good agreement with values reported for higher concentrations. Results of a typical experiment are shown in Table I. In this experiment the molarity of the potassium iodate was 0.00475, the original concentrations of potassium iodide and benzyl chloride were 0.01331 M and 0.06655 M, respectively, and the temperature was 25.00 ± 0.01°. The data reported by Conant and co-workers[2] for this reaction at 25° and for the concentration range of 0.0134 M to 0.04 M in potassium iodide and 0.0667 M to 0.20 M in benzyl chloride yield values of k varying from 1.64 to 1.97.

TABLE I

Time, hours	KIO_3, ml.	k
0	11.00	..
1.00	9.65	1.99
1.00	9.62	2.04
2.00	8.55	1.94
2.00	8.53	1.95

Since detection of the fleeting and yellow color is very difficult, starch was tried as indicator. The blue coloration produced under the conditions of this analysis was transient also, but much easier to discern than the yellow color. The results obtained with starch agreed very well with those reported in Table I.

Finally, the Andrews titration may be replaced successfully by a potentiometric titration. The cell was prepared by placing a platinum and a normal calomel electrode in a mixture of 25 ml. of distilled water, 25 ml. of concentrated hydrochloric acid and 20 to 25 g. of crushed ice. The vessel was then placed in a large ice-bath to maintain constant temperature during the titration. The solution to be analyzed was added to the cell and titrated potentiometrically with potassium iodate solution. Thorough stirring was needed to establish equilibrium after each addition of iodate. The end-point of the titration was determined by the sharp rise in potential occurring at the end-point of the reaction $KIO_3 + 2KI + 6HCl \rightarrow 3ICl + 3KCl + 3H_2O$. Tests of the method were made with known amounts of potassium iodide both in the absence and presence of acetone and with or without addition of benzyl chloride. The analyses checked to within 0.05% of the correct value.

Table II shows values of the specific rate of the benzyl chloride reaction obtained at 25° in an experiment in which the Andrews titration, using the aqueous layer as indicator, and the potentiometric method were both used. The value marked (starch) is the one obtained in the Andrews titration, starch being added to aid detection of the end-point. The potassium iodate was 0.00475 M and the reaction mixture was 0.0354 M in potassium iodide and 0.177 M in benzyl chloride. Numerous other runs were made, showing that the potentiometric method is fairly accurate in the dilute solution measurements.

TABLE II

Time, hours	KIO_3, ml.	k
0	22.40	..
1.00	16.30	1.86 (starch)
1.00	16.35	1.83
2.00	11.65	1.95

It is clear that although reliable rate data may be obtained by the Andrews method for this reaction at higher concentrations, this method must be modified or replaced in work with dilute solutions.

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Studies on Oxythiamine

BY MORRIS SOODAK AND LEOPOLD R. CERECEDO

The synthesis of oxythiamine has been reported by Bergel and Todd[1] and by Slobodin and Ziegel.[2] The former workers obtained a product which in doses of 1 mg. showed no antineuritic activity when assayed by the bradycardia method. The substance prepared by Slobodin and Ziegel was found to have only 0.5% of the activity of thiamine when tested on pigeons.

We have prepared oxythiamine by deamination of thiamine with nitrous acid. The procedure was as follows: The nitrous acid gas was generated in a flask which was open to the atmosphere through a small aperture, by the gradual addition (four to six hours) of an excess of 18% HCl to 20–30 g. of sodium nitrite. It was then passed under slight suction through a solution of 4 g. of thiamine hydrochloride in 25 cc. of water. When the thiochrome test indicated that 97–98% of the thiamine had disappeared (occasionally more nitrous acid was required), the solution was evaporated *in vacuo* until an oil was obtained. After addition of a few cc. of 95% ethyl alcohol, the solution was evaporated once more. The oil was dissolved in 75 cc. of absolute ethyl alcohol and to the solution ether added until precipitation was complete. The precipitate was taken up in 75 cc. of absolute ethyl alcohol and dry hydrogen chloride gas passed through the solution for about an hour. Heat was generated, and a white crystalline product was deposited. After cooling, the precipitate was washed with absolute ethyl alcohol and dried. A material melting at 195–200° was obtained. An additional crop of crystals separated out upon addition of absolute ether to the mother liquor. The yield varied between 50 and 70%.

Anal. Calcd. for $C_{12}H_{17}O_2N_3Cl_2S$: C, 42.60; H, 5.00; N, 12.43. Found[3]: C, 42.29; H, 4.97; N, 12.69.

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(1) Bergel and Todd, *J. Chem. Soc.*, 1504 (1937).

(2) Slobodin and Ziegel, *J. Gen. Chem.* (U. S. S. R.), **11**, 1019 (1941).

(3) 1 mg. of oxythiamine has been found to contain between 1 and 4 μg. of thiamine.

Attempts at preparing oxythiamine diphosphate by deamination of cocarboxylase have so far yielded only impure oxythiamine monophosphate.

