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Selectivity in the Reactions of Less Stable Carbocations with Magnesium Halides in Aprotic Solvents. A Theoretical Approach to the Constant Selectivity Principle.

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Abstract: The solvolysis of 7,7-bis(trifluoromethylsulfonyloxy)-2-norbornene (**1a**), 1-trifluoromethylsulfonyloxy-1-phenylethylene (**2a**), 2-methyl-1-cyclohexen-1-yl triflate (**3a**) and 4-camphenyl triflate (**4a**) in carbon disulfide or diethyl ether with added MgI_2 and $MgBr_2$ yields a mixture of the corresponding halides **5b-e**, **6b-c**, **7b-c** and **8b-c**. The ionization of the triflate group is favoured by coordination with the magnesium halides. The reaction with MgI_2 was found to be second-order and is about 50 times more reactive than $MgBr_2$. The selectivities of the intermediate cations **5-8** toward the nucleophiles MgI_2 and $MgBr_2$ are nearly constant, although the solvolysis rates differ by more than three powers of ten. A theoretical explanation of the constant selectivity principle is given.

The selectivity of reactions between carbocations and nucleophiles has so far been accounted for on the basis of two seemengly contradictory principles, namely that of reactivity-selectivity[1] and constant selectivity.[2] According to the former, the selectivity of a carbocation toward nucleophiles decreases with increasing stability of the cation and takes a limiting value of unity (no selective reaction) for very reactive cations. This principle seems to be obeyed by reactions of less stable carbocations. Thus, a plot of solvolysis rates of 16 compounds in 80% acetone containing NaN_3 at 25°C vs. the selectivity toward the pair NaN_3/H_2O gives a reasonable straight line covering a range of 10^{13} in solvolysis and 10^3 in selectivity.[3] However, such a correlation was later ascribed to the fact that reactions between carbocations and H_2O are activation controlled, while the reactions with N_3^- are diffusion controlled.[4]

According to the constant selectivity principle, the selectivity toward pairs of nucleophiles is constant and independent of the nature of the cation. So far, this principle has only been shown to be valid in reactions involving very stable carbocations.[2,4-7] The selectivity of substituted 7-norbornyl cations toward several nucleophiles has been accounted for qualitatively on the basis of the HSAB principle.[8]

In recent years, a number of reports have shown that destabilization of benzylic carbocations by electron withdrawing ring substituents leads to marked decreases in the selectivities (Hammond effects).[9] In contrast, destabilization of these cations by α-substitution leads to small increases in selectivity.[9]

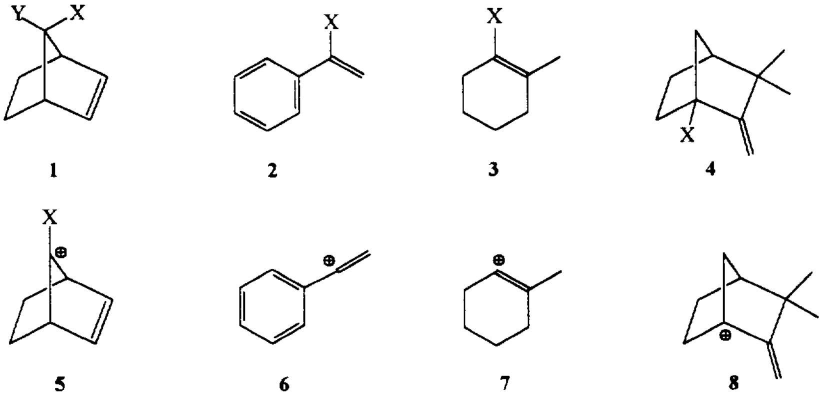
Solvation processes seem to be of crucial importance in selectivity.[7,9] However, experimental studies on the selectivity of carbocations toward anionic nucleophiles have so far been limited to protic or polar solvents.[4] This paper reports a study of the selectivity of less stable carbocations toward anionic nucleophiles in the aprotic solvents carbon disulfide and diethyl ether.

