CONCEPT OF π-DEFICIENCY IN THE CHEMISTRY OF HETEROAROMATIC COMPOUNDS (REVIEW)

A. F. Pozharskii

UDC 547.7/8:541.67

This review is the final part of our analysis [1] of the concepts of π-excess and π-deficiency in the chemistry of heteroaromatic compounds [2]. The development of quantitative criteria of π-deficiency and π-excess (π-acceptor and π-donor abilities) remains extremely relevant. Thus the search for effective organic conductors modelled on π-complexes [3] has centered on heterocyclic π-donors and π-acceptors and so the quantitative evaluation of their donor–acceptor properties has become important. Another example is the controlled synthesis of drugs, particularly sulfanilamides. The primary requirement for new and effective preparations of this series is thought to be a combination of the sulfanilamide fragment with a π-deficient center in a heteroaromatic molecule [4].

We should especially emphasize the biochemical significance of the subdivision into π-excessive and π-deficient heteroaromatic compounds. In the living organism the functions of systems based on these two types of heterocycles are very clearly differentiated. The π-excessive systems (pyrrole, indole, reduced forms of π-deficient heterocycles), possessing energy-rich electrons, carry out the transfer of these elements in the respiratory chain and are involved in reactions associated with the transmission of the nerve impulse and the activity of the central nervous system [5]. π-Deficient heterosystems (pyridinium salts, pyrimidines, purines, pteridines, etc.) are characterized by low π-orbital energy. Consequently they preferentially accept electrons. Thus there are reports that purines form molecular complexes with amino acids, indoles [6, 7], and polynuclear aromatic compounds in the process of carcinogenesis [8]. Covalent hydration is a reaction typical only of π-deficient heterocycles and is particularly important in biochemical terms [9].

CLASSIFICATION OF π-DEFICIENT HETEROSYSTEMS

We consider that an extremely convenient classification of π-deficient heterosystems would be:

I. Heterocycles containing only pyridine-type nitrogen atoms (all azines, including pyridine and its benzologs, diazines and their benzologs, naphthyridines, etc.).

II. Compounds simultaneously containing both pyridine- and pyrrole-type heteroatoms (azoles, purine, azaindoles, etc.). Many of the heterocycles of this group are intermediate in properties between typical π-deficient and π-excessive heterosystems [1].

III. Cationoid heterosystems (quaternary salts of heterocycles of the first two types, and also pyrylium, thiapyrylium, selenapyrylium salts, etc.).

IV. Heterocycles containing a heteroatom with an unoccupied orbital (borepin, phosphabenzene, arsabenzene, bismabenzene, stibabenzene, etc.). Although they also partly satisfy the physical and quantum-mechanical criteria for aromaticity, the majority differ in having lower stability and high reactivity [10].

Here we intend to deal principally with heterocycles of the first two types and to a rather lesser extent with heteroaromatic cations. We shall not consider heterocycles of the fourth group.

π-DEFICIENCY

Definition and Methods of Evaluation. Although the concept of π-deficiency is firmly entrenched in chemical terminology, it has not, surprisingly, been analyzed in quantitative terms. Obviously we must refine the concept itself and then develop appropriate criteria.

There seem to be three meaningful definitions of π-deficiency–total (TD), average (AD), and local (LD). When referring to π-deficiency, we usually mean the π-deficiency of the entire heterocyclic system as a general

Rostov State University, Rostov-on-Don 344006. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1155-1175, September, 1979. Original article submitted July 13, 1978.

0009-3122/79/1509-0939$07.50

index (excluding the heteroatoms), i.e., the total π-deficiency (TD). This is essentially the total positive π-charge remaining on the ring carbon atoms after the withdrawal of part of the π-electron density by the heteroatom and is numerically equal to the negative π-charge localized on the heteroatom. Consequently the magnitude of this π-charge can also serve as an indirect measure of the π-deficiency, particularly as it can be evaluated not only theoretically but also experimentally. Thus there is a good linear correlation between the negative π-charge on the pyridine nitrogen atom and the ^{15}N chemical shift [11].

It is extremely tempting to follow our analysis of π-excessiveness [1] by introducing the concept of the AD, meaning the average of the effective π-charges on all the carbon atoms of the hetero ring. However here we encounter several difficulties. Whereas in π-excessive heterocycles the carbon atoms are normally π-excessive and averaging is therefore justified in many respects, in π-deficient systems the π-electron density distribution is much less uniform. The fact is that the π-acceptor heteroatom causes the charges in the hetero ring to alternate and reorganizes the π-electron distribution in such a way that the electron deficiency appears exclusively in the ortho and para positions while the meta positions may even develop a slight negative π-charge. These include the β-positions in pyridine and quinoline, position 5 in pyrimidine, etc. Should these be included in evaluating the AD? If not, then what is to be done with compounds such as pyrazine, pyridazine, and related molecules in which each C atom is in the meta position to one heteroatom, but ortho or para to the other? Apparently it is valid to include in the evaluation of the AD only those carbon atoms on which there is a π-electron deficiency.

Secondly the magnitude of the AD is mainly of theoretical interest. In practice the organic chemist is more interested in the effective charges on the individual atoms, i.e., the local π-deficiency, since chemical reactions proceed at specific atoms rather than at an abstract averaged center. As the local π-deficiency we shall henceforth understand the atom with the greatest positive π-charge.

Clearly the magnitudes of the TD, AD, and LD will not necessarily vary in the same sense. This is exemplified by pyridine and pyridazine (Table 1). Quantum-mechanical calculations demonstrate that the TD index is higher in pyridazine whereas the AD and LD are greater in pyridine.

Methods for evaluating π-deficiency are essentially methods of calculating π-electron densities. In pyridine the π-deficiency can be analyzed most completely and consistently on the basis of molecular orbital calculations. The problem here is that different methods do not always give consistent results and that it is not so simple to choose an adequate method of calculation. These difficulties are graphically illustrated by the results of a calculation of the π-deficiency of positions 2 and 4 in such key compounds as pyridine, pyrimidine, and quinazoline. Thus Hückel [12], Extended Hückel [13], and SCF MO [14, 15] calculations reveal that positions 2 in these heterocycles have higher π-deficiency than positions 4, whereas CNDO/2 [16] and ab initio [17] calculations predict the opposite. In this context the need for independent, and if at all possible experimental, evaluation of π-electron charges becomes obvious.

The majority of experimental methods will provide local electron densities with varying accuracy. The NMR methods seems most important. A clear, though approximate, correlation between π-electron densities and ^{13}C chemical shifts has been reported [18, 19]. Others have claimed a better correlation if the total $(\sigma+\pi)$ electron density is used [16, 20]. The correlation of π-electron densities with proton chemical shifts is often unsatisfactory in the case of bases (because of the anisotropic effect of the lone pair of the heteroatom), but seems better for heteroatomic cations.

The NQR frequencies of ^{35}Cl atoms have been suggested as an extremely satisfactory means of calculating the π-electron charges on the carbon atoms bearing them [21]. The σ constants of the heterocyclic radicals, the NH_2 stretching frequencies in the hetaryl amines, and some other figures can be used for the same purpose.

We now consider the various experimental tests for π-deficiency agreeing with one another and with the results of theoretical calculations. Both the ^{13}C chemical shifts in azines and the results of calculations (Table 1) closely reflect the charge alternation in such compounds as pyridine, pyrimidine, and quinoline, where the meta positions have distinctly π-excessive character by comparison with benzene. Many other azines have no π-excess carbon centers.

An important result of the ^{13}C NMR method is that position 2 in pyridine, pyrimidine, quinoline, and quinazoline, and position 3 in pyridazine are more π-deficient than position 4. The same conclusion can be drawn from the ^{35}Cl NQR frequencies in chloropyridines and chloropyrimidines [21], which for example are 34.194, 35.238, and 34.739 MHz in 2-, 3-, and 4-chloropyridines respectively.

