structure predicts that the Hammett plot of log k_1 should fit for σ or σ^-; however, the contribution of the stabilities of p-$XC_6H_4S\cdot$ 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 (ρ^+ = −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-t-$C_4H_9C_6H_4SH$.[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 ($XC_6H_4SCH_2\dot{C}(CH_3)Ph$) 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 (ρ^+ = −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-$XC_6H_4S\cdot$ and in terms of the contribution of polar resonance structures such as [p-$XC_6H_4S^-$,CH_2=C(CH_3)$Ph^{+}\cdot$] 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-$BrC_6H_4S\cdot$, 31053-90-4; p-$ClC_6H_4S\cdot$, 31053-91-5; $C_6H_5S\cdot$, 4985-62-0; p-t-$C_4H_9C_6H_4S\cdot$, 81372-23-8; p-$CH_3C_6H_4S\cdot$, 31053-92-6; p-$CH_3OC_6H_4S\cdot$, 31053-93-7; p-$NH_2C_6H_4S\cdot$, 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

Dario Landini,*[1a] Angelamaria Maia,*[1b] and Gianni Podda[1a]

Centro CNR and Istituto di Chimica Industriale dell'Università, I-20133 Milano, Italy, and the Istituto di Chimica Farmaceutica e Tossicologica dell'Università, I-09100 Cagliari, Italy

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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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Table I. Influence of the Salt Concentration of the Aqueous Phase on the Reaction Rates for Nucleophilic Substitutions of Methanesulfonate by Bromide Ion in *n*-Octyl Methanesulfonate in a Chlorobenzene-Water Two-Phase System under Phase-Transfer Conditions[a] in the Presence of Quaternary Onium Bromides at 60 °C

catalyst[b]	[KBr], M	$10^5 k_{\text{obsd}}$, s^{-1}	10^2[cat]$_{\text{org}}$, M	$10^3 k_{\text{obsd}}$/[cat]$_{\text{org}}$, M^{-1} s^{-1}
1c, $C_{16}H_{33}P^+Bu_3Br^-$ [c]	1.1	11.6	4.0	2.9
	2.0	11.2	4.0	2.8
	4.0	12.8	4.0	3.2
	6.0	11.6	4.0	2.9
	>6.0[d]	12.4	4.0	3.1
2c, $Bu_4P^+Br^-$ [c]	2.0	7.3	2.6	2.8
	3.0	8.9	3.3	2.7
	4.0	10.0	3.7	2.7
	6.0	10.2	3.9	2.6
3c, $Bu_4N^+Br^-$ [c]	1.0	0.60	0.16	3.7
	2.1	1.59	0.43	3.7
	3.0	3.42	0.90	3.8
	4.0	5.97	1.6	3.7
	5.0	9.57	2.5	3.8
	6.0	12.07	3.2	3.8
	>6.0[d]	12.58	3.4	3.7

[a] A chlorobenzene solution (20 mL) of substrate (6×10^{-1} M) and an appropriate volume of an aqueous solution of KBr so that a 5:1 molar ratio of inorganic salt/substrate is obtained. [b] 0.8 mmol in the system PhCl-H_2O. [c] The same hydration state (2 molar equiv of water) was found independently of the salt concentration in aqueous phase. [d] Saturated solution.

However, the anionic reactivity increase due to the anhydrous conditions is usually cancelled by the difficulty of regenerating the nucleophile. Indeed the solubilization of the solid phase is generally rate determining, and the salt generated during the reaction can cover the crystal surface, to slow it down or stop it.[6,7]

One alternative is to work under classical liquid–liquid PTC conditions, provided that the activity of the water is conveniently diminished by the addition of an appropriate solute. A study[6] carried out by Thyrion et al. was limited to the reaction of methyl iodide with the *p*-nitrophenate anion.

Here we report a systematic study of how the nature and concentration of the salt in the aqueous phase affect anionic reactivity in aliphatic nucleophilic substitutions, catalyzed by quaternary onium salts, under PTC conditions. A comparison is made with reactions carried out under classic liquid–liquid PTC and homogeneous anhydrous conditions.

