intend by this note to point out the mechanistic discrepancy which arises when the two probes are compared and to present a caveat for the application of cyclopropylcarbinyl halides as free-radical probes in reactions with nucleophiles. Noteworthy in the latter regard is the recent report by Kinney, Jones, and Bergman,[7] who obtained anomalous results from the reactions of cyclopropylcarbinyl halides with the anionic vanadium carbonyl hydride $[(\eta^5\text{-}C_5H_5)V(CO)_3H]^-$, which was shown by other means to react with organic halides to give free radicals.

Experimental Section

All reactions involving organometallic species were conducted under nitrogen or argon atmospheres and employed syringe transfers. Tetrahydrofuran (THF) was distilled from sodium–benzophenone under nitrogen immediately before use. Gas chromatography (GC) was performed on a Varian 920 chromatograph on a 3 ft by 0.25 in. column of 5% SE-30 on 60/80 Chromosorb W. ^{1}H NMR spectra were recorded on a Varian T-60 spectrometer on samples with an internal standard of Me_4Si unless otherwise noted. IR spectra were recorded on a Beckman IR-8 spectrometer.

Materials. 6-Bromo-1-hexene (Fluka) containing <5% of impurities of 6-bromo-2-hexenes was used without purification. 6-Iodo-1-hexene was prepared from the bromohexene and sodium iodide (fivefold excess) in acetone (25 °C, 48 h) in 77% yield. (Triphenylstannyl)lithium and (trimethylstannyl)lithium were prepared by standard procedures from the corresponding chloride and bromide, respectively.

[(Trimethylstannyl)methyl]cyclopentane (5b). Cyclopentanemethanol was prepared from cyclopentylmagnesium bromide and excess gaseous formaldehyde by the method of Zelinsky.[8] Mesylation was effected by the method of Crossland and Servis.[9] Treatment of 1.0 g (10 mmol) of cyclopentanemethanol in 5.6 mL of methylene chloride with 1.2 mL of pyridine and 1.3 g (11.1 mmol) of methanesulfonyl chloride at −10 °C for 20 min followed by an extractive workup (consecutive extractions with water, 10% aqueous hydrochloric acid, saturated aqueous sodium bicarbonate solution, and saturated aqueous sodium chloride solution, all at 0 °C) and drying ($MgSO_4$) gave, upon distillation of the solvent, a residue of 1.2 g (67% yield) of (mesyloxymethyl)cyclopentane which was used without further purification: ^{1}H NMR ($CDCl_3$) δ 1.0–2.0 (m, 8 H), 2.2–2.4 (m, 1 H), 3.0 (s, 3 H), 4.1 (d, 2 H, J = 7 Hz); IR (film) 1350, 1165, 945 cm^{-1}. A solution of (trimethylstannyl)lithium prepared from 4.1 mmol of trimethyltin bromide in 10 mL of THF was maintained at 0 °C as a solution of 0.7 g (4 mmol) of (mesyloxymethyl)cyclopentane in 5 mL of THF was added dropwise. The stirred reaction mixture was maintained at 0 °C for 2 h and then allowed to warm to 25 °C. After 12 h at 25 °C, saturated aqueous ammonium chloride was added and the phases were separated. The aqueous phase was extracted twice with methylene chloride, and the combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed on silica gel (methylene chloride elution) to give 0.6 g (62% yield) of [(trimethylstannyl)methyl]cyclopentane (**5b**) which was further purified by preparative GC to give spectroscopically and chromatographically pure **5b**: ^{1}H NMR ($CDCl_3$, CH_2Cl_2 reference) δ 0.1 (s, 9 H), 0.9–1.1 (m, 2 H), 1.5–1.9 (m, 9 H).

