Heterocyclic Tautomerisms. II. An Investigation of the
2-Arylbenzothiazoline-2-(Benzylideneamino)thiophenol Tautomerism. Part 2.

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The reaction between 4-mercaptoaniline and various aromatic aldehydes was studied as a model system in order to determine which type of substitution on the aryl group in 2-arylbenzothiazolines (I) might give rise to the greatest possible stabilization of the hypothetical 2-(benzylideneamino)thiophenol tautomer (II). Regardless of electronic effect of substituents, most aldehydes reacted with 4-mercaptoaniline to form poly[4-(benzylideneamino)thiophenols] (III). Aromatic aldehydes substituted in the 2 position with the hydroxyl function reacted to form the stable, monomeric 4-(benzylideneamino)thiophenols (IV). This stabilization in the monomeric state is presumed to be due to the hydrogen-bonded nature of these compounds (V). Both monomeric and polymeric compounds reacted with benzalacetophenone in the presence of a basic catalyst in the manner to be expected of the 4-(benzylideneamino)thiophenol structure (IV) yielding correspondingly substituted 1,3-diphenyl-1-[4-(benzylideneamino)phenylthio]-3-propanones (VI).

In order to establish which type of substitution on the aryl group in 2-arylbenzothiazolines (I) might give rise to the greatest possible stabilization of the hypothetical 2-(benzylideneamino)thiophenol tautomer (II), so that this tautomer might be observed in an equilibrium of ring and chain tautomers, it was decided to study, as a model system, the reaction of 4-mercaptoaniline with various aromatic aldehydes.

Most aromatic aldehydes, in a manner regardless of electronic effect of substituents, reacted under mild conditions to give a poly[4-benzylideneamino)thiophenol] (III). Structurally, this polymer was the linear polymer apparently resulting from the poly-addition of the mercapto function of the hypothetical 4-(benzylideneamino)thiophenol (IV) across the imine linkage. This structure was derived from the satisfactory carbon, hydrogen and nitrogen analysis, the presence of absorption in the infrared region, near 3μ, characteristic of the N-H stretching frequency, the absence of either absorption in the region characteristic of S-H stretch, or absorption in the region characteristic of imine stretch (Table I). The assignment of a probable imine stretching frequency to be expected of the hypothetical 4-(benzylideneamino)thiophenol structure (IV) was derived from the imine stretching frequency of the *S*-methylated model compounds, the correspondingly substituted 4-(benzylideneamino)phenyl methyl sulfides (IV'), which were readily prepared by the reaction of 4-methylthioaniline with the appropriately substituted aldehyde (Table II).

In striking contrast to these results, the reaction of 4-mercaptoaniline with aromatic aldehydes substituted in the 2 position with the hydroxyl function resulted in the formation of pure, crystalline, monomeric imines (V). This structure was derived from the satisfactory carbon,
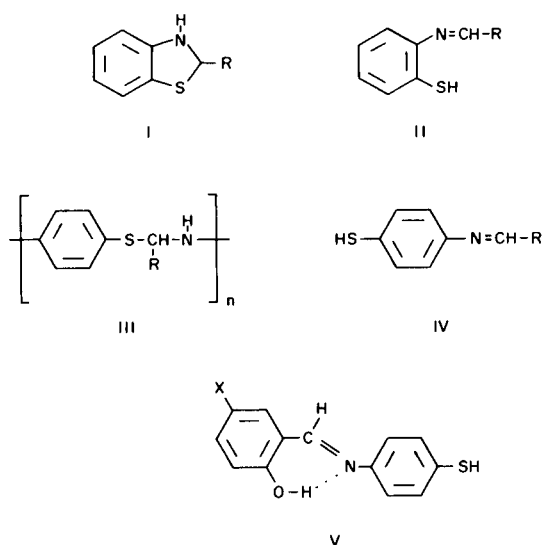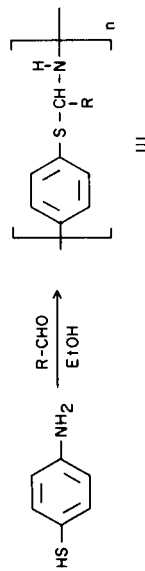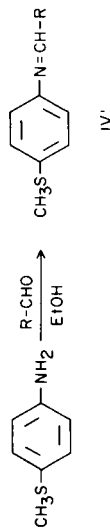
TABLE I

$$HS-\langle\text{benzene}\rangle-NH_2 \xrightarrow[\text{EtOH}]{R-CHO} \left[S-\langle\text{benzene}\rangle-\underset{R}{\overset{H}{C}}H-N \right]_n$$

