127 °C (lit.[8] mp 124.5–126.5 °C); IR (KBr) 3320, 3240, 1620, 1330, 1140 cm^{-1}; NMR ($CDCl_3/Me_2SO$-d_6, 90 MHz) δ 7.2 (d, 1 H, J = 15 Hz), 7.3–7.6 (m, 3 H), 7.75 (m, 1 H), 7.8 (d, 1 H, J = 15 Hz).

2-*tert*-Butyl-3-(*o*-nitrophenyl)-1,2-thiazetidine 1,1-Dioxide (18, R = NO_2). A solution of 1.5 g (5.1 mmol) of *N*-*tert*-butyl-2-(*o*-nitrophenyl)-2-hydroxyethanesulfonamide (**14**, R = NO_2) (prepared by the addition of dianion **12** to *o*-nitrobenzaldehyde) and 1.40 mL (10.0 mmol) of triethylamine in 10 mL of CH_2Cl_2 was cooled to 0 °C under a nitrogen atmosphere and treated with 0.60 mL (7.8 mmol) of methanesulfonyl chloride. The reaction mixture was stirred at 0 °C for 30 min and then at room temperature for 5 h. Dichloromethane (50 mL) was added and the organic layer was washed with two portions of 5% aqueous HCl and three portions of water. Drying ($MgSO_4$) and evaporation of the CH_2Cl_2 layer afforded a yellow oil from which 1.6 g (82%) of pure methanesulfonate ester **17** (R = NO_2), mp 136–138 °C dec, crystallized upon addition of ether; NMR ($CDCl_3/Me_2SO$-d_6, 90 MHz) δ 1.35 (s, 9 H), 3.2 (s, 3 H), 3.7 (m, 2 H), 6.6 (br t, 1 H, J = 6 Hz), 6.8 (br s, 1 H), 7.6–8.2 (m, 4 H).

This mesylate (1.1 g, 2.9 mmol) was added to a well-stirred suspension of 1.2 g (8.7 mmol) of anhydrous K_2CO_3 in 14 mL of dry Me_2SO. The mixture was warmed to 80 °C under a nitrogen atmosphere for approximately 1 h, allowed to cool, and then poured into 25 mL of water, causing an immediate precipitate. This solid was collected by filtration, washed well with water and ether, and dried to give 440 mg (53%) of the 1,2-thiazetidin 1,1-dioxide **18** (R = NO_2) as a white powder: mp 179–181 °C; IR (KBr) 2490, 1525, 1350, 1300, 1190, 1140 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 1.25 (s, 9 H), 3.80 (dd, 1 H, J = 2, 12 Hz), 4.69 (dd, 1 H, J = 4, 12 Hz), 5.05 (dd, 1 H, J = 2,4 Hz), 7.50 (br t, 1 H, J = 3 Hz), 7.73 (br t, 1 H, J = 3 Hz), 7.95 (br d, 1 H, J = 3 Hz), 8.23 (br d, 1 H, J = 3 Hz); MS, m/e (relative intensity) 285 (14, M + 1), 269 (38, M^+ – 15), 212 (14), 148 (27), 146 (53), 91 (15), 77 (54), 58 (100), 57 (80), 56 (45); exact mass calcd for $C_{12}H_{16}N_2O_4S$ 284.0831, found 284.0873.

Acknowledgment. I express my appreciation to Mr. Thomas P. Boyle for technical assistance and to Dr. Paul K. Tseng for performing HPLC analyses.

Registry No. **10**, 1520-70-3; **13**, 89556-99-0; **14** (R = Cl), 89557-00-6; **14** (R = NO_2), 89557-01-7; **15** (R = Cl), 89557-02-8; **16** (R = Cl), 89557-03-9; **17** (R = NO_2), 89557-04-0; **18** (R = NO_2), 89557-05-1; $CH_3SO_2NHC(CH_3)_3$, 2512-23-4; $CH_3SO_2NHCH_2Ph$, 3989-45-5; $CH_3SO_2NH(c\text{-}C_6H_{11})$, 19299-40-2; $PhCH_2SO_2NHC(CH_3)_3$, 51270-35-0; $p\text{-}ClC_6H_4CH_2SO_2NHCH(CH_3)_2$, 85952-21-2; $PhCH_2Br$, 100-39-0; $(CH_3)_3SiCl$, 75-77-4; $o\text{-}ClC_6H_4CHO$, 89-98-5; CH_3I, 74-88-4; $p\text{-}ClC_6H_4CN$, 623-03-0; $(CH_3)_2CHCN$, 78-82-0; $Ph_2C{=}O$, 119-61-9; CH_2O, 50-00-0; $PhCH_2CH_2SO_2NHC(CH_3)_3$, 89557-07-3; $(CH_3)_3SiCH_2SO_2NHCH_2Ph$, 89557-08-4; $(2\text{-}C_4H_3S)CHO$, 98-03-3; $(2\text{-}C_4H_3S)CH(OH)CH_2SO_2NH(c\text{-}C_6H_{11})$, 89557-09-5; $p\text{-}ClC_6H_4COCH_2SO_2NHCH(CH_3)_2$, 89557-10-8; $(CH_3)_2CHCOCH_2SO_2NHCH_2Ph$, 89557-11-9; $PhCH(CH_2OH)SO_2NHC(CH_3)_3$, 89557-12-0; *trans*-$2\text{-}HO_2CC_6H_4CH{=}CHSO_2NHC(CH_3)_3$, 89557-13-1; $4\text{-}ClC_6H_4CH[SO_2NHCH(CH_3)_2]CH(OH)CH_2CH_3$ (isomer 1), 89557-14-2; $4\text{-}ClC_6H_4CH[SO_2NHCH(CH_3)_2]CH(OH)CH_2CH_3$ (isomer 2), 89557-15-3; $4\text{-}ClC_6H_4CH[SO_2NHC(CH_3)_3]CHPhOH$ (isomer 1), 89557-16-4; $4\text{-}ClC_6H_4CH[SO_2NHC(CH_3)_3]CHPhOH$ (isomer 2), 89557-17-5; $Ph_2C(OH)CH(CH_3)SO_2NHC(CH_3)_3$, 89557-06-2; $o\text{-}O_2NC_6H_4CHO$, 552-89-6; $o\text{-}OHCC_6H_4CO_2CH_3$, 4122-56-9; CH_3CH_2CHO, 123-38-6; PhCHO, 100-52-7; $CH_3SO_2NHCH(CH_3)_2$, 23705-43-3; lithium diisopropylamide, 4111-54-0; butyllithium, 109-72-8; cyclohexanone, 108-94-1; *N*-benzyl-1-hydroxycyclohexanemethanesulfonamide, 89557-18-6.

