Reactions of (Chlorocarbonyl)phenylketene. Formation of Ring-Fused 4*H*-1,3-Thiazinium Betaines from Heterocyclic Thiones[1a]

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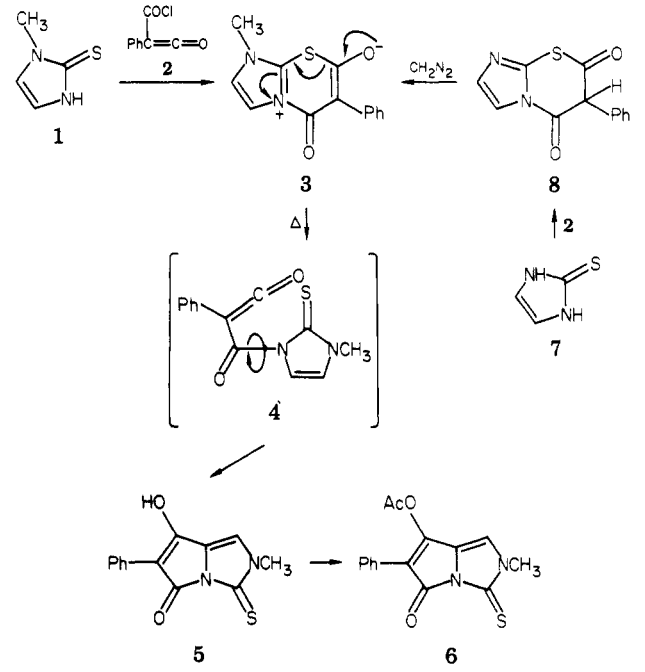
Received January 28, 1980

The betaine *anhydro*-2-hydroxy-8-methyl-4-oxo-3-phenyl-4*H*-imidazo[2,1-*b*][1,3]thiazinium hydroxide, formed from 1-methyl-2(3*H*)-imidazolethione and (chlorocarbonyl)phenylketene, underwent thermal rearrangement (220 °C) to 2,3-dihydro-7-hydroxy-2-methyl-5-oxo-6-phenyl-5*H*,3(2*H*)-pyrrolo[1,2-*c*]imidazolethione, a process involving an initial fission of the 1,2-bond and electrophilic ring closure of the resultant ketene intermediate onto the 4-position of the imidazole nucleus most likely being involved in the rearrangement. In support of this hypothesis a group of structurally related betaines derived from the (chlorocarbonyl)phenylketene and 1-methyl-5-phenyl-2-(3*H*)-imidazolethione, 1-methyl-2(3*H*)-imidazolinethione, 4-methyl-5-phenyl-3(2*H*)-1,2,4-triazolethione, and 1-methyl-5(4*H*)-tetrazolethione was found to be thermally stable as was *anhydro*-7-hydroxy-8-methyl-5-oxo-6-phenyl-5*H*-thiazolo[3,2-*a*]pyrimidinium hydroxide derived from 2-(methylamino)thiazole. 2(3*H*)-Benzothiazolethione, 2(3*H*)-benzoxazolethione, 1-methyl-2(3*H*)-benzimidazolethione, and 2-(methylamino)benzothiazole underwent reaction with (chlorocarbonyl)phenylketene in anhydrous solvents to give the appropriate tricyclic heteroaromatic betaine containing a 1,3-thiazinium nucleus. These betaines also exhibited thermal stability, and *anhydro*-2-hydroxy-4-oxo-3-phenylbenzo[*b*]-4*H*-thiazolo[2,3-*b*][1,3]thiazinium hydroxide underwent cycloaddition with acetylenic dipolarophiles to give, e.g., dimethyl 1-oxo-2-phenylbenzo[*b*]-4*H*-thiazolo[3,2-*a*]-pyridine-3,4-dicarboxylate.

In previous papers in this series the thiocarbonyl ylide dipole present in monocyclic mesoionic *anhydro*-4-hydroxythiazolium hydroxide derivatives was shown to undergo cycloaddition with olefinic and acetylenic dipolarophiles leading to substituted thiophenes and 2-pyridinones.[2] Related bicyclic mesoionic systems provided a means of annulation of the pyridinone ring to the imidazole,[3a] 1,2,4-triazole,[3a] thiazole,[3c] 1,3,4-thiadiazole,[3c] and benzothiazole[3b] ring systems. Concurrently with the above study we have been investigating alternative means of annulation, and in this publication the utilization of 1,4-dipoles present in several heterocyclic systems is described. In several mono- and bicyclic systems related 1,4-dipoles have been shown to undergo thermally induced cycloadditions with acetylenic dipolarophiles,[4] and in monocyclic 4*H*-1,3-thiazinium betaines rearrangement to 4-quinolinones was observed[5] at 80 °C. Several other ring-fused thiazinium betaines have been prepared recently[5b] from cyclic thiones and substituted malonyl dichlorides. However, the superior reactivity of (chlorocarbonyl)-phenylketene in the procedures described below makes this the method of choice.

1-Methyl-2(3*H*)-imidazolethione (**1**) and (chlorocarbonyl)phenylketene (**2**) underwent ready reaction in dry benzene or THF at room temperature, giving *anhydro*-2-hydroxy-8-methyl-4-oxo-3-phenyl-4*H*-imidazo[2,1-*b*]-[1,3]thiazinium hydroxide (**3**) as colorless prisms (85%) in a slightly exothermic reaction (Scheme I). This betaine proved to be thermally unstable and on heating to 220 °C gave an orange product which was insoluble in most organic solvents and had the same empirical composition as **3**. Treatment with hot acetic anhydride gave an orange acetyl derivative, and structures **5** and **6**, respectively, have been assigned to these rearrangement products on the basis of the following evidence.

Scheme I



Analytical and spectral data are in agreement with the betaine structure **3**, especially the delocalized carbonyl absorption at 1575 cm^{-1} and the coupled C_6 H and C_7 H of the imidazole ring at δ 8.13 and 7.83. The thermolysis product **5** was too insoluble for satisfactory NMR data to be determined, but on conversion into its acetate **6**, the NMR spectrum indicated only one hydrogen attached to the imidazole ring at δ 6.88 (s). The molecular formula was established as $C_{15}H_{12}N_2O_3S$ by mass spectral and analytical data, corresponding to the addition of an acetyl group to **5**. The chemical shift of the C_3 H also suggests that acetylation of the hydroxyl group had occurred as shown, the C_3 H being shifted upfield by this substituent.

(1) (a) Partial support of this work by U.S. Public Health Service Research Grant CA08495, National Cancer Institute, is gratefully acknowledged. (b) Abstracted in part from the Ph.D. Thesis of R.E., 1974. (c) On leave from Yamaguchi University, Japan.

(2) Potts, K. T.; Houghton, E.; Singh, U. P., *J. Org. Chem.* **1974**, *39*, 3627. Potts, K. T.; Baum, J.; Houghton, E., *ibid.* **1974**, *39*, 3631.