III

R	Yield (a) %	N-H Stretch Assignment (λ max. in μ)	Formula	Carbon		Hydrogen		Nitrogen	
				Calcd.	Found	Calcd.	Found	Calcd	Found
2-methoxyphenyl	91	2.95	$(C_{14}H_{13}NSO)_n$	69.14	68.87	5.35	5.43	5.76	5.96
3,4-dimethoxyphenyl	87	2.97	$(C_{15}H_{15}NSO_2)_n$	65.93	65.64	5.53	5.44	5.13	5.26
4-nitrophenyl	92	2.96	$(C_{13}H_{10}N_2O_2S)_n$	60.44	60.70	3.91	4.10	10.85	10.34
2-chlorophenyl	95	2.96	$(C_{13}H_{10}ClNS)_n$	63.03	62.75	4.04	4.12	5.65	5.63
2,4-dichlorophenyl	98	2.94	$(C_{13}H_9Cl_2NS)_n$	55.32	55.40	3.19	3.39	4.96	4.98
2,6-dichlorophenyl	92	2.94	$(C_{13}H_9Cl_2NS)_n$	55.32	55.09	3.19	3.44	4.96	5.07

(a) All polymers were off white, amorphous powders when freshly precipitated which softened and melted over a broad temperature range. Although the precipitated polymers rapidly darkened in air, the clear, hard, brittle, glassy solidified melt was relatively stable to oxidation. The polymers showed no absorption in the infrared region assignable to S-H stretch.

TABLE II

$$CH_3S{-}\langle\text{phenyl}\rangle{-}NH_2 \xrightarrow[\text{EtOH}]{\text{R-CHO}} CH_3S{-}\langle\text{phenyl}\rangle{-}N{=}CH{-}R$$

IV'

R	Yield %	Imine Stretch assignment (a) (λ max. in μ)	Melting Point °C	Formula	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
phenyl	74	6.15	73-74	$C_{14}H_{13}NS$	74.00	74.25	5.73	5.95
2-methoxyphenyl	80	6.20 (6.27)	64-65	$C_{15}H_{16}NSO$	70.04	70.21	5.84	6.03
3,4-dimethoxyphenyl	97	6.13 (6.29)	111-112	$C_{16}H_{18}NSO_2$	67.00	66.63	5.73	5.99
4-nitrophenyl	98	6.20 (6.29)	153-154	$C_{14}H_{12}N_2O_2S$	61.74	61.89	4.45	4.43
2-chlorophenyl	81	6.18 (6.29)	48-49	$C_{14}H_{12}ClNS$	64.24	64.08	4.59	4.62
2,4-dichlorophenyl	92	6.18 (6.31)	85-86	$C_{14}H_{11}Cl_2NS$	56.76	57.03	3.72	4.01
2,6-dichlorophenyl	97	6.13 (6.31)	49-50	$C_{14}H_{11}Cl_2NS$	56.76	56.75	3.72	3.74
2-hydroxyphenyl	98	6.18	87-88	$C_{14}H_{13}NOS$	69.14	68.80	5.35	5.44
2-hydroxy-5-chlorophenyl	99	6.18	139-140	$C_{14}H_{12}ClNOS$	60.54	60.37	4.32	4.35
2-hydroxy-5-bromophenyl	99	6.20	154-155	$C_{14}H_{12}BrNOS$	52.17	51.69	4.04	3.81

(a) The values in parenthesis are those of closely adjacent maxima also present in the polymers with the same R group. The band assigned to imine stretch in these compounds was absent in the polymers.

TABLE III
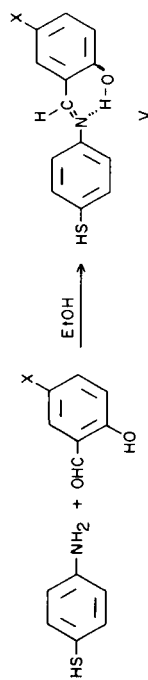
| X	Yield (a) %	Melting Point °C	Formula	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
H	98	114-115°	$C_{13}H_{11}NOS$	68.12	67.85	4.80	4.88	6.11	6.00
Cl	99	175-176°	$C_{13}H_{10}ClNOS$	59.20	58.95	3.80	3.75	5.31	5.31
Br	99	184-185°	$C_{13}H_{10}BrNOS$	50.65	50.48	3.25	3.26	4.55	4.62

(a) All these imines were bright yellow plates very closely resembling the corresponding S-methylated compounds in Table I.

