HETEROCYCLIC CHEMISTRY: AN ACADEMIC SUBJECT OF IMMENSE INDUSTRIAL IMPORTANCE

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1. HETEROCYCLES IN CHEMISTRY AND LIFE

Heterocyclic chemistry is fundamental to all life. The essence of life is the ability to reproduce, and reproduction at its simplest is found in nucleic acids generating a second molecule while leaving the first untouched. Figure 1 shows a diagram of part of a nucleic acid in the double helix form. All nucleic acids are held in the helix by hydrogen bonds between the nucleic acids pairs uracil and adenine and cytosine and guanine. When the helix unwinds, each uracil unit of the single-strand nucleic acid attracts an adenine and helps it become incorporated in the newly forming strand, which will build the identical helix to that which occurred before the unwinding had taken place. Thus, one helix becomes two new ones, and the nucleic acid has reproduced itself.

2. HETEROCYCLIC CHEMISTRY AND INDUSTRY

Heterocyclic chemistry is of the utmost importance to industry in countless ways, some of which are given on this page. We cannot imagine a society without access to the benefits of synthetic heterocycles.

The immense variety of organic structures is illustrated in Fig. 2, which compares the number of different isomers that can be constructed from say, 100 atoms with the number of atoms in the earth, the solar system, our galaxy, and the whole universe. This enormous diversity illustrates the fact that we cannot hope to make all possible compounds in any given set, and

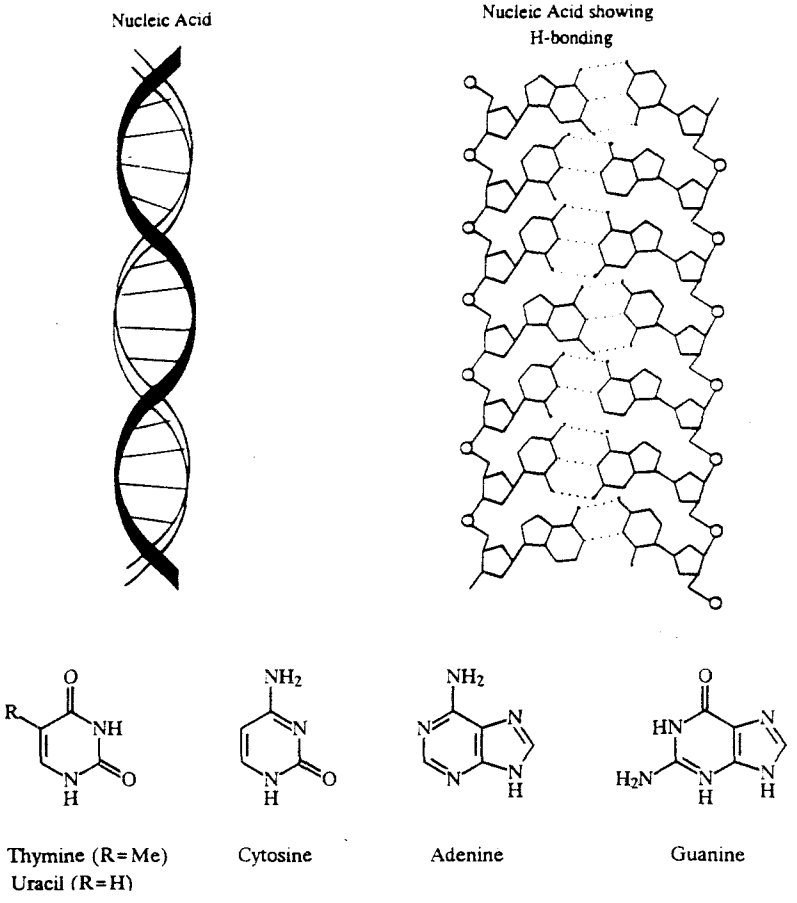

Fig. 1

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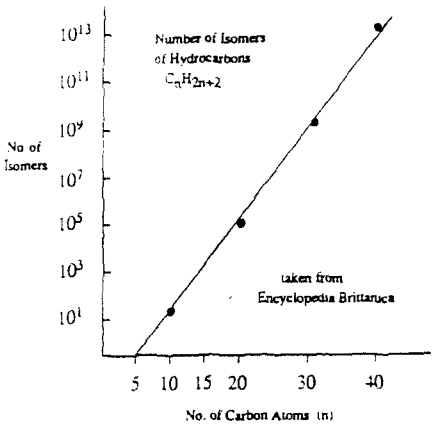
Immense Variety of Organic Molecules



The Earth

Volume = 1.1 10^{27} cu meters

Density = 5.52 g/cc

No of atoms (average AW 12) = 10^{54}

The Universe

No of atoms - 10^{80}

The Solar System

No of atoms - 10^{60}

The Galaxy

No of atoms - 10^{70}

Estimated number of compounds that could be constructed from 100 heavy atoms is 10^{50}

Fig. 2

Monocyclic Ring Systems

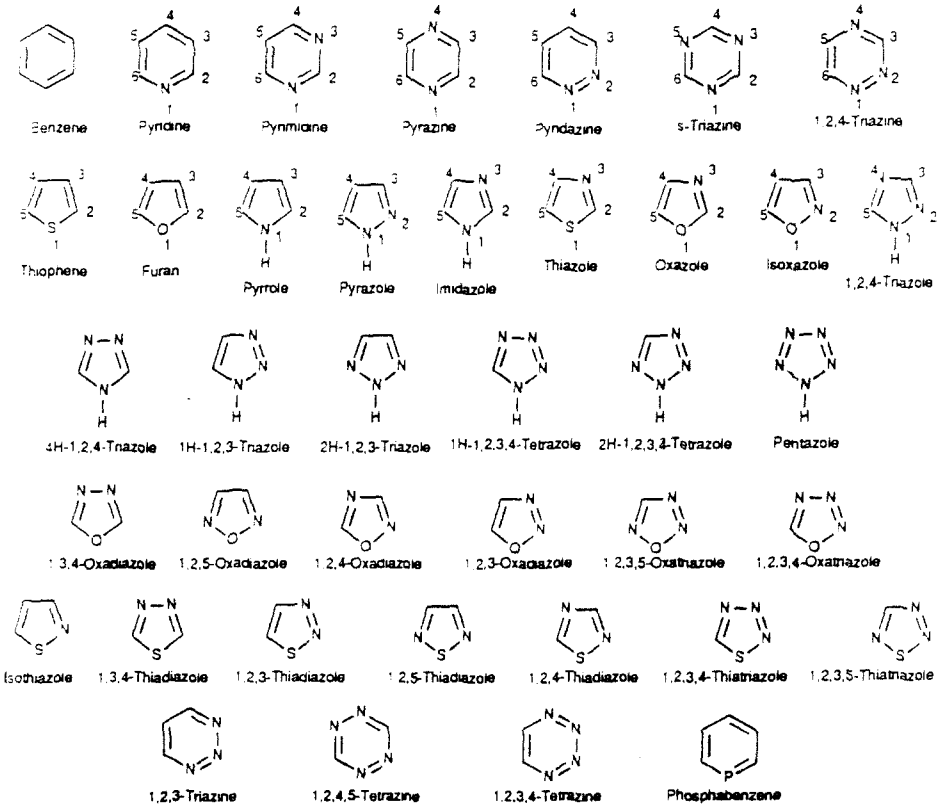


Fig. 3

The Importance of Heterocycles to Industry

A. Natural Pharmaceuticals

1. Antibiotics (penicillin, cephalosporin)
2. Alkaloids (vinblastine, ellipticine, morphine, reserpine)

3. Cardiac glycosides (digitalis)

B. Synthetic Heterocyclic Pharmaceuticals

1. Anticancer agents
2. Analeptics
3. Analgesics
4. Hypnotics
5. Vasopressor modifiers

C. Other Synthetic Biologically Active Heterocycles

1. Pesticides
2. Insecticides
3. Weedkillers
4. Rodenticides

D. Miscellaneous Application of Heterocyclics

1. Dyestuffs
2. Copolymers
3. Solvents
4. Photographic sensitizers/developers
5. Antioxidants/vulcanization accelerators
6. Intermediates used in synthesis

leads to the conclusion that we have to make the very best use of all available tools that will allow us to predict properties from structure, and thus guide our research in the most effective ways.

