Reaction of Ethyl β-Aminocrotonate with Trichloromethanesulfenyl Chloride

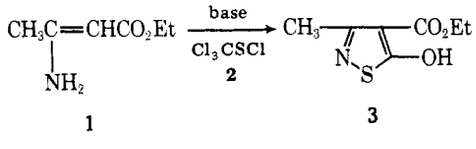
Robert K. Howe

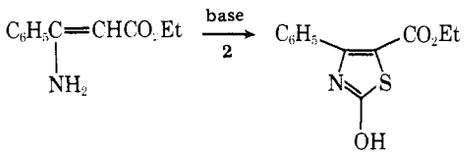
Research Department, Monsanto Agricultural Products Company, St. Louis, Missouri 63166

Received March 1, 1977

Reaction of ethyl β-aminocrotonate (1) with trichloromethanesulfenyl chloride (2) in ether or THF produced ethyl β-amino-α-(trichloromethylthio)crotonate (6) as the major product (70–79% yield). Hydrolysis of 6 in aqueous base resulted in a complex mixture in which ethyl 2-chloro-4-methyl-5-thiazolecarboxylate (8, 33% yield) and ethyl 2-hydroxy-4-methyl-5-thiazolecarboxylate (9, 27%) were the major products.

Synthesis of ethyl 5-hydroxy-3-methyl-4-isothiazolecarboxylate (3) in 30–40% yield from reaction of ethyl β-aminocrotonate (1) with trichloromethanesulfenyl chloride (2) in the presence of base was reported recently.[1] However, no physical properties were given for the product. Reaction of ethyl β-aminocinnamate with 2 in the presence of base produced ethyl 2-hydroxy-4-phenyl-5-carboxylate (4), identical

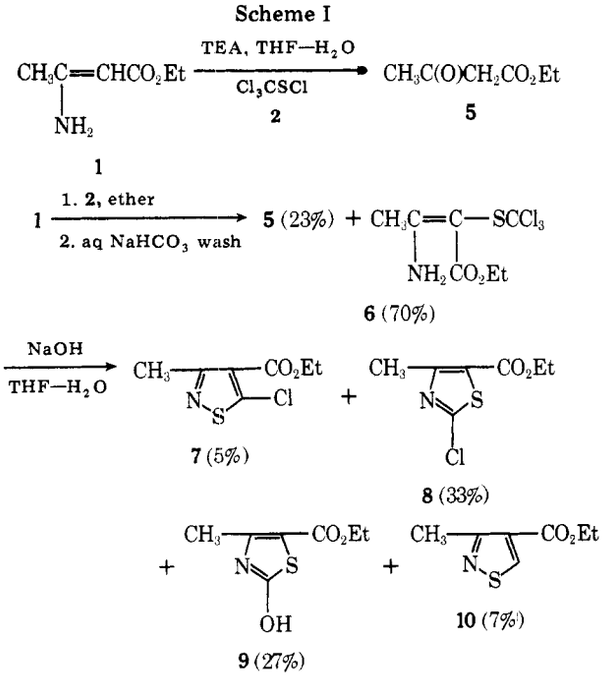




with authentic material prepared by another route.[2] Because of the apparent conflict in these results and because of our interest in isothiazoles,[3] we reinvestigated the first reaction.

