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Deprotonation of 1,2-Dialkylpyridinium Ions: A DFT Study of Reactivity and Site Selectivity

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A site-selectivity model, based on the Fukui function as a local reactivity descriptor, has been applied to 1,2-disubstituted pyridinium ions incorporating two competing sites of similar reactivity, i.e., 1-methylene and 2-methylene, which may undergo deprotonation depending on the nature of substituent present on these moieties. Applicability of the local HSAB rule, in context with the Li−Evans' generalized HSAB principle suggesting the hard−hard interactions to be controlled by minimum Fukui function, has been illustrated. Global and local reactivity descriptors have been computed by carrying out DFT calculations at B3LYP/6-31++G** level using Mulliken and NPA methods for charge analysis. A comparison with the calculated deprotonation energies involving two sites indicates that the observed site selectivity in differently substituted pyridinium ions is better explained by the Li−Evans rule of minimum Fukui function for hard−hard interactions.

I. Introduction

During the last two decades, modern physical organic chemistry has witnessed successful implementation of the density functional theory[1] (DFT) for the study of chemical reactivity. DFT has provided a sound theoretical basis for the development of a number of global and local reactivity descriptors. The global reactivity descriptors, such as electronic chemical potential[2] (μ), global chemical hardness[3] (η), global softness[4] (S), and more recently, added global electrophilicity index[5] (ω), are derived from the change in the energy of a system with respect to change in the number of electrons and have proven to be quite successful for rationalization of the observed intermolecular reactivity trends within the framework of Pearson's hard−soft acid−bases (HSAB) principle.[6] In the context of synthetic organic chemistry for planning a new synthesis, a more important aspect than the reactivity is the knowledge of intramolecular site selectivity or site specificity, i.e., the knowledge of the most favorable site in a molecule for the attack by a nucleophilic or an electrophilic reagent. Most frequently used local reactivity descriptors for this purpose are the Fukui function,[7] local softness,[4] and local hardness.[8] Several formalisms have been developed[9] for the evaluation of condensed atomic Fukui function, out of which the one given by Yang and Mortier[9a] remains most widely used so far. The softest atom in a molecule, represented by maximum Fukui function value, is expected to be the preferred site of reaction. Contrary to this anticipation, Gazquez and Mandez[10] invoked the local HSAB principle by identifying the site of the interaction between two species through the atoms with approximately equal Fukui function and not necessarily through the atoms with the largest value of Fukui function. During the same time, the suitability of the Fukui function as the key parameter for controlling chemical reactivity and selectivity was again verified by Li and Evans,[11] who further extended the "hard likes hard and soft likes soft" criterion of the HSAB principle to local selectivity and proposed a generalized rule: *"for hard−hard interactions, the site of minimal Fukui function is preferred; for soft−soft interactions, the site of maximal Fukui function is preferred*." Although, the applicability of the local HSAB principle on the basis of Fukui function has been repeatedly tested by a number of research groups,[12] Chattaraj and co-workers[13] have recently pointed out that the Fukui function is an ideal descriptor only for frontier-controlled soft−soft interactions[14] and is not reliable for the description of charge-controlled hard−hard interactions in polyfunctional systems. On the other hand, Madjarova et al.[15] employed orbital Fukui indices[16] and atom-in-molecule (AIM) softness in addition to atomic Fukui indices for the investigation of the selectivity aspect in Michael addition and once again verified the applicability of minimum Fukui indices for hard−hard interactions, in conformity with the Li−Evans rule. More recently, the Li−Evans rule has been further applied to analyze the site of protonation in strong organic superbases, and a Hammet-like linear relationship for the variation of Fukui indices has been derived.[17] The site selectivity for the attack by a hard species during electrophilic aromatic substitution has been investigated by proposing another Fukui function derived index "local hardness".[18]