Results

We have measured the rates of substitution of the $MeSO_3^-$ group in *n*-octyl methanesulfonate by a series of anions (N_3^-, Cl^-, Br^-, I^-) in a water–chlorobenzene two-phase system, in the presence of catalytic amounts of a quaternary ammonium or phosphonium salt 1–4 (reaction 1).

$$n\text{-}C_8H_{17}OSO_2Me + KY \xrightarrow[\text{PhCl-H}_2\text{O}]{Q^+Y^-} n\text{-}C_8H_{17}Y + MeSO_3K \quad (1)$$

1, $Q^+ = C_{16}H_{33}P^+Bu_3$ a, $Y^- = N_3^-$
2, $Q^+ = Bu_4P^+$ b, $Y^- = Cl^-$
3, $Q^+ = Bu_4N^+$ c, $Y^- = Br^-$
4, $Q^+ = (C_8H_{17})_4N^+$ d, $Y^- = I^-$

In a first set of experiments we varied the salt concentration in the aqueous phase, while a 1:5 substrate/inorganic salt ratio was maintained, in reaction 1 ($Y^- = Br^-$) catalyzed by ammonium or phosphonium bromide **1c**–**3c** with the inorganic salt concentration ranging from 1.0 M to saturated solutions (≥6.0 M) (Table I).

For every salt concentration in the aqueous phase (including saturated solution), the reactions follow regular pseudo-first-order kinetics (2), at least for 3 half-lives. Second-order rate constants

$$\text{rate} = k_{\text{obsd}}[\text{substrate}] \quad (2)$$

($k_{\text{obsd}}/[Q^+Y^-]_{\text{org}}$) are reported in Table I.

Reaction 1 was also studied by working with sodium hydroxide (30–50%), potassium hydroxide (30–60%), and sodium fluoride (50%) aqueous solutions added to the inorganic salt, which is the source of the nucleophile. The reactions were carried out at 35 °C with the series of tetraoctylammonium salts **4a**–**d** as catalysts, in the presence of the corresponding inorganic salts (inorganic salt/substrate ratio 5:1).[8]

Under these conditions some of the inorganic salt remains undissolved; furthermore, a study of the partition coefficients showed that, in the case of N_3^-, Br^-, and I^- anions, the whole of quaternary cation **4** is associated with the nucleophile Y^- in the organic phase.[3] The mesylate ion formed in the course of the reaction is quantitatively transferred into the aqueous phase, and equilibrium 3 is totally shifted to the right.

$$(Q^+MeSO_3^-)_{\text{org}} + (Y^-)_{\text{aq}} \rightleftharpoons (Q^+Y^-)_{\text{org}} + (MeSO_3^-)_{\text{aq}} \quad (3)$$

These reactions also follow regular pseudo-first-order kinetics, (eq 2), except for the reaction with the chloride ion. In the latter case the mesylate ion stays in the organic phase associated with the quaternary cation to reach, after about $^1/_3$ of the reaction, a 4:1 $(Q^+MeSO_3^-)_{\text{org}}/(Q^+Cl^-)_{\text{org}}$ ratio. This ratio remains constant throughout the reaction (100% conversion) (Figure 1). The plot of the integrated pseudo-first-order kinetic equation (log [substrate] vs. time) shows an initial upward curvature which becomes linear for conversions higher than 30%. Second-order rate constants have been evaluated by considering the actual Q^+Cl^- **4b** concentration present at different times in the organic phase. The data collected in these experiments are reported in Table II. Values for aqueous NaOH (30–40%), KOH (30–60%), and NaF (50%) solutions were obtained with bromide ion as the nucleophile.

So that these different systems could be directly compared, reaction rates were also measured in anhydrous chlorobenzene

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(8) Ancillary experiments showed that, in the presence of concentrated NaOH aqueous solutions, phosphonium salts readily decompose, even at room temperature. On the other hand, the corresponding ammonium salts are markedly more stable, and their decomposition rate at 35 °C can be considered negligible.

