Cleavage of the Carbon–Sulfur Bond. Kinetics of the Reaction of Thiobenzoic Acid with Aniline

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The kinetics of the reaction between thiobenzoic acid and aniline has been studied. In chlorobenzene solution, the rate is given by $k(C_6H_5COSH)(C_6H_5NH_2)$; variations in k between different samples of thiobenzoic acid are probably due to the presence of small amounts of benzoic acid as impurity. The effect of other substances on the rate has been measured. In aqueous acetic acid, the kinetics vary, depending on the composition of the solution, but most runs follow the above kinetics in the initial stage. In aniline solution, the kinetics follow the equation, rate = $k(C_6H_5COSH)^2$. The much greater rate of acylation of aniline by thiobenzoic acid, compared to benzoic acid, is discussed.

Various observations in the literature[1] indicate that the thiol acids, RCOSH, react far more rapidly with amines than the carboxylic acids, RCOOH, and the use of thiol acids as acylating agents has been studied recently from the synthetic side.[2] We have undertaken a kinetic study of the reaction between thiobenzoic acid and aniline to yield benzanilide (eq. 1) in order to determine the cause for

$$C_6H_5COSH + C_6H_5NH_2 \longrightarrow C_6H_5CONHC_6H_5 + H_2S \quad (1)$$

this marked difference between the sulfur and oxygen compounds; a second goal, so far incomplete, was to see if the acylation of amines by thiol acids could proceed by a free-radical chain process.[3]

In one series of experiments, the rate of the reaction in chlorobenzene solution was followed by acid-base titration of the unreacted thiobenzoic acid. The results gave good second-order rate constants for any one run, in agreement with the expected kinetic equation

$$\text{rate} = k_1(C_6H_5COSH)(C_6H_5NH_2) \quad (2)$$

The rate constants at 60.0° varied, from one sample of thiobenzoic acid to another, the extreme variations being $1.90–7.0 \times 10^{-3}$ mole/l./min., even though the purity of the thiol acid, as determined by iodine titration, was better than 99%. Most of the samples gave a constant very close to 2.7×10^{-3}, however, and the data in Table I on the effect of added substances were obtained on samples of thiobenzoic acid shown in each case to give this value for the constant, in the absence of added substance.

It seemed possible that the variation in different samples might be due to catalysis by benzoic acid, present in small and variable amounts as impurity in the thiobenzoic acid. The data in Table I show that benzoic acid did increase the rate constant by an amount roughly proportional to the amount of benzoic acid added; the reaction still followed second-order kinetics. One obvious explanation for this effect, the formation of benzoic anhydride (eq. 3), which then acted as the acylating agent, was made unlikely by the observation that thiobenzoic and benzoic acid do not in fact yield benzoic anhy-

$$C_6H_5COSH + C_6H_5COOH \longrightarrow (C_6H_5CO)_2O + H_2S \quad (3)$$

dride in chlorobenzene at 100°; only traces of hydrogen sulfide were formed, and benzoic acid and dibenzoyl disulfide were isolated.

This scheme (eq. 3) is also difficult to reconcile with the observed kinetics.[4]

$$C_6H_5COSH + C_6H_5COOH \longrightarrow (C_6H_5CO)_2S + H_2O$$
$$(C_6H_5CO)_2S + C_6H_5NH_2 \longrightarrow C_6H_5CONHC_6H_5 + H_2S$$

The catalytic effect of benzoic acid is most plausibly explained as due to the formation of hydrogen bonded complexes such as I between benzoic acid and thiobenzoic acid molecules; this

$$\begin{array}{ccc} & O \longrightarrow HO—C—C_6H_5 \\ & \| & \| \\ C_6H_5C—SH & & O \\ & I & \end{array}$$

makes the carbonyl carbon of the thiol acid more susceptible to nucleophilic attack by the aniline. Complexes analogous to I, but composed of two molecules of C_6H_5COSH, are not to be expected because the thiol group shows little tendency to form hydrogen bonds.[5]

Table I

Survey of Rate of Reaction of Thiobenzoic Acid with Aniline in Chlorobenzene at 60.0°