Nevertheless, there are several reports about the limitations of the Fukui function in describing observed selectivity for the systems possessing multiple sites of comparable reactivity. Pal and co-workers analyzed the factors causing failure of the Fukui function in predicting correct intramolecular reactivity trends in such cases and proposed new local reactivity descriptors namely, "relative electrophilicity" (s_k^+/s_k^-) and "relative nucleophilicity" (s_k^-/s_k^+).[19] It was demonstrated that these new descriptors, being less sensitive to the basis set and correlation effects, are better for explaining site selectivity in the aliphatic as well as aromatic carbonyl compounds. Later on, their

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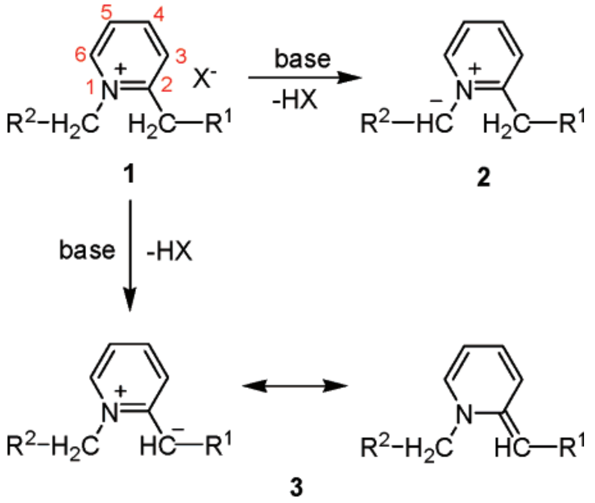
SCHEME 1: Generation of Methylide (2) or Methine (3) Intermediate from 1,2-Dialkylpyridinium Salts (1)

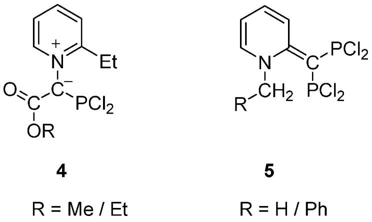


application was satisfactorily extended to the study of protonation of anilines and substituted anilines.[20] Recently, Tanwar et al. proposed two reactivity descriptors, viz., normalized Fukui function (NFF) and bond deformation kernel (BDK) for comparative studies on the systems where the number of atoms is not constant.[19b] Another dual reactivity descriptor, Δf_k (or Δs_k), based on the difference of Fukui functions (f_k^+ and f_k^-) has been recently proposed and the nucleophilic/electropilic behavior of the atom concerned has been defined in terms of the sign of Δs_k.[21]

Novel phospha analogues of the indolizine and azaindolizine have become accessible and named as phosphaindolizines;[22] the latter may be perceived as derived from the classical bridgehead-nitrogen containing heterocycle by replacing one =CH− unit of the five-membered ring by a = P− atom. A number of synthetic methods developed for these anellated azaphospholes, such as [4+1] cyclocondensation, [3+2] cyclocondensation, [3+2] cycloaddition, and 1,5-electrocyclization are analogous[23] to those available for classical anellated azoles, and several facile routes among them make use of 1,2-disubstituted pyridinium salts as starting material. Because of the versatile reactivity of *N*-methylene and 2-methylene moieties of 1,2-disubstituted pyridinium salts (**1**), reaction of a strong base like triethylamine, potassium hydroxide, or potassium carbonate may result in deprotonation at either of these positions, leading to the generation of methylide (**2**) or methine (**3**) intermediate (Scheme 1), which in turn undergo intramolecular cyclization to yield differently substituted indolizines.[24]

