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Surface-mediated reaction—A powerful technique in organic synthesis. Use of alumina and silica gel as active surface for useful synthetic transformations

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Abstract

Significant improvement in terms of convenience, yield, reaction time and selectivity has been achieved using alumina and silica gel as support or surface for several important reactions. These include : (a) Michael reaction, (b) regioselective alkylation of 1,3-dicarbonyl compounds, (c) selective bromination of alkyl-substituted aromatic hydrocarbons, (d) aldol reaction of silyl enol ethers with aldehydes, (e) regioselective reductive cleavage of epoxides, (f) regioselective hydration of alkenes, and (g) regioselective 1,2-reduction of conjugated carbonyl compounds.

Key words: Surface-mediated reaction, silica gel, alumina, Michael reaction, alkylation, aldol reaction, epoxide-cleavage, hydration of alkenes, reduction of conjugated carbonyl compounds.

1. Introduction

The technique of surface-mediated reaction is of growing interest[1] because of its advantages of ease of set-up, mild conditions, rapid reactions, selectivity, increased yields and low cost compared with their homogeneous counterparts. It has also been demonstrated that attempts to carry out the same reactions in solvent without support on surface frequently either fail or result in the formation of a mixture of products. A recent modification in this technology is the technique of surface-mediated solid phase reaction which has already gained much importance and popularity[2]. For the past few years we have been actively engaged in utilizing surface-mediated reaction for useful synthetic transformations and a brief account of our work in this area is presented here.

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2. Results and discussion

(a) Michael reaction

The Michael reaction is one of the most efficient methods for effecting carbon–carbon bond formation and has wide synthetic applications. This reaction is usually carried out in a suitable solvent in the presence of strong bases. Side reactions, frequently encountered in the presence of a base, are secondary condensations, *bis* additions, polymerisations, retrogressions and rearrangements. We have discovered that Michael reactions are carried out very efficiently and rapidly without any side reaction on the surface of alumina through a solvent-free reaction[3]. In a typical general procedure, the Michael donor was stirred on the surface of alumina at room temperature for 10 min after which the Michael acceptor was added and stirring was continued till completion of the reaction. The product was isolated in a pure state by simple filtration of the solid mass through a short plug of silica gel. Several structurally varied donors, including 1,3-dicarbonyl compounds, ethyl cyanoacetate, diethyl malonate, nitroethane underwent clean and remarkably fast additions with a variety of acceptors like methyl vinyl ketone, acrolein, methyl acrylate, etc., by this procedure (Table I). The dramatic improvement observed is with regard to reaction time. Many reactions are complete within a period of 5 minutes. Interestingly, it was found that the presence of solvent slowed the reaction.

To sum up, the attractive features of this methodology are : (i) no requirement of base, (ii) no undesirable side reactions, (iii) remarkably fast addition, (iv) mild reaction condition, (v) ease of set-up and work-up; (vi) involvement of no toxic and expensive reagent, and (vii) high yield.

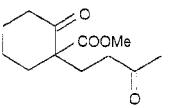
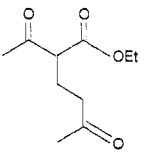
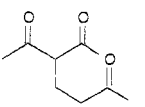
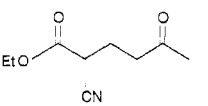
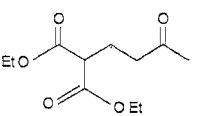
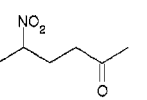
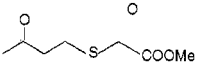
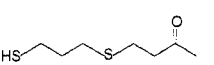
By application of this technique we have developed a novel route to the synthesis of β-keto 1,3-dithiane derivatives, an important class of synthons, through double Michael addition of 1,3-propanedithiol to α, β-acetylenic ketones on the surface of alumina[4] (Table II). The reactions are reasonably fast and high yielding.