TABLE 1. π-Electron Charges and ^{13}C and ^{15}N Chemical Shifts in the Azine Series

Compound	Position	π-Charge		Average π-charge[a]		δ, ppm[b]	
		Ab initio[17]	SCF MO	*Ab initio*	SCF MO	^{13}C[18]	^{15}N[19]
pyridine	1	−0.11	−0.100				+68
	2, 6	+0.05	+0.050	+0.057	+0.040	+21.7	
	4	+0.07	+0.020			+7.4	
	3, 5	−0.04	−0.010			−4.6	
pyridazine	1, 2	−0.06	−0.054			—	−20
	3, 6	+0.03	+0.042	+0.035	+0.028	+24.3	
	4, 5	+0.04	+0.014			+0.8	
pyrimidine	1, 3	−0.14	−0.112			—	+82
	2	+0.11	+0.100	+0.117	+0.083	+31.0	
	4, 6	+0.12	+0.074			+29.0	
	5	−0.07	−0.026			−6.4	
pyrazine	1, 4	−0.05	−0.080	+0.020	+0.040	—	+42
	2, 3, 5, 6	+0.02	+0.040			+17.1	
sym-triazine	1, 3, 5	−0.17	−0.118	+0.170	+0.118	—	+98
	2, 4, 6	+0.17	+0.118			+38.1	
sym-tetrazine	1, 2, 4, 5	−0.03	—	+0.050	—	—	—
	3, 6	+0.05	—			+33.1	

[a]Over the electron-deficient carbon atoms. [b]^{13}C chemical shifts relative to benzene; ^{15}N chemical shifts relative to the NO_3^- ion.

TABLE 2. NH_2 Stretching Frequencies (cm^{-1}) in Hetarylamines

Heterocycle (solvent)	Position of the amino group	ν_{as}	ν_s
pyridine [25] (CCl_4)	2	3509	3411
	4	3508	3413
	3	3482	3396
pyridazine [24] ($CHCl_3$)	4	3514	3415
pyrimidine [23] (CCl_4)	2	3541	3431
	4	3535	3423
	5	3486	3423
pyrazine [24] ($CHCl_3$)	2	3511	3410
quinoline [22] ($CHCl_3$)	2	3517	3413
	4	3513	3425
acridine [22] ($CHCl_3$)	9	3525	3435
cinnoline [23] (CCl_4)	3	3510	3405
quinazoline [23] (CCl_4)	2	3543	3431
	4	3537	3423

The N–H stretching force constants in hetarylamines are directly proportional to the extent of conjugation of the lone pair of the amino group with the ring [22–24]. The conjunction in turn is controlled by the electron deficiency of the carbon atom bearing the amino group. Consequently the frequencies ν_{as} and ν_s increase with the electron deficiency of this atom. This test (Table 2) also favors positions 2 in pyrimidine and quinazoline but yields no definite conclusion for pyridine and quinoline.

Measurements of the resonance constants σ_R^0 of heterocyclic radicals are sparse (Table 3). Almost all have been derived by the ^{19}F NMR method. They imply that positions 2 and 4 in pyrimidine are equally π-deficient. However the impression has arisen that this method is not sensitive enough to detect small and possibly even moderate differences in π-deficiency.

The average Hammett σ-constants of the 2-, 3-, and 4-pyridyl radicals calculated from measurements of aldoxime acidity, the kinetics of ester hydrolysis, and the exchange of chlorine for methoxy [28], are 0.71, 0.55, and 0.94 respectively, i.e., the 4-pyridyl residue has the greatest electron-accepting ability. The value of these constants for calculations of π-deficiency, however, is rather unclear because of the small amount of information and the possible superposition of dynamic effects.

In general we may conclude that the ^{13}C NMR, NQR, and IR methods give similar results when applied to hetarylamides. This agreement can hardly be fortuitous. It most probably demonstrates that these methods give a quite realistic picture of the π-electron density distribution particularly within individual heterosystems.

It is surprising that theoretical techniques such as the Hückel, Extended Hückel, and SCF MO methods give better agreement with experiment than the CNDO/2 and ab initio methods, although the latter are generally

TABLE 3. σ_R^0 Constants of Heterocyclic Radicals

Radical	σ_R^0	Radical	σ_R^0
2-pyridyl [26]	0,01	sym-triazinyl [27]	0,20
2-quinolyl [26]	0,01	2-benzimidazolyl [26]	0,05
2-pyrimidinyl [27]	0,09	2-benzothiazolyl [26]	0,10
4-pyrimidinyl [27]	0,09	2-benzoxazolyl [26]	0,14

considered to give more accurate information on the electron distribution. The origin of this discrepancy is not clear—whether it is some deficiency of these methods or that the experimental constants are not determined solely by the π-electron charges. This greatly impedes analysis of π-deficiency on a quantitative level. In view of this in the subsequent comparison of the π-deficiency of heterocycles we will offer specific conclusions only when they are justified by the majority of experimental and theoretical methods.

In the ensuing analysis of the relative π-deficiency of the major types of heterocyclic systems we shall give precedence to the TD and LD indices. We shall discuss the average π-deficiencies selectively.

Pyridine and Noncondensed Polyazines. The π-deficiency is very strongly dependent on the number and orientation of the heteroatoms. At first sight it seems natural to assume that the π-deficiency should increase with the number of pyridine-type heteroatoms in the molecule. In fact this widespread view is not completely valid. The corpus of experimental and theoretical results shows that the situation is more complex and not unambiguous.

Ab initio calculations (Table 1) indicate that both the LD and AD of azines vary in the following way (brackets enclose the most π-deficient center); sym-triazine > pyrimidine (C_4) > pyridine (C_4) > sym-tetrazine > pyridazine (C_4) > pyrazine. The SCF MO calculations summarized in Table 1 also give the same order for the LD although they favor the C_2 atom as the position with the greatest positive charge. The ^{13}C NMR method yields a slightly different correlation: triazine > tetrazine > pyrimidine (C_2) > pyridazine (C_3) > pyridine (C_2) > pyrazine. Roughly the same results come from IR spectroscopy (Table 2). These considerations suggest several conclusions regarding the LD of azines:

1) sym-Triazine has a higher LD than all other azines, including tetrazine;
2) in the diazine series the LD order is: pyrimidine > pyridazine > pyrazine;
3) the π-deficiency of pyridine is slightly higher than that of pyrazine, i.e., pyrazine is the least π-deficient of all the azines.

Two not completely clear points remain. The first concerns the relative LD of pyridine and pyridazine. Theoretical results indicate that the LD and AD are higher in pyridine but the ^{13}C NMR and IR methods imply that pyridazine has a slightly higher π-deficiency. We believe that some preference should be given to the experimental results. The second difficulty concerns the accurate location of sym-tetrazine in the LD series.

Nor has the situation regarding the TD of azines been definitively resolved. All the theoretical methods imply that the TD order is: sym-triazine > pyrimidine > pyridazine > pyridine. The various quantum-mechanical calculations give extremely discordant results for pyrazine. Thus the methods using the π-approximation place it between pyrimidine and pyridazine, whereas those using the σ, π-approximation imply that it has the lowest TD of the entire series of noncondensed azines. The same problem arises in the evaluation of the TD of tetrazine.

Unfortunately these inconsistencies are difficult to resolve experimentally by, e.g., the ^{15}N NMR method, because of its two serious inherent limitations. Firstly, the anomalously high upfield ^{15}N shifts in pyridazine, cinnoline, and phthalazine demonstrate its inapplicability to heterocycles with adjacent heteroatoms (obviously because of their mutual anisotropic effect). Secondly it is unclear whether an additive scheme can be applied to compounds with different numbers of heteroatoms. Thus the ^{15}N chemical shift in pyridine is higher than that in pyrazine. However this means only that the π-electron density on the nitrogen atom of pyridine is higher than that on either of the nitrogens of pyrazine. Clearly the total π-electron density on the two nitrogen atoms of pyrazine and consequently its total π-deficiency could be higher. If we assume additivity, we have to recognize that the TD of pyrazine is higher than that of pyridine. This problem does not exist for systems such as sym-triazine and pyrimidine. The ^{15}N NMR method quite unambiguously places them in the first two places in the total π-deficiency series.