Cyclization Reactions of Hydrazones Induced by Isocyanates. Syntheses of 1,3,4-Thiadiazoline and 1,2,4-Triazoline Derivatives

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Cyclization reactions of various hydrazones (**1**, **6**, **10**, and **13**) were found to be induced by isocyanates under mild conditions and to afford 1,3,4-thiadiazolines **3** and **11** and 1,2,4-triazolines **9**, **14**, and **18** in excellent yields. The cyclization reactions via inter- and intramolecular double additions were studied by ^1H and ^{13}C NMR spectroscopy. The syntheses of 4-(methoxycarbonyl)-Δ^2-1,2,4-triazolines **14** and **18** and derived fused heterocycles such as 1*H*,5*H*-[1,2,4]triazolo[1,2-*a*][1,2,4]triazole-1,3(2*H*)-diones **16** and 2,3-dihydro-3-thioxo-1*H*,5*H*-[1,2,4]-triazolo[1,2-*a*][1,2,4]triazol-1-ones **19** and **20** were achieved in high yields. The bicyclic structures of **16**, **19**, and **20** were confirmed by a single-crystal X-ray structure determination of **16a**.

The cycloaddition reactions of carbon–nitrogen double-bond systems with isocyanates are of great use for the syntheses of heterocyclic compounds.[1] In spite of considerable nucleophilicity of hydrazones, their cycloadditions to isocyanates have been studied only in a few limited cases.[2] The utility of hydrazones[3–7] as synthons for various heterocycles prompted us to investigate the behavior of hydrazones toward isocyanates. We found a new type of cyclization reactions of hydrazones **1**, **6**, **10**, and **13** induced by isocyanates. These reactions are characterized as a kind of inter- and intramolecular double additions. Thus, hydrazone derivatives reacted with iso-

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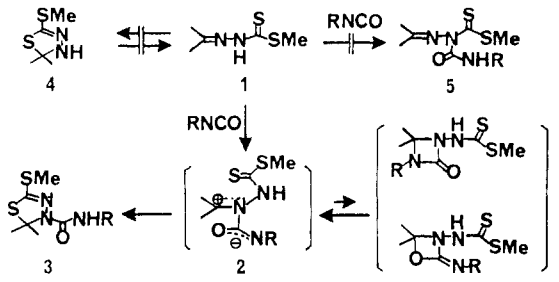
0022-3263/84/1949-1703$01.50/0

Scheme I



a, R = CH_3; b, R = t-C_4H_9

c, R = c-C_6H_{11}; d, R = C_6H_5

cyanates to afford 1,3,4-thiadiazolines **3** and **11** and 1,2,4-triazolines **9**, **14**, and **18** under mild conditions in excellent yields. Extension of 1,2,4-triazolines **14** and **18** to novel fused heterocycles such as 1*H*,5*H*-[1,2,4]triazolo-[1,2-*a*][1,2,4]triazole-1,3(2*H*)-diones **16** and 2,3-dihydro-3-thioxo-1*H*,5*H*-[1,2,4]triazolo[1,2-*a*][1,2,4]triazol-1-ones **19** and **20** was conveniently achieved in high yields.

Results and Discussion

A. Reaction of Methyl 2-Isopropylidenehydrazinecarbodithioate (1) with Isocyanates. Hydrazinecarbodithioate **1**[8] was unreactive by itself and showed no isomerization into a cyclic form (**4**) under any thermal condition below 150 °C. On treatment with isocyanates in aprotic solvents, **1** was found to undergo a cyclization reaction to give **3** (Scheme I). The reaction of **1** with an equivalent of methyl isocyanate in chloroform at room temperature was complete within 3 h and afforded a cyclic product (**3a**) in an almost quantitative yield. The structure of **3a** was determined on the basis of spectroscopic data. The IR absorption at 3330 cm^{-1} and the ^1H NMR signal of a doublet peak at δ 2.78 suggested the presence of a (methylamino)carbonyl substituent. Instead of two singlets (δ 1.96 and 2.06) due to an isopropylidene group of **1**, the ^1H NMR spectrum of **3a** exhibited one singlet (δ 1.94) whose chemical shift was similar to that (δ 1.69) of 3,5,5-trimethyl-1,3,4-thiadiazolidine-2-thione.[1b] The elemental analysis and mass spectrum (M^+, *m/e* 219) of **3a** were in agreement with the assigned structure. Similarly, 1,3,4-thiadiazolines **3b–d** were obtained in excellent yields (>90%). The structures of **3a–d** were further confirmed by ^{13}C NMR spectroscopy. Strong upfield shifts (ca. 73 ppm) of central isopropylidene carbon signals observed between **1** and **3a–d** can be attributed to the C–S bond formations. As illustrated in Scheme I, the formation of Δ^2-1,3,4-thiadiazolines **3a–d** from **1** is assumed to be a two-step reaction consisting of the first attack of an isocyanate to C=N bond and the second intramolecular addition of a sulfur atom. Possible intermediates **2** are proposed in relation to the earlier observation of 1:1 cyclic adducts[9] in the reaction of *N*-benzylideneaniline with phenyl isocyanates. In the present reaction, four-membered cyclic intermediates or simple addition products **5** were not detected by ^1H NMR spectroscopy (90 MHz) at room temperature during 2 h.