By further extension of this methodology we have achieved clean and efficient Michael addition of silyl enol ethers to methyl vinyl ketone on the solid surface of alumina impregnated with anhydrous zinc chloride[5]. The Michael addition of silyl enol ethers to α, β-unsaturated ketones has been catalysed by various Lewis acids such as $TiCl_4$, $SnCl_4$, $SbCl_5$, $BiCl_3$, $ZnCl_2$, BF_3 and salts like $TrClO_4$, $Sn(OTf)_2$, $Bu_2Sn(OTf)_2$[6]. But, a very serious limitation of most of these catalysts is toward the use of methyl vinyl ketone, the simplest enone, as an acceptor due to its high tendency to polymerise under acidic reaction conditions[6,7]. Our procedure using alumina impregnated with anhydrous zinc chloride avoids such limitation and provides a very clean reaction. A number of different trimethylsilyl enol ethers underwent additions to methyl vinyl ketone to produce the corresponding 1.5-diketones in high yields (Table III).

No side product has been isolated. Addition without alumina in the presence of $ZnCl_2$ in THF led to undesirable side reactions. On the other hand, reaction on alumina without $ZnCl_2$ is very sluggish. The combination of $ZnCl_2$ and alumina is acidic enough to catalyse the Michael addition to methyl vinyl ketone but moderate enough to suppress the undesired side reactions.

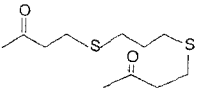
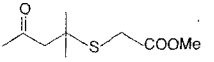
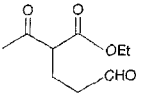
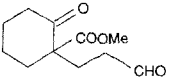
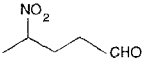
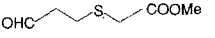
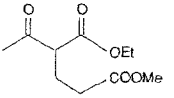
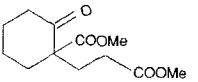
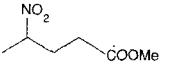
Table I

Al_2O_3-mediated Michael addition

Entry	*Donor*	*Acceptor*	*Time*	*Adduct*	*Yield (%)*[a]
1	Methyl 2-oxocyclo-hexanecarboxylate	MVK[b]	5 min		91
2	Ethyl acetoacetate	MVK	5 min		95
3	Acetylacetone	MVK	30 min		84
4	Ethyl cyanoacetate	MVK	4 h		90
5	Diethyl malonate	MVK	4 h		90
6	Nitroethane	MVK	2 h		60
7	Methyl thioglycolate	MVK	5 min		85
8	1,3-Propanedithiol	MVK (1 equiv)	5 min		75

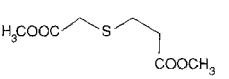
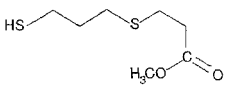
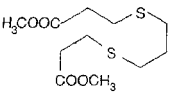
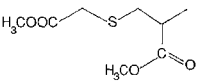
(contd)

Table 1 (contd)

Entry	*Donor*	*Acceptor*	*Time*	*Adduct*	*Yield (%)*[a]
9	1,3-Propanedithiol	MVK (2 equiv)	5 min		82
10	Methyl thioglycolate	Mesityl oxide	30 min		80
11[c]	Ethyl acetoacetate	Acrolein	5 min		90
12[c]	Methyl 2-oxycyclo-hexanecarboxylate	Acrolein	5 min		91
13[d]	Nitroethane	Acrolein	1 h		60
14[d]	Methylthioglycolate	Acrolein	10 min		90
15	Ethyl acetoacetate	MA[b]	4 h		80
16	Methyl 2-oxocyclo-hexane carboxylate	MA	4 h		88
17[c]	Nitroethane	MA	4 h		55

(contd)

Table I (contd)

Entry	*Donor*	*Acceptor*	*Time*	*Adduct*	*Yield (%)*[a]
18	Methyl thioglycolate	MA	2 h		85
19	1,3-Propanedithiol	MA (1 equiv)	30 min		76
20	1,3-Propanedithiol	MA (2 equiv)	30 min		90
21	Methyl thioglycolate	MMA[b]	2 h		75

[a]Yield of isolated pure products, fully characterized by their IR, NMR data, [b]MVK, MA and MMA are abbreviated for methyl vinyl ketone, methyl acrylate and methyl methacrylate, respectively. [c]Reactions were carried out at 0°C; [d]Reactions were carried out at −10 to −15°C (ice-salt bath).

