aryl isothiocyanates, whereas it certainly reacts as a nucleophile (HOMO-controlled, path b) with acyl isothiocyanates and sulfenes. Both pathways occur simultaneously with ketenes.
(12) R. B. Woodward and R. Hoffmann, *Angew. Chem.*, **81**, 797 (1969); *Angew. Chem., Int. Ed. Engl.*, **8**, 781 (1969).
(13) R. Gompper, *Angew. Chem.*, **81**, 348 (1969); *Angew. Chem., Int. Ed. Engl.*, **8**, 312 (1969).
(14) H. W. Moore and W. Weyler, *J. Am. Chem. Soc.*, **92**, 4132 (1970).

Studies on the Reaction of Acylimidazolidones with Ketenes[1,2]

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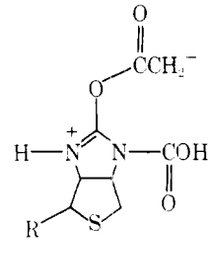
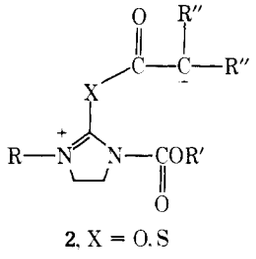
A series of substituted acylimidazolidones (**3a–d**) and acylimidazolidinethiones (**4a–d**) were treated with ketene (**6a**), bis(trifluoromethyl)ketene (**6b**), and diphenylketene (**6c**). The monosubstituted imidazolidinethiones gave N,N′-disubstituted 2:1 ketene adducts upon treatment with **6a**. 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.

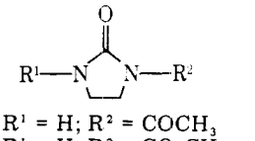


1

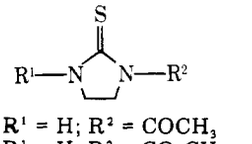


2, X = O, S

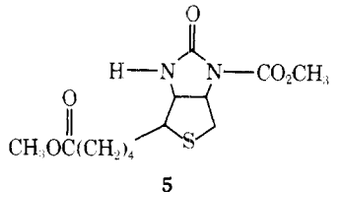
In this paper, we report our findings of the reaction of eight simple models (**3a–d** and **4a–d**) for carboxybiotin as well as *N*′-carbomethoxybiotin methyl ester (**5**) with three different ketenes (**6a–c**). Although no cases of CO_2 transfer were noted in this study, a novel S→O replacement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



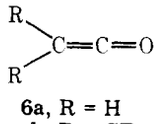
3a, R¹ = H; R² = $COCH_3$
b, R¹ = H; R² = CO_2CH_3
c, R¹ = CH_3; R² = $COCH_3$
d, R¹ = CH_3; R² = CO_2CH_3



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



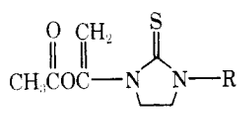
5



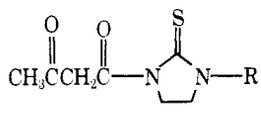
6a, R = H
b, R = CF_3
c, R = Ph

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.

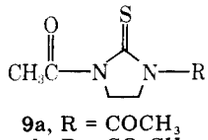


7a, R = $COCH_3$
b, R = CO_2CH_3



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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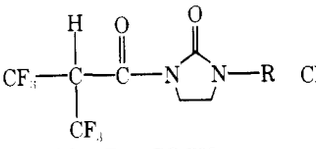
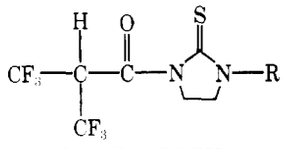
b. Bis(trifluoromethyl)ketene (6b) Reactions. Bis(trifluoromethyl)ketene (**6b**) reacts readily with nucleophiles, but unlike other ketenes it does not undergo spontaneous self-condensation with heating (<250 °C).[13] Treatment of the N–H substituted imidazolidones (**3a,b**) and imidazolidinethiones (**4a,b**) in CH_2Cl_2 with 1.1 equiv of **6b** at 65 ± 2 °C gave the expected *N*-α-*H*-hexafluoroisobutyryl adducts **10a,b** and **11a,b** in good yields. Analogously, treatment of **5** with **6b**

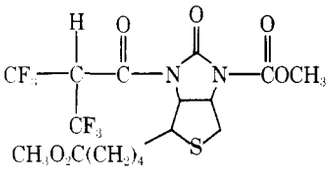


10a, R = $COCH_3$
b, R = CO_2CH_3



11a, R = $COCH_3$
b, R = CO_2CH_3

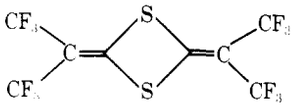
in DME gave the corresponding *N*-α-*H*-hexafluoroisobutyryl-*N'*-carbomethoxybiotin methyl ester (**12**) in quantitative yield. The ^1H NMR for these adducts showed a characteristic septet (J = 7.5 Hz) for the lone methine proton.[13]



12

Addition of the ketene **6b** to a CH_2Cl_2 solution containing the *N*-methylimidazolidones **3c** and **3d** under similar conditions led to the total recovery of starting urea in each case. The same results were observed in DME and DMF and at elevated temperatures (60–130 °C).

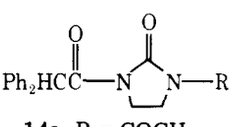
When, however, the N,N'-disubstituted imidazolidinethiones **4c** and **4d** were treated with **6b** in CH_2Cl_2, replacement of the sulfur atom occurred to give the corresponding oxygen analogues **3c** and **3d** in quantitative yield along with 2,4-bis[2,2,2-trifluoro-1-(trifluoromethyl)ethylidene]-1,3-dithietane (**13**).[14] In the case of **4d**, the S→O substitution reaction proceeded even at room temperature, with the dithietane **13** precipitating from the reaction.



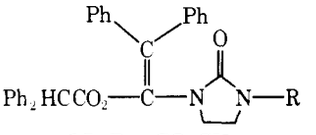
13

c. Diphenylketene (6c) Reactions. The results obtained from the treatment of carboxybiotin model compounds **3a–d**, **4a–d**, and **5** with ketene **6b** prompted us to examine the reaction of these substrates with diphenylketene (**6c**) under a variety of conditions. Ketene **6c** can be readily prepared[15] by the thermal decomposition of phenylbenzoyldiazomethane.[16]

Treatment of *N*-acetylimidazolidone (**3a**) with 1.0 equiv of freshly distilled **6c** in CH_2Cl_2 at 60 ± 2 °C gave the 1:1 N,N'-disubstituted adduct **14a** (12%). The corresponding adduct **14b** (14%) was also observed in the reaction of **6c** with *N*-carbomethoxyimidazolidone (**3b**), along with the 2:1 adduct **15** (16%).