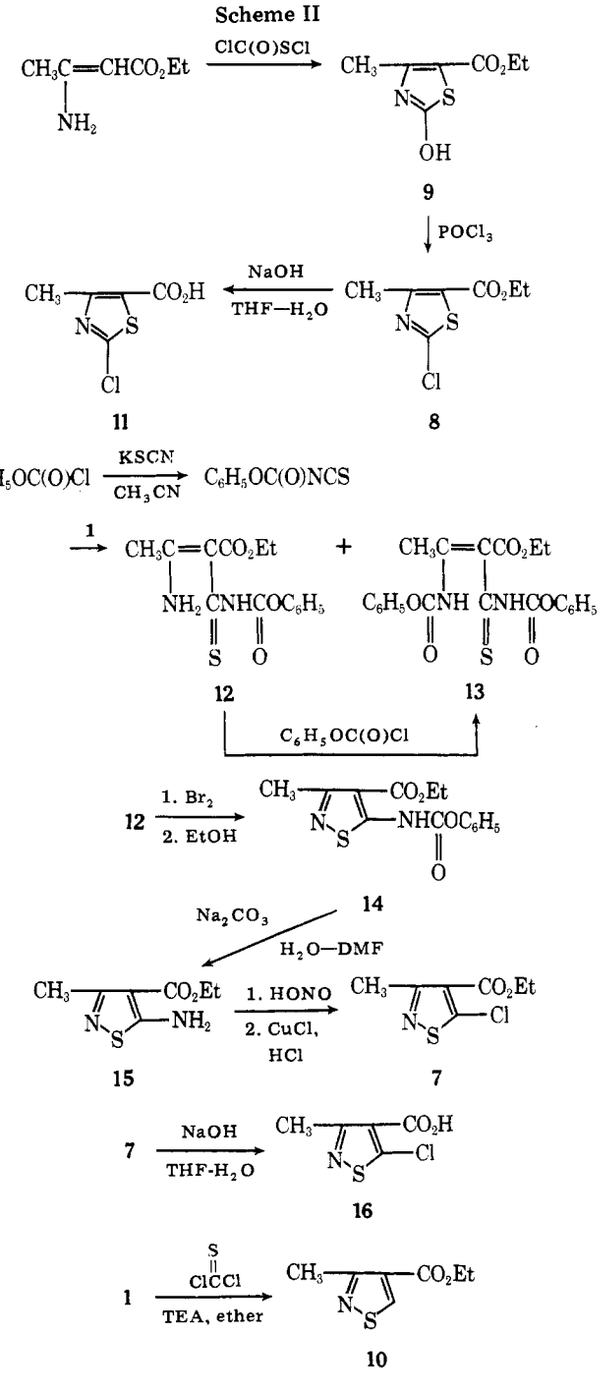
Addition of 2 to ethyl β-aminocrotonate and 4 equiv of triethylamine in aqueous THF at 0–5 °C led predominantly to ethyl acetoacetate (5) (Scheme I). Addition of 2 to 1 in ether

Scheme I

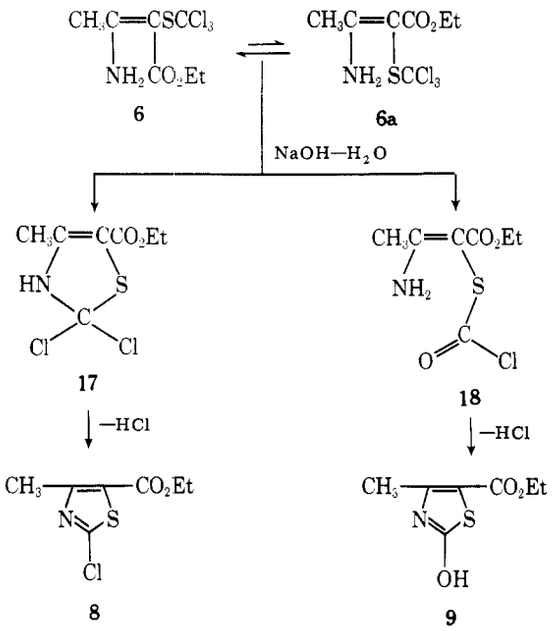


followed by an aqueous sodium bicarbonate wash gave 5 (23%) and ethyl β-amino-α-(trichloromethylthio)crotonate (6, 70%) with traces (ca. 1% each) of several other materials (NMR

Scheme II



Scheme III



analysis). Pure **6**, an unstable solid, was isolated in 24% yield and was completely characterized by elemental analysis, IR, ^{1}H NMR, and ^{13}C NMR spectra (see Experimental Section).