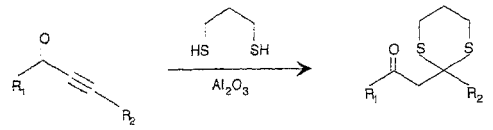
(b) Regioselective alkylation of 1,3-dicarbonyl compounds

Selective C-alkylation of 1,3-dicarbonyl compounds having two active hydrogen atoms through a simple and mild operation remains one of the more formidable problems in organic synthesis. The difficulties frequently encountered in the C-alkylation of 1,3-dicarbonyl compounds by traditional methods using bases are the presence of varying amounts of side products due to concomitant O-alkylation, di-C-alkylation, cleavage of 1,3-diketones and Claisen condensation. Although a number of methods using thallium enolates[8], cobalt and other metal complexes[9], tetralkylammonium fluorides[10] and its other derivatives[11] have been shown to be useful to overcome such difficulties, these methods have one or more limitations as regards the scope and generality of the reaction, the use of toxic materials, tedious and long reaction procedures, and/or relatively low yields of products.

We now report a solution to this problem which provides a simple and controlled procedure for the selective/mono- as well as di-C-alkylation of 1,3-dicarbonyl compounds

Table II

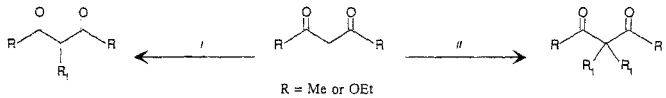
Preparation of β-keto 1,3-dithianes by Michael addition of 1,3-propanedithiol to α, β-acetylenic ketones on the surface of alumina



Entry	*R*	*R*$_2$	*Reaction time (h)*	*Yield(%)*[a]
a	i-Pr	H	4	70[b]
b	Ph	H	5	82[b]
c	4-OMe-C$_6$H$_4$	H	5	85[c]
d	3,4-(OMe)$_2$C$_6$H$_3$	H	5	80[c]
e	i-Pr	CH_2OCH_3	5	80[b]
f	Ph	CH_2OCH_3	6	75[b]

[a]All yields refer to pure isolated products, fully characterized by IR and ^{1}H NMR. [b]The reaction was carried out without solvent. The reaction was run in CH_2Cl_2.

through a solvent-free reaction on the surface of alumina impregnated with sodium or potassium alkoxide (Scheme 1)[12].



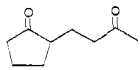
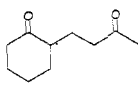
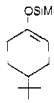
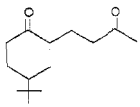
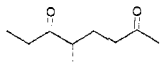
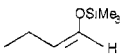
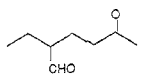
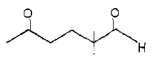
SCHEME 1. Reagents and conditions *(i)* KOBu^t or NaOEt (1equiv.) on Al_2O_3, R_1X (1 equiv.), room temp. *(ii)* NaOEt (2.5 equiv.) on Al_2O_3, R_1X (2 equiv.), room temp.

In a typical general procedure, the 1,3-dicarbonyl compound was stirred on the surface of alumina impregnated with alkoxide base for 30 min, after which the alkyl halide was added and stirring continued until completion of the reaction. The reaction conditions could be set to produce either mono- or di-C-alkylated product as desired in one step. For mono-C-alkylation, 1 equivalent of base (KOBu^t or NaOEt) and 1 equivalent of alkyl halide were used, whereas for dialkylation, 2.5 equivalents of NaOEt and 2 equivalents of alkyl halide produced best results (Table IV).

As shown in Table IV, a variety of 1,3-dicarbonyl compounds underwent selective mono- and di-C-alkylations with several alkyl halides in high yields under this procedure. No appreciable O-alkylation and di-C-alkylation was observed during mono-C-alkylation. No other side product has also been isolated during di-C-alkylation. The alkylations, in general, were complete within a reasonable time.

