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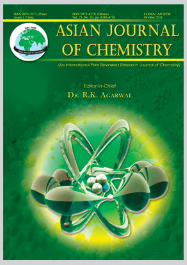

A DFT Study of Strecker Intermediates as Scavengers for Cyanides

C.A. FLORES-SANDOVAL[1,*], F. GODINEZ-SALOMON[1,2], J.M. HALLEN-LOPEZ[2], H.I. BELTRÁN[3],
R. HERNÁNDEZ-ALTAMIRANO[1], D.A. NIETO-ALVAREZ[4] and L.S. ZAMUDIO-RIVERA[5,*]

[1]Programa de Ingeniería Molecular, Instituto Mexicano del Petróleo, Eje Central Lázaro Cárdenas 152, México D.F.
[2]Departamento de Ingeniería Metalúrgica, Escuela Superior de Ingeniería Química e Industrias Extractivas, IPN, Unidad Profesional Adolfo López Mateos, México D.F.
[3]Departamento de Ciencias Naturales DCNI, UAM-Cuajimalpa, Pedro Antonio de los Santos 84, San Miguel Chapultepec, 11850, México D.F.
[4]Programa de Recuperación de Hidrocarburos, Instituto Mexicano del Petróleo, Eje Central Lázaro Cárdenas 152, México D.F.
[5]Laboratorio de Síntesis Química y Electroquímica, Instituto Mexicano del Petróleo, Eje Central Lázaro Cárdenas 152, México D.F.

*Corresponding authors: Fax: +52 55 9175 6239; Tel: +52 55 9175 8269; E-mail: caflores@imp.mx; lzamudio@imp.mx

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Bis-(aminomethyl)ethers (**1-4**) have been employed as molecular scavengers for cyanides. They are theoretically studied herein at DFT, thus enabling a theoretical study in order to elucidate why the efficiency as scavenger depends on the substituent placed at the nitrogen atom. The local softness (s^+) value for C2 from electrostatic potential analysis (ESP) shows that the following decreasing order of reactivity is in accordance with the experimental yield values: **4**, **1**, **2** and **3**. 1290 runs considering four to ten parameters such as N3-C2 and C2-O1 bond lengths, HOMO and LUMO energies, GAP, dipolar moment, partition coefficient, atomic charge, local softness, global hardness, electronegativity and ^{13}C NMR chemical shift were taken into account in a structure-activity relationship study. In particular five runs of linear combination of four (run 259), five (run 517), seven (runs 937 and 1063) and eight (run 1214) molecular indexes have shown the best F values, being the run 517, which present the highest F value 4 to 10 parameters.

Key Words: Local softness, DFT, Molecular descriptor, Molecular reactivity, Scavenger.

INTRODUCTION

Metallic cyanides are among the most common corrosive pollutants in crude oil[1-3]. In order to eliminate the cyanide ions in the petroleum feedstock, some scavengers of cyanides have been synthesized[4]. A strecker intermediates that act as scavengers of cyanides were synthesized[5]; which have shown different chemical reactivity, measured as reaction yield, between 66 and 94 %, when cyanide is the nucelophile species and thus this can be considered as their activity as cyanide scavengers.

On another hand, the electron density $\rho(r)$ distribution is a fundamental concept to understand the reactivity of molecular entities and therefore, it can explain the phenomena of nucleophilic, electrophilic and radical attacks on a particular structure. The frontier-electron density theory of chemical reactivity by Fukui[6] explained the importance of the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) in the chemical reactions. Therefore, the Fukui function $f(r)$ and local softness $s(r)$ are of great interest in chemical reactions, because these parameters could describe the most reactive site in a given molecular species. The $f(r)$ function for a molecule can be defined as[7]:

$$f(r) = \left(\delta\mu / \delta v(r)\right)_N = \left(\partial\rho(r) / \partial N\right)_{v(r)} \qquad (1)$$

where, μ is the chemical potential, N is the number of electrons, $v(r)$ is the potential acting on an electron due to all nuclei and $\rho(r)$ is the electron density. The $\rho(r)$ measures how sensitive a chemical potential is to an external perturbation at a particular point. Thus, $f(r)$ indirectly gives the reactivity of a particular site and hence acts as a reactivity index. Considering the fact that $\rho(r)$ is a discontinuous function of N, two different types of $f(r)$ can be defined for any atom or molecule corresponding to a nucleophilic and electrophilic attack. However, the evaluation of these $f(r)$ values is quite intricate. A simple procedure to calculate f_k (condensed Fukui function) was proposed by Yang and Mortie, an alternative for $f(r)$, based on the Mulliken population analysis (MPA) and the finite-difference approximation of eqn. (1). In a finite-difference approximation, for a system of N electrons, the $f(r)$ values are given as:

$$f^+(r) = q_k(N_0 + 1) - q_k(N_0) \text{ for a nucleophilic attack} \qquad (2)$$

$$f^{-}(r) = q_k(N_0) - q_k(N-1) \text{ for an electrophilic attack} \quad (3)$$

where, $q_k(N_0)$, $q_k(N_0-1)$ and $q_k(N_0+1)$ represent the electronic population in the k atom for the N_0, N_0-1 and N_0+1 electron system, respectively.

