Solvolysis Reactions of *tert*-Butyl Chloride and Methyl Tosylate in Trimethoxyborane Methanol Mixtures[1a]

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The solvolysis rates of *t*-butyl chloride and methyl tosylate were measured in various trimethoxyborane — methanol mixtures. The ionizing power and the nucleophilicity for the respective solvent mixtures were determined, and the suitability of this new solvent system for the study of solvolysis reactions is discussed. At elevated temperatures a reaction of hydrogen chloride, liberated in the solvolysis of *t*-butyl chloride, with the solvent was observed, and the results seem to indicate that methyl chloride is the reaction product.

Solvents of high ionizing power and low nucleophilicity have attracted attention in the study of solvolytic reactions for a long time[2,3]. Recently, a lot of work has been done in fluoroalcohols, trifluoroethanol[4-11] and hexafluoroisopropanol[12]. The drawback of these solvents, however, is that they are not readily available, and/or are relatively expensive. With this in mind, we have turned our attention to a new solvent mixture, trimethoxyborane-methanol, which can be easily synthesized[13] and which potentially may have all the desired properties of a convenient solvent for the study of solvolytic reactions.

Trimethoxyborane and methanol form an azeotrope (TMB·M) boiling at 54.6 °C, and having a composition[13,14] of 1 mole trimethoxyborane : 1 mole methanol. The following acid-base equilibrium between the two components can be formally written.

$$(CH_3O)_3B + CH_3OH \rightleftharpoons (CH_3O)_4\overset{-}{B}\overset{+}{H}$$

However, it was found[14] that the nature of the azeotrope was that of an equimolar mixture of $(CH_3O)_3B$ and methanol, with a very small amount of $(CH_3O)_4\overset{-}{B}\overset{+}{H}$ present. Regardless of that, it was reasonable to assume that such a solvent mixture would have quite a low nucleophilicity as well as increased proton donor character relative to methanol. On the other hand, Kreevoy et al.[15] have found that the azeotrope has a dielectric constant of 9 (comparable to that of acetic acid, 6.18, and trifluoroacetic acid, 8.22), and that it is in many respects a good ionizing solvent.

In view of all these observations, we set out to measure the solvolysis rates of *t*-butyl chloride and methyl tosylate in various trimethoxyborane--methanol mixtures, in order to probe their ionizing power and nucleophilicity. The results of these investigations are presented below.

Materials

Trimethoxyborane — Methanol Azeotrope was prepared from methanol and boric acid (molar ratio 8 : 1) in 90% yield, according to the procedure of Brown *et al.*[13], b. p. 54 °C, $n_D^{20} = 1.3483$, ^{1}H NMR (neat): δ 3.39 (s, 12), 4.14 (s, 1).

Trimethoxyborane was obtained by separating[13] the methanol from the azeotrope with anhydrous zinc chloride; yield 95%, $n_D^{20} = 1.3576$, ^{1}H NMR (neat): δ 3.36.

t-*Butyl Chloride* was carefully fractionally distilled and a centre cut was used.

Methyl p-*Toluenesulfonate* was prepared[16] from methanol and p-toluenesulfonyl chloride, ^{1}H NMR ($CDCl_3$): δ 2.38 (s, 3), 3.68 (s, 3), 7.22—7.88 (aromatic, 4).

Kinetic Measurements

Solvent mixtures were prepared by mixing measured volumes of either the trimethoxyborane — methanol azeotrope and methanol (mixtures with mole fraction methanol larger than 0.5), or trimethoxyborane and methanol (mixtures with mole fraction methanol smaller than 0.5). Rates were measured by the usual sealed ampule technique, and the reactions were followed to ca. 75% completion. The reactions were first order within experimental error over the range of concentrations investigated.

The solvolysis rate of t-butyl chloride was followed by NMR on a Varian A-60 A spectrometer. Measurements were made with ca. 0.3 M solutions and toluene was used as an internal standard. Rate constants were obtained from plots of reactant concentration *vs.* time.

