Kinetics and Mechanisms of the Bamberger Rearrangement. Part 4.[1] Rearrangement of Sterically Hindered Phenylhydroxylamines to 4-Aminophenols in Aqueous Sulphuric Acid Solution

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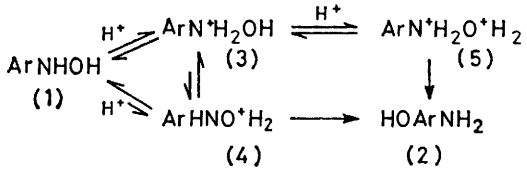
The rates of the Bamberger rearrangement of sterically hindered phenylhydroxylamines have been determined in aqueous sulphuric acid solution and the substituent effects (in particular, the steric effects) are discussed. The rate constants for phenylhydroxylamines with 2-substituents (Me, Cl, I) satisfied the Taft equation: $\log k_{rel} = \rho^*\sigma^* - \delta E_s$ with $\rho^* -1.93$ and $\delta -1.16$. The result shows that steric hindrance of the substituents, in addition to the electron-donating effect, has an accelerating effect on the rates of the Bamberger rearrangement. The rate constants for 3-substituted 2-methylphenylhydroxylamines were generally greater than those for 5-substituted 2-methylphenylhydroxylamines. The difference was attributed to the ' buttressing effect ' of neighbouring 3-substituents. This is the first example of steric acceleration of the Bamberger rearrangement.

In Part 3 [1] we determined the rate constants for the Bamberger rearrangement of 3-substituted phenylhydroxylamines (ArNHOH) as a function of pH and H_0. It was established on the basis of the kinetic measurements that (i) the rearrangement occurs by an S_Ni mechanism, (ii) the elimination of water from $ArNHO^+H_2$ is rate determining, and (iii) the active species at $[H_2SO_4] < 1.00$N (pH region) is the *O*-protonated arylhydroxylamine ($ArNHO^+H_2$), while the diprotonated species ($ArN^+H_2O^+H_2$) contributes significantly to the observed reaction rate at $[H_2SO_4] > 1.00$N (H_0 region) (Scheme 1).



Scheme 1

We here report the influence of 2-, 2,3-di-, and 2,5-disubstituents on the rates of the rearrangement from monoprotonated species. We have found that the rate constants for 2-substituted and 2,3-disubstituted phenylhydroxylamines are greater than those of corresponding 3-substituted and 2,5-disubstituted phenylhydroxylamines, respectively. The findings suggest that the rate of the Bamberger rearrangement is enhanced by steric hindrance around the hydroxylamino-group. In particular, the marked rate acceleration observed for 2,3-disubstituted phenylhydroxylamines is a rare example of the ' buttressing effect.' [2]

RESULTS AND DISCUSSION

Plots of first-order rate constants k_{obs} [see equation (1)] *versus* pH or H_0[3] are shown in Figure 1. The plots were similar to those for the rearrangement of 3-substituted phenylhydroxylamines,[1] *i.e.* k_{obs} increases with decreasing pH, then becomes almost constant between pH 1 and H_0 −1, and increases again at $H_0 < -1$. The characteristic pH(H_0)–rate profile means that monoprotonated (4) is the active species at $H_0 > -1$, while both monoprotonated (4) and diprotonated (5) are involved in the active species at $H_0 < -1$.