The local softness parameter is defined as:

$$s(r) = f(r)S \quad (4)$$

where, S is the global softness. Furthermore, the three approximate atomic $f(r)$ indexes, when they are multiplied by S, provide two different local softnesses for any particular atom (k), which can be written as:

$$s_k^{+} = [q_k(N_0+1) - q_k(N_0)]\ S \quad (5)$$

$$s_k^{-} = [q_k(N_0) - q_k(N_0-1)]\ S \quad (6)$$

Finally, the $\Delta f(r)$ descriptor defined as the difference of the nucleophilic Fukui function $f^{+}(r)$ and the electrophilic Fukui function $f^{-}(r)$[8]. The sign of the $\Delta f(r)$ describes the electrophile ($\Delta f(r) > 0$) and nucleophile ($\Delta f(r) < 0$) zones within a molecule.

On the other hand, it is well known that quantum chemistry enables tools to obtain chemical descriptors (molecular orbital energies, gap, atomic charge, *etc.*) these can be employed to carry on quantitative structure-activity relationships (QSAR). This analysis has been widely employed in the biological area, however, some works have been published in the field of corrosion science[9-12], or other scientific and industrial fields where a particular activity is acknowledged and is intended to be optimized in such a way.

In this work, we present a study performed at DFT for four already known and tested molecular scavengers. This survey takes into account the analysis of reactivity parameter (local softness) in order to relate this with the scavenging activity. In this work, we have done a structure-activity study[13] in order to account the factors that govern such activity.

EXPERIMENTAL

DFT calculations implemented in the Gaussian 98 program package[14] were done using to carry out the optimization of the structures by using a B3LYP functional[15]. The B3LYP hybrid functional defines the exchange functional as a linear combination of Hartree-Fock, local and gradient-corrected exchange terms[15-19]. The 6-31G+(d) basis set was employed in this work, where diffuse functions were employed because they are known to supply a better energy value for anionic species. The zero-point energy correction (ZPE) was calculated at same level of theory in all four molecular cases under study.

The ^{13}C NMR shielding tensors were calculated using the methodology of Gauge Independent Atomic Orbitals (GIAO)[20-23].

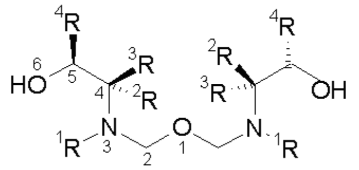
The isotropic shielding values defined as:

$$\sigma_{iso} = 1/3\ (\sigma_{11} + \sigma_{22} + \sigma_{33}) \quad (7)$$

where (σ_{ii} being the principal tensor components) were used to calculate the isotropic chemical shifts (δ) relative to TMS ($\delta^X = \sigma^{TMS} - \sigma^X$)[24-26]. Finally, the parameters for the structure-activity study were obtained at B3LYP/6-31G+(d) level, except the log P parameter, which was obtained by using Hyper Chem software.

RESULTS AND DISCUSSION

The synthesis of Strecker intermediates as *bis*-(aminomethyl)ethers (**1-4**) **1-4**, have already been reported (Fig. 1)[5]. Such compounds could act as non-pollutant scavengers for sodium cyanide, in water and solvent mixtures, that have a composition similar to -crude oil; in where the efficiency (Eff) for scavenging were of 90.7, 65.8, 58.8 and 93.5 % for **1**, **2**, **3** and **4**, respectively. The last one has a pseudo-ephedrine fragment (the most branched *N* substitution in the whole series) and it shows the highest efficiency as scavenger. Thus, the experimental yield values depend on the structure and thus the reactivity of the employed β-amino alcohols, not only to form the Strecker intermediates but also to scavenge cyanide ions in order to obtain *N* substituted glycine derivatives as the non-pollutant species. In this contribution, a theoretical study of these compounds was carried out in order to observe the effect of having different molecular fragments linked to C2 atom (Fig. 1), over some molecular parameters. The underlined importance over this atom is because of it is flanked by two, more electronegative, atoms (N3-C2-O1) and since it is the electron deficient site, due to double neighboring inductive effect and hence it is also the reactive site. In this line C2 atom acts as electrophilic site and therefore, it suffers the nucleophillic attack of the cyanide ion; due to the latter facts the quantum chemical parameters are hereafter referred to this atom.