The rates of methyl tosylate were determined in ca. 0.07 M solutions by potentiometric titration of the liberated acid using Radiometer Titrator TTT 2 and Autoburette ABU 11.

Definition of Units

1 kcal mmole^{-1} = 1000 cal$_{th}$ mole^{-1}

cal$_{th}$ = 4.184 J

e.u. = 4.184 J mole^{-1} K^{-1}

RESULTS

The rates and activation parameters for the solvolysis of t-butyl chloride and methyl tosylate in trimethoxyborane — methanol mixtures are given in Table I and II, respectively.

The graphical dependence of log k *vs.* mole fraction methanol for the solvolysis of t-butyl chloride and methyl tosylate is shown in Figure 1 and 2, respectively.

The solvolysis rates of methyl tosylate were measured by potentiometric titration of the liberated acid, while those of t-butyl chloride were measured by nuclear magnetic resonance spectroscopy[18].

Reaction of Hydrogen Chloride with the Solvent

It was observed that hydrogen chloride produced in the solvolysis of t-butyl chloride in trimethoxyborane-methanol was being consumed in the course of the reaction. This was proved further by introducing a small amount of HCl into the solvent mixture (so as to get a concentration of acid comparable to that liberated during solvolysis), sealing the solution in ampules and heating them at 100 °C for varying periods of time. The rate of HCl consumption depended on the concentration of acid and the composition of the solvent, but it was within the range of 75—85% reaction after 1 hour. The reaction between HCl and trimethoxyborane — methanol thus being proved no further attempt was made to investigate it in detail. No such reaction was observed in the solvolysis of methyl tosylate.

TABLE I

Rates and Activation Parameters for the Solvolysis of t-Butyl Chloride in Trimetoxy Borane — Methanol Mixture

Solvent[a]	Mole Fraction Methanol	Temp. ^0C	k 10^{-5} s^{-1}	$\Delta H^{\ddagger}$ kcal mole^{-1}	$\Delta S^{\ddagger}$ e. u.
Methanol	1.000	70	21.0[b]		
		90	159	24.3[c]	— 5[c]
TMB·B : MeOH					
1 : 3	0.925	70	3.20 ± 0.14		
		90	8.79 ± 0.51	11.9 ± 1.43	— 45 ± 4.30
1 : 1	0.828	70	1.41 ± 0.23		
		90	3.79 ± 0.47	11.8 ± 4.20	— 46 ± 6.06
2 : 1	0.744	70	0.896 ± 0.028		
		90	2.77 ± 0.20	13.2 ± 1.78	— 44 ± 6.34
6 : 1	0.620	80	0.734 ± 0.032		
		90	1.92 ± 0.12	23.7 ± 1.02	— 15 ± 3.05
TMB·M Azeotrope	0.500	80	0.600 ± 0.018		
		90	0.980 ± 0.019	11.8 ± 3.11	— 50 ± 6.46
TMB : MeOH					
5 : 1	0.360	90	0.480		
		100	0.648	7.4	— 63
10 : 1	0.219	90	0.208 ± 0.022		
		100	0.450 ± 0.035	19.9 ± 5.3	— 30 ± 7

[a] TMB = trimetoxy borane; TMB · M = trimetoxy borane — methanol azeotrope. [b] Reference 2a. [c] Calculated from data in reference 2a.

No separate investigation of the solvolysis products was made. However, in the solvolysis of *t*-butyl chloride some conclusions can be made from the NMR spectra of the runs. The pertinent chemical shifts in trimethoxyborane — methanol (there are small variations of these values due to different compositions of solvent) are as follows:

δ 1.60 ppm *t*-butyl chloride

2.34 ppm CH_3 group of toluene (internal standard)

1.16, 3.23 CH_3 and OCH_3 of methyl-*t*-butyl ether

2.95 assumed to be due to methyl chloride, the reaction product of HCl with the solvent

3.39 ppm OCH_3 in the solvent.