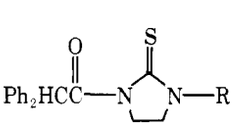


14a, R = $COCH_3$
b, R = CO_2CH_3
c, R = H

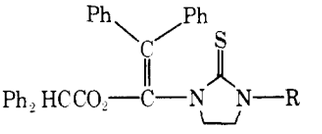


15, R = CO_2CH_3

Analogously, low yields of 2:1 adducts (**17a, 17c,** and **17b, 17c**) were detected in the reactions of **6c** with *N*-acetyl- (**4a**) and *N*-carbomethoxyimidazolidinethione (**4b**), respectively. Formation of the small amounts of the 2:1 adduct **17c** cannot



16a, R = $COCH_3$
b, R = CO_2CH_3
c, R = H

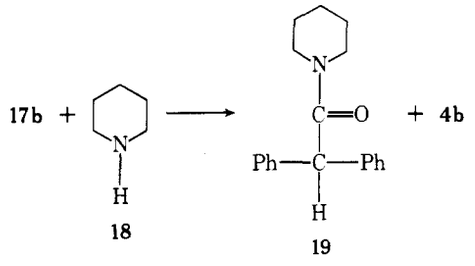


17a, R = $COCH_3$
b, R = CO_2CH_3
c, R = H

readily be explained. Preliminary ^1H NMR analysis of the product mixture before chromatographic purification indicated that deacylation had occurred during the reaction. Surprisingly, the corresponding 1:1 adducts (**16a–c**) were not observed in these reactions (40 °C, 2 days) as well as at elevated temperatures (60 °C, 2 days).

A variety of cyclic as well as linear structures can be drawn for these 2:1 adducts. Both modes of addition have previously been reported for the reaction of 2 equiv of diphenylketene with heterocyclic systems.[17–20] Doubts have been cast over the correctness of some of these structures.[17] Examination of the spectral data for **15** and **17a–c** (see Experimental Section) supported our structural assignment for these four compounds. Mass spectrometry gave a weak molecular ion peak for compounds **15** and **17a–c.** The fragmentation patterns for these adducts revealed two distinct modes of cleavage. Compounds **15, 17a,** and **17b** each gave a noticeable P–CO_2CH_2, or P–$COCH_2$ peak. This McLafferty-type rearrangement of the starting molecular ion has been observed as a characteristic fragmentation pattern for N-acyl-substituted imidazolidones.[8] A significant feature in all the spectra were the P–Ph_2CCO and P–Ph_2CHCO fragments. Comparison of the IR spectra for these compounds revealed the consistent appearance of several absorptions (i.e., 1760 cm^{-1} for the carbomethoxy carbonyl group in **15** and **17b** and a weak, broad absorption at 1650 cm^{-1} tentatively assigned to the enol ester[12]) which agree with expectation. The ^1H NMR spectra for the 2:1 adducts showed a characteristic downfield singlet (1 H) at ca δ 5.05, which can be assigned to the diphenylacetyl methine hydrogen. The ethylene pattern for the assymmetrically substituted imidazolidone ring protons was the expected AA'BB' spin system. Significantly, the *N*-acetyl methyl resonance for compound **17a** occurred at δ 2.73. This unusually low field absorption has been a reliable diagnostic peak for *N*-acetylimidazolidinethiones.[8]

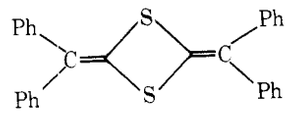
Additional support for the structural assignment for these adducts stemmed from their chemical reactivity. Each substrate gave a positive spot test for the thione group.[21] Furthermore, treatment of **17b** with 1 equiv of piperidine (**18**) in CH_2Cl_2 at room temperature (48 h) gave 2 equiv of diphenylacetylpiperidine (**19**) along with a 50% yield of *N*-carbomethoxyimidazolidinethione (**4b**).[22] This result suggested that the rate-determining step for this reaction was aminolysis of **17b** to give 1 equiv of **19** and the corresponding 1:1 adduct **16b,** which then rapidly reacted with a second equivalent of **18** to give **19** and **4b.** In order to test this hypothesis, imidazoli-



18 **19**

dinethione **16b** was synthesized (79%) by the addition of diphenylacetyl chloride[23] to a CH_2Cl_2 solution containing **4b** and pyridine. Treatment of **16b** with 1 equiv of **18** in dichloroethane or DME led to the rapid (<2 h) formation of **19** and **4b**.

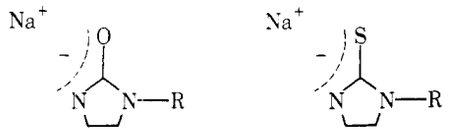
Treatment of model compound **5**, as well as the N,N′-disubstituted imidazolidones **3c** and **3d**, with **6c** at 60 ± 2 °C led to the recovery of the starting urea in each case. However, addition of ketene **6c** to CH_2Cl_2 solutions containing the N,N′-disubstituted imidazolidinethiones **4c** and **4d** (60 ± 2 °C, 3 days) resulted in the partial S→O replacement of the thione group in the starting material to give the corresponding imidazolidones **3c** and **3d** in 29 and 51% yields, respectively. In these cases, the corresponding dithietane dimer **20**[24] of



20

diphenylthioketene was also isolated. Although the isolated yields obtained in these reactions are considerably lower than those observed for ketene **6b**, ^1H NMR analysis of the crude reaction mixture showed that the S→O replacement reaction had occurred to ca. 65 and 85%, respectively.

II. Reaction of the Sodium Salts of N-Acyl-Substituted Imidazolidones with Diphenylketene. Due to the large amounts of unreacted starting material recovered in the above diphenylketene (**6c**) reactions with the N-H-, N′-acyl-substituted imidazolidones (**3a, 3b, 4a,** and **4b**), the reaction of the sodium salt of these substrates with **6c** was examined. Sodium salts (**21a, 21b, 22a,** and **22b**) were prepared by ad-

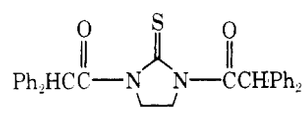


21a, R = $COCH_3$ **22a**, R = $COCH_3$
b, R = CO_2CH_3 **b**, R = CO_2CH_3

dition of the appropriately substituted imidazolidone to an equivalent of NaH in DME.

Addition of **6c** to **21a** gave only the deacylated 1:1 adduct **14c** in 70% yield. The same product (27%) was formed from the reaction of **21b** with **6c**. In this case, the 1:1 adduct **14b** (15%) was also isolated.

A similar trend was noted for the sodium salts of imidazolidinethiones **4a** and **4b**. Reaction of **22a** with **6c** gave only the 1:1 adduct **16a** (67%) while treatment of **22b** with **6c** gave adducts **16b** (48%), **16c** (3%), and a compound tentatively



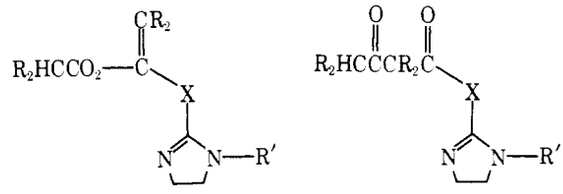
23

identified as **23** (2%). Surprisingly, unlike the neutral imidazolidinethione reactions with **6c**, no 2:1 (**17a–c**) adducts were observed.