TABLE 4. π-Electron Charges [12] and ^{13}C and ^{15}N Chemical Shifts [11, 20] in Benzoazines

Heterocycle	Position	π-Charge (Hückel)[a]	δ, ppm[b]	Total charge on benzene ring[c]
pyridine	N	−0,195	+68	
	2	+0,077	+21,7	
	4	+0,050	+7,4	
quinoline	N	−0,216	+72	
	2	+0,104	+22,4	+0,011
	4	+0,068	+7,5	
isoquinoline	N	−0,198	+68	
	1	+0,105	+24,6	+0,029
	3	+0,053	+15,3	
phenanthridine	N	−0,216	—	+0,039
	6	+0,131	—	−0,004
acridine	N	−0,254	+94	+0,019×2
	9	+0,105	+7,4	
benzo[f]quinoline	N	−0,214	—	+0,010
	2	+0,094	—	+0,009
	4	+0,059	—	
benzo[g]quinoline	N	−0,221	—	−0,001
	2	+0,112	—	+0,003
	4	+0,074	—	
benzo[h]quinoline	N	−0,209	—	+0,002
	2	+0,092	—	+0,013
	4	+0,059	—	

[a]Here and subsequently Hückel calculations were carried out with parameters $h_N = 0.5$, $k_{CN} = 1$. [b]See the note to Table 1. [c]Quoted without allowance for the bridging carbon atoms. For benzoquinolines the first number is the charge on the central benzene ring and the second that on the outer ring. For phenanthridine the charges on the isoquinoline-type benzene ring appears first and that on the quinoline-type second.

The π-deficiency does not vary strictly in the same series as the number of heteroatoms because their π-acceptor ability is most effectively exerted only with meta orientation (sym-triazine, pyrimidine, quinazoline). This can be compared with the well-known phenomenon of the consistent orientation in the aromatic series. When the heteroatoms have the ortho, para orientation, each carbon atom becomes subject to the effect of two opposing forces, the electron-accepting effect of the ortho or para nitrogen atom conjugated with it and the electron-donating effect of the meta nitrogen atom (due to the reorganization of the π-cloud). The consequence is a reduction in the π-deficiency that differs in the various systems of this type.

Benzoazines. In this section we can conveniently consider two questions—firstly, how benzoannelation affects π-deficiency and secondly how π-deficiency varies as a function of the number and orientation of the heteroatoms.

Comparing pyridine with quinoline and isoquinoline, we find an increase in both TD and LD. Quinoline and isoquinoline themselves exemplify the lack of agreement of the TD and LD indices. Thus Hückel calculations and the ^{15}N NMR method (Table 4) show that quinoline has a slightly higher TD than isoquinoline. If we consider these heterocycles as naphthalene derivatives, this reflects the well-known fact that the conjugation of the α-substituent with the nucleus is stronger than that of the β-substituent. On the other hand, isoquinoline is shown by the Hückel and ^{13}C NMR methods to have a slightly higher LD.

The correlations of the π-deficiency of the dibenzo derivatives of pyridine are even more complex (Table 4). Their TD varies in the order: acridine > benzo[g]quinoline > phenanthridine > benzo[f]quinoline > benzo[h]-quinoline. Quinoline has the same TD as phenanthridine, whereas that of isoquinoline is inferior to all these compounds. We would particularly note that the TD is enhanced by linear annelation of benzene rings (acridine, benzo[g]quinoline) to a greater extent than by angular annelation. This is a general feature of the heteroaromatic series and is also encountered for example in azoles (see below).

Annelation of benzene rings to the f and h sides of quinoline produces compounds that are even less π-deficient than quinoline itself. Phenanthridine, in which one benzene ring is of the quinoline type and the other of the isoquinoline type, occupies an intermediate position.

The order of the local π-deficiency of benzoazines is slightly different: phenanthridine > benzo[g]quinoline > acridine, isoquinoline > quinoline > benzo[f]quinoline > benzo[h]quinoline. Since we unfortunately have no

TABLE 5. π-Electron Charges and ^{13}C and ^{15}N Chemical Shifts in Benzodiazines

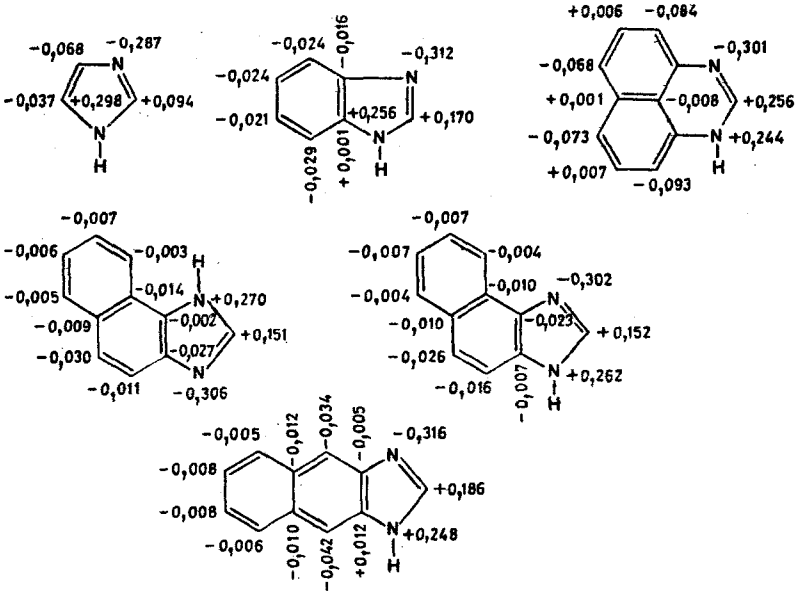
Heterocycle	Position	π-Charge (SCF MO) [15]	δ, ppm[11,20]
cinnoline	N_1	−0,059	−36
	N_2	−0,056	−36
	3	+0,032	+17,62
	4	+0,022	−3,87
phthalazine	N	−0,070	+11
	1 (4)	+0,047	+23,52
quinazoline	N_1	−0,098	+90
	N_3	−0,095	+90
	2	+0,072	+32
	4	+0,063	+27,2
quinoxaline	N	−0,082	+46
	2 (3)	+0,047	+17,2

information on the ^{13}C NMR spectra of the majority of benzoquinolines it does not seem possible to secure support for this series by an independent method.

In benzodiazines (Table 5) the TD diminishes in the order quinazoline > quinoxaline > phthalazine > cinnoline. Quinazoline also occupies the first place in the local π-deficiency series, but the theoretical and NMR results for the other compounds are contradictory. Phthalazine seems to have a higher LD than cinnoline, but the position of quinoxaline requires further clarification.

Table 4 shows that the pyridine nitrogen atom also causes benzene rings condensed with the hetero ring to acquire slight π-deficiency. Isoquinoline-type benzene rings are depleted of electrons to a much greater extent than the quinoline-type benzene rings. We should however note that in general, the effect of π-deficiency hetero rings on the properties of benzene rings condensed with them (including the π-deficiency) is considerably lower than that of π-excessive hetero rings [1]. Below we present additional examples in support of this correlation.

Azoles. As would be expected, the presence in azoles of both pyridine- and pyrrole-type heteroatoms results in a very nonuniform π-electron density distribution. Together with centers with considerable π-excess, azoles generally contain an atom with high π-deficiency, often higher than that in many azines. Imidazole systems are a typical example (see the diagram and Table 6):



In imidazole itself the donor effect of the pyrrole heteroatom prevails over the acceptor action of the pyridine nitrogen atom and consequently the net π-charge on the carbon atoms is negative, i.e., imidazole has a net π-excess rather than a π-deficiency. This is consistent with the entire chemistry of imidazole, which is typified by electrophilic rather than nucleophilic substitution reactions. We note as relevant that individual

TABLE 6. π-Charges in Imidazole Systems (Hückel Calculations) [12]

Heterocycle	π-Deficiency		Total charge on the benzene ring
	total	local (C_2)	
imidazole	−0,011	+0,094	—
benzimidazole	+0,056	+0,170	−0,098
1H-naphtho[1,2-d]imidazole	+0,036	+0,151	−0,041; −0,021
3H-naphtho[1,2-d]imidazole	+0,036	+0,152	−0,042; −0,022
naphtho[2,3-d]imidazole	+0,068	+0,186	−0,076; −0,027
perimidine	+0,057	+0,256	−0,146; −0,159

electrophilic substitution reactions (bromination, hydroxymethylation, diazo coupling) in the imidazole series also take place at the C_2 atom [29], although it is highly π-deficient.