It is the intention of this lecture to give an account of some of the work presently going on which is designed to help to increase our knowledge of the immense field of heterocyclic chemistry and to discover fundamental relationships which will help us to understand the connections between the structural formula and the chemical, physical, and biological properties of the molecules.

3. HETEROAROMATICITY

The 39 monoclinic ring systems shown in Fig. 3 are all heteroaromatic. The concept of aromaticity as a qualitative concept is a familiar one, and some of the criteria most frequently used are given in Fig. 4.

In addition to qualitative effects, aromaticity is clearly also a quantitative concept; some compounds are distinctly more aromatic than others, as is shown in Fig. 5. However, there have been great difficulties in obtaining a quantitative scale of aromaticity, and some of these are listed in Fig. 8. Indeed, the difficulties in the precise definition and measurement of aromaticity have been such that certain very eminent chemists have even suggested that the concept be abandoned. However, one has to be very eminent to make such a suggestion. Anybody who has any contact with the teaching or practice of chemistry knows that it would be quite unthinkable to abandon aromaticity from a practical point of view.

Difficulties of Establishing a Quantitative Aromaticity Scale

(I) Experimental measures of any one parameter are frequently not available for a full range of compounds.

(II) Errors in experimental measurements arise from the need to use data obtained by different investigators at different locations, or from the fact that they often represent small differences between large measured values.

(III) Most theoretical MO methods require the assumption of parameters for heteroatoms and there is no general agreement on the values to be taken for these parameters.

(IV) A particular uncertainty, affecting theoretical and experimental methods alike, is the need for comparison of actual aromatic compounds with nonaromatic models; the precise definition of these models is not easy.

4. PRINCIPAL COMPONENT ANALYSIS AND THE MANIPULATION OF DATA SETS

In these circumstances, we undertook the Principal Component Analysis of a number of characteristics that have long been considered fundamentally due to aromatic character [1].

The basic equation of Principal Component Analysis is shown in Fig. 6. It is well known that aromaticity has a major effect on the geometrical, the energetic, and the magnetic properties of molecules. Because of this, we selected criteria of these types, where I_5 and I_6 are the Bird aromaticity indices, RC is Jug's Index, and ΔN measures the differences in bond order as proposed by Pozharskii. The energetic criteria include both resonance energies and heats of formation. The magnetic criteria include the magnetic susceptibility, the exaltation, and the n.m.r. chemical shift. Because some of these criteria can be calculated in more than one way, we came up finally with a set of 12 characteristics.

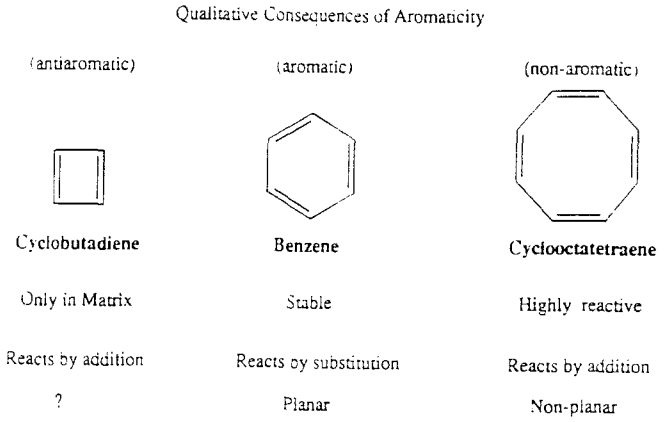


Fig. 4

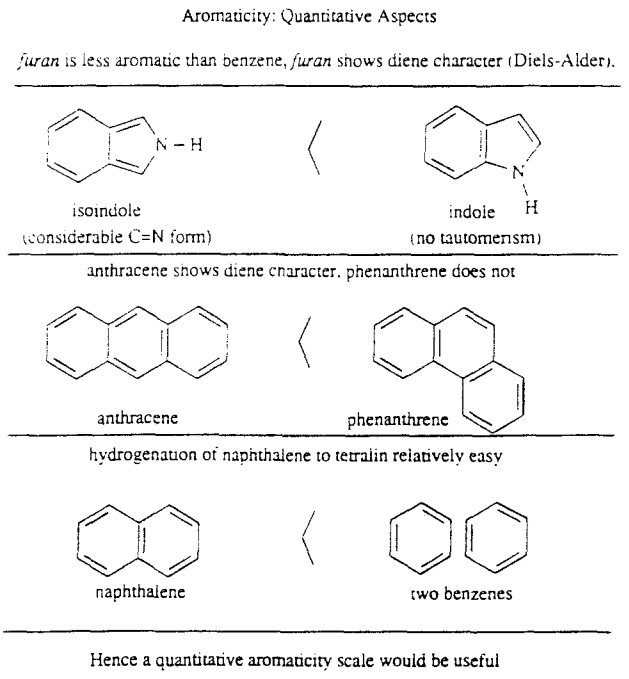


Fig. 5

Geometrical Criteria

I_5 and I_6 — the aromaticity indices of 5- and 6-membered rings
RC — the magnitude of ring current (RC) as determined by the weakest link in the ring (lowest values of bond order) (Jug's index)
ΔN — the differences in bond order

Energetic Criteria

DRE — the Dewar resonance energy
HSRE — the HessSchaad resonance energy
ΔH_f — the heat of formation

Magnetic Criteria

χ_M — the molar magnetic susceptibility
Λ — the diamagnetic susceptibility exaltation
^{15}N n.m.r. — the average N-15 chemical shift