Compound	R¹	R²	R³	R⁴	Yield (%)
1	$^7CH_2$-Ph	H	H	H	91
2	$^7CH_2$–CH_2–CH_2–CH_3	H	H	H	66
3	$^7C(CH_3)_3$	H	H	H	59
4	$^7CH_3$	CH_3	H	C_6H_5	92

Fig. 1. Structure of (*N,N*-dialkyl-amine)methyl ethers used in the study

Table-1 listed the geometric parameters from optimized structures. Fig. 2 showed the optimized structures. As can be seen from Fig. 2, all the structures present a symmetry-plane (σ) that cross through the O1 atom. The presence of this symmetry plane in the optimized structures is in accordance with the signal pattern observed in the experimental ^{1}H and ^{13}C NMR spectra[5]. In compound **4** there exists an interesting proximity of the aromatic rings, in which the HA-HB bond distance was of 2.326 Å, whereas in **1** the bond distance between both aromatic rings was of 6.82 Å. This bond distance is shorter in **4** due to ethylene moiety, which is bonded to the aromatic rings and lends more flexibility for this fragment, whereas in **1**, this flexibility is more restricted due to the presence of a benzyl moiety (R1 moiety). Thus, when other CH_2 unit was added to the benzyl fragment (this implies another degree of freedom in the chemical structure), the distance between both aromatic rings decreased approximately to 1.7 Å. In this case, both rings are almost in the same plane. Then, the addition of an ethylene fragment causes an inherent proximity of aromatic rings. Furthermore, from Table-1, the presence of *n*-butyl or *t*-butyl fragment provokes a decrease in the energy value, which could be attributed mainly to non-bonded interactions like steric hindrance.

TABLE-1
GEOMETRIC PARAMETERS FOR OPTIMIZED **1-4** STRUCTURES

Fragment	Compound			
	1	2	3	4
Bond length (Å)				
N3-C2	1.4835	1.4831	1.4802	1.4874
C2-O1	1.4129	1.4124	1.4128	1.4145
Torsion and dihedral angles (°)				
N3-C2-O1	102.2481	101.8624	112.5832	103.1177
N3-C2-O1-C2'	-170.4648	174.0940	-171.3214	-179.6984

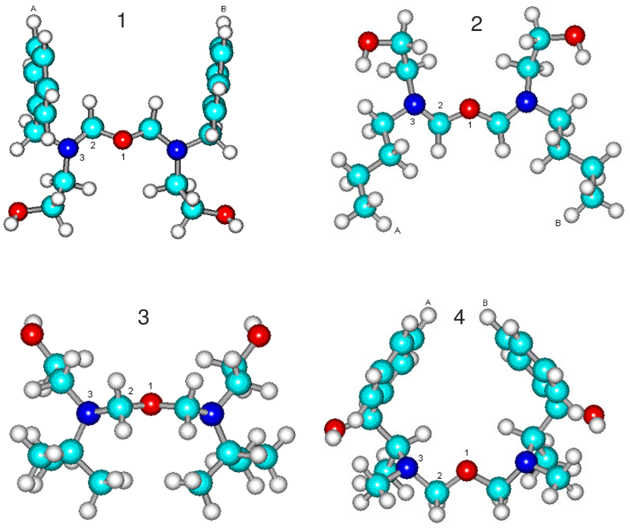


Fig. 2. Optimized structures for **1-4**

The ^{13}C NMR shielding tensors were calculated using the methodology of Gauge independent atomic orbitals (GIAO)[20-23] at the B3LYP/6-31G+(d) level. The isotropic shielding values were used to calculate the isotropic chemical shifts δ referred to TMS; the absolute $\sigma(^{13}C)$ of 184.1 ppm reported by Jameson and Jameson[25] was employed for the obtaining of the calculated chemical shift. Table-2 shows the theoretical and experimental ^{13}C chemical shifts in ppm of C2, C4, C5 and C7 for all the compounds.

TABLE-2
EXPERIMENTAL^a AND THEORETICAL^b ^{13}C CHEMICAL SHIFTS FOR **1-4** COMPOUNDS

	1	**2**	**3**	**4**
C2	86.3^a; 76.0^b	86.4^a; 76.2^b	80.6^a; 80.5^b	85.8^a; 85.8^b
C4	52.1^a; 61.0^b	53.8^a; 57.2^b	52.4^a; 54.2^b	68.0^a; 60.0^b
C5	63.2^a; 62.1^b	63.4^a; 64.23^b	66.1^a; 63.4^b	88.6^a; 77.7^b
C7	58.0^a; 53.6^b	52.3^a; 54.7^b	45.1^a; 44.6^b	36.8^a; 36.6^b

As was mentioned above, C2 atom has an electronic deficiency and is susceptible to suffer a nucleophilic attack; taking this into account, the atomic charge for this atom was obtained by using a Mulliken population analysis (MPA) and electrostatic potential analysis (ESP)[27,28]. Mulliken population analysis results are well known to strongly depend on the choice of the molecular basis set. Despite its known deficiencies, the Mulliken population analysis is still widely used, owing to its simplicity. In electrostatic potential analysis, atomic partial charges are selected to reproduce the molecular electrostatic potential. In this respect, Table-3 listed the atomic charge values ($q_k(N_0)$) for **1-4** for Mulliken population analysis and electrostatic potential analysis. Mulliken population analysis gave a negative value for **1-4**, which could be related with the employed theoretical level, however, for electrostatic potential only **1** showed a negative value, whereas **4** showed the highest positive value. The Mulliken population analysis atomic charges analyzed at the nitrogen atoms have positive values, whereas the charges obtained from electrostatic potential gave -0.1678, -0.0657, -0.7214 and -0.3573 for **1-4** compounds, respectively. Again, the absolute differences in the values obtained for Mulliken population analysis and electrostatic potential are due to the employed basis set.

