Mesoionic Compounds. 40. A Convenient Route to the *anhydro*-4-Hydroxyimidazolium Hydroxide System[1]

Kevin T. Potts* and Samuel J. Chen[1]

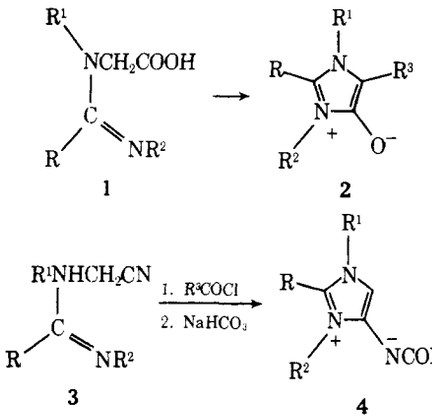
Department of Chemistry, Rensselaer Polytechnic Institute, Troy, New York 12181

Received July 27, 1976

N,N'-Disubstituted amidines and α-bromoacetyl chlorides underwent ready condensation in the presence of triethylamine to form a variety of functionally substituted derivatives of the title mesoionic system. These underwent ready 1,3-dipolar cycloaddition with acetylenic dipolarophiles forming, in turn, functionally substituted pyrroles. This mesoionic system also underwent ready hydrolysis with water to the corresponding imidazolidine-2,4-diones.

In the previous paper[2] in this series, the condensation of a suitable 1,3-binucleophile containing at least one hydrogen atom with a reactive 1,2-bielectrophile incorporating an α-bromoacyl chloride function was shown to be a particularly convenient route to several mesoionic ring systems. In addition to the ease of reaction, it enabled a variety of functional groups to be incorporated into the mesoionic system, greatly extending their potential use as precursors to other heterocycles. We now describe an extension of this synthetic route to the preparation of the *anhydro*-4-hydroxyimidazolium hydroxide system, which is difficult to prepare by other procedures.

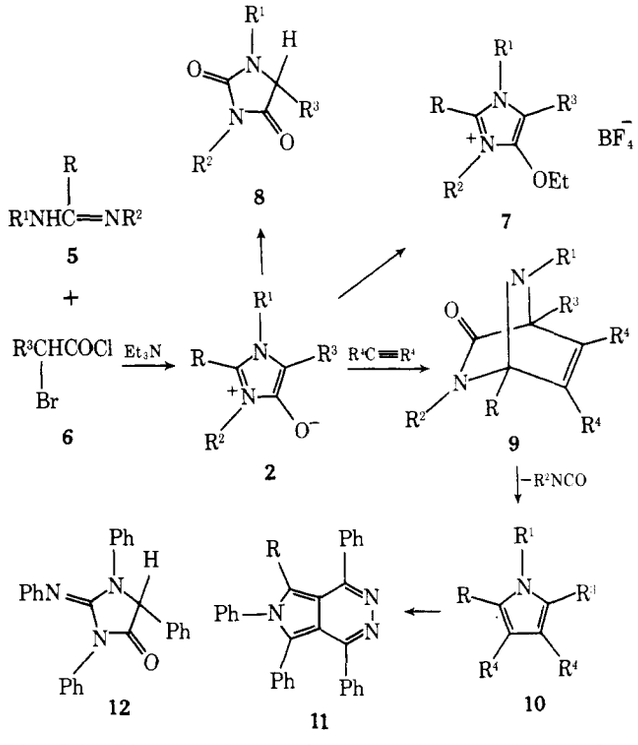
Previous attempts to prepare derivatives of this ring system have centered around the dehydrative cyclization of glycine derivatives **1** with acid anhydrides[3] to form the 4-hydroxy derivative **2**, or ring closure[4] of the corresponding nitrile **3** to the acylimino derivative **4**. However, in the cyclization of **1** to



2, an acyl substituent, R^3, corresponding to the acyl group of the acid anhydride used for the cyclization was always introduced into the 5 position of the nucleus. Representatives of this ring system with an exocyclic sulfur atom have also been prepared, in this instance the route involving reaction of *anhydro*-2,4-diphenyl-5-hydroxy-3-methyloxazolium hydroxide[5] or *anhydro*-2-aryl-5-hydroxy-3-methylthiazolium hydroxides[6] with phenyl isothiocyanate to give the appropriately substituted derivatives. Reaction of the former mesoionic ring system with phenyl isocyanate has also been reported[7] to give the corresponding *anhydro*-4-hydroxyimidazolium hydroxide system.

The 5-acetyl derivative **2** ($R^3 = COCH_3$) did not react with acetylenic or olefinic dipolarophiles,[4] and also was relatively stable to hot acids, alkali, and benzylamine,[3b] this stability being attributed to delocalization of the exocyclic negative charge over the 5-acyl substituent. MO calculations predict[3b] appreciable dipolar activity for this ring system and considerable effort has been expended to obtain derivatives without the 5-acyl substituent as well as other representatives of this ring system. Reaction of benzoylformic acid anil with trifluoroacetic anhydride in dry pyridine at 0 °C results[8] in dimerization and evolution of CO_2 with the ultimate formation of *anhydro*-4-hydroxy-1,2,3,5-tetraphenylimidazolium hydroxide (**2**, R = $R^1 = R^2 = R^3$ = Ph). More recently the reaction of symmetrically substituted amidines with α-bromophenylacetyl chloride or α-bromopropionyl chloride, followed by reaction with dimethyl acetylenedicarboxylate, was found to give substituted pyrroles,[9] a reaction which must have involved an intermediate *anhydro*-4-hydroxyimidazolium hydroxide system though this ring system was not isolated in this study.

1,3-Diphenyl-2-methyl-2-pseudothiourea (**5**, R = CH_3S;



$R^1 = R^2$ = Ph) and α-bromophenylacetyl chloride[10a] (**6**, R^3 = Ph) in the presence of 2 mol of Et_3N underwent an extremely facile condensation to give *anhydro*-4-hydroxy-2-methylthio-1,3,5-triphenylimidazolium hydroxide (**2**, R = SCH_3; $R^1 = R^2 = R^3$ = Ph) (Table I). An equally ready reaction with 2-bromo-2-ethoxycarbonylacetyl chloride[10b] (**6**, R^3 = COOEt) gave *anhydo*-5-ethoxycarbonyl-1,3-diphenyl-4-hydroxy-2-methylthioimidazolium hydroxide (**2**, R = SCH_3; $R^1 = R^2$ Ph; R^3 = COOEt). The analytical and spectral data described in Table I leave no doubt that ring closure had occurred to the desired system, and this was confirmed by further chemical transformations described below. Most of these imidazolium hydroxide derivatives could be stored for relatively long periods of time at ca. 0 °C; at room temperature decomposition occurred after several days.

