Step 2: *meso*-Diethyl 2,5-Dibromoadipate (3). A 2-L three-neck round-bottom flask was equipped with paddle stirrer and thermometer and was cooled in an ice bath. The flask was charged with ethanol (650 mL), and the crude product from the previous step (ca. 1.1 mol) was added to the flask over 45 min with the temperature maintained below 25 °C. The resulting suspension was stirred for 16 h at room temperature and was then cooled to 5 °C for 30 min. the suspension was filtered, the moist cake was reslurried briefly in fresh ethanol (250 mL at 10–15 °C), and the suspension was pulled dry once again. The white solid was dried in a vacuum oven at 30 °C. There was obtained 205 g (52%) of *meso*-3, mp 64–66 °C (lit.[10] mp 65–66 °C). The clear yellow ethanol mother liquors from above were combined and concentrated to a volume of 600 mL. The solution was seeded and was stirred overnight. After being cooled to 10 °C and stirred for 30 min, the slurry that resulted was filtered, and the moist cake was restirred in cold ethanol (150 mL). The product *meso*-3 was obtained by filtration and vacuum drying. Crop 2; 92 g (23%), mp 64–66 °C. Continued concentration of the mother liquors lead to the isolation of an additional 28 g (7%) of *meso*-3 (total yield three crops 325 g, 82%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.19 (4 H, q, J = 6 Hz), 4.19 (2 H, obscured), 2.23 (2 H, m), 2.0 (2 H, m), 1.26 (6 H, t, J = 6 Hz); ^{13}C NMR ($CDCl_3$, 75.429 MHz) δ 169.1, 62.2, 44.7, 32.4, 13.9; IR (KBr) γ 2978, 1729, 1376, 1267, 1158 cm^{-1}; MS m/e 360 (M^+). Anal. Calcd for $C_{10}H_{16}Br_2O_4$: C, 33.36; H, 4.48; Br, 44.39. Found: C, 33.51; H, 4.45; Br, 44.39.

Also prepared by procedures related to that described above were the corresponding *meso*-dimethyl and -dibenzyl adipates:

***meso*-Dimethyl 2,5-dibromoadipate (5):** 83.3% in three crops; mp 75–76 °C (lit.[12] mp 74 °C); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.2 (2 H, dd, J = 8 Hz, J = 6 Hz), 3.73 (6 H, s), 2.22 (2 H, m), 2.0 (2 H, m); ^{13}C NMR ($CDCl_3$, 75.429 MHz) δ 169.6, 53.1, 44.3, 32.4.

***meso*-Dibenzyl 2,5-dibromoadipate (6):** 55.2% in two crops; mp 81–83 °C (lit.[11d] mp 83 °C); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.36 (10 H, s), 5.2 (4 H, s), 4.26 (2 H, dd, J = 6 Hz, J = 4 Hz), 2.28 (2 H, m), 2.05 (2 H, m); ^{13}C NMR ($CDCl_3$, 75.429 MHz) δ 168.9, 135, 128.7, 128.6, 128.3, 67.8, 44.5, 32.4.

Registry No. (±)-3, 124819-16-5; *meso*-3, 54221-37-3; (±)-5, 124819-17-6; *meso*-5, 53490-47-4; (±)-6, 124756-17-8; *meso*-6, 124985-73-5; $ClCO(CH_2)_4COCl$, 111-50-2.

Silica Impregnated with Tetramethylammonium Salts as Solid–Solid–Liquid Triphase Catalysts

Onn Arrad* and Yoel Sasson

The Casali Institute of Applied Chemistry, School of Applied Science and Technology, The Hebrew University of Jerusalem, 91904 Jerusalem, Israel

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Since its introduction, phase-transfer catalysis (PTC) has become a very common synthetic tool. However, the separation of soluble phase-transfer catalysts from the reaction products is usually a laborious step, where many losses occur. In the recent decade much effort has therefore been put in the research of polymer-bound catalysts (triphase catalysis), which were usually based on polystyrene resins.[1-3] Although at first quite promising, this approach has encountered some difficulties,[4,5] and it is rarely used in synthetic chemistry.[4,6] Some of the catalysts are commercially available, but they are quite expensive.[7] Also, separation by filtration and recycling seems to be far from trivial. Their low physical stability makes them prone to pulverization when reaction mixtures are vigorously agitated,[3,4] and they have a tendency to swell and form gels.[3,4] To improve this physical instability of the catalysts, polystyrene has been substituted by inorganic supports such as silica or alumina.[3,8] But these catalysts can be loaded only to a relatively low degree,[9] their preparation requires some synthetic effort, and the supports may catalyze some side reactions by themselves.[10,11] In a different approach, the need of a phase-transfer catalyst is circumvented by impregnation of the inorganic reagent itself on a support, but then, the latter is required in large amounts.[12,13]

