In the case of PNMG and MG, treatment of the data as for the other reactions already described led to both rate and equilibrium constants for formation of the triarylmethyl thioethers. In the case of CV, the unfavorable equilibrium required studies at such high thiophenoxide concentrations that the rate became too fast to measure. In the case of MG and PNMG, the values reported in Table V were obtained at an ionic strength of 1.0×10^{-3} *M*. The CV data were obtained at an ionic strength of 5.0×10^{-3} *M*.

Reactions of Thiols with Schiff Bases in Nonaqueous Solvents. Addition Equilibria, Cleavage, and Reduction

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Abstract: The addition of thiols to the C=N bond of Schiff bases in nonaqueous solvents has been shown to involve an easily studied mobile equilibrium analogous to semimercaptal formation. A study involving substituted Schiff bases has shown that electron-withdrawing groups in either the aniline-derived ring or benzaldehyde-derived ring favors adduct formation. A Hammett plot of the equilibrium constants for the reaction of 1-butanethiol with Schiff bases substituted in the para position of the benzaldehyde-derived ring against σ^+ constants gave a straight line of slope +0.86. Strong electron-withdrawing substituents in the aniline-derived ring caused a facile cleavage of the Schiff base with resultant mercaptal formation. The reaction of benzaldehyde with *p*-toluenethiol to form the corresponding mercaptal was shown to be catalyzed by electron-withdrawing para substituted anilines. Evidence is presented to indicate that the catalysis may be due to intermediate Schiff base formation. The reduction of Schiff bases by *p*-toluenethiol at higher temperatures has been shown to be catalyzed by a free-radical initiator, thus suggesting a free-radical mechanism.

The addition of water, alcohols, thiols, and amines to the carbonyl group has been studied rather extensively.[2,3] Equilibrium measurements have shown that the tendency of thiols to add to the carbonyl group is considerably greater than that of hydroxyl compounds or of most amines.[4] Similarly, the addition equilibria of water and alcohols to imines[5,6] has received attention, but interestingly little has been done involving the addition equilibria of thiols to carbon–nitrogen double bonds. This is somewhat surprising in view of the relative stability of the adducts that can be obtained. For example, Stacy, Day, and Morath[7] have previously demonstrated that stable crystalline adducts readily form from the simple addition of thiols to Schiff bases. That these adducts are simple 1:1 adducts involving addition of the thiol to the carbon–nitrogen bond shall be further demonstrated in this work.

Indications that a mobile equilibrium existed between reactants and adducts were first given by the ease with which these adducts reverted to thiol and Schiff base under the influence of base.[7] Also, the crystalline adducts were shown to give a positive nitroprusside test even after repeated recrystallization.[8] We have also noted that the adducts readily react with heavy metal ions such as divalent lead or mercury to produce mercaptides.

Further indications that a facile dissociation was taking place in solution was given by some of the chemical reactions of the adducts. For example, Stacy, Day, and Morath[9] have shown that the acetylation of the *p*-toluenethiol adduct of *N*-benzylideneaniline proceeds with some difficulty. They generally obtained only small amounts of the anticipated *N*-acetyl derivative. The major products are now best interpreted as being formed from free thiol and Schiff base due to prior dissociation of the adduct. Reaction of the adducts with phenyl isocyanate and phenyl isothiocyanate[10] leads to a similar conclusion. A complex mixture of products was obtained when the adducts were allowed to react with phenyl isocyanate alone, but when the reaction was run in the presence of triethylamine (a potent catalyst for the reaction of thiols with isocyanates[11]), the only products obtained were *N*-benzylideneaniline and the phenyl isocyanate derivative of the thiol. All of this, taken together, suggested a ready dissociation of adducts to thiol and Schiff base.

More recent work dealing with chain tautomerism of thiazolidines has further demonstrated the existence of a reversible equilibrium for the addition of thiols to the C=N bond.[12] In this case, the authors showed that equilibrium greatly favors the ring tautomer but they demonstrated that the open-chain tautomer was a probable intermediate in many different reactions involving the incipient thiol or imino function. Spectral studies[12,13] of the thiazolidine system have not been able to detect the presence of the open-chain tautomer,

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[1] From the Ph.D. Thesis of T. R. Oakes, Washington State University, June 1963; National Science Foundation Cooperative Fellow, 1960–1962.

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[7] G. W. Stacy, R. I. Day, and R. J. Morath, *ibid.*, **77**, 3869 (1955).

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[9] G. W. Stacy, R. I. Day, and R. J. Morath, *ibid.*, **80**, 3475 (1958).

[10] G. W. Stacy, P. A. Craig, and R. I. Day, *J. Org. Chem.*, **23**, 1760 (1958).

[11] E. Dyer and J. F. Glenn, *J. Amer. Chem. Soc.*, **79**, 366 (1957).

[12] G. W. Stacy and P. L. Strong, *J. Org. Chem.*, **32**, 1487 (1967).

[13] E. D. Bergmann and A. Kaluszyner, *Recl. Trav. Chim. Pays-Bas.*, **78**, 289 (1959).

