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THE POLAROGRAPHIC AND POTENTIOSTATIC REDUCTION OF N-BROMOBENZAMIDES IN NONAQUEOUS SOLVENTS

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ABSTRACT

The polarographic reduction of N-bromobenzamides in dimethylformamide reduced in three waves; the first wave and second wave are the reduction of the nitrogen to bromine bond and the third wave is the reduction of the carbonyl linkage. Large-scale potentiostatic reductions produced evidence for a negatively charged transition state when formic acid was produced in the medium from carbon dioxide. A Hammett substituent plot produced a reaction constant (ϱ) of $+0.054$ which was consistent with a negatively charged transition state in the rate controlling step.

INTRODUCTION

N-Bromobenzamides have not been previously studied polarographically. Active halogen bonds have been reduced in nonaqueous solvents, and Wawzonek (1964) was one of the first to report the reduction of benzyl halides and ethyl chloro and bromo acetates in the aprotic solvent dimethylformamide. Grimshaw (1968) did a detailed study of the Hammett substituent plot of benzyl bromides which followed Streitwieser's study (1964) of the benzyl chlorides.

Gem-dichloro compounds have been studied, and Wawzonek (1979) reported the reduction of benzal chloride in dimethylformamide. In this laboratory we polarographically reduced 9,9-dichlorofluorene in dimethylformamide (Duty, 1974). In both cases, the reduction mechanism had a carbanion transition state as revealed by product isolation.

Casanova (1972) reduced α,α'-dibromo ketones in dimethylformamide and acetonitrile in an unsuccessful attempt to electrochemically synthesize cyclopropane structures through a carbanion postulated mechanism. Hawley (1969) reduced the nitrobenzyl halides in acetonitrile and demonstrated a one-electron reduction to the radical anion which, subsequently, lost a halide ion. Previous studies have shown the loss of a halide ion with an uptake of two electrons to generate the carbanion intermediate.

Since active bromo compounds are reduced to generate the carbanion, we studied the possibility of generating the nitrogen anion from active N-bromo compounds. To study this reaction we elected to synthesize several *N*-bromo-benzamides and ascertain if a nitrogen anion could be generated polarographically.

N-bromobenzamide undergoes a facile rearrangement in base to form phenyl isocyanates. This reaction is known as the Hofman rearrangement (Hofmann, 1882), and the nitrogen anion is generated as an intermediate by loss of a proton. Stevens (1963) unequivocally demonstrated the nitrogen anion intermediate with his bromine-82 study where he isolated *gem*-dihalides.

EXPERIMENTAL SECTION

Apparatus. A Heath Model EUW-401 polarograph with a Heath Model EUW-10-2 operational amplifier was used to record the polarograms on a Heath EUW-20A. The potentiostat was a modified design of Tackett and Knowles (1966) so that it could produce a current of 90 mA through a 1000-ohm load (Duty, 1974).

Reagents. Fisher reagent grade N,N-dimethylformamide was purified as previously described (Duty, 1974). The supporting electrolyte was Eastman reagent grade tetra-*n*-butylammonium bromide (0.175 M) and was recrystallized five times from anhydrous ethyl acetate and dried in a vacuum desiccator which contained phosphorus pentoxide.

N-Bromobenzamides and Derivatives. The *N*-bromo compounds were prepared from their corresponding amides by a modified method of Stevens (1963). The pulverized benzamide (5g) was added quickly to 150 ml solution of cold (– 3° to 0°) sodium hypobromite which was prepared by adding 15 g of bromine to 150 ml of sodium hydroxide solution (1.5 M). The mixture was shaken between 3 to 5 minutes and filtered rapidly into 125 ml of distilled water containing 9 ml of glacial acetic acid and ice. The precipitated *N*-bromobenzamide was washed with water and recrystallized from chloroform and hexane or from glacial acetic acid.

Not all of the compounds have been previously synthesized, but each one was verified by running an infrared KBr pellet of the compound and observing the singlet nitrogen-hydrogen stretch at 330 cm^{-1}. All compounds gave an immediate precipitate with silver nitrate solution. The following *N*-bromobenzamides were synthesized.

N-Bromobenzamide. Recrystallized from chloroform and hexane. The compound decomposed at 129°-130°C. (Lit. d.p. 129-131°C) (Hauser, 1937).