Principal Component Analysis

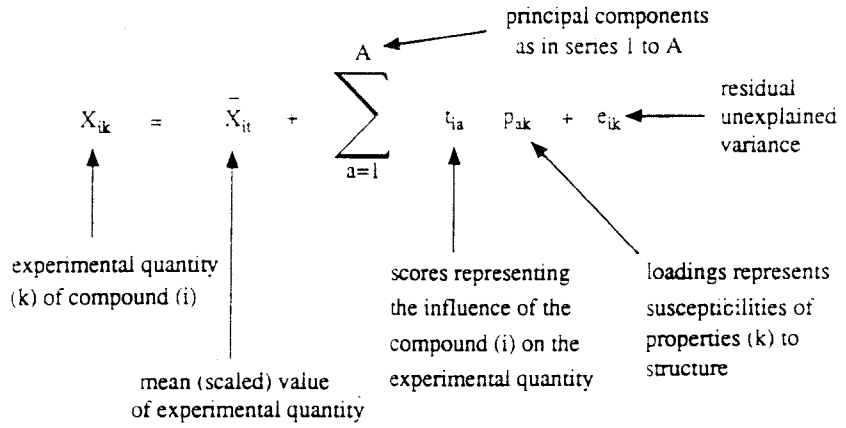


Fig. 6

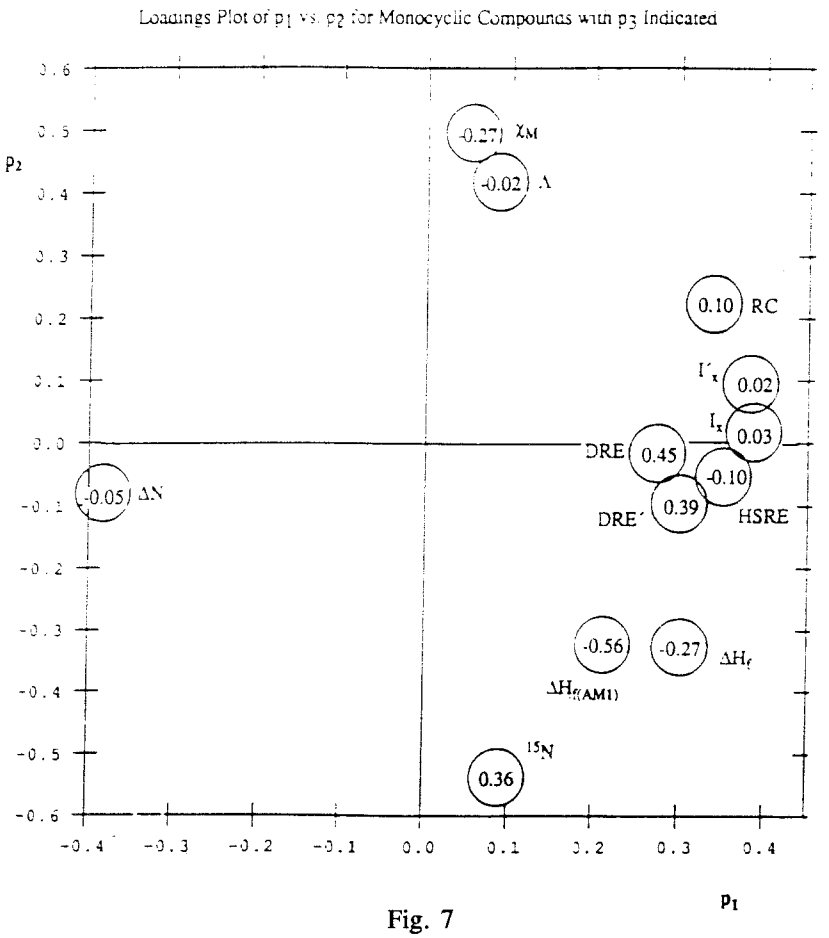


Fig. 7

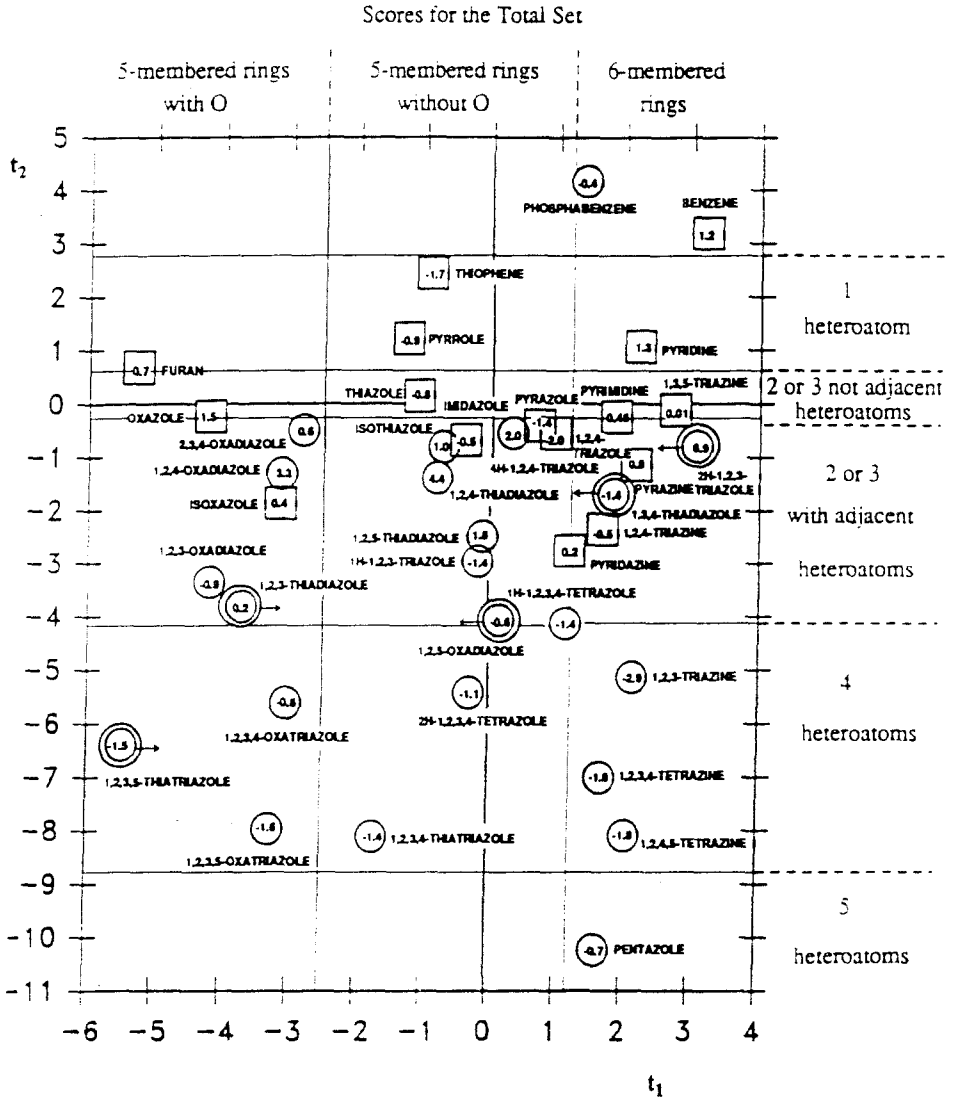


Fig. 8

Heterocyclic Tautomerism: 2-Pyridone

exists in crystalline state
dominant in aqueous solution by
factor of ca 1000 : 1

dominates in vapor phase by
factor of ca 2 : 1

Fig. 9

The results of the Principal Component Analysis disclose three principal components, of which two are highly significant. A loadings plot for the 12 characteristics is given in Fig. 7. It will be seen that these characteristics fall into three groups: those (most of the geometrical criteria) which are described almost entirely by the first principal characteristic p_1 with very small components from p_2; those (the magnetic criteria) which are described almost entirely by p_2 with very small components from p_1; and a third group including the heats of formation and RC, which have considerable components from both p_1 and p_2.

We believe that to a considerable extent, this resolves the apparent impasse between classical and magnetic aromaticity, and provides a firm basis for the consideration of aromaticity as a quantitative concept. It turns out that there are at least two

types of aromaticity. The best available measure of classical aromaticity is provided by the Bird $I_{5,6}$ parameter, and this parameter correlates well for ΔN and for DRE. The second type of aromaticity is magnetic aromaticity, which is best measured by the molar magnetic susceptibility χ_M.

The scores plot for the 39 compounds is given in Fig. 8. It is seen that the classical aromaticity is influenced mainly by the nature of the heteroatoms in the ring, and by the ring size: t_1 is greatest for six-membered rings, intermediate for five-membered rings without oxygen, and least for five-membered rings with oxygen. The measure of magnetic aromaticity (t_2) is influenced mainly by the number of heteroatoms in the ring, and by whether or not they are adjacent. Thus, it is the most positive for benzene or for heterocycles containing just one heteroatom; next, for those with two or three heteroatoms, but with the heteroatoms not adjacent; then comes two or three heteroatoms with at least two adjacent; followed by four and finally five heteroatoms.

We therefore gain an understanding of aromaticity. However, in addition, the technique provides considerable predictive power; we are able to measure this statistically and to show that there are very good grounds for believing that we will be able to progress in the prediction of chemical and physical properties by statistical approaches of this type [2].