TABLE-3
ATOMIC CHARGES ($q_k(N_0)$), f^+, f^-, s^+ AND $\Delta f(\mathbf{r})$ VALUES IN C2 ATOM FOR **1-4** BY USING A MPA AND ESP ANALYSES

Compound	Mulliken population analysis (MPA)				
	$q_k(N_0)$	f^+	f^-	s^+	$\Delta f(\mathbf{r})$
1	–0.3163	0.3850	–0.0591	1.4647	0.4441
2	–0.2259	0.4605	–0.1137	1.7409	0.5742
3	–0.1012	0.0920	–0.0335	0.3769	0.1255
4	–0.0684	0.2698	–0.0564	1.0253	0.3262
	Electrostatic potential (ESP)				
1	–0.3101	0.3683	–0.0279	1.4011	0.3962
2	0.1205	0.3311	0.0704	1.2517	0.2607
3	0.1707	0.2654	0.0824	1.0871	0.1830
4	0.5028	0.5239	0.1093	1.9914	0.4146

We carried out the calculation for the obtaining of the local softness value. In this case, only the s^+ parameter was calculated because it shows the more susceptible center to be attacked by a nucleophilic species. The f^+ and s^+ values obtained by Mulliken population analysis and electrostatic potential analysis for compounds **1-4** are listed in the Table-3. As can be observed from this table, the s^+ value directly depends on the R^1 substituent attached to N3, which affects the reactivity towards the C2 site. For Mulliken population analysis, the s^+ value increases in the following way: **3**, **4**, **1** and **2**; whereas for electrostatic potential analysis the reactivity increases as: **3**, **2**, **1** and **4**. This difference is because the Mulliken population analysis is highly dependant on the employed basis set. Regarding to electrostatic potential analysis it shows the same order than that of the yield, therefore, the substituent on N3 atom has a great effect in the reactivity of electrophilic center, C2 and therefore in the yield of the chemical reaction and thus scavenging activity.

Finally, the $\Delta f(r)$ values (Table-3) for all compounds were higher than zero, which show that C2 atom is an electrophilic site; having the same behaviour found by the local softness values.

On the other hand, we carried out a study of quantitative structure-activity relationship, in order to observe which structural and electronic parameters are the most important in these compounds. However, because only four compounds are taken into account in this work, several parameters and combinations between them have been considered to ponderate the number of compounds. The parameters that were taken into account were: N3-C2 and C2-O1 bond lengths, E_{HOMO}, E_{LUMO} and GAP energies, dipolar moment (DIP), partition coefficient (log P), C2 atomic charge (AC_{ESP}), local softness (s^+_{ESP}), global hardness (η), electronegativity (χ) and ^{13}C NMR chemical shift. Atomic charge and local softness from Mulliken population analysis were not taken into account because, this population analysis strongly depends on the employed basis set. Table-4 listed all the parameters for this study regarding compounds **1-4**. Furthermore, the data presented in Table-5 (correlation matrix) express that the electronegativity (-0.9696), N3-C2 bond length (0.8355) and local softness (0.8244) descriptors correlate well with the log Eff. Thus a linear combination model was selected due to its simplicity and thus facility in evaluation of those weighed molecular indexes in charge of a particular activity. This simple equation was constructed considering 4 to 10 parameters and was solved by using the multivariate least squares procedure present in Excel software. Those combinations where the dependent parameters E_{HOMO}/GAP, E_{LUMO}/GAP and AC_{ESP}/s^+_{ESP} are present were not considered for the study. All the 4 parameter systems were resolved adding a dummy constant in the equation in order to avoid the presumably and misestimated analytic solution of the square matrix. All equations were matched to the experimental log Eff. After obtaining the R^2 and R^2_{adj} values for all the arrays, there were only considered those, which have the lower R^2 and R^2_{adj} values (values in the range of 1E-5 and 1E-10, respectively). Subsequently, the linear regression for obtaining the Fisher variance ratio (F) value was performed and the runs with the higher F value were taken into account. A total of 1290 combination were done, obtaining a F value in the range of 1E+25 and 1E+37. Table-6 listed the runs with the lowest and the highest F values considering from 4 to 10 parameters in the linear combination model. Considering only four parameters could take a risk, seeing as the combination of parameters could give a good F value or a worse value. By contrary wise, having 8, 9, or 10 parameters, provoked a dropping in the F value, hence, in this type of compounds using more than seven parameters should be avoided. The runs 259, 517, 937, 1063 and 1214 show an F value, which is between 2.95E+37 and 8.85E+37; the equations for those runs are shown in the Table-7. As can be seen, only the AC_{ESP} parameters appear in all those runs, pointing out the importance of this parameter in the scavenging activity; whereas, the local softness is absent in those ones. Owing to this fact, the s^+_{ESP} could be omitted in