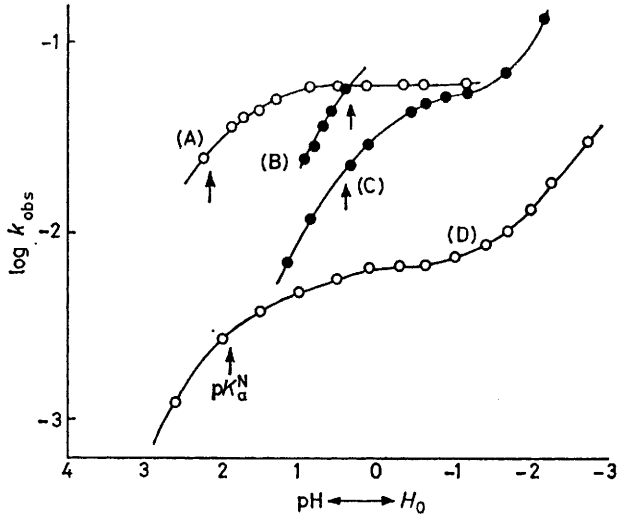
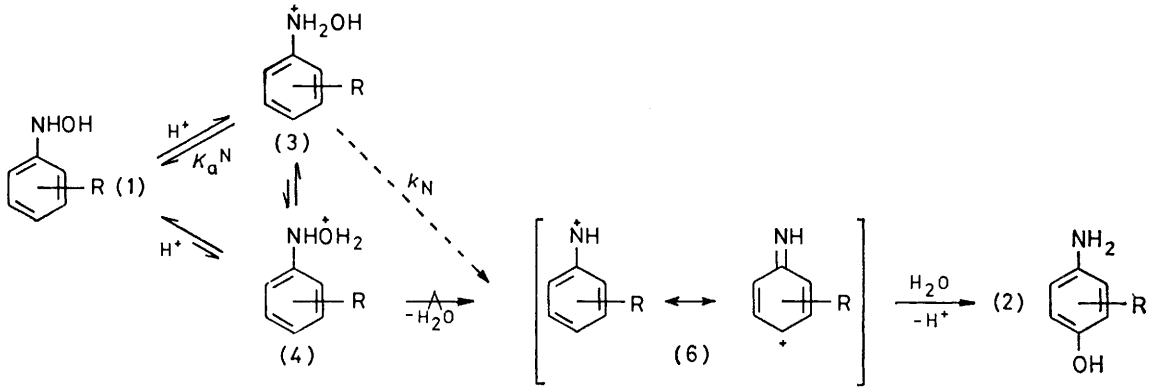


Figure 1 log k_{obs} against pH or H_0 for the rearrangement of 2-substituted phenylhydroxylamines: (A) (1; R = 2-Me) at 25.0 °C; (B) (1; R = 2-I) at 400 °C; (C) (1; R = 2-Cl) at 40.0 °C; (D) (1; R = H) at 40.0 °C

As shown in Scheme 2, the true rearrangement from monoprotonated species occurs from *O*-protonated (4) and not from *N*-protonated (3). Since the protonation of arylhydroxylamines occurs predominantly on the more basic nitrogen atom, the concentration of (4) cannot be determined spectrophotometrically. Taking the equilibrium (3) ⇌ (4) into consideration, however, one can estimate the reactivity of arylhydroxylamines by the rate constants for *N*-protonated species, k_N (for the kinetic detail, see ref. 1), from equation (1) where

$$v_{obs} = k_{obs}[(1)_{total}] = k_N[(3)]$$
$$= k_N[H^+][(1)_{total}]/(K_a^N + [H^+]) \quad (1)$$

$[(1)]_{total} = [(1)] + [(3)]$. The concentrations of (1) and (3) can be easily determined by a spectroscopic method.[1]



SCHEME 2

pK_a^N, k_N, and the activation parameters are summarised in the Table. In 3-substituted phenylhydroxylamines, only electron-donating substituents accelerated the rearrangement (Hammett ρ −3.2).[1] Examination of the Table reveals, however, that all substituents, irrespective of the electronic effect, accelerate the rearrangement. The result implies that the steric effect, rather than the electronic effect, contributes to the transition state of the Bamberger rearrangement of 2-substituted phenylhydroxylamines. We thus propose that 2-substituents facilitate the elongation of the N–O bond due to the relaxation of the steric crowding and the transition state is closer to (6) (nitrenium ion).

pK_a^N, k_N, and activation parameters for the rearrangement of phenylhydroxylamines (1) in sulphuric acid solution