The signal that was assigned to methyl chloride increased in the course of the reaction, but it was always somewhat smaller in intensity than that due to the methoxy group of the ether product.

TABLE II

Rates and Activation Parameters for the Solvolysis of Methyl Tosylate in Trimethoxyborane—Methanol Mixtures

Solvent[a]	Mole Fraction Methanol	Temp. °C	k 10^{-5} s^{-1}		$\Delta H\neq$ kcal mol^{-1}	$\Delta S\neq$ e.u.
Methanol	1.000	50	1.06[b]			
		90	42.3[c]		20.8[c]	— 17[c]
TMB·M:MeOH						
1 : 3	0.925	70	1.42	± 0.13		
		90	4.25	± 0.36	12.8 ± 2.47	— 43 ± 4.32
1 : 1	0.828	70	1.02	± 0.16		
		90	3.80	± 0.26	15.5 ± 3.95	— 37 ± 7.8
2 : 1	0.744	70	0.719	± 0.02		
		90	2.13	± 0.22	12.7 ± 2.47	— 46 ± 7.8
6 : 1	0.620	80	0.867	± 0.08		
		90	1.81	± 0.14	18.3 ± 3.08	— 31 ± 9.3
TMB·M Azeotrope	0.500	80	0.537	± 0.024		
		90	0.806	± 0.028	9.7 ± 2.03	— 58 ± 6.09
TMB : MeOH						
5 : 1	0.360	90	0.224			
		100	0.413		15.7	— 42
10 : 1	0.219	90	0.0406 ± 0.003			
		100	0.0782		16.9 ± 3.05	— 42 ± 7.15

[a] TMB = trimetoxy borane, TMB·M = trimetoxy borane — methanol azeotrope. [b] Reference 17.
[c] Calculated from data in reference 17.

DISCUSSION

The ionizing power, Y, and the nucleophilicity, N_{BS}[19], for different mixtures of trimethoxyborane and methanol are presented in Table III.
The Y values were calculated using the standard Grunwald — Winstein equation[2a], while the nucleophilicities were calculated from the general equation[23]

$$\log (k/k_0) = l\, N + m\, Y$$

according to the method recently proposed by Schleyer et al.[20,24].

For comparison, equivalent data of some other commonly used solvents are given in Table IV.

It can be seen from Table III that the ionizing power of trimethoxyborane — methanol mixtures in general is very low[27]. This is rather surprising in view of other properties of the solvent described by Kreevoy et al.[15] in the preceding papers. Increasing the amount of methanol in the solvent results in an increase in the solvolysis rate of t-butyl chloride, i. e. in an increase of the ionizing power of the solvent. The ability of the solvent to stabilize the reaction transition state seems to be strongly reduced by adding even a small quantity (7.5 mole %) of trimethoxyborane to methanol. The drastic reduction