TABLE-4
PARAMETER VALUES FOR QSAR STUDY

Parameters	Compound			
	1	2	3	4
N3-C2 (Å)	1.4835	1.4831	1.4802	1.4874
C2-O1 (Å)	1.4129	1.4124	1.420	1.4145
E_{HOMO} (eV)	-0.00163	-0.00129	-0.00499	-0.00556
E_{LUMO} (eV)	0.00114	0.00142	0.00286	0.00619
GAP	0.00277	0.00271	0.00785	0.01175
DIP (Deybe)	4.5506	5.628	1.7631	2.8559
log *P*	1.41	2.23	1.49	4.34
η	0.001385	0.001355	0.003925	0.005925
χ	-1113.987	-887.73	-887.69	-1192.64
AC_{ESP}	-0.3101	0.1205	0.1707	0.5028
s^+_{ESP}	1.4011	1.2517	1.0871	1.9914
^{13}C (ppm)	86.3	86.4	80.6	85.8

TABLE-6
F VALUES FOR COMBINATION OF
FOUR TO TEN PARAMETERS

Run	Parameters	*F* value
Four parameters		
15	N3-C2, C2-O1, GAP, log P	3.87E+25
259	GAP, log P, η, AC_{ESP}	2.95E+37
Five parameters		
319	N3-C2, C2-O1, E_{HOMO}, η, ^{13}C	1.24E+29
517	C2-O1, E_{HOMO}, η, AC_{ESP}, ^{13}C	8.85E+37
Six parameters		
838	C2-O1, E_{HOMO}, E_{LUMO}, DIP, log P, χ	1.00E+30
937	HOMO, E_{LUMO}, DIP, log P, AC_{ES}, ^{13}C	7.38E+37
Seven parameters		
1123	N3-C2, E_{HOMO}, E_{LUMO}, log P, χ, s^+_{ESP}, ^{13}C	6.84E+29
1063	N3-C2, E_{HOMO}, E_{LUMO}, DIP, log P, η, AC_{ESP}	6.32E+37
Eight parameters		
1216	N3-C2, C2-O1, E_{HOMO}, E_{LUMO}, DIP, log P, η, ^{13}C	1.60E+32
1214	N3-C2, C2-O1, E_{HOMO}, E_{LUMO}, DIP, log P, η, AC_{ESP}	1.51E+37
Nine parameters		
1282	N3-C2, C2-O1, E_{LUMO}, DIP, log P, η, χ, s^+_{ESP}, ^{13}C	1.83E+33
1287	C2-O1, E_{HOMO}, E_{LUMO}, DIP, log P, η, χ, AC_{ESP}, ^{13}C	4.68E+36
Ten parameters		
1289	N3-C2, C2-O1, E_{HOMO}, LUMO, DIP, log P, η, χ, AC_{ESP}, ^{13}C	1.01E+34
1290	N3-C2, C2-O1, E_{HOMO}, LUMO, DIP, log P, η, χ, s^+_{ESP}, ^{13}C	3.61E+34

TABLE-5
CORRELATION COEFFICIENT MATRIX

	log Eff	N3-C2	C2-O1	E_{HOMO}	E_{LUMO}	GAP	DIP	log P	η	χ	AC_{ESP}	s^+_{ESP}	^{13}C
log Eff	1.0000												
N3-C2	0.8355	1.0000											
C2-O1	-0.5704	-0.5628	1.0000										
E_{HOMO}	-0.5786	-0.8353	0.0233	1.0000									
E_{LUMO}	0.3725	0.6591	0.2353	-0.9637	1.0000								
GAP	0.1313	0.4787	0.4076	-0.8744	0.9689	1.0000							
DIP	0.1602	0.1523	-0.8920	0.3842	-0.5886	-0.6758	1.0000						
log P	0.5135	0.8781	-0.2105	-0.9525	0.8860	0.8068	-0.1480	1.0000					
η	0.2138	0.4583	0.4704	-0.8708	0.9677	0.9779	-0.7713	0.7436	1.0000				
χ	-0.9696	-0.8363	0.3672	0.7127	-0.5541	-0.3342	0.0797	-0.5995	-0.4316	1.0000			
AC_{ESP}	v0.0388	0.4475	0.2765	-0.7820	0.8679	0.9355	-0.4558	0.8208	0.8410	-0.1204	1.0000		
s^+_{ESP}	0.8244	0.9705	-0.3572	-0.9265	0.7944	0.6275	-0.0875	0.9050	0.6373	-0.8814	0.5322	1.0000	
^{13}C	0.6782	0.6903	-0.9862	-0.1831	-0.0797	-0.2700	0.8063	0.3493	-0.3238	-0.5006	-0.1695	0.5065	1.0000

TABLE-7
EQUATIONS FOR RUNS HAVING THE HIGHER F VALUE

259	log Eff. = 0.65 + 378.30*GAP + 0.10*log P – 412.67*η-2.23*AC_{ESP}	(1)
517	log Eff. = 2.66-2.53 * C2-O1-0.13 * E_{HOMO} + 64.88*η-0.33*AC_{ESP} + 0.03*^{13}C	(2)
937	log Eff. = 2.46-48.89*E_{HOMO} + 1011.04*E_{LUMO} + 0.97*DIP-2.48*log P +1.36*AC_{ESP}-0.03*^{13}C	(3)
1063	log Eff. = -0.54-0.36*N3-C2 + 33.23*E_{HOMO}-40.45*E_{LUMO} + 0.27*DIP + 0.38*log P + 604.77*η-1.68*AC_{ESP}	(4)
1214	log Eff. = -0.78-0.17*N3-C2 + 0.47*C2-O1 + 43.43*E_{HOMO}-177.52*E_{LUMO}-0.009*DIP + 0.98*log P + 449.04* η-2.05*AC_{ESP}	(5)