Table I. Properties of Schiff Bases

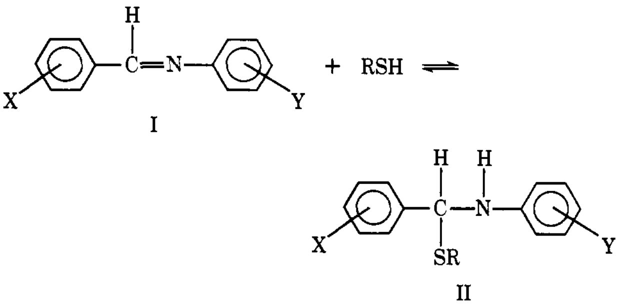
Substituent[a]	Mp, °C Obsd	Mp, °C Lit.	Ref	Bands[b] E$_1$	Bands[b] E$_2$	Bands[b] K
Hydrogen	52–53	50–51	*e*	E.a.[c]	262 (16,500)	305 (8,680)[d]
4-Methyl	46–48	46.5–48	*f*	E.a.	269 (18,300)	305 (11,600)
4-Chloro	64.5–66	65.5–66	*g*		267 (19,400)	310 (10,300)[d]
4-Methoxy	64–65.5	64	*e*	222 (17,000)	289 (18,500)	312 (10,400)[d]
4-Nitro	92–93	92	*e*	E.a.	288 (13,700)	335 (10,400)[d]
4′-Methyl	34–35	32	*h*	E.a.	262 (15,800)	316 (10,500)
		36	*i*			
4′-Chloro	63–65	60	*j*	220 (13,800)[d]	262 (17,700)	312 (10,300)
		64	*e*			
4′-Methoxy	71–72	70	*i*	229 (12,800)	264 (13,200)	330 (13,100)

[a] The notations 4 and 4′ refer to substitution in the benzaldehyde-derived ring and the aniline-derived ring, respectively. [b] The spectra were determined in anhydrous methanol. Wavelengths are in nanometers; molar absorption intensities are in parentheses. [c] E.a. denotes end absorption below 220 nm. [d] Inflection or shoulder. [e] O. H. Wheeler and P. H. Gore, *J Org. Chem.*, **26,** 3298 (1961). [f] E. J. Wayne and J. B. Cohen, *J. Chem. Soc.*, **127,** 450 (1925). [g] H. D. Law, *ibid.*, **101,** 154 (1912). [h] A. Dornow and F. Boberg, *Justus Liebigs Ann. Chem.*, **578,** 94 (1952). [i] H. H. Keasling and F. W. Schueler, *J. Amer. Pharm. Ass.*, **39,** 87 (1950). [j] M. T. Bogert and H. B. Corbitt, *J. Amer. Chem. Soc.*, **48,** 783 (1926).

however. On the other hand, the corresponding six-membered heterocycle from 3-aminopropanethiol did show infrared evidence for a chain tautomer.[14]

In this work we wish to report a study in nonaqueous solvents of the mobile equilibrium that exists between thiol, Schiff base (I), and adducts (II) in nonring systems (Scheme I).

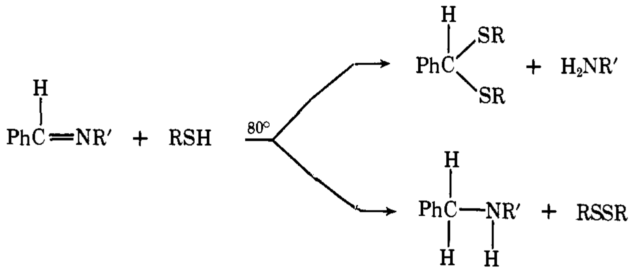
Scheme I



This reaction is analogous to hemithioacetal formation which has recently been studied by Lienhard and Jencks[4] and by Field and Sweetman.[15]

At higher temperatures two other reactions occur between thiols and Schiff bases, Schiff base cleavage resulting in mercaptal formation[7] and reduction[7,16] (Scheme II). Both of these reactions will also be discussed in this paper.

Scheme II



Experimental Section

Equilibrium data for the addition reaction of thiols to Schiff bases were obtained by two methods. The first and more accurate method involves the analysis of ultraviolet spectra in anhydrous methanol; the second, a more qualitative infrared method in carbon tetrachloride, serves to characterize the reaction more fully. It should be stressed that this second method is only semiquantitative; its value lies in showing that actual addition is taking place.

Ultraviolet Method. Materials. Methanol (Baker Analyzed Reagent) was purified by reaction with magnesium turnings followed by distillation. Eastman Grade (white label) 1-butanethiol, benzenethiol, and α-toluenethiol were distilled under nitrogen immediately before use. The Schiff bases were prepared by condensing equimolar quantities of the appropriate benzaldehyde and substituted aniline in refluxing benzene using a Dean-Stark trap to remove the water as it formed.[7] The Schiff bases were recrystallized from ethanol, or from hexane or pentane, in the case of the more soluble compounds. Their melting points, together with literature values and spectral data, are given in Table I. The monosubstituted anilines and benzaldehydes used in this study were all available commercially.

Apparatus. Spectra were recorded with a Cary Model 14 spectrophotometer using standard 1.0-cm quartz cells with 0.95-cm spacers. The temperature of the cell compartments was maintained at 23.7 ± 0.5° by circulation of water from a constant-temperature bath.

Sample Preparation. Schiff base master solutions were prepared by adding a weighed amount of the Schiff base to a volumetric flask and adding dry methanol to the mark. Thiol master solutions were prepared in dry methanol at a concentration of approximately 0.9 *M*. The exact concentration of thiol was then determined by iodometric titration.[17,18] The sample solutions were prepared from aliquots of these stock solutions. The sample solutions, in glass-stoppered volumetric flasks, were then sealed with Parafilm and let stand at room temperature for 2–3 hr before the ultraviolet spectra were determined; by this time equilibrium was generally attained.

Procedure. During the determination of ultraviolet spectra, hydrolysis of the Schiff bases was at times a problem. Hydrolysis products were detected easily by observing the entire ultraviolet spectrum of a pure Schiff base. If hydrolysis had occurred, the samples were discarded, and fresh samples were prepared. This check for hydrolysis was performed both immediately before and immediately after the spectra of the mixtures had been determined.