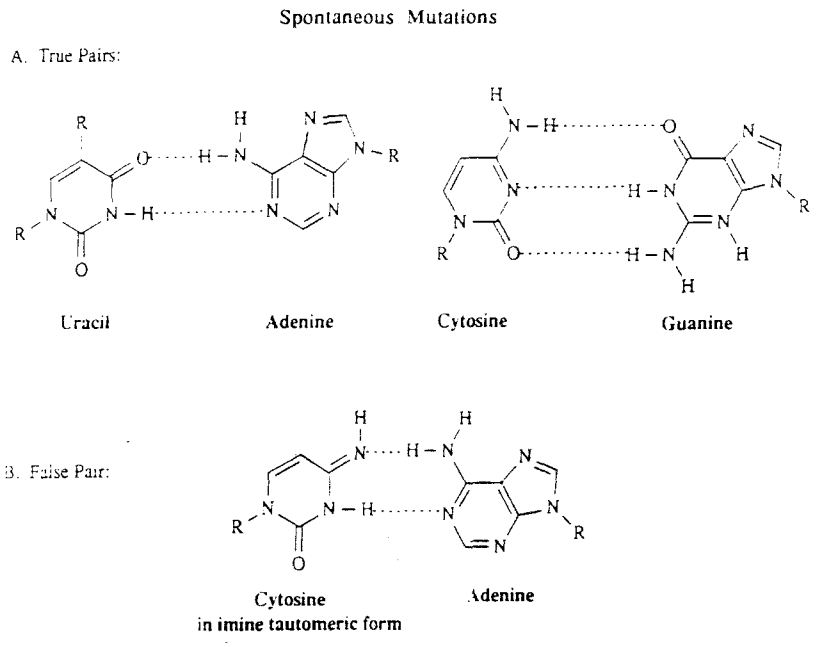


Fig. 10

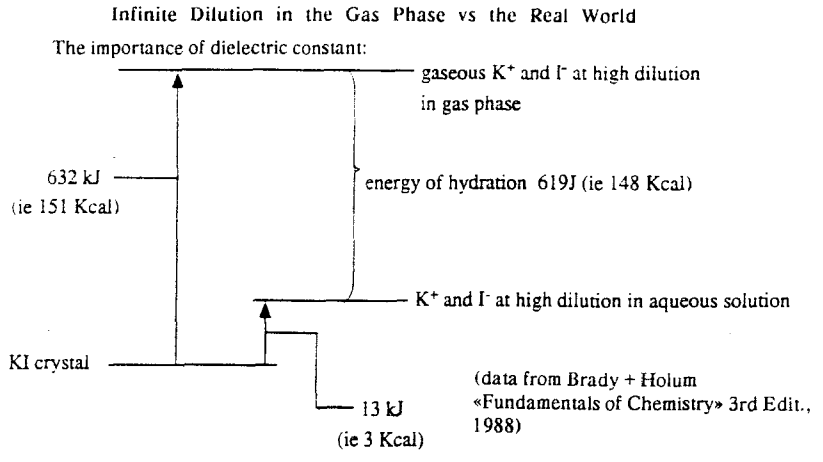


Fig. 11

5. HETEROCYCLIC TAUTOMERIC EQUILIBRIA

Figure 9 illustrates the phenomenon of heterocyclic tautomerism, where the compound 2-hydroxypyridine can exist either as such, or in the carbonyl form of 2-pyridone. This concept is of the greatest importance with relevance to the nucleic acids. In Fig. 10, the base pairing referred to above is shown, but in addition to the true base pairs of uracil and adenine, and cytosine with guanine, we also show the false base pair between cytosine and adenine. In this false pair, the cytosine is shown, not in its normally stable amino form, but in the imino form, in which it acts as a mimic of uracil. It is believed that spontaneous mutations occur because of the small possibility of such false base pairing. Clearly, tautomeric equilibrium constants are therefore of considerable biological importance.

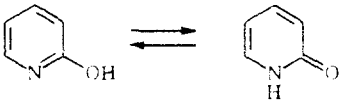
One of the difficulties in such calculations using Molecular Orbital Theory has been that the results normally refer to the state of infinite dilution in a vacuum and this, as illustrated in Fig. 11, is very different from the real world situation. This is particularly gross for charged molecules, as in the example given, but still very important for molecules which, while not containing an integral charge, have a dipole moment. This includes most real molecules.

There have been many attempts to calculate tautomeric equilibrium constants, as illustrated by Fig. 12 for 2-pyridone. It is seen that to get a reasonable agreement for the vapor phase result, one needs to use quite a sophisticated ab initio calculation, but that a result just as good is obtained by using the new AM1 semiempirical method of Dewar. Recently, by a combination of the new AM1 semiempirical theoretical method, and Reaction Field Theory, as illustrated in Fig. 13, it has become possible to reach reasonable calculations for a variety of tautomeric pyridines, as illustrated in Fig. 14 [3]. Here, 12 different compounds have been considered. For ten of these, quantitative experimental measurements are available, and for the other two, qualitative. The calculated results are in extremely good agreement (with the one exception of 3-hydroxypyridine), and this indicates that we are now really able to use readily available programs on small computers to give us results of true physical significance (cf. also [4]).

6. AQUATHERMOLYSIS OF ORGANIC COMPOUNDS

I would like now to illustrate an ideal example of academic—industrial collaboration by reference to an extensive program on the aquathermolysis of organic compounds that as been supported by the Exxon Corporation at the University of Florida.

Attempts to Calculate
Tautomeric Constant 2-Hydroxypyridine to 2-Pyridone



Experimental Data

Vapor Phase	OH favored by 0.4 kcal
Aqueous Solution	C=O favored by 4.2 kcal
Crystalline state	Only C=O form

Ab - initio Calculations - Vapor Phase

STO - 3G	C=O by 15.4 kcal
3 - 21G	OH by 1.7 kcal
MP 2/6 - 31G*	OH by 0.6 kcal

Semi-empirical Calculations - Vapor Phase

MNDO/2	C=O by 14.2 kcal
MNDO/3	C=O by 3.7 kcal
CNDO/2	OH by 11.3 kcal
AM1	OH by 0.55 kcal

Fig. 12

Basis of Dielectric Correction

$$E = \langle\psi | H_o | \psi\rangle - \frac{M^2}{2}\left\{\frac{2(\mathcal{E}-1)}{r_c^3(2\mathcal{E}+1)}\right\}$$

where $M = \langle\psi | \underline{\mu} | q\rangle$ and $\mathcal{E}$ = bulk dielectric constant

$$r_c = \text{cavity radius} = \sqrt[3]{\frac{3V_c}{4\pi N_a}}$$

solved using $[f_o - \mu g M]\,\varphi_i = \mathcal{E}_i\varphi_i$

Fig. 13

Comparison of Experimental and Calculated log K_T Values for Aqueous Solution
(Positive Values Indicate the Predominance of Pyridinoid Form)

X	Calc.	Exp.	Calc.	Exp.	Calc.	Exp.
O	-2.8	-3.1	6.7	0.1	-3.0	-3.3
S	-4.7	-4.7	-2.4	-2.2	-7.3	-4.6
NH	7.8	6.0	20.0	(large)	7.2	8.7
CH_2	14.8	13.3	25.7	(large)	14.8	13.4

Fig. 14

Aquathermolysis is defined as the behavior under the simultaneous influence of heat and water. Water changes its character very considerably as the temperature increases. In particular, its high dielectric constant (78 at 20°C), which is caused by the extensive hydrogen bonding of the ice crystal being largely retained in the liquid at lower temperature, rapidly decreases on increasing the temperature because of the breakup in this hydrogen bonding. Thus, at around 200°, water becomes an excellent solvent, not only for polar, but also for nonpolar compounds.

A study of aquathermolysis is both of great academic and of great industrial importance. It is an example of a field which has remained essentially untouched and has led to the formulation of a most interesting scenario of unusual properties and reactions.

Academic Importance of Aqueous Organic Chemistry Research

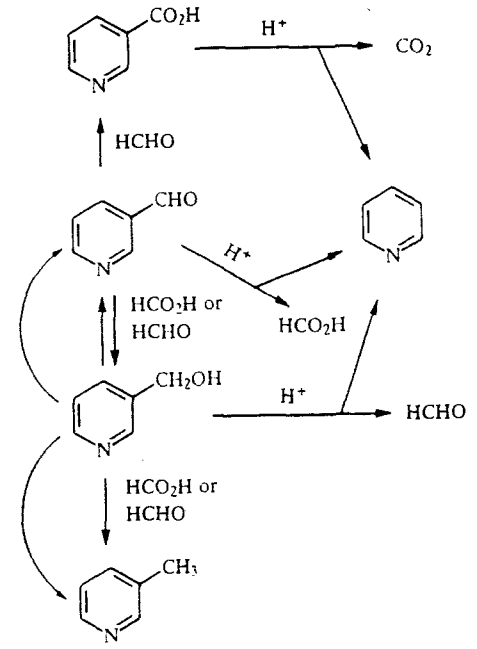
(a) Large number of novel reactions
(b) Reactivity increase with temperature particularly large because of increased dissociation to OH^- and H_3O^-
(c) Kinetics of successive reactions
(d) Autocatalysis

Industrial Importance of Aqueous Organic Chemistry Research

Kerogens are formed (diagenesis) and depolymerized (catagenesis) in aqueous environments (60-130°C) to generate petroleum.