It has been shown in this laboratory that tetramethylammonium halides are very active phase-transfer catalysts when polar solvents such as ethanol are employed.[14] These salts are very stable to relatively high temperatures and to strongly basic conditions. The chloride and bromide salts are commercially available in bulk, and because of their low molecular weight they are very cost effective catalysts.[14] Unfortunately most PTC reactions require an apolar reaction medium,[15] and it has been generally accepted that tetramethylammonium halides are not active in such systems, since they are completely insoluble in the respective solvents.[16,17]

We have taken advantage of this fact and impregnated these salts on a commercial silica support. As will be shown below for some model reactions, this combination makes very efficient "triphase catalysts," even with apolar solvents, provided the inorganic reagent is applied as a solid rather than in an aqueous solution, thus preventing the excess hydration of these hydrophylic catalysts. According to the same principle, we have shown recently the potential of some commercial ion exchange resins (of the strongly basic type) as triphase catalysts.[18]

Results and Discussion

Synthetic Features. Alkyl chlorides and bromides in aromatic hydrocarbon have been reacted with alkali salts of iodide, acetate, and formate ions in the presence of (5–7.5 mol %) tetramethylammonium halides (TMAX) impregnated on silica (Silica D 22 of Degussa Co., is a non surface treated precipitated silica;[19] its surface area is due to primary colloidal size[20]). After filtration of the two solid

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phases, clean organic solutions of the products are obtained. GC analysis indicates high yields (Table I). No reaction occurs in the absence of a catalyst. In the presence of only one of the catalyst's components the reaction conversions are less than 5%. Above a certain loading the catalyst's efficiency is strongly reduced. This maximum loading varies between about 10% (weight % of TMACl, 0.9 mequiv/g catalyst) with aliphatic and 25% (2.3 mequiv/g) with benzylic substrates (Table I). In order to avoid any halogen exchange (side) reaction between the catalyst and the substrate, the catalyst was always used with the same halide ion as the leaving group of the substrate (TMACl with benzyl or alkyl chlorides, TMABr with bromooctane).

TMAX impregnated on silica *gel* (its surface area is due to porosity[20]) instead of the colloidal silica shows a similar catalytic activity. Actually, both types of silica have a similar surface composition, containing a relative high percentage of Si–O–H bonds (corresponding to 5–10% per weight water content) even after drying at 120 °C.[20] Various other supports such as hydrophobic (sililated) silica, neutral alumina, and polystyrene are inefficient.

The intrinsic reactivity of the catalytic site is rather low, and therefore elevated temperatures are required to avoid prolonged reaction durations. Thus, with benzyl chloride as substrate, reactions were completed only after 12 h at 120 °C, compared to a few hours at 90 °C with soluble PT catalysts. Accordingly, reactions with nonactivated substrates were performed at 150 °C. At this temperature the catalyst decomposes slowly, and with substrates too sluggish (chloroalkanes) the reactions could not be completed (Table I). This catalyst decomposition has no effect on the purity of the product, since the decomposition products are insoluble in the organic phase. Thus 99.6% pure benzyl formate was isolated (0.4% benzyl alcohol) in 97% yield after neat benzyl chloride and potassium formate were reacted for 2 h at 150 °C.

The catalyst *cannot* be recycled as a unity. The wash water used to remove the inorganic salts formed during the reaction from the solid mixture would also dissolve the hydrophilic TMAX. The catalyst's components can be recovered, however, by washing of the filter cake first with a polar organic solvent (extraction of TMAX) and then with water (removal of the inorganic salts).

Unfortunately the catalysts introduced in this study are generally not applicable to PTC reactions promoted by concentrated base, since the silica support is decomposed under these conditions.[9] For example the etherification of 1-octanol with alkyl chloride comes to a standstill at an intermediate conversion. However, reactions with highly active substrates might be faster than cattalyst decomposition. This is demonstrated by the alkylation of benzyl cyanide, the yield of which increases from less than 1% in the absence of catalyst to 100% on addition of TMACl/silica.

Mechanistic Considerations. The catalysis of the exchange reaction occurs on the silica surface only. Otherwise TMAX salts should be active catalysts even in the absence of a support, or in the presence of any other support. To prove that the reactions were not catalyzed by *any* homogeneous species (e.g. complexes of TMAX and possible impurities introduced with the silica), we interrupted some of the reactions after a few hours, filtered the hot (>100 °C) organic solutions, and added more substrate and inorganic reagent. The reaction mixtures were then stirred overnight at the respective reaction temperatures, but the reactions did not proceed.

