mole) of sodium hydroxide, 240 ml. of water, 100 g. (0.80 mole) of *o*-aminothiophenol and 1.8 l. of absolute ethanol. The mixture was stirred at room temperature for 5 min. when sodium chloride suddenly precipitated. The reaction mixture was then stirred and refluxed for 2 hr. and filtered while hot. The filtrate was heated to boiling and 800 ml. of water were added with vigorous stirring. Almost immediately orange needles formed; m.p. 126–127°; 197 g.; (88%). Two recrystallizations from ethanol did not change the melting point.

Anal. Calcd. for $C_{13}H_9ClN_2O_2S$: C, 51.34; H, 3.23. Found: C, 51.46; H, 3.38.

6-Chloro-2'-formamido-2-nitrodiphenylsulfide (XVI). A mixture of 197 g. (0.7 mole) XV and 2 kg. of 90% formic acid was refluxed for 10 hr., cooled to room temperature, and poured over 2 l. crushed ice. The green gum soon solidified to a yellow-green solid. Recrystallization from aqueous ethanol (Norit) gave an orange-yellow solid, which after three recrystallizations from absolute ethanol, gave 142 g. (66%) of yellow crystals; m.p. 124–125°.

Anal. Calcd. for $C_{13}H_9ClN_2O_3S$: C, 50.57; H, 2.94. Found: C, 50.50; H, 3.02.

1-Chloro-10-formylphenothiazine (XVII). To the yellow solution of 6.2 g. (0.02 mole) XVI in 75 ml. of acetone were added 20 ml. of 1*N* ethanolic sodium hydroxide. The color changed immediately from yellow to orange and sodium nitrite precipitated. The mixture was refluxed for 2 hr. and the solid was removed. Concentration of the filtrate gave a maroon oil which solidified on standing overnight. Recrystallization from ethanol yielded 2.4 g. (52%) of XVII as a white solid; m.p. 112–113°; which gave a green color with concentrated nitric acid.

Anal. Calcd. for $C_{13}H_8ClNOS$: C, 59.70; H, 3.08; N, 5.36; Cl, 13.60. Found: C, 59.82; H, 3.24; N, 5.45; Cl, 13.60.

1-Chlorophenothiazine (XVIII). To a solution of 62 g. (0.2 mole) XVI in 750 ml. of acetone was added 400 ml. of 1*N* ethanolic sodium hydroxide. Immediately precipitation of sodium nitrite occurred. The reaction mixture was refluxed for 2.5 hr. and the solid was filtered. Concentration under reduced pressure gave a pale-brown solid. Crystallization from carbon tetrachloride followed by recrystallization from ethanol gave 20 g. (43%) of white crystals of XVIII; m.p. 92–93° (lit.[21,22] m.p. 92–93°).

Acknowledgment. The authors gratefully acknowledge the assistance of Messrs. Martin Hausman and Robert North of the Research Institute of Temple University in carrying out some of the reactions described, and of Dr. Walter Thompson and co-workers, of the Analytical and Physical Chemistry Section, Smith Kline and French Laboratories, for obtaining infrared spectral data.

PHILADELPHIA, PA.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Reaction of Ethylenethiourea with Phenacyl and *para*-Substituted Phenacyl Halides

M. FEFER[1] AND L. C. KING

Received June 6, 1960

Phenacyl and *para*-substituted phenacyl halides react with ethylenethiourea in acetone at room temperature to yield 2-phenacylmercapto-2-imidazolinium halides (I). Treatment of an aqueous solution of this salt with ammonium hydroxide yields the corresponding free base, 2-phenacylmercapto-2-imidazoline (II). When the *para* group is hydrogen, bromine, methyl mercapto or phenyl, the infrared spectra of these salts show a carbonyl absorption in the 5.9 to 6.0 μ region, the accepted position for an aryl carbonyl; however, when the *para* group is chlorine or nitro the spectra show a complete absence of a carbonyl absorption. In the case of *p*-chloro and *p*-nitro this, along with other evidence, indicates that these salts exist in the enol form in the crystalline state. In general the electronic nature of the *para* group is the determining factor as to whether the salt exists in the keto or enol form. The free bases (II) exist entirely in the enol form regardless of the *para* substituent. In this case the enol derives stability through resonance with the imidazoline portion of the molecule. The original salt in each case can be regenerated from the free base by dissolving a small amount of the base in sufficient acetone and adding 47% hydrobromic acid to yield the bromide or concentrated hydrochloric acid for the chloride. The infrared spectra of salts prepared in this manner from the free bases, are identical with the spectra of the original salts formed. In refluxing ethanol phenacyl halides and ethylenethiourea react to form the bicyclic 3-phenyl-5,6-dihydroimidazo[2,1-*b*]-thiazolium halide (III). Treatment of an aqueous solution of this salt with ammonium hydroxide yields the free base 3-phenyl-5,6-dihydroimidazo[2,1-*b*]thiazole (IV). 2-Phenacylmercapto-2-imidazolinium halide (I) (formed in acetone at room temperature) can be converted to the thiazolium type halide (III) by refluxing in ethanol, showing therefore that the salt type I is an intermediate in the formation of III in this reaction.[2]

A number of alkyl isothioureas have been reported[3]; however, relatively few *S*-alkyl derivatives of ethylenethiourea are known (2-alkylmercapto-2-imidazolines). Schacht[4] prepared the methyl and ethyl derivatives by treating ethylenethiourea with the corresponding alkyl halide. Easton and

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(2) Four basic structures will be described throughout the text (I–IV). I and III are salts, the former *via* acetone as solvent and the latter in ethanol. II and IV are the neutral or free bases of I and III respectively. Salts of type I are the open form while III is closed (bicyclic). Subscripts denote the *para* substituent of the benzene ring—this substituent being determined by the *para*-substituted phenacyl halide used in the particular reaction, *e.g.* I_H or II_{NO_2}. At times the anion of the salts of I and III will be shown, *e.g.* I_HCl or $I_{NO_2}Br$. If no anion is designated Br is understood; this will also apply to the subscript for hydrogen.