R	$10^4\ k_N/s^{-1}$ 40.0 °C	25.0 °C	pK_a^N	$\Delta H^\ddagger$/ kcal mol^{-1}	$\Delta S^\ddagger$/ cal mol^{-1} K^{-1}
2-Me	61.7 [b]	8.99	2.18 [d]	22.9	4.6
2-Cl	7.44	1.17 [b]	0.42 [c]	23.5	2.3
2-I	19.3		0.35 [c]		
2,3-(Me)$_2$	157 [b]	23.7	2.38 [d]	23.2	7.4
2,5-(Me)$_2$	106 [b]	18.2	2.40 [d]	21.4	0.5
2-Me-3-Cl	9.15	1.73 [b]	1.15 [c]	21.7	−3.0
2-Me-5-Cl	7.95	1.05 [b]	1.16 [c]	25.2	7.7
H [a]	1.08	0.14	1.90 [c]	24.8	2.4
3-Me [a]	2.37	0.31	2.15 [c]	23.8	0.7
3-Cl [a]	0.065	0.008 [b]	1.00 [c]	26.8	3.6
2,6-(Me)$_2$		820	2.2 [d]		
1-$C_{10}H_7$-HNOH		420	1.37 [d]		

[a] Ref. 1. [b] By extrapolation from an Arrhenius plot. [c] 40.0 °C. [d] 25.0 °C.

The steric effect of 2-substituents was quantitatively described by the Taft equation (2).[4] Only three 2-substituted phenylhydroxylamines (Me, Cl, and I) could be isolated as pure crystals, so that further discussion is based on the rate constants of these three materials. Provided that the rate constants are affected only by the inductive effect (polar substituent constant, σ^*) and steric effect (steric substituent constant, E_S), trial-and-error linear regression analysis of a plot of log k_{rel} − $\rho^*\sigma^*$ *versus* E_S gave the best result ($r > 0.999$, Figure 2) for ρ^* −1.93 with slope δ of −1.16.

$$\log k_{rel} = \log k_N - \log k_N(2\text{-MeC}_6\text{H}_4\text{NHOH}) \quad (2)$$
$$= \rho^*\sigma^* - \delta E_S$$

The absence of a resonance effect is supported by the prediction based on CPK model building of (6) that the benzene ring cannot enjoy coplanarity with both the 2-substituent and the imino group in the same plane. The negative ρ^* value indicates that electron-donating 2-substituents, as well as 3-substitutents, are able to accelerate the rate of the rearrangement. The negative

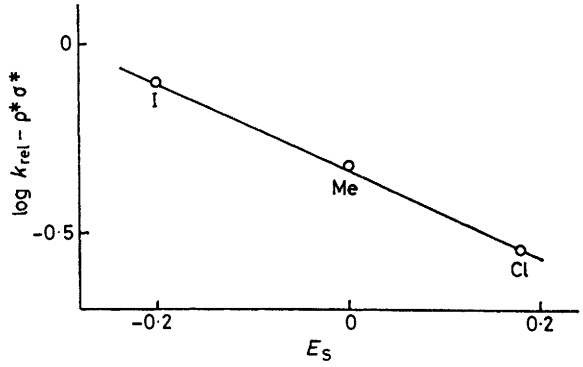


FIGURE 2 Taft plot of (log k_{rel}–$\rho^*\sigma^*$) *versus* E_S for the rearrangement of 2-substituted phenylhydroxylamines in sulphuric acid solution at 40.0 °C: ρ^* −1.93, δ (slope) −1.16

δ value indicates that the reaction rate increases with increasing steric hindrance. It is not easy to discuss the relative importance of the inductive and steric effects on the basis of the magnitude of ρ^* and δ, but the following facts suggest that the steric effect is the more important. (i) Both 2-Cl and 2-I derivatives have greater rate constants than phenylhydroxylamine itself. (ii) The rate constant for the 2-I derivative is greater than that for the 2-Cl derivative (because for the inductive effect 2-Cl > 2-I, while for the steric effect 2-Cl < 2-I). The rate constants are further enhanced by increasing steric hindrance. For example, 2,6-dimethylphenyl- and 1-naphthyl-hydroxylamine which are expected to suffer more serious steric hindrance have rate constants greater by a factor of 10^3 than phenylhydroxylamine.