Melton and Wibberley reported the synthesis of indolizines from 1,2-disubstituted pyridinium salts via an intermediacy of methine intermediate[25] of type **3**, which is already stabilized by resonance (Scheme 1). However, later work by Kröck and Kröhnke[26] showed the site of initiation of the reaction to be dependent on the extent of activation of the *N*-methylene group by a substituent. They demonstrated[26b] that, although a methine intermediate **3** was generated in the case of R^2 = H/Ph/C_6H_4-NO_2/C_6H_4Cl, the activation of the *N*-methylene group by an acyl substituent (R^2 = COR) resulted in the generation of methylide **2**, which on further cyclization yielded an indolizine. In an analogous synthesis, Kakehi et al. made use of *N*-ethoxycarbonylmethyl-2-picolinium salts for obtaining indolizinones and proposed that the action of base initially generated a methine intermediate by dehydrohalogenation.[27] Recently, Kostik et al. reinvestigated the synthesis of indolizinones and showed their formation, in the case of R^2 = electron withdrawing group like COR/CO_2R, via methylide of type **2** and not the methine of type **3**.[28] This dependence of the generation of methylide or methine from 1,2-dialkylpyridinium salts on the nature of the substituent was further confirmed while making use of the latter for the synthesis of 2-phosphaindolizines by one of the present authors. In the case of **1** having a highly electron withdrawing substituent R^2 such as alkoxycarbonyl, a dichlorophosphinylated methylide intermediate (**4**) was isolated[22b,29] and characterized by X-ray crystallography,[29] the stability of which could be assigned to the presence of negative hyperconjugation by carrying out DFT level calculations.[30] However, in the case of pyridinium salts (**1**) with R^2 = H/Ph and R^1 = H, dichlorophosphinylated anhydrobase (**5**)[31] were isolated from the reaction with Et_3N and PCl_3, which resulted from the initial deprotonation at the 2-methylene group (Scheme 2).

SCHEME 2



1,2-Dialkylpyridinium salts are well-known to act as versatile synthones for the synthesis of a wide variety of condensed heterocycles containing a bridgehead nitrogen atom.[23,24] In view of their synthetic importance, we have considered a series of differently substituted 1,2-dialkylpyridinium ions having two competing sites for deprotonation and computed the corresponding deprotonation energies. An attempt has been made to describe intramolecular site selectivity on the basis of Fukui function as the local reactivity descriptor. At the same time, global descriptors such as chemical potential, global hardness, and global electrophilicity have also been calculated to compare intermolecular reactivity trends. It has been found that the deprotonation reaction under investigation comprises a hard−hard interaction, and therefore the site is controlled by the minimum Fukui function criterion of Li and Evans.

The paper has been organized as follows. In Section II, a brief description of concerned global and local reactivity descriptors, and in Section III, methodology and computational details are presented. Section IV deals with the analysis of computed trends of deprotonation energies and local as well as global descriptors, wherein the validity of the site-selectivity model in question has been discussed.

II. Theoretical Background

The analytical definition of absolute or global hardness (η) of a chemical species as defined by Parr and Pearson[3] in terms of the second derivative of $E(N)$ is given by

$$\eta = \frac{1}{2}\left(\frac{\partial^2 E}{\partial N^2}\right)_{v(\bar{r})} = \frac{1}{2}\left(\frac{\partial \mu}{\partial \mathrm{N}}\right)_{v(\bar{r})} \qquad (1)$$

where E is the total energy, N is the number of electrons of the chemical species, and $v(\bar{r})$ is the external potential. μ is the chemical potential identified by Parr et al.[2] as the negative of the electronegativity (χ).[32] The global hardness of a system is an indicator of its stability, and its half inverse is termed as global softness (S), which indicates the reactivity of the system.[4]