Discussion

The formation of 2:1 and 1:1 linear adducts of ketenes with heterocycles has been previously observed.[17,25] Procter and Taylor obtained the 2:1 adduct, 9,10-dihydro-10-(1-methacryloyloxy-2-methylpropenyl)acridine, from the addition of excess dimethylketene to acridine.[25] In this case, only the corresponding enol acetate adduct was isolated.

The mechanism for the formation of open-chain products **7, 8, 15,** and **17a–c** probably involves initial nucleophilic attack by the heterocycle (**3b, 4a,** and **4b**) on the ketene to give a zwitterion, which then can undergo further reaction with a second molecule of ketene. It is not known whether this stepwise reaction initially occurs directly at the ring nitrogen atom or at the thione group. The latter pathway would initially give the isomeric imidazolines **24** and **25**. However, Chap-

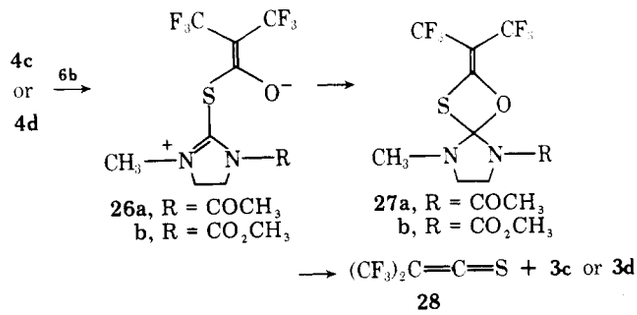


24 **25**

man-type rearrangement of **24** and **25** to the observed products should occur rapidly.[26–31]

A mechanism similar to the one postulated for the formation of the 2:1 adducts can be used to explain products **10, 11, 12, 14,** and **16**. In these cases, however, only 1 equiv of ketene is consumed to give the 1:1 adducts. Interestingly, the use of the preformed sodium salts (**21a, 21b, 22a,** and **22b**) did not significantly alter the mode of addition of **6c** to these substrates.[32] Formation of the deacylated products **14c** and **16c** may have resulted from basic hydrolysis (traces of water) of the N-acyl group during the reaction.[33]

The high yield formation of **3c** and **3d** with **6b** from **4c** and **4d** can be envisioned to occur by initial attack of the ketene by the imidazolidinethione (**4c** or **4d**) to give zwitterion **26a** and **26b**, respectively. Intermediate formation of the oxathietane ring **27** in the subsequent step, followed by ring fragmentation, would generate the observed products (**3c** or **3d**) and **28**. Bis(trifluoromethyl)thioketene (**28**) is reported



26a, R = $COCH_3$ **27a**, R = $COCH_3$
b, R = CO_2CH_3 **b**, R = CO_2CH_3

28

to dimerize to **13** in the presence of nitrogen, oxygen, and sulfur nucleophiles.[14] In an analogous fashion, reaction of either **3c** or **3d** with ketene **6b** would lead to the intermediate formation of a 1,3-dioxetane ring. However, fragmentation of this adduct in either direction leads to the regeneration of both starting materials. The appropriate labeling experiment needed to test this possibility, however, has not been conducted. A similar mechanism can also be drawn for the substitution reaction noted for **4c** and **4d** with diphenylketene (**6c**).

Isolated examples of heteroatom replacement reactions have been observed in the past.[14,34–38] Notable cases that have been reported are the conversion of amides and ureas to thioamides[34] and thioureas[35] with phosphorous pentasulfide, the sulfur–oxygen exchange between isothiocyanate and isocyanate esters,[36,37] and the reaction of **28** with electron-rich carbonyl compounds to give **6b** and the dithietane adduct of **28** and the corresponding thione.[14] Analogously, 1,3-oxathietane rings have been suggested as intermediates in the last two isosteric substitution reactions.[14]

Experimental Section

General. Melting points were determined with a Thomas-Hoover melting point apparatus and are uncorrected. Infrared spectra (IR)

were run on Perkin-Elmer Model 700 and 237B spectrometers and calibrated against the 1601-cm^{-1} band of polystyrene. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on Varian Associates Models T-60 and EM-390 instruments.

Chemical shifts are expressed in parts per million relative to Me_4Si, and coupling constants (J values) in hertz. Spin multiplicities are indicated by the symbols s (singlet), d (doublet), t (triplet), q (quartet), sept (septet), and m (multiplet). Mass spectral (MS) data were obtained at an ionizing voltage of 70 eV on a Hitachi Perkin-Elmer Model RMU-6H mass spectrometer and a Hewlett-Packard 5930 gas chromatograph–mass spectrometer. High-resolution mass spectra were performed by Dr. James Hudson at the Department of Chemistry, Rice University, or Dr. Ronald Grigsby at the Department of Biochemistry and Biophysics, Texas A&M University on CEC21-110B double focusing magnetic sector spectrometers at 70 eV. Exact masses were determined by peak matching. Elemental analyses were obtained at Spang Microanalytical Laboratories, Ann Arbor, Mich.

The solvents and reactants were of the best commercial grade available and were used without further purification unless noted. When dry solvents were required, CH_2Cl_2 was distilled from P_2O_5, benzene was distilled and then stored over sodium, dimethylformamide was stored over sodium sulfate and then distilled from CaH_2, anhydrous ether was distilled and stored over sodium metal, DME was distilled from $LiAlH_4$, and piperidine was stored and distilled from CaH_2.

All reactions were run under nitrogen and all glassware dried before use. Thick-layer preparative chromatography was run on Analtech Uniplates-GF, 1000 μm and Merck silica gel (70–230 mesh) was used for all column chromatography. Analytical thin-layer chromatography was run on Merck silica gel 60 F-254 (Catalog No. 5775).

Reaction of Substituted Imidazolidinethiones with Ketene (6a). General Procedure. Ketene (**6a**) was prepared by the pyrolysis of acetone according to the method of Williams and Hurd.[10] The ketene gas generated was then directly passed through a solution (CH_2Cl_2 or $CHCl_3$) containing the substituted imidazolidinethione for 30 min at room temperature. The reaction vessel was stoppered, stored in the refrigerator (~0 °C) overnight, and then concentrated in vacuo. The residue was further purified in the manner described below.

Treatment of *N*-Acetylimidazolidinethione (4a) with Ketene (6a). Using the above procedure, a mixture of three products (NMR analysis) was obtained from the addition of excess **6a** to 2.00 g (0.014 mol) of **4a** in $CHCl_3$ (50 mL). The mixture was chromatographed on silica gel (140 g) using CH_2Cl_2–Et_2O (90:10) as the eluent. The first eluted material (2.0 g) was tentatively identified as a 70:30 mixture of **7a** and **9a**. All attempts (recrystallization and chromatography) to further purify this viscous oil were unsuccessful. Substraction of the ^1H NMR peaks that can be attributed to **9a**[7] from the spectrum of the mixture led to the following tentative NMR assignment for **7a**: NMR ($CDCl_3$) δ 2.20 (s, 3 H), 2.80 (s, 3 H), 3.84–4.12 (m, 4 H), 5.05–5.15 (m, 2 H).