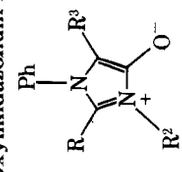
Alkylation of **2** (R = SCH_3; $R^1 = R^2$ = Ph; R^3 = Ph and COOEt) with Meerwein's reagent[11] occurred readily in methylene chloride giving the corresponding ethyl ethers **7**, readily characterized by analytical and spectral data (Experimental Section). Hydrolysis of **2** (R = SCH_3; $R^1 = R^2 = R^3$ = Ph) in refluxing ethanol/water (1:3) occurred over 3 h yielding 1,3,5-triphenylimidazolidine-2,4-dione[12] (**8**, $R^1 = R^2 = R^3$ = Ph). Similarly, the corresponding 5-ethoxycarbonyl derivative of **2** underwent ready hydrolysis. In refluxing dilute HCl, 5-ethoxycarbonyl-1,3-diphenylimidazolidine-2,4-dione[13] (**8**, $R^1 = R^2$ = Ph; R^3 = COOEt) was readily obtained, the ester function being stable under these conditions. However, further hydrolysis of **8** ($R^1 = R^2$ = Ph; R^3 = COOEt) under alkaline conditions[14] resulted in the formation of 1,3-diphenylimidazolidine-2,4-dione[15b] (**8**, $R^1 = R^2$ = Ph; R^3 = H), the intermediate β-keto acid undergoing spontaneous decarboxylation.

Dimethyl acetylenedicarboxylate underwent cycloaddition with **2** (R = CH_3S; $R^1 = R^2 = R^3$ = Ph) in refluxing benzene forming dimethyl 1,5-diphenyl-2-methylthiopyrrole-3,4-dicarboxylate (**10**, R = CH_3S; $R^1 = R^3$ = Ph; R^4 = $COOCH_3$) (Table II) in very good yield. The intermediate 1:1 cycloadduct **9** was not isolated but was undoubtedly involved in the reaction. Hydrolysis of **10** (R = CH_3S; $R^1 = R^3$ = Ph; R^4 = COOEt) with aqueous methanolic (3:1) NaOH solution gave 1,5-diphenyl-2-methylthiopyrrole-3,4-dicarboxylic acid (**10**, R = CH_3S; $R^1 = R^3$ = Ph; R^4 = COOH) (Table II). Cycloaddition also occurred readily with **2** (R = CH_3S; $R^1 = R^2$ = Ph; R^3 = COOEt) to give the corresponding pyrrole **10** (R = CH_3S; $R^1 = R^2$ = Ph; R^3 = COOEt), although in slightly reduced yield. Thus the 5-ethoxycarbonyl substituent does not retard the "masked" ylide character of this ring system in contrast to a 5-acetyl substituent when all 1,3-dipolar characteristics are suppressed. This is most likely due to a less effective delocalization of the exocyclic negative charge over the 5-ethoxycarbonyl group than in the 5-acetyl group. Dibenzoylacetylene also underwent ready cycloaddition with **2** (R = CH_3S; $R^1 = R^2 = R^3$ = Ph) in refluxing benzene forming 3,4-dibenzoyl-1,5-diphenyl-2-methylthiopyrrole (**10**, R = CH_3S; $R^1 = R^3$ = Ph; R^4 = COPh) (Table II) which was characterized further by conversion into 5-methylthio-1,4,6,7-tetraphenylpyrrolo[3,4-*d*]pyridazine (**11**, R = CH_3S) by reaction with hydrazine.

Other amidines reacted readily with the 1,2-bielectrophiles **6**, in most cases forming the desired *anhydro*-4-hydroxyimidazolium hydroxide system **2**, but in several instances difficulty in effecting adequate purification of the product resulted in their being isolated as their hydrolysis products. *N,N'*-Diphenylbenzamidine[16] (**5**, R = $R^1 = R^2$ = Ph) and α-bromophenylacetyl chloride (**6**, R^3 = Ph) underwent ready reaction as above to give *anhydro*-4-hydroxy-1,2,3,5-tetraphenylimidazolium hydroxide (**2**, R = $R^1 = R^2 = R^3$ = Ph) (Table I) in 77% yield and the corresponding 5-ethoxycarbonyl derivative **2** (R = $R^1 = R^2$ = Ph; R^3 = COOEt) was readily formed when 2-bromo-2-ethoxycarbonylacetyl chloride (**6**, R^3 = COOEt) was used as the 1,2-bielectrophile. This imidazole derivative reacted readily with Meerwein's reagent to form the corresponding ether **7** (R = $R^1 = R^2$ = Ph; R^3 = COOEt) and also underwent ready cycloaddition with dimethyl acetylenedicarboxylate and dibenzoylacetylene forming the corresponding pyrroles in good yields (Table II). Additional characterization of **10** (R = R^1 = Ph; R^3 = COOEt; R^4 = COPh) by reaction with hydrazine gave ethyl 1,4,6,7-tetraphenylpyrrolo[3,4-*d*]pyridazine-5-carboxylate (**11**, R = COOEt).

The symmetrically substituted urea derivatives above present no problem in terms of the structure of the final product. However, use of an unsymmetrically substituted 1,3-binucleophile could lead to four intermediates depending

Table I. *anhydro*-4-Hydroxyimidazolium Hydroxide Derivatives (**2**)[f]

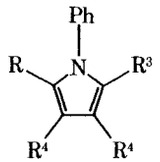


Registry no.	Substituents R	R^2	R^3	Mp, °C	Yield,[a] %	Mol formula	M^+. (rel int)	Spectral data: λ_{max} (CH_3OH), nm (log ϵ)	Spectral data: ν_{CO}	Spectral data: $\nu_{C=N}$, cm^{-1}	Spectral data: NMR, δ ($CDCl_3$)
61505-47-3	CH_3S	Ph	Ph	177–180[b]	49	$C_{22}H_{18}N_2OS$	358 (32)	237[c] (4.20), 264[c] (3.91), 353 (3.63)	1635	1600	7.65–6.90 (m, 15, aromatic), 1.90 (s, 3, SCH_3)
61505-48-4	CH_3S	Ph	COOEt	158–160[b]	52	$C_{19}H_{18}N_2O_3S$	354 (43)	226[c] (4.12), 247[c] (4.01), 327 (4.00)	1690 1670	1600	7.53 (s, 10, aromatic), 4.18 (q, 2, $COOCH_2CH_3$), 1.85 (s, 3, SCH_3), 1.17 (t, 3, $CO_2CH_2CH_3$)
54563-03-0	Ph	Ph	Ph	174–177[d]	77	$C_{27}H_{20}N_2O$		255[c] (4.23), 347 (3.73)	1640	1595	7.7–6.7 (m, aromatic)