The C/O-alkylation ratio of sodium phenolate is a reliable tool for the determination of the active-site environment.[21] C-Alkylation has been shown to occur only with solvents capable of strong hydrogen bond formation[21] or when reactions occur on the surface of the solid phenoxide.[22] The chemical reactions in phase-transfer[23,24] and triphase catalytic[25] systems occur in an apolar medium, and O-alkylation is observed selectively.[23,25] We found that mainly C-alkylation occurs in the reaction of solid sodium phenoxide with benzyl bromide in toluene, in the absence of any catalyst (as expected[22]) or in the presence of either TMAX or silica alone. But on addition of 0.3 molar equiv of TMAX (25%) on silica, O-alkylation becomes the *sole* product (the reaction rate increases by a factor of about 20), which leads to the conclusion that the TMAX/silica-catalyzed reactions proceeds in an aprotic medium.[26]

The great importance of traces of water to various solid–liquid and solid–solid–liquid phase-transfer catalytic reactions has been emphasized in numerous studies.[18,24,27–30] The water is required for efficient mass transfer,[24,28–30] but some water is always coextracted into the organic phase[30] where it reduces the nucleophilicity of the attacking ion.[30,31] As a result, the reaction rate displays a maximum as a function of the water content. This effect has been also found in the present study (Figure 1), and with our hydrophilic catalyst, the phenomena is even more pronounced. Thus, as little as 50 μL of water is enough to supress completly the esterification of benzyl chloride with potassium formate (at 120 °C). This might be caused by excessive hydration of the attacking nucleophile, but dissolution of the TMACl salt in the aqueous film is also possible. On the whole, the activity observed with the TMAX/Silica D 22 catalyst, clearly complies with the idea that "a delicate balance is required between the hydrophilic and hydrophobic nature of the entire supported system in order to achieve maximum catalytic activity".[32] The loss of activity above a certain catalyst loading (Table I), and the variation of this limit with different substrates (in the same organic solvent!), can be understood only in this connection. In our opinion this hydrophilic–hydrophobic balance, rather than some specific chemical interaction, is also responsible for the inactivity of the alternative supports, which we have tested.

Experimental Section

Materials. Unless stated otherwise all reagents were purchased from Aldrich Chemical Co. and used without further purification. Solid reagents and catalysts were dried overnight in a vacuum

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(26) This result might be somewhat surprising, since it has been found that in the same reaction, use of *hydrophobic* phase transfer catalysts bound covalently to silica gel results in partial C-alkylation (sodium phenoxide is applied in aqueous solution!).[8b,d,25]

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Table I. Solid–Solid–Liquid Substitution Reactions Catalyzed by TMAX on Silica[a]

substrate	solid reagent	catalyst loading weight %	catalyst amount molar %	product	temp, °C	time, h	yield,[b] %, GC
benzyl chloride	HCO_2K	10	5	benzyl formate	120	12	99
		25	5			11	99
		50	5			12	21
(without solvent)		25	5		150	2	100[c]
1-chlorodecane	HCO_2K	10	7.5	decyl formate	120	120	86
					150	2	14
						20	52
						72	64
		25	7.5		150	20	7
1-bromooctane	CH_3CO_2K	10	7.5	octyl acetate	120	80	99
					150	9	100
1-bromooctane	NaI	10	7.5	1-iodooctane	120	80	97
					150	25	99
		25	7.5		120	40	1

[a] 10 mL of a solution of the substrate (1 M) in *p*-xylene (for reactions at 120 °C) or *o*-chlorotoluene (for reactions at 150 °C) was magnetically stirred with the inorganic reagent (15 mmol) and the catalyst. [b] Yields are determined by GC calibrated with pure reference substances. [c] The product was isolated in 97% yield.

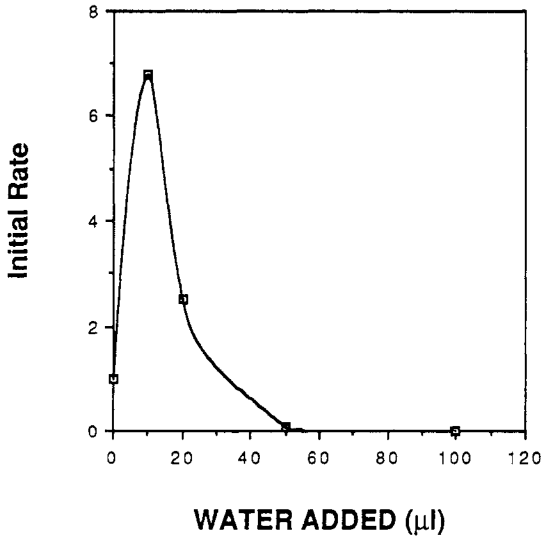

Figure 1. Effect of water on the esterification rate of benzyl chloride. Reaction conditions: Benzyl chloride (10 mmol) in *p*-xylene (10 mL) was magnetically stirred with potassium formate (15 mmol) and 0.22 g (25%) TMACl/Silica D22 at 120 °C. The reactions were followed by GC. When no water was added the reaction system contained approximately 2 µL of water (Karl Fisher). The initial rates were determined between 0 and 25% conversion. They are expressed in units of 10^5 M s^{-1}.

