−35.0° (c 0.466, EtOH). The main part of the mixture of lactones (1.67 g, 0.0121 mol) was mixed with 12 mL of 2 N NaOH solution, and the mixture was stirred for 1 h at room temperature. The same procedure described above gave 0.80 g of *endo*-lactone **15**, $[\alpha]^{25}_D$ −2.1° (c 1.09, EtOH), and hydroxy acid **20** (0.70 g), $[\alpha]^{25}_D$ +8.5° (c 0.550, EtOH). When this hydroxy acid **20** (300 mg, 1.92 mmol) was heated at 145–150 °C (5 mm) for 30 min, a white solid was observed to condense on the cold finger. This was collected and sublimed at 70–80 °C (5 mm) to yield 125 mg of *exo*-lactone **8** (48% yield), $[\alpha]^{15}_D$ −88.6° (c 0.397, EtOH).

(−)-7-*syn*-(Methoxycarbonyl)bicyclo[2.2.1]heptan-2-one (10). To a solution of (+)-**20**, $[\alpha]^{15}_D$ +13.9° (720 mg, 4.61 mmol), in 9 mL of aqueous KOH (0.46 g) solution was added a solution of potassium permanganate (1.11 g) in 15 mL of water at room temperature, and the mixture was warmed to 35 °C. This mixture was stirred for 30 min at this temperature and then for an additional 3 h at room temperature. After addition of a small amount of ethanol to decompose the excess oxidizing agent, an inorganic solid was filtered off. The filtrate was made acidic with sulfuric acid and extracted continuously for 2 days with ether. The extract was dried over $MgSO_4$, and the solvent was evaporated to give 575 mg of the keto carboxylic acid, which was esterified with diazomethane. The crude ester was distilled to yield 367 mg of **10** (47% yield): bp 120–122 °C (10 mm); $[\alpha]^{25}_D$ −4.1° (c 1.00, EtOH).

Anal. Calcd for $C_9H_{12}O_3$: C, 64.37; H, 7.19. Found: C, 64.03; H, 7.30.

Registry No.—(−)-**4**, 20507-53-3; (+)-**4**, 58001-99-3; (±)-**4**, 67999-50-2; **5** (isomer 1), 67999-51-3; **5** (isomer 2), 67999-52-4; **8**, 68035-50-7; **10**, 60133-56-4; **11**, 60133-48-4; **12**, 68035-51-8; **13**, 68035-52-9; **14**, 67999-53-5; **15**, 68035-53-0; **20**, 68035-54-1.

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4-Alkyl-5-(arylimino)-1,2,3,4-thiatriazolines as Masked 1,3-Dipoles

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The title compounds can undergo bimolecular cycloaddition–elimination reactions by two pathways (1 → **2** and 1 → **4**). The first pathway has been demonstrated in previous publications, while the second pathway is now observed with the electrophilic acyl isothiocyanates and also with sulfenes. The corresponding products of types **5** and **8** can undergo a Dimroth rearrangement under the influence of Lewis acids to give **7** and **9**, respectively. The sulfene adducts **8** react with heterocumulenes in a similar manner to give products (**11–13**) which are identical with those obtained from **1** and the same heterocumulenes. The NMR criteria used to distinguish between the isomeric reaction products are discussed.

Recent interest in the chemistry of masked 1,3-dipoles[1] has led us to investigate the behavior of 4-methyl-5-(phenylimino)-1,2,3,4-thiatriazoline (**1**) in this respect. In principle, two pathways can be considered for the reactions of **1** with unsaturated compounds, i.e., reactions involving participation of the endocyclic or exocyclic nitrogen atom of the amidine residue. We have previously reported that **1** reacts across the C=N bond of isocyanates[2] and alkyl and aryl isothiocyanates[3] to yield heterocycles of type **2** (path a). We now describe examples which can be interpreted in terms of the masked 1,3-dipole **1***, and possibly also a thiapentalene **3**, as an intermediate or transition state (path b).[4]

Reactions with Acyl Isothiocyanates. The reaction of **1** with 1 equiv of aroyl isothiocyanate or ethoxycarbonyl isothiocyanate in benzene at room temperature gave single products by NMR of structure **5**. A kinetic study of the reaction with benzoyl isothiocyanate was undertaken in two solvents of different polarity, benzene and acetonitrile.[5] The second-order rate constants and activation parameters are summarized in Table I. The small solvent effect and the moderately negative entropies of activation may indicate a concerted cycloaddition–elimination mechanism proceeding through a thiapentalene-like transition state (see structure **3** with partial bond formation of a=b and partial loss of N_2). However, these data do not rigorously exclude the alternative stepwise mechanism.[13]

