J. Org. Chem. **1982**, *47*, 2261-2264

(column μ-Bondapack, C_{18}, 10 μm, Waters; solvent H_2O–MeOH, 60:40). Spectral data compared to those of a reference sample obtained from biotin[21] confirm the structure of **2c**. The deuterium content of [6,6-$^2H_2$]dethiobiotin was determined by mass spectrometry on the purified acid: MS (CI, quasimolecular ion) *m/z* (relative intensity) 217 (d_2, 100), 216 (d_1, 3.5), 215 (d_0, 5.2).

[5,5-$^2H_2$]-*d*-Biotin Methyl Ester (11). A solution of 100 mg of biotin-*d* sulfoxide[22] in 2.5 mL of 0.93 N NaOD/D_2O was kept at room temperature for 9 days. After neutralization by HCl, the water was evaporated, the residue was dissolved in 7.5 mL of MeOH–$CHCl_3$ (2:1), and 1 mL of $TiCl_3$ was added. The mixture was refluxed for 6 h and, and then the solvent was evaporated. The residue dissolved in 2 mL of MeOH was treated with 2 mL of 1 N NaOH for 2 h. After neutralization by HCl, the solution was poured over a Dowex Ag 1-X2 column (formate form). Biotin-d_2 (49 mg, 53%) was eluted with 0.05 N formic acid. The methyl ester **11** was obtained by treatment with diazomethane: mp 128–130 °C; NMR ($CDCl_3$) δ 3.16 (m, 1 H, SCH), 4.25 (m, 1 H, H at C-3), 4.45 (d, 1 H, J = 7 Hz, H at C-4), no signal corresponding to the two hydrogens at C-5 (δ 2.66 and 2.90);[16] MS (EI) *m/z* 145, 146, 167, 187, 199, 200, 229, 260 ($M^{+}\cdot$); MS (CI, quasimolecular ion) *m/z* (relative intensity) 262 (1), 261 (100), 260 (13), 259 (2).

[3-$^2H_{1;0}$,4-$^2H_{0;1}$]-*dl*-Biotin Methyl Ester (13). Et_3SiD was prepared by $LiAlD_4$ reduction of chlorotriethylsilane.[23] Its isotopic purity (>95%) was estimated by NMR (no signal at δ 3.28 (C_6H_6 internal reference). To 50 mg (0.2 mmol) of 3-dehydrobiotin[17] **14** dissolved in 1 mL of CF_3COOH were added 50 μL (0.2 mmol) of Et_3SiD. The mixture was stirred for 15 min at 20 °C. After removal of the solvent, the crude material was esterified by diazomethane to give a mixture of two compounds. After separation by silica gel column chromatography, we obtained the following.

13: 28 mg (60%); mp 128–130 °C; NMR ($CDCl_3$)[16] δ 4.25–4.63 (m, 0.8 H, H at C-3), 4.02–4.25 (m, 0.2 H, H at C-4); MS (EI, 70 eV) *m/z* 85, 98, 144, 145,167, 186, 199, 228, 259 ($M^{+}\cdot$); MS (CI, quasimolecular ion) *m/z* (relative intensity) 260 (100), 259 (1); MIKE spectrum on *m/z* 259, *m/z* (relative intensities) 198 (2), 199 (98), 144 (37), 145 (62).

trans-[3-$^2H_{1;0}$, 4-$^2H_{0;1}$]Biotin methyl ester (noncrystallized): 14 mg (30%); NMR ($CDCl_3$) δ 1.35 (m, 8 H), 2.04 (m, 2 H, $CH_2CO_2CH_3$), 2.22–2.88 (m, 3 H, HCS), 3.26 (s, 3 H, OCH_3), 3.48 (m, 0.8 H, CN–CH), 3.90 (m, 0.2 H, NCH), 4.71 (m, 1 H, NH), 4.91 (m, 1 H, NH); mass spectrum, identical with that for **13**.