Table II. Second-Order Rate Constants for Nucleophilic Substitutions of Methanesulfonate by Anions (Y^-) in *n*-Octyl Methanesulfonate in the Presence of $(C_8H_{17})_4N^+Y^-$ at 35 °C

	phase-transfer conditions			
	PhCl-H_2O[a]			
Y^-	(10^3k), M^{-1} s^{-1}[d,e]	hydr state *n* of $Q^+Y^-\cdot nH_2O$[f]	PhCl-50% aq NaOH[b] (10^3k), M^{-1} s^{-1}[d,e]	homogeneous conditions anhyd PhCl[c] (10^3k), M^{-1} s^{-1}[e]
N_3^-	2.9	3.0 ± 0.2	11.6	11.7
Cl^-	0.26	3.4 ± 0.2	3.4	3.4
Br^-	0.42	2.1 ± 0.2[g]	1.1 (0.43)[h]	1.1
I^-	0.29	1.0 ± 0.15	0.42	0.45

[a] A chlorobenzene solution (20 mL) of substrate (6×10^{-1} M) and of $(C_8H_{17})_4N^+Y^-$ ($2\text{-}4 \times 10^{-2}$ M) and an aqueous solution (15 mL) of potassium salt (4.2 M) (sodium salt in the case of N_3^-). [b] Same amounts of PhCl, substrate, and $(C_8H_{17})_4N^+Y^-$ as in *a*, with 50% aqueous NaOH (15 mL) in the presence of KY (63 mmol), partially as solid phase. [c] [Substrate] = $2\text{-}6 \times 10^{-2}$ M, $[(C_8H_{17})_4N^+Y^-] = 3\text{-}4 \times 10^{-2}$ M. [d] *k* is defined as $k = k_{obsd}/[(C_8H_{17})_4N^+Y^-]_{org}$. [e] Average of at least three runs. [f] Average of at least four determinations. [g] The same value was found in the system PhCl-50% aqueous NaF. [h] PhCl-50% aqueous NaF.

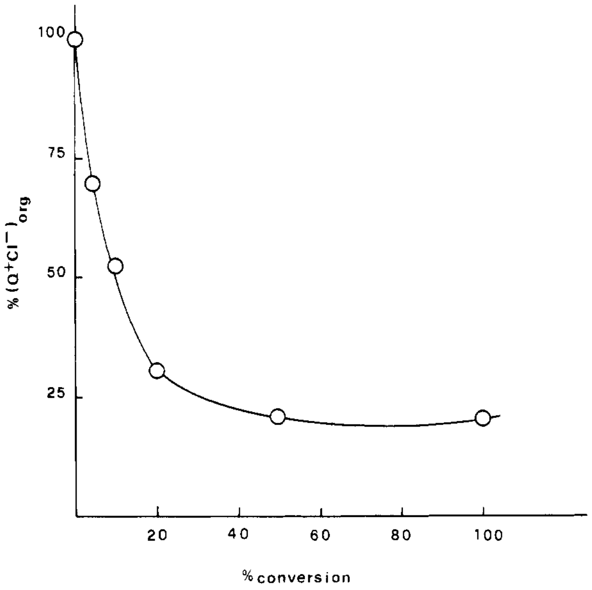

Figure 1. Dependence of the amount of Cl^- associated with tetraoctylammonium cation (4) in the organic phase on the percent conversion for the displacement of the methanesulfonate group with chloride ion in a PhCl-50% aqueous NaOH two-phase system at 35 °C. For the reaction conditions see footnote *b*, Table II.

solution (working with comparable concentrations of substrate and quaternary salt) as well as under classic liquid-liquid PTC conditions.[3] Table II shows the data obtained in these experiments.

The hydration state of the anions in the organic phase was determined for all the two-phase systems (Table I-III).

