Table III. Ratios $k(\alpha\text{-}CH_3)/k(t\text{-}\beta\text{-}CH_3)$

Parent compd	$k(\alpha\text{-}CH_3)/k(t\text{-}\beta\text{-}CH_3)$		
	ArSCl	Br_2	Hydration
Styrene	2.24	55	3147
Propene	1.26	3.2	10563

addition of 4-chlorobenzenesulfenyl chloride. This indicates that more charge is developed on the ring carbons in the bridged rate-determining transition state in the addition of bromine than arenesulfenyl chlorides. This is consistent with the greater ability of sulfur to support a positive charge.

By comparing the effect of methyl groups in the α and β positions, in terms of the ratios $k(\alpha\text{-}CH_3)/k(t\text{-}\beta\text{-}CH_3)$, we can obtain an estimate of the symmetry of the rate-determining transition state. These data are presented in Table III. To eliminate any problems due to steric hindrance, the values of the trans-β isomers are used. The difference between addition of 4-chlorobenzenesulfenyl chloride and hydration is striking. For a bridged rate-determining transition state the ratio is small (1.3–2.2) while for an open-ion-like transition state the ratio is large (10^3–10^4).

Bromination in the propene series closely resembles the addition of 4-chlorobenzenesulfenyl chloride. Clearly the rate-determining transition state for these additions is quite symmetrical. The $k(\alpha\text{-}CH_3)/k(t\text{-}\beta\text{-}CH_3)$ ratio for the bromination in the styrene series more closely resembles that of the addition of 4-chlorobenzenesulfenyl chloride than hydration. Consequently, the data are best explained by proposing a weakly bridged rate-determining transition state. Thus the structures range from strongly bridged for arenesulfenyl chloride to weakly bridged for bromination to an open one for hydration.

These data indicate that the formation of nonstereospecific products in the bromination of styrene and its derivatives is due to the intervention of open ions *after* the rate-determining step.

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Reductive Alkylation of Phenazine. Electrochemical Preparation of 5,10-Dihydro-5,10-dimethyl and 5,10-Dihydro-5,10-diethyl Derivatives

Duane K. Root, Richard O. Pendarvis, and Wayne H. Smith*

Department of Chemistry, Texas Tech University, Lubbock, Texas 79409

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In conjunction with research on the chemical behavior of certain cation radical species and as part of a more general study of reductive alkylation initiated electrochemically, a method has been developed for the facile synthesis of 5,10-dialkyl-5,10-dihydrophenazine derivatives in high yield.

Previous methods for the synthesis of *N,N'*-dialkyldihydrophenazines consisted of chemical reduction of phenazine followed by treatment with the appropriate alkylating agent. For example, Gilman and Dietrich[1] prepared the dimethyl derivative in 1,2-dimethoxyethane (DME) by reduction of phenazine with potassium metal, followed by addition of methyl iodide. Only 62% yield was reported. In a more elaborate preparation, Mikhailov and Blokhina[2] synthesized the diethyl derivative by first isolating the disodium salt of reduced phenazine after treatment with sodium metal in DME for 30–35 h. The salt was then reacted with either ethyl chloride or ethyl iodide for an additional 40 h, resulting in only 40–44% yield.

More recently, reactions of this type have been carried out electrochemically.[3,4] This technique offers the advantage of a selective reduction potential such that the parent compound can be reduced at a potential where the alkylating agent is not. Thus both reagents can be present in solution simultaneously. The alkylating agent reacts with reduced parent compound as it is generated at the cathode eliminating the need for stepwise addition of reagents or isolation of reactive intermediates.

Results and Discussion

A cyclic voltammogram of phenazine in acetonitrile shows two reduction waves, a reversible one-electron reduction at −1.60 V (vs. Ag|0.1 M Ag^+), and a second irreversible one-electron transfer at −2.41 V. The radical anion species is very stable showing completely reversible behavior at scan rates as slow as 20 mV/s. Also, controlled potential coulometry at the first reduction wave yields an n_{app} value of 1.0 (where n_{app} is the number of equivalents of electrons added per mole of substrate). The second wave exhibits irreversible behavior at scan rates as fast as 50 V/s indicating the presence of a fast following chemical reaction which is most likely protonation by solvent or trace impurities to produce the 5,10-dihydro derivative.[4]

In the presence of a fourfold excess of dimethyl sulfate, which is itself electroinactive, the first reduction wave of phenazine exhibits irreversible behavior at slow scan rates indicating a reaction between the phenazine anion radical and the added alkylating agent. Also, two new oxidation waves appear at −0.18 and +0.52 V on scan reversal. When the cyclic scan is allowed to include both reduction waves these same two oxidation waves appear in greater magnitude showing that the reaction of dimethyl sulfate with either the radical anion or dianion of phenazine yields the same product.