Reactions of Lithiostannanes with 6-Halo-1-hexenes. The following reaction is representative. A solution of 4.1 mmol of 6-bromo-1-hexene in 5 mL of THF was added dropwise to 10 mL of a 0.41 M solution of (trimethylstannyl)lithium at 0 °C over ca. 30 min. After 60 min of additional stirring at 0 °C, the mixture was quenched by addition of an aqueous saturated ammonium chloride solution. An extractive workup (methylene chloride) followed by drying ($MgSO_4$) and solvent distillation gave a residue which was shown by GC to contain no (<1%) [(trimethylstannyl)methyl]cyclopentane. Chromatography of the residue on silica gel (hexane elution) gave 0.5 g (50% yield) of 6-(trimethylstannyl)-1-hexene (**3b**) which was chromatographically and spectroscopically pure: ^{1}H NMR ($CDCl_3$, $CHCl_3$ reference) δ 0.17 (s, 9 H), 0.85–0.95 (m, 2 H), 1.0–1.7 (m, 4 H), 1.8–2.2 (m, 2 H), 4.7–5.1 (m, 2 H), 5.2–6.1 (m, 1 H). The corresponding product from the reaction of (triphenylstannyl)lithium, 6-(triphenylstannyl)-1-hexene (**3a**), had the following ^{1}H NMR spectrum: ($CDCl_3$) δ 1.1–1.7 (m, 8 H), 4.7–5.1 (m, 2 H), 5.2–5.9 (m, 1 H), 7.0–7.6 (m, 15 H).

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Registry No. **1a**, 2695-47-8; **1b**, 18922-04-8; **3a**, 73017-73-9; **3b**, 73017-74-0; **5b**, 73017-75-1; cyclopentanemethanol, 3637-61-4; [(mesyloxy)methyl]cyclopentane, 73017-76-2; (trimethylstannyl)lithium, 17946-71-3; trimethyltin bromide, 1066-44-0; (triphenylstannyl)lithium, 4167-90-2.

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General Catalyzed Condensation of Nitrosobenzene and Phenylhydroxylamine in Aqueous Solution

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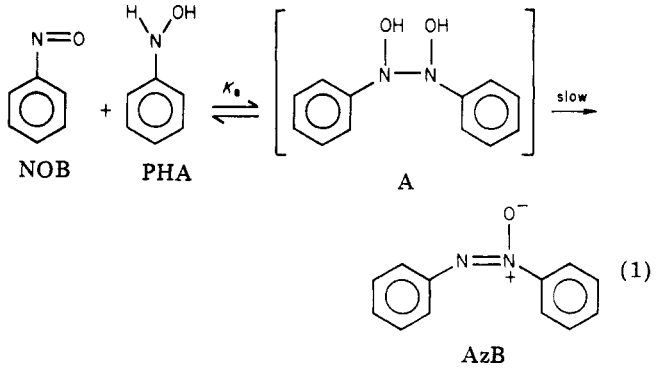
The condensation of *N*-arylhydroxylamines with aromatic nitroso compounds to form substituted azoxybenzenes has been studied in a variety of solvent systems.[1-6] Evidence[7,8] suggests that PHA and NOB in the absence of added bases (ethanol and 70% aqueous methanol solvent) react to produce a symmetrical intermediate (A) which is in rapid equilibrium with starting materials (eq 1). In ethanolic Britton–Robinson buffer, Darchen



(1)

and Moinet[9] have shown that the reaction exhibits *specific* acid and base catalysis and an undefined spontaneous term. Because of the potential importance of this con-

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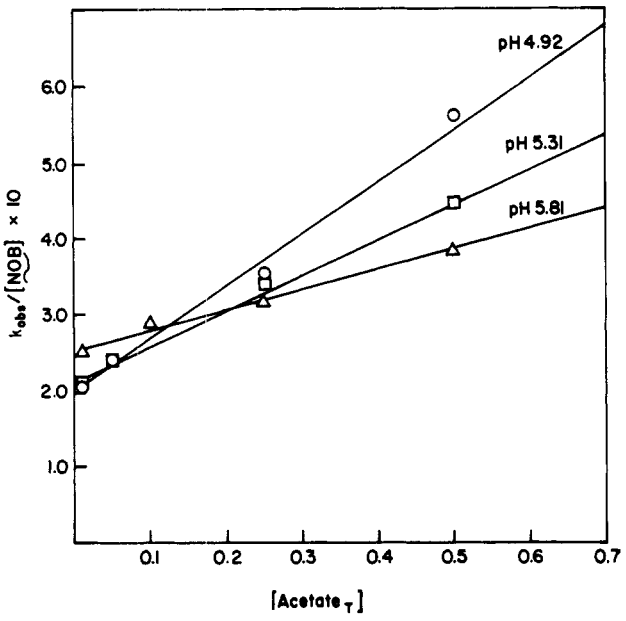