The π-electron distribution varies substantially in condensed imidazole systems. Since the acceptor effect of the pyridine nitrogen atom is now greater than the π-donor stability of the pyrrole nitrogen atom, the TD's of condensed imidazoles diminish in the order: naphtho[2,3-d]imidazole > perimidine > benzimidazole > naphtho[1,2-d]imidazole. The LD of the μ-carbon atom in these compounds increases to an even greater extent – peri-naphthoimidazole (perimidine) is notable for the particularly high positive π-charge. Linear naphthoimidazole comes next and the other compounds appear in the same order as for the TD.

The pyrrole nitrogen atom in azoles does not oppose the induction of such a high positive π-charge on the adjacent carbon atom. The reason for this is that the π-donor effect of the pyrrole nitrogen atom is exerted almost exclusively on the condensed benzene rings. In fact all the condensed imidazoles have considerable negative π-charge on the benzene rings. This particularly applies to the perimidine molecule, which we have discussed in detail earlier [1].

There is no doubt that the Hückel method gives a realistic picture of the π-electron density distribution in imidazoles (the SCF MO [30] and CNDO/2 [31] methods give essentially the same results). In agreement with these considerations, nucleophilic substitution reactions at position 2 become most typical in all condensed imidazole systems [29, 32]. Conversely electrophilic substitution reactions also proceed extremely readily on the benzene rings.

Calculations [33, 34] and ^{13}C NMR parameters [33, 35] imply that pyrazoles have lower LD than imidazoles. Thiazoles and oxazoles are more π-deficient than imidazoles (Table 3).

Systems consisting of π-excessive and π-deficient rings condensed with each other (azaindoles, purine, etc.) are of considerable interest. All the evidence indicates that the effect of the pyrrole heteroatom on the properties of the π-deficient fragment is greater than that of the pyridine atom on the properties of the π-excessive ring. Thus the pyridine nucleus in azaindoles is completely inert in nucleophilic substitution reactions, whereas the electrophilic substitution reactions that are typical of indole take place at position 3 in azaindoles, though with slightly more difficulty [36]. Similarly in purines, although the pyrimidine ring is more π-deficient than the imidazole, nucleophilic substitution reactions proceed more readily at the carbon atom of the imidazole ring [37]. This is also reflected in quantum-mechanical calculations [12, 38].

Heteroaromatic Cations. The π-deficiency of heterocyclic cations is much greater than that of their bases, but the π-deficiency orders show no great changes. Thus various quantum-mechanical calculations [12, 13] reveal that the TD order for the cations of noncondensed azines and benzoazines remains the same as that of their bases: pyrimidinium > pyridazinium > pyrazinium > pyridinium (Table 7) and acridinium > quinolinium > isoquinolinium > pyridinium (Table 8).

The situation regarding the LD is slightly more confused. Calculations imply that the LD and TD orders for the cations of noncondensed azines are identical. However the ^1H and ^{13}C chemical shifts interchange the pyrazinium and pyridinium ions (Table 7). This resembles the situation for pyrazine and pyridine (Table 1).

The PMR and quantum-mechanical methods also give conflicting results for the LD of benzoazine cations. Whereas the PMR method ranks the acridinium cation ahead of the isoquinolinium and quinolinium cations, Hückel calculations give the opposite order: isoquinolinium > quinolinium > acridinium > pyridinium (Table 8). The choice between these results remains open.

TABLE 7. π-Charges (Extended Hückel) [13] and ^1H and ^{13}C Chemical Shifts in Azine Monocations [13]

Cation	π-Deficiency		δ, ppm*	
	total	local	^1H	^{13}C
pyridinium	+0,820	+0,318 (C_2)	2,49 (2-H)	19,84 (C_4)
pyridazinium	+1,244	+0,495 (C_6)	2,50 (3,6-H)	23,21 ($C_{3,6}$)
pyrimidinium	+1,360	+0,594 (C_2)	2,84 (2-H)	30,29 ($C_{2,3}$)
pyrazinium	+1,188	+0,374 (C_2)	2,11 (2,3-H)	14,47 ($C_{2,3}$)

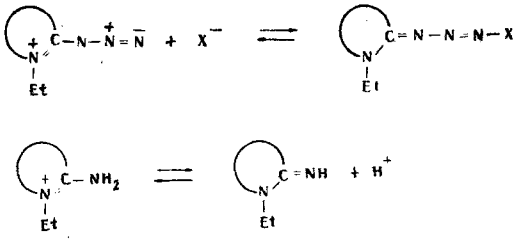
*Chemical shifts relative to benzene. The NMR spectra of the protonated species were measured in water. Consequently because of the fast reversible proton migration in the diazine cations the chemical shifts of the formally inequivalent nuclei were identical. Since conversely the quantum-mechanical calculation was carried out for cations with the charge fixed on one of the nitrogen atoms, the π-charges on all the carbon atoms were different.

TABLE 8. π-Charges (Hückel) [12] and ^1H Chemical Shifts [39] in Benzoazine Cations

Cation	π-Deficiency		δ, ppm*
	total	local	
pyridinium	+0,622	+0,248 (C_2)	8,9 (2-H)
quinolinium	+0,661	+0,306 (C_2)	9,4 (2-H)
isoquinolinium	+0,629	+0,329 (C_1)	9,87 (1-H)
acridinium	+0,716	+0,288 (C_9)	10,05 (9-H)

* PMR spectra of the methiodides in DMSO solution.

The LD's of heteroaromatic cations are clearly reflected by their σ substituent constants (Table 9). These were derived from work on two consecutive equilibria where the σ constant of the pyridinium-2-yl ion was taken as 0 [40, 41]:



Although these σ constants incorporate inductive and resonance components, we may expect both components to vary in the same sense. The figures provide support for the assignment of higher LD's to the quinolinium ion than the pyridinium and to the benzimidazolium ion than the indazolium. The benzothiazolium ion has higher LD than the thiazolium and angular naphthothiazolium ions. We have already noted this sort of variation of the LD in the series imidazole–benzimidazole–naphtho[1,2-d]imidazole and pyridine–quinoline–benzo[f]-quinoline.

We can use the benzazole cations as examples of how the nature of a second pyrrole-type heteroatom affects the LD. The LD diminishes in the order: benzoselenazolium > benzothiazolium > benzoxazolium > benzimidazolium, i.e., the electron-accepting character of the unoccupied selenium and sulfur d orbitals has considerable significance in the case of the first two compounds.

In connection with this last series we encounter the question of the relative π-deficiency of the pyrylium, thiapyrylium, and selenapyrylium ions. We have no reliable figures for the TD's of these ions. The LD indices of the various positions do not vary in the same way. Thus the PMR method [42, 43], which is in agreement with quantum-mechanical calculations using d orbitals [43], gives the LD order as thiapyrylium > selenapyrylium > pyrylium for the β-position and pyrylium > thiapyrylium > selenapyrylium for the γ-position. The α-proton

TABLE 9. σ Constants of Cationic N-Heteroaromatic Substituents [40, 41]

Substituent	σ	Substituent	σ
1-ethylpyridinium-2-yl	0	3-ethylbenzothiazolium-2-yl	4.89
1-ethylquinolinium-2-yl	1.21	3-ethylnaphtho[2,1-d]-thiazolium-2-yl	4.79
1,2-diethylindazolium-3-yl	0.41	3-ethylbenzoxazolium-2-yl	4.33
1,3-diethylbenzimidazolium-2-yl	2.52	3-ethylbenzoselenazolium-2-yl	4.98
3-ethylthiazolium-2-yl	3.60		

TABLE 10. σ_R^0 Constants of the Heteroatom in Pyridinium Ions [46]

Compound	σ_R^0	Compound	σ_R^0
pyridine	0,268	pyridine N-oxide	−0,212
1-methylpyridinium iodide	0,281	1-methoxypyridinium iodide	−0,171
pyridine borane	0,209		

chemical shifts (selenapyrylium > thiapyrylium > pyrylium) seem unsuitable for evaluating the LD of the α-positions because of the strong anisotropic effect of the heteroatom. Thus the common view, which is based mainly on reactivity data, that the pyrylium cation is most π-deficient [44] must be considered neither unambiguous nor definitively established.