61505-49-5	Ph	Ph	COOEt	236–238[e]	50	$C_{24}H_{20}N_2O_3$	384 (31)	244 (4.15), 316 (4.10)	1690 1655	1600	7.45–6.65 (m, 15, aromatic), 4.15 (q, 2, $CO_2CH_2CH_3$), 1.11 (t, 3, $CO_2CH_2CH_3$)
61505-50-8	Ph	CH_3	Ph	183–185	51	$C_{22}H_{18}N_2O$	326 (11)	232[c] (3.97), 290 (3.83), 340 (3.98)	1630	1600	7.6–6.8 (m, 15, aromatic), 3.47 (s, 3, NCH_3)
61505-51-9	Ph	CH_3	COOEt	308–310[b]	32	$C_{19}H_{18}N_2O_3$	322 (53)	223[c] (4.10), 247 (3.97), 309 (4.10)	1690 1665	1605	7.24 (s, 10, aromatic), 4.13 (q, 2, $CO_2CH_2CH_3$), 3.34 (s, 3, NCH_3), 1.18 (t, s, $CO_2CH_2CH_3$)

[a] All obtained as colorless or cream prisms or needles from $CHCl_3/Et_2O$. [b] Decomposition. [c] Shoulder. [d] Lit.[8] mp 166–168 °C. [e] Purification by PLC on silica gel using EtOAc. [f] Satisfactory analytical values (±0.4% for C, H, N) were reported for all compounds in table.

Table II. Pyrroles (10) Obtained from 2 and Acetylenic Dipolarophiles[f]



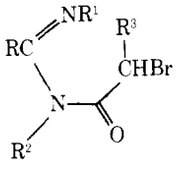
	Substituents							Spectral data		
Registry no.	R	R^3	R^4	Mp, °C	% yield[a]	Formula	$M^{+\cdot}$ (rel int)	λ_{max} (CH_3OH), nm (log ε)	ν_{CO} (KBr), cm^{-1}	NMR, δ ($CDCl_3$)
61505-52-0	CH_3S	Ph	$COOCH_3$	155–156.5	81	$C_{21}H_{19}NO_4S$	381 (100)	270[b] (4.07)	1725 1705	7.4–6.8 (m, 10, aromatic), 3.93 (s, 3, CO_2CH_3), 3.66 (s, 3, CO_2CH_3), 2.15 (s, 3, SCH_3)
61505-53-1	CH_3S	Ph	COOH	213–215	87	$C_{19}H_{15}NO_4S$	353 (1.5)	283[b] (3.90)	1695	7.25 (m, 10, aromatic), 2.14 (s, 3, SCH_3)[c]
61505-54-2	Ph	COOEt	$COOCH_3$	168.5–170.5	55[d] 72[e]	$C_{23}H_{21}NO_6$	407 (100)	268 (4.25)	1740 1720 1710	7.17 (s, 10, aromatic), 4.1 (q, 2, $CO_2CH_2CH_3$), 3.98 (s, 3, CO_2CH_3), 3.83 (s, 3, CO_2CH_3), 1.1 (t, 3, $CO_2CH_2CH_3$)
61505-55-3	CH_3S	Ph	PhCO	197–198	72	$C_{31}H_{23}NO_2S$	473 (40)	253 (4.54), 315 (3.75)	1650	7.83–6.8 (m, 20, aromatic), 2.17 (s, 3, SCH_3)
61528-39-0	Ph	COOEt	PhCO	176–178	60	$C_{33}H_{25}NO_4$	499 (100)	256 (4.58), 286[b] (4.18)	1700 1670 1645	8.1–6.77 (m, 20, aromatic), 3.83 (q, 2, $CO_2CH_2CH_3$), 0.73 (t, 3, $CO_2CH_2CH_3$)

[a] All obtained as colorless prisms from ethanol. [b] Shoulder. [c] Me_2SO-d_6. [d] Derived from 2 (R^2 = Ph). [e] Derived from 2 (R^2 = CH_3). [f] Satisfactory analytical values (±0.4% for C, H, N) were reported for all compounds in table.

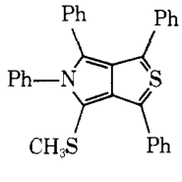
on the site of initial condensation with the 1,2-bielectrophile, and two final products could result. 1,2-Dimethyl-3-phenyl-2-pseudothiourea (**5**, R = CH_3S; R^1 = CH_3; R^2 = Ph) and α-bromophenylacetyl chloride (**6**, R^3 = Ph) underwent ready reaction with the final isolaton of a mixture of two products, one the *anhydro*-1,5-diphenyl-4-hydroxy-2-methylthio-3-methylimidazolium hydroxide (**2**, R = SCH_3; R^1 = R^3 = Ph; R^2 = CH_3) and its hydrolysis product 1,5-diphenyl-3-methylimidazolidine-2,4-dione[17] (**8**, R^1 = R^3 = Ph; R^2 = CH_3), the former being converted into the latter by hot water. Similarly reaction of **5** (R = CH_3S; R^1 = CH_3; R^2 = Ph) with 2-bromo-2-ethoxycarbonylacetyl chloride (**6**, R^3 = COOEt) and subsequent hydrolysis of the reaction product with water resulted in a product assigned the structure 5-ethoxycarbonyl-3-methyl-1-phenylimidazolidine-2,4-dione (**8**, R^1 = Ph; R^2 = CH_3; R^3 = COOEt) as its physical characteristics (mp 123–125 °C) were quite different from those of the isomeric 5-ethoxycarbonyl-1-methyl-3-phenylimidazolidine-2,4-dione[18] (**8**, R^1 = CH_3; R^2 = Ph; R^3 = COOEt) (mp 95–97 °C). This was confirmed by the hydrolysis of **8** (R^1 = Ph; R^2 = CH_3; R^3 = COOEt) with alkali to 3-methyl-1-phenylimidazolidine-2,4-dione[15a] (**8**, R^1 = Ph; R^2 = CH_3; R^3 = H).