Conversion of Dethiobiotin to Biotin. The conversion of dethiobiotin to biotin was performed by using *E. coli* C124 His$^-$, bio A^{-24} as previously described.[4] The culture medium was inoculated with 5 μg/L of deuterated *dl*-dethiobiotin diluted with [3,4-$^3H_2$]-*dl*-dethiobiotin[8] (200 mCi/mmol) in an approximate ratio of 9:1.

The bound biotin was extracted[4] and purified[25] according to the described techniques by using solvent of the highest purity available. Starting from 24 L of culture medium, we obtained 4 μg of crude biotin, yielding 700 ng of biotin methyl ester after purification by silica gel column chromatography (eluent MeOH–ACOEt, 1:4).

Acknowledgment. We thank Dr. G. Field for generous gifts of 3-dehydrobiotin. We are indebted to Dr. R. Lett for helpful advice. Dr. P.-L. Desbene is also acknowledged for HPLC separation.

Registry No. 1, 22377-59-9; **2**, 636-20-4; **2a**-*d* (isomer 1), 81477-33-0; **2a**-*d* (isomer 2), 81477-34-1; **2b**, 81477-35-2; **2c**, 81477-36-3; **3**, 14273-92-8; **4**, 81477-37-4; **5**, 81496-93-7; **6**, 81477-38-5; **7**, 81477-39-6; **8**, 81477-40-9; *cis*-**9**, 81477-41-0; *trans*-**9**, 81496-84-6; **10**, 81477-42-1; **11**, 81496-94-8; **12**, 81477-43-2; **13**-*d* (isomer 1), 81477-44-3; **13**-*d* (isomer 2), 81477-45-4; **14**, 61379-20-2; δ-valerolactone, 542-28-9; triphenylmethyl chloride, 76-83-5.

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Polar Effect in Addition Rates of Substituted Benzenethiyl Radicals to α-Methylstyrene Determined by Flash Photolysis[1]

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The absolute rate constants for the reversible addition reactions of the para-substituted benzenethiyl radicals (p-$XC_6H_4S\cdot$) to α-methylstyrene have been determined by flash photolysis. The equilibrium constants have been estimated as the relative values. From the Hammett plots vs. σ^+, the reaction constant (ρ^+) for the reactivities was estimated to be 1.72 (r = 0.9851). Since the polar effect was also found for the equilibrium constants ($\rho^+ \approx 1.4$), a portion of the polar effect on the reactivities is determined by the polar effect on the stabilities of p-$XC_6H_4S\cdot$ in terms of a linear free-energy relationship. The remaining positive portion of the polar effect on the reactivities may be attributed to the contribution of a polar resonance structure such as [p-$XC_6H_4S^-$,CH_2=$C(CH_3)Ph^{+}\cdot$] to the transition state.

Negative Hammett reaction constants (ρ or ρ^+) have been estimated from the Hammett-type linear free-energy treatments in the thiyl radical addition reactions toward substituted α-methylstyrene on the basis of the measurements of the relative reactivities.[2-4] The negative ρ^+ value has been confirmed by the Hammett plots of the absolute rate constants determined by the flash photolysis method.[5] The negative ρ^+ values suggest the polar nature of the transition state as follows:

$$[RS\cdots CH_2{=}C(CH_3)C_6H_4Y] \leftrightarrow [RS^-,CH_2{=}C(CH_3)C_6H_4Y^{+}\cdot]$$

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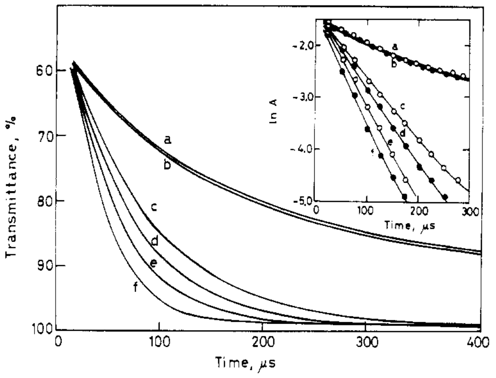