Added material	Mole/l.	$k^a \times 10^3$, moles/l./min.
None		2.72
C_6H_5COOH	0.00701	5.78
	.0166	8.00
	.0310	10.9
H_2S^b		1.70
$(C_4N_5COS)^c$	0.00523	2.98
Ascaridole^d		2.72
Benzoyl peroxide^e		4.33

^{a} This is the bimolecular rate constant, determined from the plot of $\log b(a - x)/a(b - x)$ vs. time. The aniline and thiobenzoic acid concentrations were roughly equivalent, and were in the range 0.20—0.25 molar. ^{b} Nearly saturated with H_2S. ^{c} Prepared by iodine oxidation of thiobenzoic acid, m.p. 126–128°; cf. R. L. Frank and J. R. Blegen, Org. Syntheses, 28, 16 (1948). ^{d} 0.0341 g. of ascaridole added; it was obtained by two distillations of oil of chenopodium, b.p. 50–52° (1 mm.), $n^{20}D$ 1.4740, in agreement with the literature (E. K. Nelson, This Journal, 35, 84 (1913); O. Wallach, Ann., 392, 59 (1912)). ^{e} Benzoyl peroxide (0.0485 g.) purified according to P. D. Bartlett and K. Nozaki, This Journal, 68, 1686 (1946) was used.
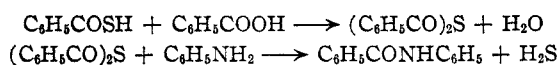
(1) (a) B. Pawlewski, Ber., 31, 661 (1898); 35, 111 (1902); (b) H. L. Wheeler, This Journal, 23, 444 (1901); (c) D. S. Tarbell and D. P. Harnish, Chem. Revs., 49, 46 (1951).

(2) M. W. Cronyn and J. Jiu, This Journal, 74, 4726 (1952); J. C. Sheehan and D. A. Johnson, ibid., 74, 4726 (1952); I. B. Wilson, ibid., 74, 3205 (1952).
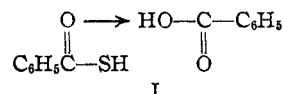
(3) This is suggested by some observations of G. Alliger, et al., J. Org. Chem., 14, 962 (1949), and of Sheehan and Johnson, ref. 2.

(4) An alternative scheme, in which the active acylating agent is dibenzoyl sulfide, as outlined below, is untenable because, according to this scheme, trace amounts of benzoic acid should have a negligible effect on the rate, and this scheme also would not give the observed kinetics.

(5) L. Hunter, Ann. Repts. of the Chem. Soc., 43, 141 (1946); ref. 2c, p. 2; also footnote 16, below.

Hydrogen sulfide had a slight inhibiting effect on the rate, but dibenzoyl disulfide and ascaridole were essentially without effect.[6] Benzoyl peroxide showed a slight accelerating effect.[7] Added triethylamine increased the rate to about the same degree as benzoic acid, but the results were erratic.

From runs at 50, 60 and 70°, the temperature coefficient was found to be small, and the Arrhenius activation energy was found to be 7.4 kcal.[8] The data (Table II) were obtained with samples of thiobenzoic acid that consistently gave the lowest rate constant at 60°. The Arrhenius plot of log k vs. $1/T$ for the data tabulated gave a good straight line, and this, together with the reproducibility of the rate constants in different runs (Table II), indicates that the value given is reliable, at any rate for the best samples of thiobenzoic acid.

TABLE II

RATE CONSTANTS AT DIFFERENT TEMPERATURES

Temp., °C.	$ka \times 10^3$, moles/l./min.	Temp., °C.	$k^a \times 10^3$, moles/l./min.
50.0	1.50	60.0	1.90
50.0	1.45	70.1	2.68
50.0	1.53	70.1	2.72
60.0	1.91	70.1	2.71
60.0	1.95		

[a] See note a to Table I.