However, the *anhydro*-4-hydroxyimidazolium hydroxide system obtained from *N*-methyl-*N'*-phenylbenzamidine (**5**, R = R^2 = Ph; R^1 = CH_3) and α-bromophenylacetyl chloride (**6**, R^3 = Ph) was obtained free of its hydrolysis product and *anhydro*-4-hydroxy-3-methyl-1,2,5-triphenylimidazolium hydroxide (**2**, R = R^1 = R^3 = Ph; R^2 = CH_3) obtained in this way is isomeric with *anhydro*-4-hydroxy-1-methyl-2,3,5-triphenylimidazolium hydroxide (**2**, R = R^2 = R^3 = Ph; R^1 = CH_3) obtained from *anhydro*-2,4-diphenyl-5-hydroxy-3-methyloxazolium hydroxide and phenyl isocyanate.[7] The physical characteristics of these two products are quite dissimilar. An interesting feature of the NMR spectrum of **2** (R = R^1 = R^3 = Ph; R^2 = CH_3) is the chemical shift of the NCH_3 group at δ 3.47; the corresponding methyl group in **2** (R = R^2 = R^3 = Ph; R^1 = CH_3) is at δ 3.03, and the downfield shift in the former is probably due to the adjacent carbonyl group. Similarly *anhydro*-5-ethoxycarbonyl-1,2-diphenyl-4-hydroxy-3-methylimidazolium hydroxide (**2**, R = R^1 = Ph; R^2 = CH_3; R^3 = COOEt) was readily formed from **5** (R = R^2 = Ph; R^1 = CH_3) and **6** (R^3 = COOEt), and in this product the chemical shift of the methyl group was at δ 3.34, indicating its closeness to the 4-carbonyl function. Additional characterization of **2** (R = R^1 = Ph; R^2 = CH_3; R^3 = COOEt) by ready cycloaddition with dimethyl acetylenedicarboxylate gave dimethyl 5-ethoxycarbonyl-1,2-diphenylpyrrole-3,4-dicarboxylate (**10**, R = R^1 = Ph; R^3 = COOEt; R^4 = $COOCH_3$) in 72% yield.

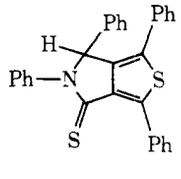
These collective results, together with the cycloaddition to pyrroles described above, remove two possibilities from consideration as the initial mode of condensation, leaving the condensation of the acid chloride function with the NCH_3 group in the amidine or reaction between the α-bromo carbon and the NPh group of the amidine to be the actual pathway followed. Unfortunately, with our present data this point cannot be resolved. Other studies[20] however, suggest a reaction sequence involving initial attack of the amidine at the acyl chloride function followed by intramolecular cyclization of the α-haloacylamidine **13**.



13



14



15

Use of a guanidine with one replaceable hydrogen atom as a 1,3-binucleophile in the initial condensation such as 1,1-diethyl-2,3-diphenylguanidine[19] (**5**, R = NEt_2; R^1 = R^2 = Ph) resulted in a product from its reaction with α-bromophenylacetyl chloride (**6**, R^3 = Ph) that could not be satisfactorily purified. The stability of the *anhydro*-4-hydroxyimidazolium hydroxide system was not improved by the introduction of a 5-ethoxycarbonyl substituent, a similar experience resulting from the use of several other guanidines. However, use of a guanidine with two replaceable hydrogen atoms, although not leading to a mesoionic system, readily gave an imidazole derivative. Thus, 1,2,3-triphenylguanidine (**5**, R = NHPh; R^1 = R^2 = Ph) and α-bromophenylacetyl chloride readily gave 2-phenylimino-1,3,5-triphenylimidazolidin-4-one (**12**). Confirmation of this structure was readily obtained by hydrolysis of the product to 1,3,5-triphenylimidazolidine-2,4-dione (**8**, R^1 = R^2 = R^3 = Ph).

The pyrroles obtained via the cycloadditions described above contain functional substituents in the α position of the nucleus that are not readily introduced by other procedures and these *anhydro*-4-hydroxyimidazolium hydroxides are quite useful in this respect. An interesting application is the possible conversion of 3,4-dibenzoyl-1,5-diphenyl-2-methylthiopyrrole (**10**, R = R^1 = Ph; R^3 = CH_3S; R^4 = PhCO) with P_4S_{10} in pyridine into the substituted thieno[3,4-*c*]pyrrole system **14** which has only been isolated with phenyl substituents in the 1, 3, 5, and 6 positions.[21] The product obtained was identified as **15** having been formed from **14** by loss of the methyl group. This ready demethylation may be due to **15** being the thermodynamically more stable product or indicative of the already noted highly reactive nature of this fused ring system but no conclusion can be made from the data currently available.

Experimental Section[22]

General Procedure for the Reaction of the Amidines 5 with the Bielectrophiles. Formation of *anhydro*-4-Hydroxy-2-methylthio-1,3,5-triphenylimidazolium Hydroxide (2, R = CH_3S; R^1 = R^2 = R^3 = Ph). 1,3-Diphenyl-2-methyl-2-pseudothiourea (727 mg, 3 mmol) in ether (10 mL) was treated dropwise with α-bromophenylacetyl chloride[10a] (0.7 g, 3 mmol) in ether (10 mL) and the reaction mixture was stirred at room temperature for 10 min. To this stirred mixture, a solution of triethylamine (606 mg, 6 mmol) in ether (5 mL) was added slowly. After stirring for 10 min the precipitate was separated by filtration and washed with water, leaving a yellow solid. Recrystallization from chloroform/ether gave cream prisms, 595 mg (49%), mp 177–180 °C dec (Table I).