Figure 1. Effect of oxygen concentration on the decay rates of $p\text{-}CH_3OC_6H_4S\cdot$ (at 520 nm) produced by the flash photolysis of the disulfide (2×10^{-4} M) in benzene at 23 ± 1 °C: (a) in degassed solution without α-methylstyrene, (b) in degassed solution with α-methylstyrene (9.7×10^{-3} M), (c) addition of oxygen (5.7×10^{-4} M) to solution b, (d) $[O_2] = 1.1 \times 10^{-3}$ M and [α-methylstyrene] = 9.3×10^{-3} M, (e) $[O_2] = 2.0 \times 10^{-3}$ M and [α-methylstyrene] = 9.3×10^{-3} M, (f) $[O_2] = 1.0 \times 10^{-2}$ M and [α-methylstyrene] = 9.3×10^{-3} M. Insert: First-order plots.

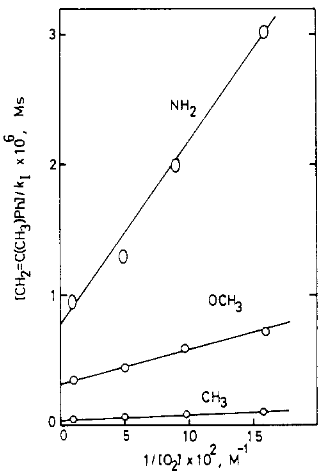

Figure 2. Plots of $[CH_2{=}C(CH_3)Ph]/k_I$ vs. $1/[O_2]$ for the reactions of $p\text{-}XC_6H_4S\cdot$ with α-methylstyrene in benzene at 23 °C.

Table I. Rate Constants (k_1) and the Equilibrium Constants (Kk_2) for the Addition Reactions of $p\text{-}XC_6H_4S\cdot$ with α-Methylstyrene in Cyclohexane at 23 °C[a]

X	k_1, M^{-1} s^{-1}	Kk_2, M^{-2} s^{-1}
Br	1.5×10^8	4×10^9 [b]
Cl	1.4×10^8	4×10^9 [b]
H	7.1×10^7	2×10^9 [b]
$t\text{-}C_4H_9$	1.6×10^7	5×10^8 [b]
CH_3	1.6×10^7	5×10^8 [b]
CH_3O	3.3×10^6	1.0×10^8
NH_2	4.8×10^5	4.4×10^6

[a] Estimation errors of ±10%. [b] Estimation errors of ±30%.

This type of the polar resonance structure predicts a positive ρ value in the addition reactions of the substituted benzenethiyl radicals to α-methylstyrene.

In 1980 Geers, Gleicher, and Church measured the relative rates of disappearance of pairs of substituted benzenethiols with α-methylstyrene and interpreted the results as measuring the relative rates of reaction of pairs of thiyl radicals with α-methylstyrene.[6] From this method a negative ρ^+ value (−0.18) was estimated. However, relative rates of disappearance of two thiols in radical–chain reactions depend on the rate constants for attack of chain-carrying radicals ($XC_6H_4SCH_2\dot{C}(CH_3)Ph$) on the thiols; i.e., the relative rate data refer to the hydrogen-abstraction step. Relative rates of reaction of different radicals with the same substrate cannot be obtained by competitive measurements but require absolute rate measurements. Since the sign and magnitude of the ρ^+ value of this reaction system are of interest and relatively few data on rates of different radicals on the same substrate are available, we have applied the flash photolysis technique to this system.

