

Correlations of  $pK_{\text{lg}}^{\text{Me}}$  with Reduction PotentialsK. R. Fountain,\*<sup>‡</sup> Kamlesh D. Patel, Timothy W. Dunkin, Janette A. Powers, and Dean A. Van Galen

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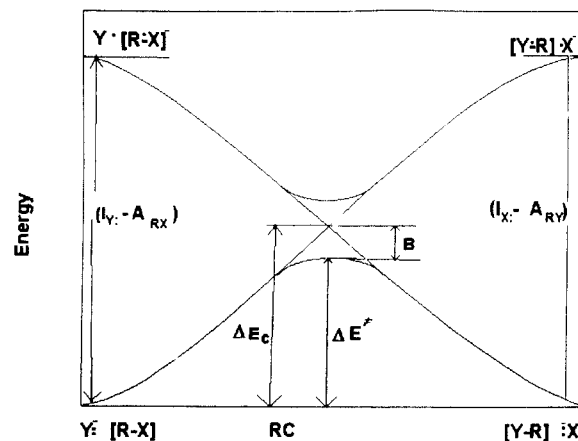
The quantitative indices for the ability of leaving groups to depart from C atoms are  $pK_{\text{lg}}^{\text{Me}}$ . In the cases of methyl transfers from arenesulfonates, these parameters have correlated a large number of nucleophilic data. A new scale of these parameters has been defined from methyl transfer data between phenylmethyl thioethers. The  $pK_{\text{lg}}^{\text{Me}}$  data from both sets of compounds correlated with both experimental  $E_{1/2}$  values and  $E_{\text{LUMO}}$  values from computational chemistry. These correlations support the SCM model of Shaik et al. which requires the leaving group to display some SET character in an  $S_{\text{N}}2$  transition state.

## Introduction

The quantitative behavior of leaving groups is important in modeling transition state behavior in the  $S_{\text{N}}2$  reaction.<sup>1</sup> Quantitative modeling of transition state data has led to important insights into the timing and detailed bonding in many reactions.<sup>2,3</sup> A recent transition state (TS) model for the  $S_{\text{N}}2$  reaction emphasizes single-electron transfer (SET) character as an important component. The principal features of this model, the state correlation diagram (SCD), or valence bond configuration mixing (VBCM) model, is summarized in Figure 1 for a thermoneutral  $S_{\text{N}}2$  reaction.

The transition state (TS) in this diagram is the result of avoided crossing of the states  $\text{N}^{\cdot}(\text{:X})^{-}$  and  $\text{N}^{\cdot-}(\text{R-X})$ . These states represent valence bond (VB) wave functions describing the intimate complex of the nucleophile and the substrate (lower left corner) and the electronically excited state (upper left corner) of this complex. Similar considerations correlate the right side (products) of Figure 1. One of the predictions of this diagram is that leaving group behavior should involve some SET character. This research explores this prediction by correlating the leaving group parameters ( $pK_{\text{lg}}^{\text{Me}}$ ) with the single electron parameter,  $E_{1/2}$ .

A recent quantitative expression of leaving group behavior is the  $\beta_{\text{lg}}^{\text{Me}}$  parameter, due to Shankweiler and Hofmann.<sup>4</sup> This parameter is the slope of a plot of  $-\log k_{\text{nuc}}$  vs  $pK_{\text{lg}}^{\text{Me}}$ . The  $pK_{\text{lg}}^{\text{Me}}$  are based on the methyl exchange data of Lewis et al.,<sup>5</sup> for methyl transfer between arenesulfonate anions. They successfully correlated a wide variety of experimental and theoretical data for nucleophilic reactivity and eliminations. Typical



**Figure 1.** State correlation diagram (SCD) for a thermoneutral  $S_{\text{N}}2$  reaction.

$\beta_{\text{lg}}^{\text{Me}}$  values for nucleophilic displacements range from 0.44 to 0.57. A typical use of this parameter is as an index of bond order (BO) in the transition state.<sup>6</sup> For a very early transition state where a nearly full bond exists between C and the leaving group,  $\beta_{\text{lg}}^{\text{Me}}$  is nearly 0.0; so when the bond is cleaved at the TS  $\beta_{\text{lg}}^{\text{Me}}$  is 1.0. The BO is then  $1.0 - \beta_{\text{lg}}^{\text{Me}}$ .