4-Ethoxy-2-methylthio-1,3,5-triphenylimidazolium Tetrafluoroborate (7, R = CH_3S; R^1 = R^2 = R^3 = Ph). *anhydro*-4-Hydroxy-2-methylthio-1,3,5-triphenylimidazolium hydroxide (727 mg, 2 mmol) in methylene chloride (10 mL) was treated with a slight excess of Meerwein's reagent[11] (0.4 g, 2.1 mmol) and the reaction mixture stirred at room temperature for 24 h. Anhydrous ether was added and the resultant precipitate recrystallized from methylene chloride/ether yielding colorless prisms: 935 mg (93%); mp 262–264 °C; IR (KBr) 3060, 2985, 2925 (CH), 1640 (CO), 1600 (C=N), 1110–1020 cm^{-1} (BF_4^-); λ_{max} (CH_3OH) 239 nm (log ε 4.12), 287 (3.93); NMR ($CDCl_3$) δ 8.15–7.05 (m, 15, aromatic), 3.94 (q, 2, OCH_2CH_3), 2.09 (s, 3, SCH_3), 0.9 (t, 3, OCH_2CH_3).

Anal. Calcd for $C_{24}H_{23}BF_4N_2OS$: C, 60.77; H, 4.87; N, 5.91. Found: C, 60.64; H, 4.86; N, 5.79.

Similarly, 5-ethoxycarbonyl-4-ethoxy-1,2,3-triphenylimidazolium tetrafluoroborate (**7**, R^1 = R^2 = Ph; R^3 = COOEt) was obtained from methylene chloride/ether as colorless prisms (81%): mp 249–251 °C; IR (KBr) 3060, 2985, 2940, 2910 (CH), 1730 (CO), 1615 (C=N), 1120–1020 cm^{-1} (BF_4^-); λ_{max} (CH_3OH) 253 nm sh (log ε 4.13); NMR ($CDCl_3$) δ 7.87–6.97 (m, 15, aromatic), 4.5 (q, 2, $CO_2CH_2CH_3$), 4.15 (q, 2, OCH_2CH_3), 1.15 (t, 3, $CO_2CH_2CH_3$), 1.05 (t, 3, OCH_2CH_3).

Anal. Calcd for $C_{26}H_{25}BF_4N_2O_3$: C, 62.42; H, 5.04; N, 5.60. Found: C, 62.81; H, 5.01; N, 5.49.

1,2-Dimethyl-3-phenyl-2-pseudothiourea (5, R = CH_3S; R^1 = Ph; R^2 = CH_3). 1,2-Dimethyl-3-phenyl-2-pseudothiourea hydriodide[23] (60.0 g, 0.195 mol) and ammonium hydroxide (300 mL) were

stirred at room temperature for 2 h. The solid precipitate was collected, washed well with water, and dried. Extraction with ether and concentration of the solution in vacuo gave an oil which solidified to colorless prisms upon cooling: 25.8 g (75%); mp 60–62 °C; IR (KBr) 3250, 3150, 2980, 2920, 1585, 1535, 1510 cm^{-1}; λ_{max} (CH_3OH) 231 nm sh (log ϵ 4.03), 277 sh (3.65); NMR ($CDCl_3$) δ 7.37–6.70 (m, 5, aromatic), 4.42 (s, 1, NH), 2.87 (s, 3, SCH_3), 2.2 (s, 3, NCH_3); mass spectrum *m/e* (rel intensity) M^+·180 (43).

Anal. Calcd for $C_9H_{12}N_2S$: C, 59.96; H, 6.71; N, 15.54. Found: C, 59.83; H, 6.71; H, 15.35.

3-Methyl-1,5-diphenylimidazolidine-2,4-dione (8, $R^1 = R^3$, ph; $R^2 = CH_3$). α-Bromophenylacetyl chloride (0.7 g, 3 mmol) in anhydrous ether (5 mL) was added dropwise to a solution of 1,2-dimethyl-3-phenyl-2-pseudothiourea (541 mg, 3 mmol) in ether (5 mL) and then the reaction mixture was stirred at room temperature for 5 min. A solution of triethylamine (606 mg, 6 mmol) in ether (5 mL) was added dropwise. After stirring for 5 min, the precipitate was collected by filtration and refluxed in water (10 mL) for 2 h. Cooling in an ice bath gave colorless crystals which were filtered and recrystallized from aqueous ethanol forming colorless needles: 0.32 g (40%); mp 187–188 °C (lit.[17] mp 185–186 °C); IR (KBr) 3030, 2930 (CH), 1765, 1700 cm^{-1} (CO); λ_{max} (CH_3OH) 237 nm (log ϵ 4.06), 248 sh (4.01); NMR ($CDCl_3$) δ 7.55–7.05 (m, 10, aromatic), 5.40 (s, 1, CH), 3.1 (s, 3, CH_3); M^+·266 (100).

Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 71.99; H, 5.50; N, 10.27.

Similarly, 5-ethoxycarbonyl-3-methyl-1-phenylimidazolidine-2,4-dione (8, R^1 = Ph; $R^2 = CH_3$; R^3 = COOEt) crystallized from aqueous ethanol as colorless prisms (13%): mp 123–125 °C; IR (KBr) 2995, 2965, 2915 (CH), 1780, 1745, 1710 cm^{-1} (CO); λ_{max} (CH_3OH) 232 nm (log ϵ 3.98), 246 sh (3.94); NMR ($CDCl_3$) δ 7.6–7.0 (m, 5, aromatic), 5.12 (s, 1, CH), 4.22 (q, 2, $CO_2CH_2CH_3$), 3.10 (s, 3, NCH_3), 1.2 (t, 3, $CO_2CH_2CH_3$); M^+·262 (41).

Anal. Calcd for $C_{13}H_{14}N_2O_4$: C, 59.53; H, 5.38; N, 10.68. Found: C, 59.14; H, 5.23; N, 10.54.

General Procedure for the Reaction of *anhydro*-4-Hydroxy-1,2,3,5-tetrasubstituted-imidazolium Hydroxides (2) with Acetylenic Dipolarophiles. Formation of Dimethyl 1,5-Diphenyl-2-methylthiopyrrole-3,4-dicarboxylate (10, R = CH_3S; $R^1 = R^3$ = Ph; R^4 = $COOCH_3$). *anhydro*-4-Hydroxy-2-methylthio-1,3,5-triphenylimidazolium hydroxide (727 mg, 2 mmol), dimethyl acetylenedicarboxylate (0.3 g, 2.1 mmol), and dry benzene (30 mL) were stirred under reflux for 24 h. Removal of the solvent under reduced pressure and trituration of the resultant residue with petroleum ether (bp 35–60 °C) afforded yellow-brown prisms. The crystals were digested with ethanol and filtered. Recrystallization from ethanol gave colorless prisms, 0.62 g (81%), mp 155–156.5 °C (Table II).