oven at 120 °C, 1 mmHg. The following catalyst supports were used: Silica SIPERNAT® D22 (Degussa Co., W. Germany, precipitated colloidal silica, not surface treated, particle size 180 Å, BET surface area 190 m^2/g, spray dried agglomerates of 40–200 µm); Silica SIPERNAT D17 (Degussa Co., sililated with alkylchlorosilane, particle size 280 Å, BET surface area 110 m^2/g; silica gel 60 (Merck Catl. No. 7733, Particle size 0.2–0.5 mm, average pore diameter 60 Å); Polystyrene Amberlite XAD-4 (Rohm and Haas Co.); aluminiumoxide S neutral, active (Riedel De Haen Co., W. Germany, Catl. No. 31164).

Catalytic Preparation. All catalysts were prepared according to the procedure described for the preparation of 25% TMACl/Silica D22: 2.5 g of tetramethylammonium chloride were dissolved in about 25 mL of methanol, in a round-bottom flask; 7.5 g of Silica D22 were added, and the suspension was stirred at room temperature for 1 h. The solvent was evaporated, and the catalyst was dried. The catalysts are strongly hygroscopic. To prevent the adsorbtion of water, they were kept in tightly closed flasks, which were opened always for a few seconds only.

General Reaction Conditions. Ten milliliters of a solution of the substrate (1 M) in *p*-xylene (for reactions at 120 °C) or *o*-chlorotoluene (for reactions at 150 °C), the inorganic reagent (15 mmol), and the catalyst were placed in a vial (Thomas Scientific 9710 D61) equipped with a 15 × 7 mm magnetic bar. In some cases (Figure 1) water was added with a syringe. The vial was closed with a Teflon-lined screw cap, placed in an oil bath, and stirred vigorously. Small samples were taken at appropriate time intervals, filtered through cotton wool, and analyzed by GC (calibrated with authentic samples) on a 10% SP 2100 on Chromosorb P column.

Preparation of Benzyl Formate. Benzyl chloride (200 mmol, 25.3 g), potassium formate (220 mmol, 18.5 g), and 25% TMACl/Silica D22 (10 mmol, 4.38 g) were stirred mechanically at 150 °C for 2 h. The reaction mixture was filtered, and the solids were washed thorougly with chloroform. After evaporation of the chloroform, 99.6% benzyl formate was obtained in a yield of about 97% (the product contained 0.4% benzyl alcohol; residual benzyl chloride was not detected by GC).

Alkylation of Benzyl Cyanide. Benzyl cyanide (5 mmol), 1-chlorobutane (20 mmol, solvent), sodium hydroxide (20 mmol, partially crushed), and 25% TMACl/Silica D 22 (0.25 mmol, 0.110 g) were stirred overnight (18 h) at room temperature. GC analysis indicated a quantitative conversion to α-butylbenzyl cyanide (78%) and α,α-dibutylbenzyl cyanide (22%).

Alkylation of Phenoxide. The reactions were carried out as described before.[27] Sodium phenoxide was prepared from phenol and sodium hydroxide;[22] 10 mL of a 0.2 M solution of benzyl bromide in toluene was stirred with sodium phenoxide (3.2 mmol) and the catalyst at 55 °C as described above. The reactions were followed by GC.

Registry No. TMABr, 64-20-0; TMAC, 75-57-0; NaOPh, 139-02-6; HCO_2K, 590-29-4; CH_3CO_2K, 127-08-2; NaI, 7681-82-5; benzyl chloride, 100-44-7; 1-chlorodecane, 1002-69-3; 1-bromooctane, 111-83-1; benzyl formate, 104-57-4; decyl formate, 5451-52-5; octyl acetate, 112-14-1; 1-iodooctane, 629-27-6.

A Facile One-Step Synthesis of *C*-Arylnitrones Using Dimethyldioxirane[1]

Robert W. Murray* and Megh Singh

Department of Chemistry, University of Missouri—St. Louis, St. Louis, Missouri 63121

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Nitrones are versatile organic compounds that are used widely in organic synthesis.[2-9] Of more recent but equal

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