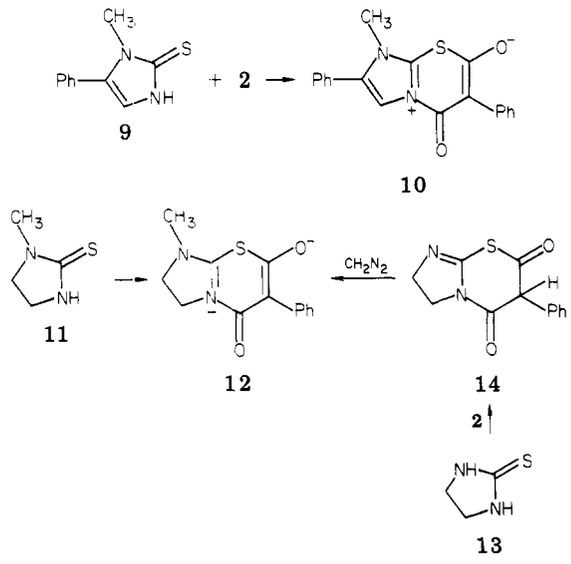
(3) (a) Potts, K. T.; Kanemasa, S., *J. Org. Chem.* **1979**, *44*, 3803. (b) Potts, K. T.; Choudhury, D. R., *ibid.* **1978**, *43*, 2697. (c) Potts, K. T.; Kanemasa, S.; *ibid.* **1979**, *44*, 3808.

(4) Potts, K. T.; Sorm, M., *J. Org. Chem.* **1971**, *36*, 8; **1972**, *37*, 1422. Prystas, M., *Collect. Czech. Chem. Commun.* **1967**, *32*, 4241. Kappe, T.; Gosler, W., *Synthesis* **1972**, 312. Kappe, T.; Lube, W., *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 825; *Monatsh. Chem.* **1971**, *102*, 781. Maki, Y.; Sako, M.; Suzuki, M., *J. Chem. Soc., Chem. Commun.* **1972**, 999.

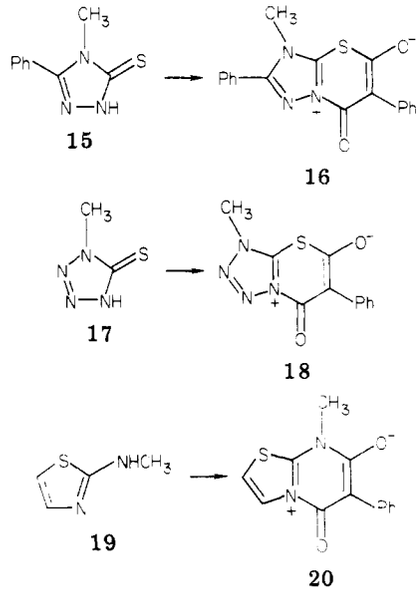
(5) (a) Potts, K. T.; Ehlinger, R.; Nichols, W. M., *J. Org. Chem.* **1975**, *40*, 2596. (b) See also: Kappe, T.; Gosler, W., *Synthesis* **1972**, 312.

0022-3263/80/1945-2474$01.00/0

Scheme II



Scheme III



The betaine **3** was also prepared in an alternative way by the action of diazomethane on 2-hydroxy-4-oxo-3-phenyl-4*H*-imidazo[2,1-*b*][1,3]thiazine (**8**), itself prepared from 2(3*H*)-imidazolethione (**7**) and (chlorocarbonyl)-phenylketene. Both N- and O-methylation occurred, and the *N*-methyl product was separated from the mixture by fractional crystallization.

The intermediate involved in the rearrangement of **3** into **5** is most likely **4**, formed by fission of the sulfur–carbonyl bond between the 1- and 2-positions. The imidazole ring in **4** contains an enamine system, and electrophilic attack of the ketene carbonyl group on the C_4-position of the imidazole ring would be expected to occur readily, giving **5**. To evaluate this hypothesis, we have prepared several betaines analogous to **3** either in which the electron density at the C_4-position has been substantially reduced or in which the 4-position has been blocked to electrophilic substitution by removing the C_4–C_5 double bond or by replacing the C_4 atom with a nitrogen atom. It was anticipated that these betaines would be thermally stable, and such was found to be the case.

1-Methyl-5-phenyl-2(3*H*)-imidazolethione (**9**) and (chlorocarbonyl)phenylketene (**2**) reacted readily at room temperature to give **10** (Scheme II) as colorless prisms (66%), mp 176–177 °C. A strong carbonyl absorption at 1590 cm^{-1} and a singlet for the C_6 H at δ 8.03, together with a molecular ion at *m/e* 334 and analytical data, are in agreement with this structure. This betaine was found to be thermally stable and also did not undergo cycloaddition with acetylenic dipolarophiles.

Similar thermal stability was found in **12**, *anhydro*-6,7-dihydro-2-hydroxy-8-methyl-4-oxo-3-phenyl-4*H*-imidazo[2,1-*b*][1,3]thiazinium hydroxide, formed from 1-methyl-2(3*H*)-imidazolinethione (**11**) and (chlorocarbonyl)phenylketene (**2**). This betaine was obtained as colorless prisms (75%, mp 267–269 °C) and was characterized by a carbonyl absorption at 1580 cm^{-1} and a molecular ion at *m/e* (relative intensity) 260 (12). It was also synthesized by reaction of **14**, formed from 2(3*H*)-imidazolinethione (**13**) and (chlorocarbonyl)phenylketene, with diazomethane. Methylation occurred exclusively on the nitrogen atom to form the betaine **12**.

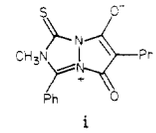
anhydro-3,7-Diphenyl-2-hydroxy-8-methyl-4-oxo-4*H*-1,2,4-triazolo[5,1-*b*][1,3]thiazinium hydroxide (**16**) was also readily obtained from 4-methyl-5-phenyl-3(2*H*)-1,2,4-triazolethione (**15**) and (chlorocarbonyl)phenylketene (Scheme III) as yellow prisms (75%). It was thermally stable until its melting point (246 °C), when it decomposed. Its infrared carbonyl absorption occurred at 1620 cm^{-1}, and the molecular ion at *m/e* (relative intensity) 335 (20) underwent fragmentation by loss of CO, a metastable transition at *m/e* 281 (335 → 307) supporting this fragmentation. The betaine **16** did not undergo cycloaddition with acetylenic dipolarophiles and although thermally stable underwent ready hydrolysis in aqueous Me_2SO solution, a process readily evident from the change in the NMR spectrum.

The addition of another nitrogen atom to the 7-position of **16**, however, reversed this ease of hydrolysis. From 1-methyl-5(4*H*)-tetrazolethione (**17**) and (chlorocarbonyl)phenylketene (**2**) was obtained[6a] *anhydro*-2-hydroxy-8-methyl-4-oxo-3-pehnyl-4*H*-tetrazolo[5,1-*b*]-[1,3]thiazinium hydroxide (**18**) as colorless prisms (73%), mp 218 °C. Its carbonyl absorption occurred at 1605 cm^{-1}, and it underwent deep-seated fragmentation on electron impact. This betaine was also thermally stable and did not undergo cycloadditions with acetylenic dipolarophiles.

Other heteroaromatic betaines of this type such as **20**, formed from 2-(methylamino)thiazole (**19**), could conceivably undergo a similar thermal isomerization. However **20**, obtained as light yellow prisms (mp 231–232 °C) was thermally stable at temperatures sufficient[4] to induce rearrangement in its monocyclic analogues.

2(3*H*)-Benzothiazolethione (**21**) and (chlorocarbonyl)-phenylketene (**2**) underwent reaction in warm anhydrous benzene to give **22** (Scheme IV) as yellow prisms in 77% yield. This betaine was stable when maintained in a dry atmosphere. The structure of **22** was evident from the analytical and spectral data, especially ν_{CO} 1601 cm^{-1} (vs), and, in addition to the aromatic protons (δ 7.0–8.1) in the

(6) (a) The isomeric structure i obtained by condensation of **2** at the nitrogen atoms of the cyclic hydrazone grouping was considered but discarded on the basis of results obtained with simpler systems where this structural ambiguity could exist (Potts, K. T.; Cody, R., unpublished results). (b) The deshielding effect of an adjacent carbonyl group on a proton in this environment is now well established in the literature and is of diagnostic importance in structural determination of isomers.



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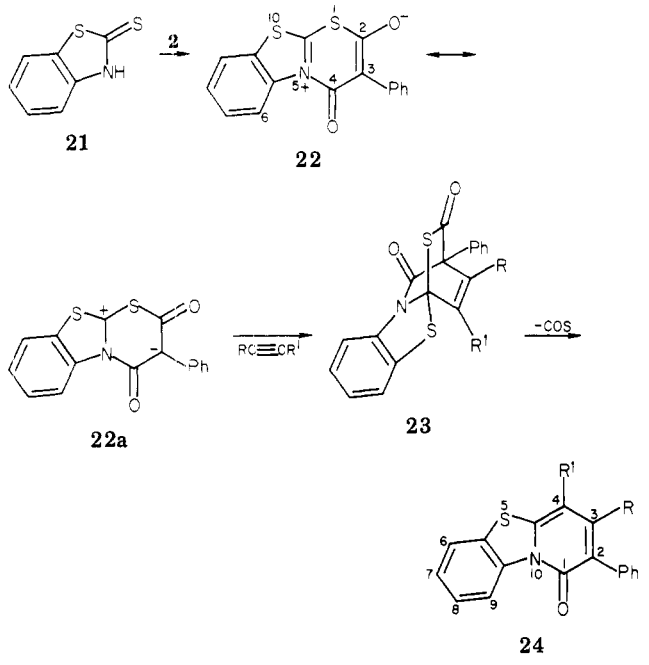
Scheme IV[a]



[a] a, R = R¹ = $COOCH_3$; b, R = H, R¹ = COOEt; c, R = COOEt, R¹ = H.

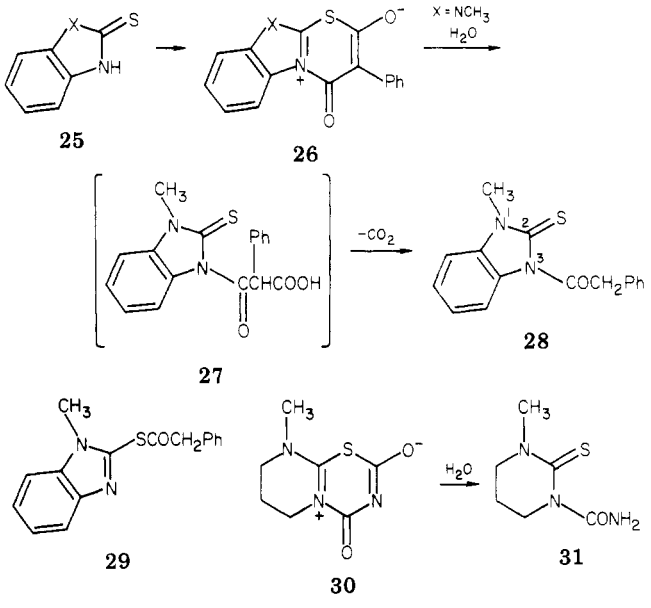
NMR spectrum, the C_6 H was shifted downfield[6b] to δ 9.9 by the deshielding effect of the 4-carbonyl group.

Dimethyl acetylenedicarboxylate reacted with **22** in boiling toluene, presumably via **22a**. The intermediate cycloadduct **23** was not isolated, carbonyl sulfide being eliminated, and the tricyclic pyridinone **24a** was obtained. This same pyridinone was produced in the reaction of dimethyl acetylenedicarboxylate and *anhydro*-3-hydroxy-2-phenylthiazolo[2,3-*b*]benzothiazolium hydroxide, in this case sulfur being extruded from the initial cycloadduct.[3b] Ethyl propiolate in refluxing benzene also reacted with **22**, giving ethyl 1-oxo-2-phenyl-1*H*-pyrido[2,1-*b*]benzothiazole-4-carboxylate (**24b**) in 83% yield. Regioselectivity was observed in this reaction, no trace of the other isomer being observed. A choice between the two possible isomeric structures **24b** and **24c** was made on the basis of the following spectral data. The C_2 phenyl protons were observed as a multiplet at δ 7.2–7.9 with the C_3 H being a sharp singlet at δ 8.23. These chemical shifts are consistent with the C_2 phenyl not being adjacent to a bulky substituent in the 3-position.[3a,c] Ethyl phenylpropiolate, however, did not undergo cycloaddition with **22** which was recovered in quantitative amount.

Olefinic dipolarophiles such as *N*-phenylmaleimide and fumaronitrile also did not undergo cycloaddition with **22** even though a wide variety of reaction temperatures and solvents were used. In all instances the betaine was recovered in nearly quantitative amounts. 2(3*H*)-Benzoxazolethione (**25**; X = O) reacted with (chlorocarbonyl)phenylketene in boiling benzene to give *anhydro*-2-hydroxybenzo[*b*]-4*H*-oxazolo[2,3-*b*][1,3]thiazinium hydroxide (**26**; X = O), obtained as yellow prisms (81%) (Scheme V). Its structure was assigned on the basis of analytical and spectral data, and it did not undergo reaction with a variety of dipolarophiles, being recovered in quantitative amounts.

1-Methyl-2(3*H*)-benzimidazolethione (**25**; X = NCH_3), on the other hand, underwent ready reaction at room temperature in benzene to give the betaine **26** (X = NCH_3) as yellow prisms (78%). In contrast to **26** (X = O), the downfield shift of the C_6 H (δ 8.90) due to deshielding by

Scheme V



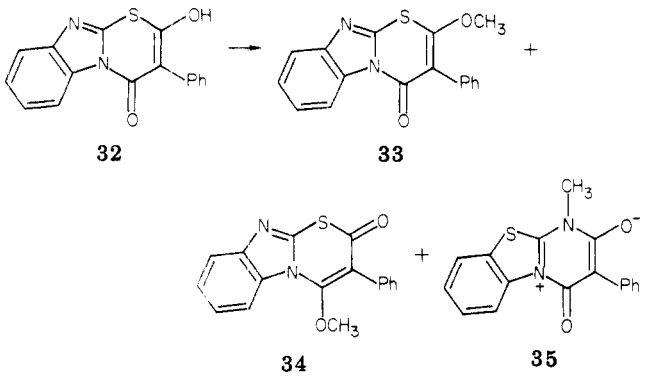
the 4-carbonyl group was clearly discernible, and also in this instance, the molecular ion *m/e* (relative intensity) 308 (9) was observed in its mass spectrum. The next fragmentation, supported by its metastable transition, was loss of CO from the molecular ion. This is in contrast to **22**, **26** (X = O), and the majority of the other heteroaromatic betaines described here which underwent deep-seated fragmentation on electron impact.

Analytical and spectral data are consistent with the assigned structure **26** (X = NCH_3). Hydrolysis in aqueous Me_2SO resulted in the formation of 1-methyl-3-phenacetyl-2(3*H*)-benzimidazolethione (**28**), formed by decarboxylation of the initial hydrolysis product **27**. This product assumes hydrolysis to occur by an initial attack on the C_2 carbonyl group. Attack on the C_4 carbonyl group to give, finally, **29** can be excluded on the basis of the following evidence. The infrared spectrum showed ν_{CO} at 1700 cm^{-1}, and no C=N absorption was present. A downfield shift of a single aromatic proton to δ 8.15 was observed and was attributed to the deshielding effect of the carbonyl group attached to N_3 in **28**. The ultraviolet spectrum [λ_{max} nm (log ε) 306 (4.26), 245 (4.04), 215 (4.07)] was consistent with the spectrum of 2(3*H*)-benzimidazolethione[7] [λ_{max} nm (log ε) 309 (4.46), 249 (4.14), 219 (4.17)] rather than with that of 1,2-dimethylbenzimidazole[8] [λ_{max} nm (log ε) 292 (3.76), 284 (3.75), 255 (3.70), 210.5 (4.73)]. This mode of ring opening is similar to that reported[9] for the hydrolysis of the 1,3,4-thiadiazinium betaine **30** to **31** and provides additional confirmation of structure **26** (X = NCH_3). Attempted cycloadditions of **26** (X = NCH_3) with a variety of dipolarophiles were unsuccessful. In all cases a nearly quantitative recovery of the betaine was obtained.

Alkylation of suitable precursors has often been used to generate heteroaromatic betaines,[10] and we have evaluated this route to **26** (X = NCH_3). Reaction of 2(3*H*)-benzimidazolethione and (chlorocarbonyl)phenylketene/Et_3N in hot, anhydrous dioxane gave 2-hydroxy-4-oxo-3-phenylbenzo[*b*]-4*H*-imidazo[2,1-*b*][1,3]thiazine (**32**). The

(7) "Sadtler Ultraviolet Spectra"; Sadtler Research Laboratories, Inc.: Philadelphia, PA, 1973, spectrum no. 19916.
(8) Reference 7, spectrum no. 1421.
(9) Hagemann, H.; Ley, K., *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 1012.
(10) Katritsky, A. R.; Waring, A. J., *J. Chem. Soc.* **1962**, 1544.

Scheme VI



chemical shift of the C_6 H at δ 8.70 indicated that this proton was deshielded, in this instance by the C_4 carbonyl group. Alkylation of **32** with diazomethane could result in the formation of three products (Scheme VI). However, a mixture of the 2- and 4-methoxy isomers, **33** and **34**, respectively, was formed, and the less soluble isomer was isolated in the pure state by fractional crystallization. The 3-phenyl group in this product was observed as a singlet, indicative of the adjacent group forcing the phenyl substituent to lose coplanarity with the thiazine nucleus. The structure of the 4-methoxy isomer was assigned principally on the effect of the 4-substituent on the C_6 H chemical shift. This was observed at δ 8.60 as compared to δ 8.90 in **26** (X = NCH_3) and δ 8.70 in **32**, two compounds having approximately the same geometry as the methylated products. For evaluation purposes, we prepared **35**, isomeric with **26** (X = NCH_3). It was readily obtained as bright yellow prisms from 2-(methylamino)benzothiazole and (chlorocarbonyl)phenylketene. The chemical shift of the C_6 H was observed at δ 9.23, indicating a strong deshielding by the C_4 carbonyl group, and in **35**, the molecular ion, *m/e* (relative intensity) 308 (100), was the most intense ion in the spectrum. This betaine proved to be stable to aqueous Me_2SO and did not undergo cycloaddition with a variety of dipolarophiles in boiling toluene.

The evidence available to date does not allow one to predict with any degree of certainty whether the 1,4-dipoles present in a variety of heteroaromatic betaines of the above type will undergo cycloaddition reactions with electron-deficient acetylenic dipolarophiles. Although mono- and bicyclic systems containing the pyrimidine nucleus[4] undergo cycloaddition with dimethyl acetylenedicarboxylate, the corresponding system containing the 1,3,5-triazine system does not.[11] The corresponding monocyclic *anhydro*-1,3-thiazinium hydroxide system undergoes rearrangement[4] to a quinolone rather than cycloaddition to dimethyl acetylenedicarboxylate, whereas **22** undergoes ready cycloaddition as does the corresponding *anhydro*-4-hydroxy-2-oxopyrido[2,1-*b*][1,3]thiazinium hydroxide system.[12] Factors controlling the reactivity of 1,4-dipoles in heteroaromatic betaines of this type are currently under study in this laboratory.

Experimental Section[13]

***anhydro*-2-Hydroxy-8-methyl-4-oxo-3-phenyl-4*H*-imidazo[2,1-*b*][1,3]thiazinium Hydroxide (3).** 1-Methyl-2-(3*H*)-imidazolethione[14] (**1**; 1.14 g, 10 mmol) was added with stirring to (chlorocarbonyl)phenylketene[15] (2.0 g, 11 mmol) in dry benzene (50 mL). After the mixture was stirred at room temperature for 1 h, the colorless product was collected and recrystallized from dioxane: 2.2 g (85%); IR (KBr) 1575 (CO) cm^{-1}; λ_{max} (CH_3OH) nm (log ϵ) 290 (sh, 3.64), 246 (4.14), 206 (4.16); NMR ($CDCl_3$) δ 8.13 (d, 1, J = 2.0 Hz, C_7 H), 7.83 (d, 1, J = 2.0 Hz, C_6 H), 7.04–7.52 (m, 5, aromatic), 3.72 (s, 3, NCH_3); mass spectrum, *m/e* (relative intensity) 258 (100, $M^{+\cdot}$), 230 (31, $M^{+\cdot}$ – CO).

Anal. Calcd for $C_{13}H_{10}N_2O_2S$: C, 60.45; H, 3.90; N, 10.85. Found: C, 60.14; H, 3.86; N, 10.77.

When **3** was heated in a melting point tube, it turned orange at about 200 °C without melting, finally melting at 271–273 °C with decomposition.

2,3-Dihydro-7-hydroxy-2-methyl-5-oxo-6-phenyl-5*H*,3-(2*H*)-pyrrolo[1,2-*c*]imidazolethione (5). The above betaine **3** was heated without solvent at 220 °C for 1 min. The orange product obtained (100%) was washed with acetone and chloroform: mp 273 °C dec. It was insoluble in most organic solvents and was finally recrystallized from DMF–water to form orange prisms: mp 273 °C dec; IR (KBr) 3060 (br s, OH), 1660 (s), 1580 (s, CO), 1390 (s, CS) cm^{-1}; mass spectrum, *m/e* (relative intensity) 258 (56, $M^{+\cdot}$), 230 (17, $M^{+\cdot}$ – CO).

Anal. Calcd for $C_{13}H_{10}N_2O_2S$: C, 60.45; H, 3.90; N, 10.85. Found: C, 60.60; H, 3.74; N, 11.24.

2,3-Dihydro-7-acetoxy-2-methyl-5-oxo-6-phenyl-5*H*,3-(2*H*)-pyrrolo[1,2-*c*]imidazolethione (6). The pyrrolo[1,2-*c*]-imidazole **5** (0.26 g, 1 mmol) was heated under reflux in acetic anhydride (3 mL) for 30 min. When the mixture cooled, orange needles separated: 0.21 g (70%); mp 200–205 °C. Recrystallization from benzene afforded orange prisms: mp 204.5–206 °C; IR (KBr) 1800 (s), 1725 (s), 1580 (w, CO) cm^{-1}; NMR ($CDCl_3$) δ 2.33 (s, 3, $COCH_3$), 3.48 (s, 3, NCH_3), 6.88 (s, 1, C_3 H), 7.2–7.5 (m, 3, aromatic), 7.6–7.9 (m, 2, aromatic); mass spectrum, *m/e* (relative intensity) 300 (72, $M^{+\cdot}$), 258 (100, $M^{+\cdot}$ – CH_2CO), 230 (34, *m/e* 258 – CO).

Anal. Calcd for $C_{15}H_{12}N_2O_3S$: C, 60.00; H, 4.03; N, 9.33. Found: C, 60.02; H, 3.81; N, 9.37.

Hydrolysis of *anhydro*-2-Hydroxy-8-methyl-4-oxo-3-phenyl-4*H*-imidazo[2,1-*b*][1,3]thiazinium Hydroxide (3). The betaine (0.15 g) was suspended in acetone (10 mL) containing 15 drops of concentrated HCl. After the mixture was heated under reflux for 30 min, the solvent was removed from the reaction mixture under reduced pressure, and the resultant yellow oil was neutralized with aqueous K_2CO_3 solution and extracted with $CHCl_3$. After the extract was dried ($MgSO_4$), the $CHCl_3$ was evaporated, yielding a pale yellow crystalline product: 0.05 g (75%); mp 146–147 °C. This product was identical[17] with 1-methyl-2(3*H*)-imidazolethione.

2-Hydroxy-4-oxo-3-phenyl-4*H*-imidazo[2,1-*b*][1,3]thiazine (8). 2(3*H*)-Imidazolethione[16] (**7**; 2.0 g, 20 mmol) was added with stirring to a solution of (chlorocarbonyl)phenylketene (3.6 g, 20 mmol) in dry THF (50 mL). After the reaction mixture was stirred for 12 h at room temperature, the solvent was removed under reduced pressure and the remaining solid recrystallized from acetone, forming yellow prisms: 4.1 g (84%); mp 273 °C dec; IR (KBr) 2500–3200 (OH), 1625 (CO) cm^{-1}; λ_{max} (CH_3OH) nm (log ϵ) 300 (3.94), 227 (4.25), 208 (4.28); NMR (Me_2SO-d_6) δ 8.14 (d, 1, J = 2.0 Hz, C_7 H), 7.80 (d, 1, J = 2.0 Hz, C_6 H), 7.40 (br s, 5, aromatic); mass spectrum, *m/e* (relative intensity) 244 (62, $M^{+\cdot}$).

Anal. Calcd for $C_{12}H_8N_2O_2S$: C, 59.00; H, 3.30; N, 11.47. Found: C, 58.76; H, 3.35; N, 11.50.

Reaction of 8 with Diazomethane. The above imidazothiazine (1.2 g, 5 mmol) in ethanol (100 mL) was added with stirring to an ethereal solution of diazomethane (ca. 1.5 g, 36 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 24 h and the solvent then removed under reduced pressure to leave a colorless product, 0.95 g. TLC (benzene–acetone, 1:1) indicated a two component mixture, shown by NMR data to be the betaine **3** and an *O*-methoxy derivative (5:1). Fractional crystallization from ethanol–diethyl ether yielded the betaine **3**,

(11) Coburn, R. A.; Bhooshan, B., *J. Heterocycl. Chem.* **1975**, *12*, 187.
(12) Kappe, T.; Gosler, W., *Chem. Ber.* **1976**, *109*, 3668.
(13) Reaction workup and spectral characterization were as reported in previous papers in this series.
(14) Wohl, A.; Marckwald, W., *Ber. Dtsch. Chem. Ges.* **1889**, *22*, 1353.
(15) Butler, K. Union of South Africa Patent 690059, 1968; *Chem. Abstr.* **1970**, *72*, P66625. Nakanishi, S.; Butler, K., *Org. Prep. Proced. Int.* **1977**, 155.
(16) Marckwald, W., *Ber. Dtsch. Chem. Ges.* **1892**, *25*, 2354.
(17) Superimposable infrared and NMR spectra and no depression in mixture melting point were used to establish identity.

identical[17] with that prepared directly from 1 and (chlorocarbonyl)phenylketene above.

***anhydro*-3,7-Diphenyl-2-hydroxy-8-methyl-4-oxo-4*H*-imidazo[2,1-*b*][1,3]thiazinium Hydroxide (10).** 1-Methyl-5-phenyl-2(3*H*)-imidazolethione[18] (1.9 g, 10 mmol) was added with stirring to (chlorocarbonyl)phenylketene (2.0 g, 11 mmol) in dry THF (50 mL). After 2 h at room temperature the product was collected and recrystallized from acetone, separating as colorless prisms: 2.2 g (66%); mp 176–177 °C; IR (KBr) 1590 (w) cm^{-1}; λ_{max} (CH_3OH) nm (log ϵ) 253 (4.45), 206 (4.45); NMR ($CDCl_3$) δ 8.03 (s, 1, C_6 H), 7.2–7.7 (m, 10, aromatic), 3.60 (s, 3, NCH_3); mass spectrum, *m/e* (relative intensity) 334 (85, $M^{+}\cdot$), 216 (100, $M^{+}\cdot$ - $PhC{\equiv}NCH_3$).

Anal. Calcd for $C_{19}H_{14}N_2O_2S$: C, 68.24; H, 4.22; N, 8.38. Found: C, 68.45; H, 4.28; N, 8.34.

***anhydro*-6,7-Dihydro-2-hydroxy-8-methyl-4-oxo-3-phenyl-4*H*-imidazo[2,1-*b*][1,3]thiazinium Hydroxide (12).** 1-Methyl-2(3*H*)imidazolinethione[14] (11; 0.9 g, 7.75 mmol) was added with stirring to (chlorocarbonyl)phenylketene (1.5 g, 8.3 mmol) in dry THF (50 mL). After an additional 2 h at room temperature, the separated product was collected and recrystallized from acetone to form colorless prisms: 1.5 g (74%); mp 267–269 °C; IR (KBr) 1580 (CO) cm^{-1}; λ_{max} (CH_3OH) nm (log ϵ) 289 (3.88), 222 (4.33), 208 (4.27); NMR ($CDCl_3$) δ 7.23 (br s, 5, aromatic), 3.60–4.35 (m, 4, CH_2), 3.03 (s, 3, NCH_3); mass spectrum, *m/e* (relative intensity) 260 (12, $M^{+}\cdot$), 232 (100, $M^{+}\cdot$ - CO).

Anal. Calcd for $C_{13}H_{12}N_2O_2S$: C, 59.98; H, 4.65; N, 10.76. Found: C, 60.06; H, 4.73; N, 10.73.

6,7-Dihydro-2-hydroxy-4-oxo-3-phenyl-4*H*-imidazo[2,1-*b*][1,3]thiazine (14). 2(3*H*)-Imidazolinethione[19] (13; 2.04 g, 20 mmol) was added with stirring to (chlorocarbonyl)phenylketene (3.6 g, 20 mmol) in dry THF (50 mL). After the mixture was stirred for 12 h at room temperature, the solvent was removed and the remaining solid recrystallized from acetone, forming bright yellow prisms: 3.6 g (73%); mp 142 °C dec; IR (KBr) 2500–3500 (br, OH), 1570 (CO) cm^{-1}; λ_{max} (CH_3OH) nm (log ϵ) 268 (3.66), 231 (4.02), 309 (4.08); NMR (Me_2SO-d_6) δ 7.2–7.7 (m, 5, aromatic), 3.2–4.8 (m, 5, CH_2, OH). The product did not give an $M^{+}\cdot$ and decomposed on standing. It was used in the preparation of 12 without undue delay.

Treatment of 14 with Diazomethane. The above thiazine 14 (2.0 g, 8.1 mmol) in ethanol (50 mL) was added with stirring to an ethereal solution of diazomethane (ca. 1.5 g, 36 mmol) at 0 °C. After stirring for 24 h at room temperature, the solvent was removed leaving a colorless residue which recrystallized from acetone forming colorless prisms: 1.5 g (74%), mp 267–269 °C. This product was identical[17] to 12 prepared above.

***anhydro*-3,7-Diphenyl-2-hydroxy-8-methyl-4-oxo-4*H*-[1,2,4]triazolo[5,1-*b*][1,3]thiazinium Hydroxide (16).** 4-Methyl-5-phenyl-3(4*H*)-1,2,4-triazolethione[20] (15; 1.91 g, 10 mmol) was added with stirring to (chlorocarbonyl)phenylketene (2.0 g, 11 mmol) in dry benzene (50 mL). After the mixture was stirred for 3 h at room temperature, the product was collected and recrystallized from acetone, forming yellow prisms: 2.4 g (72%); mp 246 °C dec; IR (KBr) 1620 (CO) cm^{-1}; λ_{max} ($CHCl_3$) nm (log ϵ) 314 (3.97), 269 (3.78), 241 (4.04); NMR ($CDCl_3$) δ 7.0–7.7 (m, 10, aromatic), 3.50 (s, 3, NCH_3); mass spectrum, *m/e* (relative intensity) 335 (20, $M^{+}\cdot$), 307 (93, $M^{+}\cdot$ - CO).

Anal. Calcd for $C_{18}H_{13}N_3O_2S$: C, 64.46; H, 3.91; N, 12.53. Found: C, 64.39; H, 3.99; N, 12.55.

***anhydro*-2-Hydroxy-8-methyl-4-oxo-3-phenyl-4*H*-tetrazolo[5,1-*b*][1,3]thiazinium Hydroxide (18).** 1-Methyl-5-(4*H*)-tetrazolethione[21] (17; 1.16 g, 10 mmol) was added with stirring to (chlorocarbonyl)phenylketene (2.0 g, 11 mmol) in dry THF (50 mL). After the mixture was stirred for 3 h at room temperature, the separated product was collected and recrystallized from ethanol, forming colorless prisms: 1.9 g (73%); mp 218 °C dec; IR (KBr) 1701, 1605 (CO) cm^{-1}; NMR ($CDCl_3$) δ 7.44 (s, 5, aromatic), 3.83 (s, 3, NCH_3).

Anal. Calcd for $C_{11}H_8N_4O_2S$: C, 50.76; H, 3.10; N, 21.53. Found: C, 50.67; H, 3.45; N, 21.44.

***anhydro*-7-Hydroxy-8-methyl-5-oxo-6-phenyl-2*H*-thiazolo[3,2-*a*]pyrimidinium Hydroxide (20).** 2-(Methylamino)-thiazole[22] (19; 1.77 g, 15.5 mmol) and (chlorocarbonyl)phenylketene (3.09 g, 17.0 mmol) were reacted together as above for 6 h. Recrystallization of the product from acetone afforded light yellow prisms: 3.2 g (80%), mp 231–232 °C; IR (KBr) 1630 (CO) cm^{-1}; λ_{max} (CH_3OH) nm (log ϵ) 320 (sh, 3.70), 298 (3.73), 250 (4.39), 204 (4.22); NMR ($CDCl_3$) δ 8.22 (d, 1, J = 4.0 Hz, C_3 H), 7.2–7.9 (m, 5, aromatic), 7.00 (d, 1, J = 4.0 Hz, C_2 H), 3.66 (s, 3, NCH_3); mass spectrum, *m/e* (relative intensity) 258 (100, $M^{+}\cdot$), 230 (86, $M^{+}\cdot$ - CO).

Anal. Calcd for $C_{13}H_{10}N_2O_2S$: C, 60.45; H, 3.90; N, 10.85. Found: C, 60.16; H, 3.86; N, 10.81.

***anhydro*-2-Hydroxy-4-oxo-3-phenylbenzo[*b*]-4*H*-thiazolo[2,3-*b*][1,3]thiazinium Hydroxide (22).** 2(3*H*)-Benzothiazolethione (1.92 g, 11.5 mmol) was added with stirring to (chlorocarbonyl)phenylketene (2.09 g, 11.5 mmol) in dry benzene (50 mL). After 15 min at room temperature the reaction mixture was refluxed for 15 min, and when the mixture cooled, the betaine 22 crystallized. It was recrystallized from absolute ethanol, forming yellow prisms: 2.76 g (77%); mp 194 °C; IR (KBr) 1601 (CO) cm^{-1}; λ_{max} (CH_3OH) nm (log ϵ) 324 (4.42), 235 (sh, 4.16), 228 (4.18); NMR ($CDCl_3$) δ 9.9 (m, 1, C_9 H), 7.0–8.1 (m, 8, aromatic).

Anal. Calcd for $C_{16}H_9NO_2S_2$: C, 61.71; H, 2.91; N, 4.50. Found: C, 61.25; H, 3.10; N, 4.55.

Dimethyl 1-Oxo-2-phenylbenzo[*b*]thiazolo[3,2-*a*]-pyridine-3,4-dicarboxylate (24a). The betaine 22 (0.93 g, 3.0 mmol), dimethyl acetylenedicarboxylate (0.43 g, 3.0 mmol), and dry toluene (50 mL) were heated together under reflux for 12 h. The solvent was removed under reduced pressure and the residue recrystallized from ethanol, forming yellow prisms: 0.79 g (67%); mp 237–239 °C; IR (KBr) 1725, 1655 (CO) cm^{-1}; λ_{max} (CH_3OH) nm (log ϵ) 372 (4.15), 358 (4.12), 308 (4.16), 227 (4.32); NMR ($CDCl_3$) δ 7.2–8.1 (m, 9, aromatic), 3.93 (s, 3, OCH_3), 3.60 (s, 3, OCH_3); mass spectrum, *m/e* (relative intensity) 393 (100, $M^{+}\cdot$).

Anal. Calcd for $C_{21}H_{25}NO_5S$: C, 64.11; H, 3.84; N, 3.56. Found: C, 64.21; H, 3.88; N, 3.56.

Ethyl 1-Oxo-2-phenylbenzo[*b*]thiazolo[3,2-*a*]pyridine-4-carboxylate (24b). The betaine (1.26 g, 4.05 mmol), ethyl propiolate (0.40 g, 4.05 mmol), and dry benzene (50 mL) were heated together under reflux for 15 h. The solvent was removed under reduced pressure and the remaining solid recrystallized from benzene–petroleum ether (bp 40–60 °C), separating as yellow prisms: 0.95 g (83%); mp 184–186 °C; IR (KBr) 1690, 1650 (CO) cm^{-1}; λ_{max} (CH_3OH) nm (log ϵ) 3.71 (4.23), 3.0 (4.14), 229 (4.33); NMR ($CDCl_3$) δ 8.23 (s, 1, C_3 H), 7.2–7.9 (m, 9, aromatic), 4.47 (q, 2, CH_2CH_3), 1.43 (t, 3, CH_2CH_3); mass spectrum, *m/e* (relative intensity) 349 (100, $M^{+}\cdot$).

Anal. Calcd for $C_{20}H_{15}NO_3S$: C, 68.75; H, 4.33; N, 4.07. Found: C, 68.90; H, 4.28; N, 4.11.

***anhydro*-2-Hydroxy-4-oxo-3-phenylbenzo[*b*]-4*H*-oxazolo[2,3-*b*][1,3]thiazinium Hydroxide (26; X = O).** 2(3*H*)-Benzoxazolethione[23] (25, X = O; 1.51 g, 10 mmol) was added with stirring to (chlorocarbonyl)phenylketene (2.0 g, 11 mmol) in anhydrous benzene (50 mL). After being stirred for 15 min at room temperature, the reaction mixture was heated under reflux for 2 h. When the mixture cooled, the product 26 (X = O) separated, and it was crystallized from benzene–petroleum ether, forming yellow prisms: 2.4 g (81%); mp 118 °C dec; IR (KBr) 1615 (CO) cm^{-1}; λ_{max} (CH_3OH) nm (log ϵ) 298 (4.44), 258 (3.99); NMR ($CDCl_3$) δ 7.0–7.7 (m, aromatic).

Anal. Calcd for $C_{16}H_9NO_3S$: C, 65.07; H, 3.07; N, 4.74. Found: C, 65.13; H, 3.38; N, 4.47.

***anhydro*-2-Hydroxy-10-methyl-4-oxo-3-phenylbenzo[*f*]-4*H*-imidazo[2,1-*b*][1,3]thiazinium Hydroxide (26; X = NCH_3).** 1-Methyl-2(3*H*)-benzimidazolethione[24] (25, X = NCH_3; 2.05 g, 13 mmol) was added with stirring to (chlorocarbonyl)phenylketene (2.40 g, 13.3 mmol) in anhydrous benzene (50 mL). After the mixture was stirred at room temperature for 3 h, the precipitated product 26 (X = NCH_3) was collected and recrystallized from acetone, forming yellow prisms: 3.0 g (78%); mp 237 °C; IR (KBr)

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1600 (CO) cm^{-1}; λ_{max} ($CHCl_3$) nm (log ϵ) 323 (4.15), 255 (4.23), 242 (sh, 4.13); NMR ($CDCl_3$) δ 8.90 (m, 1, C_6 H), 7.2–7.7 (m, 8, aromatic), 3.80 (s, 3, NCH_3); mass spectrum, *m/e* (relative intensity) 308 (9, M^+·).

Anal. Calcd for $C_{17}H_{12}N_2O_2S$: C, 66.21; H, 3.92; N, 9.09. Found: C, 65.98; H, 3.92; N, 9.08.

1-Methyl-3-[(phenylmethyl)carbonyl]-2(3*H*)-benzimidazolethione (28). The betaine **26** (X = NCH_3; 1.0 g, 3.24 mmol) was stirred in aqueous Me_2SO (4 mL of 10% solution) at room temperature for 12 h. The separated product was collected and recrystallized from THF, forming colorless plates: 0.8 g (88%); mp 180–181 °C; IR (KBr) 1700 (CO) cm^{-1}; NMR ($CDCl_3$) δ 8.15 (m, 1, C_4 H), 7.0–7.5 (m, 8, aromatic), 5.1 (s, 2, CH_2), 3.75 (s, 3, NCH_3); mass spectrum, *m/e* (relative intensity) 282 (25, M^+·).

Anal. Calcd for $C_{16}H_{14}N_2OS$: C, 68.07; H, 5.00; N, 9.93. Found: C, 68.04; H, 4.98; N, 9.96.

2-Hydroxy-4-oxo-3-phenylbenzo[*f*]-4*H*-imidazo[2,1-*b*][1,3]thiazine (32). 2(3*H*)-Benzimidazolethione[25] (6.9 g, 46 mmol) was added with stirring to (chlorocarbonyl)phenylketene (8.3 g, 46 mmol) in dry dioxane (100 mL). Triethylamine (4.65 g, 46 mmol) was added dropwise and the reaction mixture refluxed for 4 h. The solvent was removed under reduced pressure and the remaining solid washed with water (200 mL) and recrystallized from ethanol, forming colorless prisms: 14.2 g (91%); mp 293 °C dec; IR (KBr) 2500–3200 (br, OH), 1690 (CO) cm^{-1}; λ_{max} (CH_3OH) nm (log ϵ) 305 (4.33), 295 (sh, 4.26), 278 (4.18), 245 (4.29), 210 (4.43); NMR (Me_2SO-d_6) δ 12.9 (s, 1, OH), 8.70 (m, 1, C_6 H), 7.1–8.0 (m, 8, aromatic); mass spectrum, *m/e* (relative intensity) 294 (95, M^+·).

Anal. Calcd for $C_{16}H_{10}N_2O_2S$: C, 65.29; H, 3.42; N, 9.52. Found: C, 64.99; H, 3.48; N, 9.60.

Methylation of 2-Hydroxy-4-oxo-3-phenylbenzo[*f*]-4*H*-imidazo[2,1-*b*][1,3]thiazine (32). The hydroxy compound **32** (2.94 g, 10 mmol) in ethanol (50 mL) was added with stirring to an ethereal solution of diazomethane (ca. 1.5 g, 36 mmol) at 0 °C. The solution was allowed to warm to room temperature with stirring over 24 h. Removal of the solvent and recrystallization of the remaining solid product from acetone gave colorless prisms, 2.3 g. TLC in benzene–acetone (1:1) showed this to be a two-component mixture, and on fractional crystallization from THF the less soluble 4-methoxy-2-oxo-3-phenylbenzo[*f*]-4*H*-imidazo-[2,1-*b*][1,3]thiazine (**34**) was obtained as colorless prisms: 0.8 g (25%); mp 211–212 °C; IR (KBr) 1670 (CO) cm^{-1}; λ_{max} (CH_3OH) nm (log ϵ) 305 (3.67), 264 (4.57), 218 (sh, 4.22); NMR ($CDCl_3$) δ 8.60 (m, 1, C_6 H), 7.45 (br s, 8, Ph and aromatic), 3.96 (s, 3, OCH_3); mass spectrum, *m/e* (relative intensity) 308 (100, M^+·).

Anal. Calcd for $C_{17}H_{12}N_2O_2S$: C, 66.21; H, 3.92; N, 9.09. Found: C, 66.44; H, 3.93; N, 9.04.

***anhydro*-2-Hydroxy-1-methyl-4-oxo-3-phenylbenzo[*b*]-4*H*-thiazolo[3,2-*a*]pyrimidinium Hydroxide (35).** 2-(Methylamino)benzothiazole[26] (1.42 g, 8.65 mmol) was added with stirring to (chlorocarbonyl)phenylketene (1.73 g, 9.6 mmol) in dry THF (50 mL). After the mixture was stirred at room temperature for 6 h, the separated material was collected and recrystallized from acetone, forming bright yellow prisms: 2.5 g (86%); mp 205 °C; IR (KBr) 1625 (CO) cm^{-1}; λ_{max} (CH_3OH) nm (log ϵ) 330 (3.65), 255 (4.39), 213 (4.50); NMR ($CDCl_3$) δ 9.23 (m, 1, C_6 H), 7.2–7.9 (m, 8, aromatic), 3.68 (s, 3, NCH_3); mass spectrum, *m/e* (relative intensity) 308 (100, M^+·).

Anal. Calcd for $C_{17}H_{12}N_2O_2S$: C, 66.21; H, 3.92; N, 9.09. Found: C, 66.17; H, 3.89; N, 9.32.

Registry No. **1**, 60-56-0; **2**, 17118-70-6; **3**, 73395-65-0; **5**, 73384-43-7; **6**, 73384-44-8; **7**, 872-35-5; **8**, 73384-45-9; **9**, 25433-13-0; **10**, 73384-46-0; **11**, 13431-10-2; **12**, 73384-47-1; **13**, 96-45-7; **14**, 73384-48-2; **15**, 38942-51-7; **16**, 73384-49-3; **17**, 13183-79-4; **18**, 73384-50-6; **19**, 6142-06-9; **20**, 73384-51-7; **21**, 149-30-4; **22**, 73384-52-8; **24a**, 66085-23-2; **24b**, 73384-53-9; **25** (X = O), 2382-96-9; **25** (X = NCH_3), 2360-22-7; **26** (X = O), 73384-54-0; **26** (X = NCH_3), 73384-55-1; **28**, 21541-38-8; **32**, 73384-56-2; **34**, 73384-57-3; **35**, 73384-58-4; diazomethane, 334-88-3; dimethyl acetylenedicarboxylate, 762-42-5; ethyl propiolate, 623-47-2; 2(3*H*)-benzimidazolethione, 583-39-1; 2-(methylamino)benzothiazole, 16954-69-1.

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7*H*-[1,2,4]Triazolo[5,1-*b*][1,3]thiazin-7-ones by Deamination Cyclization of *S*-Acrylates of 4-Amino-3(3*H*)-1,2,4-triazolethiones

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Received January 20, 1980

Condensation of 4-amino-3(3*H*)-1,2,4-triazolethiones with methyl propiolate gave *S*-acrylic esters. *S*-Acrylic acids prepared from these esters underwent a deamination cyclization of 7*H*-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones with the loss of the elements of hydroxylamine.

The vicinal amino and mercapto functions in the tautomeric form of 4-amino-3(4*H*)-1,2,4-triazolethiones (**1**) offer nucleophilic loci for heterocyclic syntheses involving potential bridging reactings with alkynyl esters. Our earlier studies, which make these triazoles available in quantity,[1] and our continuing interest in synthetic applications of acetylene esters[2,3] prompted our investigation of the condensation of **1** and methyl propiolate.

Combination of equimolar quantities of **1a–c** and methyl propiolate (Scheme I) in refluxing anhydrous methanol resulted in 53–83% yields of 1:1 adducts identified as S-substituted acrylic esters (**2a–c**). Infrared spectra retained the characteristic primary amine bands at 3630 to 3550 cm^{-1}, and ^1H NMR spectra displayed a singlet, D_2O exchangeable and integrating for 2 protons, between δ 5.9 and 6.3, which excludes adduct formation involving the primary amino group and the alkyne.

Exclusion of the tautomeric ring nitrogen of the thiolactam as a site of Michael addition rests on both literature precedent and Raney nickel treatment of **2b**. Kovalev has

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