Commercial Ion Exchange Resins as Catalysts in Solid–Solid–Liquid Reactions

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Nucleophilic substitutions, base-catalyzed alkylations, and oxidation of a secondary alcohol have been carried out in a nonpolar solvent with inorganic *solid* reagents using polymer-bound quarternary ammonium or phosphonium catalysts. The products could be isolated simply by filtration and evaporation of the solvent. Some commercial ion exchange resins, which are known to be inactive in liquid–liquid systems, were found to have a similar or even superior activity in comparison with the usual "triphase catalysts". The resins were chemically stable under the reaction conditions, but their mechanical breakdown could be reduced only by application of unconventional means of agitation.

Introduction

The use of phase-transfer catalysis (PTC) for reactions between organic soluble substrates and inorganc reagents has become extremely popular over the past years and continues to grow in importance in synthetic organic chemistry.[1,2] Soluble phase-transfer catalysts are usually difficult to separate from the reaction mixture and are seldom reused.[3] Much effect has therfore been put in the research of polymer supported catalysts (triphase catalysis, TC).[4–6] Besides a reduced catalytic activity[7,8] they still suffer from a very limited commercial supply at extremely high prices,[9] which make them rather inconvenient to the synthetic chemist. The catalytic activity of typical commercial benzyltrimethylammonium ion exchange resins has been reported to be negligible in most TC reactions,[4–6,10,11] most likely because of their strong preference for the aqueous phase, which prevents any contact between the active site and the organic substrate. Besides a few exceptions,[8,12–14] they are of value only when applied stoichiometrically as reagents after they have been converted into the required anionic form and dried.[15–17]

So-called solid–liquid PTC has been used often with reagents unreactive or unstable in the presence of water or in order to improve reaction kinetics.[1,18] Recently it has been shown that the maximum conversion obtainable in exchange reactions of alkyl halides with formate, fluoride, or bromide ions can be dramatically increased by application of solid inorganic reagents.[19–21]

The combination of both techniques, namely the performance of reactions with a solid reagent together with a solid catalyst, has been used only rarely, either with large amounts of neutral alumina[22–24] or with specially synthesized catalysts such as silica gel and cellulose-based phosphonium and ammonium ions,[25,26] as well as polyethylene glycols and crown ethers on various supports.[27–30] Concerning polystyrene bound phosphonium or ammonium ions, only the oxidation of alcohols with periodate ion (and a preconverted catalyst) has been carried out successfully.[13,14] In other reactions the yields of the resulting products were either small or not much larger than the yields obtained in the absence of any polymer.[14]

In a recent mechanistic investigation on triphase catalysis, it was found that the reaction rates can be drastically improved through proper adjustment of the volume ratio of the two liquid phases.[31] Thus the use of the very hydrophilic commercial ion exchange resins as triphase catalysts should be generally feasible if the presence of excess water is prevented. Indeed, Ford et al.[8] have found these resins to be very active triphase catalysts in the presence of strongly desiccant 50% aqueous sodium hydroxide. Concerning the mechanism of solid–liquid PTC reactions, it has been suggested quite often that a certain amount of water is necessary to carry out the reaction effectively.[32–34] We have shown in a recent paper that in

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Table I. Formation of Benzyl Formate with Different Catalysts[a]

no.	catalyst	type[b]	RS[c]	functionality	% DVB[d]	yield,[e] % GC
Commercial Ion Exchange Resins						
1	Amberlyst A27	macro	40	$CH_2N^+(CH_3)_3Cl^-$		97
2	Amberlite IRA 904	macro	40	$CH_2N^+(CH_3)_3Cl^-$		98
3	Dowex 1 × 2	gel	60	$CH_2N^+(CH_3)_3Cl^-$	2	4
4	Dowex 1 × 4	gel	60	$CH_2N^+(CH_3)_3Cl^-$	4	2
5	Dowex 1 × 8	gel	60	$CH_2N^+(CH_3)_3Cl^-$	8	9
6	Amberlite IRA 900	macro	87	$CH_2N^+(CH_3)_3Cl^-$		2
7	Amberlyst A26	macro	87	$CH_2N^+(CH_3)_3Cl^-$		20
8	Amberlite IRA 410	gel	67	$CH_2N^+(CH_3)_2(C_2H_4OH)Cl^-$		9
9	Amberlite IRA 910	macro	83	$CH_2N^+(CH_3)_2(C_2H_4OH)Cl^-$		8
Triphase Catalysts						
10	*p*-benzyltrimethylammonium chloride	gel	14	$CH_2N^+(CH_3)_3Cl^-$	2	83
11			20		2	36
12	*p*-benzyltriethylammonium chloride	gel	12	$CH_2N^+(C_2H_5)_3Cl^-$	2	93
13			16		2	91
14	*p*-benzyltripropylammonium chloride	gel	10	$CH_2N^+(C_3H_7)_3Cl^-$	2	8
15	*p*-benzyltributylammonium chloride	gel	8	$CH_2N^+(C_4H_9)_3Cl^-$	2	19
16			9		1	20
17			14		2	4
18	*p*-benzyltributylphosphonium chloride	gel	10	$CH_2P^+(C_4H_9)_3Cl^-$	1	75
19	hexyltributylphosphonium chloride	gel	12	$(CH_2)_6P^+(C_4H_9)_3Cl^-$	2	97