TABLE IV
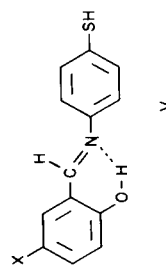
	Infrared Spectra (λ max. in μ)		(Ultraviolet Spectra (λ max. in mμ))			
	S-H Stretch assignment	Imine Stretch assignment	1% DMF in ETOH solvent		Solvent + 0.1% Triethylamine	
X			λ max.	log ε	λ max.	log ε
H	3.90	6.13	351.0	4.24	400.0	4.28
Cl	3.91	6.18	362.5	4.21	415.0	4.28
Br	3.92	6.22	362.5	4.20	417.0	4.28

TABLE V
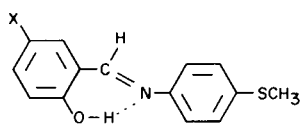
V'

Ultraviolet Spectra (a) (λ max. in mμ)

X	λ max.	log ε
H	353.5 (b)	4.30
Cl	365.5	4.28
Br	365.0	4.32

(a) 1% DMF in ETOH Solvent. (b) This maximum was not altered by addition of 0.1% triethylamine to the solution.

hydrogen and nitrogen analyses (Table III), the presence of absorption in the infrared region, near 3.9μ, characteristic of the S-H stretching frequency, the absence of absorption in the region characteristic of the N-H stretching frequency, and the presence of absorption characteristic of the imine stretching frequency (Table IV). The imine stretching frequency assigned to these compounds agreed well with that of the appropriate S-methylated models (Table II, Structure V'). The near visible ultraviolet absorption maxima of these 4-(benzylideneamino)thiophenols, partially due to the N-(4-mercaptophenyl)formimide chromophore as determined by the shifting of this maxima by the addition of a tertiary amine, agreed quite well with those of the correspondingly substituted 4-(benzylideneamino)phenyl methyl sulfides (V'), (Tables IV and V).

Whether or not the products of the reaction between aromatic aldehydes and 4-mercaptoaniline were of polymeric or monomeric structure was of little importance in determining the type of product formed by their reaction with benzalacetophenone in the presence of a basic catalyst. In both series a 1,3-diphenyl-1-[4-(benzylideneamino)phenylthio]-3-propanone (VI), derived from the apparent addition of the mercapto function of the 4-(benzylideneamino)thiophenol structure (IV) across the α,β-unsaturated function of the ketone, resulted. The structure of these compounds was derived from their satisfactory carbon and hydrogen analyses (Table VI), the presence of absorption in the infrared region characteristic absorption due to carbonyl stretching as derived by comparison with the model, 1,3-diphenyl-1-(4-amino-phenylthio)-3-propanone (VII), the presence of an imine stretching absorption as derived by comparison with the

TABLE VI

| R in VI	By Direct Addition to Benzalacetophenone (c)		By Reaction of R-CHO with VII		Formula	Carbon		Hydrogen	
	Yield %	Melting Point °C	Yield %	Melting Point °C		Calcd.	Found	Calcd.	Found
2-hydroxyphenyl(a)	76	162-163°	95	162-163°	C₂₈H₂₃NOS₂	76.85	76.60	5.31	5.23
2-methoxyphenyl(b)	52	100-102°	91	101-102°	C₂₉H₂₆NOS₂	77.13	76.86	5.59	5.63

(a) The addition to benzalacetophenone was accomplished with compound V, X = H and the aldehyde reacted with VII was 2-hydroxybenzaldehyde. (b) The addition to benzalacetophenone was accomplished with polymer III, R is 2-methoxyphenyl and the aldehyde reacted with VII was 2-methoxy-benzaldehyde. (c) The compounds prepared by both procedures had identical infrared spectra and showed no depression on mixed melting.

TABLE VII

Infrared Spectra (λ max. in μ)

Compound	N-H Stretching assignment	C=O Stretching assignment	Imine Stretching assignment
VII (a)	2.88, 2.96	5.97	None
VI, R is 2-hydroxyphenyl	None	5.96	6.18 (b)
VI, R is 2-methoxyphenyl	None	5.96	6.20 (c)

(a) This compound showed no absorption in the region characteristic of S-H stretching. The melting point was 116-118°. *Anal.* Calcd. for $C_{21}H_{19}NOS$: C, 76.27; H, 5.71; N, 4.20. Found: C, 75.96; H, 5.83; N, 4.30. (b) The imine stretching assignment of the S-methylated model (Table II) was 6.18μ. (c) The imine stretching assignment of the S-methylated model (Table II) was 6.20μ.