We have looked carefully at the behavior of a wide range of organic compounds under aquathermolysis conditions. A fairly simple example is shown by the reaction pathways of 3-substituted pyridines in Scheme 1 [5]. Under the particular conditions utilized, pyridine and 3-picoline are the synchs, but there is interconversion between the alcohol and the aldehyde, and between these compounds, the acid, and pyridine and 3-picoline. In a scheme of this degree of simplicity, it is quite feasible to consider a kinetic model in which the reactions are found to have specific first-order or second-order rate constants.

3-Substituted Pyridines: Reaction Scheme (1)



A more complex example is shown for 2-substituted pyridines in Scheme 2. The situation is now very much more complex, because not only have we possibilities found in the 3-substituted series, but now a large number of condensation products can be formed by reactions involving two different molecules [6]. In the four years of the program on aquathermolysis, many hundreds of reactions have been investigated in this way.

Some of the results of our aquathermolysis research are summarized here. The first batch of 15 papers summarizing this work will be submitted for publication shortly. We believe that a sound science base has now been established in this important field.

Products from 4-ethylaniline (10% aq. H_3PO_4, 250°C, 3 days)

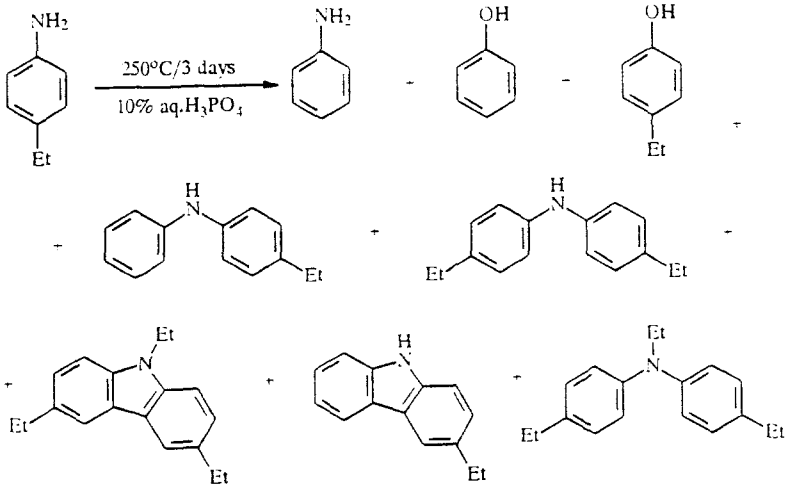
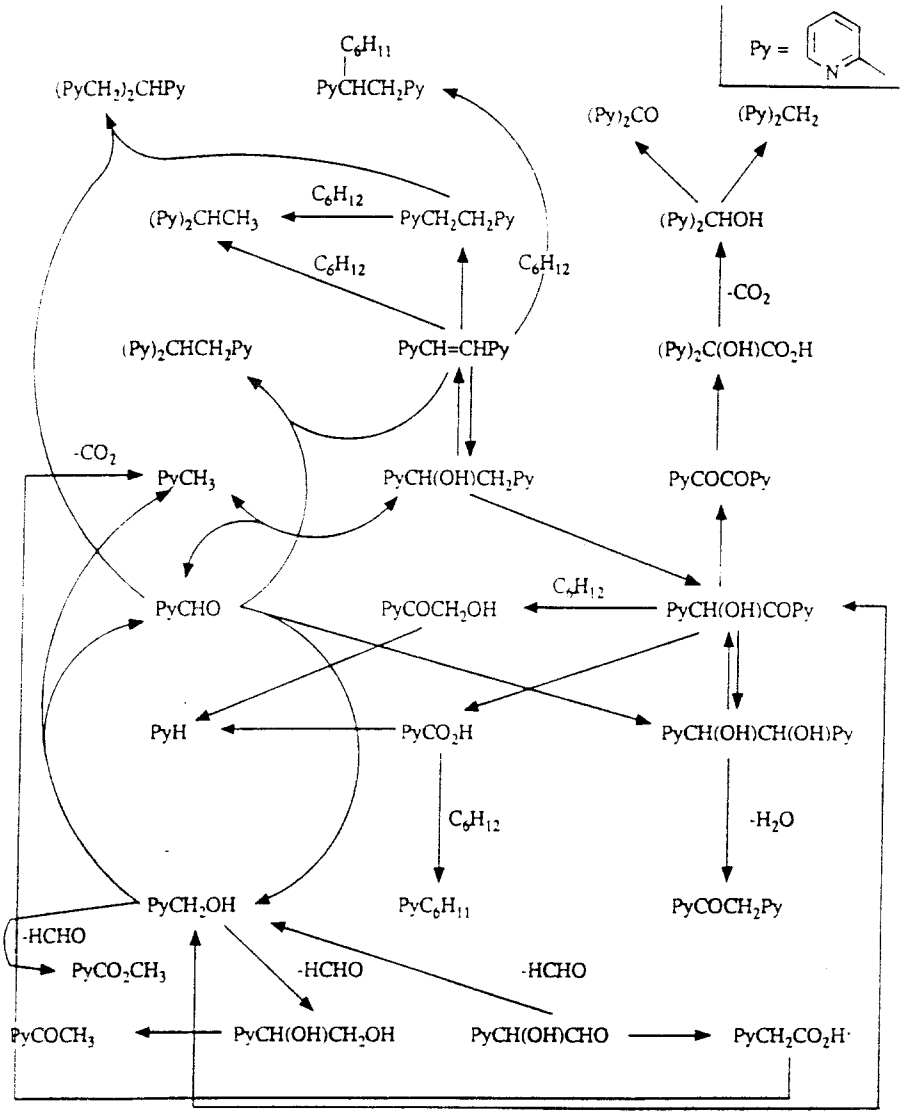
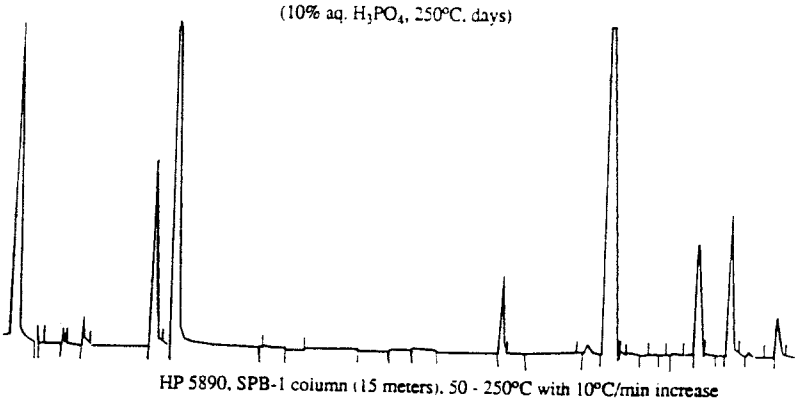


Fig. 15

2-Substituted Pyridines: Reaction Scheme (2)

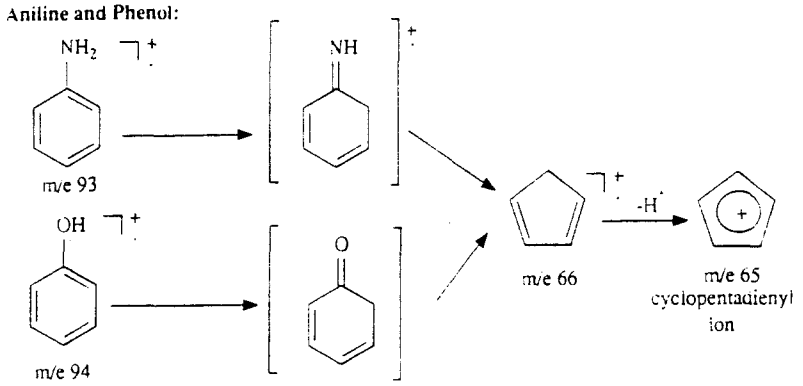


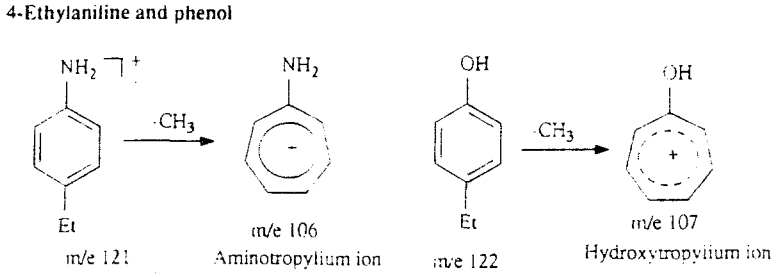
GC Trace of Reaction of Products of 4-Ethylaniline
(10% aq. H_3PO_4, 250°C, days)