Interpreting the  $\beta_{\text{lg}}^{\text{Me}}$  can be based on any model one chooses for the  $S_{\text{N}}2$  reaction. It is a quantitative expression about structure–rate relationships, but has not yet been investigated for single-electron transfer (SET) character or polar (transfer of two electrons in the TS) character. We report in this paper a correlation of the  $pK_{\text{lg}}^{\text{Me}}$  with a specific SET parameter, the reduction potential,  $E_{1/2}$ , for the positively charged methylating agent, and  $E_{\text{LUMO}}$  for the O–C bond for the neutral methylating agent.

## Experimental Section and Results

**Reduction Potentials.** The reduction potentials of a series of substituted phenyldimethylsulfonium fluoroborates were determined in acetonitrile, DMF, and DMSO. The apparatus was a BAS 100B/W electrochemical analyzer, which was used to determine all the cyclic voltametry. The working electrode,

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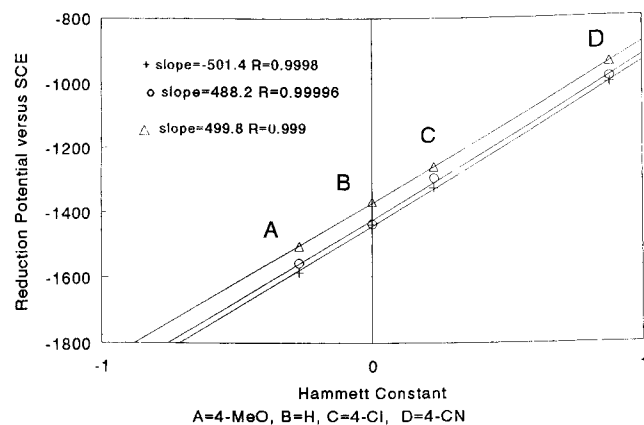
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**Figure 2.** Hammett Plot of  $E_{1/2}$  of substituted phenyldimethylsulfonium fluoroborates in acetonitrile (+), DMSO (o), and DMF ( $\Delta$ ).

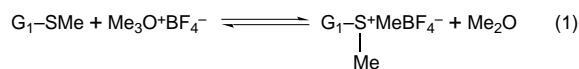
reference electrode, and auxiliary electrode were glassy carbon (BAS), Ag/AgCl (0.1 M), and Pt wire. The  $E_{1/2}$  values were obtained at a scan rate of 100 mV/s. The glassy carbon electrode was polished after every run, to remove any adsorbed species, with a 0.3  $\mu\text{m}$  OP alumina suspension for 30 s and then rinsed with distilled water before being polished with 0.05  $\mu\text{m}$  OP alumina suspension for 30 s. The electrode was once again rinsed with distilled water and sonicated for 1 min with a Branson 1200 Ultrasonic Cleaner. The electrode was once again rinsed with distilled water before use.

The reductions of methyl arenesulfonate esters were done in acetonitrile in the same manner as described above. The  $E_{1/2}$  values are summarized in Table 2. A Hammett plot (not shown:  $N = 6$ ;  $r = 567$  mV/s;  $R = 0.9998$ ) of these values showed excellent linearity and correlation.

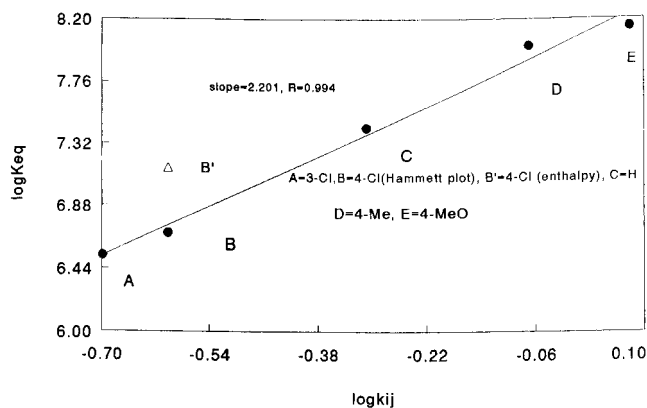
**Materials.** All of the phenyldimethylsulfonium fluoroborate salts were synthesized by known methods.<sup>5</sup> The methyl arenesulfonates were from samples previously reported.<sup>6a</sup> The supporting electrolyte was tetrabutylammonium fluoroborate (used as received from Aldrich). The solvents, acetonitrile (Fisher Scientific, HPLC grade), dimethylformamide (American Burdick & Jackson), and dimethyl sulfoxide (Fisher), were used as received. An internal reference of ferrocene is 307 mV vs the SCE electrode; thus values of  $E_{1/2}$  are vs the SCE and not Ag/AgCl.