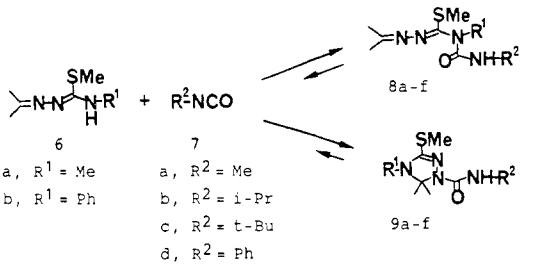
B. Reaction of 1-Isopropylidene-3-methylthioisosemicarbazides (6) with Isocyanates 7. The reaction of 1-isopropylidene-3-methylthioisosemicarbazides **6** with isocyanates **7** was examined because of the functional analogy of **6** to hydrazinecarbodithioate **1** (Scheme II, Table I). Compounds **6** were readily provided by S-methylation of 2-isopropylidenehydrazinecarbothioamides[10] with iodomethane in the presence of sodium methoxide in methanol at room temperature according to the known method.[11] In the reaction of **6b** (R^1 = Ph) with isocyanates **7a,b** in chloroform at room temperature overnight (method A), Δ^2-1,2,4-triazolines **9e,f** were selectively produced in high yields irrespective of isocyanates used (entries 7 and 8). The same treatment of **6a** (R^1 = Me) with isocyanates **7c,d** also afforded cyclic products **9c,d** predominantly (entries 5 and 6). Contrary to these results, the reaction of **6a** with alkyl isocyanates **7a,b** (except **7c** (R^2 = *t*-Bu)) gave major acyclic products **8a,b**. However, when **6a** was heated with alkyl isocyanates **7a,b** in sealed tubes at 140 °C for 5 h (method B), cyclic products **9a,b** were mainly obtained. Under the same reaction conditions as method B, acyclic compounds **8a,b** were found to isomerize into **9a,b** in the yields of 61% and 83%, respectively. In addition, retroreactions of both **8a,b** (fast) and **9a,b** (slow) into **6a,b** and **7a,b** were observed when treated in refluxing toluene during 15 h. These results above suggest the presence of thermodynamic control in the reversible reaction of **6** with **7** to give the more stable cyclic products **9** rather than the acyclic **8**. The structures of **8** and **9** were elucidated by the ^1H NMR spectra showing the differences in *gem*-methyl signals between **8** (two singlets) and **9** (one singlet).

Table I

entry	R^1	R^2	method[a]	product[b] (% yield)[c]
1	Me	Me	A	**8a** (84) + **9a** (trace)
2	Me	Me	B	**8a** (22) + **9a** (63)
3	Me	*i*-Pr	A	**8b** (79) + **9b** (7)
4	Me	*i*-Pr	B	**8b** (trace) + **9b** (88)
5	Me	*t*-Bu	A	**8c** (trace) + **9c** (87)
6	Me	Ph	A	**8d** (trace) + **9d** (76)
7	Ph	Me	A	**8e** (trace) + **9e** (71)
8	Ph	Ph	A	**8f** (trace) + **9f** (87)

[a] Method A is at room temperature overnight, and method B is at 140 °C for 5 h in a sealed tube. [b] All the products **8a,b** and **9a-f** gave satisfactory elemental analyses (±0.3% for C, H, and N). [c] Preparative yield. The trace of product **8c-f** observed by the ^1H NMR measurement was not isolated.

Scheme II



a, R^1 = Me

b, R^1 = Ph

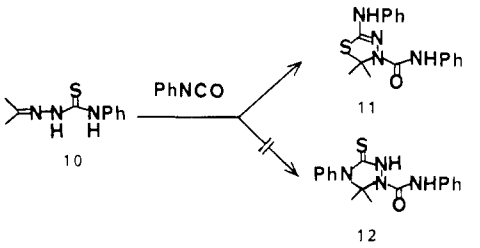
a, R^2 = Me

b, R^2 = i-Pr

c, R^2 = t-Bu

d, R^2 = Ph

Scheme III



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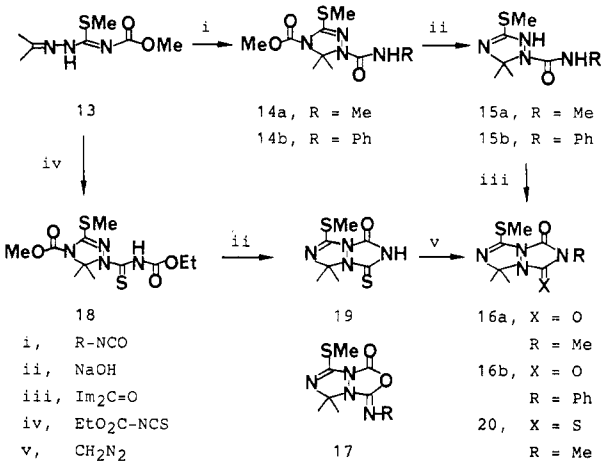
Scheme IV