[a] Reaction conditions: Benzyl chloride 10 mmol, potassium formate 15 mmol, toluene 8 mL, catalyst 0.120 g, magnetic stirring, 95 °C. [b] Macroporous or gel type. [c] RS percentage of ring substitution. [d] DVB, divinylbenzene. [e] After 15 h of reaction (not final yield).

reactions with inorganic formate salts, the ions are actually transferred into the organic phase from an aqueous film on the crystal's surface.[35]

Combination of these two findings led us to the prediction that reactions using both a solid reagent and a commercial ion exchange resin as catalyst should proceed smoothly, provided the amount of water present is adjusted properly to the reaction system.

Results and Discussion

When solid potassium formate (1.26 g, 15 mmol) and benzyl chloride (1.27 g, 10 mmol) in toluene (8 mL) were magnetically stirred for 20 h at 95 °C in the presence of previously dried Amberlyst A27 (in short: A27) ion exchange resin (0.12 g, 0.3 mequiv Cl^-), benzyl formate (eq 1) was formed quantitatively (100.0% conversion according to GC). In the absence of the catalyst only 1.3% benzyl formate was formed in 45 h.

$$C_6H_5CH_2Cl + KO_2CH(s) \xrightarrow{\text{A-27}} C_6H_5CH_2OC(O)H + KCl(s) \quad (1)$$

The reaction was performed also without solvent; benzyl chloride (purity 99%, 100 mmol), potassium formate (125 mmol), and Amberlyst A27 (0.6 g, 1.5 mequiv Cl^-) were mechanically agitated at 95 °C for 24 h. Slightly yellowish benzyl formate (purity 99%) was isolated in a yield of 93%, after addition of acetone, filtration, and acetone evaporation.

Commercial ion exchange resins might contain traces of soluble organic material. Any possible homogeneous catalysis of the reaction by such traces could be ruled out by the continuation of the reaction after filtration of the solids and addition of more benzyl chloride and potassium formate. The observed reaction rate was similar to the uncatalyzed rate (less than 1% conversion in 24 h).

Variation of Catalyst. The reaction of benzyl chloride and potassium formate was performed with a great number of catalysts, commercial ion exchange resins as well as "typical triphase catalysts".[6] We have chosen to compare the various catalysts on the basis of same weight rather than same number of moles, since the catalysts should be looked upon as one entity. The catalyst's geometrical structure and its swelling behavior, as well as intraparticle diffusion or intraparticle distribution of the various phases, strongly affects the overall activity, and very close catalytic sites can hardly be dealt with as if they were homogeneously distributed throughout the organic medium. Also, the application of variable amounts of catalyst could affect the stirring efficiency in the various reactions. In any case, the results (Table I) should not be compared *all together* due to the great number of parameters varied, such as type of catalyst (macroporous or gel type), average pore radius, surface area, functional group, percentages of cross-linking, ring substitution, etc. Still some important conclusion can be drawn: The two commercial exchange resins Amberlyst A27 (resin no. 1) and Amberlite IRA 904 (resin no. 2) which have a relatively low percentage of ring substitution (RS = 40%) perform at least as well as the best "triphase catalysts". The commercial resins with higher exchange capacity have an almost neglectable activity, except resin Amberlyst A26 which is designed for use with nonaqueous solvents. Among the typical "triphase catalysts" activity was strongly dependent on the chain length of the functional group, being highest with the triethylammonium group (resins no. 12 and 13). A phosphonium-based catalyst (resin no. 18) was again[6] more active than the corresponding ammonium based resins, and the well-known[5,6] positive effect of a spacer chain between the functional group and the polymer backbone was also observed (resin no. 19).

With neutral Alumina as catalyst conversion of benzyl chloride was low (20%) and formation of benzyl alcohol (25%) competed with the major reaction path (75%).