The later fractions that were obtained from the column yielded 0.10 g (3%) of **8a**. Reprecipitation of this solid from carbon tetrachloride–hexanes gave the purified material: mp 97–100 °C; IR (KBr) 1680, 1605 (broad) cm^{-1}; NMR ($CDCl_3$) δ 2.30 (s, 3 H), 2.74 (s, 3 H), 3.94–4.14 (m, 4 H), 4.52 (s, 2 H); MS *m/e* (rel %) 228 (57), 185 (9), 170 (11), 144 (94), 143 (38), 128 (11), 102 (100), 85 (45), 72 (40); mol wt 228.0560 (calcd for $C_9H_{12}N_2O_3S$, 228.0568).

Treatment of *N*-Carbomethoxyimidazolidinethione (4b) with Ketene (6a). Addition of excess **6a** to 3.00 g (0.019 mol) of **4b** in CH_2Cl_2 (50 mL) according to the procedure described above gave a mixture of products which was then chromatographed on silica gel (210 g) using CH_2Cl_2–Et_2O (90:10) as the eluting solvent. The initial fraction was identified as **7b** which was then further purified by reprecipitation from carbon tetrachloride–hexanes to give 3.66 g (80%) of product: mp 68–69 °C; IR (KBr) 1780, 1760, 1650 cm^{-1}; NMR ($CDCl_3$) δ 2.22 (s, 3 H), 3.85 (s, 3 H), 3.90–4.20 (m, 4 H), 5.05 (s, 2 H); MS *m/e* (rel %) 244 (4), 201 (100), 160 (16), 129 (16), 102 (18), 96 (13), 88 (28), 72 (30), 70 (13).

Anal. Calcd for $C_9H_{12}N_2O_4S$: C, 44.25; H, 4.95; N, 11.47. Found: C, 44.28; H, 4.89; N, 11.42.

The second fraction gave **8b** in 11% yield (0.50 g) after reprecipitation from carbon tetrachloride–hexanes: mp 111–113 °C; IR (KBr) 1735, 1725, 1685 cm^{-1}; NMR ($CDCl_3$) δ 2.32 (s, 3 H), 3.90 (s, 3 H), 4.00 (s, 4 H), 4.45 (s, 2 H); MS *m/e* (rel %) 244 (35), 201 (25), 160 (100), 102 (47), 88 (32), 84 (30), 72 (35), 69 (25).

Anal. Calcd for $C_9H_{12}N_2O_4S$: C, 44.25; H, 4.95; N, 11.47. Found: C, 44.20; H, 4.88; N, 11.38.

Hydrolysis of 7b to *N*-Acetyl-*N'*-carbomethoxyimidazolidinethione (9b). Compound **7b** (0.48 g, 0.002 mol) was dissolved in DME (25 mL) and then an aqueous 5% HCl solution (4 mL) was added and allowed to stir at room temperature for 4 h. The reaction was monitored by TLC to insure complete hydrolysis of the enol acetate. The reaction mixture was then diluted with CH_2Cl_2 (100 mL) and washed with aqueous 5% $NaHCO_3$ (25 mL) and H_2O (25 mL). The CH_2Cl_2 solution was dried (Na_2SO_4) and concentrated in vacuo, and then **9b** was reprecipitated from chloroform–hexanes: yield 0.34 g (84%); mp 95–96 °C (lit.[8] mp 95–97 °C).

Hydrolysis of the Mixture of 7a and 9a to *N,N'*-Diacetylimidazolidinethione (9a). The initial mixture (0.20 g) of **7a** and **9a** obtained after chromatography was subjected to the solvolysis conditions used in the preceding reaction. The reaction was then diluted with CH_2Cl_2 (50 mL), washed with aqueous 5% $NaHCO_3$ (20 mL) and H_2O (10 mL), dried (Na_2SO_4), and evaporated in vacuo. NMR analysis of the remaining solid (0.14 g) indicated only the presence of **9a**.[8]

Reaction of Substituted Imidazolidones and Imidazolidinethiones with Bis(trifluoromethyl)ketene (6b). General Procedure. Bis(trifluoromethyl)ketene[13] (**6b**) was transferred from a sealed tube via a standard vacuum line[39] to a cylindrical glass vessel fitted with a Teflon stopcock for storage. A sample (0.003 mol) of the compound to be treated with the ketene was weighed into a glass vessel (13 × 200 mm) suitable for a sealed tube reaction and then connected to the vacuum line. CH_2Cl_2 (10 mL) was condensed into the reaction tube and then **6b** (0.57 g, 0.0032 mol) was measured using a calibrated section of the vacuum line and then vapor transferred to the reaction tube. The vessel was sealed with a torch and then removed to an oil bath maintained at 65 ± 2 °C for 2 days unless otherwise noted. The sealed tube was opened and filtered if necessary and the filtrate concentrated in vacuo. The residue was then further purified in the manner outlined below to give the observed product(s).

Treatment of *N*-Acetylimidazolidone (3a) with Bis(trifluoromethyl)ketene (6b). Using the above procedure, **10a** was obtained in 92% yield (0.85 g) from **3a** and **6b**. Purification was accomplished by distillation of the viscous oil: bp 150 °C (external temperature, 0.2 mm); IR (neat, NaCl) 1765, 1715 (sh), 1705 cm^{-1}; NMR ($CDCl_3$) δ 2.58 (s, 3 H), 3.77–4.07 (m, 4 H), 5.75–6.50 (sept, J = 7.5 Hz, 1 H); MS *m/e* (rel %) 306 (100), 265 (25), 245 (25), 208 (59), 179 (36), 86 (41), 85 (45), 69 (68).

Anal. Calcd for $C_9H_8F_6N_2O_3$: C, 35.30; H, 2.63; N, 9.15. Found: C, 35.19; H, 2.76; N, 9.03.

Treatment of *N*-Carbomethoxyimidazolidone (3b) with Bis(trifluoromethyl)ketene (6b). Treatment of **3b** with **6b** according to the above procedure gave 0.34 g (35%) of **10b** as a colorless, viscous oil after distillation: bp 155 °C (external temperature, 0.2 mm); IR (neat, NaCl) 1805, 1775 (sh), 1745 (sh), 1705 cm^{-1}; NMR ($CDCl_3$) δ 3.95 (s, 3 H), 3.99 (s, 4 H), 5.78–6.58 (sept, J = 7.5 Hz, 1 H); MS *m/e* (rel %) 322 (46), 303 (11), 208 (10), 192 (21), 179 (53), 159 (22), 144 (50), 113 (17), 99 (30), 91 (33), 88 (100).

Anal. Calcd for $C_9H_8F_6N_2O_4$ (322.0388): C, 33.55; H, 2.50; N, 8.69. Found (322.0393): C, 33.62; H, 2.60; N, 8.92.

Treatment of *N*-Acetylimidazolidinethione (4a) with Bis(trifluoromethyl)ketene (6b). Utilizing the above procedure, **11a** was obtained in quantitative yield (0.96 g) from **4a** and **6b**. The product was purified by reprecipitation from chloroform–hexanes: mp 78–80 °C; IR (KBr) 1710, 1680 cm^{-1}; NMR ($CDCl_3$) δ 2.80 (s, 3 H), 3.97–4.17 (m, 4 H), 7.30–8.08 (sept, J = 7.5 Hz, 1 H); MS *m/e* (rel %) 322 (86), 303 (25), 192 (17), 179 (49), 159 (15), 144 (63), 99 (23), 88 (100).