Figure 1. $k_{obsd}/[NOB]$ vs. [acetate$_T$] at 25 °C (μ = 0.5, $NaClO_4$) at pH 4.92, 5.31, and 5.81. Each point represents data obtained at a minimum of three different values of $[NOB]_0$.

densation reaction as a detoxication pathway for carcinogenic arylhydroxylamines, this process has now been studied in purely aqueous buffer. Under these conditions, we have established that the condensation is subject to both *general* acid and base catalysis by acetate buffer (25 °C, μ = 0.5, $NaClO_4$) (pH 4.92 to 5.81) as well as proceeding by a buffer-independent pathway.

Under the experimental conditions chosen, the condensation of NOB with PHA follows pseudo-first-order kinetics in accord with eq 2. On the basis of the kinetic

$$\frac{d[AzB]}{dt} = k_{obsd}[PHA] \quad (2)$$

behavior observed in the presence of acetate buffer, k_{obsd} can be expressed by eq 3 where [acetate$_T$] refers to the

$$k_{obsd} = \left[\left(k_{ga}\frac{a_H}{K_a + a_H} + k_{gb}\frac{K_a}{K_a + a_H}\right) \times [\text{acetate}_T] + k_c\right][NOB] \quad (3)$$

total acetate concentration and K_a refers to the acid dissociation constant for acetic acid [$K_{a,HOAc} = 1.74 \times 10^{-5}$]. The oxidation of PHA under the experimental conditions, in the absence of added NOB, did not contribute to the value of k_{obsd}. Apparent third-order rate constants were obtained from plots of $k_{obsd}/[NOB]$ vs. [acetate$_T$] at three pH's (Figure 1). The intercept values thus obtained are the second-order rate constants for the buffer-independent reaction (k_c = 0.22 M^{-1} s^{-1}). Defining the apparent third-order rate constant k_r as $[k_{obsd}/([NOB] - k_c)]/[\text{acetate}_T]$ yields eq 4 from eq 3. A plot of $(k_r/K_a)/(K_a + a_H)$

$$\frac{k_r/K_a}{K_a + a_H} = k_{ga}\frac{a_H}{K_a} + k_{gb} \quad (4)$$

vs. a_H/K_a yields k_{ga} (general acid rate constant) as the slope and k_{gb} (general base rate constant) from the intercept (Figure 2). The values of k_{ga} and k_{gb} were thus determined to be 1.4 M^{-2} s^{-1} and 0.2 M^{-2} s^{-1}, respectively. High-performance LC product studies indicate that the condensation of PHA with NOB produces AzB in 85–102% yield on the basis of the initial concentration of PHA.

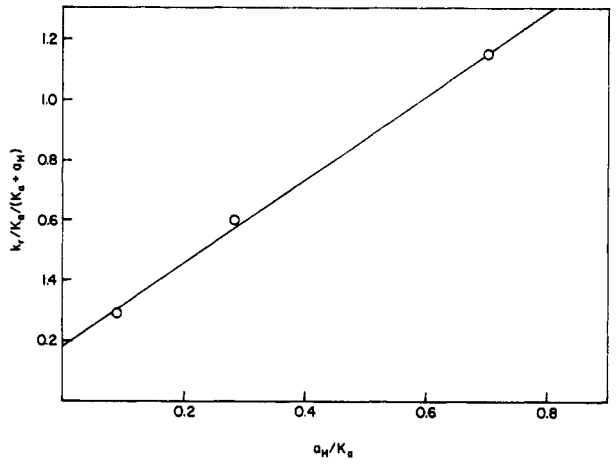
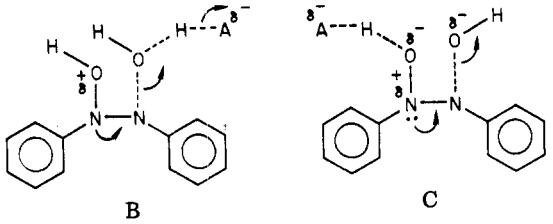


Figure 2. $(k_r/K_a)/(K_a + a_H)$ vs. a_H/K_a for pH 4.92, 5.31, and 5.81. The slope provides the value of k_{ga} with the intercept equal to k_{gb}.