The previous runs were carried out in the presence of air, and there was some loss of thiobenzoic acid in blank experiments under these conditions, presumably due to oxidation; however, the very good second-order rate constants obtained in each run, and the isolation of benzanilide in essentially quantitative yield from numerous runs indicated that, in the presence of aniline, the thiol acid was consumed only by reaction with aniline. Nevertheless, it was considered advisable, in studying the kinetics more in detail, to use a nitrogen atmosphere and to determine the thiobenzoic by iodine titration.[9] Measurements of the rate in chlorobenzene by this modifier technique likewise gave good second-

TABLE III

REACTION OF THIOBENZOIC ACID WITH ANILINE IN CHLOROBENZENE AT 59.5°

Time, min.	(C_6H_5COSH), mole/l.	$(C_6H_5NH_2)$, mole/l.	Reaction, %	$k \times 10^3$,[a] moles/l./min.
0	0.2624	0.2354	0	
67	.2527	.2257	5	2.51
180	.2364	.2094	12	2.61
406	.2108	.1838	23	2.60
1134	.1572	.1302	45	2.61
1691	.1364	.1094	54	2.45
3207	.1001	.0731	69	2.37

[a] Bimolecular rate constants; the mean (5–54%) = 2.54.

(6) Dibenzoyl disulfide has been shown to promote vinyl polymerization reactions (R. L. Frank, R. J. Blegen and A. Deutschman, J. Polymer Sci., 3, 58 (1948)).

(7) J. T. Hackmann and R. Berkenbosch (Rec. trav. chim., 68, 745 (1949)) have shown that there are marked differences in the activity of different organic peroxides in promoting the addition of ethyl mercaptan to 1-cetene.

(8) The activation energy for aldol condensation reactions is also found to be small; cf. J. D. Gettler and L. P. Hammett, THIS JOURNAL, 65, 1824 (1943); R. E. Buckles and K. G. Bremer, ibid., 75, 1487 (1953).

(9) There was no loss of thiobenzoic acid in blanks kept under nitrogen.

order constants (example in Table III); there was still some variation in the magnitude of the constant, from one sample to another, but the most consistent values were about 2.6×10^{-3} (l./moles/min.) at 59.5°, in agreement with the previous values.

Because the variations in rate were plausibly explained by the presence of varying amounts of benzoic acid, the reaction was studied in solution of acetic acid containing varying amounts of water (Table IV). The presence of the large excess of acetic acid should make negligible the effects of small variable amounts of benzoic acid on the rate; this expectation was borne out, in that samples of thiobenzoic acid, which in chlorobenzene showed second-order constants of 1.49 and 2.6×10^{-3}, now showed identical constants of 3.0×10^{-2} in acetic acid with ca. 0.4% water v./v.

TABLE IV

REACTION IN AQUEOUS ACETIC ACID AT 59.5°

(C_6H_5COSH) initial, mole/l.	$(C_6H_5NH_2)$ initial	H_2O, % v./v.	$k \times 10^2$,[a] moles/l./min.
0.1361	0.1917	0.4	3.0[b]
.1262	.2006	4.0	2.48[c]
.1251	.2860	10.0	2.33[d]
.1071	.2558	20.0	2.49[e]
.1256	.2208	30.0	2.89[f]
.1439	.1044	30.0	2.20[g]
.1881	.4721	42.0	5.42[h]

[a] The bimolecular rate constant; constant over the following range of % reaction: [b] 13–67; [c] 19–58; [d] 7–80; [e] 15–72; [f] 15–56; [g] 18–34; [h] 52–79.

The initial stages of reactions in aqueous acetic acid showed good second-order constants (i.e., eq. 2 was followed), but the constants fell off at some stage. The percentage reaction at which this falling off began appeared to be dependent on the amount of added water and the initial aniline concentration. Thus at a water concentration of 42% v./v. and initial aniline concentration of 0.1371/mole/l. the rate constants showed no region of constancy, whereas at an initial aniline concentration of 0.4721 mole/l. the constants remained constant up to 80% reaction.

Attempts to interpret these observations on the basis of rate equations such as rate = $k_2(C_6H_5COSH)(C_6H_5NH_2) + k_3(C_6H_5COSH)^2(C_6H_5NH_2)$ or rate = $k_4(C_6H_5COSH)(C_6H_5NH_2) + k_5(C_6H_5NH_2)$, among others, met with only limited success. It was not possible to explain more than a few runs on any single basis. It was shown, incidentally, that in aqueous acetic acid, benzanilide was formed exclusively, and acetanilide could not be isolated.

Whatever the complicating factors in the aqueous acetic acid runs were, it appeared desirable to eliminate the variable $(C_6H_5NH_3{}^+):(H_3O^+)$ ratio, and further runs were therefore carried out in aniline as solvents, the rate being followed by gravimetric determination of the benzanilide formed.