The data for the determination of the equilibrium constants were obtained by measuring the absorbance difference of a methanol solution of pure Schiff base in the sample cell and a Schiff base–thiol solution of the same total Schiff base concentration in the reference cell. By scanning the 280–350-nm region, the optimum wavelength for study, that is, the wavelength of largest absorbance difference, was determined. Most Schiff bases displayed two regions of largest absorbance difference; these correspond to the two absorption bands of the pure Schiff bases. Equilibrium data were obtained at the longer of these two wavelengths in order to avoid overlap of the thiol absorption. A minimum of five different thiol concentrations, with some duplicates, was used

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[14] E. D. Bergmann and A. Kaluszyner, *J. Amer. Chem. Soc.*, **78,** 327 (1959).

[15] L. Field and B. J. Sweetman, *J. Org. Chem.*, **34,** 1799 (1969).

[16] H. Gilman and J. B. Dickey, *J. Amer. Chem. Soc.*, **52,** 4573 (1930).

[17] J. W. Kimball, R. L. Kramer, and E. E. Reid, *ibid.*, **43,** 1199 (1921).

[18] J. R. Sampey and E. E. Reid, *ibid.*, **54,** 3404 (1932).

for each determination. The value of the absorption difference was determined after thermal equilibrium had been reached. This was evidenced by the constant value of the absorption difference at the chosen wavelength over a period of 5–10 min. The method of calculation of the equilibrium constants and their values are given in the section entitled Results.

Infrared Method. Materials. Mallinckrodt Analytical Reagent carbon tetrachloride was used without further purification. The thiols and Schiff bases were purified as described above.

Apparatus. The spectra were determined with a Beckman Model IR-5 spectrophotometer. The spectra of the solutions were obtained by use of a standard Beckman 1.0-mm cell against a similar reference cell containing pure carbon tetrachloride. Adequate temperature control was not available. However, the maximum temperature variations were less than 5°. This does not influence the qualitative conclusions from these experiments.

Sample Preparation. Schiff base and thiol master solutions were prepared from weighed samples made up to the desired volume with carbon tetrachloride. The sample solutions were prepared from aliquots of these stock solutions.

Procedure. This method involved the measurement of the intensity of the N–H stretching band at 3400 cm^{-1} of the Schiff base–thiol adducts in carbon tetrachloride solution. Spectra of the sample solutions were determined after the sample cell, which was mounted in the light beam, had reached thermal equilibrium with its surroundings. Spectra of the same samples, taken at different times, showed that the temperatures did not vary appreciably. In all cases, the intensity of the N–H band, at 3400 cm^{-1}, increased with increasing thiol concentration while the C=N band, at 1625 cm^{-1}, decreased. The decrease of the C=N band was, at times, difficult to observe due to high concentrations and the overlap of other absorption bands. The data and the method of calculation of the equilibrium constants are given in the section entitled Results.

In order to assure the fact that both the ultraviolet and infrared methods were measuring the postulated equilibria, the equilibria were approached also from the opposite direction. The crystalline *p*-toluenethiol adducts of *N*-benzylideneaniline, *N*-*p*-nitrobenzylideneaniline, and *N*-*p*-methoxybenzylideneaniline were prepared by the method of Stacy, Day, and Morath.[7] The infrared and ultraviolet spectra of these adducts were then determined at various concentrations in chloroform and in cyclohexane. These spectra were identical with those obtained by mixing the reactants in solution. (The reactants were mixed so as to obtain solutions of the same concentrations as those of the adducts.) Thus, the same point of equilibrium is reached from either direction.

Mercaptal Formation from Benzaldehyde and *p*-Toluenethiol Using Various Catalysts. A mixture containing 2.5 ml (2.62 g, 0.025 mol) of benzaldehyde, 12.4 g (0.10 mol) of *p*-toluenethiol, a measured volume of toluene, and a specific amount of catalyst (water or a substituted aniline) was heated under reflux for an appropriate period of time. The flask was equipped with a magnetic stirrer and a reflux condenser, and a nitrogen atmosphere was maintained. After the reflux period had been completed, the mercaptal was isolated by the method of Stacy, Day and Morath.[7] The results are summarized in Table II.

Cleavage of *N*-Benzylidene-*p*-nitroaniline by *p*-Toluenethiol. A slight modification of the procedure used by Stacy, Day, and Morath[7] for the cleavage of *m*-benzylideneaminobenzoic acid was employed. A solution of 5.66 g (0.025 mol) of *N*-benzylidene-*p*-nitroaniline and 12.40 g (0.10 mol) of *p*-toluenethiol in 100 ml of toluene was heated under reflux (nitrogen atmosphere) for 12 hr. As the reaction mixture cooled, a yellow crystalline precipitate formed. This solid proved to be *p*-nitroaniline: yield 1.28 g (38%); mp 144–148°. Its identity was confirmed by the exact comparison of its infrared spectrum to that of an authentic sample. The combined filtrate and washings were extracted with 200 ml (100, 50, 50) of a 5% sodium hydroxide solution and then with 200 ml (100, 50, 50) of a 10% hydrochloric acid solutions; finally, the solution was washed with water (two 50-ml portions). After the toluene solution had been dried over calcium sulfate, the toluene was removed (aspirator), and the solid residue was recrystallized from 30 ml of ethanol. This solid proved to be the mercaptal: yield, 4.40 g (52%); mp 78–80°; a mixture melting point determination with an authentic sample showed no depression. A second crop of impure product (0.44 g, 73–85°) was obtained by concentration of the ethanol filtrate.