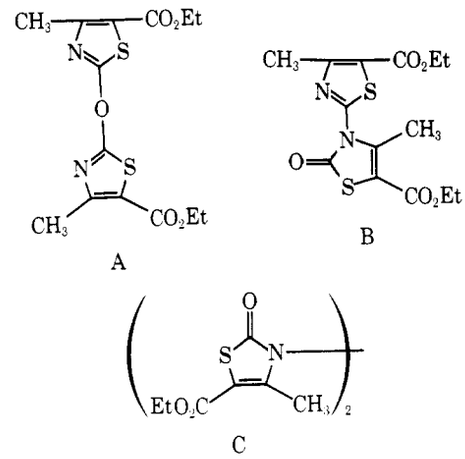
Hydrolysis of pure **6** in NaOH–H_2O–THF gave an ester mixture (Scheme I) that contained 5% of ethyl 5-chloro-3-methyl-4-isothiazolecarboxylate (**7**), 33% of ethyl 2-chloro-4-methyl-5-thiazolecarboxylate (**8**), 27% of ethyl 2-hydroxy-4-methyl-5-thiazolecarboxylate (**9**), 7% of ethyl 3-methyl-4-isothiazolecarboxylate (**10**), and at least three high-boiling materials with molecular weights of 356, 372, and 372, respectively. Pure **9** was isolated from the reaction mixture in 10% yield. Several hydrolysis experiments gave the same products, but their ratios varied, probably due largely to whether or not the THF and water layers were miscible (layer separation occurred in the 20–30 °C range) and to the particular concentrations employed.

Reaction of **2** with **1** in THF gave, after an aqueous sodium bicarbonate wash, mainly **6** (79%), with traces of other products that included **5** (4%) and **7** (6%). Hydrolysis with aqueous sodium hydroxide of the reaction mixture from treatment of **1** with **2** in THF led to a product mixture similar to that obtained from hydrolysis of pure **6**.

Product assays were performed by NMR, IR, GC–MS, and TLC analyses. Authentic samples of **7**,[4] **8**,[5] **9**,[6] and **10**[7] were prepared by literature procedures (Scheme II) to calibrate the GC–MS, NMR, TLC, and IR analyses. The procedure of Goerdeler and Horn[8] for preparation of **12** led to a mixture of **12** and **13** that had the properties reported[8] for **12**. In a separate experiment, pure **12** was converted to **13** with phenyl chloroformate. Mild hydrolysis of **8** and **7** gave **11**[9] and **16**,[4] respectively.

Quite evidently, the reaction of **6** with aqueous base is complex. The pathways for formation of **7** and **10** from **6** are unknown.[10] Certain major features are apparent, however. The predominant reaction of **1** with **2** occurs via attack of the sulfenyl chloride **2** on the α carbon of **1**, in accord with other studies[5,11] of reactions of sulfenyl chlorides with **1**. Based on the IR spectrum of **6**, which exhibits a hydrogen-bonded, conjugated carbonyl absorption at 6.07 μm, compound **6** exists mainly in the form with amino and carbethoxy groups cis to each other because of the stabilization due to intramolecular hydrogen bonding. Rotation about the double bond to give **6a** should be a facile process, however, and should occur at room temperature based on analogy with the reported[12,13] low barriers of rotation about the double bond for similar compounds. A competition exists between cyclization of **6** to **17** and partial hydrolysis to **18** (Scheme III). Compound **17** produces **8**, and **18** produces **9**. The hydrolysis of **8** to **11** (Scheme II) reveals that **8** is not a precursor of **9**. No evidence for formation of ethyl 5-hydroxy-3-methyl-4-isothiazolecarboxylate (**3**) was found.[14]

In regard to the high-boiling materials formed in the hydrolysis of **6**, the material with mol wt 356 had mass spectrum *m/e* (relative intensity; fragment) 356 (56.7, M^+), 357 (6.9 M^+ + 1), 358 (4.4, M^+ + 2), 311 (16.5, M^+ − OEt), 310 (41.8, M^+ − HOEt), 282 (100, M^+ − HOEt − CO), indicative of a structure containing an even number of nitrogen atoms, two sulfur atoms, and no chlorine atoms; this material might be either A or B, arising from reaction of the sodium salt of **9** with **8**. The materials with mol wt 372 remain unidentified, although in the mass spectrum of one of them the M^+ = 372 peak (rel intensity 35.3) and the M^+ + 2 = 374 peak (rel intensity 3.2) suggest a structure containing a even number of nitrogen atoms, two sulfur atoms, and no chlorine atoms, corresponding in gross features to a structure such as C. Formation of C conceivably could occur by N-chlorination of **9** and reaction of the *N*-chloro compound with the anion of **9**.



