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COMPARISON OF UNSTIRRED, SONICATED AND STIRRED MIXTURES ON THE TWO-PHASE DISPLACEMENT OF HALIDE BY THIOCYANATE ION

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Abstract: The two-phase catalytic reaction of alkyl halides with aqueous thiocyanate ion has been found to proceed readily in stirred, unstirred, and sonicated solutions.

The two-phase catalytic nucleophilic displacement reactions have become commonplace in recent years.[1] Usually such reactions are conducted by rapidly stirring a two-phase mixture in the presence of a suitable catalyst such as a tetraalkylammonium salt.

We have found that the two-phase catalyzed displacement of halide by thiocyanate ion to form the alkylthiocyanate proceeds smoothly and in good yield <u>without</u> stirring. As reported in Table I, several catalysts and substrates have been studied. As noted, a tremendous variance in catalytic activity has been observed. As previously observed in phase transfer catalyzed reactions[2], the highly lipophilic symmetrical catalysts appear to be the most efficient in the unstirred reactions. Tetraheptylammonium bromide was the most efficient of the catalysts studied. The magnitude of this difference was most pronounced with the longer chained primary alkyl halides. Unstirred reactions conducted at room temperature were not successful with trihexylamine as a catalyst. As noted earlier[3], this lack of reactivity is possibly due to failure to generate the tetraalkylammonium salt.

A brief study of unstirred reactions comparing catalyst concentration (1.66%, 3.33%, 6.67%, 10% molar) and interfacial surface area with reaction rate shows that the rate increases with both increased catalyst concentration and with increased interfacial surface area. While the catalyst concentration does seem to vary linearly with the rate of product formation, no simple quantitative relationship has been found which relates interfacial surface area with reaction rate. Calculations using spherical packing suggest that in all cases 10^3 to 10^4 times more catalyst is present to cover completely the interfacial surface if the catalyst is distributed at the interface.

The thiocyanate ion displacement of bromide and iodide from the n-butyl

Table I--Thiocyanate Production in Unstirred Two-Phase Reactions

Starting Material	% Yield[8]			Catalyst
	Time/hrs 4	8	24	
n-Butyl Bromide	4	13	51	TBAB
	15	30	59	THAB
	8	24	43	A336
	3	2	0	TBAC
	---	---	4	NONE
n-Pentyl Bromide	7	14	42	TBAB
	85	72	72	THAB
	81	73	50	A336
	0	1	2	TBAC
	---	---	1	NONE
n-Hexyl Bromide	7	10	34	TBAB
	8	25	68	THAB
	3	20	37	A336
	---	---	<1	TBAC
	---	---	<1	NONE
n-Octyl Bromide	2	2	6	TBAB
	15	21	39	THAB
	7	18	35	A336
	---	---	<1	TBAC
	---	---	<1	NONE
isoPropyl Bromide	4	9	21	TBAB
	6	9	22	THAB
	3	7	31	A336
	3	8	17	TBAC
	---	---	<1	NONE
Allyl Bromide*	43	63	70	TBAB
	82	85	83	THAB
	89	88	83	A336
	52	87	93	TBAC
	---	---	84	NONE

* % product composed of both isothiocyanate and thiocyanate

Catalyst key:
TBAB = tetrabutylammonium bromide
THAB = tetraheptylammonium bromide
A336 = tricaprylylmethylammonium chloride
TBAC = benzyltriethylammonium chloride

substrate has been studied with several catalysts. The reaction rates of unstirred, magnetically stirred, and ultrasonically irradiated mixtures with both levels below the ultrasound liquid level are compared (Table II). As expected, both stirring and sonicating produced substantial rate increases in the catalyzed reactions. It was also noted that differences in catalytic efficiencies were diminished in the agitated solutions.