Alkaline Hydrolysis of Dimethyl 1,5-Diphenyl-2-methylthiopyrrole-3,4-dicarboxylate (10, R = CH_3S; $R^1 = R^3$ = Ph; R^4 = $COOCH_3$). The pyrrole (0.42 g, 1.1 mmol) was refluxed in a 4% NaOH solution of a 3:1 mixture of methanol and water (20 mL) for 6 h. The methanol was removed in vacuo and the residual suspension acidified with concentrated HCl. Filtration of the precipitated solid and recrystallization from ethanol/water gave 1,5-diphenyl-2-methylthiopyrrole-3,4-dicarboxylic acid (10, R = CH_3S; $R^1 = R^3$ = Ph; R^4 = COOH) as colorless prisms, 0.34 g (87%), mp 213–215 °C (Table II).

Reaction of 3,4-Dibenzoyl-1,5-diphenyl-2-methylthiopyrrole (10, R = CH_3S; $R^1 = R^3$ = Ph; R^4 = COPh) with Hydrazine. The pyrrole (414 mg, 1 mmol) and hydrazine (50 mg, 1.56 mmol) in ethanol (20 mL) were refluxed for 24 h. The reaction mixture was concentrated in vacuo and the residual oil triturated with ether to give a yellow precipitate. Recrystallization from ethanol gave yellow prisms of 5-methylthio-1,4,6,7-tetraphenylpyrrolo[3,4-*d*]pyridazine (11, R = CH_3S): 0.38 g (81%); mp 235–237 °C; IR (KBr) 3060, 2925 (CH), 1600 cm^{-1} (C=N); λ_{max} ($CHCl_3$) 257 nm sh (log ϵ 4.36), 297 sh (4.01), 362 (3.55); NMR ($CDCl_3$) δ 8.0–6.7 (m, 20, aromatic), 1.64 (s, 3, SCH_3); M^+· 459 (100).

Anal. Calcd for $C_{31}H_{23}N_3S$: C, 79.29; H, 4.94; N, 8.95. Found: C, 79.12; H, 5.04; N, 8.80.

Similarly, ethyl 1,4,6,7-tetraphenylpyrrolo[3,4-*d*]pyridazine-5-carboxylate (11, R = COOEt) was obtained as pale yellow prisms: 0.37 g (75%); mp 236–237 °C; IR (KBr) 3055, 2975 (CH), 1705 (CO), 1600 cm^{-1} (C=N); λ_{max} ($CHCl_3$) 265 nm sh (log ϵ 4.29), 298 sh (3.97), 354 (4.04); NMR ($CDCl_3$) δ 8.00–6.65 (m, 20, aromatic), 3.60 (q, 2, $CO_2CH_2CH_3$), 0.7 (t, 3, $CO_2CH_2CH_3$); M^+· 495 (100).

Anal. Calcd for $C_{33}H_{25}N_3O_2$: C, 79.98; H, 5.08; N, 8.48. Found: C, 80.01; H, 5.15; N, 8.49.

Hydrolysis of *anhydro*-5-Ethoxycarbonyl-1,3-diphenyl-4-hydroxy-2-methylthioimidazolium Hydroxide (2, R = CH_3S; $R^1 = R^2$ = Ph; R^3 = COOEt). The mesoionic compound (0.1 g, 2.82 × 10^{-4} mol) in a 1:1 mixture of water/ethanol (10 mL) and 4 drops of concentrated HCl were refluxed for 7 h. The ethanol was removed in vacuo and the solid precipitate was filtered and washed with water. Recrystallization from aqueous ethanol gave 5-ethoxycarbonyl-1,3-diphenylimidazolidine-2,4-dione (8, $R^1 = R^2$ = Ph; R^3 = COOEt) as colorless prisms: 30 mg (33%); mp 134.5–135.5 °C (lit.[13] mp 134.5 °C); IR (KBr) 3065, 3000, 2975, 2950, 1790, 1740, 1725, 1600 cm^{-1}; λ_{max} (CH_3OH) 233 nm (log ϵ 4.31); NMR ($CDCl_3$) δ 7.44 (s, 10, aromatic), 5.29 (s, 1, CH), 4.28 (q, 2, $CO_2CH_2CH_3$), 1.20 (t, 3, $CO_2CH_2CH_3$); M^+· 324 (55).

Anal. Calcd for $C_{18}H_{16}N_2O_4$: C, 66.66; H, 4.97; N, 8.64. Found: C, 66.83; H, 4.93; N, 8.64.

Alkaline Hydrolysis and Decarboxylation of 8 ($R^1 = R^2$ = Ph; R^3 = COOEt). 5-Ethoxycarbonyl-1,3-diphenylimidazolidine-2,4-dione (0.1 g, 0.31 mol) in 1 N NaOH solution (5 mL) was heated until all the solid dissolved and then stirred at room temperature for 1 h. Acidification with HCl precipitated an oil which gradually solidified on cooling. Filtration and subsequent recrystallization from ethanol gave 1,3-diphenylimidazolidine-2,4-dione as colorless prisms which were shown to be identical with an authentic sample, 60 mg (90%), mp 135–137 °C (lit.[15] mp 136.5–137.5 °C).

Alkaline Hydrolysis and Decarboxylation of 8 (R^1 = Ph; $R^2 = CH_3$; R^3 = COOEt). 5-Ethoxycarbonyl-3-methyl-1-phenylimidazolidine-2,4-dione (0.1 g, 0.31 mmol) in 1 N NaOH solution (5 mL) was stirred at room temperature for 1 h and then acidified with concentrated HCl. The solid was recrystallized from ethanol yielding 3-methyl-1-phenylimidazolidine-2,4-dione (8, R^1 = Ph; $R^2 = CH_3$; R^3 = H) as colorless prisms, 45 mg (62%), mp 184–186 °C (lit.[15a] mp 183–185 °C).

1,3,5-Triphenylimidazolidine-2,4-dione (8, $R^1 = R^2 = R^3$ = Ph). *anhydro*-4-Hydroxy-2-methylthio-1,3,5-triphenylimidazolium hydroxide (0.15 g, 0.42 mmol) in water/ethanol (3:1) (6 mL) was refluxed for 3 h. Upon cooling, a precipitate separated and was recrystallized from aqueous ethanol forming colorless prisms: 80 mg (58%); mp 119–120 °C (lit.[12] mp 124–126 °C); IR (KBr) 3040 (CH), 1775, 1720 cm^{-1} (CO); λ_{max} (CH_3OH) 233 nm (log ϵ 4.41); NMR ($CDCl_3$) δ 7.65–6.65 (m, 15, aromatic), 5.55 (s, 1, CH); M^+· 328 (75).