The source of chlorine or hypochlorite anion required in this process could arise from an intermediate that ultimately produces **10**.[10]

Experimental Section

Ethyl β-Amino-α-(trichloromethylthio)crotonate. To a solution of 12.9 g (0.10 mol) of ethyl β-aminocrotonate in 100 mL of ether was added dropwise, during 60 min with stirring at −5 to 0 °C, 18.6 g (0.10 mol) of trichloromethanesulfenyl chloride in 25 mL of ether under dry N_2. A white precipitate formed. The mixture was stirred at 0–15 °C for 2.5 h and then was extracted with 0.20 mol of $NaHCO_3$ in 150 mL of cold water. The ether layer was dried ($CaSO_4$) and concentrated under aspirator vacuum (<30 °C) to give 23.4 g of oil that contained 70% of product **6** and 23% of ethyl acetoacetate, with traces (ca. 1% each) of at least three other materials (NMR analysis). The oil was triturated with 450 mL of hexane; the supernatant was decanted from a little insoluble black oil, treated with a little charcoal, filtered, and seeded to give 5.15 g of beige solid, mp 83–84.5 °C dec. The filtrate was cooled to −30 °C for a second crop of 3.2 g of solid, mp 78–80 °C; two rapid recrystallizations of this solid from hexane gave 1.5 g of solid, mp 83–84.5 °C. The combined yield was 23.9%.

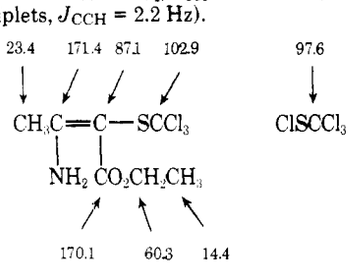
Recrystallization of 1.0 g of the beige product from hexane (charcoal) gave 0.75 g of white solid: mp 83–84.5 °C dec; IR (mineral oil mull) 2.85, 3.02 (NH_2), 6.07 (conjugated H-bonded C=O), 6.23 μm (C=C); ^{1}H NMR ($CDCl_3$) δ 9.60 (br s, 1, NH), 5.63 (br s, 1, NH), 4.20 (q, 2, OCH_2), 2.43 (s, 3, CH_3), 1.27 (t, 3, CH_3). The ^{13}C NMR spectrum of **6** in $CDCl_3$ was determined with a JEOL FX-100 spectrometer, using 8K data points plus 8K data point zero fill over a spectral width of 6024 Hz, a pulse width of 2 μs (18°), and a pulse repetition time of 0.8 s. Completely decoupled, off-resonance, and fully coupled spectra were obtained; the following spectral data are for the fully coupled

Table I. Methyl Resonances in $CDCl_3$[a]

Compd	Registry no.	CH_3, δ, ppm
1	7318-00-5	1.88
5	141-97-9	2.25[b]
6	63089-24-7	2.43
7	22131-53-9	2.63
8	7238-62-2	2.67
9	40235-78-7	2.47
10	15901-51-6	2.72

[a] EM-360 spectrometer. [b] CH_2 at δ 3.47.

spectrum of **6:** δ 171.4 (q, J_{CCH} = 5.4 Hz), 170.1 (t, J_{COCH} = 2.9 Hz), 102.9 (s), 87.1 (q, $J_{CCH} \simeq$ 3 Hz), 60.3, (t, J_{CH} = 147.1 Hz, of small quartets, J_{CCH} = 4.4 Hz), 23.4 (q, J_{CH} = 129.4 Hz), 14.4 (q, J = 127.2 Hz, of small triplets, J_{CCH} = 2.2 Hz).



Anal. Calcd for $C_7H_{10}Cl_3NO_2S$: C, 30.18; H, 3.62; Cl, 38.18; N, 5.03; S, 11.51. Found: C, 30.21; H, 3.61; Cl, 37.93; N, 4.96; S, 11.48.