(3) T. B. Johnson and J. M. Sprauge, *J. Am. Chem. Soc.*, 58, 1348 (1939).

(4) W. Schacht, *Arch. Phar.*, 235, 445 (1897).

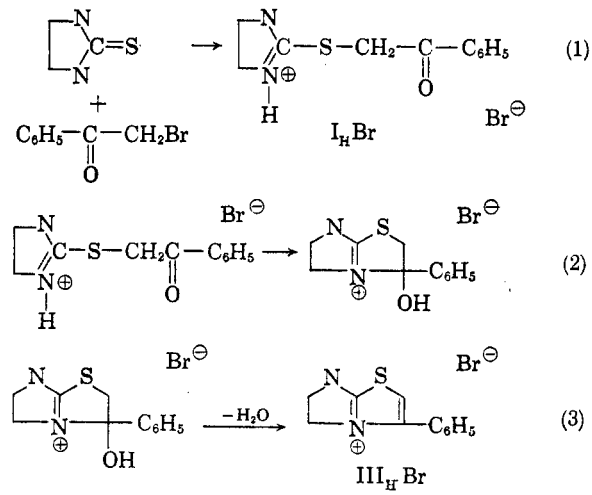
co-workers[5] have reported the synthesis of a series of substituted 2-benzylmercapto-2-imidazolines (hydro halides). 2-Alkylmercapto-2-imidazoline hydroiodides were found to be susceptible to a displacement reaction when the salt was treated with a slight excess of some primary or secondary amines yielding 2-alkylaminomercapto-2-imidazolines.[6] Some of the amines used in this study were methylamine, benzylamine, and piperidine.

2-Carboxymethylmercapto-2-imidazoline hydrochloride[7] and 2-carboethoxymethylmercapto-2-imidazoline hydrochloride were prepared from ethylenethiourea, chloroacetic acid, and ethyl chloroacetate respectively.

Baer and Lockwood[8] carried out an investigation of the acetylation and *S*-alkylation of ethylenethiourea. Acetyl chloride and acetic anhydride were used as the acetylating agents while *n*-propyl and *n*-butyl chlorides were some of the alkylating agents. 2-Acylmercapto-2-imidazolinium and 2-alkylmercapto-2-imidazolinium chlorides were the respective products obtained.

Wilson[9] treated a series of alkyl and aralkyl halides with ethylenethiourea to investigate the usefulness of these salts in the characterization of halogen compounds. Methyl iodide, *n*-hexyl bromide, 1,3-dibromopropane, 1,10-dibromodecane, and *p*-nitrobenzyl bromide were a few of the halogen compounds used. The resulting salts and their corresponding bases and picrates were prepared and the physical constants tabulated. As an extension of this general reaction Wilson and Woodger[10] carried out a study of the reaction of ethylenethiourea and certain *alpha*-halogenated carbonyl compounds. In particular, the reaction of ethylenethiourea and phenacyl bromide in refluxing ethanol yielded 3-phenyl-5,6-dihydroimidazo[2,1-*b*]thiazolium bromide (III).

This structure was formulated on the basis of ultraviolet studies and by analogy with the formation of monocyclic thiazoles from thiourea and *alpha*-halogenated carbonyl compounds. When 3-phenyl-5,6-dihydroimidazo[2,1-*b*]thiazolium bromide (III) was treated with alkali the salt was converted to the bicyclic base 3-phenyl-5,6-dihydroimidazo(2,1-*b*]thiazole (IV). A reasonable process for the formation of III can be formulated in a series of steps as shown in equations 1, 2, and 3.



If the reaction mechanism proceeds in this stepwise manner it should be possible to isolate an intermediate salt provided the experimental conditions are suitable.

The present work is an investigation of the reaction of various phenacyl halides with ethylenethiourea in acetone solution at room temperature. A study was also carried out on the free bases (2-phenacylmercapto-2-imidazolines, II) which correspond to the intermediate salts I.

RESULTS AND DISCUSSION

The reaction of phenacyl bromide (*alpha*-halocarbonyl compound) and ethylenethiourea in refluxing ethanol has been shown to yield 3-phenyl-5,6-dihydroimidazo[2,1-*b*]thiazolium bromide (III).[10]

When the same reagents were allowed to react in acetone solution at room temperature a salt with a noncyclic structure, 2-phenacylmercapto-2-imidazolinium bromide (I) was obtained. The structure of this salt was verified by microanalytical determination of C and H, by supporting structural data *via* a Volhard titration technique and by means of infrared analysis. Treatment of the salts I and III with alkali yields the corresponding bases 2-phenacylmercapto-2-imidazoline and 3-phenyl-5,6-dihydroimidazo[2,1-*b*]-thiazole respectively (II and IV).

Refluxing ethanol converts I to III, suggesting that the former may be an intermediate in the reaction of a phenacyl halide and ethylenethiourea in ethanol. Treatment of the base II in acetone solution with hydrochloric or hydrobromic acid affords the original salt I.

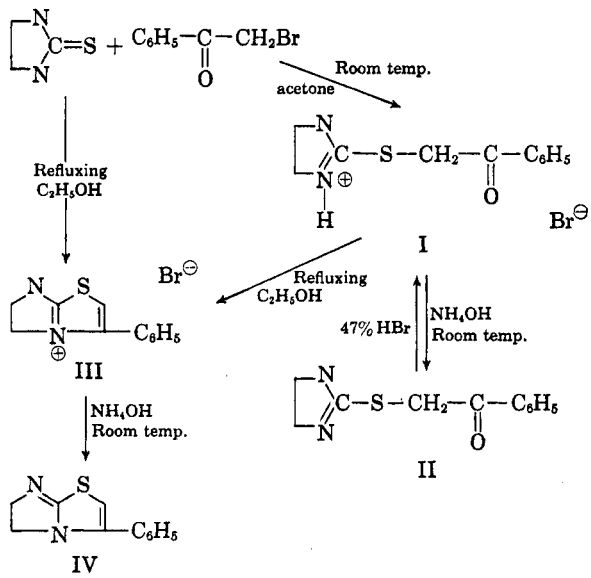
The discussion will consist of three sections, the first dealing with the reaction of phenacyl halides and ethylenethiourea in acetone solution, the second a study of the bases formed when an aqueous solution of the salt is treated with alkali and finally a discussion of the reaction of phenacyl halides and ethylenethiourea in refluxing ethanol.