Table 2, in the experimental section, summarizes the data, along with data from reduction of methyl arenesulfonates. A Hammett plot (Figure 2) allowed computation of the experimentally inaccessible  $E_{1/2}$  values for (4-nitrophenyl)dimethylsulfonium fluoroborate.

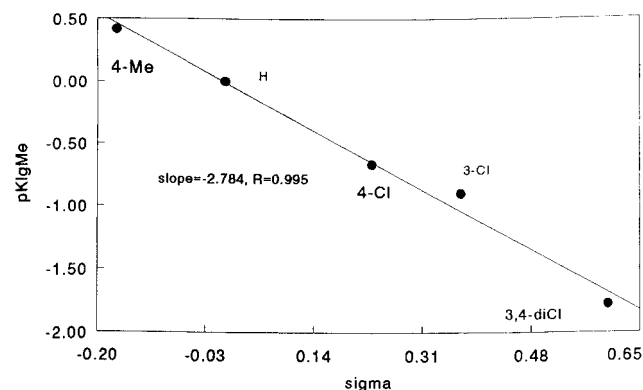
The  $pK_{\text{lg}}^{\text{Me}}$  values for the methyl arenesulfonates are reported in the literature.<sup>4</sup> Calculation of  $pK_{\text{lg}}^{\text{Me}}$  for methyl transfers between substituted phenylmethyl thioethers were computed from the rate equilibrium data in ref 5d for reaction 1 from Lewis et al.<sup>5</sup> In their paper the equilibrium constants



for  $G$  values were available for  $G_1 = 3,5\text{-di-ClC}_6\text{H}_3$ ,  $3\text{-Cl-C}_6\text{H}_4$ , and  $\text{C}_6\text{H}_5$ . Rate constants were available for  $G_1 = 4\text{-MeC}_6\text{H}_4$ ,  $4\text{-MeOC}_6\text{H}_4$ ,  $\text{C}_6\text{H}_4$ , and  $3\text{-ClC}_6\text{H}_4$ . Enthalpy values were available for all of these. The equilibrium constants for  $G = 3\text{-C}_6\text{H}_4$  and  $\text{C}_6\text{H}_5$  were used to evaluate  $T\Delta S$  terms in the Gibbs-Helmholtz equation, which were 3.03 and 1.86 kcal/mol, respectively. These values display similarity, so equating  $\Delta G$  with  $\Delta H$  and subtracting two different  $\Delta H$  values to get approximate  $\delta\Delta G$  values will perhaps be an adequate approximation. The goodness of this approximation thus depends on the constancy of the  $T\Delta S$  terms. Equation 2 shows the formula for computation of  $\delta \log K_{\text{eq}}$ . A log-log plot of the rate constants for reaction 1 vs the available  $K_{\text{eq}}$  were used to check the internal consistency of this process, Figure 3. The point for  $4\text{-ClC}_6\text{H}_4$ , from enthalpy computations, plots severely



**Figure 3.** Log  $k_{12}$  vs log  $K_{\text{eq}}$  for reaction 1. This figure justifies computation of  $K_{\text{eq}}$  values from enthalpy.



**Figure 4.** Hammett plot of  $pK_{\text{lg}}^{\text{Me}}$  for substituted phenyldimethylsulfonium ions exchanging methyl groups with substituted phenylmethyl thioethers.