C. Reaction of 2-Isopropylidene-*N*-phenylhydrazinecarbothioamide (10) with Phenyl Isocyanate. The cyclization of hydrazinecarbothioamide **10** with phenyl isocyanate was investigated in order to determine the reaction selectivity between C–S and C–N bond formations (Scheme III). Treatment of **10** with phenyl isocyanate in chloroform at room temperature for 48 h afforded cyclic product **11** in 54% yield, and 37% of **10** was recovered. The structure of **11** was suggested by the following ^1H and ^{13}C NMR spectroscopic studies. The ^1H NMR spectrum of **11** displayed a singlet peak (δ 2.07) for *gem*-methyl protons closer to that (δ 2.01) of 5,5-dimethyl-Δ^2-1,3,4-thiadiazoline (**3d**) than to that (δ 1.72) of 5,5-dimethyl-Δ^2-1,2,4-triazoline (**9f**). The ^{13}C NMR spectrum of **11** showed a signal for *gem*-methyl carbon atoms at 28.9 ppm corresponding to that (29.2 ppm) of **3a**. Accordingly, alternative structure **12** was ruled out. The selective formation of **11** can be explained by the higher nucleophilicity of a sulfur atom than that of a nitrogen atom in **10**. The reaction of **10** with alkyl isocyanates was found unsuccessful and *N*-alkyl derivatives of **10** showed no reactivity to phenyl isocyanate under the same reaction conditions.

D. Syntheses of 1*H*,5*H*-[1,2,4]triazolo[1,2-*a*][1,2,4]triazole-1,3(2*H*)-diones 16 and 2,3-Dihydro-3-thioxo-1*H*,5*H*-[1,2,4]triazolo[1,2-*a*][1,2,4]triazol-1-ones 19 and 20. The cyclization reaction descrived above was next applied to the synthesis of a novel heterocyclic system, 1*H*,5*H*-[1,2,4]triazolo[1,2-*a*][1,2,4]triazole-1,3(2*H*)-dione. 1-Isopropylidene-3-methyl-4-(methoxycarbonyl)thioisosemicarbazide (**13**) was used as a suitable synthon (Scheme IV). Compound **13** was easily prepared by the reaction of 1-isopropylidene-3-methylthioisosemicarbazide[11] with methyl chloroformate in the presence of triethylamine in refluxing chloroform. Treatment of **13** with isocyanates in tetrahydrofuran at room temperature afforded the cyclized products **14a,b** in high yields (>85%). The structures of **14a,b** were in accord with the IR and ^1H NMR spectral data summarized in the Experimental Section. The reaction of **14a,b** with 10% aqueous methanol solution of sodium hydroxide gave Δ^3-1,2,4-triazolines **15a,b** in quantitative yields. Demethoxycarbonylation of **14a,b** was verified by the disappearence of an ester group in the IR and ^1H NMR spectra. Transformation of **15a,b** into fused heterocycles **16a,b** was achieved through the cyclization reaction with 1,1′-carbonyldiimidazole at 120 °C for 1 h. Distinction between structure **16** for the product and the alternative **17** by ^1H and ^{13}C NMR spectroscopic analyses was unsuccessful. Therefore single-crystal X-ray determination was undertaken in order to solve this problem.

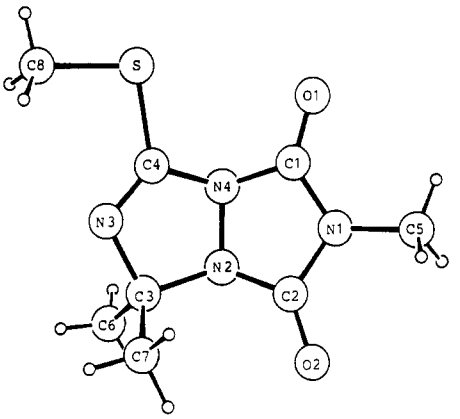


Figure 1. Stereoscopic view of 7-(methylthio)-2,5,5-trimethyl-1*H*,5*H*-[1,2,4]triazolo[1,2-*a*][1,2,4]triazole-1,3-dione (**16a**).

Figure 1 shows the final X-ray model confirming the absolute structure to be 7-(methylthio)-2,5,5-trimethyl-1*H*,5*H*-[1,2,4]triazolo[1,2-*a*][1,2,4]triazole-1,3(2*H*)-dione (**16a**). A bent structure of **16a** was manifested by the C(2)–N(2)–N(4)–C(4) torsional angle (−135.7°).

Attempts to extend this procedure for the preparation of 2,3-dihydro-3-thioxo-1*H*,5*H*-[1,2,4]triazolo[1,2-*a*]-[1,2,4]triazol-1-ones **19** and **20** from **13** were successful. The treatment of **13** with ethoxycarbonyl isothiocyanate in chloroform for 24 h afforded 4-(methoxycarbonyl)-Δ^2-1,2,4-triazoline **18** in 81% yield. The reaction of **18** with a 10% aqueous methanol solution of sodium hydroxide effected the removal of a methoxycarbonyl group and simultaneous intramolecular cyclization to give a fused heterocycle **19** in 93% yield. N2-methylation of **19** was regioselectively attained on the treatment with diazomethane in chloroform, affording **20** in 84% yield. Structures of **19** and **20** were assigned on the basis of the spectroscopic data and elemental analyses shown in Experimental Section.