Table II. Yields of Mercaptal Using Various Catalysts

Catalyst	Amount of catalyst, mol	Reflux[a] time, hr	Vol of toluene, ml	Yield of mercaptal, %
Fresh reagents[b]				
p-Cyanoaniline	0.001	12	100	28
p-Nitroaniline	0.001	12	100	26
Aniline	0.0022	12	100	5
p-Methoxyaniline	0.001	12	100	0
Water	0.011	12	100	0
Aged reagents[c]				
p-Cyanoaniline	0.001	24	90	94
p-Cyanoaniline	0.001	12	100	49
p-Chloroaniline	0.001	12.5	150	45
Aniline	0.001	12.5	150	25
Water	0.0055	12	100	4
None		12	70	6

[a] The reflux time was generally held to 12 hr so that differences in the reaction rates could be observed. [b] Benzaldehyde and *p*-toluenethiol freshly distilled under nitrogen and freshly purified anilines were used. [c] Benzaldehyde distilled 2 months previous to use and unpurified reagent grade *p*-toluenethiol and aniline were used.

Attempted Cleavage of *N*-Benzylidene-*p*-anisidine by *p*-Toluenethiol. When this same procedure was employed using *N*-benzylidene-*p*-anisidine instead of *N*-benzylidene-*p*-nitroaniline, no cleavage of the Schiff base was observed, and none of the mercaptal was obtained.

Reduction of *N*-*p*-Methoxybenzylideneaniline with *p*-Toluenethiol in the Presence of 2,2′-Azobisisobutyronitrile. A solution of 5.28 g (0.025 mol) of *N*-*p*-methoxybenzylideneaniline, 12.4 g (0.10 mol) of *p*-toluenethiol, and 100 ml of benzene was heated under reflux for 7 hr under a nitrogen atmosphere. During the reflux period, a total of 0.20 g of 2,2′-azobisisobutyronitrile was added in 0.05-g portions. The addition of the catalyst was made at the beginning of the reflux period, after 1.5 hr, after 3 hr, and after 6 hr of refluxing. The solution, contained in a stoppered flask, was then allowed to cool, and to stand overnight. An additional 50 ml of benzene was added, and the solution was extracted with 5% sodium hydroxide solution (three 50-ml portions) and then with 200 ml (100, 50, 50) of a 10% hydrochloric acid solution. The hydrochloric acid extract was allowed to stand for 2 hr to hydrolyze any unreacted Schiff base; it was then made basic with a 20% sodium hydroxide solution. This turbid solution then was extracted with ether (three 100-ml portions). The ether solution then was dried over calcium sulfate, and the solvent was removed under reduced pressure. Distillation of the residue yielded 1.23 g of aniline (53%), identified by the exact comparison of its infrared spectrum to that of an authentic sample, and 1.50 g (28%) of *N*-*p*-methoxybenzylaniline: bp 120–122° (0.05 mm); lit. bp 154–155° (2 mm).[19] Cooling caused solidification: mp 47–49°; lit. mp 48–49°.[19]

The infrared spectrum displayed a peak at 3378 cm^{-1} (m) assignable to N–H.

Reduction of *N*-Benzylideneaniline with *p*-Toluenethiol in the Presence of 2,2′-Azobisisobutyronitrile. Using this same procedure, the reduction of *N*-benzylideneaniline gave an 11% yield of *N*-benzylaniline.

Attempted Reduction of *N*-*p*-Methoxybenzylideneaniline with *p*-Toluenethiol in the Absence of 2,2′-Azobisisobutyronitrile. The same molar proportions but smaller amounts were used here as in the previous reduction. A solution of 4.44 g (0.021 mol) of *N*-*p*-methoxybenzylideneaniline, 10.54 g (0.085 mol) of *p*-toluenethiol, and 85 ml of benzene was heated under reflux for 7.5 hr (nitrogen atmosphere) and then allowed to stand overnight. No initiator was added. During the hydrochloric acid extraction, a yellow precipitate formed which dissolved on shaking. (This is typical of a Schiff base hydrochloride.) Using the same work-up as above, 1.62 g (83%) of aniline was obtained, bp 79–80° (12–15 mm). Its identity was confirmed by determination of its infrared spectrum. None of the reduced product was obtained.

Preparation of *N*-[α-(*p*-Tolylthio)benzyl]-*N*-acetyl-*p*-anisidine. This compound was prepared by a method similar to that used by Stacy, Day, and Morath[9] for the preparation of *N*-[α-(*p*-tolylthio)benzyl)acetanilide. A mixture of 11.90 g of crude *N*-(α-acetoxybenzyl)-*N*-acetyl-*p*-anisidine (prepared by the method of Snyder, Levin, and Wiley[20]) and 20.0 g of *p*-toluenethiol gave 5.0 g (38%) of

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(19) A. Roe and J. A. Montgomery, *J. Amer. Chem. Soc.*, 75, 910 (1953).

