

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/216247360>

Theoretical study of the proton affinities of 2-, 3-, and 4-monosubstituted pyridines in the gas phase by means of MINDO/3, MNDO, and AM1

ARTICLE *in* JOURNAL OF COMPUTATIONAL CHEMISTRY · JUNE 1989

Impact Factor: 3.59 · DOI: 10.1002/jcc.540100403

CITATIONS

30

READS

20

6 AUTHORS, INCLUDING:



[Jan M L Martin](#)

Weizmann Institute of Science

352 PUBLICATIONS 14,330 CITATIONS

[SEE PROFILE](#)



[Jan Yperman](#)

Hasselt University

239 PUBLICATIONS 1,797 CITATIONS

[SEE PROFILE](#)

Theoretical Study of the Proton Affinities of 2-, 3-, and 4-Monosubstituted Pyridines in the Gas Phase by Means of MINDO/3, MNDO, and AM1

R. Voets,* J.-P. François,[†] J. M. L. Martin, J. Mullens, J. Yperman, and L. C. Van Poucke
Limburgs Universitair Centrum, Departement SBM, Universitaire Campus, B-3610 Diepenbeek, Belgium

Received 31 March 1988; accepted 9 November 1988

Proton affinities (PAs) of 2-, 3-, and 4-monosubstituted pyridines in the gas phase are calculated using the MINDO/3, MNDO, and AM1 methods. The following substituents are considered: F, Cl, CN, CH₃, CF₃, CHO, NO₂, NH₂, N(CH₃)₂, OCH₃, and SCH₃. The results are compared with experimental values. It is found that all MINDO/3 PAs are ca. 6% too high (mean value) compared to the experimental results; on the other hand, the MNDO values are ca. 7% too low (mean value). However, a much better agreement has been observed for the AM1 method where the theoretical values are only ca. 2.4% too low (mean value). Correlations between the calculated proton affinities on one hand and the charges on the acid H atom and Hammett constants on the other hand are studied. Particularly good linear relationships are found for the 4-monosubstituted compounds within the AM1 formalism.

INTRODUCTION

The study of proton affinities (PA) has become in recent years a very vast and important research domain. The experimental methods by which the PA can be determined are: ion cyclotron resonance spectrometry (ICR),^{1–5} high-pressure mass spectrometry (HPMS),^{2,3,5,6} and the flow afterglow technique.^{2,3,5,7} Reviews have been published by Aue and Bowers,² by Bartmess and McIver, Jr.,^{8–10} and a general survey of the experimental studies concerning the acid-base behavior of compounds in the gas phase has been given by Moylan and Brauman.⁵ PAs in the gas phase can also be obtained using quantum mechanical methods, such as ab initio and semiempirical self-consistent field molecular orbital (SCF-MO) theories. A comprehensive bibliography of ab initio calculations of absolute and relative deprotonation enthalpies and proton affinities has been published by Dewar and Dieter.¹¹ Theo-

retical PA values for certain compounds were also obtained by means of the semiempirical MNDO^{12,13} and AM1¹⁴ methods.¹¹

In the present work, proton affinities of 2-, 3-, and 4-monosubstituted pyridines in the gas phase are studied using the MINDO/3,¹⁵ MNDO,¹² and AM1¹⁴ methods. The following substituents are considered: H, F, Cl, CN, CH₃, CF₃, CHO, NO₂, NH₂, N(CH₃)₂, OCH₃, and SCH₃. The results are evaluated by comparison with experimental values at 298.15 K. Before going into details, a brief summary of the existing experimental and theoretical studies on pyridine and on substituted pyridines is given.

Experimental Studies

A first experimental study (ICR spectrometry) concerning the influence of the substituent on the PA of substituted pyridines in the gas phase was published by Taagepera et al.¹⁶ For the 4-monosubstituted pyridines they found a linear relation between the proton affinities in the gas and liquid phases, which has been confirmed by CNDO/2 calculations. Aue et al.¹⁷ carried out a comparative study of the basicities in the gas phase and in solution for a series of 2-, 3-, and 4-

*Present address: Agfa N.V., Septestraat, B-2510 Mortsel (Belgium).

[†]Author to whom correspondence should be addressed.

monosubstituted pyridines. From the gas phase PAs and from thermodynamical data in aqueous solution they studied the solvent effects, which are for the 3- and 4-substituted pyridines similar. The 2-substituted compounds deviate due to sterical hindrance since the solvent is less easily positioned between the charged center and the substituent. Arnett et al.¹⁸ determined the relative solvation-enthalpy for a series of 3- and 4-substituted pyridinium ions. They showed that the main factor, determining the difference between the gas phase and aqueous basicity, is the influence of the substituent on the strength of the hydrogen bond between the pyridinium ion and water. A smaller contribution comes from the influence of the substituent on the hydrogen bond of the neutral pyridines, which can act as hydrogen-bond acceptors. Finally, they show, both experimentally and theoretically (ab initio, STO-3G), that the influence of the substituent on the hydrogen bond formation is about four times larger for the pyridinium ions than for the corresponding pyridines. Hopkins Jr. et al.¹⁹ investigated the relation between the gas phase basicities for 2-, 3-, and 4-substituted pyridines and the strength of the hydrogen bond for these compounds. They found for the 3- and 4-substituted pyridines a linear relation between the gas phase PAs and the Gibbs free energy change of the hydrogen-bond formation. This correlation is completely missing for the 2-substituted pyridines which is attributed by the authors to sterical hindrance.

Theoretical Studies

In the past, the pyridines have been investigated frequently by means of theoretical methods. The relative stability of monosubstituted pyridine tautomers²⁰⁻²⁴ and the hydrogen bond formation²⁵⁻²⁷ has been comprehensively studied among others. Besides, a number of papers have been published about the calculation of molecular properties (dipole moment, molecular geometry, ionization potential, . . .)²⁸⁻³⁰ and about reactions with substituted pyridines.³¹⁻³³ Only a limited number of publications deals with the determination of PAs in the gas phase.

Ab initio calculations (STO-3G and 4-31G basis) of the proton affinities for pyridine

and the diazines by Del Bene,³⁴ show that the STO-3G PAs are calculated much too high and that the 4-31G PAs are predicted ca. 10% too high. The results also show that the relative experimental sequence is only correctly predicted with the 4-31G basis and that, within a series of similar bases, an enhancement of the energy of the highest occupied molecular orbital (HOMO) correlates with an increase of the proton affinity. It finally appears from the structural data that the bonding between the proton and the proton-acceptor atom is a normal intramolecular covalent one.

Bodor and Pearlman³⁵ published a MINDO/3 study on the dihydropyridines. They found for seven isomers that the predicted relative stabilities, the proton affinities and the ionization potentials agreed well with experiment.

Catalan et al.³⁵ studied a number of 3- and 4-substituted pyridines (H, F, CH₃, CF₃, CN, NH₂, NO₂, OH, CCH) by means of ab initio calculations with a STO-3G basis. Their main findings are the existence of linear correlations between the 1s orbital energy of the nitrogen atom in the neutral compound and the energy of the HOMO on one hand and the experimental PAs on the other hand, and that there is no correlation between the charge on the nitrogen atom and the experimental proton affinity.

Taagepera et al.³⁷ analyzed the acid strength of 3- and 4-substituted pyridinium and anilinium ions in the gas phase and in aqueous solution by means of a substituent parameter approach and ab initio calculations (STO-3G basis). Their conclusions for the pyridinium ions are:

1. an increase of the acid strength is determined mainly by inductive effects and the influence of π -delocalization effects, especially in the gas phase, is less important;
2. strong π -donor (+R) substituents give rise, through the resonance effect, to a strong decrease of the acid strength;
3. the ratio of the resonance-effects in meta and para positions (R_m/R_p) is much greater in the gas phase than in aqueous solution;
4. the inductive effects correlate very well with the σ_i substituent parameters of Taft.³⁸

From a STO-3G ab initio study by Hehre et al.³⁹ it appears that for a large number of nitrogen and oxygen compounds there exists a linear relation between the PA and the charge on the proton.

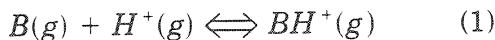
Finally, Fossey et al.⁴⁰ studied the protonation and alkylation of the 2-, 3-, and 4-aminopyridines by means of ab initio calculations (STO-3G basis). They found that the cyclic nitrogen atom is protonated rather than the nitrogen atom in the amino group.

In the present work, the PAs of the mono-substituted pyridines, stated above, are calculated using the MINDO/3, MNDO, and AM1 methods. In addition, a number of correlations are studied between the calculated PAs on one hand, and the experimental ones, charge densities and Hammett constants on the other hand.

DEFINITION OF PA, COMPUTATIONAL DETAILS, AND PROGRAMS

Proton affinity

The PA of a base B at the temperature T is defined as minus the enthalpy change of the reaction



$$PA(B) = -\Delta H_{T,\text{base}} \quad (2)$$

and can be computed by Eq. (3)

$$PA(B) = \Delta H_{f,T}^\circ(H^+, g) + \Delta H_{f,T}^\circ(B, g) - \Delta H_{f,T}^\circ(BH^+, g) \quad (3)$$

In eq. (3) $\Delta H_{f,T}^\circ$ represents the heat of formation of the species stated between parenthesis. The semiempirical quantum chemical MINDO/3, MNDO, and AM1 methods allow the calculation of the standard formation enthalpies $\Delta H_{f,298}^\circ$ so that by means of Eq. (3) the PA of a base B can be computed at 298.15 K. For $\Delta H_{f,298}^\circ(H^+, g)$ the experimental value of 367.2 kcal/mol is taken.⁴¹

Computational Details and Programs

The MINDO/3 and MNDO results were obtained using the corresponding standard methods, as implemented in an extended version of the GEOMO package.^{42,43} The geometries were optimized with respect to all geometrical variables, using a combination of Murtagh-Sargent's⁴⁴ and Davidon's cubic in-

terpolation methods.⁴⁵ The parameter EPS (minimum relative quadratic difference allowed for two consecutive values of atomic coordinates) was set equal to 1×10^{-9} . Hardwarewise, use was made of the CDC Cyber 170/825 computer at the Limburgs Universitair Centrum (LUC) under the NOS 2 operating system. A number of calculations was performed using the GEOMO package on the Cyber 205 vector processor (VSOS 2 operating system). A vectorized subroutine from the library QQLIB was introduced in the package for the computation of eigenvalues and eigenvectors. In this way, the calculations on the Cyber 205 were found to be a factor of 40 faster than on the Cyber 170/825.

All the AM1 calculations were conducted using MOPAC (Version 4.1)⁴⁶ running on the CDC Cyber 930 at the Limburgs Universitair Centrum (LUC) under the NOS/VE 1.2.3 operating system. The original VAX source code has been converted to CDC. This CDC version will be submitted to the Quantum Chemistry Program Exchange.⁴⁷ The standard values for the AM1 parameters indicated in the original VAX program were used throughout. For the elements F and Cl, the preliminary parameters included in the code were used. Geometries were optimized in Cartesian coordinates using the Broyden-Fletcher-Goldfarb-Shanno method.⁴⁸ The keyword PRECISE was used, increasing the criteria for terminating all optimizations, electronic and geometric, by the factor 100.