When the reaction of **1** was carried out with a threefold excess of benzoyl isothiocyanate in the absence of solvent, **7a** was isolated instead of **5a**. Also, the reaction of **5a** with benzoyl isothiocyanate at room temperature produced **7a** in quantitative yield. Similarly, **5c** could be isomerized into **7c** under the influence of phenyl isothiocyanate or benzoyl isothiocyanate, but no isomerization was observed by ^1H NMR when aluminum chloride or benzoyl chloride was used as a Lewis acid. The rearrangement **5** → **7** is a typical Dimroth rearrangement[6] which probably occurs via a betaine of type **6**.

Although these results would suggest that **4** is a precursor of **2** (a = CS, b = NR) in our previously reported reactions of **1** with alkyl and aryl isothiocyanates,[3] all attempts to isolate a precursor by varying the reaction conditions were unsuccessful. In the absence of direct evidence to the contrary, we consider **2** (a = CS, b = NR) as primary cycloadducts and not as products of a Dimroth rearrangement.

Reactions with Sulfenes. Sulfenes, generated in situ from

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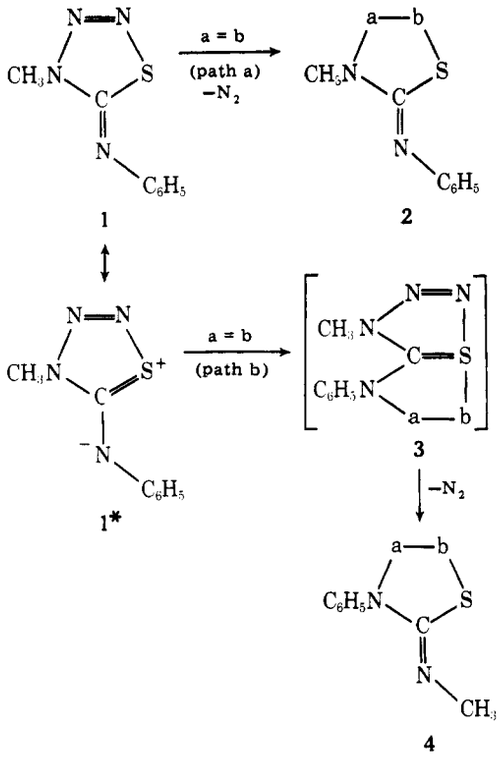
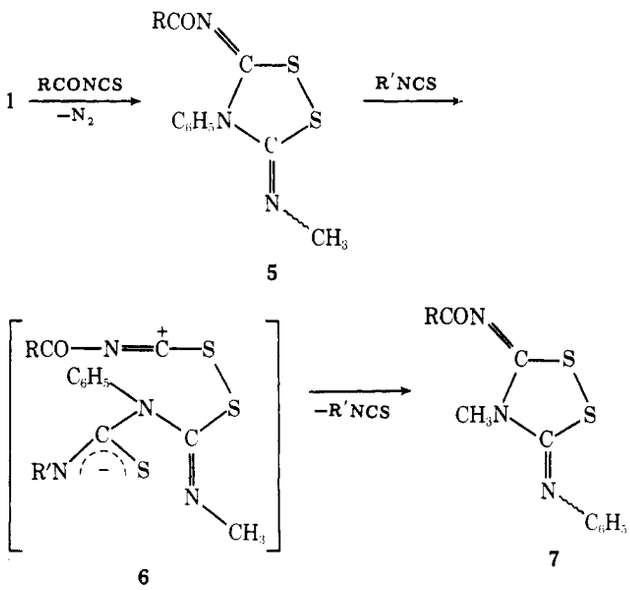




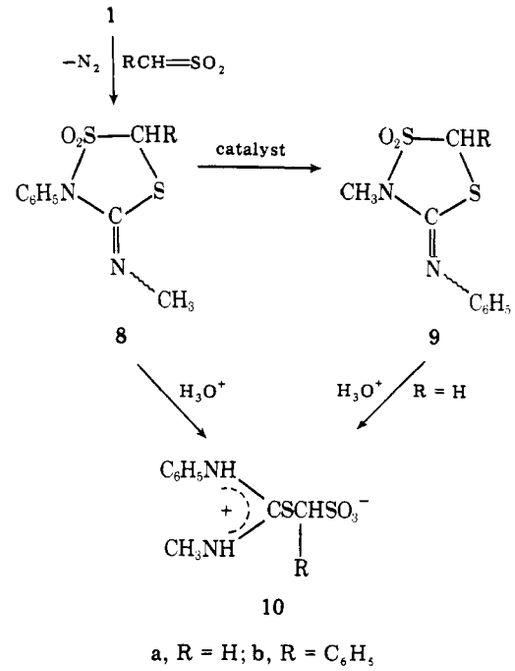
a, R = C_6H_5; b, R = *p*-ClC_6H_4; c, R = OC_2H_5