Table III. Equilibrium Constants for the Reaction of Thiols with Schiff Bases in Anhydrous Methanol[a]

Substituent[b]	Thiol	K, l./mol	ϵ_A	λ,[c] nm
4-Methoxy	1-Butanethiol	1.42 ± 0.04	3150 ± 280	312
		1.39 ± 0.03	2550 ± 190	315
4-Methyl	1-Butanethiol	2.81 ± 0.06	1020 ± 100	310
Hydrogen	1-Butanethiol	5.21 ± 0.10	1510 ± 40	305
4-Chloro	1-Butanethiol	7.63 ± 0.10	500 ± 60	315
		7.46 ± 0.30	480 ± 100	315
4-Nitro	1-Butanethiol	27.5 ± 2	1590 ± 60	340
4′-Methoxy	1-Butanethiol	0.75 ± 0.05	2660 ± 320	334
4′-Methyl	1-Butanethiol	2.11 ± 0.05	950 ± 90	320
4′-Chloro	1-Butanethiol	9.90 ± 0.50	1520 ± 100	316
Hydrogen	Benzenethiol	5.25 ± 0.40	1250 ± 140	316
Hydrogen	α-Toluenethiol	14.8 ± 0.2	360 ± 30	314

[a] At 23.7 ± 0.5°. [b] The notations 4 and 4′ refer to substitution in the benzaldehyde-derived ring and the aniline-derived ring, respectively. [c] The wavelengths at which the data were obtained.

the product; mp 74–79.5°. Several recrystallizations from petroleum ether (bp 30–60°) did not improve the melting point of the colorless prisms. This material did not react with divalent lead or mercury and it failed to react with basic nitroprusside as do the simple thiol–Schiff base adducts.

Anal. Calcd for $C_{23}H_{23}NO_2S$: C, 73.18; H, 6.14; S, 8.49. Found: C, 73.39; H, 6.23; S, 8.66

Results

The equilibrium constants given in Table III for the addition of thiols to Schiff bases have been determined using the ultraviolet method described in the Experimental Section.

The equilibrium constants were calculated by a method developed by Rose and Drago[21] for the association of molecular addition compounds of iodine.

Since the spectrum of the adduct cannot be obtained in solution due to dissociation, its absorbance is of unknown magnitude. The expression derived by Rose and Drago takes this into consideration. A slight modification of their equation gives the following

$$K^{-1} = \frac{(A^0 - A)}{(\epsilon_S - \epsilon_A)b} - (C_S + C_T) + \frac{C_S C_T(\epsilon_S - \epsilon_A)b}{(A^0 - A)}$$

$$K = C_A/C_S C_T$$

where A^0 = absorbance due to the initial concentration of Schiff base, A = absorbance of the system at a given wavelength, b = path length in centimeters (0.05 cm), C_S = initial molar concentration of Schiff base, C_T = initial molar concentration of thiol, C_A = molar concentration of adduct, ϵ_S = molar absorptivity of Schiff base, and ϵ_A = molar absorptivity of adduct. In this equation it is assumed that the thiol does not absorb in the region of study. By obtaining the equilibrium data above 280 nm this assumption is satisfied.

The equation contains two unknowns, K^{-1} and ϵ_A; each can be determined by solving simultaneous equations using the data from two different experimental trials (two different thiol concentrations). However, it was found easier to use the graphical method described by the above authors. This method involves the random selection of values of ϵ_A and calculation of the corresponding values of K^{-1} using a single set of experimental values. A curve is then constructed, plotting K^{-1} *vs.* ϵ_A. A second set of experimental values is then used, and a second curve of K^{-1} *vs.* ϵ_A is constructed. This is repeated for each set of experimental data. Since there is only one K^{-1} and only one ϵ_A, these curves should intersect at one point. In the present work, the curves obtained were straight lines due to the almost negligible contributions of the first term in the above equation. In practice, instead of passing through a single point the intersections clustered about a small area. The equilibrium constants were then determined by giving each intersection equal weight and calculating the average value. As Rose and Drago point out, this is equivalent to solving simultaneous equations for all possible pairs of data.

The data from the reaction of *N*-benzylideneaniline with 1-buthanethiol are used to demonstrate the method of calculation. The K^{-1} *vs.* ϵ_A curves are plotted in Figure 1 using the data from Table IV. The reported equilibrium constant is the average value, and the deviation given is the average deviation. In general, the intersections clustered about a relatively small area indicating good precision and reliable equilibrium constants. At low thiol concentrations the intersections were not reliable and these results are not included.

Table IV. Equilibrium Data for the Reaction of *n*-Butanethiol with *N*-Benzylideneaniline

Schiff base concn, *M*	Thiol concn, *M*	$A^0 - A$[a]
0.00200	0.5514	0.533
0.00200	0.4595	0.506
0.00200	0.3676	0.472
0.00200	0.2757	0.423
0.00200	0.1838	0.350
0.00200	0.0460	0.137

[a] At 305 nm in absolute methanol at 23.7 ± 0.5° where ϵ_S = 8680 (from Table I).

Equilibrium data for the reaction of 1-butanethiol with *N*-*p*-nitrobenzylideneaniline, *N*-benzylideneaniline, and *N*-*p*-methoxybenzylideneaniline were also obtained by the infrared method as described in the Experimental Section. The data were obtained using a Beckman IR-5 spectrophotometer which records in per cent transmission *vs.* wavelength. The transmission readings were converted to absorbance after applying base line corrections.[22] The solvent was carbon tetrachloride;

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(20) H. R. Snyder, R. H. Levin, and P. F. Wiley, *J. Amer. Chem. Soc.*, 60, 2025 (1938).

(21) N. J. Rose and R. S. Drago, *J. Amer. Chem. Soc.*, 81, 6138 (1959).

(22) G. W. Ewing, "Instrumental Methods of Chemical Analysis," McGraw-Hill, New York, N. Y., 1954, p 208.