Table III

Michael addition of silyl enol ethers to methyl vinyl ketone

Entry	*Silyl enol ether*	*Time*	*Product*	*Yield (%)*[a]
1		5 min		78
2		5 min		72
3		5 min		85
4		1 h		70
5		2 h		85
6		30 min		86

[a]Yield of isolated pure products, fully characterized by their IR, ^{1}H NMR data.

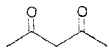
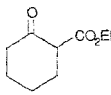
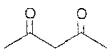
Presumably, the high efficiency of this procedure for regioselective C-alkylation is primarily due to the absence of solvent which, often, has significant contribution towards O-alkylation of ambident anions[3] and association of enolate oxygen with the surface of alumina. Anyway, convenience, simplicity of operation, general applicability with a broad spectrum of alkyl halides and high yield will make this procedure more useful and attractive in the field of organic synthesis.

(c) Selective bromination of alkyl-substituted aromatic hydrocarbons

Bromination of aromatic compounds is usually carried out with molecular bromine in a suitable solvent, but to avoid benzylic bromination and other undesired side reactions

Table IV

Selective mono- and di-C-alkylation of 1,3-dicarbonyl compounds on the surface of alumina impregnated with KOBu^t

Substrate	*RX*	*Mono-C-alkylated product*[a]	*Di-C-alkylated product*[b]
	MeI	95% (6 h)	80% (6 h)
	CH_2=CH-CH_2Br	90% (0.5 h)	90% (2 h)
	$PhCH_2Br$	85% (5 h)	81% (6 h)
	$BrCH_2CO_2Et$	75% (6 h)	70% (6 h)
	$CH_3CH(Br)CO_2Et$	80% (6 h)	
	MeI	92% (6 h)	
	CH_2=CH-CH_2Br	92% (0.5 h)	
	$PhCH_2Br$	90% (0.5 h)	
	$BrCH_2CO_2Et$	86% (6 h)	
	$CH_3CH(Br)CO_2Et$	80% (6 h) (C, 60%, O, 40%)	
	MeI	86% (22 h)	78% (24 h)
	CH_2=CH-CH_2-Br	85% (1 h)	75% (4 h)
	$PhCH_2Br$	80% (4 h)	82% (5 h)
	$BrCH_2CO_2Et$	75% (16 h)	76% (24 h)

[a]with 1 equiv. base and 1 equiv. alkyl halide; [b]with 2 equiv. base and 2 equiv. alkyl halide.

particularly when alkyl groups are attached to the aromatic ring, often special precautions like rigorous exclusion of light and catalytic presence of iodine, etc., are required. We have developed a very simple and quick procedure for exclusive ring bromination of alkyl-substituted aromatic hydrocarbons through a solvent-free reaction using molecular bromine adsorbed on the surface of alumina[14].

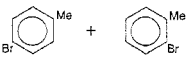
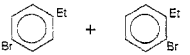
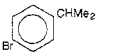
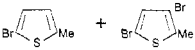
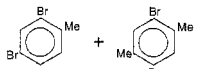
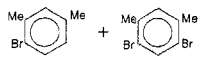
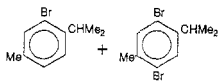
In a general procedure, bromine adsorbed on the surface of alumina was added to the aromatic substrate also adsorbed on alumina at room temperature with stirring. The reaction was complete within a minute as indicated by the disappearance of bromine colour. As usual, the product was isolated by simple filtration chromatography through a short plug of silica gel. The results with different substrates are presented in Table V.

The reaction was very clean and remarkably fast. Bromination of monosubstituted hydrocarbons led predominantly or exclusively to *p*-substitution. Disubstituted substrates furnished preferentially the monobrominated products and fused hydrocarbons like tetralin and indan produced the corresponding monobromo compounds as sole products. The yields, in general, were excellent.

For comparison, when some of the reactions were carried out neat without alumina, considerable benzylic bromination was observed together with ring substitutions. Further, the reaction was slow. The presence of solvent made the bromination sluggish and led to other side products. Thus, this procedure of ring bromination on the surface of alumina provides an attractive alternative to the currently available methods for ring bromination of aromatic compounds.