Table I. Kinetics of the Reaction 1 → 5a [a]

solvent (dielectric constant)	T, °C	$10^4 k_2$, s^{-1} L mol^{-1}	E_a, kcal mol^{-1}	$\Delta S^{\ddagger}$, eu
benzene (2.3)	31.2	1.2	19 ± 1	−12 ± 3
	37.6	2.3		
	47.0	6.6		
acetonitrile (37.5)	20.2	1.6	21 ± 2	−7 ± 7
	27.4	4.3		
	35.2	9.5		
	42.2	24.3		

[a] The reaction was followed volumetrically by measuring the amount of nitrogen gas evolved as a function of time.

alkylsulfonyl chlorides and triethylamine,[7] reacted with 1 to give sultams of structure 8. In the absence of triethylamine, 1 serves as base to generate the sulfene, but yields are low. Compound **8a** was shown to isomerize into **9a** upon heating at 60 °C in the presence of benzoyl chloride. Further, NMR-controlled test-tube reactions revealed that this isomerization also occurred under the influence of aluminum chloride and methanesulfonyl chloride. Similarly, **8b** could be isomerized into **9b** upon warming in acetone with *m*-dichlorobenzoic acid as catalyst.



a, R = H; b, R = C_6H_5

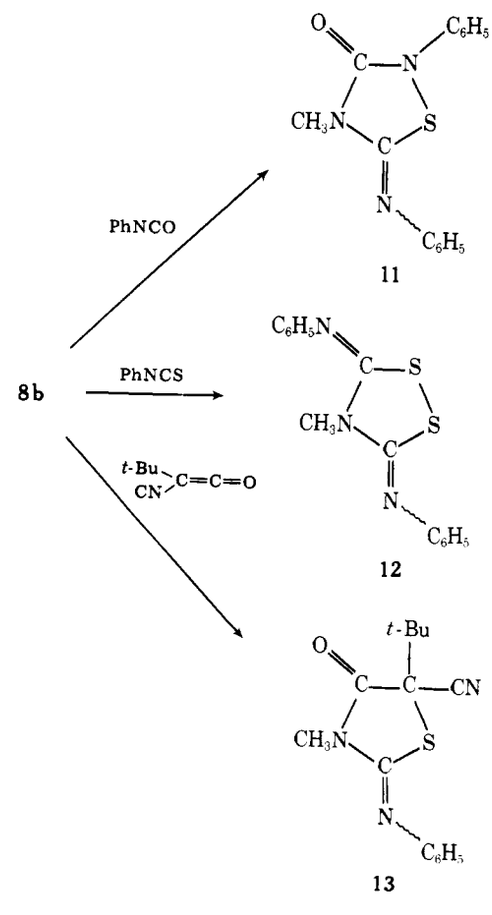


Table II. NMR Characterization of the New Heterocycles [a]

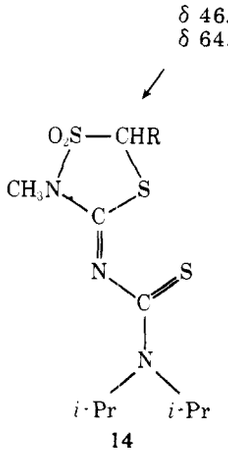
compd	^{1}H NMR		^{13}C NMR				
			N-phenyl substituent				
	CH_3	$^1J_{C-H}$, Hz	CH_3	C_1	C_o	C_p	other shift values
5a	3.1	136	40.9	139.6		129.4	C=N at 154.1 and 173.7, C=O at 177.9
5b[b]	3.13	136					
5c	3.1	136	40.5	139.1	128.4	129.6	CH_3CH_2 at 14.3 and 63.1, C=N at 153.8 and 173.9, C=O at 164.7
7a	3.80	144	36.9	149.6	121	125.3	C=N at 155.3 and 173.4, C=O at 178
7c	3.8	143	36.6	149.1	120.9	125.3	C=N at 154.7 and 173.3, C=O at 164.1
8a	3.1	137	37.5	132.5	~130		CH_2 at 46.7 ($^1J_{C-H}$ = 156.5 Hz), C=N at 145.8
8b	3.17	137	37.5	133	~130		CH at 64.8, C=N at 145.4
9a	3.35	144	28.7	147.1	121.6	125.3	CH_2 at 46.2, C=N at 145.7
9b	3.31	144	29.4	147.3	121.6	125.3	CH at 64.7, C=N at 145.8
11	3.4	142	30.3	148.9	121.2	125.4	C=N at 152.9, C=O at 150.6
12	3.56	141	35.4	149.1	121.6	125.2	C=N at 154.3
13	3.36	142.2	30.6	147.5	121.1	125.6	$(CH_3)_3C$ at 25.5 and 40.6, C≡N at 115.8, C_5 at 60, C=N at 149.9, C=O at 167.3