Most widely applied formulas to compute chemical potential and global hardness make use of three-point finite difference approximation.[3]

$$\mu \approx -\left(\frac{IP + EA}{2}\right) \tag{2}$$

$$\eta \approx \left(\frac{IP - EA}{2}\right) \tag{3}$$

Global electrophilicity, the overall electrophilic power of a chemical species, has been defined by Parr et al. in terms of chemical potential and global hardness.[5]

$$\omega = \frac{\mu^2}{2\eta} \tag{4}$$

Because the reactivity of a molecule is always related to a particular reactive site within the molecule, it becomes important, particularly for the systems having more than one reactive site, to have description of local reactivity indices. In principle, the site selectivity of a chemical system depends on the electron density distribution, and an appropriate local descriptor defined for this purpose, the local softness $s(\bar{r})$, is given by[4]

$$s(\bar{r}) = \left(\frac{\partial \rho(\bar{r})}{\partial \mu}\right)_{\upsilon(\bar{r})} = f(\bar{r})S \tag{5}$$

where ρ is the electron density at the site r and $f(\bar{r})$ is the Fukui function as defined by Parr and Yang.[7] Because of the Maxwell relations, the Fukui function can be interpreted as the change in the electron density accompanied with a change in the number of electrons. Therefore, using a finite-difference approximation, the "condensed" Fukui function for nucleophilic attack on the kth atom[9a] can be given by

$$f_k^+ = [\rho_k(N+1) - \rho_k(N)] \tag{6}$$

$\rho_k(N)$ and $\rho_k(N + 1)$ represent the condensed electronic population on an atom k for the N and $N + 1$ electron system, respectively.

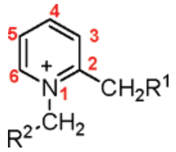
The highest (in the case of soft−soft interactions) or the lowest (in the case of hard−hard interactions) values of Fukui function (f_k^+ and f_k^-) or condensed local softness (s_k^+ and s_k^-) have been used successfully to explain experimentally observed intramolecular selectivity trends in a number of organic molecules.[12l,o,15,33]

III. Computational Methods

The density functional theory (DFT) level[1,34] calculations using Becke's three-parameter hybrid functional[35] in conjunction with the Lee, Yang, and Parr correlation potential[36] (B3LYP), were carried out with Gaussian 98 package.[37]

The pyridinium ions under investigation, **1a**−**i**, were first optimized at B3LYP/6-31+G* level without any geometrical constraints. The optimized geometries, corresponding to most stable conformations, were further utilized for the single-point calculations of species N, representing a pyridinium ion along with the corresponding $N + 1$ and $N - 1$ electron species at B3LYP/6-31++G** level in gas phase.[38] Energies of N, $N + 1$, and $N - 1$ species thus obtained were used for the calculation of global reactivity descriptors such as chemical potential, global hardness, and global philicity according to the eqs 2−4. Very recently, Hemelsoet et al. have assessed the level-of-theory dependence of global reactivity indices and found DFT-based hybrid functionals giving more accurate results.[39] Fukui functions (f_k^+) have been computed from the condensed charge on the kth atom in N and $N + 1$ systems obtained from Mulliken population analysis (MPA)[40] and natural population analysis (NPA)[41] schemes. Electronic deprotonation energies (DPE) have been computed for the reactions: (i) ion **1** → ylide **2** + H^+ and (ii) ion **1** → anhydrobase **3** + H^+ from the total energies of species **1**, **2**, and **3** calculated at B3LYP/6-31++G** level, as $DPE_1 = E(\mathbf{2}) - E(\mathbf{1})$ and $DPE_2 = E(\mathbf{3}) - E(\mathbf{1})$, respectively. The suitability of DFT level for the calculation of deprotonation energies for large systems has been discussed in several papers.[42]

TABLE 1: Experimental Site of Deprotonation in Differently Substituted Pyridinium Ions (1a−i)



	R^1	R^2	exp site	refs
1a	H	H	2-CH_3	26, 31
1b	H	Ph	2-CH_2	25b, 31
1c	Ph	H	2-CH_2	31
1d	Ph	Ph	2-CH_2	26a, 31
1e	H	$C_6H_4NO_2$-*p*	2-CH_2	26, 31
1f	H	CO_2Me	*N*-CH_2	22b, 28, 29
1g	H	COPh	*N*-CH_2	26b
1h	H	COMe	*N*-CH_2	24a, 28
1i	H	$COCMe_3$	*N*-CH_2	22a