RESULTS AND DISCUSSION

Most Stable Structures of the Substituted Pyridines and Pyridinium Ions

The conformations of the substituted pyridines and of their corresponding ions, which have to be considered for calculating the PA, are presented in Figure 1 and their molecular energies are listed in Tables I and II. The conformations have been identified with reference numbers in which the substitution position is indicated by the prefixes α , β , and γ , standing respectively for the 2-, 3-, and 4-position. A complete discussion of all the conformations, their molecular structures and properties, such as dipole moment and ionization potential, will be presented elsewhere.⁴⁹

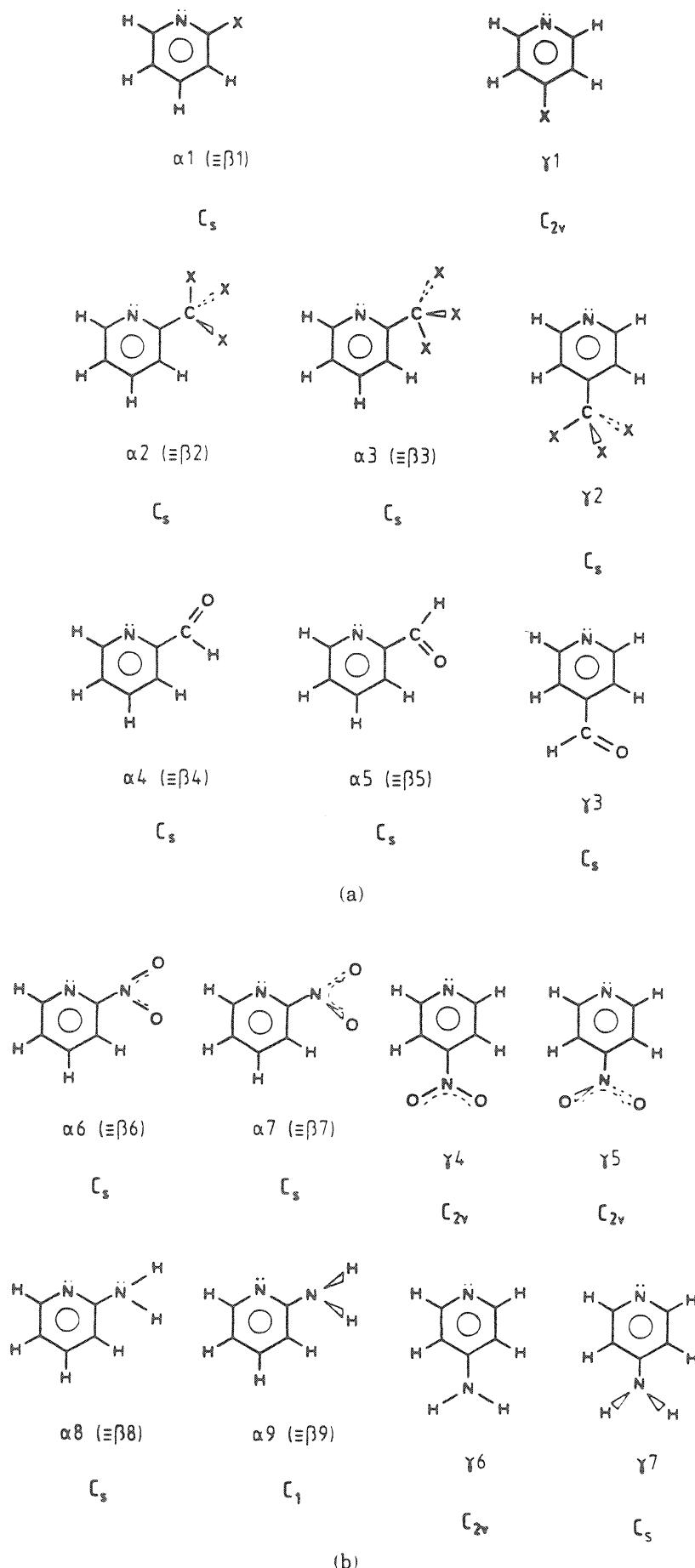


Figure 1. Conformations of the substituted pyridines and of their corresponding ions.

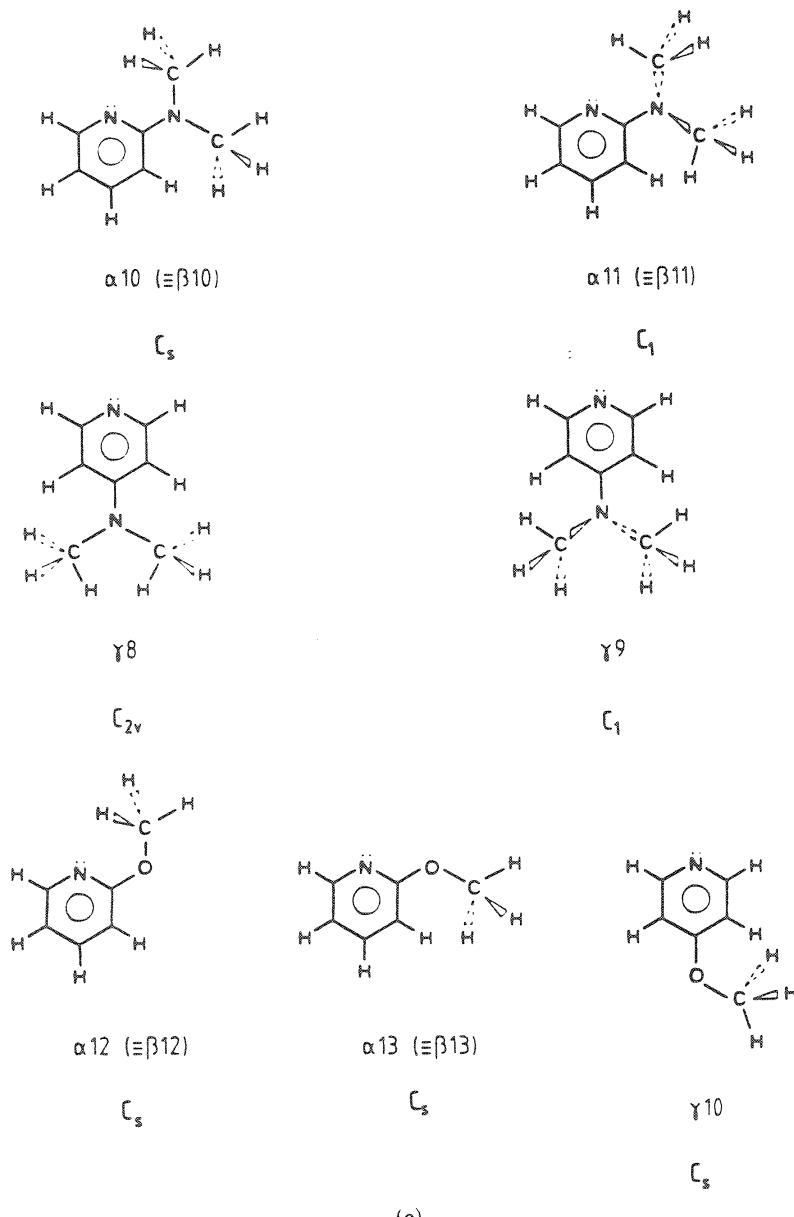


Figure 1. (continued)

PAs of the Substituted Pyridines

When the most stable conformations of the pyridines and pyridinium ions are known, the proton affinity can be computed by means of Eq. (3). For certain substituents (NO_2 , NH_2 , $\text{N}(\text{CH}_3)_2$) however, a number of stable conformations has been found which could not a priori be excluded despite the fact that they possess clearly a higher energy. For instance, MINDO/3 and MNDO find for the nitropyridines and related ions a global energy minimum corresponding to a conformation where the NO_2 group is turned out of the plane of the pyridine ring,⁵⁰ while a planar structure could be expected analogous

to nitrophenol.⁵¹ For the substituted nitropyridines, planar conformations are found as the most stable ones in the AM1 approximation; for the amino and dimethylamino pyridines nonplanar conformations are predicted to be most stable. In order to achieve completeness, the PAs for the planar as well as for the nonplanar conformations are given in Table III. This table contains also experimental PAs that have been determined mainly with ICR spectrometry. It must be remarked here that in the literature no clear information is given concerning the accuracy of the experimental values. Figures 2-4 compare in a systematic way the results obtained for respectively the 2-, 3-, and 4-

Table I. Molecular energy (eV) of different conformations of the monosubstituted pyridines.^a

Compound	Type	MINDO/3	Type	MNDO	Type	AM1
C ₅ H ₅ N	α1	-899.158	α1	-916.621	α1	-915.328
2-FC ₅ H ₄ N	α1	-1362.915	α1	-1382.089	α1	-1386.545
3-FC ₅ H ₄ N	β1	-1362.367	β1	-1381.942	β1	-1386.716
4-FC ₅ H ₄ N	γ1	-1362.487	γ1	-1381.967	γ1	-1386.734
2-ClC ₅ H ₄ N	—	—	α1	-1257.189	α1	-1275.377
3-ClC ₅ H ₄ N	—	—	β1	-1257.160	β1	-1275.421
4-ClC ₅ H ₄ N	—	—	γ1	-1257.149	γ1	-1275.419
2-CNC ₅ H ₄ N	α1	-1203.133	α1	-1236.494	α1	-1235.649
3-CNC ₅ H ₄ N	β1	-1202.842	β1	-1236.519	β1	-1235.823
4-CNC ₅ H ₄ N	γ1	-1202.791	γ1	-1236.468	γ1	-1235.783
2-MeC ₅ H ₄ N	α2	-1056.073	α2	-1073.259	α3	-1071.143
	α3	-1056.065	α3	-1073.254	α2	-1071.141
3-MeC ₅ H ₄ N	β2	-1055.869	β3	-1073.227	β3	-1071.2105
	β3	-1055.868	β2	-1073.226	β2	-1071.2104
4-MeC ₅ H ₄ N	γ2	-1055.843	γ2	-1073.210	γ2	-1071.207
2-CHOC ₅ H ₄ N	α4	-1337.417	α5	-1366.369	α5	-1363.471
	α5	-1337.357	α4	-1366.313	α4	-1363.389
3-CHOC ₅ H ₄ N	β4	-1337.206	β5	-1366.353	β5	-1363.576
	β5	-1337.192	β4	-1366.346	β4	-1363.568
4-CHOC ₅ H ₄ N	γ3	-1337.086	γ3	-1366.283	γ3	-1363.517
2-NO ₂ C ₅ H ₄ N	α7	-1697.387	α7	-1750.228	α6	-1745.882
	α6	-1697.260	α6	-1750.108	α7	-1745.863
3-NO ₂ C ₅ H ₄ N	β7	-1697.060	β7	-1750.151	β6	-1746.146
	β6	-1696.935	β6	-1750.098	β7	-1745.985
4-NO ₂ C ₅ H ₄ N	γ5	-1696.979	γ5	-1750.108	γ4	-1746.087
	γ4	-1696.782	γ4	-1750.022	—	—
2-NH ₂ C ₅ H ₄ N	α8	-1107.225	α9	-1138.389	α9	-1136.251
	α9	-1107.149	α8	-1138.255	—	—
3-NH ₂ C ₅ H ₄ N	β8	-1106.761	β9	-1138.237	β9	-1136.377
	β9	-1106.729	β8	-1138.047	—	—
4-NH ₂ C ₅ H ₄ N	γ6	-1106.879	γ7	-1138.279	γ7	-1136.420
	γ7	-1106.807	γ6	-1138.140	—	—
2-NMe ₂ C ₅ H ₄ N	α11	-1418.731	α11	-1450.565	α10'	-1446.892
	α10	-1418.696	α10	-1450.487	α10''	-1446.884
3-NMe ₂ C ₅ H ₄ N	β10	-1418.260	β11	-1450.431	β10'	-1447.012
	β11	-1418.174	β10	-1450.229	β11	-1446.942
4-NMe ₂ C ₅ H ₄ N	γ9	-1418.270	γ9	-1450.426	γ8'	-1447.050
	γ8	-1418.241	γ8	-1450.309	γ9	-1446.932
2-MeOC ₅ H ₄ N	α12	-1367.672	α12	-1395.285	α12	-1391.184
	α13	-1367.617	α13	-1395.083	α13	-1390.961
3-MeOC ₅ H ₄ N	β13	-1367.288	β13	-1394.999	β12	-1391.17397
	β12	-1367.264	β12	-1394.994	β13	-1391.17390
4-MeOC ₅ H ₄ N	γ10	-1367.395	γ10	-1395.053	γ10	-1391.220
2-MeSC ₅ H ₄ N	—	—	α12	-1311.519	—	—
	—	—	—	-1302.159 ^b	—	—
	—	—	α13	-1311.341	—	—
3-MeSC ₅ H ₄ N	—	—	—	-1301.988 ^b	—	—
	—	—	β12	-1311.345	—	—
	—	—	—	-1301.9894 ^b	—	—
	—	—	β13	-1311.343	—	—
	—	—	—	-1301.9892 ^b	—	—
4-MeSC ₅ H ₄ N	—	—	γ10	-1311.349	—	—
	—	—	—	-1301.985 ^b	—	—
2-CF ₃ C ₅ H ₄ N	α3	-2446.593	α3	-2469.412	α3	-2485.928
	α2	-2446.592	α2	-2469.407	α2	-2485.889
3-CF ₃ C ₅ H ₄ N	β2	-2446.432	β2	-2469.347	β2	-2485.968
4-CF ₃ C ₅ H ₄ N	γ2	-2446.296	γ2	-2469.281	γ2	-2485.930