The value of the buffer-independent rate constant for the condensation was found to be independent of pH over the range 4.92–5.81. Due to the constant intercept values shown in Figure 1, the value of k_c (eq 3) does not appear to include specific acid or base catalysis and therefore represents a spontaneous pathway. Darchen and Moinet[9] established that the condensation of NOB and PHA and their methyl and chloro derivatives in 20% aqueous ethanol was subject to specific catalysis and a pH-independent process and suggested the rate-determining breakdown of a tautometric form of A to account for their results. The value of k_c obtained under their experimental conditions (25 °C, Britton–Robinson buffer in ethanol–water (4:1, v/v)) was 0.32 M^{-1} s^{-1}. This is 1.5 times greater than the value obtained in our study and is surprising in view of the results of Ogata and co-workers,[7] who found that the value of k_c increased with increasing water content of the solvent.[10] In view of our findings of general catalysis, the higher value of k_c obtained by Darchen and Moinet[9] may be explained by assuming that the Britton–Robinson buffer also exhibits general catalysis.

Evidence[1-3] suggests that in strongly basic organic solutions (e.g., CH_3O^-/CH_3OH, *t*-BuOK/Me_2SO), azoxybenzene (AzB) is formed from the coupling of two nitrosobenzene radical anions [produced from nitrosobenzene (NOB) and phenylhydroxylamine (PHA)]. In organic solvents in the absence of added base (e.g., Me_2SO, *tert*-butyl alcohol, ethanol, benzene), there is evidence favoring a radical pathway by way of the phenyl nitroxide radical. From the many studies of the condensation reaction in the absence of added base in organic and aqueous–organic solutions, the evidence suggests that the slow step is preceded by a rapid preequilibrium step (eq 1). If these suggestions are also true under purely aqueous conditions, the observed general catalysis must indicate acceleration of the slow step as shown in eq 1. An intermediate such as A (eq 1) would seem to account for the results obtained in this study, and we feel no need to suggest radical intermediates. However, the present study cannot exclude the formation of phenyl nitroxide radicals (PhNHO·) either on or off the reaction pathway. If one accepts A as a logical intermediate, then the transition state for general acid catalysis can be envisioned as B where proton donation by acetic acid makes the hydroxide moiety a better leaving group. The general-base mechanism may involve ace-

(10) On increasing solvent polarity in the order benzene, CCl_4, THF, DMF, and ethanol, Knight and Saville[5] found the values of k_c at 30 °C to increase linearly from 6.8 × 10^{-3} to 0.109.



B C

tate-assisted removal of the proton from the symmetrical intermediate (as in C), increasing the electron density on the nitrogen to which the oxygen anion is bonded, facilitating electron-pair delocalization, and thereby catalyzing expulsion of hydroxide. The general catalysis rate constants determined in Figure 2 are actually apparent rate constants due to the rapid preequilibrium step shown in eq 1, i.e., $k_g = k_g'K_e$. Unfortunately, under these experimental conditions, the value of K_e is not determinable and thus neither are the actual values of k_{ga}' or k_{gb}'.

The establishment of general catalysis for the condensation of NOB and PHA provides further information regarding non-enzyme-controlled detoxication mechanisms for arylhydroxylamines at physiologically relevant pH's. Such catalysis thus offers an effective pathway for arylhydroxylamine depletion which is dependent upon catalytic groups available in an aqueous environment.

Experimental Section

NOB and AzB were obtained from Aldrich and recrystallized from methylene chloride–pentane prior to use. PHA was prepared by the method of Smissman and Corbett[11] and recrystallized from the same solvent prior to use.