Anal. Calcd for $C_9H_8F_6N_2O_2S$: C, 33.54; H, 2.50; N, 8.69. Found: C, 33.41; H, 2.45; N, 8.74.

Treatment of *N*-Carbomethoxyimidazolidinethione (4b) with Bis(trifluoromethyl)ketene (6b). Addition of **6b** to **4b** according to the procedure described above gave a quantitative yield (1.00 g) of **11b**. Reprecipitation from carbon tetrachloride–hexanes gave a yellow crystalline material: mp 130–131 °C; IR (KBr) 1750, 1685 cm^{-1}; NMR ($CDCl_3$) δ 3.95 (s, 3 H), 4.10 (s, 4 H), 7.40–8.20 (sept, J = 7.5 Hz, 1 H); MS *m/e* (rel %) 338 (39), 269 (18), 249 (21), 179 (20), 159 (29), 102 (18), 88 (64), 72 (83), 69 (100).

Anal. Calcd for $C_9H_8F_6N_2O_3S$: C, 31.96; H, 2.38; N, 8.28. Found: C, 31.92; H, 2.30; N, 8.40.

Treatment of *N*-Methyl-*N'*-acetylimidazolidinethione (4c) with Bis(trifluoromethyl)ketene (6b). Using the above procedure, **3c** was obtained in quantitative yield (0.42 g) from **4c** and **6b**. Purification of the imidazolidone was accomplished by reprecipitation from carbon tetrachloride–hexanes: mp 79 °C (lit.[8] mp 78–81 °C).

The white crystalline material which was observed upon completion of the reaction was dried in vacuo until the organic solvent was removed and identified as **13**: yield 0.57 g (100%); mp 84–85 °C (lit.[14] mp 84.5–85.5 °C); IR (KBr) 1600 cm^{-1}; MS *m/e* (rel %) 388 (30), 369 (27), 194 (100).

Treatment of *N*-Methyl-*N'*-carbomethoxyimidazolidinethione (4d) with Bis(trifluoromethyl)ketene (6b). Treatment of **4d** with **6b** at room temperature (3 days) according to the above procedure gave 0.47 g (100%) of **3d** after recrystallization from ether, mp 56–59 °C (lit.[8] mp 56–59 °C).

The precipitate that was initially observed when the tube was opened was identified as **13:** yield 0.50 g (99%); mp 84–85 °C (lit.[14] mp 84.5–85.5 °C).

Treatment of *N'*-Carbomethoxybiotin Methyl Ester (5) with Bis(trifluoromethyl)ketene (6b). Utilizing the above experimental procedure and DME (10 mL) as the reaction solvent, **12** was obtained in quantitative yield (1.48 g) from **5** and **6b.** The product was chromatographed on silica gel (100 g) using EtOAc as the eluent to give a thick viscous oil: IR (neat, NaCl) 1810, 1765, 1720 cm^{-1}; NMR ($CDCl_3$) δ 1.00–1.83 (m, 6 H), 2.03–2.40 (m, 2 H), 2.96–3.30 (m, 2 H), 3.30–3.80 (m, 1 H), 3.64 (s, 3 H), 3.94 (s, 3 H), 4.63–5.03 (m, 2 H), 5.80–6.53 (sept, J = 7.5 Hz, 1 H); MS *m/e* (rel %) 494 (3), 463 (6), 379 (1), 297 (11), 278 (5), 198 (92), 179 (38), 175 (14), 166 (64), 113 (23), 97 (44), 91 (33), 85 (44), 69 (100), 59 (85).

Anal. Calcd for $C_{17}H_{20}F_6N_2O_6S$: C, 41.29; H, 4.07; N, 5.66. Found: C, 41.36; H, 4.01; N, 5.56.

Reaction of Substituted Imidazolidones and Imidazolidinethiones with Diphenylketene (6c). General Procedure. Diphenylketene (**6c**) was prepared by the thermal decomposition of phenylbenzoyldiazomethane[16] according to the method of Smith and Hoehn,[15] bp 104–105 °C (1.0 mm) (lit.[15] bp 119–121 °C (3.5 mm)).

The substituted imidazolidone or imidazolidinethione, **6c,** and CH_2Cl_2 (3–5 mL) were added to a glass tube (13 × 200 mm), sealed with a torch, and then placed in an oil bath maintained at 60 ± 2 °C unless otherwise noted for 3 days. The vessel was opened, rinsed with acetone, and filtered if necessary, and then the filtrate was concentrated in vacuo. The residue obtained was then further purified in the manner outlined below to give the observed products.

Treatment of *N*-Acetylimidazolidone (3a) with Diphenylketene (6c). Treatment of 0.30 g (0.0023 mol) of **3a** with 0.45 g (0.0023 mol) of **6c** according to the above procedure gave a thick oil upon workup. Trituration of the oil with Et_2O (20 mL) gave a solid which was successively reprecipitated from CH_2Cl_2–CCl_4 then chloroform–hexanes to give 0.20 g (67%) of the starting imidazolidone **3a,** mp 178–181 °C (lit.[7] mp 176–177 °C).

The CH_2Cl_2–CCl_4 filtrate was concentrated in vacuo and reprecipitated twice from carbon tetrachloride–hexanes to give 0.09 g (12%) of **14a:** mp 156–158 °C; IR (KBr) 1755, 1698 cm^{-1}; NMR ($CDCl_3$) δ 2.47 (s, 3 H), 3.60–4.00 (m, 4 H), 6.50 (s, 1 H), 7.10–7.40 (m, 10 H); MS *m/e* (rel %) 322 (22), 194 (99), 167 (36), 166 (80), 165 (100), 147 (20).

Anal. Calcd for $C_{19}H_{18}N_2O_3$: C, 70.79; H, 5.03; N, 8.69. Found: C, 70.72; H, 5.70; N, 8.72.

Treatment of *N*-Carbomethoxyimidazolidone (3b) with Diphenylketene (6c). Utilizing the above procedure, 0.34 g (0.0018 mol) of **6c** was added to 0.25 g (0.0017 mol) of **3b.** Concentration of the reaction solution gave an oil which was then reprecipitated from carbon tetrachloride–hexanes. The solid was triturated with a minimum amount of CCl_4 (10 mL) and filtered, and the undissolved material was reprecipitated from chloroform–hexanes to give 0.14 g (56%) of starting material (**3b**), mp 179–180 °C (lit.[6] mp 179–180 °C).

The CCl_4 filtrate was concentrated in vacuo and then chromatographed on a thick-layer silica gel plate using CH_2Cl_2 as the eluent (double elution). The first zone (R_f 0.34) collected gave **14b:** yield 0.08 g (14%); mp 141–142 °C; IR (KBr) 1804, 1765, 1728, 1693, 1600 cm^{-1}; NMR ($CDCl_3$) δ 3.80 (s, 3 H), 3.86 (s, 4 H), 6.53 (s, 1 H), 7.10–7.55 (m, 10 H); MS *m/e* (rel %) 338 (41), 194 (100), 167 (40), 166 (70), 165 (71).