Results and Discussion

Transient absorption bands at 490–525 nm produced by the flash decomposition of para-substituted diaryl disulfides were attributed to the corresponding para-substituted benzenethiyl radicals ($p\text{-}XC_6H_4S\cdot$), since the same transient spectra were observed by the flash photolysis of the corresponding thiol.[7-9] Figure 1 shows the decay curves (transmittance vs. time) of $p\text{-}CH_3OC_6H_4S\cdot$ in benzene; the decay rate in the absence of α-methylstyrene was not affected by the addition of oxygen, suggesting the low reactivity of the thiyl radical toward oxygen. The decay rate in the presence of α-methylstyrene without oxygen was not accelerated (curve b in Figure 1). On the addition of both α-methylstyrene and oxygen, the decay rates increased (curves c–f) and the decay kinetics changed from second order to first order (insert of Figure 1). These findings suggest that the addition reaction is reversible and that oxygen acts as a selective radical trap to the carbon-centered radical (Scheme I).[10,11]

Scheme I

$$(p\text{-}XC_6H_4)_2S_2 \underset{k_r}{\overset{h\nu}{\rightleftharpoons}} 2p\text{-}XC_6H_4S\cdot$$

$$p\text{-}XC_6H_4S\cdot + CH_2{=}C(CH_3)Ph \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} p\text{-}XC_6H_4SCH_2\dot{C}(CH_3)Ph \xrightarrow[{[O_2]}]{k_2} \text{peroxy radical}$$

On the basis of the steady-state assumption, eq 2 and 3 can be derived from eq 1, where k_I refers to the pseudo-first-order rate constants estimated from the slopes of the first-order plot (insert of Figure 1).

$$-d[p\text{-}XC_6H_4S\cdot]/dt = 2k_r[p\text{-}XC_6H_4S\cdot]^2 + k_1[p\text{-}XC_6H_4S\cdot][CH_2{=}C(CH_3)Ph] - k_{-1}[p\text{-}XC_6H_4SCH_2\dot{C}(CH_3)Ph] \quad (1)$$

$$k_I = k_1[1 - k_{-1}/(k_{-1} + k_2[O_2])][CH_2{=}C(CH_3)Ph] \quad (2)$$

$$[CH_2{=}C(CH_3)Ph]/k_I = 1/k_1 + k_{-1}/k_1k_2[O_2] \quad (3)$$

The concentrations of α-methylstyrene and oxygen are being kept constant during the reaction, since [α-methylstyrene] (10^{-4}–10^{-1} M) and $[O_2]$ (6×10^{-4}–1×10^{-2} M) are higher than $[p\text{-}XC_6H_4S\cdot]$ which was estimated to be ca. 1×10^{-6} M on the basis of the assumption that the recombination rate con-

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Table II. Solvent and Temperature Effects on the Addition Rate Constants (k_1) and the Relative Equilibrium Constants (Kk_2)[a] in Benzene and *o*-Dichlorobenzene (*o*-DCB)

X	in benzene (23 °C) k_1, M^{-1} s^{-1}	in benzene (23 °C) Kk_2, M^{-2} s^{-1}	in *o*-DCB (23 °C) k_1, M^{-1} s^{-1}	in *o*-DCB (23 °C) Kk_2, M^{-2} s^{-1}	in *o*-DCB (68 °C),[c] k_1, M^{-1} s^{-1}
p-Cl	1.2×10^8	4×10^9 [b]	1.2×10^8	4×10^9 [b]	1.4×10^8
p-CH_3	1.5×10^7	9×10^8 [b]	1.5×10^7	9×10^8 [b]	1.6×10^7
p-CH_3O	3.1×10^6	3.8×10^7	2.9×10^6	2.2×10^7	3.1×10^6
p-NH_2	1.5×10^5	7.5×10^5	1.1×10^5	5.2×10^5	1.6×10^5

[a] Estimation error of ±10%. [b] Estimation error of ±30%. [c] These k_1 values were estimated approximately from the k_I values in oxygen-saturated solution.

stant of the thiyl radical (k_r) is the diffusion-controlled limit. When [O_2] and [α-methylstyrene] were low, the first-order part was separated from the mixed-order decay kinetics consisting of first- and second-order ($k_r[p\text{-}XC_6H_4S\cdot]^2$) by the graphical method.[8,9]