In conclusion, our studies indicate that the novel cyclization reactions of hydrazones **1**, **6**, **10**, and **13** with isocyanates provide an efficient route to 1,3,4-thiadiazolines **3** and **11** and 1,2,4-triazolines **9**, **14**, and **18** (Schemes I–IV). Extension of the present reaction led to a new synthesis of fused heterocycles, 1*H*,5*H*-[1,2,4]triazolo[1,2-*a*][1,2,4]-triazole-1,3(2*H*)-diones **16**, **19**, and **20**.

Experimental Section

The melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were determined on a Hitachi 260-10 spectrophotometer in Nujol. Electron-impact (EI) mass spectra were obtained on a Hitachi M-80 spectrometer equipped with a Hitachi M-003 data system and using an ionizing energy of 70 eV. ^1H NMR spectra were recorded on a Hitachi 24-B (60 MHz) or Hitachi R-900 (90 MHz) spectrometer, and ^{13}C NMR spectra were recorded on a Hitachi R-900 (90 MHz) spectrometer with teramethylsilane as the internal standard in deuteriochloroform unless otherwise noted. The ^{13}C NMR spectral data for compounds **1**, **3a–d**, **6a**, **8a**, **9a**, **10**, **11**, **13**, **14a**, **15a**, **16a**, **19**, and **20** are presented in the supplementary material section. All the new products gave correct elemetal analyses (±0.3% for C, H, and N).

(A) Reaction of Methyl 2-Isopropylidenehydrazinecarbodithioate (1) with Isocyanates. A solution containing **1** (810 mg, 5 mmol) and isocyanate (5 mmol) in 30 mL of chloroform was stirred at room temperature overnight. The solution was concentrated under reduced pressure, and the residure was recrystallized from 2-propanol–hexane to give 4-(aminocarbonyl)-5,5-dimethyl-2-(methylthio)-Δ^2-1,3,4-thiadiazoline **3**. The oily product **3b** was purified by column chromatography on silica gel using a 20% acetone–hexane mixture as the eluent. The yields, physical properties, and spectral data of **3a–d** are as follows.

3a: 91% yield; mp 106 °C; IR 3330 (NH), 1640 cm^{-1} (C=O); ^1H NMR δ 1.94 (s, 6 H), 2.46 (s, 3 H), 2.78 (d, J = 4.8, 3 H), 5.60–6.00 (br, 1 H); MS, m/e 219 (M^+, 24), 152 (59), 147 (100), 115 (66).

3b: 94% yield; oil; IR 3420 (NH), 1680 cm^{-1} (C=O); ^1H NMR δ 1.34 (s, 9 H), 1.95 (s, 6 H), 2.45 (s, 3 H), 5.86 (br s, 1 H); MS, m/e 261 (M^+, 16), 152 (74), 147 (79), 115 (100).

3c: 96% yield; mp 63 °C; IR 3310 (NH), 1640 cm^{-1} (C=O); ^1H NMR δ 0.80–2.05 (m, 10 H), 1.95 (s, 6 H), 2.45 (s, 3 H), 3.30–3.75 (br, 1 H), 5.76 (br d, J = 7.0, 1 H); MS, m/e 287 (M^+, 7), 152 (67), 147 (100), 115 (74).

3d: 97% yield; mp 78–79 °C; IR 3350 (NH), 1660 cm^{-1} (C=O); ^1H NMR δ 2.01 (s, 6 H), 2.48 (s, 3 H), 6.80–7.50 (m, 5 H), 7.86 (br s, 1 H); MS, m/e 281 (M^+, 18), 152 (58), 147 (100), 115 (66).

(B) Reaction of 1-Isopropylidene-3-methylthioisosemicarbazides 6a,b with Isocyanates 7a–d. (Method A) A solution containing **6** (5 mmol) and isocyanate **7** (5 mmol) in 30 mL of chloroform was stirred at room temperature overnight. After the reaction the solvent was removed and the residure was chromatographed on a silica gel column by using a 20% acetone–hexane mixture as the eluent. Recrystallization from 2-propanol–hexane was followed when a solid product was obtained.

(Method B) A solution containing **6** (5 mmol) and isocyanate **7** (5 mmol) in 30 mL of chloroform was heated at 140 °C for 5 h in a sealed tube. After the reaction the solution was worked up in the same way as method A.

The preparative yields of products **8a,b** and **9a–f** by methods A and B are listed in Table I. The physical properties and spectral data of **8a,b** and **9a–f** are as follows.

8a: mp 117 °C; IR 3370 (NH), 1660 cm^{-1} (C=O); ^1H NMR δ 1.92 (s, 3 H), 2.08 (s, 3 H), 2.26 (s, 3 H), 2.77 (d, J = 4.8, 3 H), 3.19 (s, 3 H), 5.48–6.00 (br, 1 H); MS, m/e 216 (M^+, 18), 144 (89), 112 (31), 88 (42), 56 (100).

8b; oil; IR 3320 (NH), 1650 cm^{-1} (C=O); ^1H NMR δ 1.14 (d, J = 7.2, 6 H), 1.93 (s, 3 H), 2.08 (s, 3 H), 2.26 (s, 3 H), 3.19 (s, 3 H), 3.64–4.35 (m, 1 H), 5.56 (br d, J = 7.2, 1 H); MS, m/e 244 (M^+, 10), 144 (100), 112 (45), 88 (25), 56 (63).

9a: mp 64–66 °C; IR 3420 (NH), 1640 cm^{-1} (C=O); ^1H NMR δ 1.63 (s, 6 H), 2.45 (s, 3 H), 2.69 (s, 3 H), 2.80 (d, J = 5.4, 3 H), 5.45–5.98 (br, 1 H); MS, m/e 216 (M^+, 11), 144 (100).