Reaction of 1 and 2 in THF. To a solution of 12.9 g (0.10 mol) of ethyl β-aminocrotonate in 100 mL of THF was added dropwise, with stirring at 0–5 °C, 18.6 g (11.0 mL, 0.10 mol) of trichloromethanesulfenyl chloride during 20 min. The cloudy mixture was stirred at 0–10 °C for 3 h. An aliquot withdrawn after this time, diluted with CH_2Cl_2, washed with ice cold $NaHCO_3$ solution, dried ($CaSO_4$), and concentrated under vacuum gave a mixture that NMR analysis indicated to contain 79% of **6,** 6% of **7,** 4% of **5,** and <1% of **8,** with other minor components below the 4% level; GC–MS data obtained on the solution confirmed the presence of **7.**

Hydrolysis of 6. To a solution of 5.1 g (0.0183 mol) of ethyl β-amino-α-(trichloromethylthio)crotonate (**6**) in 50 mL of THF was added dropwise a solution of 2.2 g (0.0549 mol, 3 equiv) of NaOH in 50 mL of water with stirring at 10–20 °C during 30 min. The mixture was stirred at 20–30 °C for 24 h (pH at 7 after this time), acidified with a few milliliters of concentrated HCl, and extracted with two 50-mL portions of $CHCl_3$. The chloroform layers were combined, dried ($CaSO_4$), and concentrated under vacuum to 50 °C at 11 Torr to give 3.8 g of semisolid. NMR analysis of this material indicated it to contain 33% of **8,** 5% of **7,** 27% of **9,** and 7% of **10.** GC–MS data confirmed the presence of these components, and in addition showed the presence of at least three high-boiling, minor components with molecular weights of 356, 372, and 372. Trituration of the semisolid with 20 mL of ether gave 0.4 g of solid, mp 160–170 °C. Recrystallization of the solid gave 0.34 g (10%) of solid **9,** mp 175.5–177.5 °C (lit.[5] mp 177–178 °C), identical with authentic **9** based on mixture melting point and IR and NMR spectral data.

Ethyl 2-Hydroxy-4-methyl-5-thiazolecarboxylate (9). Use of the procedure of Grohe and Heitzer[5] led to product, mp 167–172 °C, in 60% yield. Recrystallization of the product from benzene gave pure product, mp 176–178 °C (lit.[5] mp 177–178 °C), in 40% yield. This material was identical in all respects with an authentic sample prepared from reaction of ethyl 2-chloroacetoacetate and ammonium thiolcarbamate.[6]

Ethyl 2-Chloro-4-methyl-5-thiazolecarboxylate (8). Use of the procedure of Ganapathi and Venkataraman[6] led to the desired product, mp 46–47.5 °C (lit.[6] mp 48–51 °C) in 91% yield. Recrystallization of a 2.0-g sample from cold ethanol gave 1.0 g of white solid, mp 47–48 °C.

Ethyl β-Amino-α-[*N*-(phenoxycarbonyl)thiocarbamoyl]-crotonate (12) and Ethyl β-(Phenoxycarbonylamino)-α-[*N*-(phenoxycarbonyl)thiocarbamoyl]crotonate (13). The procedure of Goerdeler and Horn[8] was employed. A mixture of 43 g (0.275 mol) of phenyl chloroformate and 25.8 g (0.26 mol) of potassium thiocyanate in 75 mL of CH_3CN was stirred at 10–15 °C for 25 min. Then, a solution of 32.75 g (0.25 mol) of ethyl β-aminocrotonate in 50 mL of CH_3CN was added during 15 min with vigorous stirring at 10 °C. The mixture was then stirred for 30 min without cooling and was poured into 1.5 L of water. The resultant mixture was stirred for 1.5 h, and the supernatant was decanted from a viscous oil. The oil was dissolved in 500 mL of benzene, and the solution was filtered through benzene-prewet filter paper and concentrated under vacuum to a semisolid. Trituration of the semisolid with 150 mL of ethyl acetate at 5 °C gave 10.9 g of yellow solid, mp 132–133 °C dec (lit.[8] mp 130 °C dec for **12**), which was found to be a mixture of 92% of **13** and 8% of **12** by NMR analysis. Recrystallization of this solid from ethyl acetate (minimum heating time) gave 4.5 g of yellow solid, mp 146.5–147.5 °C, that was pure **13** (NMR analysis): IR (mineral oil mull) 3.1, 5.66, 5.76, 5.98, 6.16 μm; NMR ($CDCl_3$) δ 11.70 (br s, 1, NH), 9.60 (br s, 1, NH), 7.33 (m, 10, ArH), 4.30 (q, 2, OCH_2) 2.53 (s, 1, CH_3), 1.28 (t, 3, CH_3).