The NMR spectra of the reaction mixture (100% conversion) showed that the products were consistent with a normal nucleophilic substitution reaction; namely, even in reactions carried out in the presence of strongly alkaline aqueous solutions under PTC conditions, no elimination and/or hydrolysis products were observed. Blanck experiments showed that in the conditions used for kinetic runs no appreciable amount of OH^- is transferred into the organic phase. This is in agreement with the very unfavorable extraction coefficient of hydroxide ion in low-polarity media with respect to that of other common anions (Cl^-, Br^-, I^-, N_3^-, etc.).[7]

Discussion

In principle, the hydration of anions in the organic phase could be reduced by using highly concentrated aqueous solutions of the inorganic salt. As discussed above, this would enhance, as a first consequence, the anionic reactivity. However, even wide variations in salt concentration in the aqueous phase did not affect the second-order rate constants (Table I) or the hydration of the anion associated with the quaternary cation in the organic phase. In particular the Br^- hydration number was found to be 2.[2,3] The only effect of the inorganic salt concentration increase was an increase in the pseudo-first-order rate constants observed with onium salts **2c** and **3c**, partially soluble in the aqueous phase. This is due to a more favorable partition coefficient (salting out) of the catalyst with respect to the organic phase (Figure 2).[9] Indeed, second-order rate constants, which take into account the actual concentration of the catalyst in the organic phase, remained unchanged even in the case of **2c** and **3c** (Table I).

Table III. Effect of the Base Concentration in the Aqueous Phase on the Second-Order Rate Constants of the Reaction of *n*-Octyl Methanesulfonate with Bromide Ion[a] under Phase-Transfer Conditions[b]

base	% base	hydr state *n* of $Q^+Y^-\cdot nH_2O$[c]	10^3k, M^{-1} s^{-1}[d,e]
NaOH	30	2.0 ± 0.2	0.45
	40	1.0 ± 0.15	0.80
	50	$\leqslant$0.2	1.13
KOH	30	1.9 ± 0.2	0.49
	40	1.3 ± 0.15	0.75
	50	0.8 ± 0.10	0.83
	60	$\leqslant$0.2	1.18

[a] From $(C_8H_{17})_4N^+Br^-$. [b] In the system PhCl-aqueous base; for the reaction conditions see footnotes *a* and *b* of Table II. [c] Average of at least four determinations. [d] *k* is defined as $k = k_{obsd}/[(C_8H_{17})_4N^+Br^-]$. [e] Average of at least three runs.

An effective system to have unsolvated anions in the organic phase proved to be the addition to the aqueous solutions of the highly hydrophilic NaOH or KOH. The anionic reactivity under liquid-liquid PTC conditions with 50% NaOH and 60% KOH aqueous solutions was identical, indeed, with that found under anhydrous homogeneous conditions, the reactivity enhancements with respect to the classic PTC being 13.0, 4.0, 2.6, and 1.4 times for Cl^-, N_3^-, Br^-, and I^-, respectively (Tables II and III). In agreement with these results hydration measurements showed that, under these conditions, *nonhydrated anions* are transferred from the aqueous to the organic phase. Such behavior is peculiar for highly concentrated alkaline solutions (NaOH ≥ 50%, KOH ≥ 60%). At lower concentrations, as shown in Table III for Br^-, the anion associated with the quaternary cation in the organic phase retains some of the hydration sphere, progressively in-

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(9) Analogous behavior was also observed by other authors.[6,10,11]