Hammett plots of log k_N (40 °C) *versus* σ_m[5] for 5-substituted (Me, H, or Cl) 2-methylphenylhydroxylamines

gave a good linear relationship (r 0.998) with ρ_N −2.5, but a plot 3-substituted (Me, H, or Cl) 2-methylphenylhydroxylamines was not linear. Plots of $\Delta H^{\ddagger}$ *versus* $\Delta S^{\ddagger}$ are shown in Figure 3. It seems to us that 3-substituted, 2-methyl-5-substituted, and 2-methyl-3-substituted series are subject to three different linear relationships. The magnitude of the entropy control (*i.e.*, slope) is in the order: 3-substituents < 2-methyl-5-substituents < 2-methyl-3-substituents. The fact that

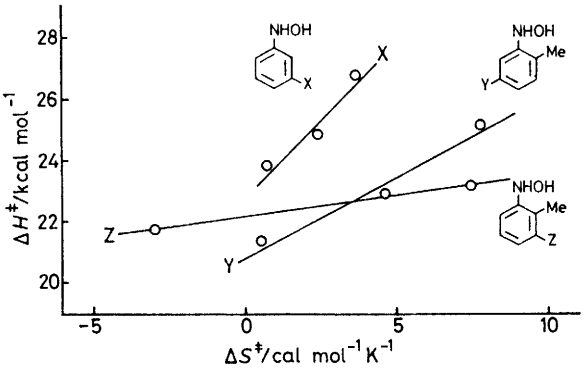


FIGURE 3 Plots of $\Delta H^{\ddagger}$ *versus* $\Delta S^{\ddagger}$ for the rearrangement of phenylhydroxylamines

the 2-methyl-3-substituted series is most significantly controlled by the entropy term is rationalised in terms of a ' buttressing effect ',[2] *i.e.* the steric interaction between 2- and 3-substituents expands the apparent bulkiness of the 2-substituents.

In conclusion, we have shown for the first time that the Bamberger rearrangement is sensitive to steric effects. In particular, the rate acceleration observed for 2,3-disubstituted phenylhydroxylamines is one of the rare examples of the buttressing effect proposed by Kistiakowsky and Smith.[2]

EXPERIMENTAL

Materials.—2-Substituted phenylhydroxylamines were prepared from the corresponding 2-substituted nitrobenzenes by zinc reduction in methanol–water containing ammonium chloride and were recrystallised from benzene–ligroin: 2-methylphenylhydroxylamine, m.p. 40.5—41 °C (lit.,[6] 44 °C); 2-chlorophenylhydroxylamine, m.p. 51.5—53.5 °C (lit.,[7] 53.5—55.5 °C); 2-iodophenylhydroxylamine, m.p. 51—52 °C (lit.,[8] 52—54 °C); 2,3-dimethylphenylhydroxylamine, m.p. 73—75 °C (lit.,[6] 74 °C); 2,5-dimethylphenylhydroxylamine, m.p. 87—89 °C (lit.,[6] 91.5 °C); 2,6-dimethylphenylhydroxylamine, m.p. 97—98.5 °C (lit.,[9] 98—98.5 °C); *3-chloro-2-methylphenylhydroxylamine*, m.p. 59—61 °C (Found: C, 53.05; H, 5.05; N, 8.75. C_7H_8ClNO requires C, 53.35; H, 5.1; N, 8.9%); *5-chloro-2-methylphenylhydroxylamine*, m.p. 70—71 °C (Found: C, 53.3; H, 5.2; N, 8.9%). 1-Naphthylhydroxylamine was prepared from 1-nitronaphthalene by reduction with ammonium sulphide in ethanol and was recrystallised from benzene, m.p. 79—81 °C (lit.,[10] 79 °C).

Kinetic Measurements.—The method of determining pK_a^N and k_N was described in Part 3.[1] The correlation coefficients for the first-order plots were always better than 0.999. The rate constants for 2,6-dimethylphenylhydroxylamine and 1-naphthylhydroxylamine were too fast to be determined by the conventional method.[1] Equation (3) which is derived from equation (1) indicates that a plot of $1/k_{obs}$ *versus* $1/[H^+]$ is linear and $1/k_N$ and K_a^N/k_N are the intercept and slope, respectively. By least-squares computation, we determined these values and then estimated pK_a^N and k_N.

$$1/k_{obs} = (1 + K_a^N/[H^+])/k_N \quad (3)$$

When this method was applied to other phenylhydroxylamines, the pK_a^N and k_N were in good accord with those determined by the conventional method [1] within experimental error.

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