Anal. Calcd for $C_{21}H_{20}N_2O_6S$: C, 58.86; H, 4.70; N, 6.53; S, 7.48. Found: C, 58.68; H, 4.65; N, 6.36; S, 7.10.

Concentration of the first ethyl acetate filtrate and crystallization of the residue from 50 mL of benzene gave 16.2 g of yellow solid, mp 112–114 °C, that was pure **12** (NMR analysis): IR (mineral oil mull) 2.97, 3.01, 5.70, 6.00, 6.07, 6.20 μm; NMR ($CDCl_3$) δ 10.0 (br s, 1, NH), 9.8–6.3 (v br, 2, NH_2), 7.30 (m, 5, ArH), 4.23 (t, 2, OCH_2), 2.32 (s, 1, CH_3), 1.20 (t, 3, CH_3).

A modification of the procedure of Goerdeler and Horn[8] was employed in another experiment. A mixture of 78.3 g (0.50 mol) of phenyl chloroformate and 48.6 g (0.50 mol) of powdered potassium thiocyanate in 150 mL of acetonitrile was stirred under N_2 at 10–15 °C for 30 min. Then, a solution of 65.0 g (0.502 mol) of ethyl β-aminocrotonate in 100 mL of acetonitrile was added with stirring during 1 min at −7 to 6 °C (ice–methanol bath). After another minute, the mixture was stirred for 1 h without cooling and then was poured into 1.5 L of water. The mixture was allowed to stand 1 h, and the aqueous supernatant was decanted from a thick oil. The oil was triturated well with two 300-mL portions of water to give a semisolid. This material was dissolved in $CHCl_3$, and the solution was dried ($CaSO_4$) and concentrated under vacuum (<40 °C). The residue, 153.2 g of red-orange oil, consisted of an 84:16 mixture of **12** and **13,** with traces of ethyl β-aminocrotonate and ethyl acetoacetate. Dilution of the residue with 300 mL of benzene and seeding with **12** resulted in crystallization of 27.6 g of pure **12,** mp 105–108 °C. Addition of 100 mL of hexane to the filtrate resulted in 15.8 g of 96% pure **12,** mp 98–104 °C. Addition of 200 mL of hexane to the last filtrate gave an oil. Trituration of the oil with 100 mL of ethyl acetate gave 6.0 g of solid, mp 129–131 °C dec, that consisted of 87% of **13** and 13% of **12.** Concentration of the last hexane filtrate and trituration of the residue with 100 mL of ethyl acetate gave 5.8 g of solid, mp 109–112 °C, that was 93% pure **12.** A total of 52.2 g of fairly pure **12** was obtained (34% yield).

Preparation of 13 from 12. To 1.50 g (5.0 mmol) of pure **12** in 25 mL of acetonitrile was added 0.78 g (5.0 mmol) of phenyl chloroformate. After 18 h, a solid had formed. The mixture was diluted with 100 mL of water and filtered to give 1.7 g (81% yield) of yellow solid **13,** mp 137–139 °C dec, that contained no residual **12.** The IR and NMR spectra of this material were identical with those of the by-product **13** isolated in the proceeding experiment. Crystallization of the 1.7 g of solid from 20 mL of benzene gave 0.95 g of solid, mp 148–149 °C dec.

Ethyl 3-Methyl-5-(phenoxycarbonylamino)-4-isothiazolecarboxylate (14). The procedure of Goerdeler and Horn[8] was employed. Pure product, mp 79–80 °C (lit.[8] mp 81 °C), was obtained in 76% yield.

Ethyl 5-Amino-3-methyl-4-isothiazolecarboxylate (15). The procedure of Goerdeler and Horn[8] was employed. The work-up procedure was modified, however. The crude solid isolated according to Goerdeler and Horn was extracted alternatively with $CHCl_3$ and water until almost all of it dissolved. The aqueous extracts were combined and extracted with $CHCl_3$. All the $CHCl_3$ layers were combined, dried ($CaSO_4$), and concentrated under vacuum to 12.1 g (85% yield) of solid, mp 114–115 °C (lit.[8] mp 113.5 °C).