Anal. Calcd for $C_{19}H_{18}N_2O_4$: C, 67.44; H, 5.36; N, 8.28. Found: C, 67.37; H, 5.24; N, 8.21.

The second zone (R_f 0.23) totalled 0.15 g. This compound was tentatively assigned structure **15:** yield 16%; mp 175–176 °C; IR (KBr) 1795, 1760, 1735, 1650 cm^{-1}; NMR ($CDCl_3$) δ 3.33–3.70 (m, 4 H), 3.83 (s, 3 H), 5.03 (s, 1 H), 6.90–7.40 (m, 20 H); MS *m/e* (rel %) (a) high gain 532, (b) low gain 475 (0.4), 474 (1), 339 (9), 338 (36), 337 (25), 309 (8), 194 (58), 168 (12), 167 (91), 166 (50), 165 (100), 152 (18).

Treatment of *N*-Acetylimidazolidinethione (4a) with Diphenylketene (6c). Using the above procedure, 0.27 g (0.0014 mol) of **6c** was added to 0.20 g (0.0014 mol) of **4a** in CH_2Cl_2 (15 mL). The solution was heated for 2 days. Evaporation in vacuo of the reaction solution left an oil which was then triturated with CCl_4. The remaining solid (0.11 g, 55%) was identified as unreacted **4a,** mp 162–164 °C (lit.[11a] mp 165–167 °C).

The CCl_4 filtrate was concentrated in vacuo and then chromatographed on a thick-layer silica gel plate using CH_2Cl_2 as the eluent. The first zone (R_f 0.41) collected gave 0.04 g (5%) of **17a:** mp 141–143 °C; IR (KBr) 1758, 1694, 1655, 1600; NMR ($CDCl_3$) δ 2.73 (s, 3 H), 3.27–3.94 (m, 4 H), 5.05 (s, 1 H), 6.93–7.04 (m, 20 H); MS *m/e* (rel %) (a) high gain 532 (100), 490 (7), 489 (9), (b) low gain 339 (10), 338 (25), 337 (64), 295 (50), 267 (18), 194 (74), 168 (10), 167 (68), 166 (55), 165 (100), 152 (20).

Anal. Calcd for $C_{33}H_{28}N_2O_3S$: C, 74.41; H, 5.30; N, 5.26. Found: C, 74.33; H, 5.20; N, 5.18.

The second fraction (R_f 0.27) was identified as **17c:** yield 0.02 g (3%); mp 83–86 °C; IR (KBr) 1755, 1655 cm^{-1}; NMR ($CDCl_3$) δ 3.10–4.00 (m, 4 H), 5.10 (s, 1 H), 6.93–7.40 (m, 20 H); N–H proton was not detected in $CDCl_3$; MS *m/e* (rel %) 490 (6), 489 (15), 296 (22), 295 (64), 194 (55), 167 (81), 166 (54), 165 (100), 152 (20); mol wt 490.1698 (calcd for $C_{31}H_{26}N_2O_2S$, 490.1714).

Treatment of *N*-Carbomethoxyimidazolidinethione (4b) with Diphenylketene (6c). Utilizing the above procedure, 0.25 g (0.0013 mol) of **6c** was added to 0.20 g (0.00125 mol) of **4b** in CH_2Cl_2 (15 mL). The solution was heated for 2 days and then evaporated in vacuo. The residue was triturated with CCl_4 and the remaining solid was reprecipitated from chloroform–hexanes and identified as **4b:** yield 0.09 g (45%); mp 156–158 °C (lit.[4] mp 156–158 °C).

The CCl_4 filtrate was concentrated in vacuo and the solid chromatographed on a thick-layer silica gel plate using CH_2Cl_2 as the eluent. The first zone (R_f 0.24) isolated was tentatively identified as **17b:** yield 0.09 g (13%); mp 124–126 °C; IR (KBr) 1760, 1720, 1700 (sh), 1650 cm^{-1}; NMR ($CDCl_3$) δ 3.36–4.06 (m, 4 H), 3.83 (s, 3 H), 5.04 (s, 1 H), 6.90–7.40 (m, 20 H); MS *m/e* (rel %) (a) high gain 548 (100), 491 (3), 490 (3), (b) low gain 354 (9), 353 (9), 195 (10), 194 (10), 167 (24), 166 (65), 165 (100), 164 (10), 163 (15), 152 (12).

The second fraction (R_f 0.15) collected was identified as **17c:** yield 0.004 g (1%); mp 83–86 °C.

Treatment of *N*-Methyl-*N'*-acetylimidazolidinethione (4c) with Diphenylketene (6c). Treatment of 0.50 g (0.0032 mol) of **4c** with 0.62 g (0.0032 mol) of **6c** according to the above procedure gave a solid residue. NMR analysis of the reaction mixture indicated that approximately 65% of the starting material had been converted to product. The residue was triturated with refluxing pentane (25 mL) and then the remaining solid reprecipitated from carbon tetrachloride–hexanes to give 0.13 g (29%) of **3c:** mp 79–80 °C (lit.[7] mp 77.5–78.5 °C).

The yellow crystalline material which was observed upon completion of the reaction was dried in vacuo and identified as **20:** yield 0.43 g (64%); mp 263–264 °C (lit.[24] mp 263 °C); IR (KBr) 1587, 1565, 1495, 1442 cm^{-1}.

Treatment of *N*-Methyl-*N'*-carbomethoxyimidazolidinethione (4d) with Diphenylketene (6c). Utilizing the above procedure, 0.56 g (0.0029 mol) of **6c** was added to 0.50 g (0.0029 mol) of **4d.** NMR analysis of the reaction mixture indicated that the reaction was approximately 85% complete. Concentration of the solvent, followed by trituration with refluxing pentane (25 mL), gave a solid which was recrystallized with Et_2O and identified as **3d:** yield 0.23 g (51%); mp 56–58 °C (lit.[8] mp 56–59 °C).

The yellow precipitate that was initially observed when the reaction vessel was opened was identified as **20:** yield 0.89 g (74%); mp 263–264 °C (lit.[24] mp 263 °C).

Treatment of 17b with Piperidine (18). Freshly distilled **18** (0.009 mL, 0.091 mmol) was added to a CH_2Cl_2 solution (15 mL) containing **17b** (0.0500 g, 0.091 mmol). Although the reaction appeared to be complete within 15 min (TLC), it was allowed to stir at room temperature for 48 h. The solution was then concentrated in vacuo and then the residue was chromatographed on a thick-layer silica gel plate using CH_2Cl_2 as the eluent. The first zone (R_f 0.43) isolated yielded 0.0222 g (44%) of starting material **17b:** mp 123–126 °C.

The second fraction isolated (R_f 0.21) was collected and reprecipitated from chloroform–hexanes to give 0.0253 g (0.091 mmol) of **19:** mp 117–118 °C (lit.[18] mp 117–118 °C); IR (KBr) 1645, 1500 cm^{-1}; NMR ($CDCl_3$) δ 1.10–1.83 (m, 6 H), 3.26–3.76 (m, 4 H), 5.23 (s, 1 H), 7.30 (s, 10 H); MS *m/e* (rel %) 279 (3), 167 (9), 166 (5), 165 (12), 113 (7), 112 (100), 84 (5).