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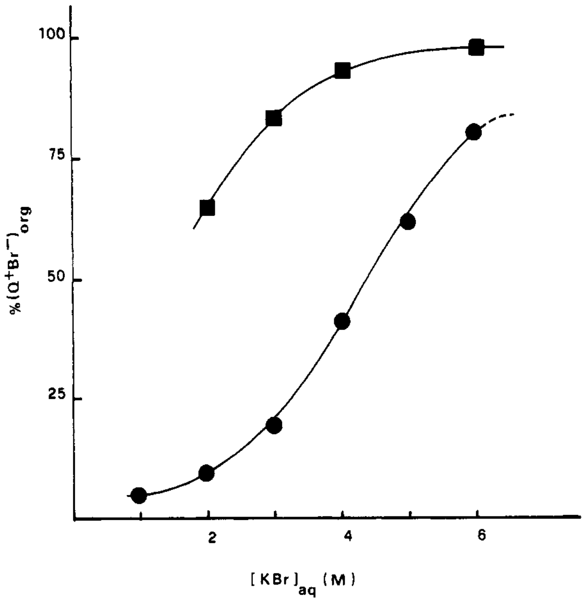

Figure 2. Dependence of the distribution of quaternary onium salts **2c** and **3c** on the KBr aqueous concentration in PhCl–H_2O two-phase system at 60 °C: $Bu_4P^+Br^-$ (**2c**) (■); $Bu_4N^+Br^-$ (**3c**) (●) (20 mL of a chlorobenzene solution of onium salts **2c** and **3c** (4×10^{-2} M) and 20 mL of an aqueous solution at various concentrations (1–6 M) of KBr).

creasing as the alkali concentration decreases. It eventually reaches the typical value for classic PTC,[2,3] i.e., 2 molar equiv, for a ≃30% concentration of base. The anionic reactivity thus decreases as the hydration number increases.

Highly concentrated solutions of analogously hydrophilic salts (50% NaF)[12,14] did not show a similar dehydrating effect: in this case, hydration state and anionic reactivity of bromide ion were identical with those in classical PTC (Table II).

Our results clearly show the desolvating power of highly concentrated NaOH and KOH solutions. Since the cation, Na^+ or K^+, is common to all the solutes examined, the different behavior of NaOH and KOH with respect to other salts (NaF and KBr) must be a consequence of a greater hydration energy ($-\Delta H$) of OH^- compared with the hydration energy of Br^- and F^-, i.e., $-\Delta H_{Br^-} < -\Delta H_{F^-} < -\Delta H_{OH^-}$. Gas-phase hydration values[13-15] for Br^-, F^-, and OH^- are consistent with this hypothesis. Namely it has been shown[13] that for a hydration number $n \geq 3$, $-\Delta H_{OH^-}$ becomes greater than $-\Delta H_{F^-}$, although for $n < 3$ the hydration enthalpies for F^- and OH^- are similar.

In conclusion, we have found an effective system for inhibiting, under PTC conditions, the hydration of the nucleophile in the organic phase by using concentrated aqueous solutions of a highly hydrophilic anion, OH^- being peculiar in producing conditions of a virtually null water activity.

Experimental Section

Nuclear magnetic resonance spectra were recorded on a Varian EM-390 90-MHz spectrometer with tetramethylsilane as internal standard. Potentiometric titrations were carried out with a Metrohm Titroprocessor E636 using silver and calomel electrodes, the latter isolated with a potassium sulfate bridge.

Materials and Solvents. *n*-Octyl methanesulfonate, bp 112–114 °C (2 mm), $n^{20}{}_D$ 1.4398, was prepared according to the literature [lit.[16] bp 110–114 °C (2 mm), $n^{20}{}_D$ 1.4392]. Inorganic salts were Analar grade commercial products used without further purification. Quaternary onium salts **1–4c** were commercially available and were purified by crystallization and dried in a vacuum desiccator before use. The ammonium salts **4a,b,d** were obtained from the commercially available tetraoctylammonium perchlorate (**4e**) by exchange with the appropriate anion according to a previously described procedure.[17] Many of these salts are hygroscopic and must be stored in a desiccator. Chlorobenzene was Analar grade chemical solvent used without further purification in the experiments carried out under liquid–liquid PTC conditions. For the reactions performed under anhydrous conditions it was carefully purified and dried by standard methods.[18] Karl Fischer analyses showed a water content ≤40 ppm.