Kinetic studies were carried out spectrophotometrically at 25 °C by monitoring the formation of AzB at 250 nm. The solutions were prepared by the addition of nitrogen-degassed metal-free[12] buffer (μ = 0.5, $NaClO_4$) to a volumetric flask containing an accurately weighed amount of NOB. After nitrogen was allowed to flow over the top of the solution and mixed, 3.0 mL was transferred to a cuvette containing PHA (concentration varied from 0.6 to 1.1 × 10^{-4} M after addition of NOB–buffer solution). Such reaction mixtures were prepared at a minimum of three NOB concentrations ($[NOB]_0$ = 1.0 to 2.1 × 10^{-3} M) at each of four buffer concentrations (0.01, 0.05, 0.25, and 0.50 M) at each of three pH's (4.92, 5.31, and 5.85). Reactions were followed for four to five half-lives under the established pseudo-first-order conditions. Values of k_{obsd} were obtained from plots of log ($OD_\infty - OD_t$) vs. time.

The rate constant for the oxidation of PHA in the absence of NOB, under the experimental conditions of the kinetic study, was determined in 0.01 and 0.50 M acetate buffer at pH 4.92 and 5.81. Product studies were performed by reverse-phase high-performance liquid chromatography on a system consisting of a Waters Model U6K injector, Model 6000 A pump, and Model 440 UV detector (Waters Associates) with an RP-18 column (Waters, μ Bondapak C_{18}). The mobile phase was 65:35 methanol–water at a flow rate of 2.0 mL/min. The concentration of AzB was monitored at 280 nm as a function of peak height on a strip chart recorder (V_R = 15 mL).

At the completion of the condensation reaction (determined by calculation from kinetic data) three high-performance LC determinations were made of the AzB concentration in each of four solutions (0.01 and 0.50 M acetate buffer at pH 4.92 and 5.81). The AzB was found to be stable in all solutions employed over the time period that reactions were monitored.

Acknowledgment. This work was supported by NIH Grant CA-19288 from the National Cancer Institute (PHS, DHEW).

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Electrochemical Reduction of the Wieland-Miescher Ketone

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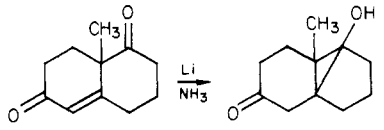
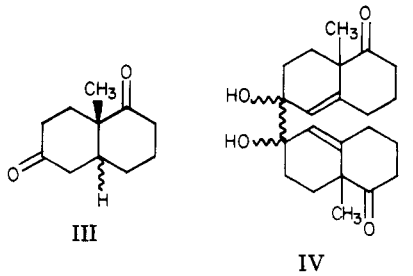
The chemistry of the reduction of the Wieland–Miescher ketone and some related compounds was reported in a series of papers by Reusch and co-workers.[1] In particular, this group was able to demonstrate that lithium/ammonia reduction resulted in a cyclopropanol derivative as the chief product, i.e., I to II. They also studied the polarography of this system and found that the half-wave reduction potentials of several enedione systems related to I were over 0.1 V more positive than the reduction potential of analogues lacking the isolated carbonyl group. This suggested very direct interaction between the enone moiety and the neighboring carbonyl group.[1]



I II

We wished to see if the polarography reported was reflected in the structure of the product of the electrochemical process, and, therefore, we undertook to effect a controlled-potential reduction of I which would allow product isolation. Toward this end, we repeated the polarography of I in 50% methanol/50% 0.1 N KCl and then carried out the controlled-potential reduction in the same medium. The crude product was chromatographically separated, and the chromatographic fractions were identified by using mass, ^1H NMR, and IR spectroscopy.

It was found that no cyclopropanol derivative II could be detected or isolated from the reduction. This material is easily distinguished from the products actually obtained, namely, III and IV, by means of its NMR spectrum.



III IV

Compound II, and similar substances, exhibits a resonance at about 1 ppm below Me_4Si, characteristic of a methyl substituting a cyclopropane ring.[1] The total crude reduction product showed no such resonance. There was recovered 85.4% product from the reduction (1.67 g of reactant yielding 1.43 g of product). Chromatography of this material gave a 79.3% recovery of fractions (1.14 g) consisting of a mixture of dihydro compounds, III (11%), and the two diastereomeric dimers of IV (89%). The mixture III was assigned structures on the basis of its IR (the presence of saturated carbonyls), NMR (no vinyl protons) and mass spectra (molecular ion at m/e 180). It

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