Ethyl 5-Chloro-3-methyl-4-isothiazolecarboxylate (7). The procedure of Machón[4] was employed. The crude product before distillation was obtained in 55% yield and was found by GC analysis to consist of 90% of **7** and 10% of ethyl 3-methyl-4-isothiazolecarboxylate (**10**). Distillation of the 7.3 g of crude product gave three fractions: (1) 2.35 g of liquid, bp 99–101 °C (5 Torr), 84% of **7** and 16% of **10;** (2) 2.00 g of liquid, bp 101–103 °C (5 Torr), mp 22–25 °C, 93% of **7** and 7% of **10;** (3) 0.75 g of liquid , bp 103 °C (5 Torr), mp 20–23 °C, 90% pure **7** [lit.[4] bp 77 °C (3 Torr)].

2-Chloro-4-methyl-5-thiazolecarboxylic Acid (11). Solutions of 1.0 g (0.00488 mol) of ethyl 2-chloro-4-methyl-5-thiazolecarboxylate in 10 mL of THF and 0.2 g (0.005 mol) of NaOH in 20 mL of water were stirred together for 30 h. The solution was acidified with dilute HCl and was extracted twice with $CHCl_3$. The $CHCl_3$ extracts were

combined, dried ($CaSO_4$), and concentrated under vacuum to 0.80 g of white solid, mp 150–155 °C dec, which was shown by IR and NMR analysis to be **11**. Recrystallization of the solid from benzene gave 0.50 g of white solid, mp 154–155 °C (lit.[9] mp 144–148 °C dec).

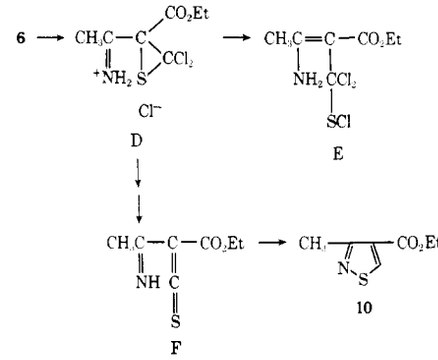
5-Chloro-3-methyl-4-isothiazolecarboxylic Acid (16). Solutions of 1.0 g (0.00486 mol) of 93% pure ethyl 5-chloro-3-methyl-4-isothiazolecarboxylate (containing 7% of ethyl 3-methyl-4-isothiazolecarboxylate) in 50 mL of THF and 1.1 g (0.0225 mol) of NaOH in 50 mL of water were stirred together for 24 h. The solution was acidified strongly with dilute HCl and extracted with three 75-mL portions of ether. The ether layers were combined, dried ($CaSO_4$), and concentrated under vacuum to 0.85 g of white solid, mp 199–205 °C, that consisted of 94% of **16** and 6% of 3-methyl-4-isothiazolecarboxylic acid (NMR analysis in basic D_2O). Crystallization of the solid from 1,2-dichloroethane gave 0.60 g of solid, mp 205–206.5 °C (lit.[4] mp 205–207 °C).

Ethyl 3-Methyl-4-isothiazolecarboxylate (10). Treatment of ethyl β-aminocrotonate with triethylamine and thiophosgene according to a literature procedure,[7a] followed by redistillation of the product thus obtained, gave pure **10**, bp 71–72 °C (1.5 Torr) [lit.[7c] bp 102–103 °C (8 Torr)].

Registry No.—**2**, 2757-23-5; **12**, 63089-25-8; **13**, 63089-26-9; **16**, 22131-56-2; phenyl chloroformate, 1885-14-9; potassium thiocyanate, 333-20-0; 3-methyl-4-isothiazolecarboxylic acid, 15903-66-9.