In the following experiments our interest was focused on the well-performing and easily available commercial resins.

Synthetic Applications. The principle demonstrated above has been applied to various typical phase transfer catalyzed reactions such as substitutions on activated (benzylic) and unactivated organic halides (eq 2), base-promoted alkylations (eq 3), and to the oxidation of an aliphatic alcohol (eq 4). The commercial ion exchange resin A27 (Cl^- form) was used as catalyst in all the reactions; the yields in the absence of catalyst are negligible. The results are summarized in Table II. Most of the

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Table II. Solid–Solid–Liquid Reactions Catalyzed by A27 Resin[a]

no.	substrate	solid reagent	amount of catalyst mol %	amount of catalyst wt %	product	temp, °C	time, h	yield,[b] GC	blank reaction[c] yield, %
Halogen Exchange									
1	benzyl chloride	NaBr	3	9	benzyl bromide	90	20	86.3	13
2	benzyl chloride	KF	3	9	benzyl fluoride	100	1000	96	
3	1-bromooctane	NaI	3	6	1-iodooctane	100	60	98	3
Esterification									
4	benzyl chloride	HCO_2K	3	9	benzyl formate	95	20	100.0	1.3
5	benzyl chloride	CH_3CO_2K	3	9	benzyl acetate	95	20	100.0	0
6	1-bromooctane	CH_3CO_2K	13	25	octylacetate	95	25	92	0.3
7	1-chlorooctane	CH_3CO_2K	5	12	octylacetate	100	140	60	0
Cyanide Displacement									
8	benzyl chloride	KCN	3	9	benzyl cyanide	100	45	92	0
9	1-bromooctane	KCN	13	25	octyl cyanide	100	35	96	0
Nitrite Displacement									
10	1-bromooctane	KNO_2	5	10	1-nitrooctane	65	90	40	
Basic Nucleophiles									
11	*p*-chloronitrobenzene	$NaOCH_3$	10	25	*p*-nitroanisole	65	4	70[d]	2
12	benzyl chloride	Kpi[e]	5	13	*N*-benzylphthalimide	90	17	100	0.5
Alcohol Oxidation									
13	2-octanol	$KMnO_4$	12	30	2-octanone	75	20	≈90	≈6
Base-Promoted Reactions									
14	nitroethane + 3-buten-2-one	KF	5	25	5-nitrohexan-2-one	25	3	100	2
15	phenol + benzyl chloride	KF	10	25	O-alkylation 99% C-alkylation 1%	85	30	95	30
16	2,4-pentanedione		10	40	3-methyl-2,4-pentanedione	40	20	≈20	
17	+ iodomethane	KF	250	1000		20	20	90	

[a] For detailed reaction conditions refer to the Experimental Section. [b] Yields are determined by GC using internal standard and pure reference substances. They are based upon the organic substrates. [c] Performed in the absence of catalyst. [d] Isolated yield. [e] Potassium phthalimide.

Table III. Effect of Water on the Cyanide Displacement of 1-Bromooctane in a Solid–Solid–Liquid System[a]

catalyst A27, g	water added, g	product distribution (% GC)[b] $C_8H_{17}CN$	$C_8H_{17}Br$	$C_8H_{17}Cl$
0.200	0.040	22.1	72.7	5.2
0.500	0.040	15.0	72.8	12.2
0.500	0[c]	4.2	83.2	12.6
	0.040	15.0	72.8	12.2
	0.100	46.7	44.0	9.3
	0.200	95.3	1.6	3.1
	0.400	91.7	7.0	1.3
	0.800	63.5	35.5	1.0

[a] Reaction conditions: 1-bromooctane 10 mmol, 1.97 g; toluene 8 mL; potassium cyanide 15 mmol, 0.98 g; magnetic stirring, 100 °C, 25 h (A27 0.50 g = 0.13 mequiv of Cl^-). [b] Normalized to 100%; a side peak (which could belong to octyl isocyanide) grew with increase in the amount of water and reached 1% with 0.800 g of H_2O. It was also observed under liquid–liquid TC reaction conditions.[4,36] [c] The dried reagents still contained a little water (a total of about 0.010 g), as was shown by Karl–Fischer titration.

reactions reported result in low yield, when performed in the presence of aqueous solutions.

$$RX(org) + MY(s) \rightarrow RY(org) + MX(s) \qquad (2)$$

$$RH(org) + R'X(org) + 2KF(s) \rightarrow RR'(org) + KX(s) + KHF_2(s) \qquad (3)$$

$$3RHOH + 2KMnO_4 \rightarrow 3R{=}O + 2MnO_2 + 2H_2O + 2KOH \qquad (4)$$

When the reaction yield is quantitative the product can be isolated simply by filtration of the solids and solvent evaporation. The solvent is needed only because agitation becomes strongly hindered when the neat substrate is mixed (magnetic stirrer) with the catalyst and the stoichiometric amount of the solid reagent. As shown before no solvent is needed when mechanical agitation is supplied.