Oxythiamine reacts with Decalso in the same manner as thiamine. It gives a positive test with the Prebluda–McCollum reagent. Although Slobodin and Ziegel reported that oxythiamine showed a slight antineuritic activity, in our experiments it has been found to produce a toxic effect on mice. Administration of 25–50 μg. of oxythiamine per day resulted after about two weeks in the death of young mice which received a thiamine-low synthetic diet supplemented with 1 μg. of thiamine per day. The effect of oxythiamine on the enzyme system of carp which destroys thiamine was studied. It was found to inhibit the action of the enzyme on thiamine. Additional microbiological studies are in progress.

CHEMISTRY DEPARTMENT
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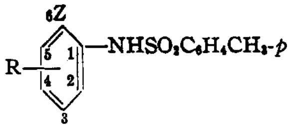
NEW COMPOUNDS

p-Toluenesulfonamides[1]

Two previously unreported *p*-tosylamides derived from substituted *o*-nitranilines and one from 4-amino-1,2-dimethylbenzene have been prepared. It has been reported[2,3] that *o*-nitro-arylamines react anomalously toward arylsulfonyl chlorides, in that the disulfonamides form much more readily than the mono compounds. This was found to be the case, but it was possible to prepare the desired monosulfonamides in a good state of purity, though in somewhat poor yield (Table I).

TABLE I

p-TOLUENESULFONAMIDES



R	Z	Yield, %	M. p., °C., cor.	Formula	Analyses, % Calculated C	H	Found C	H
2-CH$_3$	NO$_2$	15.7	121.5–3.5	$C_{14}H_{14}N_2O_4S$	54.88	4.62	54.69	4.66
2,4-Di-CH$_3$	NO$_2$	20	133.5–5.5	$C_{15}H_{16}N_2O_4S$	56.23	5.04	55.94	5.13
3,4-Di-CH$_3$	H	76	144.5–5.0	$C_{15}H_{17}NO_2S$	65.42	6.22	65.57	6.41

Procedure.—To 0.1 mole of the substituted *o*-nitraniline suspended in 400 ml. of anhydrous pyridine was added 0.1 mole of *p*-toluenesulfonyl chloride all at once, shaking vigorously to ensure homogeneity. A short air condenser topped by a Drierite tube was inserted in the flask, and the assembly was heated in a boiling water-bath for six hours. At the end of that time, the hot solution was poured into 3000 ml. of ice water with vigorous stirring. An oil admixed with crystals settled out. The supernatant liquor was decanted and the residue was washed several times with water by decantation. Boiling methanol was added to the still moist residue, causing partial solution; the insoluble material was removed by filtration through a steam-jacketed Büchner funnel. Slow cooling of the filtrate caused the deposition of well-formed crystals of the monosulfonamide. Recrystallization from ethanol or methanol, using a small quantity of Darco, gave the pure monotosylamide.

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[1] Abstracted from a thesis submitted by Frank Kipnis to the Polytechnic Institute of Brooklyn, June, 1944, for the degree of Doctor of Philosophy.

[2] Suter, "Organic Chemistry of Sulfur," John Wiley and Sons, Inc., New York, N. Y., 1942, p. 511.

[3] Bell, *J. Chem. Soc.*, 2787 (1929).

[4] The residue, not further investigated, is the disulfonamide.

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1-(4'-Diethylamino-1'-methylbutyl)-2-keto-3-methyl-1,2-dihydroquinoxaline[1]

p-1-Alkyl-3-methyldihydroquinoxalones have been prepared by Kehrmann and Messinger[2] by the interaction of N-alkyl-*o*-phenylenediamines and pyruvic acid in aqueous or alcoholic acid solution. In the present work, the use of boiling cymene in conjunction with an automatic water decanter was found convenient. The final product was isolated in approximately 60% yield and was identified as the dipicrate.

Procedure.—One-tenth mole of 1-(4'-diethylamino-1'-methylbutyl)-amino-2-aminobenzene[3] was dissolved in 200 ml. of anhydrous *p*-cymene in a 1000-ml. interjoint flask. Freshly distilled pyruvic acid (0.105 mole) was added, together with a boiling stone, and the flask vigorously shaken for about five minutes. A calibrated moisture trap (Dean–Stark) topped by an efficient water-cooled reflux condenser was inserted in the flask, and the flask contents heated gently with a free flame. A vigorous reaction ensued and water distilled. Cautious heating was continued until solution was complete (two to three hours). About 80% of the calculated volume of water was eliminated during this period. Longer heating had no effect on the final yield.

The flask contents were cooled, transferred to a separatory funnel and the base separated as the hydrochloride by shaking out three times with 50-ml. portions of 20% hydrochloric acid.

The combined acid layers were run into an excess of ice-cold 15% ammonia water with swirling. The precipitated oil was extracted with four 100-ml. portions of chloroform. The solvent was removed on the steam-bath, and the mixture was steam distilled from saturated sodium chloride solution to remove traces of cymene and unreacted triamine. About 3 liters of distillate was collected before the distillate was free of these materials.

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[1] Abstracted from a thesis submitted by Frank Kipnis to the Polytechnic Institute of Brooklyn, June, 1944, for the Degree of Doctor of Philosophy.

[2] Kehrmann and Messinger, *Ber.*, **25**, 1629 (1891).

[3] Preparation to be reported in a subsequent communication.