Table V

Results of ring bromination of aromatic hydrocarbons on the surface of alumina

Entry	*Hydrocarbons*	*Products*		*Yield (%)*[a]
1			(65:35)[b]	90
2			(90 10)[c]	92
3				88
4[d]			(80:20)[b,c]	85
5				90
6				86
7			(80:20)[c]	82
8			(96:4)[c]	84
9			(90:10)[c]	85

[a]isolated yield of brominated products; [b]by ^{1}H NMR; [c]by GC; [d]run at –10°C.

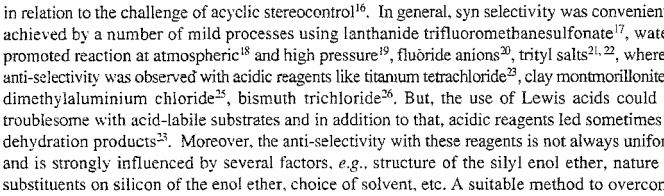
As an extension of this technology we have observed an interesting phenomenon in the iodination of a, b-unsaturated cycloalkenones on the surface of alumina. 3-Substituted cyclohexenones produced the corresponding 3-substituted phenols, while other cycloalkenones remained unaffected[15] (Table VI).

Presumably, 3-substituted cyclohexenones underwent iodination followed by dehydroiodination and aromatisation under reaction conditions to produce 3-substituted phenol. But the reasons for this reaction with only 3-substituted cyclohexenones and not with other cycloalkenones are still not clear and unexplainable to us.

(d) Aldol reaction of silyl enol ethers with aldehydes

The cross aldol reaction of silyl enol ethers with aldehydes has attracted much interest recently in relation to the challenge of acyclic stereocontrol[16]. In general, syn selectivity was conveniently achieved by a number of mild processes using lanthanide trifluoromethanesulfonate[17], water-promoted reaction at atmospheric[18] and high pressure[19], fluoride anions[20], trityl salts[21, 22], whereas anti-selectivity was observed with acidic reagents like titanium tetrachloride[23], clay montmorillonite[24], dimethylaluminium chloride[25], bismuth trichloride[26]. But, the use of Lewis acids could be troublesome with acid-labile substrates and in addition to that, acidic reagents led sometimes to dehydration products[23]. Moreover, the anti-selectivity with these reagents is not always uniform and is strongly influenced by several factors, *e.g.*, structure of the silyl enol ether, nature of substituents on silicon of the enol ether, choice of solvent, etc. A suitable method to overcome these difficulties will thus be well appreciated. In our drive to explore surface-mediated reaction we have discovered a general anti-selectivity for cross aldol products in the reaction of trimethylsilyl enol ethers with aldehydes on the solid surface of neutral alumina under sonication without any solvent (Scheme 2)[27].

Aldol reaction of silyl enol ethers with aldehydes



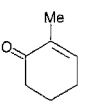
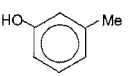
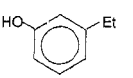
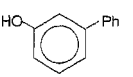
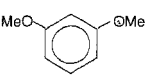
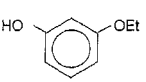
SCHEME 2 Reagents and conditions: *(i)* Al_2O_3 (neutral), ultrasound, 18 h.

The reaction procedure is very simple. Trimethylsilyl enol ether was added to activated neutral alumina under stirring. After 2 min the aldehyde was added and the resulting powder was then immersed in an ultrasonic bath for a certain period of time as required for completion. The solid mass was then taken into chloroform and filtered through a short column packed with anhydrous sodium sulfate. The filtrate was evaporated to leave the crude aldol which was further purified by column chromatography over alumina. The results of reaction of a number of structurally varied silyl enol ethers with a variety of aldehydes under this procedure are presented in Table VII.