In the absence of added aniline hydrochloride the rates agreed well with the equation

$$\text{rate} = k_6(C_6H_5COSH)^2 \qquad (4)$$

although in most cases the rate constant during the course of a run, while not showing any definite
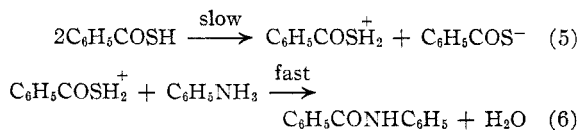
trend, showed a scatter greater than that expected from experimental error. The reaction in aniline was much faster than in chlorobenzene or aqueous acetic acid; a representative run is given in Table V, showing the bimolecular constants calculated for eq. 4. The kinetics were thus similar to those found for the reaction of aliphatic carboxylic acids in aniline as solvent.[10]

TABLE V

REACTION OF THIOBENZOIC ACID WITH ANILINE IN ANILINE SOLUTION, 59.5°

Time, min.	(C_6H_5COSH), mole/l.	Reaction, %	k, mole/l./min.[a]
0	0.0829	0	
6	.0567	32	0.49
14	.0456	45	.52
20	.0403	51	.51
40	.0292	65	.49
120	.0142	83	.46

[a] The bimolecular constant calculated from eq. 4: rate = $k(C_6H_5COSH)^2$.

The kinetics given by eq. 4 might be due to the operation of the following mechanism or some similar one, in which one molecule of thiobenzoic acid acts as an acid catalyst for the reaction of a second molecule with aniline.

$$2C_6H_5COSH \xrightarrow{\text{slow}} C_6H_5COS\overset{+}{H_2} + C_6H_5COS^- \quad (5)$$

$$C_6H_5COS\overset{+}{H_2} + C_6H_5NH_3 \xrightarrow{\text{fast}}$$
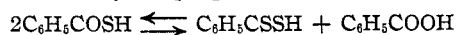$$C_6H_5CONHC_6H_5 + H_2O \quad (6)$$

The rate of the reaction was not appreciably increased by the addition of aniline hydrochloride, and hence the anilinium ion is apparently not involved in the acid catalysis.

During the aniline work, a determined effort was made to obtain thiobenzoic acid with reproducible kinetic properties. Repeated crystallization from peroxide-free ether at low temperatures in absence of air gave samples which still showed erratic behavior. Material prepared by molecular distillation behaved similarly.

Distillation under reduced pressure in nitrogen yielded samples which gave rate constants varying by ca. 20%. The following observations showed that some impurity (present only in minute amounts) was present, which affected the kinetics. The initial deep orange color of the crude acid was progressively removed by repeated distillation, accompanied by an approach to the kinetics obeying eq. 4. Exposure to air quickly removed the deep orange color, leaving a pale yellow color which did not change on continued exposure; the orange color was not discharged in a nitrogen atmosphere. A pale yellow sample prepared by distillation slowly turned orange when stored under an atmosphere of dry oxygen-free nitrogen; the contaminant appeared to be present in very small amount, as the refractive index of various samples was in the range $n^{20}D$ 1.6035–1.6040.

It was thought likely that the appearance of the orange color and of the kinetic complications was due to the presence of some thione acid or dithio

(10) H. Goldschmidt and C. Wachs, Z. physik. Chem., 24, 353 (1894); H. Goldschmidt and R. Bräuer, Ber., 39, 97 (1906).

acid, formed by disproportionation

$$2C_6H_5COSH \rightleftharpoons C_6H_5CSSH + C_6H_5COOH$$

Dithiobenzoic acid was prepared[11] and purified through the lead salt; the acid, obtained in toluene solution by treating the salt with dilute hydrochloric acid, formed a deep purple-red solution, which was not discharged by addition of benzoic acid or exposure to moist air. Hence it is apparently not the material responsible for the behavior described above.[12]

The fact that thiobenzoic acid actually reacts far more rapidly with aniline to form benzanilide than does benzoic acid was demonstrated by showing that benzoic acid and aniline in chlorobenzene solution showed no appreciable reaction after a number of hours on the steam-bath.[13] Furthermore, thiobenzoic acid in aniline as solvent reacts far more rapidly at 60° than the aliphatic carboxylic acids studied by Goldschmidt[10] react at 100° in aniline.