(5) N. R. Easton, A. Hlynsky, and H. J. Foster, *J. Am. Chem. Soc.*, **73**, 3507 (1951).
(6) S. R. Aspinall and E. J. Bianco, *J. Am. Chem. Soc.*, **73**, 602 (1951).
(7) T. B. Johnson and C. O. Edens, *J. Am. Chem. Soc.*, **63**, 3527 (1941).
(8) J. E. Baer and R. G. Lockwood, *J. Am. Chem. Soc.*, **76**, 1162 (1954).
(9) W. Wilson, *J. Chem. Soc.*, 1389 (1955).
(10) W. Wilson and R. Woodger, *J. Chem. Soc.*, 2943 (1955).

Formation and infrared study of 2-phenacylmercapto-2-imidazolinium halides. The following phenacyl and *para*-substituted phenacyl halides were allowed to react with ethylenethiourea. In each case the product was the appropriate *para*-substituted 2-phenacylmercapto-2-imidazolinium salt of type I.

$C_6H_5COCH_2Br$
$C_6H_5COCH_2Cl$
p-Br-$C_6H_4COCH_2Br$
p-Cl-$C_6H_4COCH_2Br$
p-CH_3S-$C_6H_4COCH_2Br$
p-C_6H_5-$C_6H_4COCH_2Br$
p-NO_2-$C_6H_4COCH_2Br$

CHART OF REACTIONS



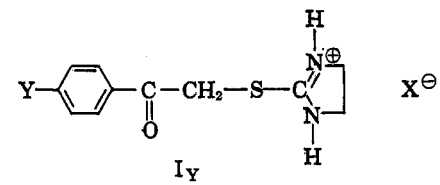
For example, phenacyl bromide reacted with ethylenethiourea in acetone solution at room temperature to yield 2-phenacylmercapto-2-imidazolinium bromide, I_H (Br); in this latter abbreviated form the subscript H refers to the *para* group and the Br to the halide salt formed. In a similar manner phenacyl chloride reacted with ethylenethiourea to give I_HCl.

In Table I the analytical data for each salt obtained in the above reactions are listed. The molecular weight determined for I_H(Cl) using the Volhard method for halogen was 269 (calculated 256). When I_H(Br) was used excellent agreement was found—in general bromides give better results than chlorides due to a sharper end point. The infrared spectra of the salts 2-phenacylmercapto-2-imidazolinium chloride and bromide were identical, both having an absorption at 5.9 μ, the accepted position for an aryl carbonyl.[11] In view of the analytical and infrared data it is clear that the salt I has the noncyclic structure as suggested previously.

p-Bromo-, *p*-methylmercapto- and *p*-phenylphenacyl bromides reacted in a similar manner with ethylenethiourea to yield the imidazolinium salts I_{Br}, I_{CH_3S}, and $I_{C_6H_5}$ respectively. The infrared spectra of these salts all possessed an absorption at approximately 6.0 μ. Microanalytical determinations for carbon-hydrogen as well as molecular weight determination from halogen analysis check for structure I with the appropriate *para* substituent. In Table I, in addition to analytical data, molecular weight, formula, and structure identification symbol are shown.

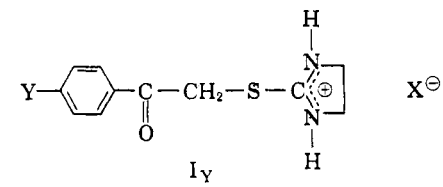
p-Chloro- and *p*-nitrophenacyl bromide reacted with ethylenethiourea to yield 2-(*p*-chlorophenacylmercapto)-2-imidazolinium bromide and 2-(*p*-nitrophenacylmercapto)-2-imidazolinium bromide, I_{Cl} and I_{NO_2}, respectively. Microanalytical data for carbon-hydrogen checked for these structures; however, the infrared spectra of these salts showed a complete absence of a carbonyl absorption.

The general formula for a *para*-substituted phenacylmercapto-2-imidazolinium halide is I_Y. In this structure the charge is not located on one



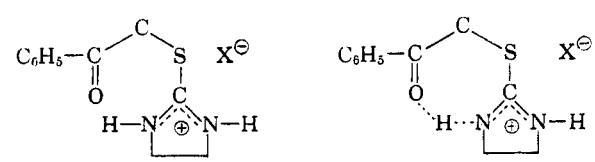
I_Y

nitrogen but is distributed so that each nitrogen atom will possess a partial positive character. Several explanations are possible to account for the



I_Y

absence of a carbonyl absorption when the *para* substituent is either chloro or nitro. One possibility is that a strong hydrogen bond exists between the carbonyl oxygen and a hydrogen atom on the nitrogen. Since both nitrogen atoms already possess a partial positive character it seems unlikely that a hydrogen bond could be established between the hydrogen atom on one of the nitrogens and the carbonyl group, destroying resonance in the imidazolinium part of the molecule. The following structures will show this more clearly.

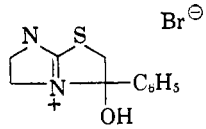


Before considering the possibility that the salt exists as an enol the following cyclic intermediate structure should be eliminated. This intermediate can be formed by attack of the electron pair of the nitrogen on the carbonyl carbon with a hydrogen

(11) L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley and Sons, N. Y., 1956.