Kinetic Measurements. The apparatus used for kinetic measurements under phase-transfer conditions has been previously described.[3] In a typical procedure, the reaction flask was charged with 15 mL of an aqueous solution of inorganic salt (4.2 M), 10 mL of chlorobenzene solution of *n*-octyl methanesulfonate (1.2 M) and benzyl phenyl ether (0.8 M) as internal standard, and 10 mL of chlorobenzene solution of catalyst ($4–8 \times 10^{-2}$ M). Stirring and timing were started. Samples of organic phase were withdrawn at various times by stopping the stirrer for 40–60 s to allow adequate separation. These were quenched by cooling in an ice bath and analyzed by ^1H NMR spectroscopy. Reaction rates were measured by following the disappearance of the triplet (CH_2OSO_2Me) centered at δ 4.05 and using the singlet at δ 4.80 (OCH_2Ph) as standard. The pseudo-first-order rate constants (k_{obsd}) were obtained by plotting log [substrate] vs. time and determining the slope of the straight lines. The second-order rate constants k were evaluated by dividing k_{obsd} by the catalyst concentration in the organic phase.

In the kinetic measurements carried on in the presence of NaOH, KOH, and NaF, aqueous solutions of these salts (15 mL) were added with 63 mmol of KY in the reaction flask thermostated at 35 ± 0.1 °C. In the case of aqueous NaOH or KOH (30–60%) KY was not completely soluble.

In the kinetic measurements under anhydrous homogeneous conditions standardized chlorobenzene solutions (10 mL) of *n*-octyl methanesulfonate ($4–15 \times 10^{-2}$ M) were added to a standardized solution (15 mL) of quaternary salt ($5–7 \times 10^{-2}$ M) in a 50-mL flask thermostated at 35 ± 0.1 °C. Samples (2 mL), withdrawn periodically, were quenched in ice-cold MeOH (50 mL), and the unchanged nucleophile was determined by using 0.01 N silver nitrate (potentiometric titration). The second-order rate constants were evaluated by using a least-squares analysis computer program, as previously described.[3]

Hydration State of Quaternary Salts. The state of hydration of quaternary salts **4a–c** was determined by stirring 20 mL of a standardized solution of the onium salt ($2–4 \times 10^{-2}$ M) for 30 min with 15 mL of an aqueous solution of the appropriate inorganic salts in a flask thermostated at 35 or 60 ± 0.1 °C. Stirring was stopped and aliquots of the organic layer were withdrawn at intervals until a constant content of water was measured (Karl Fischer, 1–3 h). Concentration of quaternary salt in the organic layer was measured in parallel by potentiometric titration.

Distribution Coefficients. The distribution coefficients for quaternary salts **1–3c** were determined by stirring 20 mL of a standardized chlorobenzene solution of onium salt (4×10^{-2} M) with 20 mL of an aqueous solution at various concentration (1–6 M) KBr in a flask thermostated at 60 ± 0.1 °C. Samples of the organic phase were withdrawn at various times by stopping the stirrer for 1–5 min, to allow separation of the organic phase

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sufficient to get a good sample, and titrated on 0.01 N silver nitrate (potentiometric titration). Results are reported in Figure 2.

In the case of onium salts **4a,c,d** equilibrium 3 was studied in the same condition as for the kinetic measurements, adding to the system 12 mmol of potassium methanesulfonate corresponding to the amount formed in reaction 1 at 100% conversion. For **4b** equilibrium 3 was studied at the following percents of reaction 1: 5, 10, 20, 50, 100% (Figure 1).

Registry No. **1c**, 14937-45-2; **2c**, 3115-68-2; **3c**, 1643-19-2; **4a**, 81389-83-5; **4b**, 3125-07-3; **4c**, 14866-33-2; **4d**, 16829-91-7; octyl methanesulfonate, 16156-52-8.

