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TRIISOPROPYLSILANOL: A NEW TYPE OF PHASE TRANSFER CATALYST FOR DEHYDROHALOGENATION

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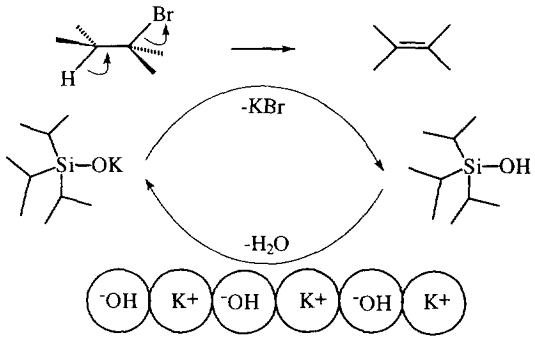
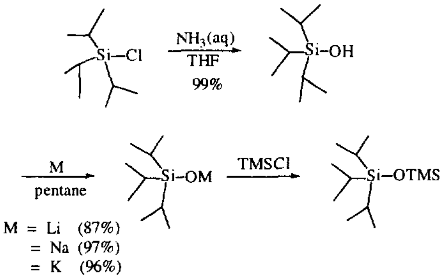
Abstract: *A new solid-liquid phase transfer catalyst, trisopropylsilanol (TIPSOH), has been developed which, through the silanol/silanoate system, allows KOH to quantitatively convert even primary alkyl halides to alkenes avoiding both ether and alcohol by-products. Its potential application in the detoxification of mustard gas analogues and environmental pollutants has been demonstrated.*

Silanols and their corresponding oxygen anions (silanoates) find increasing use in organic synthesis as organic-soluble equivalents of water and hydroxide and in organometallic chemistry as stable bulky ligands.[2,3] In addition, silanols are good hydrogen-bond acceptors and even better hydrogen-bond donors.[4] Our previous studies with TIPS systems[5] suggested that the new silanol, triisopropylsilanol, held promise as a potentially versatile new type of phase transfer catalyst (PTC) in dehydrohalogenation reactions.

The catalytic cycle which we envisaged takes advantage of the high solubility of both KOTIPS and TIPSOH in organic solvents (*i.e.* pentane, DMF, DMSO, THF, EE) in contrast to the low solubility of KOH in these media. Second, it also benefits from the favorable thermodynamics of the deprotonation of the silanol compared to alcohols with KOH, a fact which provides the silanoate base in high concentration from the KOH/TIPSOH system, in contrast to KOH/ROH systems. Third, it utilizes the steric bulk of the TIPS group to retard its S_N2 reactions at the carbon centers (*i.e.* Williamson ether synthesis), thereby favoring elimination (E2) over substitution. These properties distinguish the silanol system from other existing PTC systems (*e.g.* R_4NX, polyethylene glycols).[6]



The preparation of TIPSOH is particularly straightforward, it being readily available from the ammoniacal hydrolysis of TIPSCl. Compared to unhindered silanols (*e.g.* TMSOH), TIPSOH is very stable showing no tendency to disproportionate into water and its disiloxane, behavior which is well-known for silanols containing bulky substituents which limit access to the silicon center. In this sense, TIPSOH is a true silyl alcohol, undergoing smooth reaction with alkali metals leading efficiently to isolable metal silanoates. The hygroscopic solids were analyzed chromatographically as their TMS ethers and spectroscopically by ^{1}H and ^{13}C NMR.



Because both TIPSOH and its metal silanoates are highly soluble in non-polar solvents, the TIPSOH/KOTIPS couple represented a promising system for bringing a very hindered base to haloalkane substrates in a medium where common bases such as KOH are insoluble. It remained to establish that such bases could effectively deprotonate TIPSOH as a key feature of this system which would permit the development of a new solid-liquid phase transfer catalysis process based on this acid/base couple.

The relative acidity of TIPSOH and *t*-BuOH were initially examined to establish that TIPSOH exhibited behavior similar to other known silanols. Through an equilibrium association to the base diethyl ether, silanols exhibit IR band (OH) shifts (Δv^{-1} (free vs associated)) nearly twice as great as do the corresponding carbinols, a phenomenon which has been interpreted as an indication that the silanols are more acidic than are carbinols.[4a] This methodology was examined with *t*-BuOH which gave a $\Delta \upsilon = 115\ \text{cm}^{-1}$ compared to $\Delta \upsilon = 210\ \text{cm}^{-1}$ for TIPSOH. Based on this evidence, TIPSOH, like other silanols, appeared to be significantly more acidic than *t*-BuOH.

The equilibrium acidities for over 1200 compounds have been determined in DMSO solution.[7] Under the same conditions employed for H_2O (pK_a 31.2) and *t*-BuOH (pK_a 32.2), the pK_a of TIPSOH was determined titrametrically employing the overlapping indicator method (pK_a 24.4 (1,1,3-triphenyl-2-aza-1-propene, pK_a 24.3); 24.5 (9-*t*-butylfluorene, pK_a 24.35)) resulting in an average pK_a value of 24.4±0.1 for TIPSOH in this solvent. The fact that TIPSOH, in contrast to *t*-BuOH or related alcohols, is much more acidic than water clearly suggested that KOH(s) should be quite effective in generating KOTIPS from TIPSOH in a new catalytic cycle for dehydrohalogenations in a dipolar aprotic medium where the low solubility of KOH in this medium would preclude its direct interaction with the substrate.