RESULTS AND DISCUSSION

The solvolysis of 7,7-bis(trifluoromethylsulfonyloxy)-2-norbornene(**1a**), 1-trifluoromethylsulfonyloxy-1-phenylethylene (**2a**), 2-methyl-1-cyclohexen-1-yl triflate (**3a**) and 4-camphenyl triflate (**4a**) in CS_2 or Et_2O, buffered with triethylamine, in the presence of MgI_2 and $MgBr_2$ yields a mixture of the corresponding halides **5-8b-e** (Scheme 1) and magnesium triflate (Table 1). No solvolysis of **2a** is observed in diethyl ether without MgI_2 or $MgBr_2$ even at 140°C (ampoule). These results show an accelerating effect of the magnesium halides, and point to the formation of a complex with the triflate group.

All the solvolysis rates decrease with increasing concentration of triethylamine, indicating a preferential coordination of the base to the magnesium halide.

Scheme 1 .Substrates, Cations and Products



a: X=Y= -OTf; b: X=Y= I; c: X=Y= Br; d: X= I, Y= Br; e: X= Br, Y= I

We have measured the kinetics of solvolysis in the presence of different concentrations of magnesium halides to study quantitatively their accelerating effects. The results are listed in Table 1.

The reaction of **1a**-**4a** with magnesium halides in CS_2 and Et_2O conforms to pseudo first-order kinetics, whose straight range increases with the concentration of the magnesium halide and amounts to about 90% at a substrate/MgI_2/$MgBr_2$ mol ratio of 1.0/4.0/4.0. The pseudo first-order rate constants *k*(Table 1) were determined by the initial rate method. The rate was measured by monitoring the reaction using gas liquid chromatography.

Table 1. Products and Selectivity in the Solvolysis of the Triflates **1-4a** (4.0x10^{-2}M) in Buffered (Et$_3$N, 4.0x10^{-2}M) Carbon Disulfide or Diethyl Ether with Added Magnesium Halides

Substrate/ Solvent	m. r.[a]	k(s^{-1})[b]	T(°C)	Yield (%)[c]	Products[d]	Cation/S
1a/Et$_2$O	1.0/1.5/0.0	> 10^{-2} [e]	20	71	**1b**(100)	
	1.0/0.0/1.5	1.05x10^{-3}	20	68	**1c**(100)	
	1.0/0.5/0.5	1.52x10^{-3}	20	81	**1b**(22)+**1c**(27)+ **1d**(35)+**1e**(16)	**5a**/2.0;**5b**/ 0.55;**5c**/0.51
1a/CS$_2$	1.0/1.5/0.0	> 10^{-2} [e]	20	72	**1b**(100)	
	1.0/4.0/4.0	> 10^{-2} [e]	20	71	**1b**(62)+**1c**(2.3)+ **1d**(24)+**1e**(11)	**5a**/6.8;**5b**/ 2.7;**5c**/4.8
2a/Et$_2$O	1.0/0.0/0.0	no react.	140	0		
2a/CS$_2$	1.0/2.0/0.0	4.64x10^{-3}	45	91	**2b**(100)	
	1.0/0.0/2.0	8.88x10^{-5}	45	63	**2c**(100)	
	1.0/0.5/0.5	3.43x10^{-4}	45	79	**2b**(72)+**2c**(28)	**6**/3.4
	1.0/4.0/4.0	1.57x10^{-2}	45	60	**2b**(88)+**2c**(12)	**6**/7.5
3a/CS$_2$	1.0/2.0/0.0	6.35x10^{-6}	45	73	**3b**(100)	
	1.0/1.5/1.5	4.19x10^{-6}	45	86	**3b**(74)+**3c**(29)	**7**/3.1
	1.0/4.0/4.0	2.38x10^{-5}	45	67	**3b**(78)+**3c**(22)	**7**/3.5
4a/Et$_2$O	1.0/2.0/2.0	1.10x10^{-6}	140	48[f]	**4b**(19)+**4c**(81)	**8**/0.22
	1.00/0.0/2.0	5.50x10^{-8}	140	--[g]	**4c**(100)	
4a/CS$_2$	1.0/2.0/0.0	4.22x10^{-6}	45	80	**4b**(100)	
	1.0/1.5/1.5	2.10x10^{-6}	45	69	**4b**(70)+**4c**(30)	**8**/2.4
	1.0/4.0/4.0	2.05x10^{-5}	45	90	**4b**(78)+**4c**(32)	**8**/2.4