In substitution reactions of 1-bromooctane, 1-chlorooctane is formed as a byproduct (eq 5). Due to the much lower reactivity of 1-chlorooctane, the final reaction yield of RY (eq 2) is less than 100%. (details: [reaction no., % product (GC), % 1-chlorooctane GC], [3, 98%, 1%], [6, 92%, 8%], [9, 96%, 3%]).[36] The utility of this synthetic

$$A27\text{-}Cl^- + C_8H_{17}Br \rightarrow A27\text{-}Br^- + C_8H_{17}Cl \qquad (5)$$

tool is limited mainly by the reaction temperature which chould not exceed 100 °C, since catalyst decomposition sets in. Thus substrates with rather poor leaving groups react very slowly (e.g., reaction no. 7) and substitution reactions with potassium fluoride (reaction no. 2) are almost endless. At temperatures of 110 °C and above, the reactions proceeded, although more slowly, even after the catalyst had been filtered off, and fresh solid reagent had been added.[37] This phenomenon indicates that decomposition products of the catalyst had dissolved in the medium during the

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(36) We repeated the cyanide displacement on 1-bromooctane under conditions substantially identical with those described by S. L. Regen (ref 4, toluene–water for 18 h, at 110 °C without stirring, catalyst: PS bound benzyltrimethylammonium chloride–14% ring substitution). Here too, 1-chlorooctane formation was observed. Continuation of the reaction (now with magnetic stirring) after filtration of the catalyst and addition of more bromooctane and potassium cyanide resulted in a reaction rate *quite close to the rate observed in the presence of the catalyst.* In the absence of stirring no reaction was observed. (Compare to Regen, S. L. *J. Am. Chem. Soc.* **1976**, *98*, 6270).

(37) In a few reactions, this phenomenon was observed, to a minor extent, also below 100 °C. It is most likely due to impurities present on the commercial resin (Farall, M. J.; Frechet, J. M. J. *J. Org. Chem.* **1976**, *41*, 3880), which are capable to catalyze these reactions. The effect could be prevented by preextraction of the resin with *o*-dichlorobenzene at 90 °C for 16 h (for details refer to the Experimental Section).

heterogeneous reaction, and they catalyzed the reaction to a certain degree.[36]

Halogen Exchange and Esterification Reactions. To achieve maximum conversions in the nucleophilic displacement of alkyl chlorides with fluoride, bromide, and formate ions, solid inorganic reagents are applied instead of aqueous solutions.[19-21] The presented results prove that the A27 resin can be used instead of a soluble catalyst in these reactions. The yields are above 90% except for reaction no. 1 which reached equilibrium (86.3% benzyl bromide) and reaction no. 7 which was stopped after 140 h.

Cyanide Displacement. In their classical paper on PTC, Starks and Owens[32] have shown that the rate of the cyanide displacement of bromooctane displays a maximum as a function of the amount of water added to the reaction. Without water the reaction did not proceed at all, and with too much water the rate was reduced due to the hydration of the attacking nucleophile. We found that this was true also for the A27-catalyzed reaction (Table III). Similar to our findings on soluble PTC-catalyst,[35,38] we found that addition of excess catalyst might cause inhibition of so-called solid–liquid[39] PTC reactions since the inorganic solid is stripped of its aqueous film by the strongly hygroscopic resin. The effect can be cancelled by the addition of more water (Table III).

The cyanide displacement of benzyl chloride (reaction 8) was performed in the presence of 0.020 g of H_2O only. Even at this low water content (Table III), benzyl alcohol (1.5%) was formed as a byproduct by hydrolysis. The yield (GC) of phenyl acetonitrile was 92% after 45 h and 98% after 85 h.