TABLE 2: Different Global Descriptor Values (in eV) and Calculated Deprotonation Energies (in kcal/mol) for the Pyridinium Ions (1a−i)

	chemical potential μ	hardness η	global philicity ω	DPE_1[b]	DPE_2[c]
1a	−9.50	4.91	9.18	274.789	261.473
1b	−8.33	4.02	8.63	285.588	266.029
1c	−8.25	3.72	9.15	276.619	258.887
1d	−7.83	3.60	8.50	274.529	263.359
1e	−8.78	4.05	9.51	259.158	258.922
1f	−9.17	4.61	9.12	263.708	262.476
1g	−8.32	3.87	8.95	262.376	266.556
1h	−9.01	4.45	9.12	253.798	263.024
1i	−8.64	4.16	8.98	261.564	265.883
Et_3N	−3.65	4.31	1.55		

[a] All calculations at B3LYP/6-31++G** level on B3LYP/6-31+G* optimized geometries. [b] $DPE_1 = E(\mathbf{2}) - E(\mathbf{1})$. [c] $DPE_2 = E(\mathbf{3}) - E(\mathbf{1})$.

IV. Results and Discussion

The optimized geometries and numbering of the two reactive sites of nine differently substituted pyridinium ions (**1a**−**i**; Table 1) under investigation are given in Figure 1. Selected global reactivity descriptors, viz., chemical potential, global hardness, and global philicity in eV, as calculated from energy considerations (from total energies of N, $N + 1$ and $N - 1$ systems) for **1a**−**i** along with those for triethylamine, are reported in Table 2. Because these global quantities are associated with reactivity of the molecule, they may be used to identify the ease with which it undergoes a reaction and therefore may be used to compare reactivity within the series of related compounds. The generation of ylide **2** or anhydrobase **3** from the reaction of pyridinium ion **1** results due to the abstraction of a proton from either of the two methylene groups by a strong base such as triethylamine (Scheme 1). From Table 2, one can see that there is considerable difference in chemical potential of species **1a**−**i** with respect to the triethylamine. This large difference in chemical potential implies that their interaction is