^aα10', α10'', β10', and γ8' are nonplanar conformations.^bComputed with the new set of S parameters published in: M. J. S. Dewar, C. H. Reynolds, J. Comp. Chem., 7, 140 (1986).

Table II. Molecular energy (eV) of different conformations of the monosubstituted pyridinium ions.

Compound	Type	MINDO/3	Type	MNDO	Type	AM1
C ₅ H ₆ N ⁺	α1	-908.156	α1	-923.888	α1	-922.387
2-FC ₅ H ₅ N ⁺	α1	-1371.561	α1	-1389.008	α1	-1393.408
3-FC ₅ H ₅ N ⁺	β1	-1370.994	β1	-1388.857	β1	-1393.479
4-FC ₅ H ₅ N ⁺	γ1	-1371.189	γ1	-1388.996	γ1	-1393.615
2-CIC ₅ H ₅ N ⁺	—	—	α1	-1264.159	α1	-1282.290
3-CIC ₅ H ₅ N ⁺	—	—	β1	-1264.156	β1	-1282.285
4-CIC ₅ H ₅ N ⁺	—	—	γ1	-1264.182	γ1	-1282.350
2-CNC ₅ H ₅ N ⁺	α1	-1212.079	α1	-1243.357	α1	-1242.349
3-CNC ₅ H ₅ N ⁺	β1	-1211.762	β1	-1243.405	β1	-1242.487
4-CNC ₅ H ₅ N ⁺	γ1	-1211.767	γ1	-1243.388	γ1	-1242.486
2-MeC ₅ H ₅ N ⁺	α2	-1065.192	α3	-1080.565	α2	-1078.3704
	α3	-1065.183	α2	-1080.564	α2	-1078.3695
3-MeC ₅ H ₅ N ⁺	β2	-1064.927	β2	-1080.515	β2	-1078.342
	β3	-1064.923	β3	-1080.513	β3	-1078.338
4-MeC ₅ H ₅ N ⁺	γ2	-1064.958	γ2	-1080.535	γ2	-1078.394
2-CHOC ₅ H ₅ N ⁺	α4	-1346.120	α4	-1373.387	α4	-1370.405
	α5	-1346.041	α5	-1373.287	α5	-1370.255
3-CHOC ₅ H ₅ N ⁺	β4	-1345.907	β4	-1373.381	β4	-1370.402
	β5	-1345.874	β5	-1373.347	β5	-1370.355
4-CHOC ₅ H ₅ N ⁺	γ3	-1345.816	γ3	-1373.302	γ3	-1370.329
2-NO ₂ C ₅ H ₅ N ⁺	α7	-1705.494	α7	-1756.549	α6	-1752.320
	α6	-1705.366	α6	-1756.504	α7	-1752.149
3-NO ₂ C ₅ H ₅ N ⁺	β7	-1705.371	β7	-1756.689	β6	-1752.485
	β6	-1705.244	β6	-1756.626	—	—
4-NO ₂ C ₅ H ₅ N ⁺	γ5	-1705.356	γ5	-1756.656	γ4	-1752.438
	γ4	-1705.153	γ4	-1756.549	—	—
2-NH ₂ C ₅ H ₅ N ⁺	α8	-1116.460	α8	-1145.772	α8	-1143.640
	α9	-1116.305	α9	—	—	—
3-NH ₂ C ₅ H ₅ N ⁺	β8	-1115.998	β9	-1145.567	β8	-1143.630
	β9	-1115.895	β8	-1145.538	—	—
4-NH ₂ C ₅ H ₅ N ⁺	γ6	-1116.356	γ6	-1145.935	γ6	-1144.003
	γ7	-1116.157	γ7	—	—	—
2-NMe ₂ C ₅ H ₅ N ⁺	α11	-1427.941	α11	-1458.033	α10	-1454.442
	α10	-1427.936	α10	-1458.013	—	—
3-NMe ₂ C ₅ H ₅ N ⁺	β10	-1427.416	β11	-1457.785	β10	-1454.377
	β11	-1427.354	β10	-1457.757	—	—
4-NMe ₂ C ₅ H ₅ N ⁺	γ8	-1427.738	γ9	-1458.143	γ8	-1454.754
	γ9	-1427.419	γ8	-1458.143	—	—
2-MeOC ₅ H ₅ N ⁺	α12	-1376.758	α13	-1402.607	α13	-1398.339
	α13	-1376.732	α12	-1402.442	α12	-1398.293
3-MeOC ₅ H ₅ N ⁺	β12	-1376.352	β13	-1402.306	β13	-1398.268
	β13	-1376.349	β12	-1402.269	β10	-1398.242
4-MeOC ₅ H ₅ N ⁺	γ10	-1376.640	γ10	-1402.559	γ10	-1398.489
2-MeSC ₅ H ₅ N ⁺	—	—	α13	-1318.697	—	—
	—	—	—	-1309.333 ^a	—	—
3-MeSC ₅ H ₅ N ⁺	—	—	α12	-1318.586	—	—
	—	—	—	-1309.225 ^a	—	—
4-MeSC ₅ H ₅ N ⁺	—	—	β13	-1318.603	—	—
	—	—	—	-1309.249 ^a	—	—
2-CF ₃ C ₅ H ₅ N ⁺	α2	-2455.411	α3	-2475.941	α3	-2492.499
	α3	-2455.214	α2	-2475.934	α2	-2492.484
3-CF ₃ C ₅ H ₅ N ⁺	β2	-2455.247	β2	-2476.042	β2	-2492.548
4-CF ₃ C ₅ H ₅ N ⁺	γ2	-2455.068	γ2	-2475.963	γ2	-2492.507

^aComputed with the new set of S parameters published in: M. J. S. Dewar, C. H. Reynolds, *J. Comp. Chem.*, 7, 140 (1986).

substituted pyridines. The dotted lines represent PAs of conformations which will not be used in the following discussion. The division of the schemes according to the substi-

tution position is not only based on practical grounds but is also useful—as it will appear later—for the investigation of correlations between certain computed physical quantities.

Table III. Computed and experimental proton affinities of the substituted pyridines (kcal/mol).

Compound	MINDO/3	MNDO	AM1	Experimental ^a
C ₅ H ₅ N	234.2	208.1	215.1	220.4; 218.1 ^{b,d,e} ; 217.4 ^c
2-FC ₅ H ₄ N	226.1	200.1	210.5	211.8; 208.8 ^c ; 208.4 ^e
3-FC ₅ H ₄ N	225.7	200.0	208.3	214.8; 211.5 ^e
4-FC ₅ H ₄ N	227.4	202.6	211.0	216.9; 214.2 ^e
2-CIC ₅ H ₄ N	—	201.3	211.7	214.8; 211.8 ^{c,e}
3-CIC ₅ H ₄ N	—	201.9	210.6	215.7; 212.3 ^{b,e} ; 212.7 ^c
4-CIC ₅ H ₄ N	—	202.7	212.1	217.8; 215.0 ^{b,e}
2-CNC ₅ H ₄ N	233.0	198.8	206.8	208.9; 205.9 ^c ; 205.6 ^e
3-CNC ₅ H ₄ N	232.4	199.3	206.0	209.5; 206.8 ^{b,e} ; 206.5 ^c
4-CNC ₅ H ₄ N	233.7	200.1	206.8	210.6; 207.6 ^b
2-MeC ₅ H ₄ N	237.0	209.0	218.9	223.7; 221.6 ^b ; 220.7 ^c
3-MeC ₅ H ₄ N	235.6	208.6	216.7	222.8; 220.8 ^{b,e} ; 219.8 ^c
4-MeC ₅ H ₄ N	236.9	209.4	218.0	223.7; 222.1 ^b ; 220.6 ^c ; 223.1 ± 2.0 ^d
2-CHOC ₅ H ₄ N	227.4	202.4	212.2	—
3-CHOC ₅ H ₄ N	227.4	202.6	209.7	—
4-CHOC ₅ H ₄ N	228.0	202.4	209.4	215.2
2-NO ₂ C ₅ H ₄ N p	213.7	188.0	200.7	—
3-NO ₂ C ₅ H ₄ N p	218.4	191.1	198.5	—
4-NO ₂ C ₅ H ₄ N p	219.8	191.1	198.7	209.5; 201.1 ± 2.0 ^d ; 206.2 ^e
2-NO ₂ C ₅ H ₄ N np	213.7	186.3	—	—
3-NO ₂ C ₅ H ₄ N np	218.4	191.3	—	—
4-NO ₂ C ₅ H ₄ N np	219.9	191.5	—	209.5; 201.1 ± 2.0 ^d ; 206.2 ^e
2-NH ₂ C ₅ H ₄ N p	239.7	213.9	—	223.8; 220.8 ^c
3-NH ₂ C ₅ H ₄ N p	239.7	213.3	—	221.0
4-NH ₂ C ₅ H ₄ N p	245.3	220.3	—	229.0
2-NH ₂ C ₅ H ₄ N np	237.9	210.8	222.7	223.8; 220.8 ^c
3-NH ₂ C ₅ H ₄ N np	238.1	209.6	219.5	221.0
4-NH ₂ C ₅ H ₄ N np	242.3	217.1	227.1	229.0
2-NMe ₂ C ₅ H ₄ N p	239.8	214.1	—	229.2; 226.3 ^c
3-NMe ₂ C ₅ H ₄ N p	239.8	214.1	—	229.9
4-NMe ₂ C ₅ H ₄ N p	245.7	221.2	—	235.7; 232.7 ^b ; 232.7 ^c
2-NMe ₂ C ₅ H ₄ N np	239.1	212.8	226.4	229.2; 226.3 ^c
3-NMe ₂ C ₅ H ₄ N np	237.9	210.1	222.1	229.9
4-NMe ₂ C ₅ H ₄ N np	245.1	218.5	229.9	235.7; 232.7 ^b ; 232.7 ^c
2-MeOC ₅ H ₄ N	236.3	209.4	217.3	221.3; 218.3 ^c ; 219.2 ^e
3-MeOC ₅ H ₄ N	235.7	209.0	215.9	222.5; 221.1 ^e
4-MeOC ₅ H ₄ N	239.9	213.6	219.9	226.6; 224.8 ^b ; 226.1 ± 2.0 ^d
2-MeSC ₅ H ₄ N	—	206.1	—	222.0
		206.0 ^f		
3-MeSC ₅ H ₄ N	—	207.9	—	—
		207.9 ^f		
4-MeSC ₅ H ₄ N	—	210.0	—	225.5
		210.6 ^f		
2-CF ₃ C ₅ H ₄ N	230.7	191.1	203.8	211.8; 209.0 ^e
3-CF ₃ C ₅ H ₄ N	230.7	194.9	204.0	212.8; 210.0 ^{b,e}
4-CF ₃ C ₅ H ₄ N	229.7	194.6	204.0	213.0; 210.3 ^{b,e} ; 207.1 ± 2.0 ^d

^aD. H. Aue and M. T. Bowers, Stabilities of positive ions from equilibrium gas-phase basicity measurements, Chapter 9 in *Gas Phase Ion Chemistry*, Vol. 2: M. T. Bowers, Ed., Academic Press, New York (1979).