9b: oil; IR 3400 (NH), 1630 cm^{-1} (C=O); ^1H NMR δ 1.15 (d, J = 6.0, 6 H), 1.61 (s, 6 H), 2.42 (s, 3 H), 2.65 (s, 3 H), 3.55–4.20 (m, 1 H), 5.50 (br d, J = 7.2, 1 H); MS, m/e 244 (M^+, 7), 144 (100).

9c: mp 84–86 °C; IR 3400 (NH), 1640 cm^{-1} (C=O); ^1H NMR δ 1.37 (s, 9 H), 1.62 (s, 6 H), 2.46 (s, 3 H), 2.68 (s, 3 H), 5.77 (br s, 1 H); MS, m/e 258 (M^+, 6), 144 (100).

9d: mp 91–93 °C; IR 3380 (NH), 1670 cm^{-1} (C=O); ^1H NMR δ 1.72 (s, 6 H), 2.53 (s, 3 H), 2.76 (s, 3 H), 6.55–7.60 (m, 5 H), 7.82 (br s, 1 H); MS, m/e 278 (M^+, 3), 144 (100).

9e: mp 113–114 °C; IR 3330 (NH), 1640 cm^{-1} (C=O); ^1H NMR δ 1.64 (s, 6 H), 2.36 (s, 3 H), 2.82 (d, J = 4.8, 3 H), 5.50–6.60 (br, 1 H), 6.98–7.50 (m, 5 H); MS, m/e 278 (M^+, 9), 206 (100).

9f: mp 132 °C; IR 3360 (NH), 1670 cm^{-1} (C=O); ^1H NMR δ 1.72 (s, 6 H), 2.44 (s, 3 H), 6.75–7.52 (m, 10 H), 7.83 (br s, 1 H); MS, m/e 340 (M^+,9), 206 (100).

Thermal Isomerization of 8a,b. A solution of **8** (5 mmol) in 30 mL of chloroform was heated at 140 °C for 5 h in a sealed tube. After the reaction the solution was worked up in the same way as method A above. The main product was identified to be **9** on the basis of an identical ^1H NMR spectrum and R_f value on silica gel TLC as the authentic sample obtained by method B. The yields of **9a** and **9b** were 61% and 83%, respectively.

Retroreaction of 8a,b. A solution of **8** (2 mmol) in 10 mL of toluene was refluxed for 3 h. The solution was worked up in the same way as method A above. The main product was idetified to be **6** on the basis of an identical ^1H NMR spectrum and R_f value on silica gel TLC as the authentic sample. The yields of **6a** and **6b** were 78% and 90%, respectively.

Retroreaction of 9a,b. A solution of **9** (2 mmol) in 10 mL of toluene was refluxed for 15 h. The solution was woked up in the same way as method A above. The main product was identified to be **6** on the basis of an identical ^1H NMR spectrum and R_f value on silica gel TLC as the authentic sample. The yields of **6a** and **6b** were 58 and 67%, respectively.

(C) Reaction of 2-Isopropylidene-*N*-phenylhydrazinecarbothioamide (10) with Phenyl Isocyanate. A solution containing **10**[10] (830 mg, 4 mmol) and phenyl isocyanate (480 mg, 4 mmol) in 30 mL of chloroform was stirred at room temperature for 48 h. The solvent was removed under reduced pressure and the residue was chromatographed on a silica gel column by using a 33% acetone–hexane mixture as the eluent. The major fraction was recrystallized from 2-propanol to give 710 mg (54%) of yellow crystals, mp 155–156 °C, whose structure was determined to be 2-anilino-5,5-dimethyl-Δ^2-1,3,4-thiadiazoline **11** on the basis of following spectral data:

IR 3380, 3250 (NH), 1625, 1600 cm^{-1} (C=O); ^1H NMR δ 2.07 (s, 6 H), 6.37 (br s, 1 H), 6.85–7.50 (m, 10 H), 7.88 (br s, 1 H); MS, m/e 326 (M^+, 18), 207 (47), 192 (100), 119 (56), 77 (55).

(D) 1-Isopropylidene-3-methyl-4-(methoxycarbonyl)thioisosemicarbazide (13). To a solution containing 1.45 g (10 mmol) of 1-isopropylidene-3-methylthioisosemicarbazide[11] and 1.21 g (12 mmol) of triethylamine in 50 mL of chloroform was added dropwise over 10 min a solution containing 0.95 g (10 mmol) of methyl chloroformate in 5 mL of chloroform. The mixture was refluxed for 10 min and cooled to room temperature. The crude reaction mixture was poured into 50 mL of ice-water and extracted with an additional 30 mL of chloroform. The chloroform extract was dried over $MgSO_4$ and concentrated. The residual oil was chromatographed on a silica gel column using a 10% acetone–hexane mixture as the eluent. The major fraction was recrystallized from hexane to give 1.2 g (59%) of **13** as white crystals (mp 54–55 °C). The spectral and analytical data are as follows: IR 3310 (NH), 1750 (C=O); ^1H NMR δ 2.01 (s, 3 H), 2.06 (s, 3 H), 2.35 (s, 3 H), 3.74 (s, 3 H). Anal. Calcd for $C_7H_{13}N_3O_2S$: C, 41.37; H, 6.45; N, 20.68. Found: C, 41.11; H, 6.56; N, 20.65.

Reaction of 13 with Isocyanates. A solution containing 1.22 g (6 mmol) of **13** and isocyanate (6 mmol) in 30 mL of anhydrous tetrahydrofuran was stirred at room temperature overnight. The solution was concentrated under reduced pressure and the residue was recrystallized from 2-propanol–hexane to give 4-(methoxycarbonyl)-Δ^2-1,2,4-triazoline **14** as white crystals. The yields, physical properties, and spectral data of 14a,b are as follows.