**Table 1. Experimental and Computed Equilibrium Constants for Reaction 1 and  $pK_{\text{lg}}^{\text{Me}}$  Values for Reaction 3**

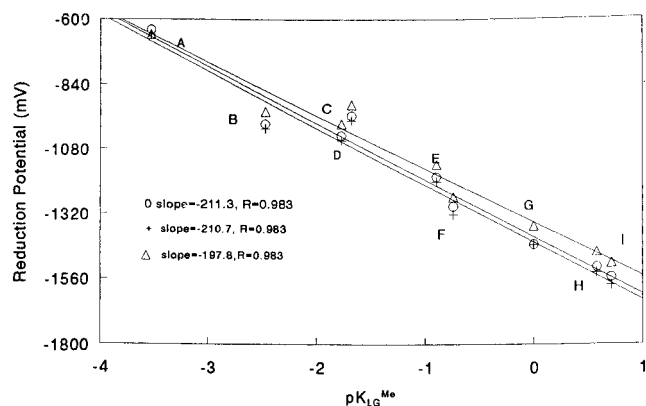
G	$K_{\text{eq}} (\times 10^6)$	$pK_{\text{lg}}^{\text{Me} b}$	$pK_{\text{lg}}^{\text{Me}}$ computed
H	7.8	0	
4-Me	20.3 <sup>a</sup>	0.579	
4-Cl	7.14 <sup>a</sup>	-0.744	
3-Cl	0.98	-0.900	
3,4-diCl	0.13	-1.778	
4-NO <sub>2</sub>			-3.532( $\sigma^-$ )
4-MeO			0.712
4-CN			-2.479( $\sigma^-$ )
3,5-diCl			-1.683

<sup>a</sup> Computed from the equation from Figure 3. <sup>b</sup> Computed by  $-\log K_{\text{H}} + \log K_{\text{C}}$ .

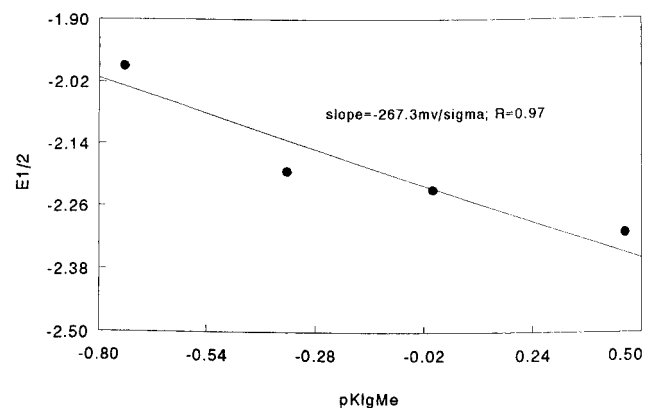
off the line, as demonstrated. All the other points lie on a fairly good line. A Hammett plot of the experimental and computed  $\log K_{\text{eq}}$  values (not shown; 5 points,  $\rho = -2.845$ ,  $R = 0.996$ ) excluding 4-Cl also showed Cl plotting off the line. The Hammett plot was used to calculate  $\log K_{\text{eq}}$  data for  $4\text{-ClC}_6\text{H}_4$  in Figure 3.

$$\frac{\Delta H - \Delta H_2}{2.303(1.98)(308)} = \delta \log K_{\text{eq}} \quad (2)$$

The computations of  $pK_{\text{lg}}^{\text{Me}}$  for eq 2 were made by the subtraction of the logs of the experimental and computed  $K_{\text{eq}}$  from Figure 3 to give the  $pK_{\text{lg}}^{\text{Me}}$  column in Table 1. A Hammett plot of the values in the  $pK_{\text{lg}}^{\text{Me}}$  column in Table 1 appears in Figure 4. The equation is  $pK_{\text{lg}}^{\text{Me}} = -2.784\sigma - 0.0121$  (points = 5;  $R = 0.995$ ). A complete set of  $pK_{\text{lg}}^{\text{Me}}$  values is thus present in Table 1. This procedure is analogous to that of Shankweiler and Hofmann, except that three  $K_{\text{eq}}$

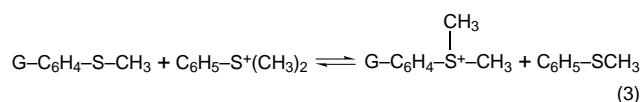


**Figure 5.** Plot of  $pK_{lg}^{Me}$  in Table 1 for  $E_{1/2}$  values of phenyldimethylsulfonium fluoroborates in acetonitrile (+), DMF ( $\Delta$ ), and DMSO ( $\circ$ ): A = 4-NO<sub>2</sub>; B = 3,5-diCl; C = 4-CN; D = 3,4-diCl; E = 3-Cl; F = 4-Cl; G = H, H = 4-Me; I = 4-MeO.