^bE. M. Arnett, B. Chawla, L. Bell, M. Taagepera, W. J. Hehre, R. W. Taft, *J. Am. Chem. Soc.*, **99**, 5279 (1977).

^cH. P. Hopkins, Jr., C. J. Alexander, and S. Zakir Ali, *J. Phys. Chem.*, **82**, 1268 (1978).

^dM. Taagepera, W. G. Henderson, R. T. C. Brownlee, J. L. Beauchamp, D. Holtz, and R. W. Taft, *J. Am. Chem. Soc.*, **94**, 1369 (1972).

^eP. Kebarle, *Ann. Rev. Phys. Chem.*, **28**, 445 (1977).

^fComputed with the new set of S parameters published in: M. J. S. Dewar, C. H. Reynolds, *J. Comp. Chem.*, **7**, 140 (1986).

From Table III and from Figures 2–4 it immediately appears that all MINDO/3 values are ca. 6% too high (mean value) compared to the experimental values in reference a; on the other hand, the PAs computed with the MNDO method are ca. 7% too low (mean

value). However, the AM1 results are in much better agreement with the experimental values since they are only about 2.4% too low (mean value). 4-nitropyridine shows the largest percentual error (−5.2%). The MINDO/3 approximation gives strikingly

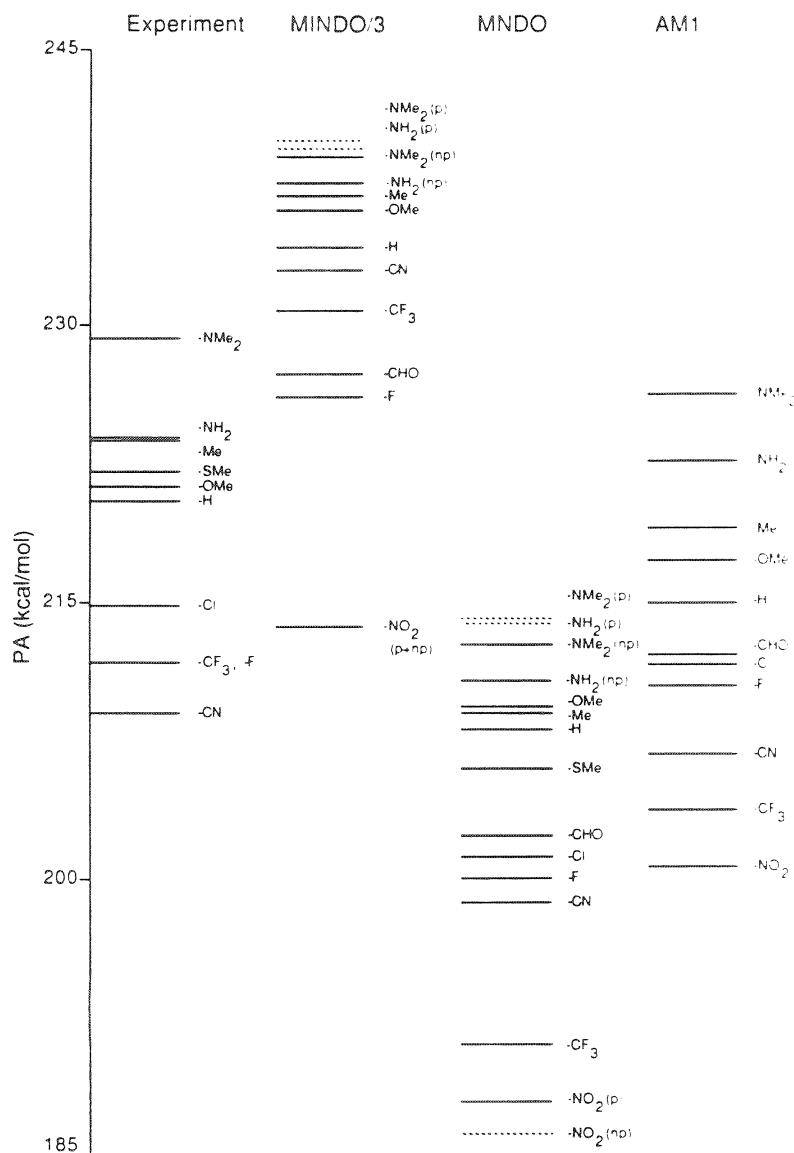


Figure 2. Comparison of the experimental and theoretical PAs of the 2-substituted pyridines (*p* stands for planar, *np* for nonplanar).

bad results for the CN and CF₃ substituents with percentual errors of respectively ca. 11% and ca. 8.5%. These compounds, which clearly appear to be outliers in the MINDO/3 method, will not be considered in the following discussion concerning the MINDO/3 results. In Figures 5(a) and 5(b) all computed PAs are plotted against the experimental ones (Table III, reference a). These figures show clearly that the best correlation is obtained for the AM1 results (MINDO/3: slope $a = 0.633$, correlation coefficient $R = 0.82$; MNDO $a = 0.937$, $R = 0.92$; AM1 $a = 1.045$, $R = 0.95$). From the correlation study between the computed and experimental PAs it appears that the CF₃ substituent influences the MNDO corre-

lation in an unfavorable way; it must be remarked that this substituent shows the largest percentual error (ca. 9%) in the MNDO approximation. From Figure 6 it appears that the correlation becomes somewhat better when the CF₃ compounds are neglected: the slope becomes 0.842 and the correlation coefficient improves to 0.94. This suggests us to consider the MNDO results for the CF₃ substituted pyridines as outliers and neglect them during the further discussion of the MNDO results. Figure 6 shows clearly that when the CN and CF₃ compounds are eliminated, the MINDO/3 correlation becomes markedly better; indeed, the slope becomes 0.916 and the correlation coefficient improves to 0.94. Figures 5(b)

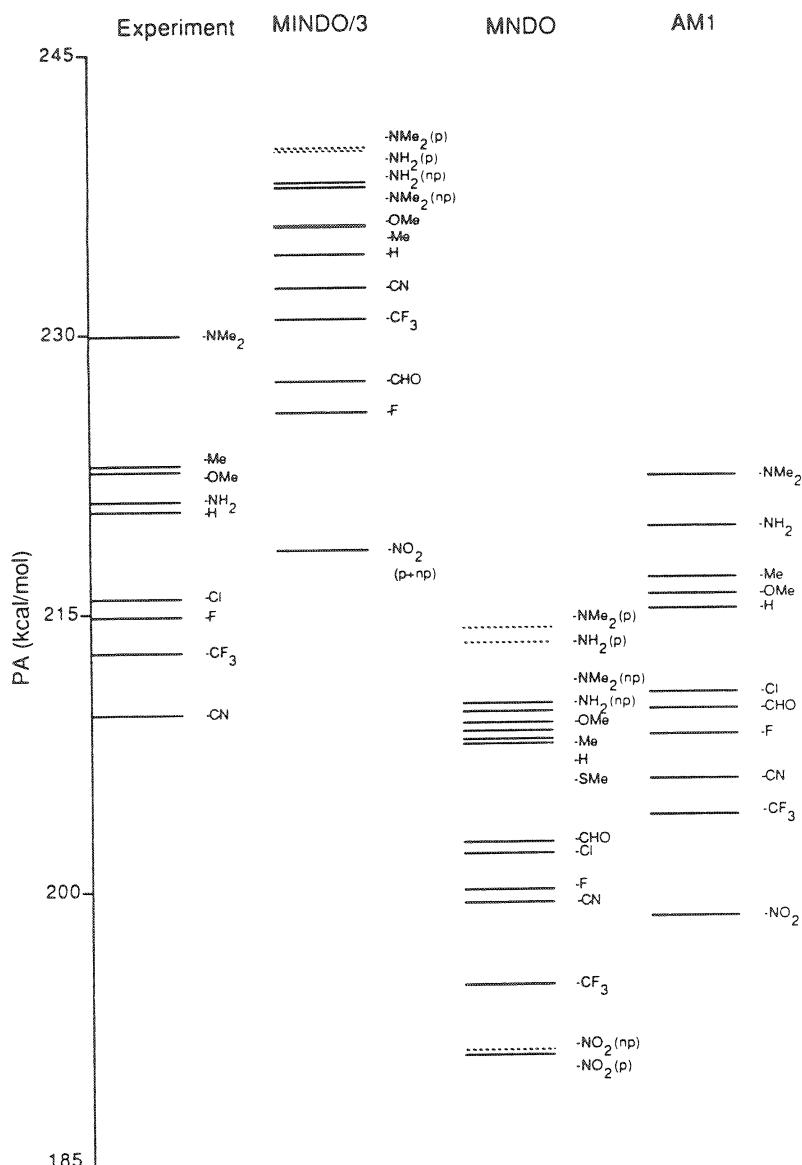


Figure 3. Comparison of the experimental and theoretical PAs of the 3-substituted pyridines (*p* stands for planar, *np* for nonplanar).

and 6 reveal that the MNDO and AM1 methods predict a strikingly low PA for 4-nitropyridine.

