Communications

Alumina As a Triphase Catalyst[1]

Summary: Commercial grade neutral alumina has been found to catalyze iodide, chloride, cyanide, and acetate displacement on 1-bromooctane as well as permanganate oxidation of alcohols conducted as solid–liquid–solid reactions.

Sir: Triphase catalysis is receiving growing interest as a synthetic technique complementary to phase-transfer catalysis.[2-4] Until now, all triphase catalysts reported in the literature have been based on insoluble polymers or surface-functionalized inorganic supports where catalytically active sites were covalently attached. In the course of related studies,[5] we have discovered that *commercial grade neutral alumina can catalyze solid–liquid biphase reactions*.[6,7] Data which we now provide demonstrate the extraordinary ability of this common support material to function as a triphase catalyst in solid–liquid–solid systems,[8] and also show that this chemistry is broad in scope.

When 0.5 g of neutral alumina and 0.75 g (5.0 mmol) of sodium iodide were suspended in 4.0 mL of a toluene solution which was 0.25 M in 1-bromooctane, and the resulting mixture was heated to 90 °C for 24 h with vigorous stirring, analysis of the liquid phase by GLC indicated a 95% conversion to 1-iodooctane.[9-11] Similar experiments carried out in the absence of alumina showed no loss of the alkyl bromide in the organic phase after heating for 40 h at 90 °C. Displacement was also attempted when alumina and sodium iodide were physically separated by means of adjoining culture tubes (Figure 1).[12] No evidence of reaction could be detected after stirring for 40 h at 90 °C under these conditions. The latter result indicates that intimate physical contact between alumina and the reagent is important for catalysis.

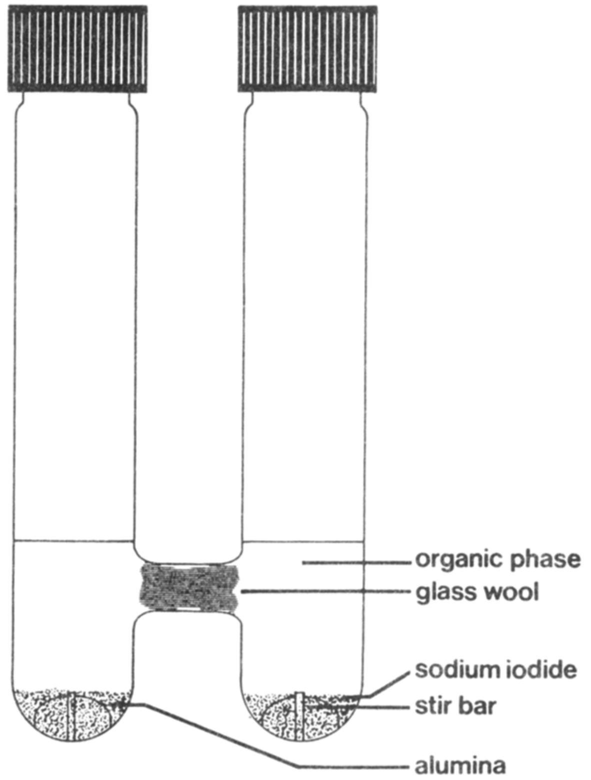

Figure 1. Adjoining culture tubes (Corning No. 9826, 25 × 150 mm) containing 1-bromooctane in toluene, alumina, sodium iodide, and two Teflon-coated magnetic stirring bars ($^{1}/_{2} \times {}^{5}/_{16}$ in. octagonal bar with pivot ring).

We have also found that alumina catalyzes a series of related displacement reactions as well as permanganate oxidation of alcohols. Our results are summaried in Table I. Also included are the results obtained using silica gel as the catalyst. In nearly all cases alumina was found to have superior activity. For purposes of comparison, we have carried out chloride, cyanide, iodide, and acetate displacement on 1-bromooctane conducted as solid–liquid phase-transfer reactions using 1,4,7,10,13,16-hexaoxacyclooctadecane (18-crown-6) as the catalyst. Data reported in Table II reveal that the crown ether catalyst yielded greater rates with acetate and iodide as the nucleophile, while alumina was more effective for chloride and cyanide displacement. It is noteworthy that triphase catalytic oxidation of alcohols using alumina–toluene–$KMnO_4$ is milder, experimentally simpler, and more amenable to large-scale synthesis than impregnated permanganate reagents previously described.[5] A preparative-scale oxidation of cyclododecanol is illustrative. When 5.0 g of

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(1) Supported by the National Science Foundation (Grant No. CHE-77-28366).

(2) For a description of the triphase catalytic method see, Regen, S. L. *J. Am. Chem. Soc.* **1975**, *97*, 5956.