[a] All of the spectra (δ values in parts per million from Me_4Si) were recorded in $CDCl_3$. [b] This compound was not sufficiently soluble for ^{13}C NMR analysis.

As expected, acid hydrolysis of both **8a** and **9a** yielded the same betaine **10a.** Compound **8b** could also be hydrolyzed into **10b,** but **9b** could not. The sultams 8 can also react as masked 1,3-dipoles, eliminating the sulfene moiety during cycloadditions with heterocumulenes. Thus, reaction of **8b** with phenyl isocyanate, phenyl isothiocyanate, and *tert*-butylcyanoketene yielded **11–13**, respectively. These cycloadducts were also obtained independently by reacting **1** with the corresponding heterocumulene according to path a (see Experimental Section).

Structure Assignment by NMR. The structures of type **2** and **4** are easily distinguished on the basis of the position of the methyl resonance in the ^{1}H and ^{13}C NMR spectra (see Table II). In addition, the coupling constant $^1J_{C-H}$ for the methyl group, whose value is known to be related to the degree of charge localization on the nitrogen atom,[8] further allows structure assignment. The values found for **5** and **8** ($^1J_{C-H}$ = 136–137 Hz) and for **7** and **9** ($^1J_{C-H}$ = 143–144 Hz) are in agreement with those of analogous systems.[3] Finally, an inspection of the chemical shifts of the *N*-phenyl carbon peaks in the ^{13}C NMR spectra also contributes to structure elucidation (see Table II). Indeed, as expected[9] for structures **7** and **9**, the C_1 atom peak (δ 147–149) is shifted downfield, whereas the C_o (δ 121) and C_p (δ 125) atom peaks are shifted upfield compared with those in **5** and **8** (C_1 at δ 139 and 133; C_o and C_p at δ 128–130). The ^{13}C NMR absorptions of **11–13** are in complete agreement with those of **7** and **9** (see Table II).

The regiochemistry of the isothiocyanate adducts (**5** and **7**) has been discussed in a previous paper,[3] while that of the sulfene adducts (**8** and **9**) is indicated by the chemical shifts



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of the ring sp^3 C atoms in the ^{13}C NMR spectra (see Table II). The shifts are found exactly at the same position as the corresponding C_2 resonance in reference compound **14,** prepared by Linden and Goerdeler.[10]

Conclusions

In this paper we have demonstrated that 4-methyl-5-(phenylimino)-1,2,3,4-thiatriazoline behaves as a masked 1,3-dipole **1*** toward acyl isothiocyanates and sulfenes.[11] The dipole **1*** is isoelectronic with the allyl anion, and hence is allowed to react concertedly with 2π-electronic systems in a suprafacial manner.[12] Although the kinetic results obtained with benzoyl isothiocyanate may point to this conclusion, a stepwise mechanism is not excluded,[13] especially since the cycloaddition–elimination reactions were only found to occur with the highly polar heterocumulenes. No cycloadducts were formed between **1** and dimethyl fumarate, dimethyl acetylenedicarboxylate, and *trans*-dimethylaminostyrene at 70 °C.

Experimental Section

Melting points were determined on a Leitz apparatus and are uncorrected. Infrared spectra were recorded with a Perkin-Elmer 157 G spectrometer, mass spectra with an AEI MS-12 instrument, and ^{1}H NMR spectra with a JEOL MH-100 or Varian XL-100 spectrometer. For ^{13}C NMR spectra, the XL-100 apparatus was equipped with a device for pulsed Fourier transform operation. The chemical shifts given are in δ values in parts per million relative to Me_4Si in $CDCl_3$ solutions unless otherwise stated. Compound **1** was prepared from 5-(phenylamino)-1,2,3,4-thiatriazole and diazomethane as reported.[3]

Reactions of 1 with Acyl Isothiocyanates. Equimolar amounts (0.01 mol) of **1** and acyl isothiocyanate were stirred in dry benzene (15–30 mL) for 1 day (4 days in the case of **5b**) at room temperature. The precipitate was filtered off and crystallized from ethanol–benzene. The filtrate was shown in each case to contain only unreacted reagents.