The dehydrohalogenation of haloalkanes has been extensively studied.[8] No alkoxide base, even KO(*t*-Bu), has solved the problem of substitution (*vs* elimination) in the case of *primary* haloalkanes. The best results[8a,b] reported are found with KO(*t*-Bu) in DMSO ($E2/S_N2 = 3.3$) while

KOH gives the worst result ($E2/S_N2 < 0.067$). We felt that the selectivity of KOTIPS should be superior to even KO(*t*-Bu) because of its increased steric bulk. The above results suggested that transforming the inexpensive base, KOH, into the highly hindered KOTIPS was feasible. Therefore, this silanol-based catalytic process was examined at 25 °C employing DMF solvent, conditions which we found to give no significant reaction in the absence of added silanol catalyst.

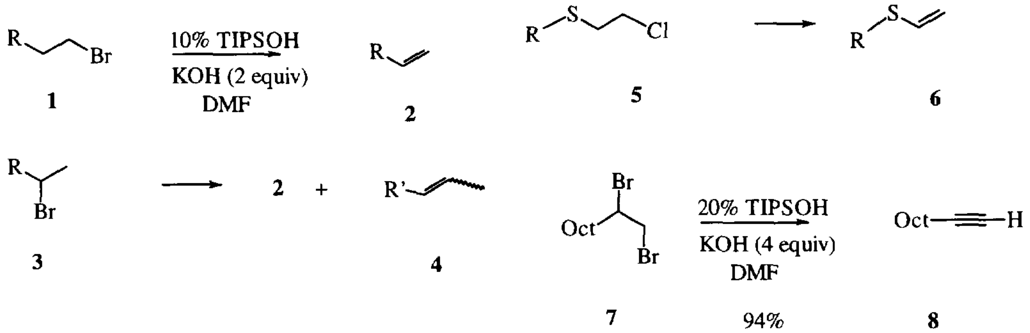


Table 1. Dehydrohalogenation of 1° and 2° haloalkanes with KOH/TIPSOH in dry DMF at 25 °C.[a]

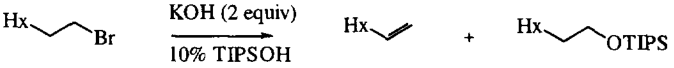
		Yield [%]		
Haloalkane	R	1-alkene	2-alkene	1-alcohol
1a	Hx[b]	97	0	0
1b	Ph	100	0	0
3a	Hx	41	51[c]	0
3b	Ph	100	0	0
5	Et	100	0	0

[a] KOH/Halide = 2:1. GC yields employing an internal standard.[b] Hx = n-C_6H_{13} [c] A *cis/trans* ratio of 1:6 was obtained which was corroborated by photoisomerization (450 W Hg lamp (190-600 nm) in C_6D_6).

From the above results summarized in Table 1, it can be observed that elimination is the exclusive process for both 1°- and 2° halides under these conditions. However, the process is not regioselective, forming both terminal and internal olefins (**4a**) from 2-bromooctane (**3a**). The mustard analogue **5** also undergoes smooth dehydrohalogenation suggesting this as a potential method for detoxifying these materials prior to combustive disposal. All of the isomeric vinyl bromides were identified in the double dehydrohalogenation of **7**. However, their rates of formation approximated their rates of decomposition so that these were converted directly to the alkyne **8** (94%). Moreover, a comparison of the *n*-octyl halides in competitive experiments clearly revealed that the relative reactivities follow the order: I > Br > Cl.

For **1a** (0.6 M), the process in DMSO was found to only consume the silanoate catalyst (S_N2).

Under similar conditions, with DMF as the solvent, 1-octene is formed (87%), but the silanoate is wholly consumed to give the silyl ether (10%). With more dilute conditions in DMF, **1a** (0.3 M) is efficiently converted to 1-octene (97%). We attribute the silyl ether formation to the greater polarity[9] of DMSO ($\varepsilon_{25^\circ C} = 46.6$) *vs* DMF ($\varepsilon_{25^\circ C} = 36.7$), favoring S_N2 over E2, a selectivity further enhanced by the production of water ($\varepsilon_{25^\circ C} = 78.3$) as the reaction proceeds. This effect is minimized with more dilute DMF solutions allowing the E2 process to reach completion before the catalyst is consumed.[10]



1a

DMSO (0.6M)	0%	10%
DMF (0.6M)	87%	10%
DMF (0.3M)	97%	----

The use of TIPSOH as a phase transfer catalyst in the dehydrohalogenation of haloalkanes circumvents competitive substitution reactions even for *primary* haloalkanes. Moreover, the process uses the inexpensive KOH, efficiently transforming it into a highly soluble, sterically hindered silanoate which effects the dehydrohalogenation and is regenerated by the KOH to repeat the cycle.

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10. GC analysis of the reaction mixtures revealed the complete consumption of the haloalkane normally in 3-6 h, with faster reactions resulting from pulverized KOH (rather than pellets).

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