Diastereoselectivities, in general, are good and a general trend for anti-selectivity was observed in all the reactions irrespective of the nature of silyl enol ether and aldehydes. No side products including the dehydrated olefin were observed. Interestingly, the presence of

Table VI

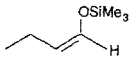
Iodination of cycloalkenones on the surface of alumina

Entry	*Cycloalkenone*	*Time (hours)*	*Product*	*Yield(%)*[a]
1		48	No reaction	
2		48	No reaction	
3		48	No reaction	
4		48		30
5		120		10
6		120		25
7		48		50[b]
8		48		40[c]

[a]The yield was calculated on the basis of isolated products after purification. [b]Presumably, this product was formed through the methylation of the initial product 3-methoxyphenol by 3-methoxycyclohexenone under the reaction conditions. [c]Some amount (10%) of resorcinol diethyl ether was also formed.

Table VII

Aldol reaction of silyl enol ethers with aldehydes on the solid surface of alumina

Entry	*Silyl enol ether*	*Aldehyde*	*Time (h)*	*Yield(%)*[a]	*anti/syn*[b]
1	 (1)	PhCHO	27	75	77/23
2	1	$CH_3CH_2CH_2CHO$	25	70	75/25
3	1	*p*-O_2N-C_6H_4CHO	30	90	60/40
4	 (2)	PhCHC	18	68	75/25
5	2	*p*-O_2N-C_6H_4CHO	28	70	67/33
6	2	*p*-MeO-C_6H_4CHO	30	70	70/30
7	2	*p*-Cl-C_6H_4CHO	30	85	75/25
8	 (8)	PhCHO	30	82	65/35
9	3	*p*-O_2N-C_6H_4CHO	30	88	60/40
10		PhCHO	28	65	65/35

[a]All yields refer to isolated products; [b]*Anti/syn* ratio was calculated by ^1H NMR analysis.

solvent retarded the reaction to a great extent. The progress of reaction of 1-trimethylsilyloxy cyclohexene with benzaldehyde under identical condition in dichloromethane is practically nil, while in THF the reaction proceeded to the extent of only 10%, although *anti/syn* ratio is the same as in solid phase reaction. This indicates that alumina surface plays the decisive role in controlling the stereochemistry of aldol in the absence or presence of solvent. On the other hand, the reaction was also very slow under stirring without sonication. Thus, solid alumina surface and ultrasound are two important contributors towards the progress of the reaction.

The procedural simplicity, mild and neutral reaction condition and above all, suppression of undesired side reactions make this method useful with regard to acyclic stereocontrol.

(e) Regioselective reductive cleavage of epoxides

The reductive cleavage of epoxides to alcohols is one of the most useful reactions in organic synthesis. In principle, an unsymmetrical alkyl-substituted epoxide can produce the more substituted carbinol or the less-substituted alcohol depending on the cleavage of the C–O bond to the less substituted carbon atom or the more substituted one. Thus, realisation of the methods for the regioselective ring opening of epoxides is of great importance. In general, more substituted alcohols are easily obtained by reduction of epoxides with nucleophilic hydride transferring agents, whereas access to less-substituted alcohols by reverse opening is not so simple. Electrophilic hydride reagents have been used for this purpose but mixtures of alcohols usually result. Satisfactory results have been achieved only with a limited number of reagents[28,29]. But high toxicity and cost of these reagents often restrict their usage. We have developed a simple methodology for the reductive cleavage of unsymmetrical epoxides to the less-substituted alcohols using zinc borohydride supported on silica gel[30,31].

In a typical procedure, the epoxide was stirred with zinc borohydride supported on silica gel in dry THF at room temperature for 24 h. The reaction mixture was then decomposed with careful dropwise addition of water and filtered. The filtrate was extracted with ether and the extract was evaporated to leave the pure product. The results of cleavage of a variety of epoxides by this procedure are reported in Tables VIII and IX.

Regioselectivity in cleavage of all types of epoxides is excellent. The less-substituted alcohols are produced exclusively or predominantly. Cleavage of cyclic epoxides occurred in a stereoselective manner producing Z-alcohols predominantly or exclusively. Conversion of E-stilbene oxide to 1,2-diphenyl ethanol implies that this supported reagent is mild and does not induce any rearrangement as observed with sodium cyanoborohydride and boron trifluoride etherate[28].