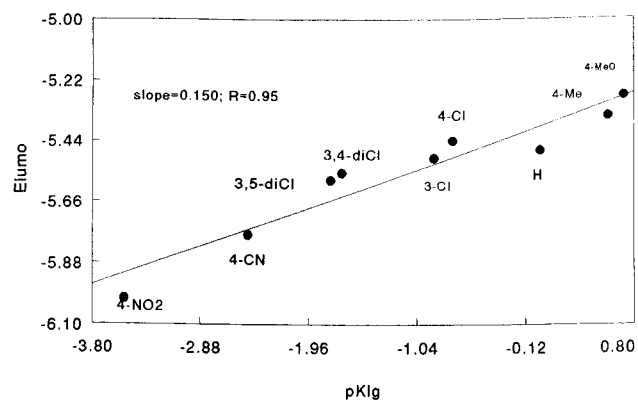
**Figure 6.** Correlation of  $E_{1/2}$  values for methylarenesulfonate esters with  $pK_{lg}^{Me}$ .

values were approximated by calculations from enthalpy to obtain the Hammett plot for computations of the complete set.

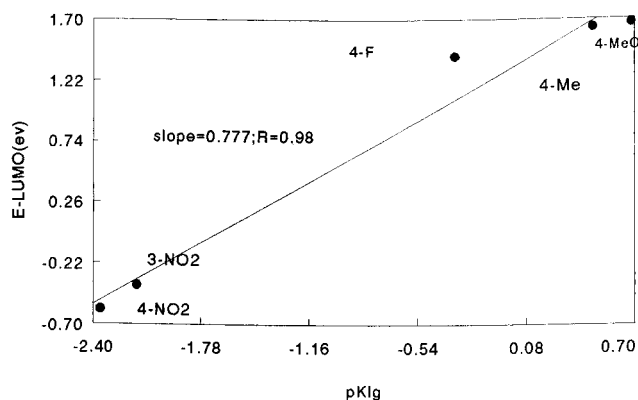


**Correlations of the Electrochemical and Quantum Data.** The correlations for the  $E_{1/2}$  values vs these  $pK_{lg}^{Me}$  for the substituted phenyldimethylsulfonium salts are displayed in Figure 5. The corresponding  $E_{1/2}$  values of the methylarenesulfonate esters vs  $pK_{lg}^{Me}$  are in Figure 6. These correlations for the substituted phenyldimethylsulfonium ions are very consistent for the order of the substituent effects and have nearly the same equations in all three solvents.

Figures 7 and 8 show correlations of  $E_{1/2}$  with the lowest occupied molecular orbital (LUMO) of a series of calculated structures of substituted methyl arenesulfonates and substituted phenyldimethylsulfonium salts Table 2. These computations were done by MOPAC6.0, MOPAC7.0, HyperChem, or Spartan. All structures were inspected visually after convergence, and vibrational studies confirmed all positive eigenvalues for the Hessian matrix. The energies of the unoccupied molecular orbitals which had significant antibonding character on the C atom of the methyl group in the methylarenesulfonates were plotted vs  $pK_{lg}^{Me}$ . There was no correlation between the LUMOs and the  $E_{1/2}$  values for methyl arenesulfonates. Saeva et al.<sup>8</sup> have pointed out the  $\sigma^*$  nature of the LUMO for arylmethylsulfonium salts to be largely centered on the S-C bond with some contributions from the aryl-S