HP 5890, SPB-1 column (15 meters), 50 - 250°C with 10°C/min increase

Fig. 16





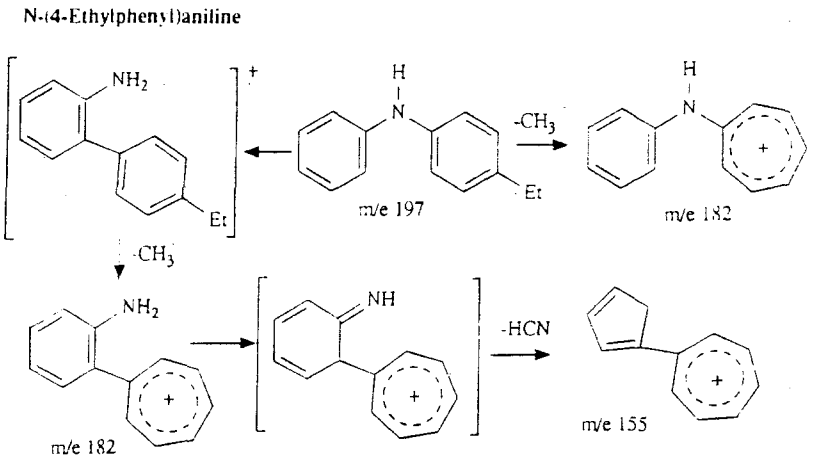


Fig. 17

Summary of Progress in Aqueous Chemistry 1985-1991

Ionic chemistry predominates
Water can behave like an amphoteric catalyst
Many side chains are cleaved
Cleaved fragments can behave as catalysts, reactants
Bonds formed as well as broken
Thermal pathways compete in more reactive systems
Large range of reactivity and stability of organic functional groups
Comprehensive kinetic analysis feasible

TABLE 1 Weights and Averages of the Variable Included in the PLS Analysis*

No.	Symbol	Variable	No.	Symbol	Variable
1	RF_{Dietz}	Response Factor	10	C=N	No. of C=N Double Bonds
2	MW	Molecular Weight	11	C≡N	No. of C≡N Triple Bonds
3	C	No. of C Atoms	12	Rings	No. of Rings
4	H	No. of H Atoms	13	$-CO_2H$	No. of Carboxyl Groups
5	O	No. of N Atoms	14	—OH or —SH	No. of Hydroxyl Groups
6	N	No. of M Atoms	15	—CHO	No. of Aldehyde Groups
7	S	No. of S Atoms	16	$C-CO_2-C$	No. of Ester Grops
8	C=C	No. of C=C Double Bonds	17	$-NH_2$	No. of Amino Groups
9	C=O	No. of C=O Double Bonds	18	C—O—C or C—S—C	No. of Ether or Sulfide Groups

* Variable 2—18 are the «explanatory» variables (X Block); variable 1 is the dependent variable.

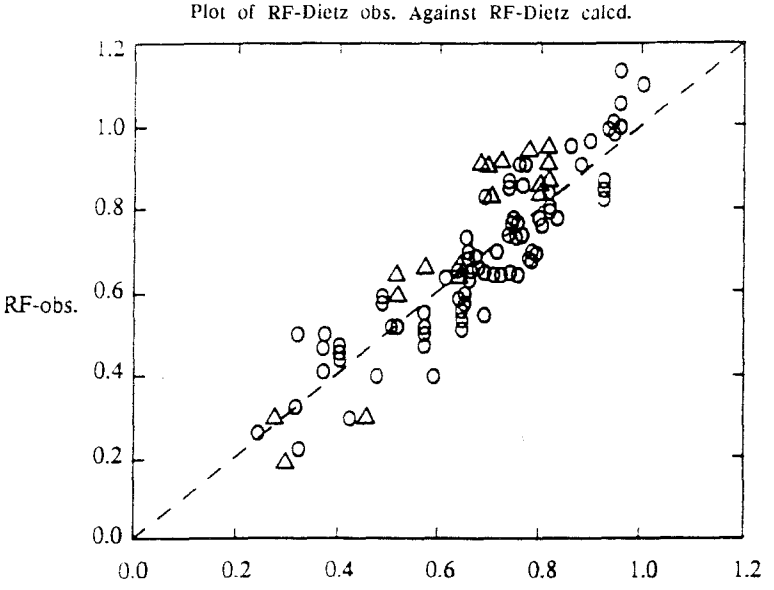


Fig. 18

7. CALCULATION OF GC-RESPONSE FACTORS

In the aquathermolysis research just mentioned, it was necessary to analyze complex reaction mixtures, as illustrated, for example, in Fig. 15.

Using a combination of gas chromatography and mass spectroscopy, the analytical chemist now has an immensely powerful tool for such work. Thus, the gas chromatograph resolves the mixture into its individual components, and the mass spectrum of each component is taken individually, and then this allows the identification of the structure of that component. The setup is illustrated in Fig. 17 for the gas-chromatographic separation, and in Fig. 16 the mass spectral fragmentation pattern can be used to deduce the structure.

In this way, the analytical chemist is able to carry out a qualitative analysis of a complex mixture. However, to convert this qualitative analysis to a quantitative analysis, it is necessary to know the relationship of the area under the peak in the gas chromatograph, and the weight of the compound causing the peak. This is known as the response factor. The classical way of measuring a response factor is quite simply to take authentic specimens of each compound and to run the gas chromatogram and measure the relationship of the weights directly. However, in the work referred to previously, this was not possible because many of the products were not available, and some of then were even unknown.

In these circumstances, we have carried out a Principal Component Analysis using molecular descriptors [7]. The descriptors are shown in Table 1, and in Fig. 18 the calculated vs. predicted response factors are shown both for the 100 compounds used in the Principal Component Analysis and also for 20 extra compounds. It is seen that an average error of 8% is achieved. While the error is still appreciable, it is certainly a far better procedure than giving all response factors as equal to unity, which would lead to gross errors in the interpretation.

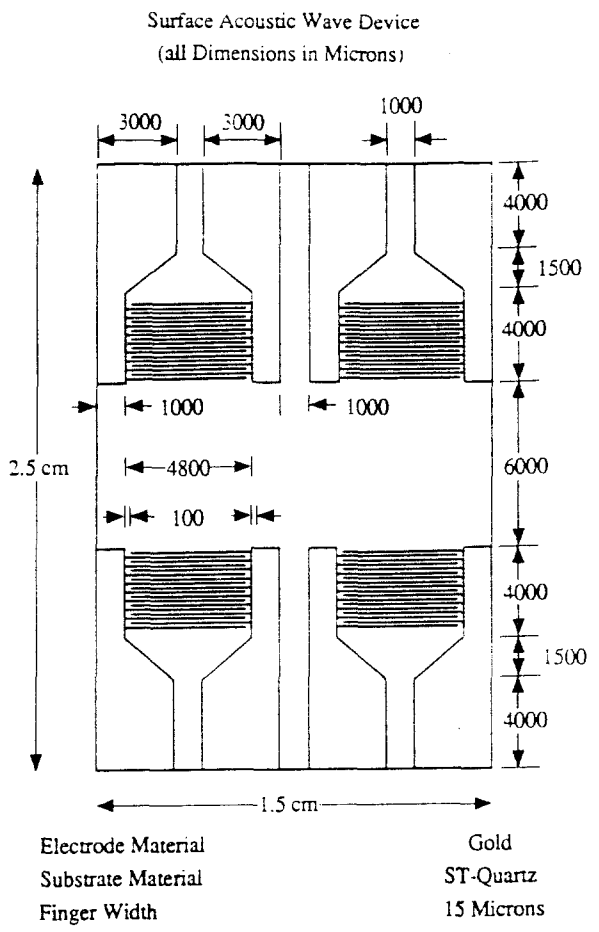


Fig. 19

8. CHEMICAL SENSORS

Chemical sensors are of wide potential utility [8]. Their definition and potential for development are given below. Potential applications include numerous safety devices in manufacturing plants, a wide range of environmental uses, testing for spoiling of foodstuffs, and many others.