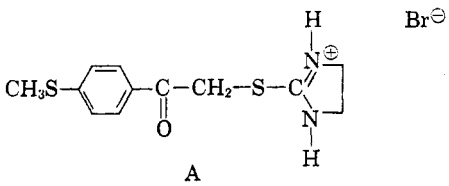
TABLE I

Name	Formula	M.W. Calcd.	M.W. Found	C, % Calcd.	H, % Calcd.	C, % Found	H, % Found
2-Phenacylmercapto-2-imidazolinium chloride (I_HCl)	$C_{11}H_{13}ON_2SCl$	256	269	51.40	5.06	51.60	5.25
2-Phenacylmercapto-2-imidazolinium bromide (I_HBr)	$C_{11}H_{13}ON_2SBr$	301	304	43.84	4.32	43.26	4.25
2-(*p*-Bromophenacylmercapto)-2-imidazolinium bromide ($I_{Br}Br$)	$C_{11}H_{12}ON_2SBr_2$	380	386	34.73	3.15	34.73	3.15
2-(*p*-Chlorophenacylmercapto)-2-imidazolinium bromide ($I_{Cl}Br$)	$C_{11}H_{12}ON_2SBrCl$	335	342	39.30	3.57	39.43	3.42
2-(*p*-Methylmercaptophenacylmercapto)-2-imidazolinium bromide ($I_{CH_3}Br$)	$C_{12}H_{15}ON_2S_2Br$	—	—	41.50	4.32	41.54	4.41
2-(*p*-Phenylphenacylmercapto)-2-imidazolinium bromide ($I_{C_6H_5}Br$)	$C_{17}H_{17}ON_2SBr$	—	—	54.10	4.52	55.45 (See Experimental)	4.65
2-(*p*-Nitrophenacylmercapto)-2-imidazolinium bromide ($I_{NO_2}Br$)	$C_{11}H_{12}O_3N_3SBr$	—	—			(See Experimental)	

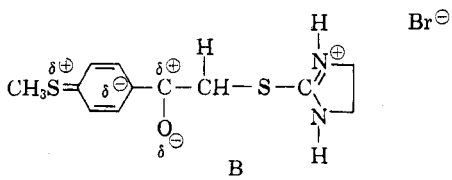


shift to oxygen (Equation 2). It will be shown later that the original imidazolinium salt can be regenerated from the free base (imidazole) by treatment of an acetone solution of the free base with concentrated hydrochloric or 47% hydrobromic acid. The possibility that the above cyclic structure would revert to the open form under these mild conditions seems unlikely.

As was noted previously *p*-hydrogen, *p*-bromo-, *p*-methylmercapto- and *p*-phenyl-phenacyl bromides reacted with ethylenethiourea to yield imidazolinium salts, the infrared spectra of which showed a carbonyl absorption. Using 2-(*p*-methylmercaptophenacylmercapto)-2-imidazolinium bromide as an example of a salt that possesses an electron donating group, the following structures can be drawn (with polarization of the carbonyl).

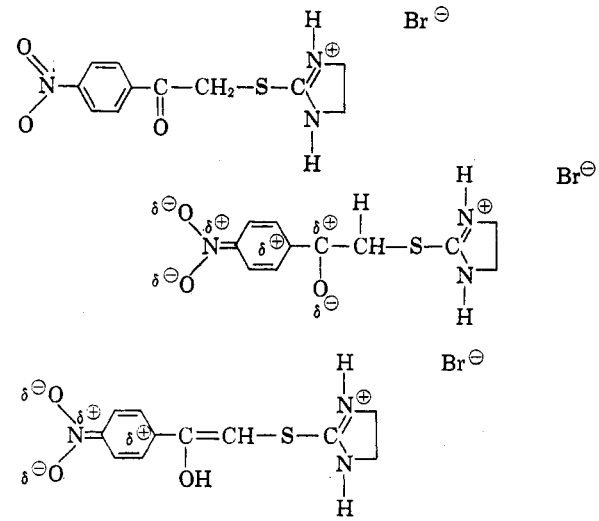


A



B

An entirely different situation is encountered when the *para* group is electron withdrawing, *e.g.* *p*-nitro. In this case, due to the inductive effect of the *p*-nitro group, the salt has two adjacent positive charges (*i.e.* with polarization of the carbonyl group). This relatively unstable situation can be eliminated if one qisualizes a pair of electrons *alpha* to the carbonyl group shifting in to neutralize the charge on the carbonyl carbon, with a shift of the hydrogen atom to oxygen (enol form).



In Table II the absence or presence of infrared evidence for a carbonyl function is correlated with the Hammett[12] *sigma* values for several *para*-substituted phenacylmercapto-2-imidazolinium salts. It should be noted that bromine and chlorine appear to be out of order according to Hammett's values.

TABLE II

para-Substituted Phenacyl Halide	Carbonyl	Hammett *sigma* Value
CH_3S—	+	−0.047
H—	+	0.000
H— (chloride)	+	0.000
C_6H_5—	+	0.009
Cl—	−	0.227
Br—	+	0.232
NO_2—	−	0.778

(12) L. P. Hammett, *Physical Organic Chemistry*, McGraw Hill Book Co., New York, p. 188.

Ozog[13] and Ozog, Comte, and King[14] studied the formation and kinetics of formation of substituted mercaptopyrylium salts. They found that in benzene or acetone solution the reaction of phenacyl bromide and 2,6-dimethyl-4-thiopyrone was first order with respect to each of the reacting species. They also determined the effect on the reaction rate of *para* substituents in the phenacyl bromide at 14.8 and 25.4°. Plotting log k versus σ the results they obtained could be described by the Hammett equation fairly well considering the broad application of the equation. If, however, the values of the σ constant were modified so as to fit a straight line having a slope of unity at 14.8° ($\rho = 1.00$), it was found that these modified σ values were also in excellent agreement with the kinetic data obtained at 25.4°. The modified σ values were described as σ' and a tabulation of those values is shown in Table III.