14a: 88% yield; mp 133 °C; IR 3340 (NH), 1720, 1650 cm^{-1} (C=O); ^1H NMR δ 1.94 (s, 6 H), 2.40 (s, 3 H), 2.84 (d, J = 5.4, 3 H), 3.82 (s, 3 H), 5.50–5.90 (br, 1 H); MS, m/e 260 (M^+, 14), 203 (9), 188 (100), 144 (29).

14b: 94% yield; mp 101 °C; IR 3380 (NH), 1720, 1650 cm^{-1} (C=O); ^1H NMR δ 1.96 (s, 6 H), 2.42 (s, 3 H), 3.82 (s, 3 H), 6.90–7.50 (m, 5 H), 7.68 (br s, 1 H); MS, m/e 322 (M^+, 16), 203 (14), 188 (100), 144 (14).

Demethoxycarbonylation of 4-(Methoxycarbonyl)-Δ^2-1,2,4-triazolines 14a,b. A solution containing **14** (5 mmol) and sodium hydroxide (0.40 g, 10 mmol) in 50 mL of 10% aqueous methanol was stirred at room temperature for 4 h. After the reaction the solution was neutralized with acetic acid and concentrated under reduced pressure. The residue was extracted with ethyl acetate (50 mL × 2), and the combined extracts were washed with water (30 mL), dried over $MgSO_4$, and evapolated. The crude product was recrystallized from 2-propanol to give Δ^3-1,2,4-triazoline **15** as white crystals. The yields, physical properties, and spectral data of **15a,b** are as follows.

15a: 91% yield; mp 146 °C; IR 3430, 3260 (NH), 1630 cm^{-1} (C=O); ^1H NMR δ 1.68 (s, 6 H), 2.42 (s, 3 H), 2.77 (d, J = 4.8, 3 H), 4.68 (br s, 1 H), 5.37–5.85 (br, 1 H); MS, m/e 202 (M^+, 9), 130 (100).

15b: 96% yield; mp 253 °C; IR 3380, 3240 (NH), 1640 cm^{-1} (C=O); ^1H NMR δ 1.72 (s, 6 H), 2.46 (s, 3 H), 4.60 (br s, 1 H), 6.84–7.48 (m, 5 H), 7.67 (br s, 1 H).

5,5-Dimethyl-7-(methylthio)-1*H*,5*H*-[1,2,4]triazolo[1,2-*a*][1,2,4]triazole-1,3(2*H*)-diones 16a,b. A mixture of Δ^3-1,2,4-triazoline **15** (2 mmol) and 1,1′-carbonyldiimidazole (0.65 g, 4 mmol) was stirred at 120 °C for 1 h. The crude reaction mixture was chromatographed on a short silica gel column by using a 25% acetone–hexane mixture as the eluent to give white crystals of **16**. The yields, physical properties, and spectral data of **16a,b** are as follows.

16a: 86% yield; mp 104 °C; IR 1770, 1720 cm^{-1} (C=O); ^1H NMR δ 1.68 (s, 6 H), 2.51 (s, 3 H), 3.05 (s, 3 H); MS, m/e 228 (M^+, 6), 155 (40), 100 (100).

16b: 90% yield; mp 140–141 °C; IR 1780, 1720 cm^{-1} (C=O); ^1H NMR δ 1.75 (s, 6 H), 2.52 (s, 3 H), 7.36 (s, 5 H); MS, m/e 290 (M^+, 9), 217 (49), 119 (100), 100 (68).

X-ray Structural Determination of 16a. A single crystal of **16a**, obtained by slow crystallization from acetone–2-propanol, was monoclinic, space group $C2/C$, with a = 22.106 (1) Å, b = 7.207 (1) Å, c = 15.821 (1) Å, β = 117.95 (1)°, V = 2226.6 Å^3, and d_{calcd} = 1.362 g cm^{-3} for Z = 8 ($C_8H_{12}N_4O_2S$, M_n = 228.27). The intensity data were measured on an Enraf-Nonius CAD 4 diffractometer (Cu Kα radiation, λ = 1.5418 Å; graphite monochromator; ω–2θ scan mode, $1 < \theta < 70°$, $\omega = (0.8 + 0.15 \tan \theta)°$; number of reflections measured, 2101). The determination and refinement of the crystal structure is based on 1785 reflectios with $I > 3(I)$. The structure was solved by direct methods with MULTAN78[12] and was refined by full-matrix least-squares methods. In the final refinement, anisotropic thermal parameters were used for the non-hydrogen 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 = 0.060. All calculations were performed on a PDP 11-34 computer with an Enraf-Nonius SDP software. Bond distances, bond angles, torsional angles, final positional parameters, and anisotropic thermal parameters are presented in the supplementary material section for compound **16a**.

Reaction of 13 with Ethoxycarbonyl Isothiocyanate. A solution containing **13** (2.03 g, 10 mmol) and ethoxycarbonyl isothiocyanate (1.44 g, 11 mmol) in 50 mL of chloroform was stirred at room temperature for 24 h. The solvent was removed under reduced pressure and the residue was chromatographed on a silica gel column by using 20% acetone–hexane mixture as the eluent. The major fraction gave 2.7 g (81%) of 4-(methoxycarbonyl)-Δ^2-1,2,4-triazoline **18** as yellow crystals (mp 126–127 °C). The spectral and analytical data are as follows: IR 3350 (NH), 1755, 1720 cm^{-1} (C=O); ^{1}H NMR δ 1.26 (t, J = 7.2, 3 H), 2.26 (s, 6 H), 2.40 (s, 3 H), 3.80 (s, 3 H), 4.16 (q, J = 7.2, 2 H); MS, m/e 334 (M$^+$, 27), 298 (25), 273 (19), 188 (100). Anal. Calcd for $C_{11}H_{18}N_4O_4S_2$: C, 39.51; H, 5.42; N, 16.75. Found: C, 39.51; H, 5.42; N, 16.55.