in rate can be best seen in Figure 1. How the structure of the solvent is reflected by these observations remains to be discussed. One obvious explanation is that the lone electron pairs of the oxygen atom in methanol are much less efficient in stabilizing the positive charge produced in the reaction transition state, since they are involved in some kind of interaction with the electron deficient boron compound. It is interesting to note that the properties of the solvent, as reflected by solvolysis rates, seem to change the least in the region of approximately 0.6—0.9 mole fraction methanol. This can be seen from both Figures 1 and 2.
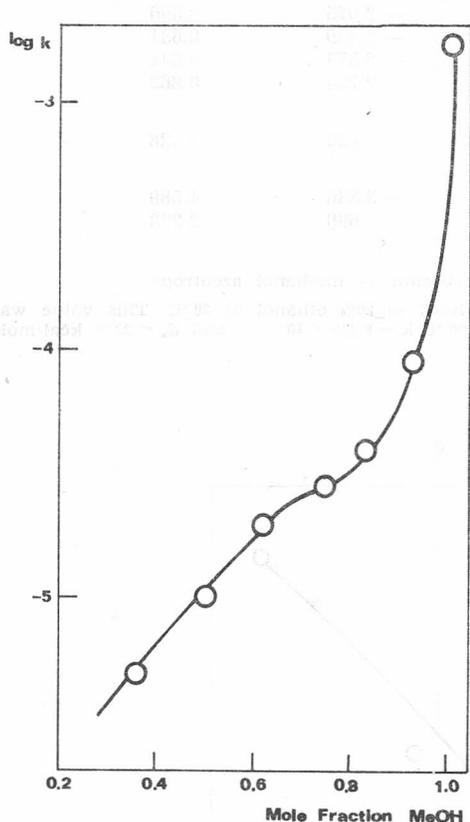
Figure 1.
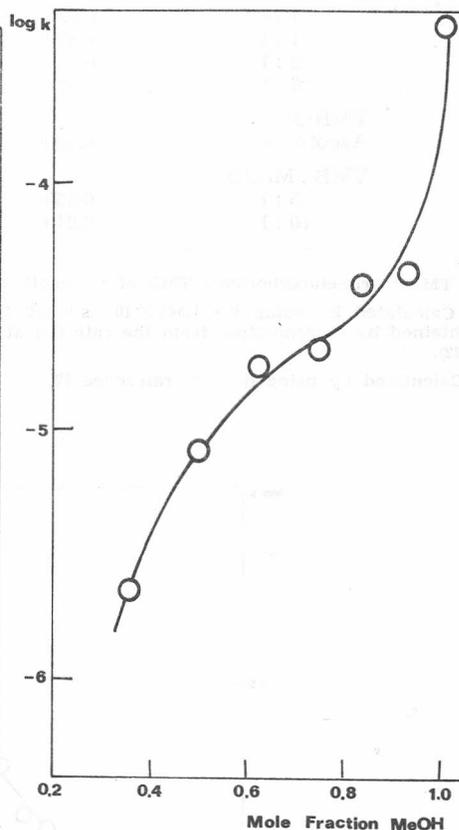
Figure 2.

Figure 1. Dependence of log k vs. mole fraction methanol for the solvolysis of t-butyl chloride in trimethoxyborane — methanol mixtures.

Figure 2. Dependence of log k vs. mole fraction methanol for the solvolysis of methyl tosylate in trimethoxyborane — methanol mixtures.

When the nucleophilicities of various trimethoxyborane — methanol mixtures (Table III) are compared with those of some other solvents (Table IV), the conclusion can be made that the former are, as expected, indeed very low. However, the nucleophilicities of the mixture change significantly depending on the composition of the solvent. In the range under study the nucleophilicities change to an even larger extent than the ionizing powers. Inspection of Figures 1 and 2 results in an unexpected observation: both t-butyl chloride and methyl

TABLE III

Ionizing Powers, Y, *and Nucleophilicities*, N_{BS}, *for Trimethoxyborane—Methanol Mixtures*

Solvent[a]	Mole Fraction Methanol	Y[b]	N_{BS}[c]
TMB : MeOH	1.000	— 1.090	+ 0.013
TMB·M : MeOH			
1 : 3	0.925	— 2.075	— 0.690
1 : 1	0.828	— 2.439	— 0.631
2 : 1	0.744	— 2.575	— 0.841
6 : 1	0.620	— 2.734	— 0.863
TMB·M Azeotrope	0.500	— 3.026	— 1.128
TMB : MeOH			
5 : 1	0.360	— 3.336	— 1.589
10 : 1	0.219	— 3.699	— 2.223

[a] TMB = trimehoxyborane; TMB·M = trimethoxyborane — methanol azeotrope.

[b] Calculated by using $k = 1.042 \times 10^{-2}$ s^{-1} for t-BuCl in 80% ethanol at 90 °C. This value was obtained by extrapolation from the rate (21) at 20 °C $k = 9.376 \times 10^{-6}$ s^{-1}, and $E_a = 23.06$ kcal/mole (22).