With diethyl sulfate as an alkylating agent, no change is observed in the first reduction wave indicating that the reaction between the phenazine radical anion and diethyl sulfate is very slow. With inclusion of the second reduction wave in the cyclic scan two new oxidation waves appear at −0.28 and +0.48 V and a third, smaller wave at −0.46 V, showing a rapid reaction does occur with the phenazine dianion.

Ethyl bromide is electrochemically reducible at a more negative potential than either reduction process exhibited by phenazine. Its effect on the phenazine reduction however is similar to that observed on addition of diethyl sulfate: slow reaction with the radical anion, and rapid reaction with the dianion species. The anodic portion of the scan includes the new oxidation waves at −0.28 and +0.48 V, the latter obscured by the oxidation of Br^-, a reaction by-product. A wave at +0.78 V corresponding to the oxidation of Br_3^- is also observed.

Controlled potential coulometry at the first reduction wave of phenazine yields an n_{app} of 2.0 when any of the three alkylating agents is added in excess to the solution. Since an n_{app} value of 1.0 is observed in the absence of alkylating agent, the alkylating agents must react with the phenazine radical anion

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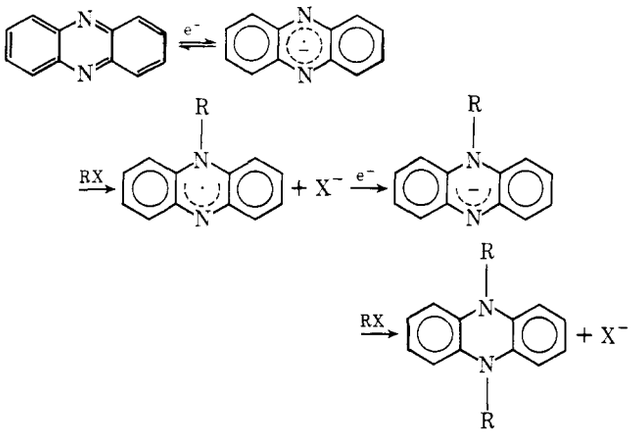
to produce an intermediate species which is further reducible at the applied potential. Also, a minimum of 2 equiv of alkylating agent is required for complete reaction. The following mechanism is suggested:



where R = CH_3 or C_2H_5 and X = Br, $[SO_4CH_3]$, or $[SO_4C_2H_5]$

Qualitatively, dimethyl sulfate is the fastest reacting alkylating agent as evidenced by the fact that the deep purple color indicative of the radical anion never develops in solution during electrolysis. Diethyl sulfate is somewhat slower reacting with build-up of the radical anion during electrolysis, although for both alkylating agents the total electrolysis time is approximately 30 min. Ethyl bromide is the slowest alkylating agent requiring over 90 min for complete reaction under similar conditions. The inconvenience of longer reaction time is offset by the wider range of phenazine derivatives available from alkyl halides than from alkyl sulfates.

On completion of the electrolysis with dimethyl sulfate or diethyl sulfate two reversible one-electron oxidation waves are observed whose wave heights are the same as the height of the reduction waves of neutral phenazine. In addition, controlled potential electrolysis at the first oxidation wave of either product yields an n_{app} of 1.0 and a deep green solution of the cation radical. Both results indicate a 100% yield of the dialkylated product, which is a substantial improvement over existing procedures. The only loss occurs during product work-up where the light green color of the crystals suggests contamination by the salt of air-oxidized dialkyl derivatives.

The electrochemically initiated reductive alkylation reaction provides a convenient route to the synthesis of 5,10-dihydro-5,10-dialkylphenazines and shows substantial improvement on both time and product yields of existing procedures.