The question of the π-deficiency of N-heteroaromatic cations has another interesting aspect, involving the form in which the onium nitrogen atom exists. Thus the γ-proton chemical shift implies that the LD of position 4 in pyridinium ions varies in the order: N-phenylpyridinium > pyridinium > N-methoxypyridinium > N-methylpyridinium > N-aminopyridinium [45]. The σ_R^0 constants of the heteroatoms calculated from the integrated intensity of the 1600 cm^{-1} band [46] (Table 10) show that the N-oxide and N-methoxy groups are resonance donors, i.e., they reduce the π-deficiency of the ring even by comparison with pyridine itself (see also [47]).

π-ACCEPTOR PROPERTIES

Pyridine-type heteroatoms, possessing considerable electron-acceptor ability, reduce the energy of all the MO's, including the lowest unoccupied π-orbital. This causes an increase in electron affinity (EA) in π-deficient heterocycles. As a result many now typically form more or less stable radical anions [48]. We should emphasize that π-excessive heterocycles will also form radical anions with great difficulty under specific conditions but this is accompanied by radical changes in molecular structure [49, 50].

There is very little information on direct methods of measuring the EA's of heterocycles in the gas phase. Thus the electron impact technique has been used to establish that pyridine has a negative EA, −0.62 eV (benzene has −1.15 eV) [51]. This demonstrates the instability of the radical anion of pyridine, which is also reflected by the difficulty of detecting it [52]. Diazines and triazines form more stable radical anions, whose EA's are usually positive [51]: sym-triazine (0.45 eV), pyrazine (0.40 eV), pyridazine (0.25 eV), and pyrimidine (0.00 eV). Unfortunately the electron impact technique is not suitable for the determination of positive EA's, and so the figures quoted here were derived indirectly on the basis of the linear correlation between the EA and the polarographic reversible reduction potential.

The ease of measurement of half-wave reduction potentials makes the polarographic method perhaps the first choice at the present time for the quantitative evaluation of the electron-acceptor properties of π-deficient heterocycles. Of course the electron is assumed to enter the lowest unoccupied π-orbital. This is supported by the existence of a good linear correlation between $E_{1/2}$ (reduction) and the energy of the lowest unoccupied orbital, calculated by LCAO MO methods, which has been reported on several occasions [53-55].

Table 11 summarizes $-E_{1/2}$ for nitrogen heterocycles and their cations. The potentials in the first column were derived by cyclic voltametry, i.e., they are reversible. The figures in the two other columns were measured by normal polarography and represent essentially the irreversible electron reduction process. Neverthe-

TABLE 11. Polarographic One-Electron Reduction Potentials ($-E_{1/2}$, V) of π-Deficient Heterocycles and Their Cations

Heterosystem	Base		Cation in DMF [55]
	in DMF [53]	in CH_3CN [54]	
pyridine	2,20	2,62	1,27
pyrimidine	1,82	2,34	0,94
pyridazine	1,66	2,12	0,74
pyrazine	1,57	2,08	0,73
sym-triazine	1,53	—	—
sym-tetrazine	0,29	—	—
quinoline	1,60	2,11	0,84
isoquinoline	1,64	2,22	1,05
phenanthridine	—	2,12	—
acridine	—	1,62	0,32
benzo[f]quinoline	—	2,14	—
benzo[h]quinoline	—	2,21	—
phthalazine	1,43	1,98	0,86
quinazoline	1,26	1,80	0,33
quinoxaline	1,10	1,70	0,37
cinnoline	0,98	1,69	0,53
phenazine	—	1,23	—
pteridine	0,53	—	—

less in all cases, regardless of the nature of the solvent, the relative ease of reduction of the heterocycles remains the same. We can draw several conclusions from the figures of Table 11.

1. Heteroaromatic cations have considerably greater π-acceptor ability than the neutral heterocycles (the difference between the figures in the first and third columns in fact is even greater, since the reference electrode is a mercury pool in the first case and the saturated calomel electrode in the second; the pyridinium cation has $E_{1/2}$ of -0.75 V relative to the mercury pool). It is vital here that the ease of reduction of the neutral heterocycles varies in the same way as that of their cations with one exception (cinnoline). Thus in those cases where the neutral heterosystem is polarographically inactive (imidazole systems for example), polarographic reduction of the cation can provide a measure of the π-acceptor ability of the neutral heterosystem.

2. In the noncondensed azines, the π-acceptor ability diminishes in the order: sym-tetrazine > sym-triazine > pyrazine > pyridazine > pyrimidine > pyridine, i.e., the π-acceptor properties intensify with the number of heteroatoms in the molecule. Among diazines, pyrazine has the greatest π-acceptor ability and pyrimidine the lowest, which is the opposite of the π-deficiency series.

3. Like π-deficiency, the π-acceptor properties are not a simple function of the number of benzene rings, but are highly dependent on their orientation. Thus quinoline and isoquinoline have higher acceptor ability than pyridine but the π-acceptor abilities of benzo[f]quinoline and benzo[h]quinoline are slightly lower than that of quinoline. The π-acceptor ability is enhanced to the greatest extent by linear annelation of benzene rings, as in acridine and phenazine in the azine series and naphtho[2,3-d]imidazole in the imidazole series [56]. Comparison of quinoline and isoquinoline reveals that annelation of a benzene ring to positions 2 and 3 of pyridine produces more strongly π-accepting systems than does 3,4-annelation. In benzodiazines, benzoannelation also slightly modifies the relative order of π-acceptor ability relative to noncondensed diazines. The first place is occupied by cinnoline among neutral heterocycles and by the quinazolinium ion among cations.

Polarography of benzazole cations reveals that in these heterosystems the π-acceptor properties diminish in the order: benzoxazole > benzothiazole > indazole > benzimidazole [57].

Another technique for the indirect measurement of EA's uses the spectra of charge-transfer complexes between π-deficient heterosystems (normally cations) and various π-donors [58]. The basis of this method is that the frequency of the charge-transfer band, $h\nu_{CT}$, is related to the EA by the equation:

$$h\nu_{CT} = IP - EA + W,$$

where IP is the ionization potential of the donor, EA is the electron affinity, and W is the free term, which is approximately constant for CT complexes of a particular type and is on average 1.2 eV. Table 12 summarizes the EA's derived by this method for several heteroaromatic cations. Plainly these figures are in complete agreement with the results of polarographic measurements.

Thus these considerations imply that, like π-excess and π-donor ability [1], the π-deficiency and π-acceptor ability do not vary in the same sense. This necessitates a dualistic interpretation of the concept of

TABLE 12. Electron Affinities of Some Heteroaromatic Cations Measured by the Charge-Transfer Technique

Cation	EA, eV	Cation	EA, eV
N-methylpyridinium [59]	5,0	N-methylacridinium [60]	6,1
N-methylisoquinolinium [59]	5,4	phenazinium [61]	6,8
N-methylquinolinium [59]	5,6	xanthylium [62]	6,75

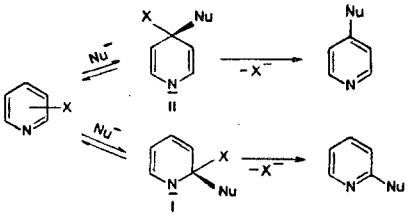
electrophilicity as regards π-deficient heterocycles and their cations. Apparently we should differentiate between orbital electrophilicity (or electron affinity) and atomic or local electrophilicity, which is usually understood to be the affinity of the π-deficient center for the electron pair of the nucleophile. These questions are discussed in rather more detail in the next section.

REACTIVITY OF π-DEFICIENT HETEROSYSTEMS

The reactivity of π-deficient heterocycles is an extremely complex problem and, despite numerous studies and several detailed reviews [63-67], is still very far from a definitive solution. Although π-deficiency and π-acceptor ability are properties of the ground state of heterocyclic molecules, organic chemists have become accustomed to interpreting their reactivity in these terms. In fact, chemical work shows that the π-deficiency controls the possibility of nucleophilic substitution reactions, the ease of reduction reactions, the increased reactivity of the protons of the methyl groups, etc. In this context we encounter the question of whether the relative local π-deficiency of heterocycles or their π-acceptor properties can be assessed from reactivity data—in other words, whether these parameters quantitatively determine the ease of interaction with a nucleophile. It is now well known that there is no single answer to these questions and that there are few reactions where this sort of correlation is satisfactory.