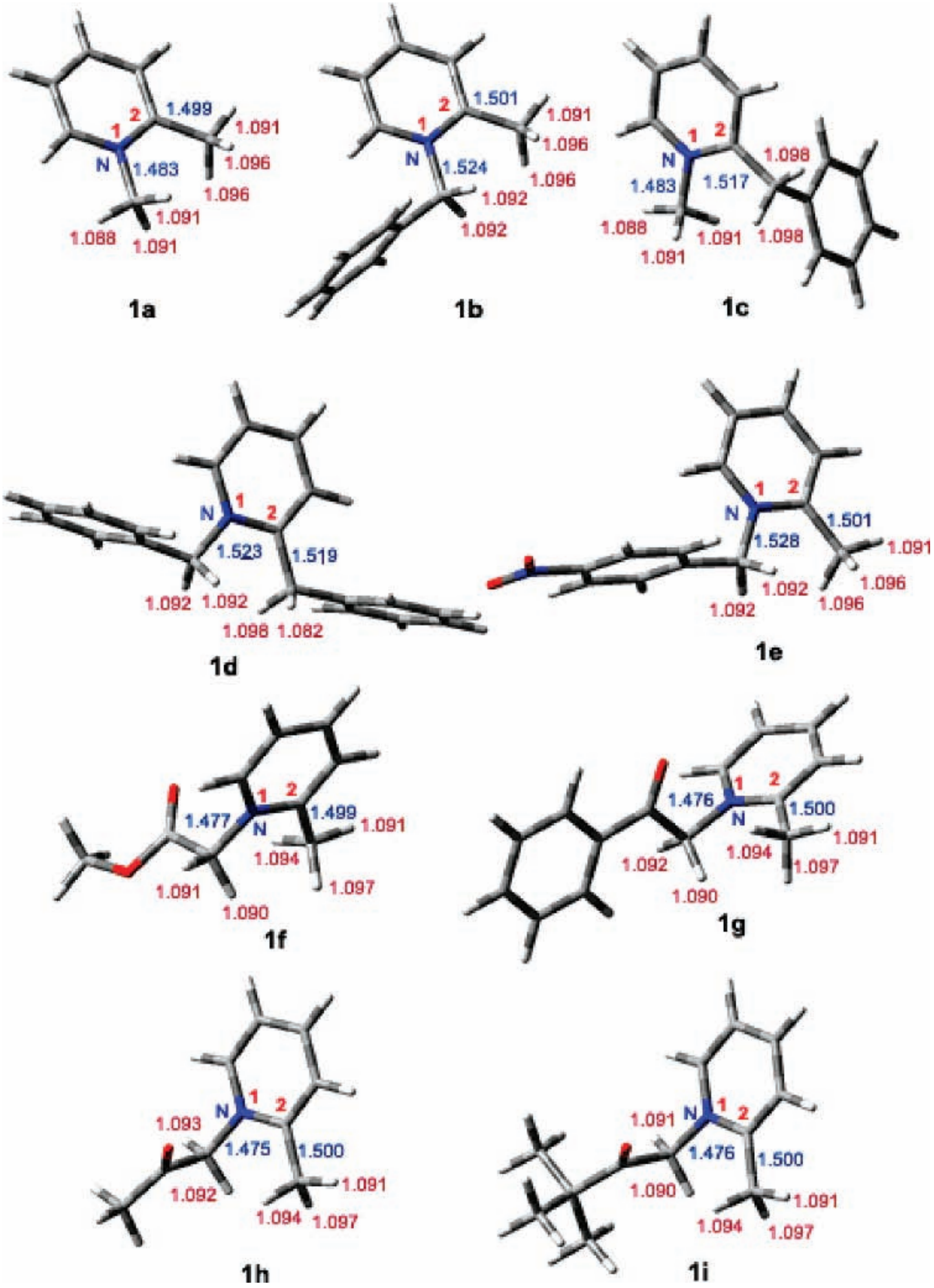


Figure 1. B3LYP/6-31+G* optimized geometries of pyridinium ions **1a**−**i** (selected bond lengths in Å).

charge controlled. The values of the hardness of these molecules reported in Table 2 are close to those of the known or reported "hard" molecules in literature (see, for example, Table 5 of ref 13). It is well-known that charge-controlled interactions are "hard−hard" ones.

The site selectivity within a molecule may be determined from the difference in the local reactivity of atoms in the molecule and has been often related to the Fukui function, a natural local descriptor of reactivity. In view of the Li−Evans local HSAB rule of minimum Fukui indices for hard−hard interactions, triethylamine, being a hard nucleophile, will have predisposition to develop an interaction with the hard substrate, i.e., pyridinium ion, by attacking the hardest hydrogen atom, the latter represented by minimum condensed-to-site Fukui function value among the reactive N-CH_2/CH_3 and 2-CH_2/CH_3 protons.

As illustrated by Fuentealba and co-workers[12l] previously, the protonation reaction of alkylamines is regarded as a *hard*−*hard* interaction that follows the local HSAB principle. Furthermore, in agreement with the Li−Evans interpretation of Pearson's HSAB rule, the enhanced basicity at the nitrogen site within a series of alkylamines could be associated with minimum values of Fukui function, the latter indicating an increase in local hardness at the basic site. More recently, Chamorro et al. have analyzed site selectivity and reactivity in a series of organic superbases and discussed a linear relationship between global energy-dependent quantities such as proton affinities and the low values of condensed-to-site Fukui functions within the framework of the local HSAB principle.[17] Thus, it is obvious that the protonation reactions of alkylamines should be satisfactorily assessed by applying the Li−Evans selectivity rule of minimum Fukui function value governing a hard−hard interaction.