Experimental Section

The electrochemical cell is similar to one described previously.[6] The total cell volume is approximately 140 mL with 70 mL in the working compartment. A platinum wire sealed in soft glass and ground to a flat disk was used as a working electrode for cyclic voltammetry. Controlled potential coulometry was carried out on a large surface area platinum gauze electrode. All potential measurements are vs. a $Ag|Ag^+$ (0.10 M) reference electrode.

Acetonitrile (Eastman, 0.05% H_2O), solvent for all electrochemical experiments, was vacuum distilled over P_2O_5 and stored over dried molecular sieves. Tetraethylammonium perchlorate (TEAP) (Southwestern Analytical Chemicals, Inc., Polarographic grade), supporting electrolyte for all experiments, was ground to fine powder and stored under vacuum. Phenazine (Aldrich, Technical grade) was purified by vacuum sublimation. Dimethyl sulfate (Aldrich, Gold Label) was used as received. Diethyl sulfate (Eastman, Practical grade) was vacuum distilled. Ethyl bromide (J. T. Baker, Reagent grade) was used as received. Electrochemical experiments were performed with a PAR Model 170 electrochemistry system using positive feedback to compensate for solution resistance.

A General Procedure for Electrochemical Generation of 5,10-Dihydro-5,10-dialkylphenazine. Phenazine (0.288 g) was added to the working compartment of the cell containing 70 mL of AN/0.3 M TEAP for a total concentration of 0.023 M in phenazine. The solution was degassed for 10 min with N_2 prior to addition of the alkylating agent and a steady flow of N_2 was maintained over the solution throughout all electrochemical manipulations. Sufficient alkylating agent was added to give a total concentration of 0.092 M and the solution was electrolyzed at −1.90 V until the current had decayed to 0.1% of its initial value signaling 99.9% completion of the reaction. Following the reduction, the solvent was removed on a rotary-evaporator and the solid residue was partitioned with 1:1 degassed benzene/water. The benzene fraction was evaporated and the solid was filtered using degassed methanol for transfer and washing. Both dimethyl- and diethylphenazine were recrystallized from ethanol/methanol mixtures.

5,10-Dihydro-5,10-dimethylphenazine from Dimethyl Sulfate. Dimethyl sulfate (16 mL, 6.4 mmol) was added directly to the working compartment of the cell containing 1.6 mmol of phenazine in 0.3M TEAP/AN. The solution was electrolyzed at −1.90 V and gave an n_{app} of 2.0 with a total electrolysis time of 30 min. The solution was then oxidized at the first product oxidation wave yielding an n_{app} = 1.0 and producing a deep green solution whose spectra matched that reported for the cation radical of 5,10-dihydro-5,10-dimethylphenazine in AN[7] (λ_{max} 720, 650, 600, 455, 447, 435, 320). The sample was reduced back to the neutral compound, isolated from the solution, and recrystallized. Colorless crystals (0.30 g) were collected: 91% yield; mp 153 °C (lit.[1] mp 153–155 °C).

5,10-Dihydro-5,10-diethylphenazine from Diethyl Sulfate. Diethyl sulfate (0.84 mL, 6.4 mmol) was added to 1.6 mmol of phenazine in 0.30 M TEAP/AN and electrolyzed at −1.90 V, n_{app} = 2.0, time of electrolysis was 30 min. Product collected: 0.349 g of silvery light green crystals; 91% yield; mp 129 °C (lit.[2] mp 130–131 °C).

5,10-Dihydro-5,10-diethylphenazine from Ethyl Bromide. Ethyl bromide (0.48 mL, 6.4 mmol) was added to 1.6 mmol of phenazine in 0.30 M TEAP/AN and electrolyzed at −1.90 V, n_{app} = 2.0, time of electrolysis was 96 min. Product collected: 0.35 g of silvery light green crystals; mp 129 °C.

Registry No.—5,10-Dihydro-5,10-dimethylphenazine, 15546-75-5; dimethyl sulfate, 77-78-1; phenazine, 92-82-0; 5,10-dihydro-5,10-dimethylphenazine radical cation, 56545-30-3; 5,10-dihydro-5,10-diethylphenazine, 62248-00-4; diethyl sulfate, 64-67-5; ethyl bromide, 74-96-4.

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