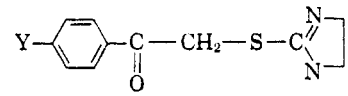
TABLE III

para Substituent	σ	σ'
H—	0.000	0.000
C_6H_5—	0.009	0.093
Br—	0.232	0.225
Cl—	0.227	0.242
NO_2—	0.778	0.780

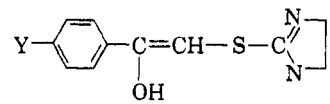
It should be noted that bromine and chlorine are now reversed, agreeing with the experimental evidence tabulated in Table II. The reactants and reaction conditions used by Ozog, *et al.* are very similar to those used in the present investigation. It is also noteworthy that in both instances the data are best explained by using the values calculated by Ozog, that is, the order (magnitude) of the σ values of *p*-chloro and *p*-bromo are reversed.

Formation and infrared study of 2-phenacylmercapto-2-imidazoline and the para-substituted compounds. When each of the substituted mercaptoimidazolinium salts described in the previous section was treated with aqueous ammonia or hydroxide ion, conversion to a substituted mercaptoimidazoline was obtained, *e.g.* 2-phenacylmercapto-2-imidazolinium bromide, I_H(Br), treated with ammonia gave 2-phenacylmercapto-2-imidazoline, II_H. The assignment of the imidazoline structure is based on elementary analysis for carbon-hydrogen. (see Table IV). In each case it is evident from analysis that no water has been removed from the molecule and hence cyclization to the corresponding 2-phenyl-5,6-dihydroimidazo[2,1-*b*]thiazole, IV_H, has not taken place.

If no cyclization to the thiazole occurred one would expect each of the imidazoles prepared above to display infrared evidence of a carbonyl function. The infrared spectra for all of these bases was examined in potassium bromide pellets—the expected band for the carbonyl absorption was absent in all of these compounds. The general formula for a *para*-substituted free base is:

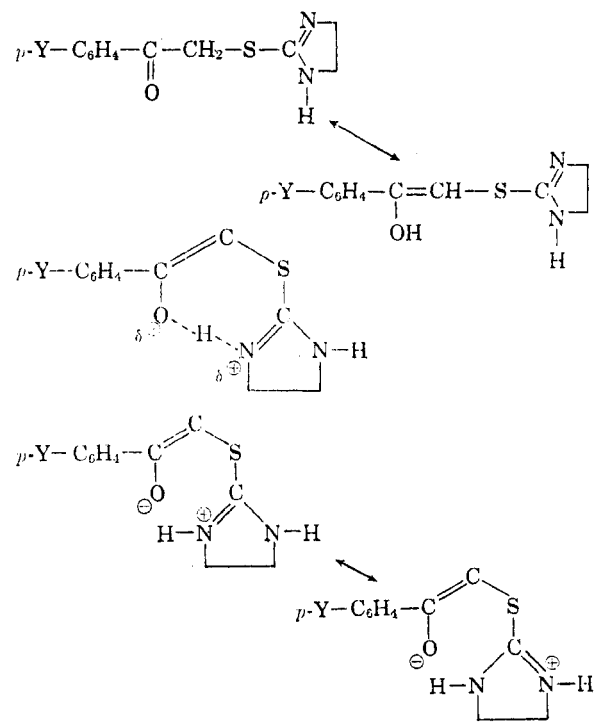


However, it is also possible for this structure to exist in an enol form:

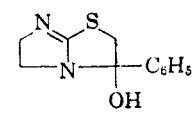


In the salts of Type I the important factor that leads to an enol structure was shown to be related to the electronic nature of the *para* substituent, an electron donating group repressing the formation of an enol and an electron withdrawing group aiding its formation.

In the free bases of Type II_Y this effect is absent or unimportant since all of the compounds fail to exhibit a carbonyl function. The following structures support the argument for the absence of a carbonyl function in the infrared spectra of the free bases.



A structure of the type:



(13) F. Ozog, Doctoral Dissertation, Northwestern Univ., 1950.

(14) F. Ozog, V. Comte, and L. C. King, *J. Am. Chem. Soc.*, **74**, 6225 (1952).

TABLE IV

Name	Formula	M.W.	C, % Calcd.	H, % Calcd.	C, % Found	H, % Found
2-Phenacylmercapto-2-imidazoline (*via* Cl) (II_H)	$C_{11}H_{12}ON_2S$	220	60.00	5.46	60.44	5.41
2-Phenacylmercapto-2-imidazoline (*via* Br) (II_H)	$C_{11}H_{12}ON_2S$	220	60.00	5.46	60.00	5.35
2-(*p*-Bromophenacylmercapto)-2-imidazoline (II_{Br})	$C_{11}H_{11}ON_2SBr$	300	44.00	3.67	43.00	3.54
2-(*p*-Chlorophenacylmercapto)-2-imidazoline (II_{Cl})	$C_{11}H_{11}ON_2SCl$	255	51.75	4.32	51.71	4.42
2-(*p*-Methylmercaptophenacylmercapto)-2-imidazoline (II_{CH_3S})	$C_{12}H_{14}ON_2S_2$	266	54.20	5.25	53.80	5.22
2-(*p*-Phenylphenacylmercapto)-2-imidazoline ($II_{C_6H_5}$)	$C_{17}H_{16}ON_2S$	296	69.00	5.40	69.07	5.32
2-(*p*-Nitrophenacylmercapto)-2-imidazoline (II_{NO_2})	$C_{11}H_{11}O_3N_3S$	265	(See Experimental)			

TABLE V

SUMMARY OF MELTING POINTS FOR PRODUCTS OF REACTION OF ETHYLENETHIOUREA AND *para*-SUBSTITUTED PHENACYL HALIDES IN REFLUXING ETHANOL AND ACETONE AT ROOM TEMPERATURE

para-Substituted Halide Used	Acetone Salt M.P.	Acetone Base M.P.	Refluxing Ethanol Salt M.P.	Refluxing Ethanol Base M.P.
$C_6H_5COCH_2Br$	248–249	143–144	248–250	110–111
p-Br—$C_6H_4COCH_2Br$	290–300	152–153	290–300	145–146
p-CH_3S—$C_6H_4COCH_2Br$	270–273	144–145	271–273	118–119
p-Cl—$C_6H_4COCH_2Br$	270–272	148–149	272–274	113–114
p-NO_2—$C_6H_4COCH_2Br$	281–283	168–169	287–290	216–218

was again eliminated from consideration since it was possible to convert the base of Type II_Y to the original imidazolinium salt, Type I, by treating the base in acetone solution at room temperature with one drop of concentrated hydrochloric acid or two to three drops of 47% hydrobromic acid solution. The spectra of the regenerated salts were identical to the original ones.