TABLE-8
EXPERIMENTAL AND CALCULATED log *Eff* VALUES

Comp.	log Eff_{exp}	log Eff_{calc}				
		259	517	937	1063	1214
1	1.95904139	1.95904139 (0)	1.95904139 (-2E-16)	1.95904139 (-1E-15)	1.95904139 (-6E-16)	1.95904139 (0)
2	1.81954394	1.81954394 (4E-16)	1.81954394 (0)	1.81954394 (-4E-16)	1.81954394 (0)	1.81954394 (6E-16)
3	1.77085201	1.77085201 (-2E16)	1.77085201 (6E-16)	1.77085201 (-4E-16)	1.77085201 (4E-16)	1.77085201 (-4E-16)
4	1.97312785	1.97312785 (2E-16)	1.97312785 (-2E-16)	1.97312785 (-2E-16)	1.97312785 (-2E-16)	1.97312785 (0)

*Values in parentheses are the difference between the log Eff_{calc} and the log Eff_{exp}.

this study, which would reduce the amount of runs, even though, as was mentioned above, the local softness showed a well relation with the log Eff. Regarding the other two parameters, χ and N3-C2, the last one is only considered in runs 1063 and 1214. Besides, although the highest F value was found with 5 parameters, a combination of 6 parameters and even seven parameters could be taken into account, seeing that those gave an acceptable value of F. Table-8 shows the experimental and calculated log Eff values for runs 259, 517, 937, 1063 and 1214, in where it can observe the high correlation between experimental and theoretical values.

On the other hand, an evaluation of the weighed molecular indexes was done for the runs 259, 517, 937, 1063 and 1214. Thus, the F values calculated when a single parameter in the equations (1) to (5) was eliminated, are listed in Tables 9-13.

TABLE-9
EFFICIENCIES CALCULATED AND R^2 VALUES WHEN ONE PARAMETER IS ELIMINATED FOR RUN 259
log Eff = 0.65 + 378.30*GAP + 0.10*log P-412.67* η-2.23*AC_{ESP}

	log Eff_{calc}	log Eff_{calc} - log Eff_{exp}	R^2	F
GAP	0.9110	−1.0481	0.0042	0.008
	0.0451	−1.7744		
	−1.2014	−2.9722		
	−2.4823	−4.4554		
log P	1.8179	–0.1412	0.0547	0.116
	1.5926	–0.2269		
	1.6193	–0.1516		
	1.5287	–0.4444		
η	2.5304	0.5714	0.0991	0.221
	2.3747	0.5552		
	3.3879	1.6171		
	4.4078	2.4347		
AC_{ESP}	1.2673	–0.6917	0.009	0.018
	2.0843	0.2647		
	2.1489	0.3781		
	3.0839	1.1108		

In run 259, GAP index show to have the main contribution in this equation, whereas the log P has a minor contribution.

For run 517, the C2-O1 bond showed to be the index with more weight in this run, although it gave a good R^2 value and furthermore, the higher F value. On the contrary, E_{HOMO} showed to be the parameter with less importance in this run. Regarding run 937, the partition coefficient (log P), quite the opposite to run 259, presented to be the parameters most important in this equation.

TABLE-10
EFFICIENCIES CALCULATED AND R^2 VALUES WHEN ONE PARAMETER IS ELIMINATED FOR RUN 517
log Eff = 2.66-2.53*C2-O1-0.13*E_{HOMO}+64.88*η-0.33*AC_{ESP} + 0.03*^{13}C

	log Eff_{calc}	log Eff_{calc} - log Eff_{exp}	R^2	F
C2-O1	5.4414	3.4824	0.9901	200.5433
	5.3003	3.4808		
	5.2769	3.5061		
	5.4597	3.4866		
E_{HOMO}	1.8666	–0.0925	0.999	0.0319
	1.7268	–0.0928		
	1.6837	–0.0871		
	1.8738	–0.0993		
η	1.7769	–0.1821	0.1946	0.4831
	1.6390	–0.1805		
	1.4297	–0.3411		
	1.4966	–0.4765		
AC_{ESP}	1.7644	–0.1946	0.4234	0.0223
	1.7667	–0.0528		
	1.7407	–0.0302		
	2.0469	0.0738		
^{13}C	–0.7222	1.2368	0.3019	0.8648
	–0.8651	0.9545		
	–0.7336	1.0372		
	–0.6929	1.2802		

In run 1063, excepting the energy of the frontier orbitals, the other parameters seemed to have the same importance in this equation.

Finally, in run 1214, again the log P was the parameter, which most affected the Eff_{calc} value. Therefore, the index, which has more weight in each equation, depends on the array of parameters that was taken into account.