The reaction mixture (1.05×10^{-3} mol alkyl halide, 6.2×10^{-4} mol catalyst, 0.5 ml cyclohexane as internal standard, and 3.1 molar excess of 50% aqueous KSCN) was monitored by gas chromatography with a 12' X 1/8" stainless steel column packed with a UCON oil 50HB 2000 in a 10% chrom.W 60/80 M. Samples taken during

Table II--Thiocyanate Ion Displacements from n-Butyl Substrates

Compound yield/hr	% Yield			Catalyst
	Time/hrs 2	6	18	
n-Butyl Bromide stand	11	29	70	TBAB
	15	36	78	THAB
	11	26	59	A336
	4	20	53	TBPA
	---	---	<1	NONE
stir	8	43	97	TBAB
	53	70	96	THAB
	8	33	87	A336
	17	45	82	TBPA
	---	---	8	NONE
ultrasound	22	62	97	TBAB
	13	58	94	THAB
	6	43	89	A336
	28	74	95	TBPA
	---	---	19	NONE
	Time/hrs 1	2	6	
n-Butyl Iodide stand	3	25	75	TBAB
	10	43	86	THAB
	11	16	73	A336
	2	64	85	TBPA
	---	---	2	NONE
stir	15	38	90	TBAB
	53	79	93	THAB
	12	37	93	A336
	18	40	91	TBPA
	---	---	5	NONE
ultrasound	16	38	77	TBAB
	---	50	90	THAB
	16	40	90	A336
	31	52	86	TBPA
	---	---	3	NONE

Catalyst Key:
TBAB = tetrabutylammonium bromide
THAB = tetraheptylammonium bromide
A336 = tricaprylylmethylammonium chloride
TBPA = tetrabutylphosphonium acid acetate

the reaction did not affect the organic/aqueous volume ratio. Chromatographic column temperatures ranged from 60 to 140°. Reactions in Table I were run in 20 X 150 mm test tubes lain horizontally, while those in Table II were run in 50 ml Erlenmeyer flasks.

Recently, reports have appeared demonstrating the effect of ultrasound on non-catalyzed two-phase reactions.[5,6] Our results differ in that a catalyst is necessary for appreciable formation of product. While we have noted a rate acceleration in the presence of ultrasound irradiation, current results do not differentiate among rate increases due to cavitation, agitation, or a combination of the two. Furthermore, it should be noted that a slight temperature increase

(7 ± 1°C) occurred during the ultrasound reactions.

The most surprising aspect of this study was the occurrence of facile nucleophilic displacement reactions in undisturbed solutions. While the thiocyanate ion is distributed into the lipophilic layer[7], it was found that other anion such as cyanide will also function as nucleophiles in undisturbed solutions even though these have less affinity for the organic media.[1a] Even with this distribution of ions into the lipophilic media, it should be emphasized that a phase transfer catalyst is essential for significant reaction.

Finally, this result suggest a word of caution for those who would attempt to interrupt or stop a phase transfer catalyzed reaction simply by discontinuing stirring.

We are currently examining other nucleophiles and substrates to ascertain the scope and limitations of these phenomena.

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References and notes:

1. a.) Dehmlow, E.V., and Dehmlow, S.S., Phase Transfer Catalysis, Verlag Chemie, Deerfield Beach, Florida, 1980. b.) Weber, W.P., and Gokel, G.W., Phase Transfer Catalysis in Organic Synthesis, Springer-Verlag, New York, 1977. c.) Starks, C.M., and Liotta, C., Phase Transfer Catalysis, Academic Press, New York, 1978.
2. Reeves, W.P., Bothwell, T.C., Rudis, J.A., and McClusky, J.V., Synthetic Communications, 12(13), 1071 (1982).
3. Reeves, W.P., and Hilbrich, R.G., Tetrahedron 2235 (1976).
4. Sonication experiments were conducted in a Branson Ultrasonic Laboratory Cleaner.
5. Regen, S.V., and Singh, A., J. Org. Chem., 1982, 47, 1587.
6. Moon, S., Duchin, L., and Cooney, J.V., Tetrahedron Lett., 1979, 3917.
7. Makosza, M., Two-Phase Reactions in Organic Chemistry, in "Survey of Progress on Chemistry", Vol. 9; Arthur F. Scott, Ed.; Academic Press, New York, 1980; p. 8.
8. Yields were determined by gas chromatographic analysis using cyclohexane as internal standard.

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