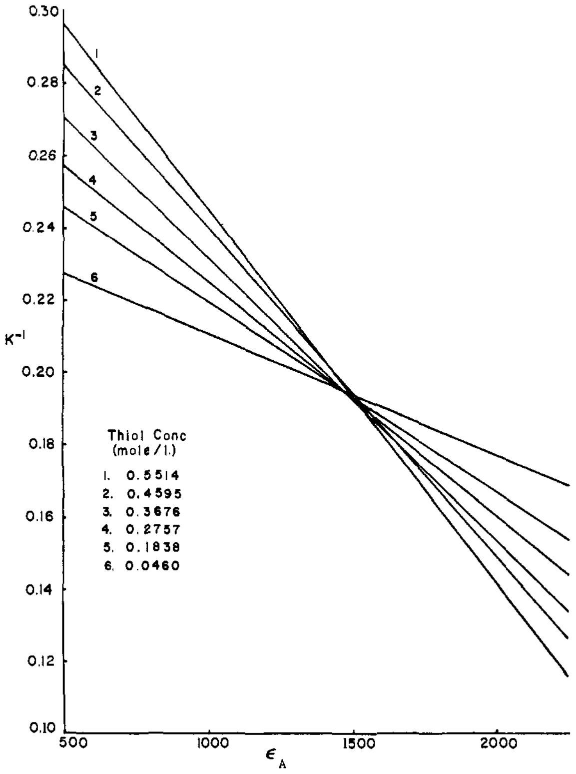


Figure 1. Plot of K^{-1} *vs.* ϵ_A for the reaction of 1-butanethiol with *N*-benzylideneaniline using the data from Table IV.

the absorption band studied was the N–H stretching band near 3400 cm^{-1}.

The equilibrium constants were calculated by a method similar to the above but with a slight modification. In this case, the N–H band of the adduct is the only absorption band in the region of study; hence, $A^0 = 0$. The equation of Rose and Drago is thus modified to the following

$$K^{-1} = \frac{A}{b\epsilon_A} - (C_S + C_T) + \frac{bC_TC_S\epsilon_A}{A}$$

In treating the ultraviolet data, the graphical method was easily applied since straight lines were obtained, and individual intersections could be read directly from the graph without solving sets of simultaneous equations. In the equation for the infrared work, the term $A/b\epsilon_A$ is not negligible, as it was in the ultraviolet study, and straight lines are not obtained. Accordingly, simultaneous equations were solved using all possible pairs of data. The data are summarized in Table V. The reported equilibrium constants are averaged values obtained from all pairs of data; in some cases (at low thiol concentrations), values lying far outside the norm were rejected.

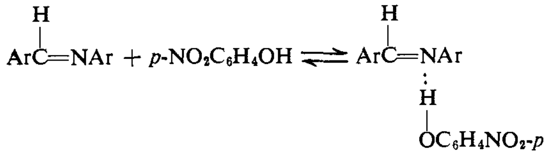
Table V. Qualitative Equilibrium Data Obtained by the Infrared Method for the Reaction of 1-Butanethiol with Schiff Bases in Carbon Tetrachloride

Schiff base[a] substituent	Schiff base concn, *M*	Thiol concn, *M*	A^b
4-Nitro	0.200	0.392	0.365
	0.200	0.314	0.335
	0.200	0.235	0.287
	0.200	0.157	0.219
	K = 11.8 l./mol, ϵ_A = 25		
Hydrogen	0.201	0.392	0.217
	0.201	0.314	0.195
	0.201	0.235	0.167
	0.201	0.157	0.122
	K = 6.9 l./mol, ϵ_A = 17		
4-Methoxy	0.201	0.392	0.126
	0.201	0.314	0.106
	0.201	0.235	0.083
	0.201	0.157	0.058
	K = 1.13 l./mol, ϵ_A = 22		

[a] In the benzaldehyde-derived ring. [b] The absorption of the N–H band of the adduct near 3400 cm^{-1}.

Discussion

Data presented in the Results require that the reactions studied be a single equilibrium. That this equilibrium is not a mere acid–base reaction but one involving true addition is supported by the work of Weinstein and McInich.[23] These authors have examined the base strengths of para substituted Schiff bases by studying the following equilibrium



$$\mathrm{Ar\overset{H}{C}{=}NAr} + p\text{-}\mathrm{NO_2C_6H_4OH} \rightleftharpoons \mathrm{Ar\overset{H}{C}{=}NAr\cdots H{-}OC_6H_4NO_2}\text{-}p$$

They demonstrated that hydrogen bonding was favored by electron-donating substituents. Thus, the base strength of the nitrogen atom is increased by electron donation as would be expected. In the present study, the opposite effect was noted. Thus, the reaction under study is not primarily dependent upon the basicity of the nitrogen atom but rather upon the ability of the C═N bond to react with a nucleophile.

The ir method also serves to prove the nature of the reaction. Upon mixing the reagents, an N–H band appears immediately at 3400 cm^{-1} while the C═N band at 1625 cm^{-1} diminishes. The same kind of substituent effect is noted in both the ir and uv methods. The differences in the equilibrium constants measured by the two methods are a reflection of a change in solvents and of the qualitative nature of the ir method.

These differences do not affect the qualitative conclusions however. The addition of the thiol to the C═N bond takes place rapidly in solution and equilibrium is attained quickly. Electron-withdrawing substituents favor adduct formation while electron-donating groups have the opposite effect. These results help to substantiate the conclusion that the reaction being studied is one of actual addition.

As mentioned earlier, addition reactions to the weakly electronegative C═N group are quite limited as compared to the addition reactions that carbonyl compounds undergo. Only the more nucleophilic reagents will add appreciably to the azomethine linkage and, as a result, the factors influencing the addition of nucleophiles across this linkage have been studied less extensively. Jencks,[24] in studying oxime and semicarbazone formation, was able to obtain equilibrium constants for the addition of water to the C═N linkage of furfural and pyruvate semicarbazones, *viz.*, 8.3 × 10^{-6} and 5.1 × 10^{-5}, respectively. This author points out that these unfavorable equilibrium constants, for the

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[23] J. Weinstein and E. McInich, *J. Amer. Chem. Soc.*, **82**, 6064 (1960).