Conclusion

Even though that the set of compounds is small, this piece of work is related to the statistical significant molecular indexes

TABLE-11
EFFICIENCIES CALCULATED AND R^2 VALUES WHEN ONE PARAMETER IS ELIMINATED FOR RUN 937
$\log \text{Eff.} = 2.46-48.89*E_{HOMO} + 1011.04*E_{LUMO} + 0.97*\text{DIP}-2.48*\log P + 1.36*AC_{ESP}-0.03*{}^{13}C$

	log Eff_{calc}	log Eff_{calc} - log Eff_{exp}	R^2	F
E_{HOMO}	1.5191	–0.4399	0.2797	0.7766
	1.3963	–0.4232		
	1.1807	–0.5901		
	–1.1648	–3.1379		
E_{LUMO}	0.4462	2.4053	0.116	0.2625
	0.0237	1.8433		
	–1.4669	0.3039		
	–4.7049	–2.7318		
DIP	–2.8153	–0.8562	0.0133	0.0269
	–3.9998	–2.1802		
	–0.2855	1.4853		
	–1.2168	0.7564		
log P	5.0956	3.1366	0.2842	0.7939
	6.9898	5.1702		
	5.1199	3.3490		
	12.3167	10.3435		
AC_{ESP}	2.0206	0.0615	0.0383	0.0797
	1.2955	–0.5240		
	1.1925	–0.5783		
	0.8697	–1.1035		
^{13}C	4.1878	2.2288	0.7974	7.8730
	4.0519	2.2318		
	3.8427	2.0718		
	4.1275	2.1543		

TABLE-12
EFFICIENCIES CALCULATED AND R^2 VALUES WHEN ONE PARAMETER IS ELIMINATED OF RUN 1063
$\log \text{Eff.} = -0.54-0.36*\text{N3-C2} + 33.23*E_{HOMO}-40.45*E_{LUMO} + 0.27*\text{DIP} + 0.38*\log P + 604.77*\eta-1.68*AC_{ESP}$

	log Eff_{calc}	log Eff_{calc} - log Eff_{exp}	R^2	F
N3-C2	2.4828	0.5237	0.9883	169.3855
	2.3437	0.5241		
	2.3077	0.5368		
	2.5209	0.5477		
E_{HOMO}	2.0029	0.0438	0.4137	1.4113
	1.85263	0.0331		
	1.9406	0.1698		
	3.8330	1.8599		
E_{LUMO}	1.9948	0.0358	0.6641	3.9539
	1.8672	0.0477		
	1.8905	0.1196		
	2.2358	0.2627		
DIP	0.7200	–1.2390	0.0035	0.0071
	0.2902	–1.5293		
	1.2988	–0.4721		
	1.2143	–0.7588		
log P	1.4129	–0.5461	0.1234	0.2816
	0.9624	–0.8572		
	1.2086	–0.5623		
	0.3362	–1.6369		
η	1.1111	–0.8479	0.0197	0.0401
	0.9903	–0.8293		
	–0.5989	–2.3698		
	–1.5979	–3.5709		
AC_{ESP}	1.4277	–0.53131	0.0197	0.0401
	2.0122	0.1927		
	2.0616	0.2907		
	2.8301	0.8569		

TABLE-13
EFFICIENCIES CALCULATED AND R^2 VALUES WHEN ONE PARAMETER IS ELIMINATED FOR RUN 1214
$\log \text{Eff.} = -0.78-0.17*\text{N3-C2} + 0.47*\text{C2-O1} + 43.43*E_{HOMO}-177.52*E_{LUMO}-0.009*\text{DIP} + 0.98*\log P + 449.04*\eta-2.05*AC_{ESP}$

	log Eff_{calc}	log Eff_{calc} - log Eff_{exp}	R^2	F
N3-C2	2.2094	0.2503	0.9995	4046.8569
	2.0719	0.2524		
	2.0199	0.2490		
	2.2286	0.2555		
C2-O1	1.2931	–0.6659	0.9993	3008.1824
	1.1559	–0.6636		
	1.1008	–0.6700		
	1.3109	–0.6622		
E_{HOMO}	2.0279	0.0689	0.4001	1.3341
	1.8758	0.0563		
	1.9849	0.2141		
	4.3904	2.4173		
E_{LUMO}	2.15956	0.2005	0.3075	0.8881
	2.0719	0.2523		
	2.2759	0.5051		
	3.0746	1.1014		
DIP	1.9981	0.0391	0.9783	89.9937
	1.8704	0.0509		
	1.7840	0.0132		
	2.0014	0.0283		
log P	0.5753	–1.3837	0.2067	0.5211
	–0.3656	–2.1852		
	0.3080	–1.4628		
	–2.2775	–4.2506		
η	1.3352	–0.6238	0.0128	0.0259
	1.2113	–0.6082		
	0.0057	–1.7651		
	–0.6848	–2.6579		
AC_{ESP}	1.3215	–0.6376	0.0119	0.0243
	2.0668	0.2473		
	2.1182	0.3473		
	3.0065	1.0333		

in order to determine and rationalize the structural and physicochemical features to obtain a certain activity of compounds type *bis*-(aminomethyl)ethers, which are employing in the oil industry. Thus, chemical reactivity descriptors, such as Fukui functions, local softness and $\Delta f(r)$ descriptors, calculating from NPA populational analysis, have shown to explain in good way the experimental behaviour of cyanides scavengers. Beside this, the reactivity of the electrophilic carbon atom (C2) can be modulated thought electronic and steric effects, which could permit to design new prototypes of cyanides scavengers with overcome performance. Finally, even only four compounds were considered in this work, the developed structure-activity study indicates that the eqn. 2, showing in Table-7, gives the best correlation for kind of compounds.