[a] Substrate/MgI$_2$/MgBr$_2$ mol ratio. [b] Experimental error ±10%. [c] Yield of the isolated product mixture. [d] Composition (in %) of the reaction mixture determined by GLC (s. Experimental). The concentrations ([]) (s. eq. (3)) were calculated by the relation: []= (%)(yield)4.0x10^{-6}M. [e] Too fast to be measured with our method (s. Experimental). [f] Without triethylamine. [g] After 168 h, only 2.4% of **4a** had reacted.

The real rate constants k' and the reaction orders n were calculated from the observed pseudo first-order rate constants k for the substrates **2-4** by eqs. (1) and (2). The reaction orders n were assumed to be equal for both magnesium halides (Table 2).

$$k = k'_{\mathrm{MgI_2}}[\mathrm{MgI_2}]^n + k'_{\mathrm{MgBr_2}}[\mathrm{MgBr_2}]^n \qquad (1)$$

$$k = k_{\mathrm{MgI_2}} + k_{\mathrm{MgBr_2}} \qquad (2)$$

A rate ratio $k_{\mathrm{MgI_2}}/k_{\mathrm{MgBr_2}} = 52$ was calculated from the k values observed in the solvolysis of **2a** in CS_2 at the mol ratios 1.0/2.0/0.0 and 1.0/0.0/2.0 (Table 1).

Table 2. Real Rate Constants k'

Substrate	n[a]	k'[b]
2a	1.8	$4.3\mathrm{x}10^{-1}$
3a	1.7	$4.4\mathrm{x}10^{-4}$
4a	2.0	$2.1\mathrm{x}10^{-2}$

[a] Experimental error : 10%

[b] Experimental error : 15%

These results clearly show that the triflate group becomes coordinated by two molecules of the magnesium halide (fast and reversible step) before the ionization (slow step) takes place. Additionaly these data show that the leaving group is $^{-}OTf.2MgX_2$. The structure of the substrates **1-4a** precludes any nucleophilic assistance by the magnesium halides[10], so that the solvolysis follow a k_c-mechanism (Scheme 2).

The carbocations thus formed, probably as internal ion-pairs **9**, are attacked by the nucleophile (MgX_2), yielding the corresponding reaction products. The magnesium triflate, which is insoluble in the organic solvents, results from the disproportionation of two molecules of MgX(OTf) (Scheme 2).

Scheme 2. Mechanism of the Solvolysis

$$\mathrm{ROTf + 2MgX_2 \xrightleftharpoons{fast} ROTf.\,2MgX_2 \xrightarrow[slow]{k} \underset{\mathbf{9}}{R^{\oplus}\,{}^{\ominus}OTf.\,2MgX_2} \xrightarrow{MgX_2} RX + MgXOTf + 2MgX_2}$$

$$\mathrm{2MgXOTf \longrightarrow Mg(OTf)_2\downarrow + MgX_2} \qquad \mathrm{R} = \mathbf{5 - 8}$$

The halides **5**-**8b**-**e** are stable under the reaction conditions and therefore they are formed in ratios depending on the corresponding rates of formation (kinetic control).

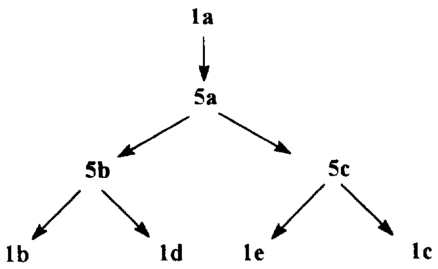
The selectivity (S in Table 1) of the reactions between the ion-pairs **9** (Scheme 2) and the magnesium halides, which should not be different from that of the corresponding free cations,[11] was calculated from eq. (4), an integrated form of eq. (3). This equation also gives the selectivity when the initial concentration of the magnesium halides is low.