[c] Calculated by using data in reference 17.
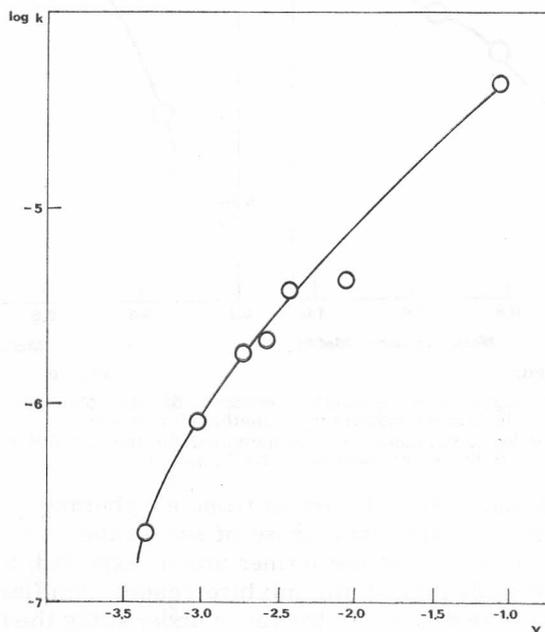
Figure 3. Dependence of log k vs. the ionizing power, Y, of the solvent for the solvolysis of methyl tosylate in trimethoxyborane — methanol mixtures.

TABLE IV

Ionizing Powers, Y, *and Nucleophilicities*, N_{BS}, *of Some Commonly Used Solvents*

	Y	$N_{BS}{}^{a}$
Ethanol	− 2.033[b]	+ 0.09
80⁰/₀ v/v aq. ethanol	0.000[b]	0.00
50⁰/₀ v/v aq. ethanol	1.655[b]	− 0.20
Water	3.493[b]	− 0.26
50⁰/₀ w/w aq. dioxane	1.361[b]	− 0.41
Acetic acid	− 1.639[b]	− 2.05
Formic acid	2.054[b]	− 2.05
97⁰/₀ w/w aq. trifluoroethanol	1.148[c]	− 2.59[g]
50⁰/₀ w/w aq. trifluoroethanol	2.229[c]	− 0.96[g]
97⁰/₀ w/w aq. hexafluoroisopropanol	2.458[d]	− 4.18[h]
Trifluoroacetic acid	5[e]	− 5.55
Fluorosulfonic acid	∼ 20[f]	− 5.5

[a] Reference 20 unless stated otherwise.
[b] Reference 2b.
[c] Reference 4.
[d] Reference 12a.
[e] Reference 26.
[f] Reference 29.
[g] Reference 30.
[h] Reference 12c.

tosylate reflect the changes of solvent composition to a similar extent and in the same way. This is surprising since they represent standard substrates for completely different solvolytic behaviour S_N1-type, and S_N2-type, respectively. In our case, where methyl tosylate is concerned, the insensitivity to changes in ionizing power seems to be more than compensated for by the changes of the solvent nucleophilicity.

The dependence of the solvolysis rate of methyl tosylate *vs.* ionizing power of trimethoxyborane — methanol mixtures is shown in Figure 3.

It is obvious that the correlation is not linear, and that the simple Grunwald — Winstein equation[2a] is not satisfied. This is not surprising, since this equation is applicable[23] only to limiting S_N1-type solvolyses, or to S_N2 substrates, when mixed solvents with components of approximately the same nucleophilicity (*e. g.* ethanol-water, acetic acid-formic acid) are used. Otherwise a dispersion of points with most primary and secondary substrates in a wider range of solvents is observed[23a]. Since there is a marked difference in nucleophilicity between methanol and trimethoxyborane, the dispersion of points observed in Figure 3 is in accordance with previous results.