The reason for the complexity of the situation is primarily that nucleophilic substitution reactions in heterocycles can proceed by several very different mechanisms, the most important of which are S_N2Ar, S_N1Ar, aryne, S_RN1 [68], and ANRORC [69]. Secondly within each of these mechanisms the contributions of the individual stages can vary in turn. Finally the reactivity is also strongly affected by such specific factors as the α-aza effect, the preliminary interaction of the heteroatom with the nucleophile or the solvent, the phenomenon of autocatalysis, the nature of the nucleophile and the leaving group, the different polarizabilities of the reaction centers, etc. [64, 65].

Hence it is clear that the relation between π-deficiency and reactivity can best be analyzed in the context of a single, most typical mechanism and a simultaneously chosen set of reactions where the effects of specific factors reduce to a minimum or are zero. These requirements are most closely satisfied by S_N2Ar reactions. These include the stage of addition of the nucleophile, which generates σ-complex (I) or (II) (which can be detected in many cases [70]), and the stage of elimination of the leaving group with regeneration of the aromatic structure:



Three types of potential energy curve are possible here (Fig. 1).

The occurrence of any one pathway will depend mainly on the nature of the leaving group, the nucleophile, and the heteroaromatic molecule itself. Obviously a quantitative comparison of rate data is meaningful only for reactions with the same energy profile. Thus the positive charge on the carbon atom can be correlated with the ease of amination of nitrogen heterocycles by sodium amide only in small groups of related compounds [71]. The reaction for this is [72] that all three types of curves can occur in the Chichibabin reaction, depending on the nature of the heterocycle. Curve b is found for heterocycles with an extended π-system (acridine, phenanthridine, perimidine, etc.), i.e., an extremely stable σ-complex is formed, which requires high temperatures for aromatization. Conversely monocyclic compounds (pyridine, imidazole) typically follow curve a (an unstable and difficultly formed σ-complex). Bicyclic systems—isoquinoline, benzimidazole—occupy an intermediate

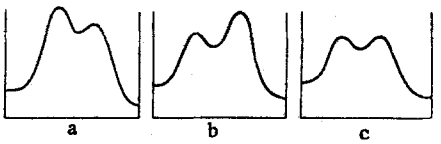


Fig. 1. Types of potential energy curve for S_N2Ar reactions (the abscissa axis is the reaction coordinate and the ordinate axis the potential energy): a) limited by the addition stage; b) limited by the elimination stage; and c) the contributions of both stages are roughly the same.

TABLE 13. Rate Data for the Reactions

$$HetSO_2CH_3 + CH_3O^- \rightarrow HetOCH_3 + CH_3SO_2^- \quad (1)[73]$$

$$HetCl + C_2H_5O^- \rightarrow HetOC_2H_5 + Cl^- \quad (2)[74]$$

Heterocyclic radical	Reaction (1)		Reaction (2)*
	temperature, °C	$k \cdot 10^5$ (liter mole^{-1}sec^{-1})	$k \cdot 10^5$ (liter mole^{-1} sec^{-1})
2-pyridyl	108,7	1,97	0,00022
4-pyridyl	110,5	40,2	0,00087
3-pyridazinyl	30,2	9,71	—
4-pyridazinyl	30,3	121	—
2-pyrazinyl	29,9	3,86	—
2-quinolinyl	60	2,72	0,063
4-quinolinyl	60,3	7,20	0,065
1-isoquinolinyl	59,1	5,19	0,069
9-acridinyl	—	—	6,2
2-quinoxalinyl	14,9	209	828
2-quinazolinyl	—	—	298
4-cinnolinyl	15,1	137	477
1-phthalazinyl	15,1	117	186

*These are the rate constants at 20°C.

position; the rapidity of their reaction with sodium amide is due to the optimum combination of the ease of addition of amide ion and the ease of abstraction of hydride ion from the σ-complexes (curve c).

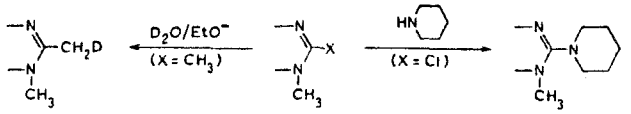
The substitution reactions of such good leaving groups as Cl, Br, SO_2CH_3, etc., on different nucleophilic residues are most common in the heteroaromatic series and have received most attention. Their energy profile is of type a and consequently it is among these reactions that we may hope to detect a correlation between the π-charge and the ease of reaction. Analysis of a considerable amount of rate data reveals that these hopes are only partially fulfilled. Even in pyridine itself these groups are substituted far more easily at position 4 than at the more π-deficient position 2 (Table 13). Similarly in pyridazine, pyrimidine, and quinoline position 4 is more reactive than the α-position. Comparison of various heterocycles with each other also reveals a direct correlation of reactivity with π-deficiency in some but not all cases.

The figures of Table 13 for substitution of methylsulfonyl by the methoxy group and other results [64, 65] reveal that in terms of their reactivity toward nucleophiles the noncondensed azines fall in the order: symtriazine > pyrimidine > pyridazine > pyrazine > pyridine. Although this series is very similar to the π-deficiency series (Table 1), there is one exception—the less π-deficient pyrazine appears ahead of pyridine. Similarly 9-chloroacridine is much more reactive than the chloro derivatives of quinoline and isoquinoline, although their local π-deficiencies are similar. In the benzodiazine series, despite the relative π-deficiency 2-chloroquinazoline is less reactive than to 2-chloroquinoxaline (which however is less reactive than 4-chloroquinazoline [74]) while 1-chlorophthalazine is less reactive than 4-chlorocinnoline.

The cause of all these inconsistencies is undoubtedly that, since the structure of the transition complex in the limiting stage of these reactions lies much nearer the σ-complex than the original reactant, the rate of the reaction is controlled not so much by the charge as by the stability of the σ-complex. The different polarizabilities of the reaction centers also seem significant.

We may expect that the discriminatory effect of these factors would be strongly reduced in a set of very similar compounds in which the reaction center has the same molecular environment and that the correlation between reactivity and π-deficiency will than be more satisfactory. This conjecture is in fact justified in several cases. Thus the lability of chlorine in reactions with the CH_3O^- ion and with piperidine diminishes in the

TABLE 14. Rate Data for the Piperidinolysis Reaction of 2-Chloro Derivatives of Imidazole Systems [72] and Kinetic Acidity of the Methyl Group in 2-Methylimidazoles [78, 79]



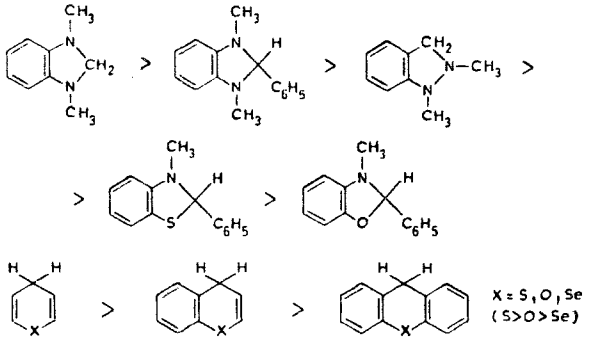
Compound type	q_2^+	X=Cl	X=CH3
		k, sec^{-1} (40°)	$-\lg k_{so}$
perimidine	0,256	$2,56 \cdot 10^{-3}$	2,7
naphtho[2,3-d]imidazole	0,186	$2,01 \cdot 10^{-4}$	3,0
benzimidazole	0,170	$5,25 \cdot 10^{-7}$	5,0
3H-naphtho[1,2-d]imidazole	0,152	$6,05 \cdot 10^{-6}$	5,9
imidazole	0,094	no reaction	6,6

same order as the positive π-charge on the carbon atom bearing the chlorine in the series 1-chloronaphtho[2, 3-d]pyridazine > 1-chlorophthalazine > 3-chloropyridazine [75, 76] and 2-chlorobenzoxazole > 2-chlorobenzothiazole > 2-chloro-1-methylbenzimidazole [77]. The rate of piperidinolysis of 2-chloro derivatives in imidazole systems in general also depends on the local π-deficiency index (Table 14), although there is one exception, in that 3-methyl-2-chloronaphtho[1, 2-d]imidazole is slightly more reactive than 1-methyl-2-chlorobenzimidazole, the positive π-charge on the μ-carbon atom in which is slightly greater.