N-Bromo-p-toluamide. Recrystallized from chloroform and hexane. The decomposition point was 129°-132°C. (Lit. d.p. 131-133°C) (Hauser, 1937).

*N-Bromo-p-methoxybenzamide.*Recrystallized from chloroform and hexane and decomposed at 145°C.

N-Bromo-p-chlorobenzamide. Recrystallized from 50% glacial acetic acid (70-80°C). The decomposition point was 190-193°C. (Lit. d.p. 170-174°C) (Hauser, 1937).

N-Bromo-m-methoxybenzamide. Recrystallized from chloroform and hexane with a decomposition point of 95°-96°C.

N,N-bis(p-anisyl)oxamide. The oxamide was prepared from p-anisidine oxalyl chloride, and was recrystallized from a 50-50 mixture of ethyl alcohol and water. The solid melted sharply at 265-266°C. (Lit. 260-261°C) (Beilstein and Castellaneta, 1930).

N,N.Bis(p-ainsyl)urea. The urea derivative was prepared from p-anisidine and phosgene. The product was recrystallized from 95% ethyl alcohol and melted at 236-238°C. (Lit. 234°C) (Beilstein and Cazeneuve, 1930).

Procedure. A current-voltage curve was recorded for a solution which was 10^{-3} M in *N*-bromo compound and 0.175 M in supporting electrolyte. The capillary had a drop time of 3.50 sec (8.44 mg/drop) at a mercury height of 56 cm with an $m^{2/3}t^{1/6}$ value of 5.04. The capillary was checked against the I_d value for thallium ion with a solution containing 1.13×10^{-3} M thallium chloride. The $E_{1/2}$ for thallium was -0.46 v *vs* the S.C.E., and the experimental I_d was 2.70. (Lit. $E_{1/2} = -0.46$, $I_d = 2.70$) (Meites, 1965). The polarograms were recorded with a Ag/AgBr electrode as the reference electrode as used previously in a polarographic study (Duty, 1983).

The large-scale reduction cell had anolyte and catholyte compartments of 25 ml each and has been described elsewhere (Duty, 1974). The catholyte was charged with 2 g of the *N*-bromo compound and 20 ml of 0.175 M supporting electrolyte. The anolyte was charged with only 20 ml of 0.175 M supporting electrolyte. The cell was placed in the temperature-controlled bath at -11°C. Dry nitrogen was bubbled through the anolyte and dry carbon dioxide was bubbled through the catholyte during the entire reduction which ran for 30 hrs. The reduction potential was set at $+1.75$ V *vs* the Ag/AgBr reference electrode. The current in the cell began at a maximum 18 ma and fell to 5 ma during the course of the reduction.

The catholyte was rotary evaporated under reduced pressure (1 mm), and gas chromatographic analysis (2.4 × 0.64 cm o.d. column, 3% silicone at 120°) of the distillate indicated only dimethylformamide.

The residue was extracted with three-15 ml portions of hot 5% HCl, three-15 ml portions of diethyl ether and three-15 ml portions of benzene. The residue which remained after these extractions weighed 1.5 g. The residue, after washing with p-dioxane, had a m.p. of 260-265°. An infrared pellet (KBr) was run and revealed a carbonyl stretch at 1690 cm^{-1} and ill-defined stretching vibrations at 3100 cm^{-1} and 3300 cm^{-1} for nitrogen-hydrogen symmetric and asymmetric stretch, respectively. The residue was slightly soluble in dimethylsulfoxide, but not sufficiently soluble at 140° to obtain a variable temperature probe NMR spectrum (60 MHz).

Upon cooling of the three solutions from the extractions, small quantities of soilds formed in each. Infrared, KBr pellets of each were run, and in all cases the IR spectrum agreed with the p-methoxybenzamide spectrum with carbonyl stretch at 1658 cm^{-1}, nitrogen-hydrogen symmetric and asymmetric stretches at 3200 cm^{-1} and 3400 cm^{-1}, respectively, and nitrogen-hydrogen scissoring at 1623 cm^{-1}.

The 5 per cent hydrochloric acid extraction was steam distilled with the first 5 ml of distillate analyzed on a Porapak column (2.4 m × 0.64 cm o.d.) at 170° for formic acid (1.6 min for H_2O and 5.4 min for formic acid at 60 ml/min He).