Anal. Calcd for $C_{21}H_{16}N_2O_2$: C, 76.81; H, 4.91; N, 8.53. Found: C, 76.43; H, 4.83; N, 8.54.

2-Phenylimino-1,3,5-triphenylimidazolidin-4-one (12). A solution of α-bromophenylacetyl chloride (700 mg, 3 mmol) in benzene (10 mL) was added dropwise to a solution of 1,2,3-triphenylguanidine (862 mg, 3 mmol) in benzene (10 mL) and the reaction mixture was then stirred at room temperature for 5 min. To this stirred mixture was added dropwise a solution of triethylamine (606 mg, 6 mmol) in benzene (10 mL). After about 10 min, the precipitated triethylamine hydrohalide salts were removed by filtration and the filtrate evaporated in vacuo. Trituration of the oily residue with ethanol gave 700 mg (58%) of colorless solid which crystallized from ethanol as colorless prisms: mp 162–163.5 °C; IR (KBr) 1750, 1660 (CO), 1595 cm^{-1} (C=N); λ_{max} (CH_3OH) 275 nm (log ϵ 4.08); Nmr)me_2SO-d_6) δ 7.65–6.50 (m, 20, aromatic), 5.82 (s, 1, CH); M^+· 403 (100).

Anal. Calcd for $C_{27}H_{21}N_3O$: C, 80.37; H, 5.25; N, 10.41. Found: C, 80.31; H, 5.26; N, 10.44.

4-Thio-4,6-dihydro-1,3,5,6-tetraphenylthieno[3,4-*c*]pyrrole (15). 3,4-Dibenzoyl-1,5-diphenyl-2-methylthiopyrrole (474 mg, 1 mmol), phosphorus pentasulfide (222 mg, 1 mmol), and dry pyridine (10 mL) were refluxed for 6 h. Upon cooling, the reaction mixture was poured into 5% sodium hydroxide solution. A dark brown solid was separated by filtration and washed well with water. Recrystallization from ethanol or chloroform/ether gave golden-yellow prisms: 400 mg (87%); mp 219–220 °C; IR (KBr) 1590, 1480, 1450, 1380 cm^{-1}; λ_{max} ($CHCl_3$) 281 nm (log ϵ 4.46), 316 sh (4.25), 337 sh (4.13); NMR ($CDCl_3$) δ 8.1–6.9 (m, 20, aromatic), 6.0 (s, 1, CH); M^+· 459 (84).

Anal. Calcd for $C_{30}H_{21}NS_2$: C, 78.39; H, 4.61; N, 3.05. Found: C, 78.58; H, 4.66; N, 2.92.

Registry No.—**5** (R = CH_3S; $R^1 = R^2$ = Ph), 5416-30-8; **5** (R = $R^1 = R^2$ = Ph), 2556-46-9; **5** (R = R^1 = Ph; $R^2 = CH_3$), 2397-29-7; **5** (R = CH_3S; R^1 = Ph; $R^2 = CH_3$), 58432-39-6; **5** (R = NHPh; $R^1 = R^2$ = Ph), 101-01-9; **6** (R^3 = Ph), 19078-72-9; **6** (R^3 = COOEt), 41141-81-5; **7** (R = CH_3S; $R^1 = R^2 = R^3$ = Ph), 61505-57-5; **7** (r, $r^1 = R^2$ = Ph; R^3 = COOEt), 61505-59-7; **8** ($R^1 = R^3$ = Ph; $R^2 = CH_3$), 6716-39-8; **8** (R^1 = Ph; $R^2 = CH_3$; R^3 = COOEt), 56598-96-0; **8** ($R^1 = R^2$ = Ph; R^3 = COOEt), 56598-97-1; **8** ($R^1 = R^2 = R^3$ = Ph), 61505-60-0; **11** (R = CH_3S), 61505-61-1; **11** (R = COOEt), 61505-62-2; **12**, 61505-63-3; **15**, 61505-64-4; $R^4C{\equiv}CR^4$ (R^4 = $COOCH_3$), 762-42-5; $R^4C{\equiv}CR^4$ (R^4 = COPh), 1087-09-8; 1,2-dimethyl-3-phenyl-2-pseudothiourea hydriodide, 61505-65-5.

References and Notes

(1) (a) Partial support of this work by USPHS Research Grant CA 08495, National Cancer Institute, is gratefully acknowledged; (b) abstracted from the Ph.D. Thesis of S. J. Chen, 1976.
(2) K. T. Potts, S. J. Chen, J. Kane, and J. L. Marshall, *J. Org. Chem.*, preceding paper in this issue.
(3) (a) A. Lawson and D. H. Miles, *J. Chem. Soc.*, 2865 (1959); (b) E. B. Roche and D. W. Stansloski, *J. Heterocycl. Chem.*, **7**, 139 (1970). See also M. J. S. Dewar and I. J. Turchi, *J. Chem. Soc., Perkin Trans. 2*, 548 (1976).
(4) K. T. Potts and S. Husain, *J. Org. Chem.*, **36**, 3368 (1971).
(5) R. Huisgen, E. Funke, F. C. Schaefer, H. Gotthardt, and E. Brunn, *Tetrahedron Lett.*, 1809 (1967).
(6) K. T. Potts, J. Baum, E. Houghton, D. N. Roy, and U. P. Singh, *J. Org. Chem.*, **39**, 3619 (1974).
(7) T. Shiba and H. Kato, *Bull. Chem. Soc. Jpn.*, **43**, 3941 (1970).
(8) G. Singh and P. S. Pande, *Tetrahedron Lett.*, 2169 (1974).
(9) M. Hamaguchi and T. Ibata, *Chem. Lett.*, 169 (1975).
(10) (a) E. Fischer and J. Schmidlin, *Justus Liebigs Ann. Chem.*, **340**, 19 (1905); (b) H. Staudinger and H. Becker, *Ber.*, **50**, 1076 (1917); D. S. Breslow, E. Baumgarten, and C. R. Hauser, *J. Am. Chem. Soc.*, **66**, 2186 (1944); G. T. Morgan and E. Walton, *J. Chem. Soc.*, 1744 (1931).
(11) H. Meerwein, *Org. Synth.*, **46**, 113 (1966).
(12) G. A. Holmberg, *Fin. Kemistsam. Medd.*, **59**, 25 (1950); *Chem. Abstr.*, **46**, 8651 (1952).
(13) P. Ruggli and R. Grand, *Helv. Chim. Acta*, **20**, 373 (1937).
(14) W. Reeve and E. Barron, *J. Org. Chem.*, **34**, 1005 (1969).
(15) (a) J. Nematollahi and R. Ketcham, *J. Org. Chem.*, **28**, 2378 (1963); (b) J. F. Klebe and H. Finkbeiner, *J. Am. Chem. Soc.*, **90**, 7255 (1968). We would like to express our thanks to Dr. H. Finkbeiner, General Electric Corporate Research and Development Center, for an authentic sample of this compound.
(16) A. C. Hontz and E. C. Wagner, *Org. Synth.*, **31**, 48 (1951).
(17) M. S. Saettone, *J. Org. Chem.*, **31**, 1959 (1966).
(18) H. Finkbeiner, *J. Org. Chem.*, **30**, 3414 (1965).
(19) H. Bredereck and K. Bredereck, *Chem. Ber.*, **94**, 2278 (1961).
(20) K. T. Potts and S. J. Chen, unpublished results.
(21) For a recent summary of this topic see M. P. Cava and M. V. Lakshmikantham, *Acc. Chem. Res.*, **8**, 139 (1975).
(22) Spectral characterizations were carried out as in preceding papers in this series.
(23) J. N. Baxter, J. Cymerman-Craig, M. Moyle, and R. A. White, *J. Chem. Soc.*, 659 (1956); W. G. Finnegan, F. A. Henry, and E. Lieber, *J. Org. Chem.*, **18**, 779 (1953).