Figure 2 shows the plots of equation 3 for *p*-$NH_2C_6H_4S\cdot$, *p*-$CH_3OC_6H_4S\cdot$, and *p*-$CH_3C_6H_4S\cdot$; linear plots were obtained. From the intercept and slope, the reciprocals of the k_1 and Kk_2 ($K = k_1/k_{-1}$) values were estimated, respectively. These values obtained in cyclohexane at 23 °C are summarized in Table I; since the slopes of the plots for $C_6H_5S\cdot$, *p*-$ClC_6H_4S\cdot$, and *p*-$BrC_6H_4S\cdot$ were small, the approximate Kk_2 values are listed. The values in benzene (at 23 °C) and in *o*-dichlorobenzene (at 23 and 68 °C) are summarized in Table II; these experimental conditions were chosen in order to compare the data with the relative reactivities reported by Geers, Gleicher, and Church.[6] The k_1 values for *p*-$NH_2C_6H_4S\cdot$ decrease with an increase in the solvent polarity; this effect is specific to *p*-$NH_2C_6H_4S\cdot$ because this radical is very polarizable.[12] A slight decrease in the k_1 values observed for *p*-$ClC_6H_4S\cdot$ in aromatic solvents may be attributed to the charge-transfer-type interaction.[13] The k_1 values at 68 °C were estimated by assuming that the k_1 values are approximately equal to $k_I/[CH_2{=}C(CH_3)Ph]$ in the O_2-saturated solution, since the O_2 concentrations at high temperature were not precisely controlled. Slight increases in the k_1 values were observed with raising of the temperature. In the Arrhenius equation ($k_1 = A \exp(-E_a/RT)$), the log *A* values of the free-radical addition reactions were estimated to be 8.5 ± 0.5;[14,15] thus the activation energies (E_a) for the reactions of *p*-Cl- and *p*-$NH_2C_6H_4S\cdot$ with α-methylstyrene were calculated to be ca. 0.5 and ca. 5 kcal/mol, respectively. The temperature dependences in the k_1 values shown in Table II are reasonable within the estimation errors. The experimental errors are mainly attributed to the flash measurements and O_2 concentrations; from these causes the errors are at most ca. 5%. Further errors arise from the estimation of each k_I value from the first-order plot (e.g., insert of Figure 1) and the estimation of k_1 or Kk_2 from eq 3 (Figure 2). With the summation of these errors, each rate constant in the tables may contain an error of ±10%. The k_1 values at 68 °C in Table II may contain higher errors since they were estimated by an approximate method.

The Hammett plots of log k_1 and log Kk_2 are shown in Figure 3; a better linear plot for log k_1 was found for the plot vs. σ^+ rather than vs. σ or σ^-. The ρ^+ for log k_1 was estimated to be 1.72 ($r = 0.9851$). The log k_1 values for *p*-$NH_2C_6H_4S\cdot$ estimated in cyclohexane were fitted to the lines at $\sigma^+ = 1.2$–1.3. A positive slope was also found for the plot of log Kk_2 vs. σ^+ ($\rho^+ \approx 1.4$). The log Kk_2 values are a measure of the thermodynamic stabilities of *p*-$XC_6H_4S\cdot$ since the k_2 values and the stabilities of *p*-$XC_6H_4SCH_2\dot{C}(CH_3)Ph$ may be invariant with the changes of the substituents X; *p*-$XC_6H_4S\cdot$ becomes stable with a decrease in the log Kk_2 value or with an increase in the electron-donating ability of the substituent. From the linear free-energy relationship, it is suggested that a part of the ρ^+ value in the reactivities is determined by the ρ^+ value in the stabilities of *p*-$XC_6H_4S\cdot$ (eq 4). By the citation of the α value from Semenov's empirical value (α = 0.75),[16] about a half of the positive polar effect in the reactivities is determined by the polar effect in the stabilities of *p*-$XC_6H_4S\cdot$.