Compound **5a** was obtained in 58% yield: mp 205 °C; IR (KBr) 1640, 1600 cm^{-1}. Anal. Calcd for $C_{16}H_{13}N_3OS_2$ (327): C, 58.70; H, 4.00. Found: C, 58.56; H, 3.91.

Compound **5b** was obtained in 79% yield: mp 205 °C; IR (KBr) 1630 cm^{-1}. Anal. Calcd for $C_{16}H_{12}ClN_3OS_2$ (362): C, 53.18; H, 3.35. Found: C, 53.15; H, 3.29.

Compound **5c** was obtained in 48% yield: mp 196–198 °C; IR (KBr) 1620–1640 cm^{-1}. Anal. Calcd for $C_{12}H_{13}N_3O_2S_2$ (295): C, 48.81; H, 4.44. Found: C, 48.93; H, 4.37.

In another experiment, **1** (0.96 g) was treated with a threefold excess of benzoyl isothiocyanate at room temperature for 18 h and then heated at 40 °C for another 2 h. Chromatographic separation of the mixture on silica gel with *n*-hexane–ether as the eluent furnished unreacted isothiocyanate, sulfur (40 mg), and **7a** (350 mg, 20%): mp 145 °C; IR (KBr) 1610 cm^{-1}. Anal. Calcd for $C_{16}H_{13}N_3OS_2$ (263): C, 58.71; H, 4.00. Found: C, 58.70; H, 4.37.

Isomerization of 5 into 7. When **5a,c** in deuteriochloroform were treated with a few drops of benzoyl isothiocyanate at room temperature and the test-tube reactions were monitored by ^1H NMR, isomerization into **7a,c** was observed within 5–10 days (90–100% conversion). The reaction with **5c** was repeated on a preparative scale as follows. Compound **5c** (0.5 g) was allowed to react with a threefold excess of phenyl isothiocyanate (1.24 g) at 100 °C for 6 h. The reaction mixture was then chromatographed on silica gel using hexane–ether (70:30) as the eluent to give **7c** in 80% yield: mp 100 °C (ether); IR (KBr) 1620, 1510–1530 cm^{-1}. Anal. Calcd for $C_{12}H_{13}N_3O_2S_2$ (295): C, 48.81; H, 4.44. Found: C, 48.70; H, 4.37.

Kinetic Measurements. Compound **1** (ca. 0.5 g) was allowed to react with 1 or 2 equivalents of benzoyl isothiocyanate in benzene or acetonitrile (5 mL) at constant temperature. The amount of nitrogen evolved was measured, and the results were plotted in the appropriate diagrams for second-order reactions. The measurements were made at several temperatures, and the energies of activation were determined graphically from $\log k_2$ vs. $1/T$. The entropies of activation were calculated from the rate constants using $\Delta S^{\ddagger} = 4.576 \log k_2$ (s^{-1} L mol^{-1}) $- 49.14 - 4.576 \log T + E_a/T$.

Reactions of 1 with Sulfenes. To an ice-cooled solution of **1** (1.4 g) and triethylamine (2 g) in dry ether was added dropwise with stirring a threefold excess of alkylsulfonyl chloride in 40 mL of ether. The reaction mixture was then stirred at room temperature for 12 h. The precipitate was filtered off and washed with ether (2 × 100 mL). The combined filtrate and ether washings were cooled to give **8a,b.**

Compound **8a** was obtained as white needles in 78% yield: mp 124–126 °C; IR (KBr) 1655 cm^{-1}. Anal. Calcd for $C_9H_{10}N_2O_2S_2$ (242): C, 44.61; H, 4.16. Found: C, 44.55; H, 4.26.

Compound **8b** was obtained in 75% yield: mp 147–148 °C; IR (KBr) 1660 cm^{-1}. Anal. Calcd for $C_{15}H_{14}N_2O_2S_2$ (318): C, 56.58; H, 4.43; N, 8.79. Found: C, 56.68; H, 4.47; N, 8.71.