**Figure 7.** Correlation of  $E_{1/2}$  with LUMO of substituted phenyldimethylsulfonium ions.



**Figure 8.** Correlation of  $E_{1/2}$  with LUMO of substituted methylarenesulfonate esters.

**Table 2.  $E_{1/2}$  Values for Substituted Methylarenesulfonates in Acetonitrile vs SCE**

G	$E_{1/2}$ (V)	G	$E_{1/2}$ (V)
3-CF <sub>3</sub>	-1.910	4-Br	-1.994
3-Me	-2.210	4-MeO	-2.430
4-F	-2.258	3-MeO	-2.200
Me	-2.310		

bond. Since we are comparing these two substrates, it is necessary to compare the same types of orbitals, centered on the CH<sub>3</sub> groups and the leaving group. Visual inspection of the LUMOs of these compounds via ChemPlus (a graphical user interface, GUI) especially for this purpose) in HyperChem showed the noncorrelating orbitals to be largely centered on the aromatic rings. The LUMOs of the phenyldimethylsulfonium ions, which were centered on the S-CH<sub>3</sub> region, correlated very well, and the methyl arenesulfonates orbitals largely located between the C and O somewhat less well, but both show a relationship between  $E_{1/2}$  and LUMO. This correlation is actually surprising since studies have shown<sup>9</sup> that in cyclic voltammetry experiments a single electron most likely initially resides on the S atom of the sulfonate portion, giving products from cleavage of S-OCH<sub>3</sub> and C-S bonds, rather than O-C bonds. The quality of the  $E_{1/2}$  correlations of these compounds are thus not surprisingly poorer. They serve some purpose because they show the capability of the SO<sub>3</sub> group as a single electron acceptor.

## Discussion

These correlations show that the parameters  $pK_{lg}^{Me}$  from both methyl arenesulfonates and phenyldimethylsulfonium ions are related to SET phenomena such as  $E_{1/2}$  values. The behavior of these leaving groups as

(8) Saeva, F. D.; Breslin, D. T.; Martic, P. A. *J. Am. Chem. Soc.* **1989**, *111*, 1328.

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single-electron acceptors has not been well studied, yet the SCM model makes specific predictions that inclusion of some SET character is present in both the attack of the nucleophile and departure of the leaving group. The correlations with the gas phase computations, LUMO vs  $pK_{\text{lg}}^{\text{Me}}$ , and the solution phase  $E_{1/2}$  values indicates that, for these substrates, solvation of the incipient molecule or ion of the leaving group in the TS is not very important. Savéant et al. have shown that the phenyldimethylsulfonium salts insert a single electron into the C–S  $\sigma^*$  bond and not into the  $\pi^*$  orbitals of the ring.<sup>8,10</sup> This insertion in the case of phenyldimethylsulfonium salts is nearly concomitant with release of the  $\text{CH}_3$  radical.

Lund suggests that when the potentials are right and there is significant steric hindrance a reaction path intermediate between the classical  $\text{S}_{\text{N}}1$  path and  $\text{S}_{\text{N}}2$  involving a nonchain electron transfer is possible.<sup>11</sup> In the present case the departure of the leaving group is putatively involving a certain amount of SET character mixed into the wave function of the transition state, and

(10) Andrieux, C. P.; Robert, M.; Saeva, F. D.; Savéant, J.-M. *J. Am. Chem. Soc.* **1994**, *116*, 7864.

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not a full SET transfer. It is this character that we claim to correlate with  $pK_{\text{lg}}^{\text{Me}}$ .

The consistency of the phenyldimethylsulfonium salts in the three solvents used here is not surprising because it shows that the use of  $pK_{\text{lg}}^{\text{Me}}$  to model leaving group behavior for phenyldimethylsulfonium ions will not vary much from solvent to solvent. Determinations of  $E_{1/2}$  values in protic solvents, such as methanol, are not possible because the solvent background obscures the potential for the solute. We have previously discussed the solvent dependency of the  $pK_{\text{lg}}^{\text{Me}}$  scale for methyl arenesulfonates, which also shows solvent independence.<sup>6</sup> Together these two scales show that the type of charge disposition, positive charge vs neutral, of the substrate does not much affect the use of  $pK_{\text{lg}}^{\text{Me}}$ . This makes this  $pK_{\text{lg}}^{\text{Me}}$  scale a good one for mapping transition states.

Subsequent papers will explore the use of  $pK_{\text{lg}}^{\text{Me}}$  with common nucleophiles, phenolate anions, and  $\alpha$ -nucleophiles. The use of this set of parameters is justified by the self-consistency they show in a variety of nucleophilic reactions in various solvents.

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