RESULTS AND DISCUSSION

The reduction of N-bromobenzamide's nitrogen-bromine bond occurs in two separate steps. The first reduction occurs at approximately −0.24 volts and is a one electron reduction which is illustrated by:

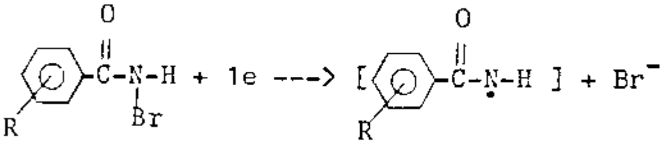

Fig. 1

The second reduction, at approximately-1.50 volts, is a two electron reduction which generates a nitrogen anion intermediate:

Fig. 2

The half-wave potentials of the five *N*-bromobenzamides are given in Table I along with their diffusion-current constants. To prove the nitrogen anion intermediate does exist, we conducted a controlled-potential, large-scale electrolytic reduction over a pool of mercury while degassing the cell continuously with carbon dioxide gas.

We theorized that if the nitrogen anion is formed as an intermediate, it would be possible to lose a hydrogen to a hydride ion scavenger such as carbon dioxide. Carbon dioxide is known to be reduced by metal hydrides (Brown, 1951), consequently it appeared reasonable for the carbon dioxide to abstract a hydride ion from the nitrogen anion.

Four of the five *N*-bromobenzamides were reduced on a large scale with most of our attention directed at the *N*-bromo-*p*-methoxybenzamide. The methoxy group is a moderate activating group and would be capable of enriching the electron density around the nitrogen atom, therefore enhancing the leaving ability of the hydride ion.

The reductions of the N-bromo compounds of *p*-chloro, p-methyl, *p*-methoxy and *p*-hydrogen were carried out at −10° and only *N*-bromo-*p*-methoxybenzamide produced traces of formic acid. However, by increasing the reduction temperature to +10° for the *p*-methoxy derivative, a formic acid peak was obtained which corresponded to a 28% yield based on the starting material of the N-bromo-*p*-methoxybenzamide (2 g.).

After substantiating that the nitrogen anion is capable of losing a hydride ion to carbon dioxide, we directed our attention to the product that would be formed from the nitrogen anion after it loses the hydride ion. In the Hofmann degradation of amides by sodium hyprobromite, the anion of the N-bromo compound is formed which rearrange simultaneously to the isocyanate and ultimately is hydrolyzed to the amine (Hofmann, 1882).

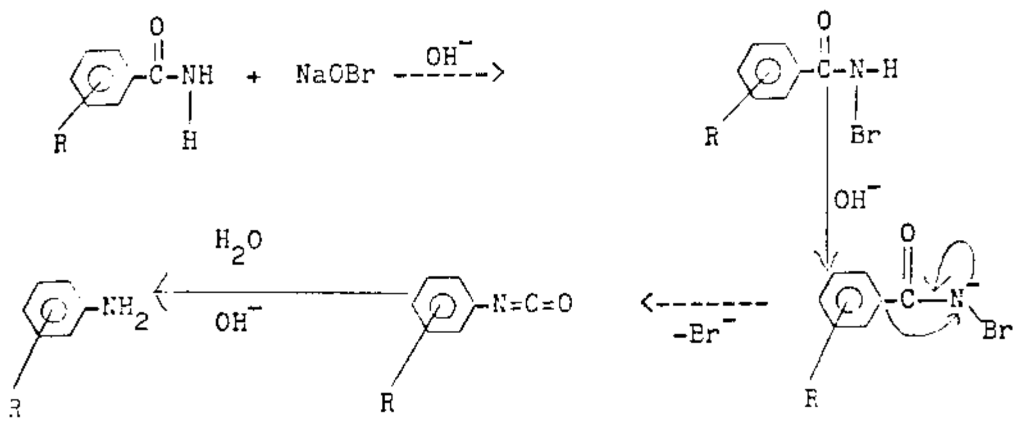

Fig. 3

In the reduction of the N-bromo compound, the nitrogen anion would have the same options available:

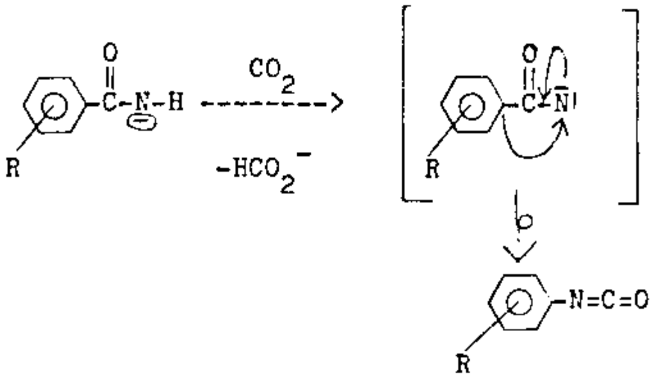

Fig. 4

We observed no evidence for an isocyanate during or at the conclusion of the large-scale electrolytic reductions. The isocyanate stretching vibration is easily observed by infrared spectrometry (see the experimental section).

Isocyanates also are reduced at the dropping mercury electrode and have been reported to reduce with two electrons (Shapaval, 1967). If this happened, one possible derivative could be an oxamide derivative formed as follows:

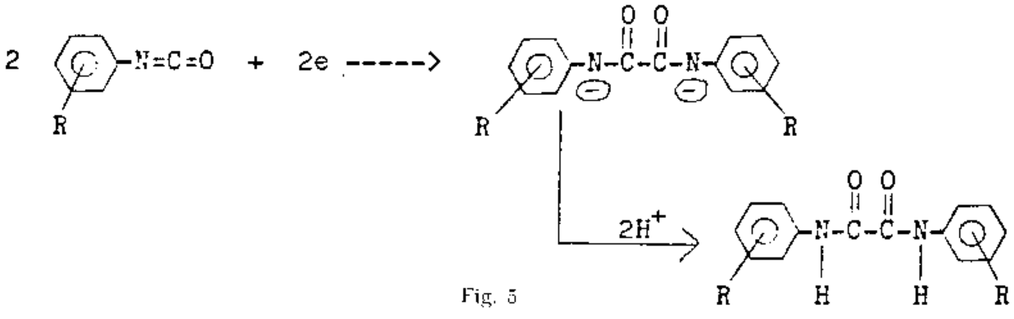

Fig. 5

N,N-Bis(*p*-anisyl)oxamide was synthesized and revealed a carbonyl stretching vibration of 1650 cm^{-1}. The unknown residue from the large-scale reduction had a carbonyl stretching vibration at 1700 cm^{-1} and was, therefore, ruled out as an oxamide derivative.

The isocyanate could also reduce to the amine, *p*-anisidine. Again, no evidence for this was observed by checking the ether extractions on the gas chromatograph.

A third possible pathway for the isocyanate to react would be to combine with any *p*-anisidine that could be generated to form a substituted urea, *N*,*N*-bis(*p*-anisyl)urea. The infrared spectrum again ruled out the urea derivative as a possible product because of the carbonyl stretching vibration occurring at 1640 cm^{-1} instead of 1700 cm^{-1} as observed for the unknown residue.

At this point in the investigation we began to doubt the authenticity of the formic acid resulting from the hydride ion abstraction by carbon dioxide. It was possible the formic acid could come from the solvent, *N*,*N*-dimethylformamide. We checked this source of formic acid by reducing *N*-bromo-*p*-methoxybenzamide in exactly the same manner as previously described except we lowered the reduction potential to − 1.0 volt. This voltage was higher than the one-electron reduction but lower than the two-electron reduction which was responsible for generating the nitrogen anion intermediate. The exact procedure was followed in the removal of solvent and in the extractions of the residue with ether. However, when the steam distillate was analyzed on the gas chromatograph, no trace of formic acid was found. Consequently, the formic acid was formed from the abstraction of the hydride ion by carbon dioxide at a potential (− 1.75v) more negative than that for the two electron reduction (− 1.72v) but less negative than that for the reduction of the carbonyl amide linkage (− 2.22v).

The unsuccessful attempt at identifying the residue may in part be caused from a reaction between the solvent and the reaction intermediate. *N*,*N*-Dimethylformamide has been reported to react with isocyanates to form cyclic compounds (Weiner, 1960 and Ulruk, 1968). Consequently, the residue which was insoluble in hot ether, hot 5% hydrochloric acid and hot benzene is possibly polymeric or a high molecular weight addition product of the solvent.