[24] W. P. Jencks, *ibid.*, **81**, 475 (1959).

addition of water, reflect the relatively low affinity of water oxygen for carbon as well as the relatively low susceptibility of the C=N group to undergo addition reactions. The greater stability of the adducts formed from thiols adding to the C=N linkage is obvious from studies involving ring-chain tautomerism. Thus, Schiff bases of *o*-aminobenzenethiol exist almost exclusively as cyclic tautomers[25] whereas Schiff bases of *o*-aminophenol exist as open-chain tautomers.[26,27] It is, therefore, consistent that a favorable equilibrium exists for the addition of thiols to the C=N linkage.

This favorable addition of thiols, in contrast to the unfavorable addition of alcohols, to Schiff bases may be explained on several counts. The large polarizability of sulfur, the bond energies involved in adduct formation, and the lack of strong hydrogen bonding of thiols all favor adduct formation. In contrast, the small polarizability of oxygen, the unfavorable bond energies for adduct formation, and the necessity of breaking strong hydrogen bonds between molecules during adduct formation contribute to the lack of reactivity of most oxygen nucleophiles.

It is true that oxygen nucleophiles will react with the azomethine linkage, but such reactions are often followed by cleavage of the C–N bond, and simple addition involves an unfavorable prior equilibrium before cleavage occurs; thus, the addition reaction is normally obscured. In contrast to this, the addition of thiols to the azomethine linkage takes place to an appreciable extent, and the simple addition reaction is not obscured by subsequent cleavage. The factors that influence addition to this linkage are, therefore, more easily observed and structural correlations are facilitated.

Figure 2 shows a Hammett plot for the equilibrium data of the reaction of 1-butanethiol with 4-substituted Schiff bases. (The notation 4 and 4′ refer to para substituents in the benzaldehyde ring and in the aniline ring, respectively.) A better correlation is obtained by using σ^+ constants rather than σ constants; using σ^+ constants, a straight line of slope +0.86 is obtained. Cordes and Jencks[28] have proposed an explanation for their σ^+ correlations involving semicarbazone formation from substituted benzaldehydes; as in the present study, positive values for ρ^+ were obtained. They explained that the correlation with σ^+ values, rather than with σ values, reflects the high degree of stabilization of the starting materials by para substituents capable of donating electrons by resonance. They pointed out in an earlier paper[6] that such resonance stabilization is expected to be less important for the C=N group in the product than for the highly polar C=O group of the starting material. This same type of argument would seem to apply in the present case; thus, resonance stabilization would be expected to be of much more importance for the C=N group of the starting material than for the RSCN(-H) group of the product. It seems reasonable that this type of argument is even more applicable to the present case since the conjugated system is shortened during the reaction, whereas in semicarbazone formation the relative stabilization of reactant and product by resonance is merely a matter of degree.

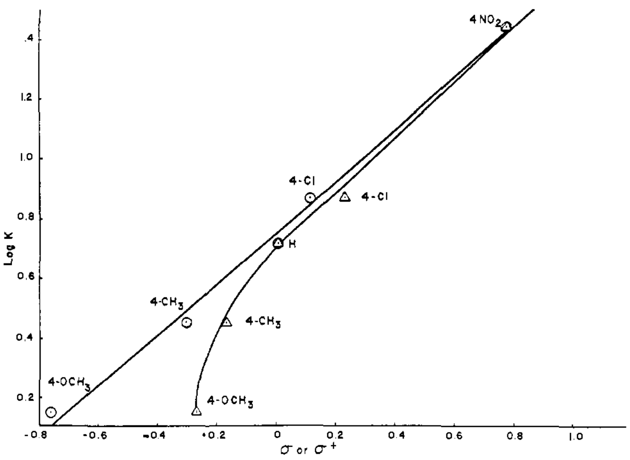

Figure 2. Hammett plot of equilibrium constants for the reaction of 4-substituted Schiff bases with 1-butanethiol: △, using σ constants; ⊙, using σ^+ constants. (The substituents are in the benzaldehyde-derived ring.)

The addition of two other thiols to *N*-benzylideneaniline was also studied. When the equilibrium constants for the addition of the three thiols—1-butanethiol, α-toluenethiol, and benzenethiol—are compared, no correlation appears obvious. The differences in the equilibrium constants are probably due to both the steric requirements and the acidities of the thiols. At this time, insufficient information is available to explain these differences. In further studies, it may be of interest to study substituted benzenethiols in which the steric requirements remain constant. Systematic studies of other thiols may also be useful in determining the nucleophilicities of mercaptans.

When attempts were made to obtain equilibrium data using Schiff bases with strongly electron-withdrawing substituents in the aniline ring, unexpected bathochromic shifts appeared in the ultraviolet spectra of the Schiff bases upon the addition of the thiol solutions. These shifts were especially apparent in the case of the 4′-nitro compound, and the appearance of the new bands occurred in the region of absorbance of *p*-nitroaniline. This suggested that cleavage of the Schiff base was taking place. This observation, together with the known cleavage of *N*-benzylideneaminobenzoic acids by *p*-toluenethiol[7] and the apparent lack of cleavage of *N*-benzylideneaniline under similar conditions, suggested that cleavage may be aided by electron-withdrawing groups in the aniline ring. (In the known cleavage of *N*-benzylideneaminobenzoic acids, an alternate explanation involved the acidity of the carboxyl group.) That electron-withdrawing groups do favor cleavage was demonstrated by treating *p*-toluenethiol with *N*-benzylidene-*p*-nitroaniline and *N*-benzylidene-*p*-methoxyaniline. The former gave a 52% yield of the mercaptal, α,α-bis(*p*-tolylthio)toluene, but in a latter case no cleavage was observed. Streitwieser[29] has pointed out that in cases in which the leaving atom is the same, the ease of displacement parallels the ability of the leaving group to bear a negative

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(25) A. H. Land, *Heterocycl. Compounds*, 5, 508 (1957).