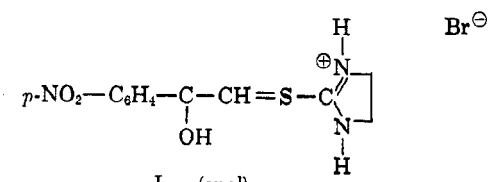
Reaction of phenacyl halides and ethylenethiourea in refluxing ethanol. (Preparation of imidazo-[2,1-*b*] thiazolium salts). When Wilson and Woodger[10] allowed phenacyl bromide to react with ethylenethiourea in refluxing ethanol the product was III_H.

In acetone solution at room temperature the salt obtained from the same reactants has the following noncyclic structure I_H

The melting points of the salt from the refluxing ethanol and the salt from acetone solution at room temperature were 248–250° and 248–249° respectively. The noncyclic form in all probability ring closes as the melting point is approached. Notable differences however can be seen in the melting points recorded for the free bases (see Table V).

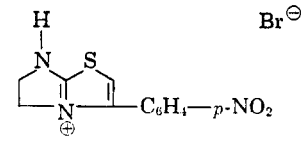
The infrared spectra of the salts clearly showed the differences when the experimental conditions are changed (*i.e.*, refluxing ethanol or acetone at room temperature). As stated previously the salts obtained, Type I, exhibited a carbonyl absorption in the infrared dependent upon the *para* substituent on the benzene ring. When there was no carbonyl function the evidence obtained showed that the salt of Type I_Y existed as an enol where Y is *p*-chloro or *p*-nitro. In refluxing ethanol the salt of Type III_Y was obtained and in no case was a carbonyl function evident. Inspection of the infrared spectra showed major differences for the free bases of Types II_Y and IV_Y.

The only phenacyl halide used by Wilson and Woodger[10] in refluxing ethanol was phenacyl bromide. Their reaction with phenacyl bromide as well as *p*-nitro-, *p*-chloro-, *p*-bromo-, and *p*-methylmercaptophenacyl bromides with ethylenethiourea in refluxing ethanol was carried out in the present



I_{NO_2}(enol)

2-(*p*-Nitrophenacylmercapto)-2-imidazolinium bromide (white)



III_{NO_2}

3-(*p*-Nitrophenyl)-5,6-dihydroimidazo[2,1-*b*]-thiazolium bromide (yellow)

work. Table V gives a summary of the physical constants for the salts and free bases using both sets of experimental conditions.

Refluxing of the noncyclic form of the salt, Type I_Y, in absolute ethanol converts it to the cyclic structure, the *p*-nitro derivative serving as an example. The melting point and spectrum of this salt were identical with the melting point and spectrum of the salt when it was originally obtained from refluxing ethanol.

EXPERIMENTAL

Molecular weight determination—Volhard halogen method. In order to support suggested structures of the salts prepared in acetone solution (*e.g.*, 2-phenacylmercapto-2-imidazolinium bromide, I_H), it was decided to assume that the salt was composed of only one ionic halogen per molecule and run a Volhard halogen determination. Standard 0.1000*N* silver nitrate was prepared by weighing out reagent grade silver nitrate and diluting to volume. An approximately 0.1*N* potassium thiocyanate solution was prepared and it was found that 7.84 ml. of potassium thiocyanate was equivalent to 10.00 ml. of silver nitrate or the ratio potassium thiocyanate/silver nitrate of 0.98 ml. A known amount of the salt was dissolved in water and approximately 10 drops of indicator was added. The indicator was prepared by dissolving 10 g. of ferric nitrate in 10 ml. of concd. nitric acid and then diluting to 50 ml. To the solution of salt and indicator was added enough potassium thiocyanate solution to produce a persistent dark red color. The silver nitrate solution was then added in excess after the formation of a white precipitate and back-titrated with the potassium thiocyanate solution to the first appearance of a red coloration on the precipitate. From a knowledge of the weight of starting material and number of milliliters of silver nitrate used, the molecular weight can be calculated. The results are summarized in Table I.

The run using phenacyl chloride is off by a considerable amount; however, in this determination chloride ion does not give as good a result as does the bromide ion. It should be noted that the error in this case is in the right direction, *i.e.*, showing a higher value indicating no ring closure.

Reaction of phenacyl halides and ethylenethiourea in acetone. Phenacyl chloride: Preparation of 2-phenacylmercapto-2-imidazolinium chloride (I_HCl). To 0.77 g. (0.005 mole) of phenacyl chloride in 50 ml. of acetone was added 0.51 g. (0.005 mole) of ethylenethiourea dissolved in 100 ml. of acetone. A white crystalline product formed quickly (at room temperature). It was filtered, washed with cold acetone and dried in an oven at 60°. Yield, based on the sum of materials used, was 0.80 g. (61%). In the present case only one crop of crystals was obtained. In other runs using less solvent and recovery of several crops, the yield was as high as 92%, m.p. 219–220°.

Preparation of 2-phenacylmercapto-2-imidazoline (II_H). To an aqueous solution of the salt, concentrated ammonia was added until basic to litmus paper. The resulting white flocculent precipitate was allowed to stand, then was filtered and washed with distilled water; m.p. 145–146°.