If the PAs of the 2-, 3- and 4-substituted pyridines are considered separately, it clearly appears from Figures 7(a), (b), and (c) that the correlations for the 2- and 4-substituted compounds are much better than for the 3-substituted ones and that this trend is most pronounced in the MINDO/3 approximation. This fact is confirmed when it is examined to what extent both methods reproduce the experimental sequence of the PAs. From Figure 2 it appears that the experimental sequence of the 2-substituted pyridines CN < CF₃ < F < Cl < H < OCH₃ < SCH₃ < CH₃ < NH₂ < N(CH₃)₂ is predicted

correctly by MINDO/3 if the substituents CN and CF₃ are omitted, as pointed out previously. With the exception of CF₃ (too low), the experimental sequence is also correctly predicted by AM1. On the other hand, the MNDO calculations give, omitting the CF₃ substituent, the sequence CN < F < Cl < SCH₃ < H < CH₃ < OCH₃ < NH₂ < N(CH₃)₂, which deviates from the experimental one because the PAs of the SCH₃ and CH₃ substituted pyridines are underestimated. The experimental sequence of the 3-substituted compounds (Fig. 3) CN < CF₃ < F < Cl < H < NH₂ < OCH₃ < CH₃ < N(CH₃)₂ is reproduced least satisfactorily. According to the MINDO/3 method, the sequence F < H < CH₃ < OCH₃ <

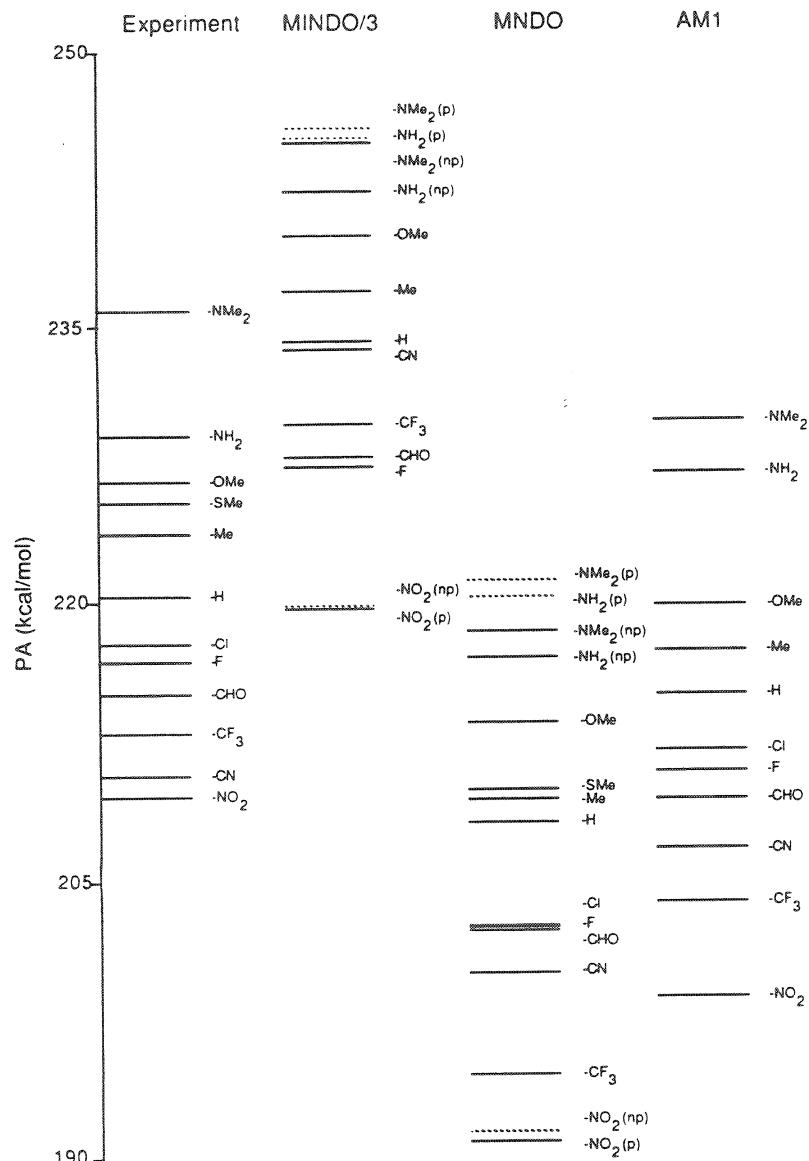


Figure 4. Comparison of the experimental and theoretical PAs of the 4-substituted pyridines (*p* stands for planar, *np* for nonplanar).

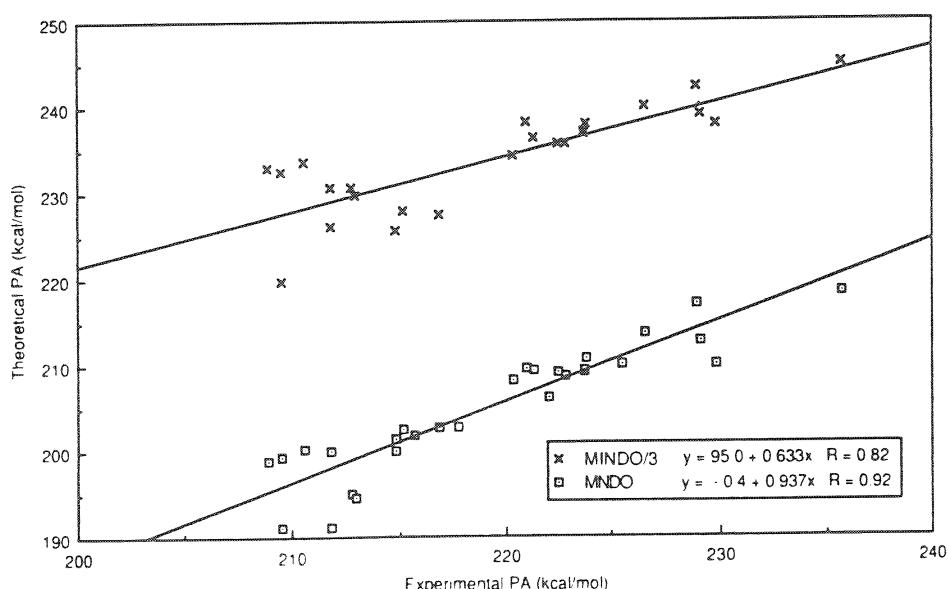


Figure 5(a). Relation between the computed (MINDO/3, MNDO) and experimental PAs of the substituted pyridines.

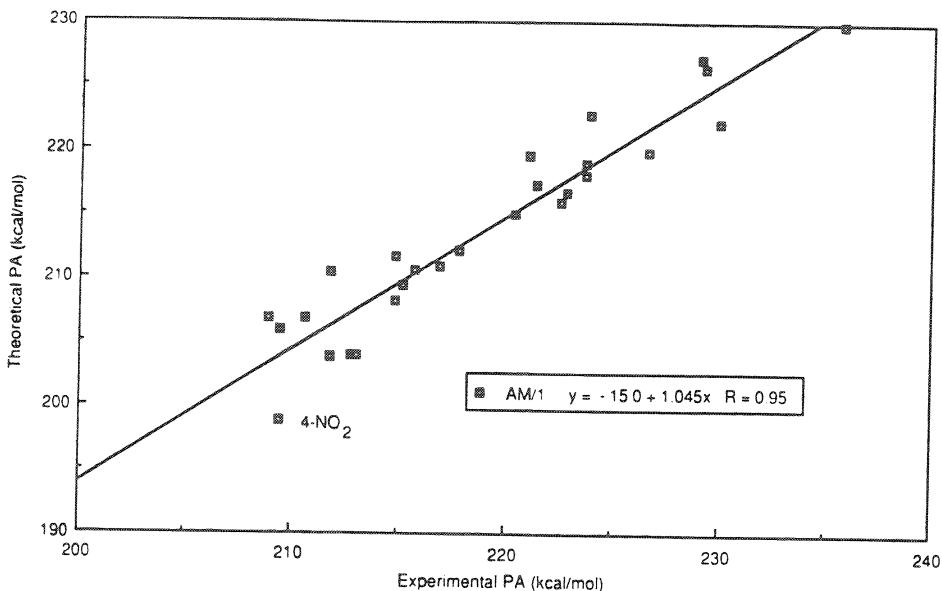


Figure 5(b). Relation between the computed (AM1) and experimental PAs of the substituted pyridines.

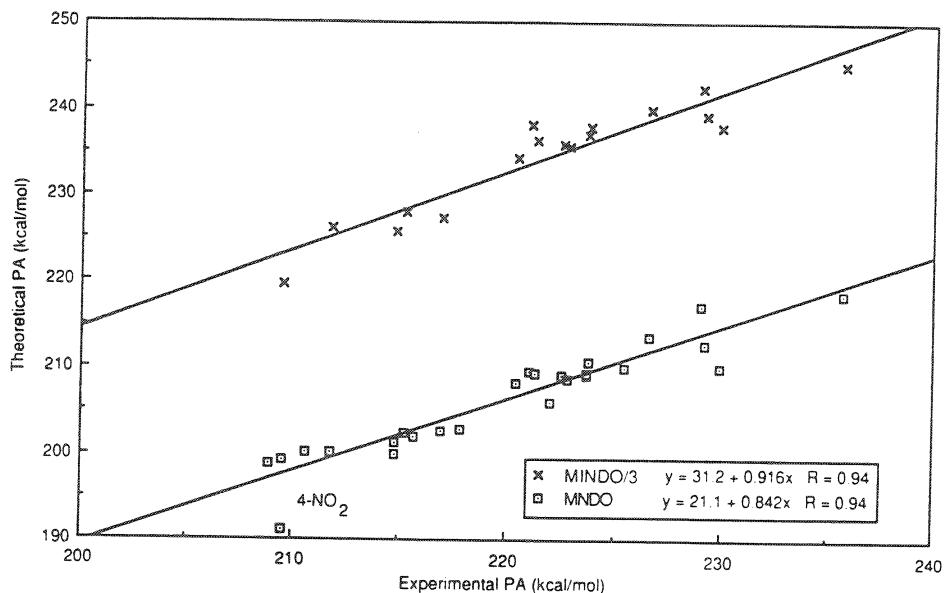


Figure 6. Relation between the computed and experimental PAs of the substituted pyridines when the CF₃(MINDO/3, MNDO) and CN(MINDO/3) compounds are deleted.

NH₂ < N(CH₃)₂ is found, where the PA for NH₂ is computed clearly too high and OCH₃ and CH₃, lying experimentally very close together, are mutually reversed. The MNDO approximation classifies the 3-substituted pyridines as follows: CN < F < Cl < H < CH₃ < OCH₃ < NH₂ < N(CH₃)₂. Compared to the MINDO/3 sequence, NH₂ and N(CH₃)₂ are reversed here. Very striking is the fact that, especially for the 3-substituted pyridines, the PA of CN is overestimated and that of N(CH₃)₂ clearly underestimated by

the MNDO method. The AM1 sequence NO₂ < CF₃ < CN < F < CHO < Cl < H < OCH₃ < CH₃ < NH₂ < N(CH₃)₂ corresponds to the experimental one, except that CN and CF₃ are reversed and that NH₂ is predicted relatively too high.

The experimental sequence of the 4-substituted compounds (Fig. 4), for which more experimental data are available, is most satisfactorily predicted. The experimental trend NO₂ < CN < CF₃ < CHO < F < Cl < H < CH₃ < SCH₃ < OCH₃ < NH₂ <

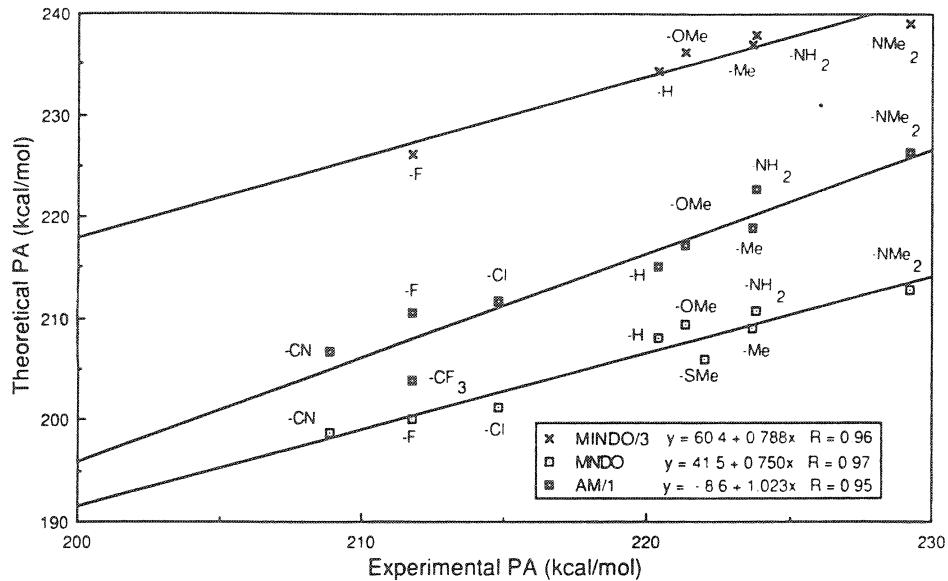


Figure 7(a). Relation between the computed (MINDO/3, MNDO, AM1) and experimental PAs of the 2-substituted pyridines.