(26) J. W. Cornforth, *ibid.*, 5, 429 (1957).

(27) A. W. Baker and A. T. Shulgin, *J. Amer. Chem. Soc.*, **81**, 1523 (1959).

(28) E. H. Cordes and W. P. Jencks, *ibid.*, **84**, 4319 (1962).

(29) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill, New York, N. Y., 1962, p 29.

charge. The above observations are in accord with this notion.

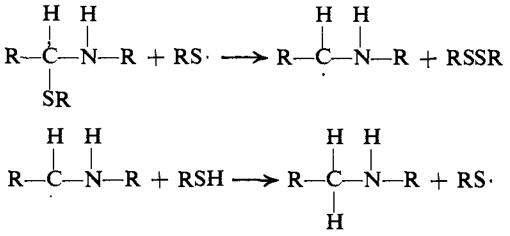
Withdrawing groups in the aniline ring not only stabilize the leaving group but also increase the concentration of adduct as demonstrated by the equilibrium data. The results of the cleavage reactions in no way prove that the adduct is an intermediate, but the favorable conditions for C–N cleavage of the adduct when electron-withdrawing groups are present does indicate that it is a possible intermediate.

The work of Cordes and Jencks[30] provides an analogy to the above cleavage. These authors demonstrated that anilines catalyze the formation of semicarbazones and that Schiff bases are intermediates in this reaction. Because of this aniline-catalyzed semicarbazone formation, it was of interest to determine if anilines would catalyze mercaptal formation. This was found to be the case. Furthermore, it was demonstrated that anilines containing strong electron-withdrawing groups are the best catalysts. The absence of catalysis using *p*-methoxyaniline and the lack of cleavage of its benzal derivative, together with the large catalytic effect of *p*-nitroaniline and the ready cleavage of its benzal derivative, indicate that Schiff bases may be intermediates in these reactions.

The increased yields of mercaptal using aged reagents probably reflect the presence of benzoic acid. Since both Schiff base formation and mercaptal formation are acid catalyzed, these results are not surprising. Even in this case, anilines substituted with electron-withdrawing groups were the best catalysts and water had a negligible catalytic effect.

The evidence that Schiff bases are intermediates in this reaction is as follows: (1) the equilibria for Schiff base–adduct formation from thiols appear to be more favorable than hemithioacetal formation; (2) the rate of mercaptal formation from Schiff bases containing negative substituents in the aniline ring is much faster than mercaptal formation from the parent aldehyde; (3) electron-withdrawing groups in the aniline ring of the Schiff base have been shown to facilitate Schiff base cleavage, and these same anilines have the largest catalytic effect on mercaptal formation. This is in direct analogy to the work of Cordes and Jencks.[20] If Schiff bases are intermediates in these reactions, this may provide a means for nonacid-catalyzed additions to the carbonyl linkage.

The reduction of Schiff bases by *p*-toluenethiol has been demonstrated previously[7,16] but little is known of the mode of this reaction. Reduction normally takes place only at high temperatures and extended reaction periods are necessary. Walling[31] suggested that this reduction may be a free-radical process. It has now been shown that a free-radical source, 2,2′-azobisisobutyronitrile, is an effective catalyst for this reduction; relatively short reaction periods and low temperature were used to effect reduction. In the absence of this initiator no reduction occurred. This supports the idea that the reaction is indeed a free-radical process. The reported ease of homolytic cleavage of some C–S bonds[32] suggests the following mechanism. The better



$$\mathrm{R{-}\underset{SR}{\overset{H}{C}}{-}\overset{H}{N}{-}R + RS\cdot \longrightarrow R{-}\underset{\cdot}{\overset{H}{C}}{-}\overset{H}{N}{-}R + RSSR}$$

$$\mathrm{R{-}\underset{\cdot}{\overset{H}{C}}{-}\overset{H}{N}{-}R + RSH \longrightarrow R{-}\underset{H}{\overset{H}{C}}{-}\overset{H}{N}{-}R + RS\cdot}$$

yield obtained in the reduction of *N*-*p*-methoxybenzylideneaniline may reflect stabilization of the benzyl radical by the methoxy group.

The preparations of the acetyl derivatives of the Schiff base–thiol adducts serve to demonstrate that the ready dissociation of the adducts is due to the presence of an N–H bond. In contrast to the actual adducts, the acetyl derivatives displayed no tendency to dissociate in solution.

Due to the ready dissociation of the adducts, it is not generally practical to obtain the acetyl derivatives by direct acetylation. When Stacy, Day, and Morath[9] attempted to acetylate *N*-[α-(*p*-tolylthio)benzyl]aniline, they observed extensive C–N cleavage; the reaction of a variety of acetylating agents gave the acetyl derivative in yields of only 14–21%. Along with the expected acetyl derivative, these authors usually obtained greater amounts of acetanilide and the mercaptal. The formation of these latter products can now be explained; the ready dissociation of the adducts results in the formation of free thiol, which in turn results in mercaptal formation. The presence of acetic acid would assist this cleavage due to protonation of the leaving aniline group.

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(30) E. H. Cordes and W. P. Jencks, *J. Amer. Chem. Soc.*, **84**, 826 (1962).

(31) C. Walling. "Free Radicals in Solution," Wiley, New York, N. Y., 1957, p 326.

(32) Reference 31, p 523.