$$dS = [A]d[MgBr_2]/[B]d[MgI_2] \qquad (3)$$

$$S = \sum_{i=1}^{n} (1/i)([A]/m[MgI_2])^i / \sum_{i=1}^{n} (1/i)([B]/m[MgBr_2])^i \qquad (4)$$

In each case, the series expansion (x-value) was extended until S became constant. The ratio of equivalents, m, was equal to 2 for the reactions of **2a**-**4a** and 1 for **1a**. [A] and [B] denote the concentration of the iodide and bromide, respectively, at the end of the reaction. The selectivity of the intermediate carbocation in the solvolysis of **1a** was calculated taking into account the precursor-product relations shown in Scheme 3.

Scheme 3. Precursor-Product Relations in the Solvolysis of **1a**



cation	[A] / [B]
5a	$\frac{[1b]+[1d]}{[1e]+[1c]}$
5b	$\frac{[1b]}{[1d]}$
5c	$\frac{[1e]}{[1c]}$

Since the nucleophilic attack at norbor-2-en-7-yl cations takes place almost exclusively *anti* to the π bond,[10c] we can assume that **1d** and **1e** are formed exclusively from **5b** and **5c**, respectively. The [A]/[B] ratios corresponding to the cations **5a-c** were calculated from the yields of the reaction products indicated in Scheme 3.

The selectivity of the carbocations **2a**-**4a** is relatively insensitive to changes in the overall concentration of the magnesium halide. This results show that : (i) The two molecules of magnesium halide coordinated to the triflate group do not react with the carbocations. Thus the selectivity is determined by the reaction of the ion-pairs **9** (Scheme 2) with "external" magnesium halides. (ii) The reactions of the carbocations with magnesium halides are not diffusion-controlled. In fact, if the processes in question were diffusion-controlled, the selectivity should be (or tend to) 0.6-0.9 on increasing the overall concentration of the nucleophiles.[4,12]

There is no relationship between the solvolysis rate and the selectivity of the reactions of the carbocations **5**-**8** with the magnesium halides in carbon disulfide or diethyl ether (Table 1). Therefore cation **5** is formed at a much higher rate (at least 10^3-fold) than cations **7** and **8**, but all three cations have a comparable selectivity (both in CS_2 and Et_2O). Our results can be explained by the constant- selectivity principle. The deviation from the S mean values, 0.82 ± 1.2 in Et_2O and 4.07 ± 3.4 in S_2C can be regarded as normal if compared with the results of other authors.[13]

A theoretical explanation of the relatioship between the stability of a carbocation and its selectivity can be accounted for by the Marcus relation[14] (eq. 5).

$$\Delta G^{\neq} = w^r + \lambda/4 + \Delta G^0/2 + (\Delta G^0)^2/4\lambda \qquad (5)$$

where $\Delta G^{\neq}$ is the free energy of activation, ΔG^0 the standard free energy of reaction, w^r the energy of formation of the encounter complex and λ the intrinsic barrier of activation.

Since the Brønsted coefficient, α, is defined as $d\Delta G^{\neq}/d\Delta G^0$, differentiation of eq. (5) gives eq. (6).

$$\alpha = 1/2 + \Delta G^0/2\lambda \qquad (6)$$

A true constant selectivity can therefore only be observed when α remains constant for a series of related reactions. Limiting cases are very exothermic reactions in which α is close to 0 and then $\Delta G^0 \simeq -\lambda$. This seems to occur in the case of the reaction of carbocations with nucleophiles[7,14] . Hence, the selectivity should be only determined by the actual values of Δw^r and therefore, it is independent of the structure of the reacting carbocations. However, in some carbocation-nucleophile combination reactions, α does not remain constant, causing a Hammond effect or even an inversion of the reactivity-selectivity relationship.[9,15] On the other hand, the values of Δw^r are solvent dependent,[14] so that a change of selectivity with the solvent is to be expected. This is also in agreement with our results.

In summary, the reaction of less stable carbocations with magnesium halides in aprotic solvents fulfill the constant-selectivity principle. A theoretical explanation of these results is given on the basis of the Marcus theory.