$$\Delta\log k_1 = \alpha\Delta\log Kk_2 \qquad (4a)$$

$$\rho^+(k_1) = \alpha\rho^+(Kk_2) \qquad (4b)$$

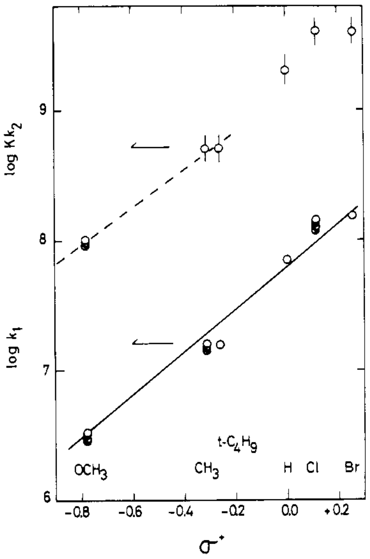

Figure 3. Hammett plots for log k_1 and log Kk_2 vs. σ^+ for the reactions of *p*-$XC_6H_4S\cdot$ with α-methylstyrene: in cyclohexane (○), in benzene (◐), in *o*-dichlorobenzene at 23 °C (◐), in *o*-dichlorobenzene at 68 °C (●).

The negative ρ^+ value for the rates of benzenethiyl radical toward substituted α-methylstyrene was reported from the relative reactivities ($\rho^+ = -0.38$)[4] and from the absolute rates ($\rho^+ = -0.30$);[5] this suggests a polar transition state such as $[PhS^-, CH_2{=}C(CH_3)C_6H_4Y^{+}\cdot]$. From this type of polar transition state, a positive ρ^+ value would be anticipated for the reactions of *p*-$XC_6H_4S\cdot$ toward α-methylstyrene. The rest of the polar effect in the reactivities which can be calculated from $\rho^+(k_1) - \alpha\rho^+(Kk_2)$ is ca. 0.9; thus this positive polar effect is ascribed to the contribution of the resonance structure $[p\text{-}XC_6H_4S^-, CH_2{=}C(CH_3)Ph^{+}\cdot]$ to the transition state. This type of resonance

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structure predicts that the Hammett plot of $\log k_1$ should fit for σ or σ^-; however, the contribution of the stabilities of $p\text{-XC}_6\text{H}_4\text{S}\cdot$ to the polar effect in the reactivities (eq 4) may draw the plot of $\log k_1$ toward σ^+.

The $\rho^+(k_1)$ (=1.72) is larger than that for styrene (ρ^+ = 1.37); this may be attributed to an increase in the above type of polar nature of the transition state since the *e* value of α-methylstyrene ($e = -1.27$) is more negative (more electron rich) than that of styrene ($e = -0.80$).[18,19] The $\rho^+(k_1)$ value estimated in the present study differs from the ρ^+ value estimated from the relative reactivities in benzene–*o*-dichlorobenzene (5:1) at 70 °C ($\rho^+ = -0.18$) which was reported by Geers, Gleicher, and Church.[6] It was reported that the reaction of 1-cyano-1-cyclohexyl radical with substituted benzenethiols has a negative ρ value (−0.52).[20] It was also reported that the absolute rate constants for hydrogen abstraction of the triarylmethyl radical from substituted benzenethiols tend to give a negative ρ^+ value except for $p\text{-}t\text{-C}_4\text{H}_9\text{C}_6\text{H}_4\text{SH}$.[21] Both these reported facts and our finding in this study suggest that the relative rates of disappearance of a pair of substituted benzenethiols with α-methylstyrene cannot be attributed to the relative rates of the addition reaction of the pair of thiyl radicals to α-methylstyrene but probably can be attributed to the relative rates for the hydrogen-abstraction reaction of chain-carrying radicals ($\text{XC}_6\text{H}_4\text{SCH}_2\dot{\text{C}}(\text{CH}_3)\text{Ph}$) to the pair of thiols.

