PL 3

SOME APPLICATIONS OF THE ^{13}C NMR IN THE FIELD OF HETEROAROMATIC COMPOUNDS

José Elguero

Laboratoire de Chimie Moléculaire, Université d'Aix-Marseille III, rue Henri Poincaré, 13397 Marseille Cédex 4, France.

The aim of this conference will be to review the work done by our research group, between 1974 and 1978, on ^{13}C nmr studies of heteroaromatic compounds (references 1—24). Our research has been mainly concerned with five-membered rings together with their benzoderivatives but some results have also been obtained in the case of pyridines (Table I).

First the assignment methods will be described, though they not differ from those already employed by others authors; an important part of this talk will be devoted to them. At present ^{13}C nmr spectroscopy is such that it is important to attribute, without ambiguity, the carbons of a large number of heterocycles, in order to systematize the results. The methods we used are the following ones:

— Replacement of an hydrogen atom by a substituent which does not disturb as a deterium, or disturbs a little such a chlorine atom, or disturbs much as a nitro group does.

— Interpretation of the ^{1}H-^{13}C coupling constants through one or several bonds.

— Effects induced by the LSR.

— Selective decoupling experiments.

The attribution being done, we have to our disposal a collection of chemical shifts ($\delta^{13}C$) and coupling constants ($J^{1}H$-^{13}C). The chemical shifts will be discused as a function of:

a) A topological model which takes in account only the number and position of nitrogen atoms.

b) The total charge $q_{\pi+\sigma}$ calculated by the CNDO methods.

In the substituents on a given heterocyclic nucleus vary, the chemical shifts of all the carbons are modified. These shifts induced by a substituent (SIS) depend on its position and nature. Attempts of correlations with one or several parameters (σ_p,σ_m,σ_I,σ_R,F,R,Q) have been made with more or less success.

The junction of a benzenic ring, annelation, has been analysed as a special case of substituent effect.

The interest of ^{13}C nmr spectroscopy in the determination of position isomerism of N-substituted azoles will be pointed out. But the difficulties involved in its use to mesure the equilibrium constants concerning the azidoimine ⇌ tetrazole isomerism will also be discussed.

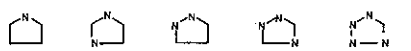
The annular tautomerism of azoles can be studied by ^{13}C nmr spectroscopy in two ways. The first one consists of an interpolation of the average chemical shift with those of N-methylated fixed compounds. The limitation of this method will be discussed and a general conclusion will be tentatively drawn. In the second way the protonic exchange is slowed enough so that both tautomers can be observed. Concerning this second method, the kinetic aspects of prototropy will be discussed as well as the influence of substituents, concentration and solvent. The study of the coupling occuring between carbons and the tautomeric proton bonded to nitrogen is particularly interesting.

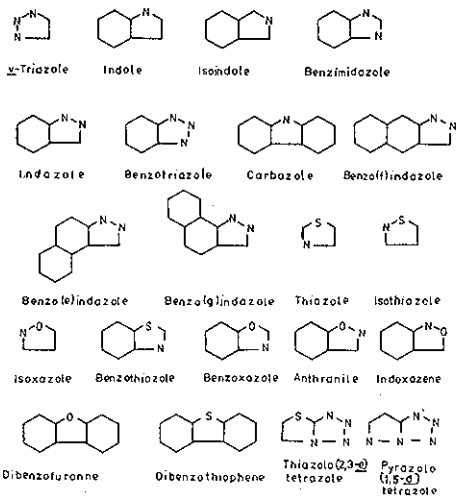
The cases in which ^{13}C nmr can be used to determine the protonation site of a heterocycle polybase will be discuss. As a preliminary, it is necessary to understand the complex effects induced by quaternization.

At last the conformational information which can be deduced from ^{13}C nmr experiments will be examined: in the case of systems related to biphenyle (N-arylazoles, C-pyridylazoles, C-arylpyridines and bipyridines) the results are very interesting but disappointing in that of azolides.

In conclusion the contribution of ^{1}H, ^{13}C and ^{15}N resonance spectroscopy to heterocyclic chemistry will be compared, pointing out their advantages, disadvantages and their complementary character.

TABLE I





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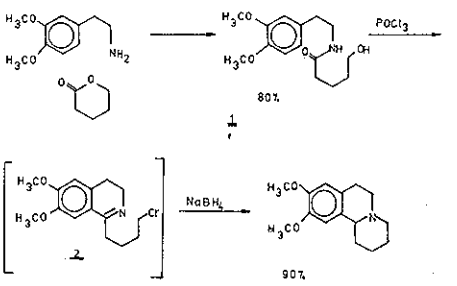
PL 4

LACTONES AS BUILDING BLOCKS FOR THE SYNTHESIS OF ALKALOID LIKE HETEROCYCLES

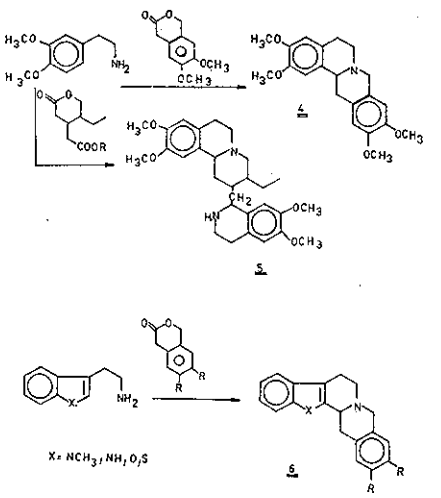
Felix Zymalkowski*, Werner Meise,

Pharmozeutisches Institut der Universität, Bonn

By reaction of γ-butyro- or δ-valerolactones with homoveratrylamine ω-hydroxyalkyl carboxamides **1** are obtained, which are cyclized by phosphorus oxychloride to give 1-(ω-chloroalkyl)-3,4-dihydroxyquinolines **2**. Immediate treatment of the not isolated rough product with sodium borohydride affords benzoquinolizines (**3**) or benzoindolizines respectively in very good yields, for example:



This simple two step synthesis can be used with good success for the preparation of quinolizidine alkaloids of the types **4**, **5** and **6**:



Replacing tryptamine by benzofuranyl or thionaphthyl ethylamines as starting material allows the preparation of oxa or thia analogous of the yohimbine ring system. These compounds are significant in respect to their biological effects.

Some investigations about scope and limitation of this synthetic pathway are discussed. Using the lactone like phthalaldehydic acid **7** the Bischler-Napieralsky ring closure is displaced by the Pictet-Spengler reaction. For example by the influence of thionaphthyl ethylamine **7** is converted to the thionaphthylbenzoindolizone **8**, the Pictet-Spengler reaction being combined with an intramolecular N-acylation: