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(9) Empirical estimates.
(10) In this work we consider structural isomers which result from nitrogen inversion as conformers.
(11) We only consider chair conformations because there is no evidence of very strong interactions which would force the molecule to have one or more rings in boat conformation; see, e.g., G. M. Kellie and F. G. Riddell, *Top. Stereochem.*, **8**, 225 (1974).
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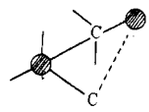
(13) Followed by ring inversion of the adjacent piperidine ring.
(14) RE = generalized anomeric effect, "rabbit ear effect". For gauche interactions the following notations are used:



Gl = butane segment (C–C–C–C)
Gl′ = 2-azabutane segment (C–N–C–C)
Gl_N = propylamine segment (C–C–C–N)
Gl_N' = 2-azapropylamine segment (C–N–C–N)

(15) C. H. Bushweller, M. Z. Lourandos, and J. A. Brunelle, *J. Am. Chem. Soc.*, **96**, 1591 (1974).
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(17) I.e., at −90 °C the contribution of A is less than 5%.[31]
(18) Whereas in smaller cyclic systems distinct ^{13}C chemical shift increments caused by alkyl substitution were successfully applied for calculation of nonbridgehead carbons in methylcyclohexanes,[20a] methyldecalines,[20b] methylpiperidines,[5b-d,21] alkyldecahydroquinolines,[5c,f] and methylquinolizidines,[22] this method may lead to wrong values of bridgehead or bridgehead neighbored carbon atoms in polycyclic systems such as methyldecalines[20b] and perhydrophenanthrenes and -anthracenes.[20c] For recent results see ref 5k.
(19) It is also possible to build up the data for PHT using the *experimental* values from corresponding segments of perhydroanthracenes and perhydrophenanthrenes. This results in a slightly better agreement with the observed data. As a consequence also assignments of some carbon signals in the less significant high-field region may have to be interchanged.
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(23) The *A* parameter only considers the nearest nitrogen position. The *B* parameter is the sum of the literature values for the three nitrogen positions. We neglected δ and ϵ effects, which are expected to be small.
(24) C-3″ and C-5″ in F, G, and H suffer the effect of an antiperiplanar lone pair of N-1″. One expects an upfield shift of about −3.5 ppm[25] compared to the calculated values. In our case such an effect could be present in an amount of maximally 2–4 ppm if we change the assignments in the high-field region, but when one does this the standard deviation between observed and calculated values increases.
(25) (a) The observed effect in the pairs **2, 2m,** and **19, 19m** in ref 5f amounts to about −9.5 ppm. It contains also the upfield shifting "γ_g" and "buttressing" effects[5f] (about −6 ppm). (b) E. L. Eliel, V. S. Rao, F. W. Vierhapper, and Z. Juaristi, *Tetrahedron Lett.*, 4339 (1975).
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(31) H. Kessler and G. Zimmermann, *Chem. Ber.*, in press.
(32) **Note Added in Proof.** A low temperature investigation of **3** gives evidence for conformational heterogenity of isotripiperideine (65% I, 23% K, and 12% L at −110 °C). This ratio leads to

$$1\ RE = 1\ Gl_N + 1\ Gl_N' + 1\ Gl' - 0.35\ kcal/mol \quad (5)$$

With the assumptions made above ($Gl_N' \approx Gl_N$) it follows that 1 RE = 1.85 kcal/mol.[33]
(33) The relative high value of RE could origin from the rigidity of the polycyclic ring system, whereas the literature values are derived from monocyclic compounds in which ring deformation is facilitated.

Syntheses and Chemistry of *N*-Acyl Substituted Dihydroimidazo[2,1-*b*]thiazolium Salts

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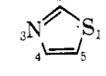
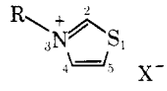
The syntheses of both *N*-acetyl- (**5**) and *N*-carbomethoxy-5,6-dihydroimidazo[2,1-*b*]thiazolium fluoroborate (**6**) from the corresponding *N*-acyl substituted thioimidazolines (**7** and **8**) are described. The reactivity of each of these salts with bases has been evaluated. Treatment of both **5** and **6** with methoxide yielded the known deacylated 3-phenyl-5,6-dihydroimidazo[2,1-*b*]thiazole (**14**). Addition, however, of triethylamine to nitromethane solutions containing **5** and **6** gave yellow, crystalline solids, **15** and **17**, respectively. Spectral analysis indicated that the products obtained were 1:1 adducts of the salts and the solvent. Substitution of nitroethane for nitromethane in each of these reactions yielded the expected homologous adducts (**16** ad **18**). The structure of one of these adducts, **15**, was determined by x-ray crystallography. Formation of **15–18** is believed to occur by the initial nucleophilic addition of the conjugate base of the solvent to the thiazolium ring of the salt to generate a tetrahedral intermediate. Fragmentation of this intermediate in the subsequent step leads to the observed adducts.

Although thiazoles (**1**) and thiazolium salts (**2**) are stable, isolable aromatic compounds, they readily undergo a variety of interesting reactions with nucleophiles.[1,2] The alkylated salts (**2**) are substantially more reactive toward nucleophilic agents than are their neutral precursors (**1**).[1,2]

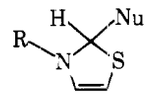


1

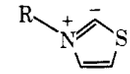


2

Three general pathways have been observed for the interaction of nucleophiles with thiazolium salts (**2**). Typically, the nucleophile adds directly to the aromatic nucleus **2**.[1-4] Addition occurs at C-2 unless this position is sterically hindered, to give the tetrahedral intermediate **3**. Fragmentation of the ring (**3**) usually occurs in a subsequent step. Alternatively, the nucleophilic species can abstract one of the thiazolium ring protons to generate a zwitterion.[5,6] In the parent salt (**2**), the C-2 hydrogen is the most acidic. Deprotonation in this case yields the zwitterion **4**. This last process has been proposed for the initial step in the numerous enzymatic reactions observed for thiamin (vitamin B_1) with α-keto acids.[5,6] In addition to these two types of reactions, the *N*-alkyl substituent in **2** can be attacked by the incoming nucleophile to displace the parent thiazole (**1**).[7]



3



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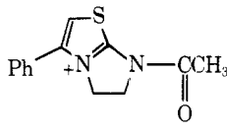
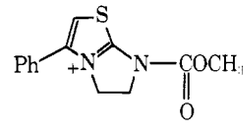
In light of this diverse group of reactions it was of interest to us to examine the reactivity of two recently prepared 5,6-dihydroimidazo[2,1-*b*]thiazolium salts **5** and **6**. Both of these



5 BF_4^-



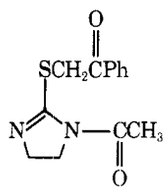
6 BF_4^-

substrates also contain an activated carbonyl system, thereby further increasing the potential number of sites for nucleophilic attack. These salts were initially synthesized as potential model substrates for a current study dealing with the mechanism of biotin catalysis.[8]

In this communication we would like to report both the syntheses and reactivity of these thiazolium compounds as well as their neutral precursors. Of particular interest here is the reactivity of these substrates with various nucleopiles. In a number of cases studied, these reactions led to the isolation of stable crystalline adducts possessing many of the structural features that have been proposed for the active intermediate in the decarboxylation and condensation reactions of α-keto acids by vitamin B_1.[5,6]

Results and Discussion

The thiazolium salts (**5** and **6**) were synthesized directly from the neutral percursors **7** and **8**. In turn, the substituted thioimidazolines (**7** and **8**) could be prepared in two steps from the commercially available imidazolidinethione.[8,9] Although most of the physical and chemical properties for **7** and **8** were consistent with their close similarity in structure, the rectivity of each of these substrates toward methoxide ion was markedly different.



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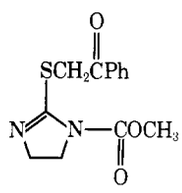
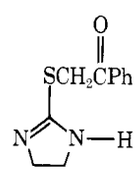
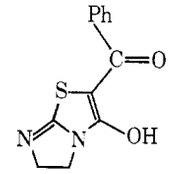


8

Reactivity of 7 and 8 toward Methoxide Ion. Treatment of **7** in CH_2Cl_2 with 1 equiv of 0.5 M sodium methoxide–methanol solution gave a 91% yield of the known deacylated 2-phenacylthioimidazoline (**9**).[10] However, when **8** was treated with 1 equiv of sodium methoxide under the identical conditions used for **7**, the deacylated thioimidazoline (**9**) was not



9

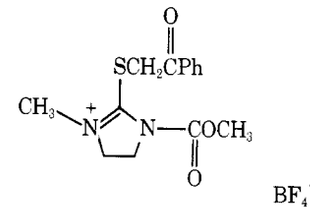


10

obtained. Instead the bicyclic 2-benzoyl-3-hydroxy-5,6-dihydroimidazo[2,1-*b*]thiazole (**10**) was isolated in 71% yield.[8]

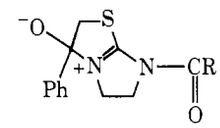
Formation of the bicyclic adduct (**10**) can be envisioned to occur by initial nucleophilic attack of the carbomethoxy carbonyl group by the enolate anion of **8**. Substitution in this case proceeds with the expulsion of methoxide ion to give the bicyclic adduct (**10**) rather than the release of a thioimidazoline anion.

Syntheses of 5 and 6. Methylation of **7** in nitromethane with 1.3 equiv of trimethyloxonium fluoroborate[11] gave the thiazolium salt (**5**) in 46% purified yield along with at least two other products (NMR analysis). *N*-Acetyl-3-phenyl-5,6-dihydroimidazo[2,1-*b*]thiazolium fluoroborate (**5**) was isolated by the selective extraction of the unidentified compounds from the product mixture with chloroform. Similarly, when **8** was treated with 1.5 equiv of trimethyloxonium fluoroborate[11] *N*-carbomethoxy-3-phenyl-5,6-dihydroimidazo[2,1-*b*]thiazolium fluoroborate (**6**) as well as the N-alkylated *N*-methyl-*N'*-carbomethoxy-2-phenacylthioimidazolinium fluoroborate (**11**) were isolated in 27 and 61% yields, respectively.[8] In this case again, **6** could be isolated by trituration of the product mixture with chloroform.



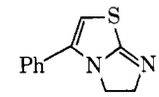
11

The formation of both **5** and **6** can be envisioned to occur by the initial tautomerism of **7** and **8**, respectively, to give the isomeric N-substituted 3-oxido-3-phenyl-2,3,5,6-tetrahydroimidazo[2,1-*b*]thiazolium salts (**12** and **13**). Subsequent methylation at oxygen followed by rearomatization by loss of methanol would give the bicyclic thiazolium salts, **5** and **6**. Analogously, it has been reported that treatment of *N*-methyl-2-phenacylthioimidazoline with hydrobromic acid gave the corresponding *N*-methyl-3-phenyl-5,6-dihydroimidazo[2,1-*b*]thiazolium bromide.[12]



12; R = CH_3
13; R = OCH_3

Reactivity of 5 and 6 with Bases. The structural assignments of **5** and **6** are supported by the reaction of these salts with methoxide ion. In both cases, methanolysis gave the known 3-phenyl-5,6-dihydroimidazo[2,1-*b*]thiazole (**14**)[9,10] in 56 and 72%[8] yields, respectively.



14

Treatment of thiazolium salts **5** and **6** with triethylamine in nitromethane, however, did not lead to the deacylated

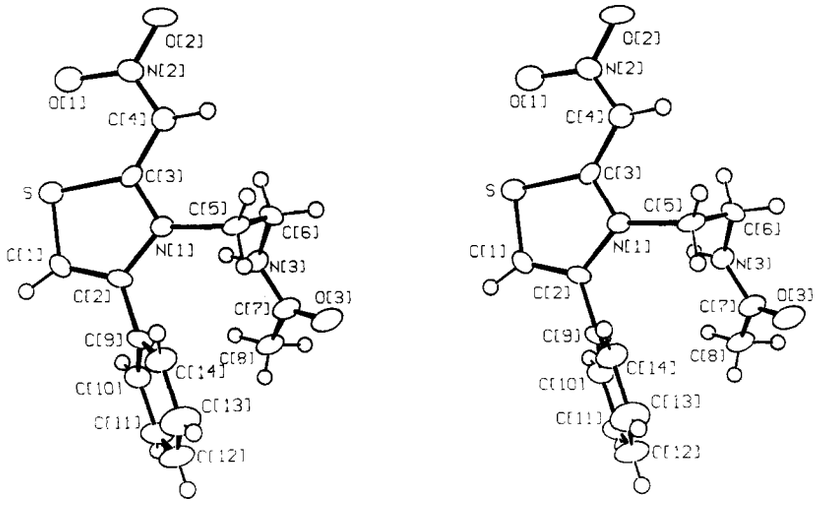


Figure 1. Stereoscopic representation of **15**, showing the atoms numbering scheme used in the presentation and discussion of crystallographic results.

product **14** observed in the sodium methoxide reactions. Instead, a brilliant yellow crystalline material (**15**) was isolated from the reaction of **5** with 1 equiv of the amine in nitromethane. Mass spectrometry showed a molecular ion at *m/e* 305. The infrared spectrum showed a strong band at 1675 cm^{-1} and the absorption was tentatively assigned to an acetamide carbonyl group.[13] This assignment, however, was jeopardized by the corresponding ^1H NMR spectrum. The Me_2SO-d_6 NMR sample did not show a peak in the δ 2.0 region typically observed for acetamide methyl protons.[14] Instead a sharp singlet was obtained at δ 1.62, a position which is considerably higher field than previously reported for acetamide methyl protons.[14] Examination of the proton decoupled ^{13}C NMR spectrum, on the other hand, revealed three carbon resonances (22.4, 36.2, 46.9 ppm) in the 20–50-ppm region. In a selective decoupling experiment (irradiation at δ 7.12), one of these peaks (22.4 ppm) gave rise to a residual quartet pattern. Unlike the ^1H NMR data, comparison of this chemical shift position to ^{13}C NMR correlation tables[15] suggested that the resonance at 22.4 ppm was due to an acetamide methyl group.

Elemental analysis (C, H, N, S) of **15** is consistent with an empirical formula of $C_{14}H_{15}N_3O_3S$, and in agreement with the earlier obtained mass spectral data. Although the precise structure of the adduct eluded us, the combined results of the elemental analysis and the mass spectral data strongly suggested that **15** was a 1:1 adduct of the salt (**5**) with the solvent, nitromethane. It was of interest, therefore, to rerun the reaction in nitroethane.

Treatment of **5** with 1 equiv of triethylamine in nitroethane again led to a brilliant yellow crystalline material **16** upon workup. Mass spectrometry showed a parent peak at *m/e* 319. The infrared spectrum showed a potential acetamide carbonyl absorption at 1660 cm^{-1}, while the ^1H NMR again exhibited the unusually high field singlet at δ 1.62. In addition, the low-field singlet (1 H) in **15** at δ 7.82 was replaced by a sharp singlet (3 H) in **16** at δ 2.53. The empirical formula of $C_{15}H_{17}N_3O_3S$ obtained from elemental analysis (C, H, N, S) was in agreement with the mass spectral data. Both **15** and **16** then appeared to arise from an interaction of **5** with the solvent.

Substitution of the *N*-carbomethoxy-3-phenyl-5,6-dihydroimidazo[2,1-*b*]thiazolium fluoroborate[8] (**6**) for **5** in each of the above two reactions (nitromethane and nitroethane) led to the isolation of two additional yellow crystalline compounds, **17** and **18**, respectively. Examination of the spectral data for these four compounds (**15–18**) (see Experimental Section) reinforces the conclusions that these compounds fall into two homologous series (**15, 16** and **17, 18**) and that these two series of compounds are structurally related.

The structural identity, however, of any one of these four compounds still remained obscure. In order to clarify this problem, a single crystal x-ray structure determination of **15** was carried out. A stereoview illustrating the molecular conformation for **15** is depicted in Figure 1, which also presents the (arbitrary) numbering system used in the presentation and discussion of the crystallographic results.

Bond distances are consistent with considerable delocalization through the sequence N(1)–C(3)–C(4)–nitro: C(3)–N(1), 1.352 (9); C(3)–C(4), 1.386 (11); C(4)–N(2), 1.348 (12); N(2)–O(1), 1.268 (8); and N(2)–O(2), 1.259 (8) Å. Thus, the C(3)–N(1) distance agrees well with the corresponding distance in one other structure in which such conjugation occurs: 1.353 (6) Å in 2-mercaptobenzothiazole.[16] This distance is noticeably longer than in structures in which the bond is largely double in character: 1.324 (4) Å in 2-(α-hydroxyethyl)-3,4-dimethylthiazolium bromide;[17] 1.32 Å (average, no esd reported) in 1-phenyl-3-(thiazolin-2-yl)-2-thiourea;[18] 1.280 (9) Å in 2-(*o*-hydroxyphenyl)benzothiazole;[19] 1.308 (5) Å in *N*-benzyl-4-methylthiazolium bromide;[20] 1.297 (3) Å in 2-methylaminobenzothiazole;[21] and 1.307 (2) Å in 2-amino-4,5-dihydro-7,8-dimethyoxy[1,2-*d*]thiazole.[22]

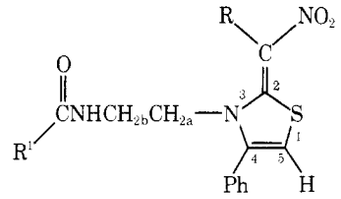
The atoms S, N(1), C(1), C(2), C(3) of the five-membered ring are coplanar to within 0.02 Å, with atom C(4) also in this plane to within experimental error. The nitro group is twisted out of this plane by only 5.6°.

Conclusions

After the structure for **15** was revealed by the x-ray study, the peak assignments in the ^1H NMR spectra for compounds **15–18** were made (Table I).

Of interest in the ^1H NMR spectra are the high field assignment to the substituted acetamide methyl protons in **15** and **16**, and the apparent quartet observed for the high field methylene protons (CH_{2b}) in **16, 17,** and **18.** Although at first surprising, this high field assignment is not unprecedented after the NMR solvent (Me_2SO-d_6) used in this study is taken into consideration. In a control experiment, the chemical shift position of the acetamide methyl resonance in acetamide itself was determined in $CDCl_3$ and Me_2SO-d_6. An upfield shift from δ 1.99 to δ 1.83 was noted in going from $CDCl_3$ to Me_2SO-d_6. On the other hand, the apparent quartet patterns

Table I. ^{1}H NMR Data for 15–18[a]



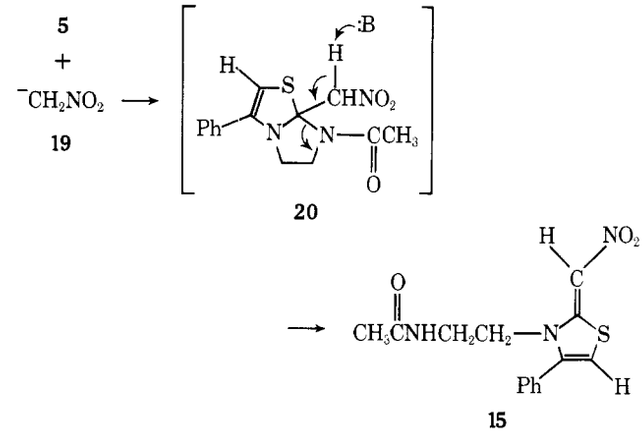
	15	16	17	18
R: H	7.82		7.78	
CH_3		2.53		2.54
R^1: CH_3	1.62	1.62		
OCH_3			3.30	3.37
Ph	7.50	7.42	7.45	7.57
C_5H	7.12	7.12	7.12	7.23
CH_{2a}	3.76–4.10 (t)[b]	4.13–4.40 (t)[b]	3.90–4.12 (t)[b]	4.27–4.47 (t)[b]
CH_{2b}	2.97–3.38 (m)	2.75–3.13 (q)[b]	2.97–3.24 (q)[b]	2.78–3.08 (q)[b]
NH	7.72–8.06[c]	7.60–7.75 (m)	6.98–7.10 (m)	7.03–7.14 (m)

[a] NMR spectra were run in Me_2SO-d_6 and chemical shifts are expressed in parts per million relative to Me_4Si. [b] $J \sim 6$ Hz. [c] Broad singlet.

(J = 6 Hz) observed for the high field methylene protons (CH_{2b}) are due to the extra coupling with a coincident J_{N-H} coupling of the neighboring N–H proton. This observation substantiates the assignment of these peaks in the ^{1}H NMR spectra to the CH_{2b} protons.

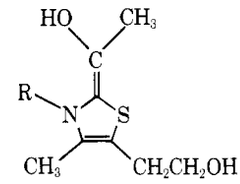
With the identity of the structure for **15** secure, a reasonable mechanism for the formation of this adduct can be formulated (Scheme I). Under the basic conditions of the reaction, proton abstraction from the solvent, nitromethane (pK_a = 10),[23] would give the corresponding conjugate base (**19**). Nucleophilic attack by this carbanion (**19**) at the central carbon of the thiazolium nucleus (C-2) gives the tetrahedral intermediate (**20**). In a subsequent step fragmentation of the ring (**20**) leads directly to **15**.

Scheme I



The eventual site of the nucleophilic attack in the thiazolium salts **5** and **6** is apparently a function of the structure of the nucleophilic species. With the carbanion (**19**), nucleophilic attack at the thiazolium nucleus leads initially to the tetrahedral intermediate (**20**), which subsequently fragments to **15**. Examples of the addition of nitromethide ion to quaternized heteroaromatic molecules have previously been observed.[24–27] On the other hand, with methoxide the product observed is the deacylated thioimidazoline (**14**). In this case formation of a comparable tetrahedral intermediate apparently does not lead to an isolable product.

The structure found for **15** is reminiscent of the proposed active intermediate for the decarboxylation and condensation reactions of α-keto acids by vitamin B_1.[5,6,28] Breslow has suggested that, for example, with pyruvic acid the thiazolium zwitterion reacts to give, after loss of carbon dioxide, the active intermediate **21**. Subsequent reaction of **21** with a proton source, a biological oxidant, or another carbonyl containing



21

compound leads to the observed enzymatic products.[6] Methylene adducts similar to those obtained in this study have previously been isolated.[1,2,29–31] In most cases, however, the compounds obtained were relatively unstable.

Experimental Section

General. Melting points were determined with a Thomas-Hoover melting point apparatus and are uncorrected. Infrared spectra (ir) were run on a Perkin-Elmer Model 700 and 237B spectrometer and calibrated against the 1601-cm^{-1} band of polystyrene. Proton nuclear magnetic resonance (NMR) spectra were recorded on a Varian Associates Model T-60 and EM-390 instruments. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra, the corresponding ^{1}H spectra, as well as a series of selective decoupling experiments were determined at the JEOL Co. Laboratories, Cranford, N.J., on a JEOL FX60 spectrometer, through the courtesy of Mr. R. Omstead and Dr. K. Goto. 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), 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. 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, dichloromethane was distilled from phosphorus pentoxide, dimethoxyethane was distilled from lithium aluminum hydride, anhydrous ether was stored over sodium metal, and nitromethane and nitroethane were freshly distilled. All reactions were run under nitrogen, and all glassware was dried before use.

Reaction of *N*-Acetyl-2-phenacylthioimidazoline (7) with Sodium Methoxide. Preparation of 2-Phenacylthioimidazoline (9). To a stirred CH_2Cl_2 solution (25 ml) containing 7[9] (0.79 g, 3 mmol), 6 ml of 0.5 M sodium methoxide in methanol (3 mmol) was added. The solution was stirred for 4 h at room temperature and then aqueous 5% $NaHCO_3$ (15 ml) added. The addition of the bicarbonate solution resulted in the immediate precipitation of a white solid. The

Table II. Experimental Summary

A. Crystal Data for 15 at −35 °C

$C_{14}H_{15}N_3O_3S$	Crystal system: monoclinic
Formula weight 305.36	Space group: $P2_1/c$ (no. 14)
a = 11.994 (3) Å	Z = 4; $F(000)$ = 640 e
b = 8.791 (3) Å	d_{calcd} = 1.46 g cm^{-3}
c = 13.230 (4) Å	d_{obsd} (room temperature, flotation in aqueous $ZnCl_2$) = 1.40 g cm^{-3}
β = 92.85 (3)°	
V = 1393.2 Å^3	

B. Data Collection at −35 °C

Radiation: Mo K$\bar{\alpha}$, = 0.71069 Å
Mode: ω scan
Scan range: symmetrically over 1.0° about K$\alpha_{1,2}$ maximum
Background: offset 1.0° in ω from K$\alpha_{1,2}$ maximum, each counted for time equal to $^1/_2$ the scan time
Scan rate: variable, 1.0 to 4.0° min^{-1}
Check reflections: four remeasured after every 96 reflections
2θ range: 4.0° to 50.0°
Reflections measured: 2458
Reflections accepted for structure analysis and refinement: 1467 with $I_o \geq 2.0\sigma(I_o)$
Absorption coefficient (Mo K$\bar{\alpha}$): 7.2 cm^{-1}; no absorption correction applied

precipitate was filtered from the H_2O-CH_2Cl_2 mixture, and then triturated with cold $CHCl_3$ and dried in vacuo, yield 0.24 g of **9.** The H_2O–CH_2Cl_2 mixture was then separated and the organic layer dried (Na_2SO_4), concentrated in vacuo, triturated with cold $CHCl_3$, and dried in vacuo to give an additional 0.36 g of **9,** total recovered yield 0.60 g (91%), mp 143–145 °C (lit.[10] mp 145–146 °C): ir (KBr) 1590 cm^{-1}; NMR (Me_2SO-d_6) δ 2.97–4.15 (m, 7 H), 6.70 (s, 1 H), 7.30–7.70 (m, 5 H).

Preparation of *N*-Acetyl-3-phenyl-5,6-dihydroimidazo[2,1-*b*]thiazolium Fluoroborate (5). Trimethyloxonium fluoroborate[11] (5.77 g, 39 mmol) in freshly distilled nitromethane (40 ml) was added dropwise to a stirred slurry containing **7**[9] (7.86 g, 30 mmol) in nitromethane (250 ml). The solution was allowed to stir at room temperature overnight and the products isolated by precipitation with Et_2O. The residue was dried in vacuo, and then triturated with $CHCl_3$. The remaining $CHCl_3$ insoluble, white solid was further purified by reprecipitation with Et_2O from a 1:1 nitromethane–dichloromethane solution: yield 4.60 g (46%); mp 204–205 °C; ir (KBr) 1675, 1515, 1415, 1315, 1125–1025 cm^{-1}; NMR (CD_3NO_2) δ 2.38 (s, 3 H), 4.97 (s, 4 H), 7.30 (s, 1 H), 7.58 (s, 5 H).

Anal. Calcd for $C_{13}H_{13}N_2OSBF_4$: C, 47.01; H, 3.95; N, 8.44. Found: C, 47.16; H, 3.92; N, 8.47.

Reaction of *N*-Acetyl-3-phenyl-5,6-dihydroimidazo[2,1-*b*]thiazolium Fluoroborate (5) with Sodium Methoxide. Preparation of 3-Phenyl-5,6-dihydroimidazo[2,1-*b*]thiazole (14). 5 (1.33 g, 4 mmol) was added to 8 ml (4 mmol) of 0.5 M sodium methoxide in methanol and the solution allowed to stand overnight. The solution was then adjusted to pH 9 by the gradual addition of aqueous 5% HCl, and then concentrated in vacuo. The residue was added to aqueous 5% $NaHCO_3$ (20 ml) and then extracted with CH_2Cl_2 (2 × 20 ml). The combined organic layer extracts were washed with H_2O (20 ml), dried (Na_2SO_4), and evaporated in vacuo to give 0.45 g (56% yield) of **14:** mp 109–112.5 °C (lit.[9] mp 112–113 °C); ir (KBr) 1600 cm^{-1}; NMR ($CDCl_3$) δ 3.52–4.40 (m, 4 H), 5.64 (s, 1 H), 7.37 (s, 5 H); MS *m/e* (rel intensity) 202 (100), 201 (69), 147 (12), 142 (22), 105 (95), 102 (47), 100 (44), 99 (50), 77 (18).

Preparation of (2*Z*)-3-(2′-Acetylaminoethyl)-2-nitromethylene-4-phenyl-2,3-dihyrothiazole (15). To a stirred nitromethane solution (30 ml) containing 0.76 g (2.3 mmol) of **5,** 0.23 g 2.3 mmol) of Et_3N was added. The solution was stirred for 48 h at room temperature during which time a yellow crystalline material separated. The solid was collected, dried (0.49 g), and then recrystallized from deionized H_2O: yield 0.30 g (43%); mp 237–238 °C; ir (KBr) 3320, 3110, 2930, 1675, 1520, 1490 cm^{-1}; NMR (Me_2SO-d_6) δ 1.62 (s, 3 H), 2.97–3.38 (m, 2 H), 3.28 (s, HOD), 3.76–4.10 (t, J = 6 Hz, 2 H), 7.12 (s, 1 H), 7.50 (s, 5 H), 7.72–8.06 (broad s, 1 H), 7.82 (s, 1 H). Upon addition of D_2O to the NMR sample the broad singlet at δ 7.72–8.06 disappears and the multiplet at δ 2.97–3.38 broadens. Addition of 1 N NaOD–D_2O (2 drops) to the sample results in the rapid exchange of the peaks at δ 7.12 and 7.82. Of the two, the higher field peak exchanges the most rapidly. The rest of the spectrum remains relatively unchanged upon the addition of base. ^{13}C NMR (Me_2SO-d_6) 22.4, 36.2, 46.9, 107.4, 110.2, 128.8, 129.3, 129.8, 143.7, 161.3, 169.6 ppm. Irradiation of the protons at δ 3.76–4.10, 7.12, and 7.82 in successive selective proton decoupling experiments identified the corresponding carbon resonances at 46.9, 110.2, and 107.4 ppm, respectively. MS *m/e* (rel intensity) 305 (23), 245 (5), 221 (53), 220 (23), 204 (17), 176 (22), 175 (73), 174 (71), 135 (17), 134 (100), 102 (44), 86 (96), 85 (35), 77 (21).

Anal. Calcd for $C_{14}H_{15}N_3O_3S$: C, 55.07; H, 4.95; N, 13.76; S, 10.50. Found: C, 55.05; H, 5.00; N, 13.72; S, 10.54.

X-Ray Structure Analysis. Crystals of **15** obtained by slow evaporation of a methanol solution were yellow plates. All x-ray work was carried out on a Syntex $P2_1$ autodiffractometer equipped with graphite monochromator and a Syntex LT-1 inert gas (N_2) low temperature (−35 °C) delivery system. Cell parameters were determined by least-squares analysis of 45 carefully centered reflections, 14° ≤ 2θ ≤ 23°. Details of crystal data and intensity data collection appear in Table II.

Data reduction and assignment of standard deviations (with p = 0.02) to the measured intensities were carried out as previously described.[32] Analysis of the 29 sets of check reflections revealed a mild fall-off of intensity with time. This fall-off was described[33] by the equation $X = 1 + At + Bt^2$, where t is exposure time in hours, and the least-squares values of A and B, respectively, were 0.000278 ± 0.000165 and −0.000006 ± 0.000002. A multiplicative correction, $1/X$, applied to the intensity data, ranged from 0.997 to 1.018. No correction for absorption was applied.

The structure was solved by application of direct methods, implemented by the program package MULTAN[34a] and refined by full-matrix least-squares methods.[34b] During the early stages of structure refinement, all nonhydrogen atoms (except sulfur) were assigned carbon atom scattering factors. Consideration of resulting B values and distances and angles soon verified the identity of the N and O atoms. After a few cycles of anisotropic refinement, a difference map revealed the positions of most hydrogen atoms. However, when these failed to refine satisfactorily, hydrogen atoms were included in the refinement in calculated ideal positions. Refinement then proceeded smoothly with all nonhydrogen atoms treated anisotropically and all hydrogen atoms isotropically.

Convergence was reached at $R = \Sigma||F_o| - |F_c||/\Sigma|F_o| = 0.067$ and $R_W = [\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2]^{1/2} = 0.079$. In the final cycle of least-squares refinement, all shifts in nonhydrogen positional parameters were less than 20% of a corresponding estimated standard deviation (esd). No shift in an anisotropic thermal parameter exceeded 30% of its esd in this final cycle. All hydrogen position shifts were less than 30% of an esd and no hydrogen temperature factor shifted by more than 75% of an esd. The function minimized in refinement was $\Sigma w(|F_o| - |F_c|)^2$, where the weight w of each reflection was taken as the reciprocal square of the standard deviation of $|F_o|$. Neutral atom scattering factors for S, O, N, C,[35] and H[36] were used; the real and imaginary corrections due to anomalous dispersion were applied to the S atom scattering factor.[37] A final difference map showed only random features, not exceeding 0.4 eÅ^{-3}.

Final fractional coordinates for the nonhydrogen atoms appear in Table III. Supplementary data consisting of tables of final thermal parameters for nonhydrogen atoms, coordinates and thermal parameters for hydrogen atoms, bond lengths and angles, torsion angles, and selected least-squares planes will be found in the microfilm edition of this journal.[38]

Preparation of (2*Z*)-3-(2′-Acetylaminoethyl)-2-nitroethylidene-4-phenyl-2,3-dihydrothiazole (16). Et_3N (0.23 g, 2.3 mmol) was added to a stirred solution of **5** (0.76 g, 2.3 mmol) in 25 ml of nitroethane. The solution was heated at 40 °C for 24 h and the product isolated by precipitation with ether (450 ml). Purification of **16** was accomplished by dissolving the crude precipitate in CH_2Cl_2 (200 ml) and washing with H_2O (2 × 50 ml). The organic layer was dried (Na_2SO_4), concentrated in vacuo, and reprecipitated from chloroform–ether: yield 0.18 g (25%); mp 208–211 °C; ir (KBr) 3280, 1660, 1540, 1350, 1325 cm^{-1}; NMR (Me_2SO-d_6) δ 1.62 (s, 3 H), 2.53 (s, 3 H), 2.75–3.12 (q, J = 6 Hz, 2 H), 3.27 (s, HOD), 4.13–4.40 (t, J = 6 Hz, 2 H), 7.12 (s, 1 H), 7.42 (s, 5 H), 7.60–7.75 (m, 1 H); MS *m/e* (rel intensity) 319 (10), 245 (9), 235 (25), 218 (7), 203 (8), 190 (10), 189 (33), 188 (100), 135 (7), 134 (17), 102 (12), 91 (8), 86 (24).

Anal. Calcd for $C_{15}H_{17}N_3O_3S$: C, 56.41; H, 5.37; N, 13.16; S, 10.04. Found: C, 56.30; H, 5.37; N, 13.07; S, 9.97.