Nitrite Displacement. This PTC reaction is preferentially carried out using solid alkali nitrite, since the application of aqueous solutions results in low yields.[1,40] Even then the yields obtained are only moderate ($\approx$ 30%[41]–65%[42-44]) due to the competing formation of alkyl nitrites and the subsequent destruction of the nitroalkane, which is decomposed by the joint action of nitrite ion and alkyl nitrites.[45] 1-Nitropropane has been prepared in 47% yield by using 2 mol of preconverted Amberlite IRA 900 (NO_2^-) for every mole of 1-bromopropane.[46]

We obtained similar yields ($\approx$40%) of 1-nitrooctane with both soluble (tetrabutylammonium bromide) and insoluble (Amberlyst A27) catalysts, but the reaction time required rose from 1 h (at 20 °C) to 90 h (at 65 °C).

Displacement Reactions with Basic Nucleophiles. In the absence of any catalyst (or in the presence of polymer-bound benzyltributylammonium chloride, catalyst 16 in Table I) *p*-chloronitrobenzene reacts with sodium methoxide to yield a sticky dark brown material which precipitates on the solid reagent. Only traces (2%) of *p*-nitroanisole are detected. In the presence of A27 (10 mol %) the product can be isolated in 70% yield and a purity of 98% (2% starting material); the side products are filtered off together with the solids. (With the same molar amount of soluble tetrahexylammonium chloride catalyst a yield of more than 90% (GC) is obtained in 1 h but the product isolation is quite laborious.)

N-Alkyl phthalimides are intermediates in the Gabriel synthesis of primary amines. They can be prepared from alkyl halides with solid potassium phthalimide and a soluble phase-transfer catalyst, but the latter is required in rather large amounts[47,48] (except for phosphonium-based catalysts[49]) due to its decomposition by the strongly basic reagent. The use of silica gel supported phase transfer catalysts (5 mol %) has been reported (98% yield with benzyl chloride).[26] We found that 5 mol % of A27 was sufficient to obtain *N*-benzyl phthalimide quantitatively.

Alcohol Oxidation. 2-Octanol can be oxidized in high yield ($\approx$90%) when reacted with solid potassium permanganate and a phase-transfer catalyst. Use of Amberlyst A27 results in a rate about half the one observed with soluble tetrabutylammonium chloride (same molar amount of catalyst). The latter can be used also in liquid–liquid PTC, but the yield is significantly lower (30%) and potassium permanganate decomposition is the major reaction pathway.

Reactions Promoted by Potassium Fluoride. The use of fluoride ion as a base[50] has become quite popular, although it has to be applied in twice the stoichiometric amount in most reactions.[50] The Michael reaction of nitroethane and 3-buten-2-one has been studied as a model reaction to compare the activities of various sources of fluoride ion.[51] We performed the reaction with potassium fluoride and chlorobenzene (instead of acetonitrile) as solvent. The Amberlyst A27 catalyzed reaction was completed in 3 compared to 15 min required with homogeneous tetrabutylammonium chloride, and a negligible yield in the absence of any catalyst.

The reaction of phenol with benzyl chloride in the presence of fluoride ion may produce four different products, namely O-alkylated and C-alkylated phenol, benzyl alcohol and benzyl fluoride.[52] Only traces of these were detected when the reaction was performed in toluene (20 h, 85 °C) with oven-dried potassium fluoride as promoter in the absence of any catalyst. KF containing some water of hydration (2%) catalyzed the two alkylation reactions (30% conversion), resulting in a mixture of O-alkylated (85%) and C-alkylated (15%) phenol. Addition of Amberlyst A27 resulted, besides an increase in the reaction rate (95% conversion) in selective O-alkylation (>99%), typical for homogeneous reactions in aprotic medium.[52]

The alkylation of 2,4-pentanedione (0.01 mol) with iodomethane (0.01 mol) in THF in the presence of preconverted A27 (F^- form, 0.035 mol) has been reported to yield 70% of 3-methyl-2,4-pentanedione.[53] We performed the reaction with some excess of iodomethane (25%). With catalytic amounts of A27 the yield was low, but with 250 mol % of A27 (Cl^- form) a yield of 90% (GC, 100% conversion) was obtained, thus showing that the "conversion of the resin" can be performed in situ.