The third zone (R_f 0.10) collected was recrystallized from CCl_4 and identified as **4b:** yield 0.0075 g (50%); mp 156–158 °C (lit.[4] mp 156–158 °C).

Treatment of *N*-Carbomethoxy-*N'*-diphenylacetylimidazolidinethione (16b) with Piperidine (18). The preceding reaction was repeated using 0.056 mL (0.566 mmol) of **18** and 0.20 g (0.565 mmol) of **16b** in dimethoxyethane (10 mL). Although the reaction appeared to be complete within 15 min, the solution was allowed to stir at room temperature for 2 h. The solution was then concentrated in vacuo and the residue was chromatographed on a thick-layer silica gel plate using CH_2Cl_2 as the eluent (triple elution). The first zone (R_f 0.58) was isolated and reprecipitated from carbon tetrachlo-

ride–hexanes to give 0.1223 g (78%) of **19:** mp 117–118 °C (lit.[18] mp 117–118 °C).

The second fraction (R_f 0.49) was collected and reprecipitated from carbon tetrachloride–hexanes to yield 0.0292 g (17%) of **16c:** mp 181–182 °C.

The third zone (R_f 0.14) collected was recrystallized from CCl_4 and identified as **4b:** yield 0.0742 g (82%); mp 156–158 °C (lit.[4] mp 156–158 °C).

Reaction of the Sodium Salt of N-Acyl-Substituted Imidazolidones and Imidazolidinethiones with Diphenylketene. General Procedure. NaH (50% mineral oil dispersion) (1 equiv) was washed with DME and additional DME was added. The imidazolidone or imidazolidinethione was then cautiously added in small increments via a solid addition funnel and the mixture allowed to stir at room temperature for 3 h. Diphenylketene (**6c**) (1 equiv) in DME was then added and the mixture stirred at room temperature for 18 h. H_2O was then added and the mixture was diluted with Et_2O or CH_2Cl_2 and extracted with H_2O (4×). The organic layer was dried (Na_2SO_4) and concentrated in vacuo, and the residue was treated in the manner outlined below to give the observed products.

Treatment of the Sodium Salt of *N*-Acetylimidazolidone (21a) with Diphenylketene (6c). Utilizing the above procedure, **14c** was obtained in 70% yield (0.78 g) from 0.004 mol of **21a** and 0.78 g (0.004 mol) of **6c.** The residue was then triturated with CCl_4 (2 × 30 mL) and filtered and the solid was recrystallized from $CHCl_3$: mp 221–222 °C; IR ($CHCl_3$) 1735, 1675 cm^{-1}; NMR (Me_2SO-d_6) δ 3.05–4.06 (m, 4 H), 6.74 (broad s, 1 H), 7.34 (s, 10 H), 7.66 (broad s, 1 H); MS *m/e* (rel %) 280 (70), 194 (98), 167 (64), 166 (100), 165 (91), 152 (16).

Anal. Calcd for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99. Found: C, 72.77; H, 5.84; N, 10.01.

Treatment of the Sodium Salt of *N*-Carbomethoxyimidazolidone (21b) with Diphenylketene (6c). Using the above procedure, 0.39 g (0.002 mol) of **6c** was added to **21b** (0.002 mol). The residue obtained was triturated with CCl_4 (2 × 25 mL) and the CCl_4 layers were combined, dried (Na_2SO_4), and concentrated in vacuo. The solid was chromatographed on silica gel (10 g) using CH_2Cl_2–Et_2O (90:10) as the eluent. Only one major fraction was isolated, which was then reprecipitated from carbon tetrachloride–hexanes to give 0.10 g (15%) of **14b,** mp 141–142 °C.

The residue remaining from the CCl_4 trituration was recrystallized from $CHCl_3$ to give **14c:** yield 0.15 g (27%); mp 221–222 °C.

Treatment of the Sodium Salt of *N*-Acetylimidazolidinethione (22a) with Diphenylketene (6c). Treatment of 0.005 mol of **22a** with 0.97 g (0.005 mol) of **6c** according to the above procedure gave 1.10 g (67%) of **16a** after chromatography on silica gel (50 g) using CH_2Cl_2–Et_2O (90:10) as the eluent. Compound **16a** was recrystallized from CCl_4: mp 119–120 °C; IR (KBr) 1690 cm^{-1}; NMR ($CDCl_3$) δ 2.74 (s, 3 H), 3.72–3.92 (m, 4 H), 7.28 (s, 10 H), 7.55 (s, 1 H); MS *m/e* (rel %) 338 (34), 295 (8), 194 (100), 167 (63), 166 (84), 165 (92), 158 (28).

Anal. Calcd for $C_{19}H_{18}N_2O_2S$: C, 67.43; H, 5.36; N, 8.28. Found: C, 67.31; H, 5.30; N, 8.25.

Treatment of the Sodium Salt of *N*-Carbomethoxyimidazolidinethione (22b) with Diphenylketene (6c). Addition of 3.88 g (0.02 mol) of **6c** to 0.02 mol of **22b** according to the above procedure gave a mixture of products which was separated by chromatography (silica gel, 120 g) using CH_2Cl_2 as the eluent. Three compounds were isolated. The first eluted material (0.20 g) was tentatively identified as **23:** yield 2%; mp 54–55 °C; IR (KBr) 1690 (broad), 1670 (broad) cm^{-1}; NMR ($CDCl_3$) δ 3.94 (s, 2 H), 7.24 (s, 10 H), 7.45 (s, 1 H); MS *m/e* (rel %) 490 (6), 295 (10), 194 (27), 181 (55), 164 (50), 151 (9), 104 (100), 76 (80).

The second material eluted from the column was the major fraction. Recrystallization from CCl_4 gave 3.40 g (48%) of **16b:** mp 146–147 °C; IR (KBr) 1740, 1680 cm^{-1}; NMR ($CDCl_3$) δ 3.80 (s, 3 H), 3.80–4.10 (m, 4 H), 7.25 (s, 10 H), 7.70 (s, 1 H); MS *m/e* (rel %) 354 (15), 194 (100), 166 (67), 165 (73), 160 (12), 152 (8).

Anal. Calcd for $C_{19}H_{18}N_2O_3S$: C, 64.38; H, 5.12; N, 7.90. Found: C, 64.46; H, 5.10; N, 7.83.

The last compound obtained from the column was identified as **16c.** Reprecipitation of this solid from chloroform–hexanes gave 0.15 g (3%) of purified compound: mp 183–184 °C; IR (KBr) 1650 cm^{-1}; NMR (Me_2SO-d_6) δ 3.28–4.43 (m, 4 H), 7.12–7.46 (m, 10 H), 8.05 (s, 1 H), 9.95 (broad s, 1 H). Upon addition of D_2O to the NMR sample the broad singlet at δ 9.95 disappeared. MS *m/e* (rel %) 296 (39), 194 (77), 167 (75), 166 (87), 165 (100), 152 (19), 129 (20).

Anal. Calcd for $C_{17}H_{16}N_2OS$: C, 68.89; H, 5.44; N, 9.45. Found: C, 68.87; H, 5.43; N, 9.32.