Isomerization of 8 into 9. Equimolar amounts (10^{-3} mol) of **8a** and benzoyl chloride were dissolved in chloroform (5 mL) and heated at 60 °C. After 2 h, complete isomerization into **9a** had occurred as evidenced by the disappearance of the methyl singlet resonance at δ 3.1 and the appearance of a new signal at δ 3.35 in the ^1H NMR spectrum. The solvent was removed in vacuo, and the residue was chromatographed on silica gel using hexane–ether (70:30) as the eluent. This furnished pure **9a** in 55% yield: mp 72–74 °C (ether); IR (KBr) 1630 cm^{-1}. Anal. Calcd for $M^{+\cdot}$: 242.01836. Found: 242.01835.

When **8a** (100 mg) was dissolved in deuteriochloroform (1 mL) and heated with a catalytic amount of aluminum chloride at 60 °C in an NMR tube, complete conversion into **9a** was observed after 2.5 h. This isomerization occurred much more slowly with methanesulfonyl chloride, being complete after 110 h.

An acetone solution (10 mL) of **8b** (0.6 g) and *m*-dichlorobenzoic acid (0.3 g) was heated for 7 h. After removal of the solvent in vacuo, the solid residue was treated with warm ether (30 mL) and filtered, and the filtrate was subjected to column chromatography on silica gel with hexane–ether (60:40) as the eluent. This furnished **9b** in 50% yield: mp 110–113 °C (hexane–ether); IR (KBr) 1635 cm^{-1}. Anal. Calcd for $C_{15}H_{14}N_2O_2S_2$ (318): C, 56.58; H, 4.43; N, 8.79. Found: C, 56.71; H, 4.32; N, 8.89.

Hydrolysis of 8 and 9. Compound **8a** (100 mg) decomposed when heated in methanol at reflux temperature for 12 h. The solvent was removed, and the residue was crystallized from ethanol to give **10a** in 40% yield: mp 252 °C dec; IR (KBr) 1630 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 3.0 (s, 3 H), 4.1 (s, 2 H), 7.3–7.4 (m, 5 H), 10.6 (br, 2 NH, exchangeable with D_2O); ^{13}C NMR (Me_2SO-d_6) δ 31.7 (CH_3, $^1J_{C-H}$ = 141.7 Hz), 43.8 (CH_2, $^1J_{C-H}$ = 148.5 Hz), 127, 128.6, 129, and 136 (phenyl C atoms), 168 (CN_2). Anal. Calcd for $C_9H_{12}N_2O_3S_2$ (260): C, 41.52; H, 4.65; N, 10.76. Found: C, 41.50; H, 4.68; N, 10.88.

This compound was also obtained when **9a** (0.2 g) was heated with 2 mL of hydrochloric acid (2 N) in ethanol (5 mL) at reflux temperature for 6 h. Removal of the solvent and crystallization of the residue from ether yielded pure **10a** in 60% yield.

For compound **8b,** an acetone solution (500 mg in 15 mL) was refluxed for 1 h in the presence of 5 mL of hydrochloric acid (1 N). The solution was concentrated and cooled to give **10b** in 90% yield: mp 245 °C dec (ethanol); IR (KBr) 2900–3400, 1640 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 2.9 (s, 3 H), 5.55 (br, 1 H), 7.1–7.4 (m, 10 H), 10.5 (NH); ^{13}C NMR (Me_2SO-d_6) δ 31.8 (CH_3), 65.7 (CH), 136.1 (C_1 phenyl), 166.4 (CN_2). Anal. Calcd for $C_{15}H_{16}N_2O_3S_2$ (336): C, 53.55; H, 4.79; N, 8.33. Found: C, 53.49; H, 4.76; N, 8.36.

Reactions of 8b with Heterocumulenes. A mixture of **8b** (1 g) and a tenfold excess of phenyl isocyanate or phenyl isothiocyanate was heated at 70–80 °C for 4–5 days (70–90% conversion by ^1H NMR). The excess of heterocumulene was distilled off in vacuo, and the residue was chromatographed on silica gel with hexane–ethyl acetate as the eluent.

Compound **11** was obtained in 50% yield: mp 78–80 °C (hexane–ether, 9:1); IR (KBr) 1710 (C=O), 1630 cm^{-1} (C=N). This compound was also prepared by reacting **1** (5 mmol) with an equimolar amount of phenyl isocyanate at room temperature for 10 min, followed by column chromatography on silica gel with CCl_4–ethyl acetate (90:10) as the eluent, yield 80%. Anal. Calcd for $C_{15}H_{13}N_3OS$ (283): C, 63.58; H, 4.62. Found: C, 63.47; H, 4.64.