2,3-Dihydro-5,5-dimethyl-7-(methylthio)-3-thioxo-1*H*,5*H*-[1,2,4]triazolo[1,2-*a*][1,2,4]triazol-1-one (19). A solution containing 4-(methoxycarbonyl)-Δ^2-1,2,4-triazoline **18** (1.0 g, 3 mmol) and sodium hydroxide (0.24 g, 6 mmol) in 30 mL of 10% aqueous methanol was stirred at room temperature for 6 h. After the reaction the solution was worked up as described above for the preparation of **15**. This method gave 0.63 g (93%) of **19** as yellow crystals (mp 200–201 °C). The spectral and analytical data are as follows: IR 3590 (NH), 1770, 1730 cm^{-1} (C=O); ^{1}H NMR δ (Me_2SO-d_6) 1.84 (s, 6 H), 2.50 (s, 3 H), 7.20–7.80 (br, 1 H); MS, m/e 230 (M$^+$, 100), 157 (33), 114 (36). Anal. Calcd for $C_7H_{10}N_4OS_2$: C, 36.52; H, 4.38; N, 24.34. Found: C, 36.38; H, 4.38; N, 24.11.

N^2-Methylation of 19. To a suspension containing 0.46 g (2 mmol) of **19** in 30 mL of chloroform was slowly added diazomethane (10 mmol) in 20 mL of ethyl ether below 10 °C. The mixture was stirred at room temperature for 2 h and concentrated under reduced pressure. The residue was chromatographed on a silica gel column by using 25% acetone–hexane as the eluent. The major fraction gave 0.41 g (84%) of **20** as white crystals (mp 110–112 °C). The structure of **20** was determined to be 2,3-dihydro-7-(methylthio)-3-thioxo-2,5,5-trimethyl-1*H*,5*H*-[1,2,4]triazolo[1,2-*a*][1,2,4]triazol-1-one on the basis of the following spectral and analytical data: IR 1730 cm^{-1} (C=O); ^{1}H NMR δ 1.90 (s, 6 H), 2.59 (s, 3 H), 3.26 (s, 3 H); MS, m/e 244 (M$^+$, 100), 171 (58), 114 (60), 98 (60). Anal. Calcd for $C_8H_{12}N_4O_2S$: C, 42.09; H, 5.30; N, 24.54. Found: C, 42.06; H, 5.38; N, 24.48.

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Registry No. 1, 27268-57-1; **3a**, 89578-89-2; **3b**, 89578-90-5; **3c**, 89578-91-6; **3d**, 89578-92-7; **6** (R^1 = H), 41208-11-1; **6a**, 89578-93-8; **6b**, 89578-94-9; **7a**, 624-83-9; **7b**, 1795-48-8; **7c**, 1609-86-5; **7d**, 103-71-9; **8a**, 89578-95-0; **8b**, 89578-96-1; **9a**, 89578-97-2; **9b**, 89578-98-3; **9c**, 89578-99-4; **9d**, 89579-00-0; **9e**, 89579-01-1; **9f**, 89579-02-2; **10**, 14673-56-4; **11**, 89579-03-3; **13**, 89579-04-4; **14a**, 89579-05-5; **14b**, 89579-06-6; **15a**, 89579-07-7; **15b**, 89579-08-8; **16a**, 89579-09-9; **16b**, 89579-10-2; **18**, 89579-11-3; **19**, 89579-12-4; **20**, 89579-13-5; ClC(O)OMe, 79-22-1; HNCO, 75-13-8; 1,1′-carbonyldiimidazole, 530-62-1; ethoxycarbonyl isothiocyanate, 16182-04-0; cyclohexyl isocyanate, 3173-53-3.

Supplementary Material Available: ^{13}C NMR values (Table II) and X-ray analytical data (Tables III–VII) (7 pages). Ordering information is given on any current masthead page.

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Chirality Transfer in the [2,3] Wittig Rearrangement

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The [2,3] Wittig rearrangement of (*S*)-1-methyl-2-methylenecyclododecyl allyl ether (**9**) was carried out and the stereochemistry of the alcohol product **10** was determined. The (*S*)-ether **9** afforded principally the (*R*)-alcohol **10**. The optically active ether **9** was prepared from 2-carbethoxycyclododecanone via the enol phosphate **3** which was coupled with lithium dimethylcuprate to give the *cis*-ester **4**. Reduction with Dibah and Sharpless epoxidation of alcohol **5** using (+)-diisopropyl tartrate as the coordinating ligand afforded the (1*S*, 2*S*)-epoxy alcohol **6**. Reduction of the mesylate derivative **7** afforded the allylic alcohol **8**, the precursor of ether **9**. The configuration of the allylic alcohol product (*R*)-**10** was determined from the CD spectrum of the *p*-bromobenzoate. The chirality transfer observed in the conversion of ether **9** to alcohol **10** is in accord with a chairlike envelope transition state for the rearrangement.

The [2,3] Wittig rearrangement of diallylic ethers has received close scrutiny recently as a carbon–carbon bond forming reaction of potential application to the stereodirected synthesis of acyclic alcohols.[1,2] The observed regioselectivity of allyl anion formation, the preference for *E* orientation in the newly formed double bond, and the *E* → threo, *Z* → erythro diastereoselectivity of the reaction suggest a highly ordered transition state (Figure 1).[1]

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