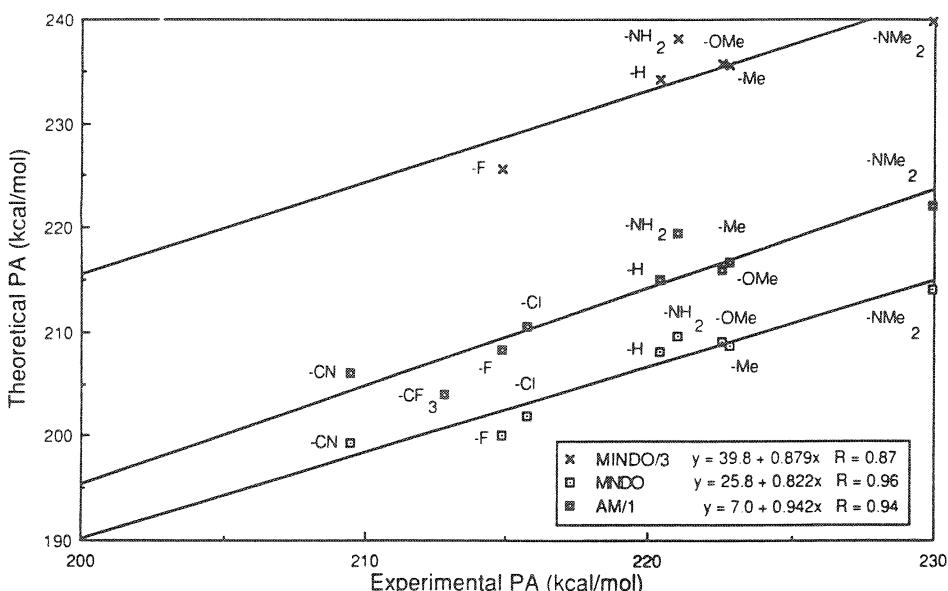


Figure 7(b). Relation between the computed (MINDO/3, MNDO, AM1) and experimental PAs of the 3-substituted pyridines.

$\text{N}(\text{CH}_3)_2$ corresponds completely with the MNDO and AM1 predictions, with the exception of an inversion between CF_3 and CN, and is also confirmed, with the exception of an inversion between F and CHO, by the MINDO/3 calculations.

The experimental results show that the PAs of all 2-substituted pyridines are lower than those of the corresponding 4-substituted compounds (except for the methylpyridines where they are equal). This trend—with the exception of CH_3 —is reproduced for all substituents in the MNDO and AM1 methods

and for all noneliminated substituents in the MINDO/3 approximation.

From the experiment it also appears that the PAs of the 3-substituted compounds, being generally close to the 2-values, are lower than the 4-ones, which is confirmed by the three approximations. An exception is the CF_3 substituent, where MINDO/3 and MNDO, as well as AM1, predict a higher value for the 3- CF_3 compound.

Due to the fact that the experimental PAs of the 2- and 3-substituted pyridines are close together, the mutual experimental se-

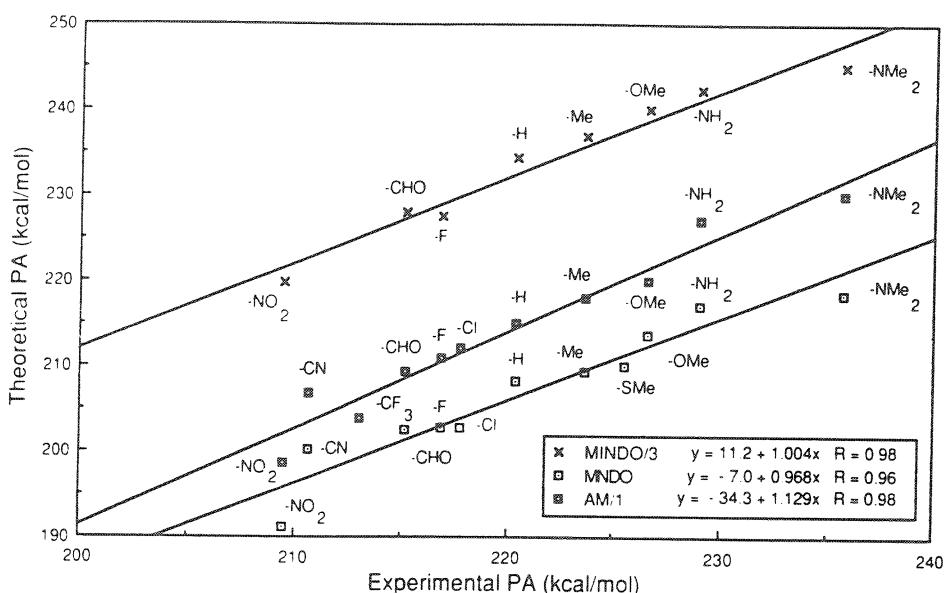


Figure 7(c). Relation between the computed (MINDO/3, MNDO, AM1) and experimental PAs of the 4-substituted pyridines.

quence is much less well predicted. The experimental sequence is reproduced for the substituents Cl, CN, CH₃, NH₂, and CF₃ by the MNDO approximation, and for CH₃, NH₂, and CF₃ by the AM1 method; however, the MINDO/3 method is only successful for CH₃.

Relation Between the Computed Charge Densities and the Proton Affinities

Many phenomena in the organic chemistry are described as a function of the electron attracting or donating properties of the substituents, which include inductive effects besides resonance interactions. For this reason, Reynolds et al.⁵² investigated the influence of the substituent on the atomic charges, obtained by ab initio calculations with a minimal STO-3G basis, and on the corresponding energies of proton transfer reactions for a series of substituted methylamines, ethylamines, anilinium and pyridinium ions. They found for all the compounds, mentioned above, a linear relationship between the energy of the proton transfer reaction and the corresponding charge difference. This charge difference, computed with Mulliken's population analysis,⁵³ is the difference between the charges of the acid proton on the substituted and on the non-substituted ion.

Application on a series of 4-substituted benzoic acids also gives linear relationships

between the proton transfer energy on one hand and the charges on the acid H atom, the OH group and the O⁻atom on the other hand. From this, they concluded that there exists for a broad range of acid reaction centers an analogous relation, which has been confirmed for a large series of nitrogen-, oxygen-, and carbon-containing acids and bases by an extensive ab initio (STO-3G) study of Hehre et al.³⁹ among others. They furthermore concluded that this linear relationship is only applicable for the charge on the H atom which is directly involved in the reaction.

Catalan et al.³⁶ investigated a potential linear dependence between the Mulliken charge on the N atom in 3- and 4-substituted pyridines and their proton affinity, obtained by means of ab initio calculations. The conclusion of their work is that there exists no simple relationship between both quantities. They suggest that rather a linear dependence should exist between the PA and the charge shift on the N atom due to protonation. In this work, these relationships are tried out for all the MINDO/3, MNDO, and AM1 studied pyridines and pyridinium ions. If all the compounds are taken together, a satisfactory linear dependence is found in the MNDO and AM1 methods between the computed PAs and the charge on the acid H atom (Table IV) regardless of the substitution position ($R = 0.87$ for both approximations). In the MINDO/3 method however,

Table IV. Computed charge on the acid hydrogen atom in the substituted pyridinium ions.

Substituent	MINDO/3			MNDO			AM1		
	2-	3-	4-	2-	3-	4-	2-	3-	4-
H	0.111	0.111	0.111	0.252	0.252	0.252	0.298	0.298	0.298
F	0.157	0.114	0.124	0.265	0.258	0.256	0.306	0.305	0.302
Cl	—	—	—	0.262	0.256	0.255	0.302	0.301	0.300
CN	0.107	0.109	0.109	0.258	0.257	0.256	0.306	0.304	0.302
CH ₃	0.101	0.107	0.108	0.256	0.250	0.251	0.292	0.296	0.296
CHO	0.116	0.114	0.110	0.261	0.255	0.254	0.311	0.302	0.300
NO ₂	0.128	0.121	0.115	0.279	0.263	0.262	0.321	0.311	0.308
NH ₂	0.106	0.101	0.111	0.239	0.249	0.244	0.282	0.294	0.291
NMe ₂	0.098	0.102	0.108	0.236	0.246	0.242	0.279	0.291	0.288
OCH ₃	0.116	0.100	0.114	0.257	0.251	0.247	0.304	0.299	0.295
SCH ₃	—	—	—	0.255	0.251	0.249	—	—	—
CF ₃	0.242	0.112	0.110	0.263	0.260	0.260	0.309	0.306	0.305

this relationship is much less pronounced ($R = 0.27$; if the CF₃, CN, and 2-F substituents are deleted R becomes 0.71). From Figures 8(a–c) it appears that in the AM1 method the linear dependence is expressed very clearly when the 2-, 3-, and 4-substituted compounds are considered separately and that the correlation coefficient increases from position 2 (0.92) to 3 (0.99) and 4 (0.99). The same trend is observed for MNDO where the correlation coefficient increases from 2 (0.91) to 3 (0.97) and 4 (0.99). On the other hand, the MINDO/3 method gives in this respect no satisfactory results and does not confirm—contrary to AM1 and MNDO—the ab initio results.

If the computed charge density on the H atom is plotted against the experimental PA, it appears that the linear relationships

become in all the cases somewhat less favorable. In addition, the three semiempirical methods confirm the conclusion of the ab initio studies, according to which there exists no simple relation between the computed PA and the charge on the N atom in the substituted pyridines. Finally, it should be pointed out that the three methods find no relation between the calculated PA and the charge shift on the N atom due to protonation, $\Delta q = q_N(\text{pyridine}) - q_N(\text{pyridinium})$.

Relation between the Substituent Parameters and the Calculated Proton Affinities

There has always been a great interest in relations between substituent parameters and computed or experimental quantities.

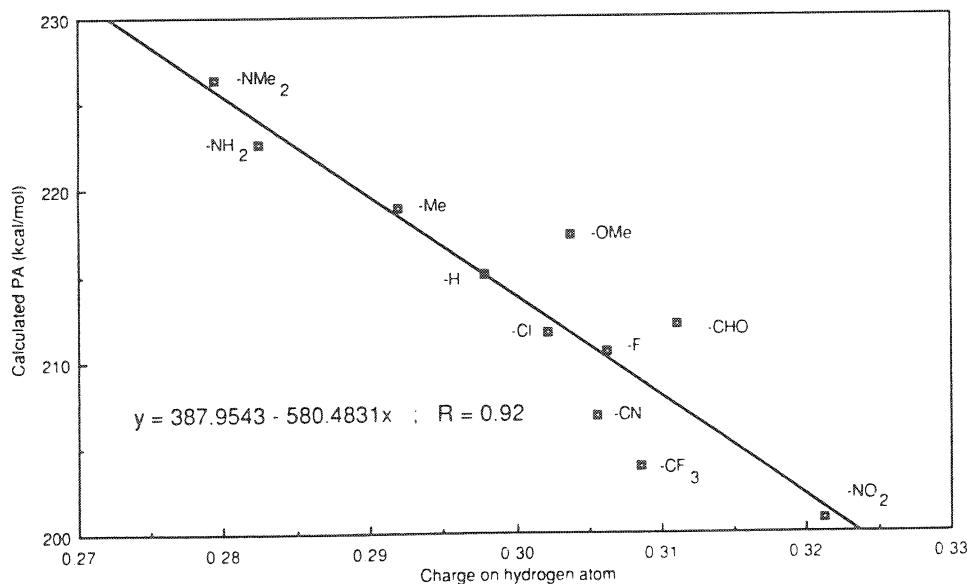


Figure 8(a). Relation between the computed charge density on the acid hydrogen atom of the 2-substituted pyridinium ions and the computed PA (AM1).