Preparation of (2*Z*)-3-(2′-Carbomethoxyaminoethyl)-2-nitromethylene-4-phenyl-2,3-dihydrothiazole (17). To a stirred nitromethane solution (35 ml) containing 1.28 g (3.7 mmol) of **6,**[8] 0.37 g (3.7 mmol) of Et_3N was added. The solution was stirred for 48 h at room temperature during which time a yellow crystalline material

Table III. Fractional Coordinates for Nonhydrogen Atoms of 15[a]

Atom	x	y	z
S	−0.0690 (1)	0.7509 (2)	0.1169 (1)
O(1)	−0.1417 (4)	0.4750 (6)	0.1242 (4)
O(2)	−0.0517 (4)	0.2592 (6)	0.1408 (4)
O(3)	0.4747 (4)	0.8198 (6)	0.2220 (4)
N(1)	0.1405 (4)	0.7196 (6)	0.1054 (4)
N(2)	−0.0506 (5)	0.4018 (7)	0.1304 (5)
N(3)	0.3052 (5)	0.7698 (7)	0.2810 (5)
C(1)	0.0119 (6)	0.9100 (9)	0.1088 (6)
C(2)	0.1210 (6)	0.8771 (8)	0.1000 (5)
C(3)	0.0471 (5)	0.6361 (8)	0.1157 (5)
C(4)	0.0458 (6)	0.4792 (9)	0.1251 (6)
C(5)	0.2538 (6)	0.6524 (9)	0.1139 (6)
C(6)	0.2894 (7)	0.6291 (9)	0.2252 (6)
C(7)	0.3991 (6)	0.8533 (9)	0.2763 (6)
C(8)	0.4057 (7)	0.9873 (11)	0.3464 (7)
C(9)	0.2104 (6)	0.9866 (8)	0.0780 (5)
C(10)	0.2338 (6)	1.1082 (9)	0.1408 (6)
C(11)	0.3178 (8)	1.2108 (10)	0.1189 (7)
C(12)	0.3740 (8)	1.1946 (11)	0.0323 (7)
C(13)	0.3514 (8)	1.0758 (12)	−0.0315 (7)
C(14)	0.2696 (6)	0.9698 (9)	−0.0103 (6)

[a] See Figure 1 for identity of the atoms. Numbers in parentheses are the estimated standard deviations in the last significant digit.

separated out. The solid was collected, triturated with Et_2O, and reprecipitated from dichloromethane–hexanes: yield 1.03 g (87%); mp 233.5–235.5 °C; ir (KBr) 3290, 3100, 2960, 1710, 1510, 1420, 1350 cm^{-1}; NMR (Me_2SO-d_6) δ 2.97–3.24 (q, J = 6 Hz, 2 H), 3.30 (s, 3 H), 3.43 (s, HOD), 3.90–4.12 (t, J = 6 Hz, 2 H), 6.98–7.10 (m, 1 H), 7.12 (s, 1 H), 7.45 (s, 5 H), 7.78 (s, 1 H). Addition of D_2O to the NMR sample results in the disappearance of the multiplet at δ 6.98–7.10 and the broadening of the quartet at δ 2.97–3.24. Ms m/e (rel intensity) 321 (4), 221 (10), 204 (10), 186 (12), 175 (30), 174 (100), 134 (71), 102 (44), 101 (26), 89 (16), 77 (19).

Anal. Calcd for $C_{14}H_{15}N_3O_4S$: C, 52.32; H, 4.71; N, 13.08; S, 9.98. Found: C, 52.35; H, 4.67; N, 13.08; S, 10.09.

Preparation of (2Z)-3-(2′-Carbomethoxyaminoethyl)-2-nitroethylidene-4-phenyl-2,3-dihydrothiazole (18). Et_3N (0.10 g, 1 mmol) was added to a stirred solution of **6**[8] (0.35 g, 1 mmol) in 10 ml of nitroethane. The solution was allowed to stir at room temperature for 72 h, during which time a yellow solid separated. The precipitate was collected, washed with Et_2O, and reprecipitated from dichloromethane–hexanes: yield 0.27 g (81%); mp 199.5–201.5 °C; ir (KBr) 3290, 3080, 2945, 1695, 1525, 1400, 1325 cm^{-1}; NMR (Me_2SO-d_6) δ 2.54 (s, 3 H), 2.78–3.08 (q, J = 6 Hz, 2 H), 3.37 (s, 3 H), 3.43 (s, HOD), 4.27–4.47 (t, J = 6 Hz, 2 H), 7.03–7.14 (m, 1 H), 7.23 (s, 1 H), 7.57 (s, 5 H). Addition of D_2O to the NMR sample results in the disappearance of the multiplet at δ 7.03–7.14 and the broadening of the quartet at δ 2.73–3.08. MS m/e (rel intensity) 335 (9), 261 (5), 235 (18), 218 (6), 202 (10), 189 (32), 188 (100), 134 (19), 102 (22), 84 (13).

Anal. Calcd for $C_{15}H_{17}N_3O_4S$: C, 53.72; H, 5.11; N, 12.53; S, 9.56. Found: C, 53.66; H, 5.03; N, 12.40; S, 9.56.

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Registry No.—**5,** 60498-93-3; **6,** 59864-00-5; **7,** 60498-94-4; **8,** 59863-93-3; **9,** 32188-99-1; **14,** 36065-41-5; **15,** 60498-95-5; **16,** 60498-96-6; **17,** 60498-97-7; **18,** 60498-98-8; trimethyloxonium fluoroborate, 420-37-1; nitromethane, 75-52-5; nitroethane, 79-24-3.

Supplementary Material Available. Tables of final thermal parameters for nonhydrogen atoms, coordinates and thermal parameters for hydrogen atoms, bond lengths and angles, torsion angles, and least-squares planes (8 pages). Ordering information is given on any current masthead page.

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