In conclusion, we may summarize our results as follows. A positive ρ^+ value (=1.72) was estimated for the addition reactions of the substituted benzenethiyl radicals toward α-methylstyrene from the absolute rate constants determined by the flash photolysis technique. This value differs from the ρ^+ value estimated from the relative reactivities ($\rho^+ = -0.18$); the latter value can be attributed to the chain-carrying step. A large positive ρ^+ value in the reactivities estimated in the present study was rationally interpreted both in terms of the polar effect in the stabilities of $p\text{-XC}_6\text{H}_4\text{S}\cdot$ and in terms of the contribution of polar resonance structures such as $[p\text{-XC}_6\text{H}_4\text{S}^-,\text{CH}_2{=}\text{C}(\text{CH}_3)\text{Ph}^{+}\cdot]$ to the transition state. This idea is in good agreement with that presented by Davis and Pryor in the polar effect on hydrogen abstraction.[22]

Experimental Section

Diaryl disulfides, α-methylstyrene, and *o*-dichlorobenzene were purified by recrystallization or by distillation under reduced pressure. Cyclohexane and benzene were of spectrophotometric grade. The oxygen concentrations of solutions were calculated from the Henry law after dissolving oxygen in them under partial pressure.[23] The flash photolysis apparatus was of standard design; the half-duration of the xenon flash lamp (Xenon Corp., N-851) was ca. 10 μs, and the flash energy was ca. 100 J. The flash photolysis measurements were made in a cylindrical cell (optical path of 10 cm) at 23 ± 1 or 68 ± 2 °C.

Registry No. $p\text{-BrC}_6\text{H}_4\text{S}\cdot$, 31053-90-4; $p\text{-ClC}_6\text{H}_4\text{S}\cdot$, 31053-91-5; $\text{C}_6\text{H}_5\text{S}\cdot$, 4985-62-0; $p\text{-}t\text{-C}_4\text{H}_9\text{C}_6\text{H}_4\text{S}\cdot$, 81372-23-8; $p\text{-CH}_3\text{C}_6\text{H}_4\text{S}\cdot$, 31053-92-6; $p\text{-CH}_3\text{OC}_6\text{H}_4\text{S}\cdot$, 31053-93-7; $p\text{-NH}_2\text{C}_6\text{H}_4\text{S}\cdot$, 31053-94-8; α-methylstyrene, 98-83-9.

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Nonhydrated Anion Transfer from the Aqueous to the Organic Phase: Enhancement of Nucleophilic Reactivity in Phase-Transfer Catalysis

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A systematic study of how the nature and concentration of the inorganic salt affect hydration and reactivity of anions transferred into the organic phase under conditions of phase-transfer catalysis (PTC) has been performed. The inorganic salt concentration in the aqueous phase up to saturated solution (≥6 M), does not affect the hydration and hence the reactivity of the anion in aliphatic nucleophilic substitutions. On the other hand, in concentrated aqueous alkaline solutions (50% NaOH or 60% KOH) *unhydrated anions* are transferred from the aqueous to the organic phase. The anionic reactivity thus becomes identical with that found under anhydrous homogeneous conditions, the rate enhancement being 13.0, 4.0, 2.6, and 1.4 times for Cl^-, N_3^-, Br^-, and I^-, respectively. The same dehydrating effect was not observed with less concentrated alkaline solutions or with 50% aqueous NaF. These data show the unique property of OH^- in producing conditions of virtually null water activity under PTC conditions.

Under classical liquid–liquid phase-transfer catalysis (PTC) conditions, specific anion solvation by a limited number of water molecules in the organic phase decreases the reaction rate. Said effect is particularly striking in the case of anions with localized and/or less polarizable charge (Cl^-, CN^-, N_3^-).[2-5] Furthermore undesired hydrolytic side reactions are possible. Therefore, from a practical point of view, the anion hydration should be reduced or totally eliminated.

A possible solution is to work under solid–liquid PTC conditions, with the anionic reactant as solid phase suspended in an anhydrous organic solution of the substrate.

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