The observed reaction of HCl with trimethoxyborane-methanol can be rationalized on the basis of the following mechanism:

$$Cl^- + H_3C\text{—}O\text{—}B(OCH_3)_2 \rightarrow H_3C\text{—}Cl + HO\text{—}B(OCH_3)_2$$

$$(CH_3O)_2BOH + CH_3OH \rightleftharpoons (CH_3O)_3B + H_2O$$
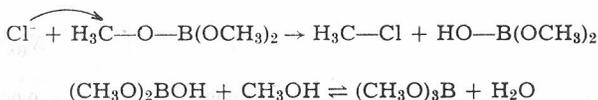
It can be argued that in a reaction of nucleophilic attack of chloride ion on carbon, a much better leaving group is present in trimethoxyborane — methanol, than in pure methanol. This would explain why such a small concentration of HCl (less than 0.05 M) is sufficient to chlorinate methanol in trimethoxyborane and, alternatively, why the same reaction was not observed in pure methanol under the given reaction conditions. In the solvolysis of methyl tosylate in trimethoxyborane — methanol no such reaction was observed, which is in accordance with the much lower nucleophilicity of the *p*-toluenesulfonate ion relative to that of the chloride ion. Although methyl chloride was not unambiguously determined as reaction product, there is a strong indication that the signal of increasing intensity with reaction time at δ 2.95 ppm in the proton NMR spectrum is due to this compound.

The only other reaction product detected in the solvolysis of *t*-butyl chloride in trimethoxyborane — methanol mixtures was *t*-butylmethyl ether. Although no signals due to isobutene were observed in the proton NMR spectrum, the elimination product cannot be rejected, since it is probably not stable under the reaction conditions.

Finally, it can be concluded that most of our assumptions with respect to the properties of trimethoxyborane — methanol mixtures as solvent for solvolytic reactions were verified. The system under study is indeed a solvent of very low nucleophilicity, such as would be required in the study of limiting type reactions. On the other hand, unfortunately, the ionizing power of the solvent is low, too, which makes it too slow a solvent for most practical purposes. In spite of that the trimethoxyborane — methanol system should be seriously considered as a convenient alternative to *e. g.* fluorinated alcohols, or carboxylic acids as solvents, when fast solvolytic reactions are concerned. One should, however, keep in mind that the nucleophilicity of the solvent, although always very low, still changes drastically when the concentration of methanol in the solvent is changed. Therefore, in order to get results comparable to each other, the same mixture should be used for each set of experiments.

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24. The procedure[20] used is as follows:
Methyl tosylate was taken as the standard substrate for evaluating the nucleophilicity term for any solvent. l = one was assigned to methyl tosylate, and an »m« value of 0.30 was used (determined from log $(k/k_0) = mY$ by using[23a,25] acetic and formic acids, which should be reasonably good approximations for the susceptibility of substrates to solvent ionizing power). When all this is taken into account, the nucleophilicity can be calculated from the equation

$$N_{BS} = \log (k^{CH_3OTs}/k_0^{CH_3OTs}) - 0.30 \ Y,$$

where k^{CH_3OTs} is the rate constant for solvolysis of methyl tosylate in a solvent of ionizing power Y, and $k_0^{CH_3OTs}$ is the rate constant for solvolysis of methyl tosylate in 80⁰/o ethanol.
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SAŽETAK

Reakcije solvolize *tert*-butilklorida i metil tosilata u smjesama trimetoksiboran-metanol

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Mjerene su brzine solvolize *t*-butilklorida i metiltosilata u raznim smjesama trimetoksiboran—metanol. Određena je ionizacijska snaga i nukleofilnost tih smjesa i razmotrena je prikladnost toga novog otapala za studij solvolitičkih reakcija. Opaženo je da klorovodik koji nastaje solvolizom *t*-butilklorida na povišenoj temperaturi, reagira s otapalom. Postoje indikacije da je produkt te reakcije metilklorid.

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