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EXPERIMENTAL

Starting materials were used as received from commercial suppliers. Solvents were purified following standard procedures. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker-AC 250 MHz spectrometer in $CDCl_3$ and chemical shifts are expresed in ppm. IR spectra were recorded on a Perkin-Elmer 781 spectrometer. Mass spectra were recorded on a Varian-MAT 711 instrument.

7,7-Bis(trifluoromethylsulfonyloxy)-2-norbornene (1a)[8] (yield 78%), **1-trifluoromethylsulfonyloxy-1-phenylethylene (2a)**[16] (85%) and **2-methyl-1-cyclohexen-1-yl triflate (3a)** (64%) were prepared by reaction of the corresponding ketones with triflic anhydride (Tf_2O) following usual procedures.[8,16] **4-Camphenyl triflate (4a)** (88%) was prepared by reaction of camphor with Tf_2O.[17]

General procedure for the solvolysis of the triflates 1a-4a. A solution containing 1.20 mmol of the triflate, anhydrous magnesium halides[18] in the ratios given in Table 1 and 0.121g (1.20 mmol) of triethylamine in 30 ml of Et_2O or CS_2, was heated in a glass ampoule placed in a thermostat (Table 2). The reaction times were 1h for **1a**, 10 h for **2a** and 150 h for **3a-4a**. The reaction mixture was successively washed with 2 x 25 ml of saturated $NaHCO_3$ and 2 x 25 ml of water and dried over $MgSO_4$. The solvent was evaporated and the residue was analyzed and the reaction products isolated by GLC (10% UCC, Chromosorb W-AW-DMCS, 80-100 mesh, 3 m x 1/8"). Compounds **1d** and **1e** could not be separated, so their yields were determined by ^{1}H-NMR.

The kinetic of the solvolysis was monitored by taking samples at appropriate times. The rate constants were calculated from at least five points.

7,7-Diiodo-2-norbornene (1b),[8] **7,7-dibromo-2-norbornene (1c)**,[19] **1-iodo-1-phenylethylene (2b)**,[20] **1-bromo-1-phenylethylene (2c)**,[21] **4-iodocamphene (4b)**[22] and **4-bromocamphene (4c)**[22] were identified by comparing their IR, ^{1}H-NMR and MS spectra with the reported in the literature.

1-Bromo-2-methyl-1-cyclohexene (3c). IR(film): ν=1670 (C=C) cm^{-1}. ^{1}H-NMR(CCl_4): δ=2.35 (m, 2H, CH_2); 1.75 (s, 3H, CH_3); 1.65 (m, 4H,CH_2). MS(100 eV): m/e (%B) = 174(22,M^+), 95(100,M^+-Br). $C_7H_{11}Br(M^+)$, cal. 174.0044, obs. 174.0044 (MS).

7-*anti*-Bromo-7-*syn*-iodo-2-norbornene (1d). IR(CCl_4): ν=3080 (=C-H); 1575 (C=C) cm^{-1}. ^{1}H-NMR(CCl_4): δ = 5.80 (m, 2H, =C-H); 3.10 (m, 2H, 1-H and 4-H); 2.20 (m, 2H, *exo*-H); 1.00 (m,2H,*endo*-H). ^{13}C-NMR($CDCl_3$): δ = 132.60 (2-C and 3-C); 58.60 (1-C and 4-C); 48.71 (7-C); 22.66 (5-C and 6-C). MS(100 eV): m/e (%B) = 298 (85, M^+); 170 (45, M^+-C_2H_4); 92 (71, $C_7H_8^+$); 91 (100, $C_7H_7^+$). $C_7H_8BrI(M^+)$, cal. 297.8853, obs. 297.8849 (MS).

7-*syn*-Bromo-7-*anti*-iodo-2-norbornene (1e). The IR and MS spectra of **1e** are consistent with those of **1d**. ^{1}H-NMR(CCl_4): δ = 5.95 (m, 2H, =CH); the rest, as for **1d**. ^{13}C-NMR($CDCl_3$): δ = 137.43 (2-C and 3-C); 59.05 (1-C and 4-C); 49.71 (7-C); 19.49 (5-C and 6-C).

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