There are a number of factors which may contribute to this difference between C_6H_5COSH and C_6H_5COOH. Consideration of the bond strengths for the C–O and C–S bonds[14] indicates that if the transition state for the two reactions is considered to be essentially that below, the thiol acid should react faster than the oxygen acid. This assumes that

$$\begin{array}{ccc} H & & O \\ | & & \| \\ C_6H_5N & \cdots\cdots\cdots & C & \cdots\cdots\cdots SH \\ | & & | \\ H & & C_6H_5 \end{array}$$
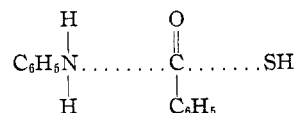
the difference in electronegativity of sulfur and oxygen in the transition state will not counterbalance the difference in bond strength, and further that the effects of solvation in chlorobenzene solution can be neglected.

The higher rate of reaction of the thiol acid is likewise favored by the fact that benzoic acid exists as a stable dimer in solution,[15] while thiobenzoic acid is probably not appreciably associated.[16] Although detailed discussion is not warranted, the energy required to dissociate the carboxylic acid dimer would increase the activation energy for the reaction with aniline, compared to that for the thiobenzoic acid, which is already in the monomeric form.

(11) F. Bloch, Compt. rend., 204, 1342 (1937).

(12) Dibenzoyl sulfide, $(C_6H_5CO)_2S$, is evidently colorless (E. Fromm and P. Schmoldt, Ber., 40, 2862 (1907)) and can thus be ruled out. It is possible that dibenzoyl polysulfides, $C_6H_5COS_xCOC_6H_5$, may be formed by some sort of disproportionation process; however, the tetrasulfide ($x = 4$) is nearly white, and the trisulfide probably is also (I. Block and M. Bergmann, Ber., 53, 961 (1920)).

(13) The preparative method for benzanilide ("Organic Syntheses," Coll. Vol. I, 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1941, p. 82) indicates that the reaction with benzoic acid requires temperatures well over 100°.

(14) L. Pauling, "Nature of the Chemical Bond," Second Ed., Cornell University Press, Ithaca, N. Y., 1945, p. 53, gives for C–O, 70.0, and for C–S, 54.5 kcal./mole.

(15) The heat of dissociation of dimeric benzoic acid in benzene solution has been given variously as 8.7 kcal. (W. S. Hendrixson, Z. anorg. Chem., 13, 73 (1897), and as about 21 kcal. (M. M. Davies, Trans. Faraday Soc., 33, 334 (1937)).

(16) There appear to be no data available on thiobenzoic acid, but thioacetic acid shows no association from infrared studies (W. Gordy and S. C. Stanford, THIS JOURNAL, 62, 499 (1940)), and cryoscopic studies show only slight association in benzene (K. Auwers, Z. physik. Chem., 30, 532 (1899)).

Experimental

Thiobenzoic acid was prepared from benzoyl chloride and potassium hydrosulfide,[17] and had $n^{20}D$ 1.6030; purity by titration with iodine was about 99.5%.

Chlorobenzene[18] was washed with concd. sulfuric acid, then with dilute bicarbonate solution, with water and, after drying over anhydrous potassium carbonate, was distilled, the material of b.p. 131–132° being collected.

Aniline.—Mallinckrodt Analytical Reagent was fractionated until colorless, and the fraction of b.p. 183.5–184.5° was used.

Procedure.—The data given in Table I were obtained as follows. A standard solution of aniline in chlorobenzene was pipetted into a 100-cc. volumetric flask containing a weighed sample of thiobenzoic acid (0.02–0.025 m.) and some chlorobenzene. The solution was made up to 100 cc., and 10-cc. aliquots were removed and placed in 50-cc. glass-stoppered erlenmeyers in an oil thermostat at 60.0 ± 0.2°. The first 10-ml. aliquot was pipetted directly into an excess of standard base and back-titrated immediately with standard acid. This initial concentration was compared to the amount of thioacid weighed and if comparable the run was continued. The agreement was consistently within 0.5%. The samples were removed at intervals, the flask washed down with benzene to facilitate removal of hydrogen sulfide and aspirated free of hydrogen sulfide on the water-pump by means of a ground-glass connection. The complete removal of hydrogen sulfide was shown by blank determinations; after three minutes aspiration no titer with 0.1 N iodine was observed and lead acetate paper was not discolored. The contents of the flask was washed into an excess of standard alkali, and the unreacted thiobenzoic acid determined by back-titration with standard acid potentiometrically with a Beckman pH meter to a predetermined pH of 7.5–8.