Catalyst Stability. The chemical stability of Amberlyst A27 resin is satisfactory (no change in the number of active sites occurs during the reaction) as long as the re-

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action temperature does not exceed 100 °C. No reduction in the catalytic activity was observed when the reaction of benzyl chloride and potassium formate was performed with recycled catalyst. But, similar to what has been found for various triphase catalysis reactions,[7,54] the physical stability of the catalyst particles is low; after 2 h of magnetic stirring the catalyst is pulverized completely (to particles sizes of 5–50 μm). The catalyst can be recovered (as powder) from the initial filter cake (obtained on separation of the organic liquid phase) only by repeated alternating washings with acetone (which removes traces of the organic phase) and water (which removes the inorganic salts). Except for resins Amberlite IRA 910 and Amberlyst A26 this picture is true for all the catalysts tested, including the commercial catalysts, which are known for their improved mechanical stability.[6] After 24 h of reaction with IRA 910 and A26 (which has been shown before to be rather tough[53]) their particle size was in the range of 100–500 μm (intact, and partially broken beads); unfortunately, their activity is quite low. Thus we decided to look for a less destructive mode of mixing. In contrast to liquid–liquid triphase catalysis,[54] even slow mechanical agitation did not avoid the catalyst's pulverization, but reaction rates were reduced. On the other hand, no reaction occurred when a shaking bath was used as a mixing device.

When the reaction was stirred by vibrations (transferred from a laboratory vortex apparatus), intact A27 particles (>95%) were recovered, and the reaction rate was about 20% of the magnetically stirred rate. Finally, we arrived at ultrasonic agitation which seems to be the ultimate answer to "fast" reactions (rates were slightly higher than with magnetic stirring) as well as catalyst recovery. After filtration of the organic solution the intact particles (about 75% of the initial amount, after 15 h of reaction) can be recovered from the solid mixture simply by washing the cake with water or by the addition of a liquid of intermediate density (e.g. chloroform), which causes them to float. The catalyst is dried and ready for reuse.

Reaction Kinetics. The reaction of benzyl chloride and potassium formate (A27 15% by weight, 95 °C) was found to follow zero order up to about 70% conversion, after which it becomes first order. A variable time lag (up to 1 h) is also observed. Magnetic and ultrasonic mixing give a similar picture. This observation makes it rather difficult to determine rate constants comparable to other means of catalysis. This transition from zero to first order might suggest that the reaction is initially controlled by slow mass transfer between the inorganic solid and the polymer, but becomes chemically controlled, as the substrate concentration decreases during the reaction. Extensive work on the kinetics of various reactions, catalysts, and mixing modes is now in progress and will be published soon.

Summary

After the feasibility of "solid–solid–liquid phase transfer catalyzed reactions" has been established, various aspects of the relevant mechanisms require clarification. This includes evaluation of the catalytic site environment and the rate-determining reaction step, as well as investigation of the way the nucleophlic reagent is transferred between the inorganic solid and the polymer.

Experimental Section

Materials. Unless stated otherwise, all reagents were purchased form Aldrich Chemical Co. and use without further purification. Solid reactions were dried overnight in a vacuum oven at 120 °C, 1 mmHg.

Resin catalysts 1–9, 16, 18, and 19 (Table I) were purchased from Fluka AG. Resins 10–15 and 17 were prepared according to established procedures[5] by reacting commercially obtained chloromethylated polystyrene beads (resins 10, 12, 14, and 15 from Aldrich Catalog No. 22,150-3, 2% DVB, ≈1 mequiv Cl/g; resins 11, 13, and 17 from Fluka Catalog No. 63874, 2% DVB, ≈2 mequiv Cl/g) with the corresponding trialkylamines and washing the resulting resin repeatedly. The percentage of ring substitution was calculated from the chloride ion content, which was measured by a modified Volhard procedure.[55] In order to remove any adsorbed impurities, the commercial ion exchange resins 1–9 were soaked overnight with 1,2-dichlorobenzene (dcb) at 95 °C after which they were washed with acetone until dcb was undetectable by GC. The "triphase catalysts" 10–19 were not treated with dcb since we found surprisingly that this treatment almost cancelled the catlaytic activity of resins 15 and 16 (a commercial and a self-prepared resin), which were the only "triphase catalysts" we tried to submit to this extraction procedure. The chloride ion titer of these treated resins was reduced to less than 10% of the inital value, a process we cannot explain. No reduction in the chloride ion content was detected with resins 1–9. All the resins were dried in a vacuum oven at 90 °C, 1 mmHg prior to use.

Procedure for Formate Ion Displacement on Benzyl Chloride. (a) Catalyst Variation. A solution of benzyl chloride (1.27 g, 10 mmol) in toluene (8 mL), dried resin (0.120 g), and potassium formate (1.26 g, 15 mmol) were placed in a 16-mL vial (Thomas Scientific 9710 D61) equipped with a 15 × 7 mm magnetic bar. The vial was sealed with a Teflon-lined screw cap, placed in an oil bath maintained at 95 ± 0.5 °C, and stirred vigorously. After 15 h the reaction was stopped, the solid mixture was filtered off and washed with a little toluene, and the organic phase was analyzed by GC (calibrated with authentic samples). In all the reactions with a yield of 20% and more, benzyl chloride was added to the organic phase to restore the initial concentration (GC). After addition of a new portion of solid reagent the reaction was continued (now without catalyst) under otherwise identical conditions. GC analysis after 20 h proved that the reaction rate was now similar to the uncatalyzed rate.