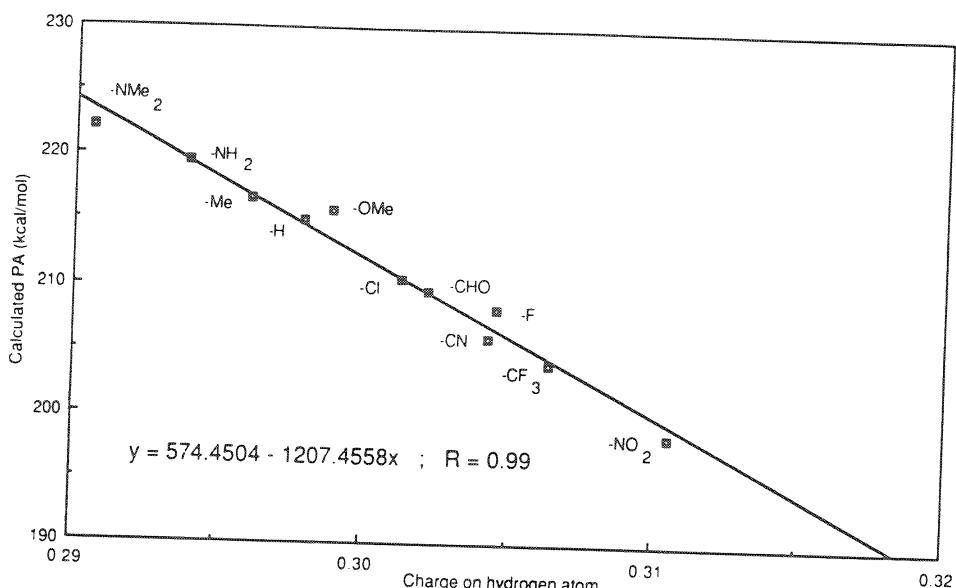


Figure 8(b). Relation between the computed charge density on the acid hydrogen atom of the 3-substituted pyridinium ions and the computed PA (AM1).

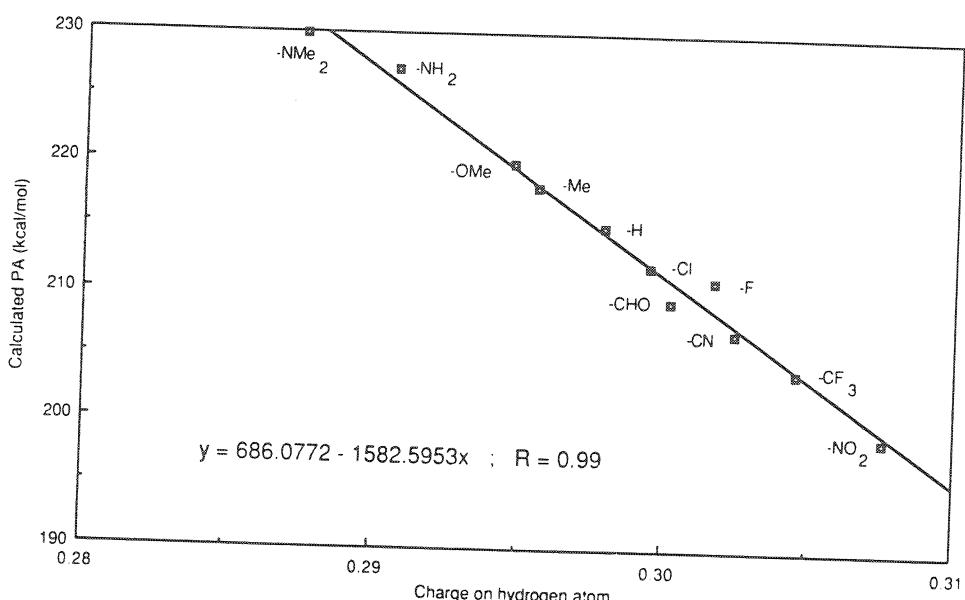


Figure 8(c). Relation between the computed charge density on the acid hydrogen atom of the 4-substituted pyridinium ions and the computed PA (AM1).

Inuzuka⁵⁴ found for a number of 4-substituted pyridinium ions a linear relation between the stabilization energy, computed with the INDO method, and the Hammett constant. The stabilization energy is defined by this author as the energy difference between a substituted pyridine and its corresponding ion. Taagepera et al.³⁷ analyzed the aqueous and gas phase acidities of a series of 3- and 4-substituted pyridinium and anilinium ions by means of a substituent parameter and an ab initio (STO-3G) approach. These investigators were able to make, for each substituent, a separate estimation of the inductive and

resonance effects on the acid-base behavior of the studied compounds. In addition, they determined substituent parameters merely on an ab initio basis and found a good correspondence with the values obtained via experimental data.

Figures 9–11 are plots of the AM1 proton affinities versus the Hammett σ -values^{55,56} (Table V). From these plots it appears clearly that the conclusions of Inuzuka can be generalized. The AM1 method gives for a larger range of substituents, regardless of the substitution position, a very good correlation between the PA, which is closely related to

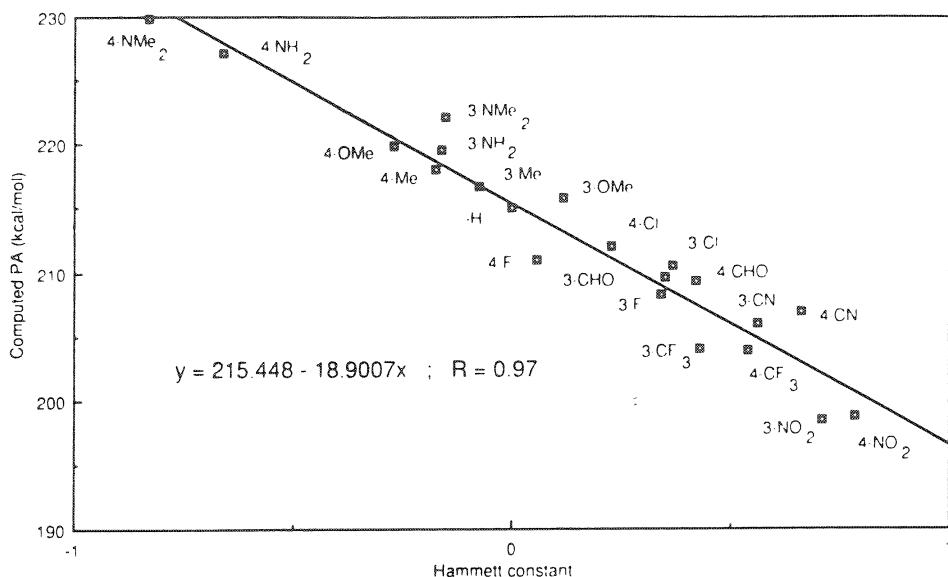


Figure 9. Relation between the Hammett σ values and the AM1 PAs of the 3- and 4-substituted pyridines.

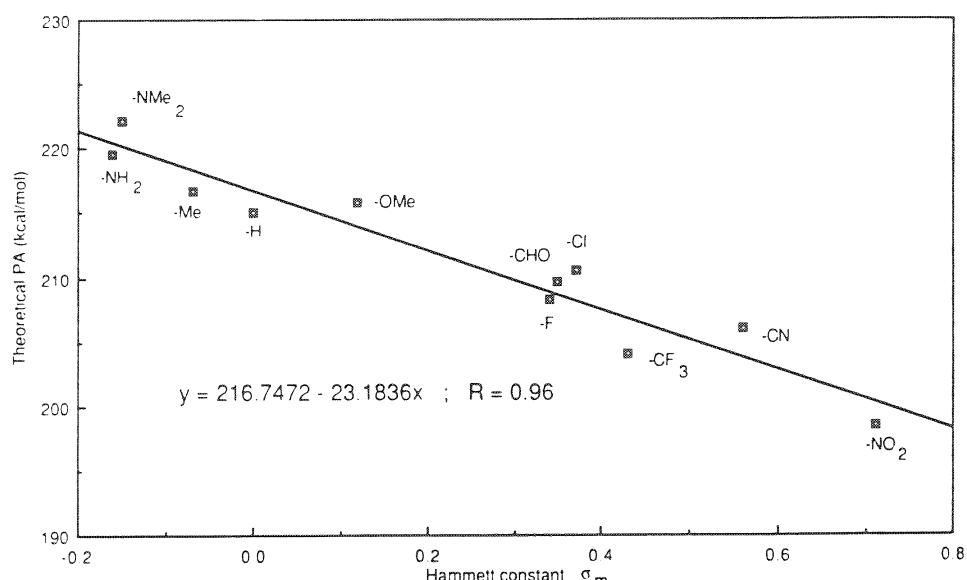


Figure 10. Relation between the Hammett σ_m constants and the AM1 PAs of the 3-substituted pyridines.

Table V. Substituent parameters.

Substituent	σ_m	σ_p	σ_m^*	σ_p^*	σ_p^{**}	σ_t
H	0.0	0.0	0.0	0.0	0.0	0.0
F	+0.34	+0.06	+0.35	-0.07	—	+0.50
Cl	+0.37	+0.23	+0.40	+0.11	+0.23	-0.46
CN	+0.56	+0.66	+0.56	+0.66	+0.88	+0.56
CH ₃	-0.07	-0.17	-0.07	-0.31	-0.17	-0.04
CHO	+0.35	+0.42	—	—	+1.04	-0.32
NO ₂	+0.71	+0.78	+0.67	-0.79	+1.27	+0.65
NH ₂	-0.16	-0.66	-0.16	-1.3	-0.66	+0.12
NMe ₂	-0.15	-0.83	—	-1.7	—	+0.06
OCH ₃	+0.12	-0.27	+0.05	-0.78	-0.27	+0.27
SCH ₃	+0.15	0.0	—	-0.6	—	+0.23
CF ₃	+0.43	+0.54	+0.52	+0.61	—	-0.45

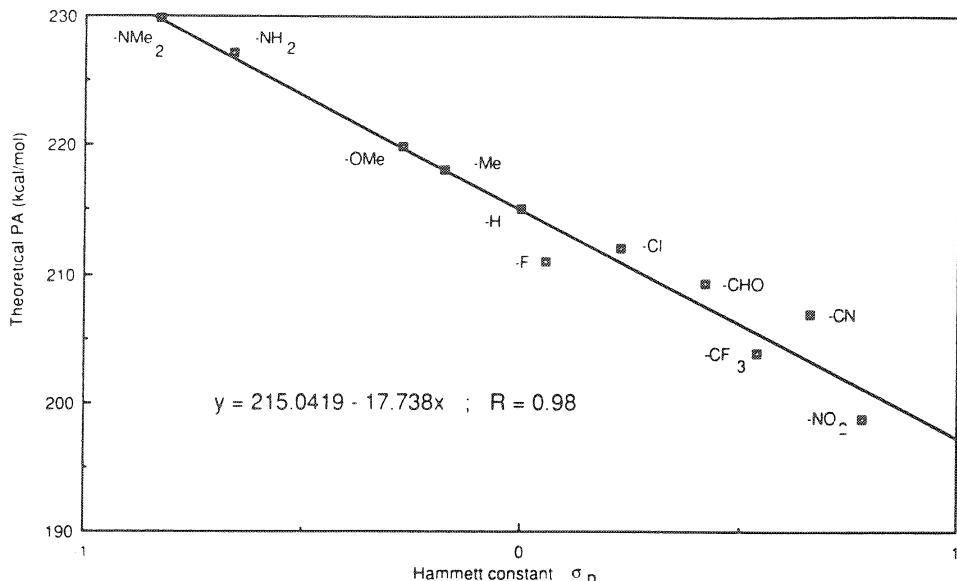


Figure 11. Relation between the Hammett σ_p constants and the AM1 PAs of the 4-substituted pyridines.

the stabilization energy of Inuzuka, and the Hammett constants. Somewhat less good correlations are found for the MINDO/3 ($R = 0.95$ (substitution positions 3 and 4), 0.98 (position 3), 0.96 (position 4)) and the MNDO ($R = 0.94$ (positions 3 and 4), 0.94 (position 3), 0.95 (position 4)) methods.