Compound **12** was obtained in 30% yield after crystallization from hexane–petroleum ether, mp 134–135 °C. It was identical in all respects with the minor component obtained from **1** and phenyl isothiocyanate.[3]

For **13,** a mixture of **8b** (0.5 g) and a double excess of *tert*-butylcyanoketene[14] was heated in benzene (5 mL) for 2 h. Column chromatographic separation of the mixture on silica gel with hexane–ether (80:20) as the eluent furnished stilbene (52%), **9b** (10%), and **13** (52%). The latter was crystallized from methanol: mp 83–84 °C; IR (KBr) 1725, 1630 cm^{-1}. Anal. Calcd for $C_{15}H_{17}N_3OS$ (287): C, 62.69; H, 5.96. Found: C, 62.57; H, 5.85.

For an alternative synthesis of **13,** a solution of **1** in benzene (5 × 10^{-3} mol in 20 mL) was added with stirring over a period of 30 min to an equimolar amount of *tert*-butylcyanoketene in benzene (20 mL) at room temperature. The solvent was then removed on a rotary evaporator, and the residue was fractionally crystallized from methanol to give **13** (65%) and 4 [a = CO, b = C(*t*-Bu)CN] (10%). The latter was recrystallized from methanol: mp 114–116 °C; IR (KBr) 1725, 1655 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.16 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 25.5 and 41 (*t*-Bu C atoms), 38.9 (CH_3, $^1J_{C-H}$ = 136 Hz), 59.7 (C_5), 116 (C≡N), 128.1–129.8 (C_o and C_p phenyl), 134.9 (C_1 phenyl), 148.7 (C=N), 166.7 (C=O). Anal. Calcd for $C_{15}H_{17}N_3OS$ (287): C, 62.69; H, 5.96. Found: C, 62.59; H, 5.77.

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Registry No.—**1,** 34551-29-6; **4,** 68014-07-3; **5a,** 68013-96-7; **5b,** 68013-97-8; **5c,** 68013-98-9; **7a,** 68013-99-0; **7c,** 68014-00-6; **8a,** 68014-01-7; **8b,** 68014-02-8; **9a,** 65168-83-4; **9b,** 68014-03-9; **10a,** 68014-05-1; **10b,** 68014-06-2; **11,** 61249-40-9; **12,** 61249-39-6; **13,** 68014-04-0; benzoyl isothiocyanate, 532-55-8; chlorobenzoyl isothiocyanate, 16794-67-5; ethoxycarbonyl isothiocyanate, 16182-04-0; methylsulfonyl chloride, 124-63-0; phenylmethylsulfonyl chloride, 1939-99-7.

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(5) Compound **1** alone decomposes at 90–110 °C to give 2-(methylamino)-benzothiazole.[3] The first-order rate constants (10^5 k_1, s^{-1}), determined by ^1H NMR techniques in deuteriotoluene as solvent, are as follows: 0.94 (at 90 °C), 2.55 (at 98 °C), 3.08 (at 100 °C), and 8.75 (at 110 °C). The activation parameters are E_a = 31.4 kcal/mol and $\Delta S^{\ddagger}$ = +3 eu.

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(11) The reason why some heterocumulenes follow pathway a and others b in their reactions with **1** is uncertain. It is possible that **1** reacts as an electrophilic species (LUMO-controlled, path a) with isocyanates and alkyl and

aryl isothiocyanates, whereas it certainly reacts as a nucleophile (HOMO-controlled, path b) with acyl isothiocyanates and sulfenes. Both pathways occur simultaneously with ketenes.
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Studies on the Reaction of Acylimidazolidones with Ketenes[1,2]

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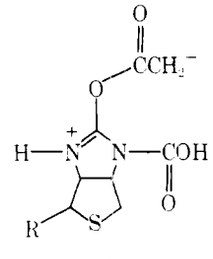
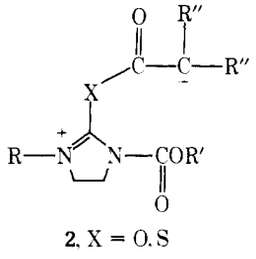
A series of substituted acylimidazolidones (**3a–d**) and acylimidazolidinethiones (**4a–d**) were treated with ketene (**6a**), bis(trifluoromethyl)ketene (**6b**), and diphenylketene (**6c**). The monosubstituted imidazolidinethiones gave N,N′-disubstituted 2:1 ketene adducts upon treatment with **6a**. Analogously 2:1 and 1:1 ketene adducts were noted for the reactions of monosubstituted imidazolidones and imidazolidinethiones with **6c**, while only 1:1 adducts were isolated using ketene **6b**. Treatment of N,N′-disubstituted imidazolidinethiones with either **6b** or **6c** led to a novel S → O replacement reaction at the thione position to give the corresponding imidazolidone in high yields.