In principle a correlation between π-deficiency and reactivity would most logically be expected in those cases where the structure of the transition complex in the limiting stage closely resembles that of the original reactant. These reactions are conveniently referred to as charge-controlled and occur with rigid, difficultly polarizable nucleophiles [80]. Only one reaction of this type seems to be known in the nitrogen heterocyclic series—direct hydroxylation using solid alkali [32, 71, 81]. The process usually takes place at such high temperatures that there are no problems with the aromatization of the σ-complexes and the ease of this reaction is entirely determined by the positive π-charge.

Strange as it may seem at first, a correlation between π-deficiency and reactivity is also possible in principle for reactions whose energy profile corresponds to curve b (Fig.1). A necessary condition here is that the transition complex in the aromatization stage and the end product of the reaction have similar structures. There seem to be no reliably identified examples of such reactions in the heteroaromatic series. The closest are possibly the reactions of abstraction of hydride ion from dihydro derivatives of heterocycles, which form heteroaromatic cations. Since rate data for these reactions unfortunately are extremely sparse (they refer mainly to 1,4-dihydropyridines) we have to limit the analysis to qualitative information.

Crossed hydride transfer between dihydro derivatives of heterocycles and various heteroaromatic cations has been used to derive several hydride lability series [57, 82]:



These series generally follow the relative LD's of the heteroaromatic cations conjugated with the dihydro compounds. However although the LD's of benzimidazolium cations are higher than those of indazolium cations, benzimidazolines are stronger hydride donors. This implies that the π-deficiency of the cations is not the sole factor responsible for hydride lability.

The not infrequently encountered correlation of the reactivity of π-deficient heterocycles with their π-acceptor properties demands particular attention. Thus the hydride lability of dihydro derivatives of heterocycles

TABLE 15. Half-Wave Reduction Potentials and Ease of Addition of Bisulfite Ion for Some Heteroaromatic Systems [83]

Compound	$-E_{1/2}$, V	lg k_{add}
quinazolinium ion	0,40	8,55
acridinium ion	0,53	6,04
pyrimidinium ion	0,62	4,49
2-aminopyrimidinium ion	0,71	3,26
purinium ion	0,83	1,34
adenine	1,12	very slow

correlates closely with the ease of polarographic reduction of the corresponding heteroaromatic cations: greater difficulty of reduction of the cation is accompanied by higher hydride reactivity of the conjugate dihydro derivative [57]. In particular the reduced hydride reactivity of indazolines relative to benzimidazolines is consistent with the markedly greater ease of reduction of the indazolium ion by comparison with the benzimidazolium ion [57]. There is also a good linear correlation between the ease of addition of bisulfite ion to the C=N bond of π-deficient heterosystems and the ease of their polarographic reduction (Table 15) [83].

The existence of such correlations implies that electron transfer from the nucleophile to the lowest unoccupied orbital of the heterocyclic compound is of considerable significance in the limiting stage of these reactions. These reactions are conventionally referred to as being controlled by the energy of the frontier orbitals [80].

At first sight it seems tempting to use measurements of the kinetic carbon acidity of heterocycles to evaluate the relative π-deficiency, since more π-deficient centers should correlate with more acidic C–H bonds. However no correlation has been found, probably because of the existence of the α-aza effect, which destabilizes the carbanionic center lying next to the heteroatom [78, 84].

The situation regarding the correlation between the carbon acidity of the methyl group in C-methyl-substituted heterocycles and the π-charge on the atom bearing the CH_3 group closely resembles that for S_N2Ar reactions. Thus 4-methyl-substituted pyridines and quinolines have higher acidity than the 2-methyl derivatives while the methyl group in 2-methylpyrazine is three orders of magnitude more acidic than that in 2-methylpyridine. This is not consistent with the relative LD's. The observed order of the carbon acidity of these methyl groups is thought to be due mainly to the relative stability of the carbanions that are formed [79]. On the other hand closely related compounds in which the methyl groups have identical molecular environments usually show a correlation between their acidity and the LD of the atom to which they are bonded. This is clearly exemplified by 2-methyl-substituted imidazole systems (Table 14).

The chemistry of π-deficient heterocycles has several other interesting aspects. These include in particular the effect of π-deficient hetero rings on the reactivity of benzene rings condensed with them, the reactivity of systems consisting of a π-deficient and a π-excessive fragment, etc. However discussion of these points would take us beyond the confines of this review.

CONCLUSIONS

The problems associated with π-deficiency thus have much in common with those of π-excess. Our aim should primarily be to develop a single scale for π-excess and π-deficiency based on some easily measurable and reliable experimental parameter or on an adequate quantum-mechanical method. With this we could both clarify the relative π-deficiency of heterocyclic compounds and assign them more precisely to one particular class. Benzimidazole could act as this reference compound – in Albert's terminology it belongs with the π-excessive compounds (six π-electrons in a five-membered ring) but in addition it distinctly displays net π-deficiency.

Secondly chemists have to date used the concept of π-excess and π-deficiency mainly as a convenient model classification and have not given due attention to its use as a guiding principle in quantitative work on reactivity and physical properties. Expansion of this work would be useful and here progress in our knowledge of the mechanism of nucleophilic substitution reactions would have no small part. The π-acceptor ability, like the π-donor ability, is a parameter that is highly amenable to precise definition and measurement.

I thank Corresponding Member of the Academy of Sciences V. P. Mamaev and Professors O. N. Chupakhin and A. K. Sheinkman for valuable discussions of the questions dealt with in this review.