Regeneration of 2-phenacylmercapto-2-imidazolinium chloride (I_HCl). A small amount of the base was dissolved in acetone at room temperature and 3 drops of concd. hydrochloric acid was added. A white crystalline product was obtained, identical in all respects to the original salt.

Phenacyl bromide: Preparation of 2-phenacylmercapto-2-imidazolinium bromide (I_HBr). To 1 g. (0.005 mole) of phenacyl bromide in 15 ml. of acetone was added 0.5 g. (0.005 mole) of ethylenethiourea dissolved in 50 ml. of acetone. Upon standing at room temperature for a short time a white crystalline material separated. It was filtered, washed with cold acetone, and dried at 60°; yield 1.39 g. (93%), m.p. 248–249°.

Preparation of 2-phenacylmercapto-2-imidazoline (II_H). Concentrated ammonia was added to an aqueous solution of the salt until basic to litmus. The resulting white flocculent precipitate was allowed to stand, then filtered, washed with distilled water, and dried; m.p. 143–144°.

Regeneration of 2-phenacylmercapto-2-imidazolinium bromide (I_HBr). A small amount of the free base was dissolved in acetone at room temperature and 5 drops of 47% hydrobromic acid was added. A white crystalline product formed. It was filtered, washed and dried, and was identical in all respects to the original salt.

p-Methylmercaptophenacyl bromide: Preparation of 2-(p-methylmercaptophenacylmercapto)-2-imidazolinium bromide ($I_{CH_3S}Br$). To 0.62 g. (0.0025 mole) of *p*-methylmercaptophenacyl bromide in 30 ml. of acetone was added 0.25 g. (0.0025 mole) of ethylenethiourea dissolved in 25 ml. of acetone. Upon standing at room temperature a white crystalline material separated. It was filtered, washed and dried at 60°; yield 0.7 g. (80%), m.p. 270–272° with shrinkage at 220–250°.

Preparation of 2-(p-methylmercaptophenacylmercapto)-2-imidazoline (II_{CH_3S}). Concentrated ammonia was added to an aqueous solution of the salt until basic or until no further formation of a white flocculent precipitate took place. The product was filtered, washed, and dried; m.p. 145–146°.

Regeneration of 2-(p-methylmercaptophenacylmercapto)-2-imidazolinium bromide ($I_{CH_3S}Br$). A small amount of the free base was dissolved in acetone at room temperature and 5 drops of 47% hydrobromic acid was added. In some cases it was found that instead of reforming the bromide it was easier to get the chloride. The melting points would be different but the infrared spectra would be the same. In this case the chloride was formed and showed a carbonyl absorption in the same position as the original salt.

p-Bromophenacyl bromide: Preparation of 2-(p-bromophenacylmercapto) 2-imidazolinium bromide ($I_{Br}Br$). To 0.7 g. (0.0025 mole) of *p*-bromophenacyl bromide in 15 ml. of acetone was added 0.25 g. of ethylenethiourea dissolved in 40 ml. of acetone. Upon standing at room temperature a white crystalline material separated. It was filtered, washed and dried at 60°; yield 0.84 g. (88%), m.p. 290–300°.

Preparation of 2-(p-bromophenacylmercapto)-2-imidazoline (II_{Br}). To an aqueous solution of the salt was added concentrated ammonia until basic to litmus. The white flocculent precipitate formed was allowed to stand, and was then filtered, washed, and dried; m.p. 155–156°.

Regeneration of 2-(p-bromophenacylmercapto)-2-imidazolinium salt (I_{Br}). In this case the chloride was prepared. The infrared spectra were identical.

p-Chlorophenacyl bromide: Preparation of 2-(p-chlorophenacylmercapto)-2-imidazolinium bromide (I_{Cl}). To 0.58 g. (0.0025 mole) of *p*-chlorophenacyl bromide in 15 ml. of acetone was added 0.25 g. of ethylenethiourea dissolved in 50 ml. of acetone. A white crystalline material separated on standing. It was filtered, washed, and dried; yield 0.4 g. (50%), m.p. 270–272°.

Preparation of 2-(p-chlorophenacylmercapto)-2-imidazoline (II_{Cl}). To an aqueous solution of the salt was added concentrated ammonia until precipitation was complete. The flocculent precipitate was filtered, washed, and dried; m.p. 149–150°.

Regeneration of 2-(p-chlorophenacylmercapto)-2-imidazolinium salt (I_{Cl}). The infrared spectra was identical to the original salt.

p-Phenylphenacyl bromide: Preparation of 2-(p-phenylphenacylmercapto)-2-imidazolinium bromide ($I_{C_6H_5}Br$). To 0.69 g. (0.0025 mole) of *p*-phenylphenacyl bromide in sufficient acetone to bring about solution was added 0.25 g. of ethylene thiourea (0.0025 mole) dissolved in 50 ml. of acetone. Upon standing at room temperature and then in an ice room overnight a buff material crystallized. It was filtered,

washed, and dried; yield 0.6 g. (one crop obtained 62%), m.p. range was 290–300°.

Anal. Calcd. for $C_{17}H_{17}ON_2SBr$: C, 54.10; H, 4.52. Found: C, 55.45; H, 4.65.

This analysis was quite poor; however, the corresponding free base had an excellent analysis. Because of this and the fact that the infrared spectrum showed a carbonyl absorption, a repeat analysis was not performed.

Preparation of 2-(p-phenylphenacylmercapto)-2-imidazoline ($II_{C_6H_5}$). To an aqueous solution of the salt was added concentrated ammonia until precipitation was complete. The product was filtered, washed, and dried; m.p. 140–141°.

Regeneration of 2-(p-phenylphenacylmercapto)-2-imidazolinium salt ($II_{C_6H_5}$). The spectrum of this salt was found to be identical with the original salt prepared. As was stated previously, at times, as in this case, the chloride was obtained rather than the bromide.

p-Nitrophenacyl bromide: Preparation of 2-(p-nitrophenacylmercapto)-2-imidazolinium bromide ($I_{NO_2}Br$). To 0.3 g. (0.0012 mole) of p-nitrophenacyl bromide in 60 ml. of acetone was added 0.17 g. of ethylenethiourea dissolved in 30 ml. of acetone. Upon standing a white precipitate separated. It was filtered, washed, and dried; yield 0.36 g. (77%), m.p. 281–283°.