S-methylated models (Table VII), and comparison of the properties (melting point, infrared spectra) with compounds prepared by the reaction of appropriately substituted aldehydes with VII which was prepared by the reaction of 4-mercaptoaniline with benzalacetophenone (Table VI). The structure of VII was derived from its analysis for carbon, hydrogen and nitrogen and its infrared spectrum.
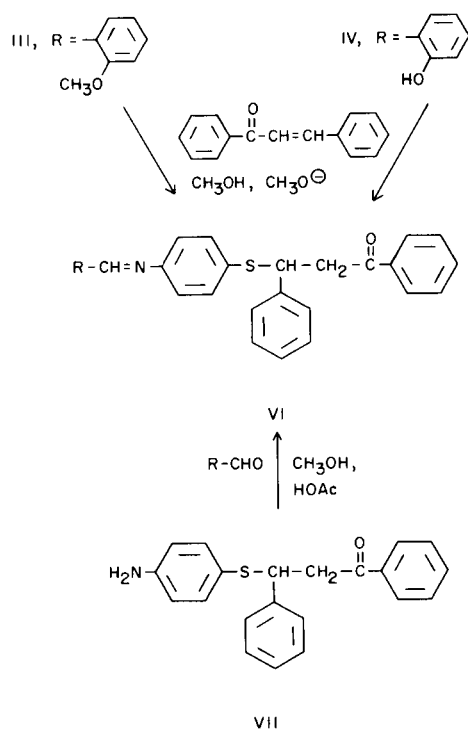
It is expected, in the light of these results, that if 2-arylbenzothiazoline-2-(benzylideneamino)thiophenol equilibria are to be observed, those compounds having aryl substituents with a hydroxyl function in the 2 position

might be most likely to give rise to observable concentrations of the 2-(benzylideneamino)thiophenol tautomer. Certainly, this hydrogen-bonded effect is much stronger than any electronic influence in stabilizing the imine tautomer.

A system with such substitution might be of particular interest since such substitution may permit the operation of a completely internal mechanism of proton transfer acting in a manner to substantially lower the apparent activation energy of tautomerization so that neither acid nor base nor protic solvent nor bimolecular reaction will be necessary to mobilize equilibrium. This matter is presently being investigated in detail.

EXPERIMENTAL

Preparation of the Polymers (III). (Table I).

In an atmosphere of pure nitrogen, 0.01 mole of 4-mercaptoaniline in 10 ml. absolute ethanol was added at once to 0.01 mole of the aldehyde (for 4-nitrobenzaldehyde, equivalent aldehyde as a saturated solution at 25° was used) in 50 ml. absolute ethanol with rapid stirring. The polymers first separated as a thick tar but on further standing this became granular and the polymer finally separated as a fine precipitate which was easily filtered and washed with 50 ml. of ethanol. The polymers were dried at room temperature *in vacuo* (10 mm/Hg).

Preparation of the Imines (IV', V, V'), (Tables II, III).

The imines were prepared by addition of 0.01 mole of the appropriate amine (2-mercaptoaniline for V, 2-methylthioaniline for IV' and V') to 0.01 mole of the aldehyde in 50 ml. of absolute ethanol. If the imine did not separate on standing for 1 hour a few drops of acetic acid was added and the imine isolated by stepwise concentration and cooling. The imines of series V crystallized from the reaction mixture in a state of analytical purity and only washing with ethanol was necessary for purification. All other imines were recrystallized from benzene-methylcyclohexane for analysis.

Preparation of 1,3-Diphenyl-1-(4-aminophenylthio)-3-propanone (VII), (Table VII).

To a solution of 0.01 mole (2.1 g.) of benzalacetophenone in 25 ml. warm ethanol (50°) was added 0.01 mole (1.25 g.) of 4-mercaptoaniline and one drop of 40% benzyltrimethylammonium methoxide in methanol. The colorless, crystalline adduct rapidly separated in almost pure condition. The yield was 3.2 g. (95%). The analytical sample was recrystallized from ethanol.

Preparation of 1,3-Diphenyl-1-[4-(benzylideneamino)phenylthio]-3-propanones (Table VI).

A. From the Monomer V or Polymer III.

A suspension of the monomer or polymer (0.002 equiv.) in 30 ml. of 2% N,N-dimethylformamide in absolute ethanol containing 1 drop of 40% benzyltrimethylammonium methoxide in methanol was stirred at reflux under pure nitrogen with 630 mg. (0.003 mole) benzalacetophenone until all insoluble material dissolved. The adduct was obtained by stepwise concentration and cooling after 2 days at room temperature.

B. From VII.

A solution of VII (660 mg. or 0.002 mole) in 30 ml. of 2% N,N-dimethylformamide and the appropriate aldehyde (0.002 mole) with 1 drop acetic acid was refluxed under nitrogen for 6 hours. The imine was obtained by stepwise concentration and cooling. The analytical sample was recrystallized from N,N-dimethylformamide-ethanol.