For the sake of completeness a study of Johnson⁵⁶ is mentioned here in which, among others, the Hammett equation is applied to heteroaromatic systems. The author suggests that the electron withdrawing effect of (-I, -R) substituents is strongly weakened with respect to benzoic acid, due to the presence of the electronegative N atom in the pyridine ring, and that the influence of such substituents can be best described by means of the σ_i parameters of Taft.³⁸ On the other hand, (+R) substituents will have a greater tendency, compared to benzoic acid, to give electrons to the pyridinium ion, which carries a positive charge. The effects of such substituents are described better with the σ^+ parameters. It must be remarked here that the numerical values of the different parameters vary strongly from one author to the other. In this work the σ_i parameters of Taft³⁷ and the σ^+ values of Johnson⁵¹ are used. Studies with these sets of parameters yield no better linear correlations than those obtained with the Hammett σ values. It further appears that the correlations become somewhat better if the 3- and 4-substituted pyridines are considered separately.

CONCLUSION

From the present study it can be concluded that especially the AM1 proton affinities of 2-, 3-, and 4-monosubstituted pyridines are in agreement with the experimental values. The AM1 results are ca. 2.4% too low (mean value): on the other hand, the MINDO/3 PAs are ca. 6% too high and the MNDO PAs ca. 7% too low (mean values). Correlations between the calculated proton affinities on one hand and the charges on the acid H atom and Hammett σ constants on the other hand are studied. The best linear relationships are found for the AM1 method. Particularly good linear relationships are observed for the 4-monosubstituted compounds within the AM1 formalism.

One of us (J. P. F.) wishes to thank the Belgian National Fund of Scientific Research (N.F.W.O./F.N.R.S.) for a computer time grant on the Cyber 205. Prof. Dr. J. L. Rivail and Dr. D. Rinaldi (Laboratoire de Chimie Théorique, Université de Nancy I, France) receive many thanks for providing the authors with a copy of the extended GEOMO program and for their kind discussions. The authors are also indebted to Mr. M. Thoelen, the system engineer at the LUC computer center, for a lot of help. Mrs. L. Govarts-Vangerven is thanked for putting the drawings in their final form.

References

1. J. L. Beauchamp, *Ann. Rev. Phys. Chem.*, **22**, 527 (1971).
2. D. H. Aue and M. T. Bowers, Stabilities of positive ions from equilibrium gas-phase basicity measurements, Chapter 9 in *Gas Phase Ion*

- Chemistry*, Vol. 2, M. T. Bowers, Ed., Academic Press, New York (1979).
3. P. Kebarle, *Ann. Rev. Phys. Chem.*, **28**, 445 (1977).
 4. A. G. Wren, P. T. Gilbert and M. T. Bowers, *Rev. Sci. Instrum.*, **49**, 531 (1978).
 5. C. R. Moylan and J. I. Brauman, *Ann. Rev. Phys. Chem.*, **34**, 187 (1983).
 6. A. J. Cunningham, J. D. Payzant and P. Kebarle, *J. Am. Chem. Soc.*, **94**, 7627 (1972).
 7. D. K. Bohme, R. S. Hemsworth, H. W. Rundle and H. I. Schiff, *J. Chem. Phys.*, **58**, 3504 (1973).
 8. J. E. Bartmess and R. T. McIver, Jr., The gas-phase acidity scale, Chapter 11 in *Gas Phase Ion Chemistry*, Vol. 2, M. T. Bowers, Ed., Academic Press, New York (1979).
 9. J. E. Bartmess, J. A. Scott and R. T. McIver, Jr., *J. Am. Chem. Soc.*, **101**, 6046 (1979).
 10. J. E. Bartmess, J. A. Scott and R. T. McIver, Jr., *J. Am. Chem. Soc.*, **101**, 6056 (1979).
 11. M. J. S. Dewar and K. M. Dieter, *J. Am. Chem. Soc.*, **108**, 8075 (1986).
 12. M. J. S. Dewar and W. Thiel, *J. Am. Chem. Soc.*, **99**, 4899, 4907 (1977).
 13. R. L. DeKock and C. P. Jasperse, *Inorg. Chem.*, **22**, 3839 (1983).
 14. M. J. S. Dewar, E. G. Zoebisch, E. F. Healy, and J. J. P. Stewart, *J. Am. Chem. Soc.*, **107**, 3902 (1985).
 15. R. C. Bingham, M. J. S. Dewar, and D. H. Lo, *J. Am. Chem. Soc.*, **97**, 1285, 1294, 1302, 1307 (1975).
 16. M. Taagepera, W. G. Henderson, R. T. C. Brownlee, J. L. Beauchamp, D. Holtz, and R. W. Taft, *J. Am. Chem. Soc.*, **94**, 1369 (1972).
 17. D. H. Aue, H. M. Webb, M. T. Bowers, C. L. Liotta, C. J. Alexander, and H. P. Hopkins, Jr., *J. Am. Chem. Soc.*, **98**, 854 (1976).
 18. E. M. Arnett, B. Chawla, L. Bell, M. Taagepera, W. J. Hehre, and R. W. Taft, *J. Am. Chem. Soc.*, **99**, 5729 (1977).
 19. H. P. Hopkins, Jr., C. J. Alexander, and S. Zakir Ali, *J. Phys. Chem.*, **82**, 1268 (1978).
 20. R. Czerminski, B. Lesyng, and A. Pohorille, *Int. J. Quant. Chem.*, **16**, 1141 (1979).
 21. J. Mirek and A. Sygula, *J. Mol. Struct.*, (THEOCHEM), **86**, 85 (1981).
 22. G. La Manna, *J. Mol. Struct.*, (THEOCHEM), **85**, 389 (1981).
 23. H. B. Schlegel, *Int. J. Quant. Chem.*, **22**, 1041 (1982).
 24. M. J. Scanlan, I. H. Hillier and A. A. McDowell, *J. Am. Chem. Soc.*, **105**, 3568 (1983).
 25. J. E. Del Bene, *J. Am. Chem. Soc.*, **101**, 7146 (1979).
 26. J. E. Del Bene, *J. Am. Chem. Soc.*, **102**, 5191 (1980).
 27. H. Tanaka and K. Nishimoto, *J. Phys. Chem.*, **88**, 1052 (1984).
 28. D. A. Case, M. Cook and M. Karplus, *J. Chem. Phys.*, **73**, 3294 (1980).
 29. G. Buemi, S. Fasone, D. Grasso and C. Gandolfo, *Croatica Chemica Acta*, **52**, 213 (1979).
 30. J. I. Seeman, J. C. Schug, and J. W. Viers, *J. Org. Chem.*, **48**, 2399 (1983).
 31. M. C. Anthony, W. L. Waltz, and P. G. Mezey, *Can. J. Chem.*, **60**, 813 (1982).
 32. P. H. M. Budzelaar, A. J. de Koning, and B. G. K. van Aarsen, *J. Chem. Soc. Perkin Trans. II*, **989** (1983).
 33. J. C. Schug, J. W. Viers, and J. I. Seeman, *J. Org. Chem.*, **48**, 4892 (1983).
 34. J. E. Del Bene, *J. Am. Chem. Soc.*, **99**, 3617 (1977).
 35. N. Bodor and R. Pearlman, *J. Am. Chem. Soc.*, **100**, 4946 (1978).
 36. J. Catalan, O. Mo, P. Pérez and M. Yanez, *J. Am. Chem. Soc.*, **101**, 6520 (1979).
 37. M. Taagepera, K. D. Summerhays, W. J. Hehre, R. D. Topsom, A. Pross, L. Radom and R. W. Taft, *J. Org. Chem.*, **46**, 891 (1981).
 38. S. Ehrenson, R. T. C. Brownlee, and R. W. Taft, *Progr. Phys. Org. Chem.*, **10**, 1 (1973).
 39. W. J. Hehre, M. Taagepera, R. W. Taft, and R. D. Topsom, *J. Am. Chem. Soc.*, **103**, 1344 (1981).
 40. J. Fossey, A. Loupy, and H. Strzelecka, *Tetrahedron*, **37**, 1935 (1981).
 41. D. R. Stull and H. Prophet, Eds., *JANAF Thermochemical Tables*, Natl. Stand. Ref. Data Ser., Natl. Bur. Stand., NSRDS-NBS 37, U.S. Govt. Print. Off., Washington, D.C.
 42. D. Rinaldi, R. Voets, and J.-P. François, *QCPE* 485; *QCPE Bulletin*, **4**, 108 (1984).
 43. D. Rinaldi, G. Schmidling, R. Voets, and J.-P. François, *QCPE* 487, *QCPE Bulletin* 5, 27 (1985).
 44. B. A. Murtagh and R. W. H. Sargent, *The Computer Journal*, **13**, 185 (1970).
 45. W. C. Davidon, A. E. C. Research and Development Report, ANL-5990 (Rev.), Argonne National Laboratory (1959).
 46. J. J. P. Stewart, QCPE program number 455, Quantum Chemistry Program Exchange, Indiana University, Bloomington, Indiana.
 47. J. M. L. Martin and J. P. François, CDC version of MOPAC, to be submitted to the QCPE.
 48. a. C. G. Broyden, *J. Inst. Math. Appl.*, **6**, 76, 222 (1970); b. R. Fletcher, *Comput. J.*, **13**, 317 (1970); c. D. Goldfarb, *Math. Comput.*, **24**, 23 (1970); d. D. F. Shanno, *Math. Comput.*, **24**, 647 (1970); e. See also W. H. Press, B. P. Flannery, A. A. Teukolsky, and W. T. Vetterling, *Numerical Recipes*, Cambridge University Press, Cambridge (1986).
 49. R. Voets, J.-P. François, J. M. L. Martin, J. Mullens, J. Yperman, and L. C. Van Poucke, to be published.
 50. J. J. P. Stewart, *QCPE Bulletin* 3, 54 (1983).
 51. M. Perrin, A. Thozet, G. Bertholon, C. Decoret, and J. Royer, *J. Mol. Struct.*, **70**, 87 (1981).
 52. W. F. Reynolds, P. G. Mezey, W. J. Hehre, R. D. Topsom, and R. W. Taft, *J. Am. Chem. Soc.*, **99**, 5821 (1977).
 53. R. S. Mulliken, *J. Chem. Phys.*, **23**, 1833, 1841 (1955).
 54. K. Inuzuka, *J. Chem. Soc. Jpn.*, **3**, 355 (1977).
 55. H. Maskill, *The Physical Basis of Organic Chemistry*, Oxford University Press, Oxford (1985).
 56. C. D. Johnson, *The Hammett Equation*, Cambridge University Press, Cambridge (1973).