When this cleavage reaction was carried out with zinc borohydride in THF, it was found to be very sluggish and the epoxide remained almost unaffected. Presumably, silica gel in the supported reagent activates the epoxide towards nucleophilic attack by the hydride at the site best able to accommodate a carbonium ion.

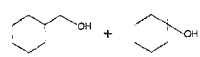
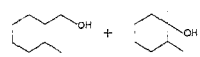
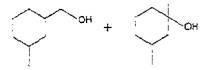
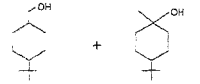
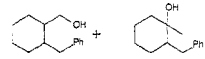
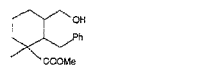
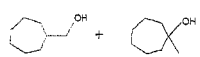
The major advantages of this methodology are the easy availability of this reagent, mild condition and much improved regioselectivity in reductive cleavage of epoxides and these make this procedure more useful and attractive in the field of organic synthesis.

(f) Regioselective hydration of alkenes

Hydration of alkenes to alcohols is one of the important reactions in organic synthesis. An unsymmetrical alkyl-substituted carbon–carbon double bond on such reaction can produce the more substituted carbinol or the less-substituted alcohol depending on the mode of hydration in the Markovnikov or anti-Markovnikov manner, respectively. In general, oxymercuration–demercuration[32] of alkenes provides a very efficient method for the Markovnikov addition and, on the other hand, hydroboration–oxidation[33] leads to the anti-Markovnikov hydration.

Table IX

Reductive cleavage of methylenecycloalkane oxides with silica gel-supported zinc borohydride in THF

Entry	*Epoxide*	*Product*	*Product-Ratio* [a]	*Yield(%)* [b]
1			98:2	95
2			87(55+32):13	92
3			90(58+32):10	91
4			70.30	92
5			84(56+28).16	90
6				87
7			80(46+34):20	90
8			93:7	94

[a]The percentage compositions of products were determined by GC; the figures in parenthesis showed the percentage ratio of stereoisomers in the less-substituted alcohol. [b]Yields refer to total isolated products.

reduction of the double bonds. This leads to saturated alcohols and/or ketones due to competing 1,2- *vs* 1,4-attack by hydride. Considerable progress has been made in the development of various reducing agents for this purpose, but few have proven general and practical in scope. We have found that our silica gel-supported zinc borohydride provides an efficient and highly selective reduction of conjugated ketones and aldehydes to the corresponding allylic alcohols[36]. The results of reduction are summarized in Table XI.

Table VIII

Reductive cleavage of epoxides with supported reagent

Epoxide	*Product*	*Yield(%)*
Nonene-1-oxide	$C_7H_{15}CH_2CH_2OH$	88
Epichlorohydrin	$ClCH_2CH_2CH_2OH$ (70%) + $ClCH_2CH(OH)CH_3$(30%)	85
Styrene oxide	$PhCH_2CH_2OH$ + $PhCH(OH)CH_3$ (trace)	90
α-Methylstyrene oxide	$PhCH(Me)CH_2OH$	91
trans-Stilbene oxide	$PhCH(OH)CH_2Ph$	88
1-Methylcyclohexene oxide	*cis*-2-Methylcyclohexanol + *trans*-2-Methylcyclohexanol (10%)	85
1-Methylcycloheptene oxide	*cis*-2-Methylcycloheptanol	84
Indene oxide	Indan-2-ol	90

Recently, various combinations of Lewis acids and borohydrides[34] have also been reported to effect hydration of olefins in an anti-Markovnikov manner. We have discovered[35] that the reaction of zinc borohydride in DME with alkenes on silica gel support furnished clean regioselective anti-Markovnikov hydration to produce the less-substituted alcohols in excellent yields. In a general procedure, a solution of zinc borohydride was added to alkene uniformly adsorbed on activated silica gel and the reaction was continued at room temperature under stirring till completion. The reaction mixture was then decomposed with water and extracted with ether to isolate the product.