References and Notes

(1) J. A. Waite and K. R. H. Wooldridge, *Tetrahedron Lett.*, 327 (1972).
(2) R. R. Crenshaw, J. M. Essery, and A. T. Jeffries, *J. Org. Chem.*, **32**, 3132 (1967).
(3) R. K. Howe and J. E. Franz, *J. Chem. Soc., Chem. Commun.*, 524 (1973).
(4) Z. Machón, *Diss. Pharm. Pharmacol.*, **21**, 135 (1969).
(5) K. Grohe and H. Heitzer, *Justus Liebigs Ann. Chem.*, 1018 (1973).
(6) K. Ganapathi and A. Venkataraman, *Proc. Indian Acad. Sci., Sect. A*, **22**, 362 (1945); *Chem. Abstr.*, **40**, 4059 (1946).
(7) (a) U.S. Patent 3 403 209 (1968); (b) R. B. Woodward, *Harvey Lect.*, **59**, 34–37 (1965); (c) D. Buttimore, D. H. Jones, R. Slack, and K. R. H. Wooldridge, *J. Chem. Soc.*, 2032 (1963).
(8) J. Goerdeler and H. Horn, *Chem. Ber.*, **96**, 1551 (1963).
(9) *Beilstein*, **27**, 316.
(10) Several mechanistic possibilities can be postulated starting, for example, with D and E, but the mechanisms are so highly speculative that we prefer not to dignify them with enumeration. Along these speculative lines, dechlorination and dehydrochlorination of D or an intermediate (other than E) formed from D could lead to F and thus **10**. Species F is probably an intermediate in the reaction[7] of thiophosgene with **1** to produce **10**.



(11) R. Gompper, H. Euchner, and H. Kast, *Justus Liebigs Ann. Chem.*, **675**, 151 (1964).
(12) A. Mannschreck and U. Koelle, *Tetrahedron Lett.*, 863 (1967).
(13) Y. Shvo, E. C. Taylor, and J. Bartulin, *Tetrahedron Lett.*, 3259 (1967).
(14) Dr. Waite has acknowledged in a most cordial fashion that their structure assignment[1] for **3** rested strongly on analogies[1] and that, in light of the present work, the material that they isolated must have been **9**, the product that we obtained [J. A. Waite, private communication].

Reductive Sulfenylation. A General Method for the α-Sulfenylation of Cyclic Ketones

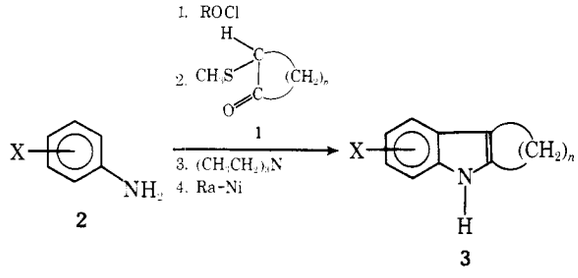
Paul G. Gassman,* David P. Gilbert, and Susan M. Cole[1]

Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455

Received March 15, 1977

A general method has been developed for the reductive sulfenylation of cyclic α,β-unsaturated ketones. Sulfenylation with dimethyl disulfide has been shown to occur by preferential pseudoaxial attack on the intermediate enolate anions. The regiospecificity and preferential pseudoaxial attack were established by a combination of NMR and circular dichroism studies.

As part of our general program of exploring the scope and utility of our versatile indole synthesis,[2] and in anticipation of our utilization of this process in the preparation of polycyclic natural product intermediates, we found ourselves in need of highly specific methods for the addition of an α-methylthio function to a variety of cyclic ketones. The availability of cyclic ketones of general formula **1** would permit the conversion of anilines of general formula **2** into indoles of general formula **3** according to the procedure outlined. Thus,



we had a particular interest in regiospecifically methylsulfenylating cyclic ketones. While a variety of methods have appeared in the literature for the sulfenylation of ketones,[2–5] most of these methods can be traced back to the initial functionalization of a mixture of the thermodynamically most stable enolate anion[2,3] or enol form of the ketonic precursor[4,5] and the thermodynamically less stable enolate or enol form. This provides little control over regiospecificity. In view of the regiospecificity attained in the reductive alkylation of α,β-unsaturated ketones,[6] we investigated the sulfenylation of lithium enolates generated from the lithium in liquid ammonia reduction of α,β-unsaturated ketones. We now wish to report that the reductive sulfenylation of α,β-unsaturated ketones is a useful method for the regiospecific introduction of the thiomethoxyl moiety.

In a general procedure, a solution of 1 equiv of α,β-unsaturated ketone and 1 equiv of *tert*-butyl alcohol in ether was added to a solution of 2.2 equiv of lithium in liquid ammonia. After 1 h, 1 equiv of dimethyl disulfide was added and allowed to react, and the product was isolated. In this way, **4** could be