(b) Reactions with A27 Resin. When the reaction described above was performed with A27 resin as catalyst, the reaction was continued until GC indicated 100.0% benzyl formate (≈19 h).

(c) Reactions without Solvent. Benzyl chloride (purity 99%, 12.7 g, 100 mmol), potassium formate (10.5 g, 125 mmol), and resin A27 (0.6 g, 1.5 mequiv Cl^-) were mechanically agitated (at 600 rpm) at 95 °C. After 24 h the mixture was cooled, acetone was added, and the solids were filtered off and washed three times with 20 mL of actone. The filtrates were combined, and the acetone was evaporated. Benzyl formate was obtained as a slightly yellowish liquid of 99% purity (GC) in a yield of 93%.

(d) Variation of Agitation Mode. Shaking of the reaction mixture was achieved by connecting the reaction vial, which was immersed in an oil bath, to a shaking apparatus (Tuttnauer Co., Model 14-300, 15 strokes per minute) by means of a short rod. Vibrations were transferred similarly, from a laboratory Vortex machine (Heidolph Co., Reax 2000, 42 W, 2000 rpm). The mechanically mixed reactions (200 rpm) were carried out in a round-bottom flask (20 mL) equipped with a stoppered side arm and a small condenser (also stoppered) through which a mechanical glass stirrer with a curved Teflon blade was introduced.

For ultrasonic mixing an ultrasonic generator (W-375, Heat Systems Ultrasonics Inc.) with a flat tip (1 cm^2) was used at an output level of 50 W. The reagents' quantities were doubled. Three further changes had to be introduced to the experimental procedures.

(1) Xylene had to be used as solvent instead of toluene since ultrasound is ineffective when the vapor pressure of the system is too high.[56] The conventionally stirred reaction proceeded the same with either solvent.

(2) The ultrasonic head had to be immersed in the reaction medium, thus an open vial (25 mL) was used as the reaction vessel. (It is strictly forbidden to introduced the tip through any kind

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of seal.) Mass balance showed that solvent evaporation was negligible.

(3) In order to account for the heat released by the ultrasonic source the thermostated bath was held at 90 °C. The reaction temperature, which was measured inside the vial with a thermocouple, varied between 92 and 95 °C, but the latter was never exceeded.

(e) Catalyst Recovery and Recycle. The catalyst powder (magnetic stirring) was recovered from the filter cake by 3–4 alternating washings with acetone and water and was dried as usual. (The catalyst was free of potassium ions, which was affirmed by Energy Dispersive Spectrometry.) The particle size was investigated both with a light microscope and by SEM. The percent of active sites remaining in the recovered catalyst was determined by conversions of the catalyst back to its original chloride form,[11] and chloride ion titration was performed in the usual way. The catalytic activity of the recovered catalyst powder was measured by repeating the reaction as described in paragraph a. Catalyst particles bigger than ≈ 100 μm (as obtained from the reactions with unconventional agitation) were separated from the filter cake by mixing the cake (manually, by means of a spatula) with chloroform. The floating particles were decanted, washed twice with acetone, and dried as usual.

(f) Reaction Kinetics. The reaction conditions were the same as described above (using 15% by weight of A27 catalyst), but samples were taken every hour and analyzed by GC.

Synthetic Applications. (a) Halogen Exchange, Esterification, and Cyanide Displacement Reactions (Reactions 1–9 in Table II). The ractions were performed with A27 resin as catalyst according to the procedure described for formate ion displacement of benzyl chloride. The reaction temperatures and the amount of catalyst (in percent of the organic substrate) are summarized in Table II. Water was added to reactions 2, 6, 8 (20 μL each), and 9 (200 μL). The reactions were followed by GC analysis of samples taken at appropriate time intervals. The dependency of the cyanide displacement of 1-bromooctane on the water content (Table III) was investigated under the same reaction conditions except for the reduced reaction time (25 h) and the variable amount of water added.

(b) Nitrite Displacement. The reaction conditions were the same as those described in paragraph a, except for 0.5 mL of xylene which was added as internal standard (the solvent's volume was reduced to 7.5 mL). The GC integrator was calibrated for 1-bromooctane, 1-nitrooctane, and 1-octyl nitrite.