Several structurally varied alkenes underwent clean regioselective anti-Markovnikov hydration by this procedure to give the corresponding less-substituted alcohols in high yields. The regioselectivity, in general, is excellent. The reactions are reasonably fast and no side products were observed.

The mechanism of this reaction is not yet very clear, but the following observations are noteworthy. Silica gel or zinc borohydride alone failed to promote any hydration. Replacement of zinc borohydride with other zinc salts like zinc acetate, zinc sulfate, zinc oxide and zinc chloride also produced no alcohols. A combination of zinc borohydride and silica gel is essential for this reaction to proceed.

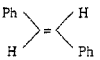
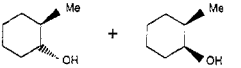
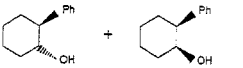
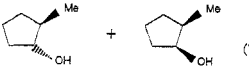
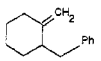
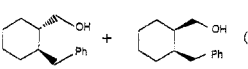
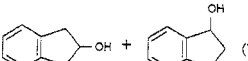
Whatever be the exact nature of reaction path, the present combination of zinc borohydride and silica gel provides an efficient methodology for the regioselective *anti*-Markovnikov hydration of alkenes producing less-substituted alcohols and will find important applications in systems containing sensitive functionalities.

(g) Regioselective 1,2-reduction of conjugated ketones and aldehydes

Selective reduction of conjugated ketones and aldehydes to the corresponding allylic alcohols is a challenging problem since it is usually associated with varying amounts of concomitant

Table X

Hydration of alkenes with silica gel-supported zinc borohydride

Entry	*Alkene*	*Time (h)*	*Product* [a]	*Yield (%)* [b]
1	$CH_3(CH_2)_6CH=CH_2$	0.5	$CH_3(CH_2)_7CH_2OH$	95
2	$PhCH=CH_2$	1	$PhCH_2CH_2OH$ (80%)[c] + $PhCH(OH)CH_3$(20%)	85
3		1.5	$PhCH(Me)CH_2OH$	90
4		24	$PhCH(OH)CH_2Ph$	70
5		0.5		85
6		0.5	 (70:30)[c]	80
7		24	 (75:25)[c]	70
8		0.5	 (70:30)[c]	70
9		1	 (55:45)[c]	90
10		1	 (75:25)[c]	90

[a] All compounds were identified by direct comparison of physical data with those of authentic samples. [b] All yields refer to isolated pure products. [c] The ratio of regio- and stereoisomers was estimated by ^1H NMR and GC.

Table XI

Reduction of conjugated carbonyl compounds with silica gel-supported zinc borohydride to the corresponding allylic alcohols

Entry	*Starting carbonyl compound*	*Yield (%)*
1	3-Methylcyclohex-2-en-1-one	80
2	4-Carbethoxy-3-methyl-2-cyclohexen-1-one (Hagemann's ester)	82
3	(s)-Carvone	87
4	3-Carbmethoxycyclohex-2-en-1-one	85
5	α-ionone	85
6	Ph–CH = $CHCOCH_3$	90
7	Mesityl oxide	70
8	Cinnamaldehyde	92
9	Citral	95
10	Crotonaldehyde	80
11	4-Nitrobenzaldehyde	90

3. Conclusion

It is clear from these illustrations that simple materials like alumina and silica gel can have an important role in dictating the course of many reactions. Although the exact nature of their activities is not yet very clear, it is generally assumed that the effectiveness of silica gel and alumina may be due to a combination of several factors : (i) an increase in the effective area for reaction, (ii) the presence of pores which contain both substrate and reactant and thus lower the entropy of activation of reactions, (iii) an activation of the reagent, (iv) a synergistic effect resulting from bringing electrophile and nucleophile into proximity, while at the same time enhancing the nucleophilicy and basicity of the latter. The potentialities of this technology are hitherto not fully exploited and wider application of this technology in organic synthesis is desirable. The present account it is hoped will attract more attention to this area.

Acknowledgements

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