Preparation of *N*-Diphenylacetyl-*N'*-carbomethoxyimidazolidinethione (16b). To a stirred CH_2Cl_2 solution (30 mL) containing **4b** (0.80 g, 0.005 mol) and pyridine (0.48 g, 0.006 mol), diphenylacetyl chloride[23] (1.38 g, 0.006 mol) was slowly added. The solution was stirred at room temperature overnight and then washed with H_2O (2 × 25 mL), dried (Na_2SO_4), and evaporated in vacuo. Purification of the desired compound was accomplished by recrystallization from CCl_4: yield 1.40 g (79%); mp 146–147 °C.

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Registry No.—**3a,** 5391-39-9; **3b,** 41730-78-3; **3c,** 61076-68-4; **3d,** 61076-69-5; **4a,** 5391-52-6; **4b,** 59863-98-8; **4c,** 60546-76-1; **4d,** 60546-78-3; **5,** 4795-59-9; **6a,** 463-51-4; **6b,** 684-22-0; **6c,** 525-06-4; **7a,** 67845-07-2; **7b,** 67845-08-3; **8a,** 67845-09-4; **8b,** 67845-10-7; **9a,** 5391-53-7; **9b,** 61076-72-0; **10a,** 61709-50-0; **10b,** 61687-02-3; **11a,** 61709-51-1; **11b,** 61687-03-4; **12,** 67845-11-8; **13,** 7445-61-6; **14a,** 67845-12-9; **14b,** 61687-04-5; **14c,** 67845-13-0; **15,** 67849-33-0; **16a,** 67845-14-1; **16b,** 61687-05-6; **16c,** 67845-15-2; **17a,** 67845-16-3; **17b,** 67845-17-4; **17c,** 67845-18-5; **18,** 110-89-4; **19,** 4107-00-0; **20,** 54191-85-4; **21a,** 67845-19-6; **21b,** 67845-20-9; **22a,** 67845-21-0; **22b,** 67845-22-1; **23,** 67845-23-2.

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Studies on the Reaction of Thiocarbonyl-Containing Compounds with Ketenes[1]

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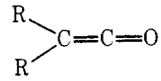
The reactivity of thiocarbonyl-containing compounds with bis(trifluoromethyl)ketene (**1b**) and diphenylketene (**1c**) has been investigated. Replacement of the sulfur atom at the thione position by an oxygen atom was observed for *N*-(diphenylacetyl)-*N'*-carbomethoxyimidazolidinethione (**2a**), 1,3-diethyl-2-thiobarbituric acid (**3a**), and *N*-methylbenzothiazole-2-thione (**4a**) with ketene **1b**. A similar reaction was observed for thione **4a** and *N*-methyl-*N'*-carbomethoxybenzimidazole-2-thione (**10a**) with ketene **1c**. However, treatment of N–H substituted thiones [2-mercaptobenzimidazole (**11a**), 2-mercaptobenzothiazole (**12a**), and *N*-methyl-2-mercaptobenzimidazole (**13a**)] with **1c** led to the formation of 4:1, 2:1, and 1:1 adducts. In these cases, reaction occurred at the nitrogen site. Addition of **1c** to either ethylene trithiocarbonate (**6**) or *N,N*-dimethylthioformamide (**15**) gave the corresponding alkenes **16** and **17** along with COS. Finally, treatment of thiobenzophenone (**7**) and 4,4'-dimethoxythiobenzophenone (**8**) with ketene **1c** gave the corresponding β-thiolactones **20** and **21**, respectively. These two compounds have been incorrectly assigned by previous workers as the isomeric thietanones **23** and **24**.

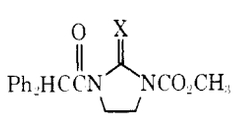
In the preceding paper we reported on the reactivity of acyl-substituted imidazolidones and imidazolidinethiones with ketenes **1a–c**.[3] Significantly, with *N,N'*-disubstituted imidazolidinethiones a novel S→O replacement reaction occurred at the thione position in high yields with ketenes **1b** and **1c**. The reactivity of thiocarbonyl containing compounds with ketenes has not been extensively investigated.[4] We have, therefore, tested the generality of this unique substitution reaction for thiones of varying structure with both **1b** and **1c**.



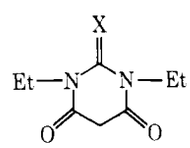
1a, R = H
b, R = CF_3
c, R = Ph

Three types of reactions have been detected. The results of this investigation are reported in the present paper.

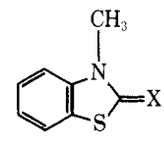
Bis(trifluoromethyl)ketene (1b) Reactions with Thiones. Compounds **2–7** were each treated with 1.1 equiv of ketene **1b**[5] at 60 ± 2 °C. No attempt was made to optimize yields due to the limited supply of the ketene. In only three cases was reaction noted. Thiones **2a**,[3] **3a**, and **4a** gave the S→O replacement products **2b**,[3] **3b**,[6] and **4b**[7] in 100, 43, and 30% yields, respectively. A mechanism similar to the one previously postulated[3] can be drawn for these reactions.



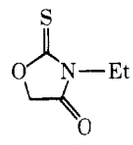
2a, X = S
b, X = O



3a, X = S
b, X = O



4a, X = S
b, X = O



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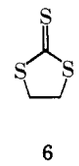

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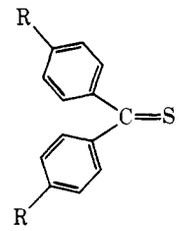
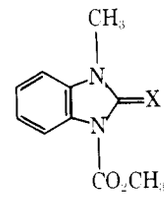


7, R = H
8, R = OMe
9, R = NMe_2



10a, X = S
b, X = O

Diphenylketene (1c) Reactions. The accessibility of diphenylketene[8,9] (**1c**) coupled with our earlier observations[3] prompted us to examine the reactivity of **1c** with a series of thiones. Treatment of *N*-methyl-*N'*-carbomethoxybenzimidazole-2-thione (**10a**) and *N*-methylbenzothiazole-2-thione (**4a**) with **1c** for a period of 4 days at 60 ± 2 °C gave the carbonyl-containing compounds **10b** and **4b**[7] in moderate yield (54 and 20%, respectively). No reaction, however, was detected when thione **5** was treated with **1c**.

When, however, ketene **1c** was added to a thione which contained an active N–H proton flanking the thione group reaction occurred exclusively at the nitrogen site. Treatment of excess **1c** with **11a** and **12a** gave the 4:1 adduct **11b** and the 2:1 adduct **12b** in 74 and 76% yields, respectively. Correspondingly, a mixture of the 2:1 adduct **13b** (43%) as well as the 1:1 adduct **13c** (15%) was observed for the reaction of **13a**[10] with **1c**.

Partial support for the enol acetate structural assignment for these 2:1 and 4:1 adducts stemmed from a favorable comparison of their IR and ^1H NMR spectra with those adducts previously obtained from the reaction of ketene **1c** with imidazolidinethiones.[3] Notable similarities included the tentative assignment of the absorptions at ca. 1760 and 1650

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