The reaction under present investigation is important in a sense because here, for the first time, the site selectivity in the

TABLE 3: Average Fukui Function (f_k^+) and Average Charge Values of N-CH$_2$/CH$_3$ and 2-CH$_2$/CH$_3$ Hydrogen Atoms of Pyridinium Ions 1a−i Calculated at B3LYP/6-31++G//B3LYP/6-31+G* Level**

		MPA		NPA	
	site	f_k^+	charge	f_k^+	charge
1a	N-CH$_3$	0.0400	0.2005	0.0328	0.2604
	2-CH$_3$	0.0351	0.2022	0.0378	0.2726
1b	N-CH$_2$	0.0462	0.2104	0.0263	0.2641
	2-CH$_3$	0.0342	0.1953	0.0362	0.2693
1c	N-CH$_3$	0.0364	0.2065	0.0317	0.2607
	2-CH$_2$	0.0234	0.1947	0.0250	0.2755
1d	N-CH$_2$	0.0397	0.1823	0.0258	0.2629
	2-CH$_2$	0.0447	0.2249	0.0329	0.2710
1e	N-CH$_2$	0.0377	0.2174	0.0244	0.2676
	2-CH$_3$	0.0279	0.1959	0.0289	0.2706
1f	N-CH$_2$	0.0243	0.2240	0.0252	0.2854
	2-CH$_3$	0.0368	0.2045	0.0371	0.2729
1g	N-CH$_2$	0.0264	0.2520	0.0259	0.2747
	2-CH$_3$	0.0303	0.2012	0.0306	0.2713
1h	N-CH$_2$	0.0260	0.2278	0.0263	0.2770
	2-CH$_3$	0.0358	0.2042	0.0368	0.2721
1i	N-CH$_2$	0.0239	0.2335	0.0255	0.2767
	2-CH$_3$	0.0363	0.2029	0.0364	0.2714

substrate, which provides a proton to the alkylamine, is being investigated. Therefore, by considering the validity of the Li−Evans rule in the present case also, the formation of an ylide or an anhydrobase due to the deprotonation by a base at different sites has been explained on the basis of minimum condensed-to-site Fukui function values of active hydrogen sites in the respective pyridinium ion. Average total atomic charges and average electrophilic Fukui function (f_k^+) values of the hydrogen atoms of the N-CH$_2$/CH$_3$ and 2-CH$_2$/CH$_3$ moieties in differently substituted pyridinium ions **1a**−**i** calculated from MPA and NPA schemes have been summarized in Table 3; individual f_k^+ values and atomic charge on all relevant hydrogens are available in Supporting Information (Table SI-2).

Our aim is to assess the suitability of electrophilic Fukui function (f_k^+) as a site-selectivity descriptor in differently substituted pyridinium ions (**1a**−**i**) and make a comparison with the deprotonation energies of possible deprotonation reactions. For this purpose, the calculated deprotonation energies of two competing reactions, i.e., generation of ylide **2** and generation of methine **3,** have been included in Table 2. As mentioned earlier, in the case of **1a**, deprotonation at 2-methyl group leads to the generation of the anhydrobase of type **3** by the action of Et$_3$N or K$_2$CO$_3$.[26b,31] Similarly, in the case of **1b**−**e** also, the experimental site of the reaction has been identified to be 2-CH$_2$/CH$_3$.[31] However, in the case of pyridinium salts having an electron-withdrawing substituent like CO$_2$Me, CO$_2$Et, or COPh at the N-methylene group, the isolation of a dichlorophosphinylated pyridinium ylide[22b,31] of type **4** indicates the initial deprotonation at N-CH$_2$ moiety. A similar observation was made during the benzoylation of **1g**.[26b] Thus, the experimental evidence indicates that the preferred site of deprotonation is 2-methylene in **1a**−**e**, while N-methylene is in **1f**−**i** (Table 1) and depending on the nature of the substituents on 1- and 2-methylene groups, two different mechanistic pathways exist for the synthesis of indolizines[26] and phosphaindolizines[23a,31] involving intermediacy of either a methylide or a methine intermediate.