(3) Review of triphase catalysis: Regen, S. L. *Angew. Chem., Int. Ed. Engl.* in press.

(4) For a detailed discussion of phase-transfer catalysis, see: Weber, W. P.; Gokel, G. W. "Phase-Transfer Catalysis in Organic Synthesis"; Springer-Verlag: New York, 1977. Dehmlow, E. V. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 493. Brandstrom. A. *Adv. Phys. Org. Chem.*, **1977**, *15*, 267.

(5) Regen, S. L.; Koteel, C. *J. Am. Chem. Soc.*, **1977**, *99*, 3837.

(6) Neutral alumina used in this study was purchased from Bio-Rad Laboratories, Richmond, California (AG-7, 100-200 mesh).

(7) For a recent review dealing with alumina in organic chemistry, see: Posner, G. H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 487. An interesting use of alumina related to the chemistry described herein is the catalytic displacement on alkyl halides by carboxylic acids: McNulty, J. G.; Walsh, W. L. U. S. Patent 3 510 499, May 5, 1970. We are grateful to a referee for bringing the latter to our attention.

(8) Polymers have previously been employed in solid–liquid–solid triphase catalytic systems: Regen, S. L.; Nigam, A; Besse, J. J. *Tetrahedron Lett.* **1978**, 2757. McKenzie, W. M.; Sherrington, D. C. *J. Chem. Soc., Chem. Commun.* **1978**, 541. Yanagida, S.; Takahashi, K.; Okahara, M. *J. Org. Chem.* **1979**, *44*, 1099. Activated charcoal has been used in liquid–solid–liquid triphase catalytic reactions: Starks, C. M.; Johnson, M. A.; Yang, K. U. S. Patent 3 839 399, Oct. 1, 1974. Johnson, M. A.; Yang, K. U. S. Patent 3 812 211, May 21, 1974. Johnson, M. A.; Starks, C. M.; Yang, K. U. S. Patent 3 994 985, Nov. 30, 1976.

(9) Both alumina and inorganic salts used in this study were pulverized together in a mortar prior to addition. In general, we have found comparable results when reagent and alumina are ground together or separately.

(10) All experiments reported in this paper were carried out in 50-mL culture tubes (Corning No. 9826, 25 × 150 mm). Stirring was accomplished by means of a $^{1}/_{2} \times {}^{5}/_{16}$ in. octagonal Teflon-coated stirring bar with a pivot ring.

(11) Product mixtures were analyzed by GLC on a Hewlett-Packard Model 5830 A flame ionization instrument. In all cases, an internal standard was added to each mixture prior to GLC analysis.

(12) In this experiment, 1.0 g of neutral alumina and 1.5 g of sodium iodide were placed separately in each chamber of the "H" tube and allowed to react with 20 mL of 0.1 M 1-bromooctane in toluene. Both alumina and sodium iodide were stirred vigorously by means of a Teflon-coated stirring bar.

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Table I. Alumina and Silica Gel as Triphase Catalysts[a]

reagent	reactant	product	temp, °C	time, h	yield, %[b] alumina	yield, %[b] silica gel
NaI	1-bromooctane	1-iodooctane	90	24	95	24
				44	100 (98)[d]	
KI	1-bromooctane	1-iodooctane	90	44	95	
LiCl	1-bromooctane	1-chlorooctane	90	68	10	9
NaCl	1-bromooctane	1-chlorooctane	90	68	1	0
KCl	1-bromooctane	1-chlorooctane	90	68	15	0
KCl	1-iodooctane	1-chlorooctane	90	68	4	
NH_4Cl	1-bromooctane	1-chlorooctane	90	68	30	2
NaCN	1-bromooctane	1-cyanooctane	90	68	38[c]	6
KCN	1-bromooctane	1-cyanooctane	90	68	65[c]	6
KCN	1-iodooctane	1-cyanooctane	90	68	6	
NaOAc	1-bromooctane	octyl acetate	90	68	0	0
KOAc	1-bromooctane	octyl acetate	90	100	89	7
KOAc	1-iodooctane	octyl acetate	90	68	13	
$KMnO_4$	cyclododencanol	cyclododencanone	25	20	95	
			25	40	100[e] (95)[d]	
$KMnO_4$	2-octanol	2-octanone	25	20	100	

[a] Unless stated otherwise, reactions were carried out by stirring 0.5 g of alumina, 5.0 mmol of reagent, plus 1.0 mmol of reactant dissolved in 4 mL of toluene in a 50-mL culture tube using the indicated temperature and reaction time. Control experiments carried out for each reaction in the absence of alumina showed no loss of starting material. [b] Yields were determined by GLC using internal standards. Mass balance in all cases was >95%. [c] A small yield (~10%) of 1-octanol plus an unidentified side product were also formed. [d] Isolated yield from preparative-scale reaction using procedures described in the text. [e] Control experiments carried out without alumina showed 3% oxidation when the concentration of alcohol was 0.1 M after 48 h and 20% oxidation of 0.5 M cyclododecanol in toluene after 72 h.