Today's sensors are still rather clumsy; a typical example is shown in Fig. 19. However, the microelectronic engineering aspects of sensor technology are receiving much attention, and it is expected that the dimensions will decrease by a factor of 100, and that the sensitivity will increase by a factor of 100 within the next decade. This will allow, above all, the construction of arrays of sensors, in which many different materials can be sensed for at the same time.

We have looked at sensors under contract from the Department of Defense for their possibility for agent detection. We have examined a wide range of new coatings, frequently containing hetrocyclic compounds. In Fig. 20 three examples are shown which illustrate the selectivity for three different compounds: to the agent simulants, dimethyl methylphosphonate and chloroethyl ethyl sulfide, and to water. It will be seen that these three different compounds can be readily detected in the presence of each other, and even a semiquantitative analysis carried out.

Figure 21 gives some illustrations of organic synthesis, which have been used for the preparation of these materials for sensor coatings. The particular example given is the synthesis of a pyridinium salt from a pyrylium analog. We have been trying to vastly extend the range of organic compounds that have been used in sensor coatings, and in this context we have synthesized a wide variety of new derivatives, including pyridines [9], dihydronicotinic acid derivatives [10], phosphonic acid and esters [11], thiadiazoles [12], and other compounds.

9. ORGANIC SYNTHESIS

Organic synthesis can be carried out for a variety of reasons, some of which are given below. In the work to be described here, we are interested particularly in point 4, and also in point 3 as a help to achieving point 4 more easily.

We have looked recently particularly at the chemistry of benzotriazole, some of whose characteristics are given in Fig. 22. Benzotriazole is a readily available, inexpensive material which possesses some outstandingly useful characteristics. It is readily introduced into an organic compound, confers useful properties while it is there (behaving as a tame halogen substitute), and can easily be displaced in various ways. Thus, whereas α-halogeno amines and ethers are dangerous physiologically active compounds, the benzotriazole analogs are stable, nonvolatile, and much safer analogs.

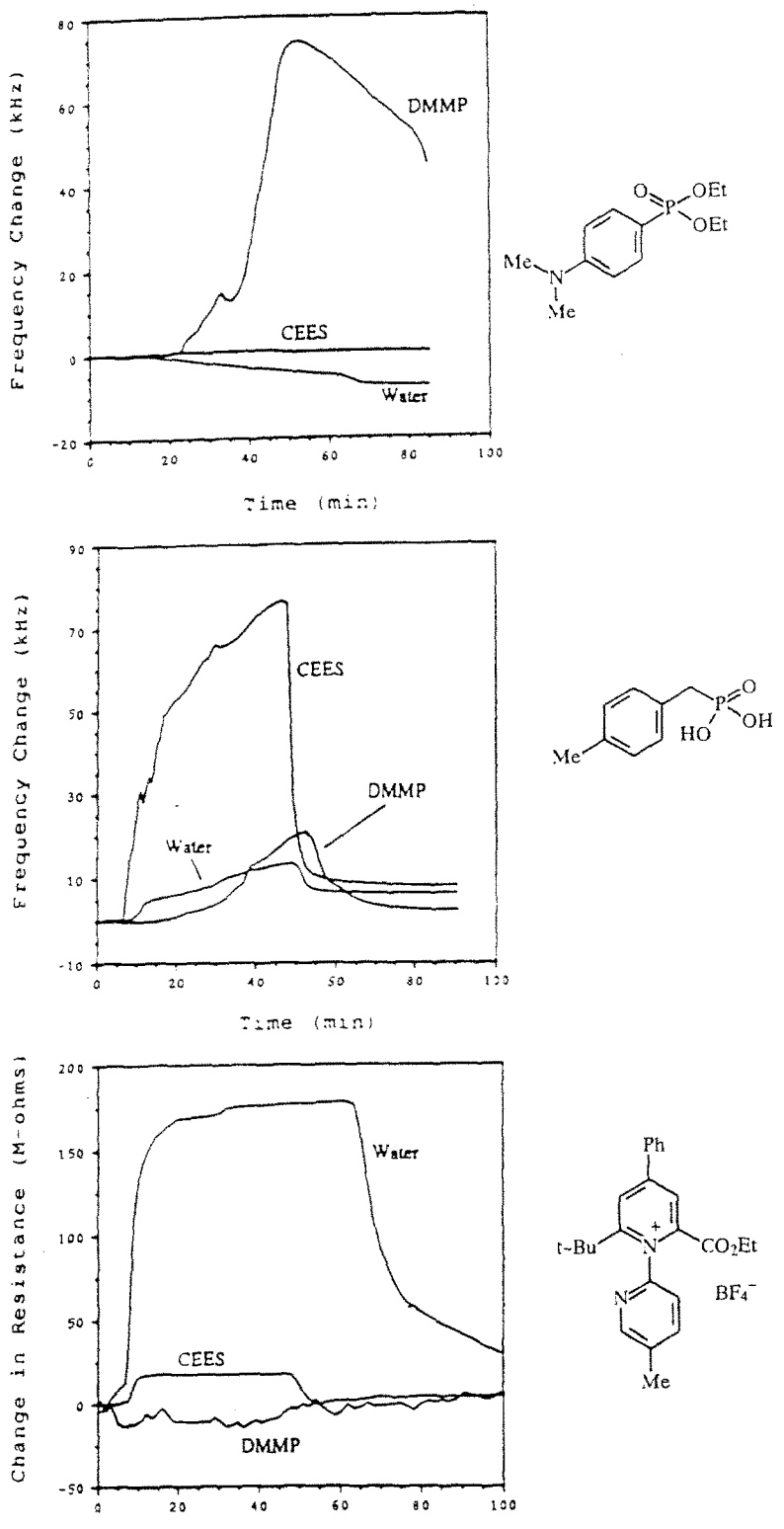


Fig. 20

With the use of benzotriazole we have been able to develop new syntheses for a wide variety of amines. In Fig. 23 the methods are shown diagrammatically for the preparation of a wide variety of different types of amine, each using an organometallic derivative and a synthon for an α-amino carbocation. All these synthons are available by utilizing N-benzotriazolyl groups.

Synthesis of a Heterocyclic Material for Sensor Coating

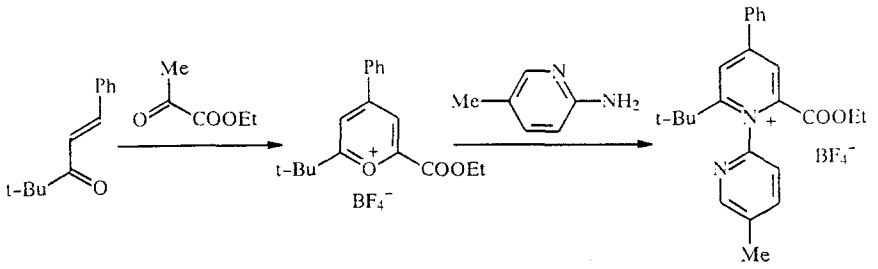


Fig. 21

Benzotriazole — A Tame Halogen Substitute

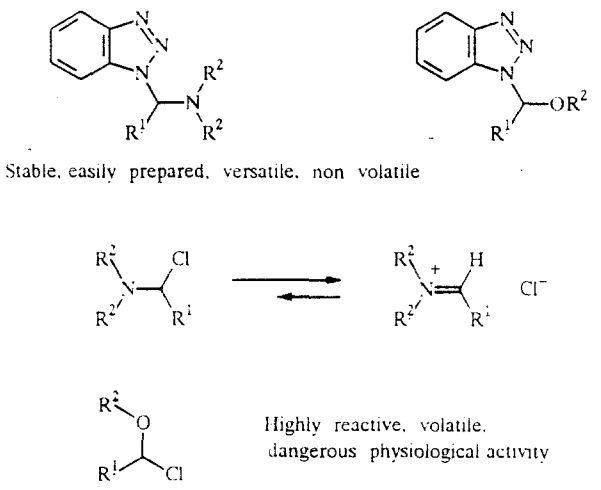


Fig. 22

Development of New Microsensors

Coatings Desiderata

1) Selectivity to vapors
2) Sensitivity to vapors
3) Form stable films on aqueous media
4) Transfer easily and reproducibly to surface acoustic wave (SAW) devices
5) Coatings show reversibility
6) Chemically and physically durable

Candidates

1) Pyridine N-oxides
2) Acridinium betaines
3) Pyridinium salts
4) Metal chelators
5) Phosphonic acids and esters
6) Other heterocyclic systems

Organic Synthesis — Justifications

1. The confirmation of the structure of a natural product (outmoded).
2. As an intellectual exercise (the Mt. Everest syndrome).
3. To gain understanding of reactivity and extend knowledge base.
4. To synthesize products more effectively, selectively, safely, and cheaply.