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REFERENCES

1. D. Brodel, R. Edwards, A. Hayman, D. Hill, S. Metha and T. Semerad, *Oilfield Rev.*, **35**, 4 (1994).

2. L.A.C.J. Garcia, C.J.B.M. Joia, E.M. Cardoso and O.R. Mattos, *Electrochim. Acta*, **46**, 3879 (2001).
3. D. Urban, S. Frisbie and S. Croce, *Environ. Prog.*, **16**, 171 (1997).
4. L.S. Zamudio-Rivera, A. Estrada-Martinez, A. Morales-Pacheco, J.L.R. Benitez-Aguilar, R. Roldan-Perez, J.L. Yañez-Ayuso, J. Marin-Cruz and M.G. Guzman-Pruneda, *Mex. Pat. Req.* 2002Pa/a/2002/006434.
5. F. Godinez-Salomon, J.M. Hallen-Lopez, H. Höpfl, A. Morales-Pachecho, H.I. Beltrán and L.S. Zamudio-Rivera, *Green Chem.*, **7**, 716 (2005).
6. K. Fukui, *Science*, **218**, 747 (1982).
7. R.G. Parr and W. Yang, *J. Am. Chem. Soc.*, **106**, 4049 (1984).
8. C. Morell, A. Grand and A. Toro-Labbé, *J. Phys. Chem. A*, **109**, 205 (2005).
9. F.B. Growcock, *Corrosion*, **45**, 1003 (1989).
10. F.B. Growcock and W.W. Freinier, *Corrosion*, **45**, 1007 (1989).
11. P.G. Abdul-Ahad and S.H.F. Al-Madfai, *Corrosion*, **45**, 978 (1989).
12. S.G. Zhang, W. Lei, M.Z. Xia and F.Y. Wang, *J. Mol. Struct. Theochem*, **732**, 173 (2005).
13. Hyper Chem Version 6.0, Hypercube Inc. Ontario, Canada.
14. M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, V.G. Zakrzewski, J.A. Montgomery Jr., R.E. Stratmann, J.C. Burant, S. Dapprich, J.M. Millam, A.D. Daniels, K.N. Kudin, M.C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G.A. Peterson, P.Y. Ayala, Q. Cui, K. Morokuma, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J. Cioslowski, J.V. Ortiz, A.G. Baboul, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, J.L. Andres, C. Gonzalez, M. Head-Gordon, E.S. Replogle and J.A. Pople, Gaussian 98, Revision A.9, Gaussian, Inc., Pittsburgh (1998).
15. A.D. Becke, *J. Chem. Phys.*, **98**, 5648 (1993).
16. P.J. Stephens, F.J. Devlin, C.F. Chabalowski and M.J. Frisch, *J. Phys. Chem.*, **98**, 11623 (1994).
17. S.H. Vosko, L. Wilk and M. Nusair, *Can. J. Phys.*, **58**, 1200 (1980).
18. J.A. Pople, H. Head-Gordon, D.J. Fox, K. Raghavachari and L.A. Curtiss, *J. Chem. Phys.*, **90**, 5622 (1989).
19. L.A. Curtiss, C. Jones, G.W. Trucks, K. Raghavachari and J.A. Pople, *J. Chem. Phys.*, **93**, 2537 (1990).
20. R. McWeeny, *Phys. Rev.*, **126**, 1028 (1962).
21. R. Ditchfield, *Mol. Phys.*, **27**, 789 (1974).
22. J.L. Dodds, R. McWeeny and A.J. Sadlej, *Mol. Phys.*, **41**, 1419 (1980).
23. K. Wolinski, J.F. Hilton and P. Pulay, *J. Am. Chem. Soc.*, **112**, 8251 (1990).
24. P. d'Antuono, E. Botek, B. Champagne, M. Spassova and P. Denkova, *J. Chem. Phys.*, **125**, 144309 (2006).
25. C.J. Jameson and A.K. Jameson, *Chem. Phys. Lett.*, **134**, 461 (1987).
26. D. Vikic-Topic and L. Pejov, *J. Chem. Inf. Comput. Sci.*, **41**, 1478 (2001).
27. B.H. Besler, K.M. Merz Jr. and P.A. Kollman, *J. Comp. Chem.*, **11**, 431 (1990).
28. U.C. Singh and P.A. Kollman, *J. Comp. Chem.*, **5**, 129 (1984).