LITERATURE CITED

1. A. F. Pozharskii, Khim. Geterotsikl. Soedin., No. 6, 723 (1977).
2. A. Albert, Heterocyclic Chemistry. An Introduction, Athlone Press, University of London, London (1958); 2nd ed. (1968).
3. F. Wudl, M. L. Kaplan, B. K. Teo, and J. Marshall, J. Org. Chem., 42, 1666 (1977).
4. C. Hansch, J. Chem. Educ., 51, 360 (1974).
5. A. Szent-Györgyi, Introduction to a Submolecular Biology, Academic Press (1960).
6. M. A. Slifkin, Charge Transfer Interactions of Biomolecules, Academic Press, New York (1971).
7. H. Sigel and C. F. Naumann, J. Am. Chem. Soc., 98, 730 (1976).
8. N. E. Giacintov, T. Prusik, and J. M. Khosrofian, J. Am. Chem. Soc., 98, 6444 (1976).
9. A. Albert and W. L. F. Armarego, Adv. Heterocycl. Chem., 4, 1 (1965).
10. M. J. Cook, A. R. Katritzky, and P. Linda, Adv. Heterocycl. Chem., 17, 255 (1975).
11. M. Witanowski, L. Stefaniak, H. Jannszewski, and G. A. Webb, Tetrahedron, 27, 3129 (1971).
12. A. F. Pozharskii, Dissertation Submitted for the Academic Degree of Doctor of Chemical Sciences, Rostov State Univ., Rostov-on-Don (1972).
13. R. J. Pugmire and D. M. Grant, J. Am. Chem. Soc., 90, 697 (1968).
14. T. E. Peacock, J. Chem. Soc., No. 4, 1946 (1960).
15. P. J. Black, R. D. Brown, and M. L. Heffernan, Aust. J. Chem., 20, 1305 (1967).
16. J. E. Bloor and D. L. Breen, J. Am. Chem. Soc., 89, 6835 (1967).
17. J. Almlof, B. Roos, U. Wahlgren, and H. Johanson, J. Electron Spectrosc. Relat. Phenom., 2, 51 (1973).
18. P. C. Lauterbur, J. Chem. Phys., 43, 360 (1965).
19. T. Tokuhiro and G. Fraenkel, J. Am. Chem. Soc., 91, 5005 (1969).
20. R. J. Pugmire, D. M. Grant, M. J. Robins, and R. K. Robins, J. Am. Chem. Soc., 91, 6381 (1969).
21. E. Lucken, in: A. R. Katritsky, Physical Methods in Heterocyclic Chemistry, Vol. 6, Academic Press (1974).
22. L. N. Short, J. Chem. Soc., No. 12, 4584 (1952).
23. L. N. Short, J. Chem. Soc., No. 11, 4200 (1956).
24. S. F. Mason, J. Chem. Soc , No. 10, 3619 (1958).
25. J. D. S. Goulden, J. Chem. Soc., No. 7, 2939 (1952).
26. G. P. Syrova, Dissertation Submitted for the Academic Degree of Candidate of Chemical Sciences, Rostov State Univ., Rostov-on-Don (1973).
27. O. P. Shkurko, E. P. Khmeleva, S. G. Baram, M. M. Shakirov, and V. P. Mamaev, Khim. Geterotsikl. Soedin., No. 7, 996 (1978).
28. J. H. Blanch, J. Chem. Soc. B, No. 10, 937 (1966).
29. A. F. Pozharskii, A. D. Garnovskii, and A. M. Simonov, Usp. Khim., 35, 261 (1966).
30. V. I. Minkin and B. Ya. Simkin, Khim. Geterotsikl. Soedin., No. 5, 678 (1971).
31. A. F. Pozharskii, E. N. Malysheva, A. N. Suslov, and L. L. Popova, Khim. Geterotsikl. Soedin., No. 5, 692 (1979).
32. A. F. Pozharskii and A. M. Simonov, Chichibabin Amination of Heterocycles [in Russian], Rostov State Univ., Rostov-on-Don (1971).
33. R. J. Pugmire and D. M. Grant. J. Am. Chem. Soc., 90, 4232 (1968).
34. V. I. Minkin, A. F. Pozharskii, and Yu. A. Ostroumov, Khim. Geterotsikl. Soedin., No. 4, 551 (1966).
35. M. Begtrup, R. M. Claramunt, and J. Elguero, J. Chem. Soc., Perkin Trans. II, No. 2, 99 (1978).
36. L. N. Yakhontov, Usp. Khim., 37, 1258 (1968).
37. G. B. Barlin and D. J. Brown, in: R. N. Castle (editor), Topics in Heterocyclic Chemistry, Wiley, New York (1969), p. 122.
38. Z. Neimann, Experientia, No. 8, 996 (1975).
39. O. N. Chupakhin, Dissertation Submitted for the Academic Degree of Doctor of Chemical Sciences, Rostov State Univ., Rostov-on-Don (1977).
40. H. Balli, B. Hellrung, and H. Hinsken, Helv. Chim. Acta, 57, 1174 (1974).
41. H. Balli, B. Hellrung, and A. Kneubuhler-Hof, Helv. Chim. Acta, 57, 1178 (1974).
42. J. Degani, L. Lunazzi, and F. Taddei, Boll. Sci. Fac. Chim. Ind. Bologna, 23, 131 (1965).
43. S. Yoneda, T. Sugimoto, and Z. Yoshida, Tetrahedron, 29, 2009 (1973).
44. V. G. Kharchenko, S. N. Chalaya, and T. M. Konovalova, Khim. Geterotskil. Soedin., No. 2, 147 (1975).
45. A. K. Sheinkman, Dissertation Submitted for the Academic Degree of Doctor of Chemical Sciences, Rostov State Univ., Rostov-on-Don (1972).

46. A. R. Katritzky, C. R. Palmer, F. J. Swinbourne, T. T. Tidwell, and R. D. Topsom, J. Am. Chem. Soc., 91, 636 (1969).
47. A. R. Katritzky and F. J. Swinbourne, J. Chem. Soc., No. 12, 6707 (1965).
48. J. Chaudhuri, S. Kume, J. Jagur-Grodzinski, and M. Szwarc, J. Am. Chem. Soc., 90, 6421 (1968).
49. P. Kasai and D. McLeod, J. Am. Chem. Soc., 95, 27 (1973).
50. P. H. Kasai and D. McLeod, J. Am. Chem. Soc., 95, 4801 (1973).
51. J. Nenner and G. J. Schulz, J. Chem. Phys., 62, 1747 (1975).
52. V. Kalyanaraman, C. N. R. Rao, and M. V. George, J. Chem. Soc. B, No. 12, 2406 (1971).
53. K. B. Wiberg and T. P. Lewis, J. Am. Chem. Soc., 92, 7154 (1970).
54. S. Millefiori, J. Heterocycl. Chem., 7, 145 (1970).
55. O. N. Chupakhin, V. N. Charushin, I. M. Sosonkin, E. G. Kovalev, G. L. Kalb, and I. Ya. Postovskii, Khim. Geterotsikl. Soedin., No. 5, 690 (1977).
56. A. V. Lizogub and A. F. Pozharskii, Khim. Geterotsikl. Soedin., No. 1, 110 (1979).
57. A. V. El'tsov and M. Z. Girshovich, Zh. Org. Khim., 3, 1332 (1967).
58. V. Kampars and O. Neilands, Usp. Khim., 46, 945 (1977).
59. V. Kampars and O. Neilands, Zh. Obshch. Khim., 47, 442 (1977).
60. M. Feldman and S. Winstein, Theor. Chim. Acta, 10, 86 (1968).
61. H. Inone, S. Hayashi, and E. Imoto, Bull. Chem. Soc. Jpn., 37, 336 (1964).
62. H. J. Dauben and J. D. Wilson, Chem. Commun., No. 24, 1929 (1968).
63. R. Zahradnik and J. Koutecky, Adv. Heterocycl. Chem., 5, 69 (1965).
64. G. Illuminati, Adv. Heterocycl. Chem., 3, 285 (1964).
65. R. G. Shepherd and J. L. Fedrick, Adv. Heterocycl. Chem., 4, 145 (1965).
66. V. P. Mamaev, O. A. Zagulyaeva, and S. M. Shein, Khim. Geterotsikl. Soedin., No. 6, 723 (1973).
67. J. Reed, in: A. R. Katritzky, Physical Methods in Heterocyclic Chemistry, Vol. 6, Academic Press (1974).
68. J. F. Wolfe, J. C. Greene, and T. Hudlicky, J. Org. Chem., 37, 3198 (1972).
69. Gy. Simig, H. C. van der Plas, and C. A. Laudheer, Rec. Trav. Chim., 95, 113, 125 (1976).
70. J. A. Zoltewicz and L. S. Helmick, J. Am. Chem. Soc., 94, 682 (1972).
71. A. F. Pozharskii, A. M. Simonov, and V. N. Doron'kin, Usp. Khim., 47, 1933 (1978).
72. V. N. Doron'kin, A. F. Pozharskii, and I. S. Kashparov, Khim. Geterotsikl. Soedin., No. 2, 257 (1979).
73. G. B. Barlin and W. V. Brown, J. Chem. Soc. B, No. 7, 648, 736 (1967).
74. N. B. Chapman and D. Q. Russell-Hill, J. Chem. Soc., No. 6, 1563 (1956).
75. J. H. Hill and J. G. Krause, J. Org. Chem., 29, 1642 (1964).
76. J. H. Hill and J. H. Ehrlich, J. Org. Chem., 36, 3248 (1971).
77. A. Ricci and P. Vivarelli, Gazz. Chim. Ital., 97, 741 (1967).
78. A. F. Pozharskii, L. P. Smirnova, A. I. Belyashova, N. N. Zatsepina, and I. F. Tupitsyn, Khim. Geterotsikl. Soedin., No. 7, 961 (1979).
79. N. N. Zatsepina and I. F. Tupitsyn, Khim. Geterotsikl. Soedin., No. 12, 1587 (1974).
80. G. Klopman, J. Am. Chem. Soc., 90, 223 (1968).
81. I. S. Kashparov and A. F. Pozharskii, Khim. Geterotsikl. Soedin., No. 1, 124 (1971).
82. I. Degani, R. Fochi, and G. Vincenzi, Boll. Sci. Fac. Chim. Ind. Bologna, 23, 21 (1965).
83. I. H. Pitman and L. A. Sternson, J. Am. Chem. Soc., 98, 5234 (1976).
84. J. A. Zoltewicz, G. Grahe, and C. L. Smith, J. Am. Chem. Soc., 91, 5501 (1969).