Out of the two calculated electronic deprotonation energies, DPE$_1$ and DPE$_2$ for each ion (Table 2), the lower value should correlate with the more favorable reaction pathway. In the case of pyridinium ions **1a**−**d**, a reasonably lower value of DPE$_2$ is in good agreement with the experimentally observed deprotonation at 2-CH$_2$/CH$_3$, while for **1e**, the difference between DPE$_2$ and DPE$_1$ is small enough to describe site selectivity. Alternatively, in the case of **1g**−**i**, the value of DPE$_1$ is lower again, corresponding to the correct deprotonation site (Table 1). It can be seen that **1f** is an exceptional case, where the difference between two deprotonation energies is much smaller and does not match the experimental site selectivity. On the other hand, in view of the Li−Evans selectivity rule, one would expect the said hard−hard interactions to be controlled by the smaller f_k^+ value. Accordingly, when the f_k^+ values of hydrogens corresponding to N-CH$_2$/CH$_3$ and 2-CH$_2$/CH$_3$ groups obtained from Mulliken population analysis are considered, the correct site of reaction is justified by the smallest f_k^+ in all the cases except **1d**. It is worthwhile to mention here a recent report prescribing the charge to be a better descriptor of selectivity than Fukui function for hard−hard interactions.[13] Although, in the case of aminothiols in the referred paper, minimum Fukui function consideration also explains the correct site of protonation along with the charge criterion. Moreover, in a good number of cases of hydroxylamines, the charge too does not give the correct site of protonation when minimum Fukui function fails.[13] In the present investigation, if we consider maximum positive atomic charge criterion for the attack of a nucleophile, the correlation does not match the correct site of reaction in several cases (i.e., **1b,c,e**), thereby justifying the applicability of minimum Fukui function rule in such interactions. Although, in the present case, when f_k^+ and atomic charge values obtained from natural population analyses (NPA) are considered, the minimum Fukui function criterion presents some exceptions in predicting the correct site of reaction (Table 3). It is apparent from the above assessment that, for the description of site-selectivity in ionic pyridinium compounds using Fukui functions, the MPA scheme gives more appropriate results.

The present case deals with the explanation of site selectivity in molecules with two different sites of comparable reactivity, the latter varying with the change of substituents. It is apparent from above discussion that, within the context of Li−Evans' criterion, the electrophilic Fukui function (f_k^+) obtained from the MPA scheme provides fairly good explanation to the observed site selectivities in differently substituted pyridinium ions that act as a hard substrate during deprotonation.

V. Conclusion

Applicability of Li−Evans' criterion of minimum Fukui function for site selectivity in the reactions comprising hard−hard interaction has been verified by considering the deprotonation of pyridinium ions. For this purpose, B3LYP/6-31++G** level calculations of deprotonation energies and Fukui functions by MPA, NPA analysis have been performed. In a good number of cases, minimum Fukui function justifies the observed site selectivity in the investigated case of hard−hard interaction. Results obtained from the MPA scheme are closer to the description obtained from deprotonation energies.

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Supporting Information Available: The total energies of pyridinium ions (**1a**−**i**), ylides (**2a**−**i**), anhydrobases (**3a**−**i**), and triethylamine calculated at B3LYP/6-31++G**//B3LYP/6-31+G* level. Individual f_k^+ values and atomic charges on all relevant hydrogen atoms of *N*-CH_2/CH_3 and 2-CH_2/CH_3 groups. Cartesian coordinates of B3LYP/6-31+G* optimized geometries of **1a**−**i** and triethylamine in gas phase. This material is available free of charge via the Internet at http://pubs.acs.org.

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