Preparation of 2-(p-nitrophenacylmercapto)-2-imidazoline (II_{NO_2}). To a small amount of the salt dissolved in water was added ammonia until basic to litmus. The precipitate was filtered, washed, and dried; m.p. 165–166°.

The analyses in this series were off by a considerable margin. It was noted that in all cases an ash was formed, making the results inconclusive.

Reaction of phenacyl halides and ethylenethiourea in refluxing ethanol. Phenacyl bromide: Preparation of 3-phenyl-5,6-dihydroimidazo[2,1-b]thiazolium bromide (III_HBr). This was a repeat of the work done by Wilson and Woodger.[8] The physical constants checked very well; their reported melting point was 248–249°. The present preparation had a m.p. of 248–250°. No analysis was performed on this salt or the following free base.

Preparation of 3-phenyl-5,6-dihydroimidazo[2,1-b]thiazole (IV_H). The free base was obtained by treating an aqueous solution of the salt with sodium hydroxide solution. The melting point of this compound checked exactly with that prepared previously.

p-Chlorophenacyl bromide: Preparation of 3-(p-chlorophenyl)-5,6-dihydroimidazo[2,1-b]thiazolium bromide ($III_{Cl}Br$). A solution of 0.58 g. (0.0025 mole) of p-chlorophenacyl bromide and 0.25 g. (0.0025 mole) of ethylenethiourea in 70 ml. of absolute ethanol was refluxed for 2 hr. Upon cooling, a crystalline product separated which was filtered, washed, and dried; yield 0.6 g. (one crop) (73%), m.p. 272–274°.

Anal. Calcd. for $C_{11}H_{10}N_2SBrCl$: C, 41.50; H, 3.15. Found: C, 41.52; H, 3.08.

Preparation of 3-(p-chlorophenyl)-5,6-dihydroimidazo[2,1-b]thiazole (IV_{Cl}). To an aqueous solution of the salt was added sodium hydroxide until basic to litmus. The resulting precipitate was filtered, washed, and dried; m.p. 113–114°.

Anal. Calcd. for $C_{11}H_9N_2SCl$: C, 55.75; H, 3.79. Found: C, 55.41; H, 3.69.

p-Bromophenacyl bromide: Preparation of 3-(p-bromophenyl)-5,6-dihydroimidazo[2,1-b]thiazolium bromide ($III_{Br}Br$). A solution of 0.7 g. (0.0025 mole) of p-bromophenacyl bromide and 0.25 g. (0.0025 mole) of ethylenethiourea in 100 ml. of absolute ethanol was refluxed for 2 hr. Upon cooling a crystalline material separated which was filtered, washed, and dried; yield 0.7 g. (one crop) (70%); m.p. 290–300°.

Anal. Calcd. for $C_{11}H_{10}N_2SBr_2$: C, 36.48; H, 2.76. Found: C, 35.92; H, 2.70.

Preparation of 3-(p-bromophenyl)-5,6-dihydroimidazo[2,1-b]thiazole (IV_{Br}). To a small amount of the salt dissolved in water was added sodium hydroxide until basic to litmus. The resulting product was filtered, washed, and dried; m.p. 145–146°.

Anal. Calcd. for $C_{11}H_9N_2SBr$: C, 47.00; H, 3.20. Found: C, 46.58; H, 3.06.

p-Methylmercaptophenacyl bromide: Preparation of 3-(p-methylmercaptophenyl)-5,6-dihydroimidazo[2,1-b]thiazolium bromide ($III_{CH_3S}Br$). A solution of 0.62 g. (0.0025 mole) of p-methylmercaptophenacyl bromide and 0.25 g. (0.0025 mole) of ethylenethiourea in 100 ml. of absolute ethanol was refluxed for 2 hr. Upon cooling a crystalline material separated which was filtered, washed, and dried; yield 0.6 g. (one crop) (69%), m.p. 271–273°.

Anal. Calcd. for $C_{12}H_{13}N_2S_2Br$: C, 43.75; H, 3.94. Found: C, 43.49; H, 4.03.

Preparation of 3-(p-methylmercaptophenyl)-5,6-dihydroimidazo[2,1-b]thiazole (IV_{CH_3S}). To a small amount of the salt dissolved in water was added sodium hydroxide until basic to litmus. The resulting product was filtered, washed, and dried; m.p. 118–119°.

Anal. Calcd. for $C_{12}H_{12}N_2S_2$: C, 57.75; H, 4.82. Found: C, 56.54; H, 4.74.

p-Nitrophenacyl bromide: Preparation of 3-(p-nitrophenyl)-5,6-dihydroimidazo[2,1-b]thiazolium bromide ($III_{NO_2}Br$). A solution of 0.3 g. (0.0023 mole) of p-nitrophenacyl bromide and 0.17 g. (0.0013 mole) of ethylenethiourea in 100 ml. of absolute ethanol was refluxed for 2 hr. The resulting yellow product was filtered, washed, and dried; yield 0.3 g. (64%), m.p. 287–290°.

Preparation of 3-(p-nitrophenyl)-5,6-dihydroimidazo[2,1-b]-thiazole (IV_{NO_2}). To a small amount of the salt dissolved in water was added sodium hydroxide until basic to litmus. The yellow solution turned deep red and a solid material separated. The color of the free base was red; m.p. 216–218°.

Attempted analysis of the salt and free base in the p-nitro series gave erratic results. Usually an ash was formed which made the results inconclusive. The infrared spectra however showed the difference in these compounds from those obtained in acetone solution.

Acknowledgment. The authors wish to thank Abbott Laboratories, E. I. du Pont de Nemours Co., and the Stauffer Chemical Co. for supporting funds in carrying out this investigation.

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