Preparation and Rearrangement of 1,2-Dialkenylcyclobutanols. A Useful Method for Synthesis of Substituted Cyclooctenones

Robert C. Gadwood* and Reneé M. Lett

Department of Chemistry, Northwestern University, Evanston, Illinois 60201

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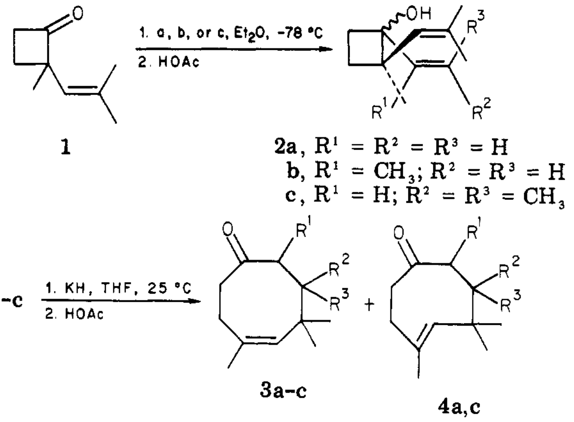
The syntheses and anionic oxy-Cope rearrangements of 1,2-dialkenylcyclobutanols are reported. Reaction of 2-methyl-2-(2-methylpropen-1-yl)-1-cyclobutanone (**1**) with vinyl-, isopropenyl-, or isobutenyllithium led to formation of cyclobutanols **2a–c**. Treatment with potassium hydride induced rearrangement to *Z* and *E* cyclooctenones **3a–c** and **4a,c**. Reaction of 5-methylenespiro[3.5]nonan-1-one (**8**) with the same alkenyllithium reagents afforded directly a mixture of rearranged and ring-opened products (**11a–c** and **12a–c**). Reaction of spiro[3.5]non-5-en-1-one (**17**) with vinyl- or isopropenylmagnesium bromide produced a mixture of diastereomeric cyclobutanols **18a,b** and **19a,b** which underwent anionic oxy-Cope rearrangement to bicyclo[5.3.1]undec-1-(11)-en-4-ones **20a,b** in high yield. A mechanism for the rearrangement of stereodistal 1,2-dialkenylcyclobutanols is proposed.

There are several important classes of natural products which contain eight-membered rings. Cyclooctanes appear in the fused-ring systems of the ophiobolin,[1] ceroplastol,[2] cotylenol,[3] and fusiococcin[4] families of natural products and also in the bridged, bicyclic skeletons of pleuromutilin[5] and taxol.[6]

Syntheses of cyclooctanes from acylic precursors tend to be only marginally successful[7] due to unfavorable entropic factors as well as large increases in enthalpy resulting from transannular and torsional strain. Somewhat more successful preparations of cyclooctanes have involved one- and two-carbon ring expansions of cycloheptanes[8] and cyclohexanes,[9] respectively, and also fragmentation of bicyclic precursors.[8,10] However, these reactions are far from general, and new methodology for cyclooctane synthesis is needed. We report the results of our investigation of a novel and versatile cyclooctane synthesis based upon ring expansion of cyclobutane precursors.

Scheme I



1

2a, $R^1 = R^2 = R^3 = H$
b, $R^1 = CH_3$; $R^2 = R^3 = H$
c, $R^1 = H$; $R^2 = R^3 = CH_3$

2a–c

3a–c

4a,c

[a] (a) $CH_2{=}CHLi$, (b) $CH_2{=}C(CH_3)Li$, (c) $(CH_3)_2C{=}CHLi$.

The Cope rearrangement of *cis*-1,2-divinylcyclobutane has been studied in detail by Berson and others.[11,12,16] Driven by a significant release of ring strain, this rearrangement occurs at much lower temperatures than the acyclic variant. We felt that the anionic oxy-Cope version of this rearrangement would be particularly suitable as a general method for the synthesis of substituted cyclooctenones for several reasons: (1) the required dialkenylcyclobutanols could, in principle, be prepared directly from readily available 2-alkenylcyclobutanones;[13] (2) rearrangement should be possible under mild conditions (room temperature or below) due to the accelerating effect

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