The modified procedure, using an iodine titration for the thiobenzoic acid and hydrogen sulfide, was carried out as follows. A sealed glass ampoule containing about 10 cc. of the chlorobenzene solution of thiobenzoic acid (about 0.2 M) was broken under an excess of standard iodine solution (0.1 N) in 300 cc. of water containing 20 cc. of 20% potassium iodide solution. The mixture was shaken for 5 min., an excess of sodium thiosulfate was added and shaken for 5 min. more. The excess thiosulfate was then back-titrated with frequent shaking to a starch indicator. In the acetic runs, the excess iodine could be back-titrated directly with thiosulfate.

Comparison of weighed and determined quantities are given below and are taken from run data where initial con-

Thiobenzoic acid, moles/l.

Taken	0.2784	0.2667	0.2749
Detd.	0.2762	0.2659	0.2763

(17) P. Noble and D. S. Tarbell, *Org. Syntheses*, **32**, 101 (1952).

(18) We are indebted to the Dow Chemical Company for this material.

centrations were determined from the iodine titrations of two ampoules having identical histories, one previously evacuated of dissolved H_2S.

The decomposition of thiobenzoic acid was essentially eliminated by maintaining an atmosphere of dry, oxygen-free (Fieser solution) nitrogen above the solution in the ampoules. The constancy of the iodine titration (both with and without evacuation to remove hydrogen sulfide) and of the acid–base titration is sufficient to establish the absence of decomposition.

The runs in ampoules were carried out as follows. Ampoules, previously flushed with oxygen-free nitrogen, were filled from a calibrated automatic pipet with a known volume of the chlorobenzene solution of weighed quantities of thiobenzoic acid and aniline. Two tubes were chilled in Dry Ice–acetone immediately after filling and used for the determination of initial concentration, i.e., by a comparison of the iodine titrations with and without evacuation. The remaining tubes were placed in the thermostat, and two tubes removed after 5 min. and the determined concentration used as that at zero time. The remaining tubes were removed at suitable time intervals, quenching the reaction by immersion of the tubes in Dry Ice–acetone. The thiobenzoic acid concentrations were deduced from the initial concentration and the increase in iodine titer due to the hydrogen sulfide formed in the reaction.

The Kinetic Runs in Aniline.—Due to the iodination of the aniline, it was not possible in these runs to use the iodine method to follow the course of the reaction. Attempts to suppress the iodination, by conducting the titrations in a strongly acid solution, were not successful. While it was shown that in the acetic acid runs, the acidity was sufficient, at the low aniline concentrations, to completely suppress the iodination, it was not possible at the higher aniline concentration to attain conditions which would both suppress the iodination and not obscure the starch end-point. The acids tried were acetic, formic, oxalic, phosphoric, hydrochloric and sulfuric.

The gravimetric determination of thiobenzoic acid by the arsenic salt, and the volumetric determination by titration of the arsenic salt with iodine solution or by oxidation of the arsenic salt with peroxide, followed by reduction of the arsenic pentoxide with potassium iodate solution, were investigated but proved unsuccessful. The method finally adopted was the direct weighing of the benzanilide isolated by the following method:

The contents of the ampoule, previously chilled in Dry Ice–acetone to stop reaction, were washed into 100 cc. of 10% hydrochloric acid, stirred to dissolve the aniline and filtered at the pump using a sintered glass crucible. The benzanilide was washed with water, with 50 cc. of ice-cold hexane (to remove thiobenzoic acid), dried (100–110°) and weighed. The empty weight of the crucible was then determined by dissolving out the benzanilide (with acetone), drying and reweighing. Blank determination showed a loss in such a procedure of approximately 1%, using 0.25 g. of benzanilide.

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