In light of our continuing interest in the mechanism of biotin catalysis and the potential intermediacy of compounds of general structure 1 in acyl-CoA carboxylation reactions,[4] we have undertaken a general study of the reactions of substituted imidazolidones with ketenes. Conceptually, a model for **1** should be synthetically accessible in one step! Treatment of N-acyl-substituted imidazolidones or imidazolidinethiones with ketenes is envisioned to give **2** directly.

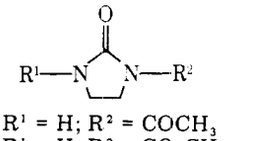


1

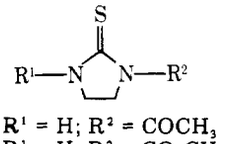


2, X = O, S

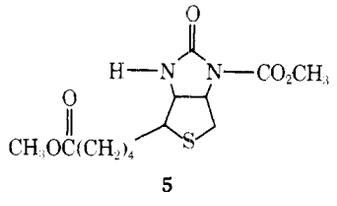
In this paper, we report our findings of the reaction of eight simple models (**3a–d** and **4a–d**) for carboxybiotin as well as *N*′-carbomethoxybiotin methyl ester (**5**) with three different ketenes (**6a–c**). Although no cases of CO_2 transfer were noted in this study, a novel S→O replacement reaction occurred in high yields at the thione group in N,N′-disubstituted imidazolidinethiones (**4c** and **4d**) with ketenes **6b** and **6c**.



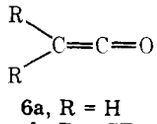
3a, R¹ = H; R² = $COCH_3$
b, R¹ = H; R² = CO_2CH_3
c, R¹ = CH_3; R² = $COCH_3$
d, R¹ = CH_3; R² = CO_2CH_3



4a, R¹ = H; R² = $COCH_3$
b, R¹ = H; R² = CO_2CH_3
c, R¹ = CH_3; R² = $COCH_3$
d, R¹ = CH_3; R² = CO_2CH_3



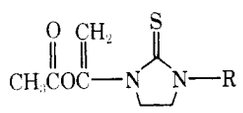
5



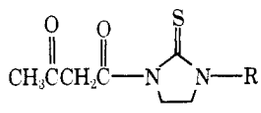
6a, R = H
b, R = CF_3
c, R = Ph

Results

I. Reaction of Acylimidazolidones with Ketenes. a. Ketene (6a) Reactions. Treatment of imidazolidones **3a–d**,[5–8] imidazolidinethiones **4c**[8] and **4d**,[8] and *N*′-carbomethoxybiotin methyl ester[9] (**5**) with excess ketene[10] (**6a**) gave only recovered starting material. When, however, the monosubstituted acylimidazolidinethiones **4a**[11] and **4b**[4] were treated with excess **6a**, two isomeric 2:1 ketene adducts were produced in each reaction (**7a**, **8a** (3%), and **7b** (80%), **8b** (11%), respectively). Since imidazolidinethiones are considerably more reactive toward alkylating agents than the corresponding imidazolidones[8] it was not surprising that only **4a** and **4b** reacted with ketene (**6a**). Enol acetate adduct **7a** could not be isolated in pure form. All purification attempts (recrystallization and chromatography) led to mixtures of the desired compound (**7a**) and the corresponding 1:1 adduct, *N,N*′-diacetylimidazolidinethione (**9a**). The structural assignment given to these pairs of linear isomers stemmed from a combination of spectral and chemical properties. In the ^1H NMR, the terminal vinylic protons in **7a** and **7b** appeared at ca. δ 5.05, while the corresponding resonance for the methylene unit in the acetoacetate residue in **8a** and **8b** occurred at ca. δ 4.50. The infrared spectrum for **7b**, unlike that of **8b**, showed strong absorptions at 1780 and 1650 cm^{-1} which can tentatively be assigned to the ester carbonyl and double bond groups in the enolic acetate residue.[12] Finally, both **7a** and **7b** undergo rapid acid-catalyzed hydrolysis to the 1:1 adducts, **9a**[7] and **9b**[8] in DME.

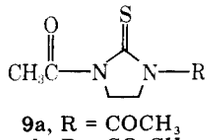


7a, R = $COCH_3$
b, R = CO_2CH_3



8a, R = $COCH_3$
b, R = CO_2CH_3

5% aq HCl/DME



9a, R = $COCH_3$
b, R = CO_2CH_3

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