Mesoionic Compounds. 41. *anhydro*-4-Hydroxy-2,3,5-trisubstituted-1,3-selenazolium Hydroxides and *anhydro*-4-Hydroxy-6-oxo-2,3,5-trisubstituted-4*H*-1,3-selenazinium Hydroxides

Kevin T. Potts,* Frank Huang, and Rangin K. Khattak

Department of Chemistry, Rensselaer Polytechnic Institute, Troy, New York 12181

Received July 27, 1976

Reaction of a variety of monoprotonic selenoamide derivatives with 1,2-bielectrophiles such as α-bromophenylacetyl chloride and 2-bromo-2-ethoxycarbonylacetyl chloride gave representatives of the *anhydro*-4-hydroxy-1,3-selenazolium hydroxide mesoionic ring system possessing varying degrees of stability. These reacted with dimethyl acetylenedicarboxylate giving the corresponding pyridones with extrusion of selenium from the initial 1:1 adduct, a reaction pathway in contrast to the correspondingly substituted sulfur system where thiophene derivatives were usually formed. With phenyl isothiocyanate, selenium was also extruded from the initial 1:1 adduct leading to the *anhydro*-4-mercapto-6-oxopyrimidinium hydroxide system, the first example of the conversion of a five-membered mesoionic ring system into a six-membered mesoionic system. With chlorocarbonylphenylketene, the selenoamides readily formed the *anhydro*-4-hydroxy-6-oxo-4*H*-1,3-selenazinium hydroxide system.

In the two preceding papers in this series,[2] the introduction of various functional groups into several five-membered mesoionic ring systems was readily achieved by variation of both the 1,3-binucleophilic component of the reaction system and its 1,2-bielectrophilic counterpart, making this general procedure the one of choice for the synthesis of these ring systems. Extension of this method to selenium-containing 1,3-binucleophiles now provides a convenient synthesis of several endocyclic selenium mesoionic systems whose physical and chemical characteristics are described below.

The only example of a selenium-containing mesoionic ring system with an endocyclic selenium atom is *anhydro*-4-hydroxy-2,3,5-triphenyl-1,3-selenazolium hydroxide (**2**, R = R^1 = Ph), which was prepared[3] recently by dehydrative cyclization of the appropriate α-seleno acid (**1**, R = R^1 = Ph; Y = OH) with Ac_2O/Et_3N. Our studies, commenced prior to this report, have also focused in part on this ring system as the selenocarbonyl dipole represented by **2a** would be expected to influence the ability of the ring system to undergo a variety of 1,3-dipolar cycloadditions with dipolarophiles and a comprehensive study of the synthesis and reactions of this ring system is thus of particular interest. The utility of the corresponding sulfur-containing ring system in cycloadditions and as a source of other heterocycles is now well established[4] and the lesser stability of the C–Se bond compared to the C–S bond[5] suggested that the reactions of the ring system **2** would show a surprising individuality.

Synthesis. The requisite selenium-containing 1,3-binucleophiles have all been described in the literature[6] and, by the use of the appropriate selenoamide derivatives, it was possible to introduce aryl, alkylthio, and disubstituted amino substituents into the 2 position of **2**. Thus selenoanisanilide (**3**, R = *p*-$CH_3OC_6H_4$), prepared from *N*-phenylanisimidoyl chloride and sodium hydroselenide,[7] and α-bromophenylacetyl chloride (**4**, R^1 = Ph) in anhydrous benzene in the presence of Et_3N gave *anhydro*-3,5-diphenyl-4-hydroxy-2-*p*-methoxyphenyl-1,3-selenazolium hydroxide (**2**, R = *p*-$CH_3OC_6H_4$; R^1 = Ph) as deep-red needles (Table I). It is logical to assume that the intermediate **1** (R = *p*-$CH_3OC_6H_4$; R^1 = Ph; Y = Cl), or the ketene derived from it, was involved in the reaction and that the product formed was not the isomeric system **5**. This was confirmed by ring closure of the acid **1** (R = *p*-$CH_3OC_6H_4$; R^1 = Ph; Y = OH), prepared[3] from selenoanisanilide and α-bromophenylacetic acid, with Ac_2O/Et_3N. Attempted recrystallization of **2** (R = *p*-$CH_3OC_6H_4$; R^1 = Ph) resulted in decomposition and, on warming with ethanol, addition of a molecule of ethanol occurred across the 2,5 positions of the system giving 3,5-diphenyl-2-ethoxy-2-*p*-methoxyphenylselenazolidin-4-one (**6**). This reaction is similar to that occurring when 1,3,4-oxadiazolium salts are treated