Synthons for the Preparation of Amines Using Carbanions
(RMgBr, RLi or $NaBH_4$)

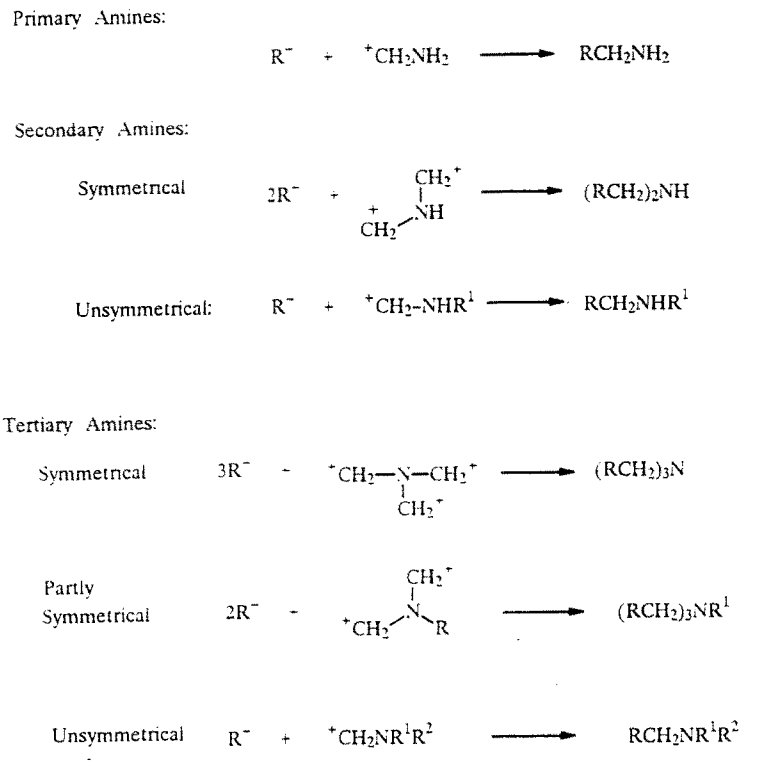


Fig. 23

N,N-Dialkylhydrazines

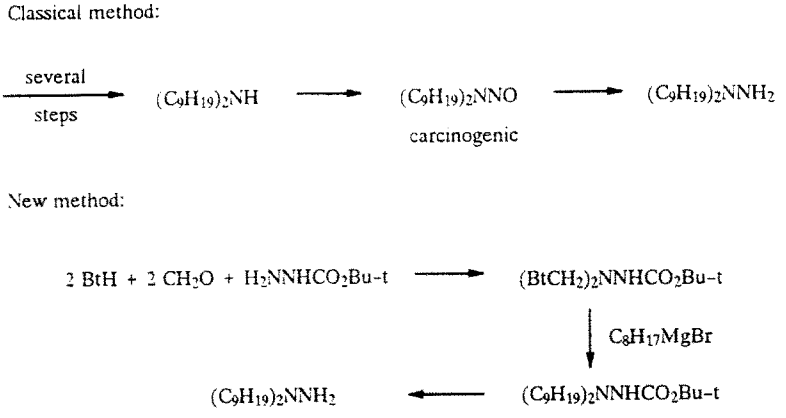


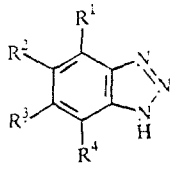
Fig. 24

Many of these methods are the preferable ones for the preparation of these industrially important amine derivatives from the point of view of convenience and efficiency. Full details of this work have been published or are presently in press [13, 14].

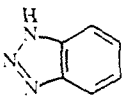
Benzotriazole can be used in many other synthetic applications, one of which is outlined in Fig. 24. The classical method for the preparation of 1,1-dialkylhydrazines involves the conversion of the corresponding secondary amine (itself needing several steps to prepare) through the corresponding N-nitroso derivative into the desired hydrazine. Unfortunately, N-nitroso compounds are known to be highly carcinogenic. By contrast, our new method [15] involves three simple stages from easily available starting materials and avoids the hazardous N-nitroso compound.

Structure Search: Available Benzotriazoles

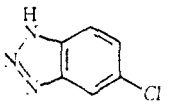
Target Substructure:



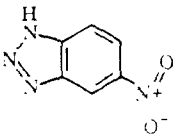
Structures Retrieved:



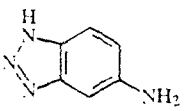
Benzotriazole



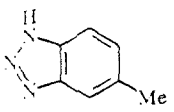
5-Chlorobenzotriazole



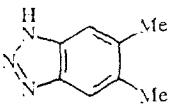
5-Nitrobenzotriazole



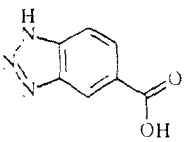
5-Aminobenzotriazole



5-Methylbenzotriazole



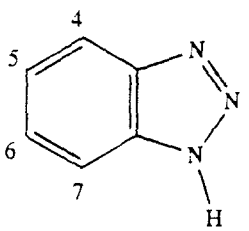
5,6-Dimethyl- 1H-Benzotriazol



Benzotriazole-5- Carboxylic Acid 99%

Fig. 25

Available N-Unsubstituted C-Substituted Benzotriazoles



parent

4-Substituted : Me

5-Substituted : Cl, NO_2, NH_2, Me, CO_2H

5,6-Disubstituted : di-Me

Details of 5-Nitro-, 5-Amino- and 5-Carboxy-6-benzotriazoles

5-Aminobenzotriazole	K & K	K21269	3325-11-9
	Lancaster	LAN-6660	3325-11-9
5-Nitrobenzotriazole	Aldrich	17618-4	2338-12-7
	Chemalog	66-4020-00	2338-12-7
	Frinton	FR-0235	2338-12-7
	P & B	N07290	2338-12-7
	TCI	N0173	2338-12-7
Benzotriazole-5-carboxylic acid	Aldrich	30423-9	23814-12-2

Fig. 26

10. LITERATURE OF HETEROCYCLIC CHEMISTRY

Heterocyclic chemistry has an enormous literature. There are many ways of accessing this literature. Classically, it has been done by means of compendia, which can be comprehensive (such as *Chemical Abstracts* or *Beilstein*) or which can be selective (such as *Comprehensive Heterocyclic Chemistry* or *Advances in Heterocyclic Chemistry*). However, more and more it becomes important to use computational aids to access the literature of heterocyclic chemistry, and great progress has been made in this at the moment.

For example, we can now use the *ChemQuest Online* or the *Fine Chemical Directory In-House* to find out what organic compounds, including heterocyclic compounds, are available. Thus, we wish to know which benzotriazoles are commercially available, and Figs. 25 and 26 illustrate this. In particular, Fig. 25 shows that seven and only seven N-unsubstituted benzotriazoles are commercially available. It would be almost impossible to come to this conclusion by manually searching through catalogs because it is very difficult to know just how these compounds would be named. In Fig. 26 further details are given of the sources for these derivatives.

The *FCD*-searching in-house mentioned above is a specific example of the more general category of chemical databases. All organic chemists should now be making extensive use of these. *FCD* is available to search using MACCS (Molecular ACCess System) from Molecular Design Ltd. The program allows the storage and retrieval of molecular structures and associated information and data. The system is customizable, allowing the user to set up his own data fields, menus, and displays. The program can also act as a chemical front-end to a number of industry standard data management systems.

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