We also checked for the formation of a nitrogen to phenyl linkage by hydrolyzing the insoluble residue in basic solution. The residue was refluxed in a 50/50 mixture of water and ethylene glycol that was 2.5m in sodium hydroxide. The residue was refluxed for 4 hrs and steam distilled. The distillate was extracted 3 times with diethyl ether, and the ether extract was analyzed by gas chromatography which revealed peaks for only ether and water. No *p*-anisidine was found on the 3% silicone column at 180°C. We theorized that if the nitrene were formed and rearranged, a nitrogen to phenyl linkage would form. Thus, if one hydrolyzes the residue from the electrolytic reductions, the presence of *p*-anisidine would support the nitrene as an intermediate.

From the infrared spectrum of the residue, which has a carbonyl stretch at 1700 cm^{-1}, and its negative test for *p*-anisidine upon hydrolysis, these results also suggest the residue is polymeric with a phenyl ring attached to the carbonyl group and not to a nitrogen.

To ascertain if the polarographic currents were kinetic currents, adsorption currents or diffusion controlled currents, four *N*-bromobenzamides (*N*-bromobenzamide, *N*-bromo-p-chlorobenzamide, *N*-bromo-p-methylbenzamide and

N-bromo-p-methoxybenzamide) were run at mercury heights of 39, 49, 59, 69 and 79 cm. The diffusion currents for the first reduction wave were plotted *vs.* the square root of mercury height and in each case a linear positive slope was observd which suggests a diffusion-controlled current was produced.

The half-wave potential of the second reduction was plotted *vs.* the Hammett substituent constants and a positive slope was observed (Figure 6). A positive slope suggests that the reactive intermediate has a negative charge in the transition state, and that electron-contributing groups stabilize this transition state (Streitwieser, 1964 and Sease, 1964). This would be the case if the *N*-bromobenzamides reduced with two electrons to form the nitrogen anion.

CONCLUSIONS

N-Bromobenzamides are reduced at the dropping mercury electrode in three waves. The second wave generated a nitrogen anion which was the precursor to the hydride ion. This hydride ion was abstracted by carbon dioxide to form formic acid. Only in the case of *N*-bromo-p-methoxybenzamide was formic acid produced. In addition, no formic acid was produced at a potential less than the reduction potential of the second wave and higher than the reduction potential of the first wave. A Hammett sigma-rho plot substantiated the formation of a negative transition state in the rate controlling step of the mechanism.

Table 1. Polarographic Half Wave Potentials and Diffusion Current Constants for N-Bromobenzamides

Compound	Half wave potential (volts) E1/2 (1st wave)	E1/2 (2nd wave)	Diffusion current constant E1/2 (3rd wave)	Id
N-bromobenzamide	−0.27	−1.54	−2.14	0.784
N-bromo-p-methylbenzamide	−0.23	−1.57	−2.15	0.730
N-bromo-p-chlorobenzamide	−0.20	−1.46	−1.86	0.600
N-bromo-p-methoxybenzamide	−0.21	−1.72	−2.22v	0.771
N-bromo-m-methoxybenzamide	−0.25	−1.64	−.2.21v	0.750

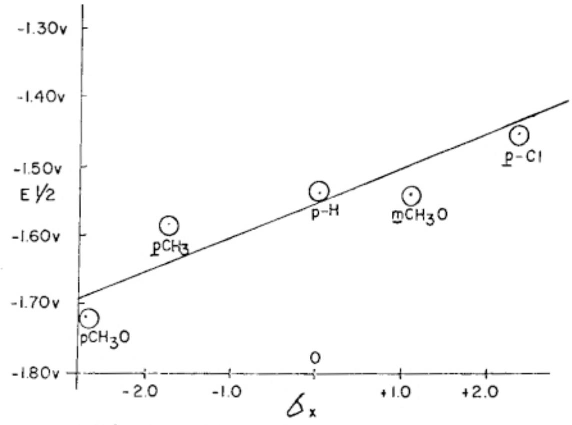

Fig. 6 E1/2 *vs.* Hammett Substituent Constants

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