Table II. Solid-Liquid Phase-Transfer Catalyzed Displacement[a]

reagent	reactant	product	time, h	yield, %[b]
KI	1-bromooctane	1-iodooctane	4	85
KOAc	1-bromooctane	octyl acetate	20	70
KCl	1-bromooctane	1-chlorooctane	47	3
KCN	1-bromooctane	1-cyanooctane	47	23
KOAc	1-iodooctane	octyl acetate	20	34

[a] Reactions were carried out by stirring 1.0 mmol of the reactant, 5.0 mmol of reagent, plus 0.1 mmol of 18-crown-6 in 5 mL of toluene in a 50-mL culture tube at 90 °C for the indicated reaction time. [b] Yields were determined by GLC using internal standards. Mass balance in all cases was >95%.

neutral alumina plus 7.9 g (50.0 mmol) of $KMnO_4$ were suspended in 50 mL of toluene containing 1.84 g (10.0 mmol) of cyclododecanol and the reaction mixture was stirred at room temperature for 30 h, analysis of the liquid phase by GLC indicated complete conversion to cyclododecanone. The ketone was isolated by filtering the product mixture through Celite, washing the spent and unused reagent plus alumina with 100 mL of toluene, and removing the solvent from the combined filtrate under reduced pressure yielding 1.75 g (95%) of cyclododecanone as a colorless solid which melted at 58–59 °C.[13] The IR and ^{1}H NMR spectra were identical with those of an authentic sample.

Although we have only begun to examine the full scope of this chemistry, preliminary results reveal unusual selectivity features. Specifically, 1-bromooctane exhibits significantly greater reactivity toward nucleophilic displacement by chloride, cyanide, and acetate ion as compared to 1-iodooctane (Table I). Thus stirring 1 mmol each of 1-bromooctane and 1-iodooctane dissolved in 7 mL of toluene with crushed potassium acetate (0.5 g, 5.0 mmol) plus 0.5 g of neutral alumina converted 60% of the organic bromide and 0% of the organic iodide to octyl acetate.[14]

The mechanistic details underlying these complex three-phase reactions are not presently understood and kinetic as well as stereochemical studies are now underway in an effort to elucidate the nature of the catalysis. Nonetheless, the low cost and ready availability of alumina, coupled with the experimental simplicity associated with its use, strongly suggest that it will be of considerable value as a triphase catalyst.

Registry No. Alumina, 1344-28-1; silica gel, 7631-86-9; 1-bromooctane, 111-83-1; 1-iodooctane, 629-27-6; 1-chlorooctane, 111-85-3; 1-cyanooctane, 2243-27-8; octyl acetate, 112-14-1; cyclododecanol, 1724-39-6; cyclododecanone, 830-13-7; 2-octanol, 123-96-6; 2-octanone, 111-13-7; KI, 7681-11-0; LiCl, 7447-41-8; NaCl, 7647-14-5; KCl, 7447-40-7; NH_4Cl, 12125-02-9; NaCN, 143-33-9; KCN, 151-50-8; NaOAc, 127-09-3; KOAc, 127-08-2; $KMnO_4$, 7722-64-7.

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[13] An authentic sample from Aldrich Chemical Co. had mp 57–61 °C.

[14] Surprisingly, similar experiments carried out as solid–liquid phase-transfer reactions using 18-crown-6 gave identical results.

β-Acylvinyl Anion Equivalents: Preparation of 1-Lithio-3-(*tert*-butyldimethylsiloxy)-1,3-cyclohexadiene and Its Reaction with Electrophiles

Summary: 1-Lithio-3-(*tert*-butyldimethylsiloxy)-1,3-cyclohexadiene (**21**), conveniently prepared by transmetalation of the trialkylstannyl derivatives **18** and **20** with methyllithium and *n*-butyllithium, respectively, reacts smoothly with various electrophilic reagents to form, in excellent yields, the corresponding 1-substituted 3-(*tert*-butyldimethylsiloxy)-1,3-cyclohexadienes (**23**).

Sir: Previous work in our laboratory has demonstrated that β-bromo- (**1**) and β-iodo-α,β-unsaturated ketones (**2**)[1] serve as excellent synthetic equivalents of β-acylvinyl cations **3**.[2] For example, treatment of **1** and/or **2** with a

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[1] E. Piers and I. Nagakura, *Synth. Commun.*, **5**, 193 (1975).