(c) *p*-Nitroanisole. *p*-Chloronitrobenzene (pCNB, 8 mmol, 1.25 g), sodium methoxide (16 mmol, 0.85 g), A27 (0.8 mmol, 0.3 g), and toluene (8 mL) are magnetically stirred for 4 h at 65 °C. The solids are filterd off and washed twice with toluene. The solvent is evaporated, and the product is dried overnight at 60 °C, 1 mmHg. The solid product (0.93 g, mp 48 °C) contains 98% *p*-nitroanisole (5.9 mmol, yield 74%) and 2% pCNB according to GC analysis.

(d) *N*-Benzylphthalimide. Benzyl chloride (10 mmol, 1.27 g), potassium phthalimide (12 mmol, 2.22 g), A27 (0.5 mmol, 0.17 g), xylene (internal standard, 0.5 mL), and toluene (7.5 mL) are magnetically stirred overnight at 90 °C. A quantitative yield (100%) of *N*-benzylphthalimide is obtained (GC calibration with authentic samples).

(e) Alcohol Oxidations. 2-Octanol (2.5 mmol, 0.352 g), potassium permanganate (7.5 mmol, 1.18 g), A27 (0.3 mmol, 0.10 g), nonane (internal standard, 0.1 g), and toluene (6 mL) were mixed for 20 h at 75 °C. Analysis by GC showed a conversion of 98% and a yield of 90% (according to the peak area ratio of product to standard; additional peaks were not observed).

(f) Michael Addition (Reaction 14). 3-Buten-2-one (10 mmol, 0.7 g), nitroethane (20 mmol, 1.5 g), A27 (0.5 mmol, 0.17 g), potassium fluoride (5 mmol, 0.30 g), toluene (internal standard, 0.3 g), and chlorobenzene (5 mL) were magnetically stirred at room temperature. The reaction solution was analyzed by GC after 2 and 3 h. Potassium fluoride containing 2% water and dried potassium fluoride had the same effect. Less than 2% of the product was obtained when A27 or potassium fluoride was applied alone.

(g) Alkylation of Phenol. Benzyl chloride (3 mmol, 0.38 g), phenol (5 mmol, 0.47 g), A27 (0.3 mmol, 0.10 g), potassium fluoride (2% H_2O, 10 mmol, 0.6 g), dodecane (internal standard, 0.2 g), and toluene (8 mL) were stirred in the standard reaction vial at 85 °C for 30 h. GC analysis was calibrated with benzyl chloride, benzyl phenyl ether, and *o*- and *p*-hydroxydiphenylmethane. Conversions are based on benzyl chloride.

(h) Methylation of 2,4-Pentanedione (Reaction 16/Reaction 17). 2,4-Pentanedione (5 mmol, 0.5 g/1 mmol, 0.10 g), iodomethane (12.5 mmol, 1.78 g/1.25 mmol, 0.178 g), A27 (0.5 mmol, 0.2 g/2.5 mmol, 0.85 g), KF (20 mmol, 1.2 g/4 mmol, 0.24 g), and THF (8 mL/4 mL) were magnestically mixed (at 40 °C/20 °C) for 20 h. Reaction yields were calcualted from GC analysis.

Lewis Acid Induced Nucleophilic Substitution Reaction of β-Nitro Sulfides

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The nitro group of β-nitro sulfides is readily substituted by an allyl or a cyano group or hydrogen on treatment with allyltrimethylsilane, cyanotrimethylsilane, or triethylsilane in the presence of an appropriate Lewis acid. The intramolecular Friedel–Crafts reaction of β-nitro sulfides is also induced by a Lewis acid. Primary and secondary nitro groups as well as tertiary and benzylic nitro groups undergo this substitution reaction. These replacements of the nitro group cannot proceed when the adjacent phenylthio group is absent. Unsymmetrical β-nitro sulfides afford mixtures of two regioisomers. In particular, 1,2-migration of the phenylthio group predominates when the nitro group is located on primary position. This reaction proceeds in a stereospecific way. Stereochemical study reveals that the substitution reaction proceeds via the retention of configuration. These results suggest that episulfonium ions are the intermediates of the reaction. Thus, the β-nitro sulfides–Lewis acid system provides a new method for the generation of episulfonium ions.

Since the nitro group acts as an effective activating group in a carbon–carbon bond formation, aliphatic nitro compounds represent versatile intermediates in organic synthesis.[1] For example, the aldol reaction or the Michael addition reaction using aliphatic nitro compounds proceeds under very mild conditions to form new carbon–carbon bonds. Nitro compounds are also useful in organic syn-

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