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Isotopic exchange in heterocyclic quaternary salts I.
Deuteration of 2,3-dimethylbenzothiazolium iodide

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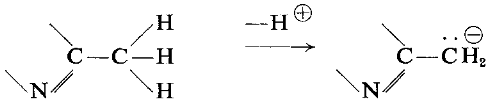
Summary

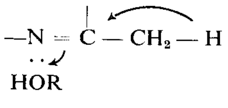
The H/D exchange in 2,3-dimethylbenzothiazolium iodide was studied. The deuteration took place exclusively at the methyl group in position 2, and the non-catalyzed reaction followed a first order kinetics.

Introduction

It has been generally considered that the characteristic condensation reactions of an active-CH_3 group in heterocyclic compounds, as well as its H/D isotopic exchange, depend on the ability of this group to cleave a proton yielding an intermediary carbenate ion.

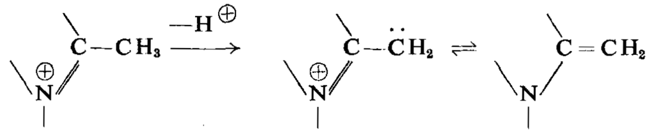


Kinetic measurements carried out on certain substances of analogous structure (α-picoline : chinaldine, γ-picoline : lepidine) pointed out that the rate of isotopic exchange, which proceeds through a type A complex, increases with the basicity of the heterocyclic ring (1, 2, 3).



The available experimental data do not seem to confirm this regularity in the benzazole series (2).

In the case of heterocyclic quaternary salts the problem is different. In process B the rate-determining step of the deuteration, i.e. the conversion of cation I into the active intermediate (methylene — base II) proceeds the faster the less basic II is (4).



I. II. (B)

In the series of quaternary 2-methylazolium salts no comparative studies were performed untill now. Papers published in this field (2, 3, 5) mentioned only the expected increase of the deuteration rate of certain derivatives as compared to the non-quaternized parent compounds.

Since we were interested in the preparation of the deuterated 2,3-dimethylbenzothiazolium iodide, we considered that a kinetic study of the isotopic exchange would be of interest.

The labelling of 2,3-dimethylbenzothiazolium iodide was performed through a non-catalyzed reaction with deuterium oxide, in a very dilute solution, at a molar ratio iodide : $D_2O = 5.50 \times 10^{-6}$. Preliminary investigations showed that heating at 90° C for 10 hours rezulted in the obtention of an isotopic concentration of 30 % in the product; this value remained unchanged by prolonging the reaction time up to 50 hours. It follows, therefore, that complete labelling of the methyl group in position 2 (three hydrogen atoms) took place under these conditions, while the N-CH_3 group and the benzene nucleus (seven hydrogen atoms in all) remained unaffected.

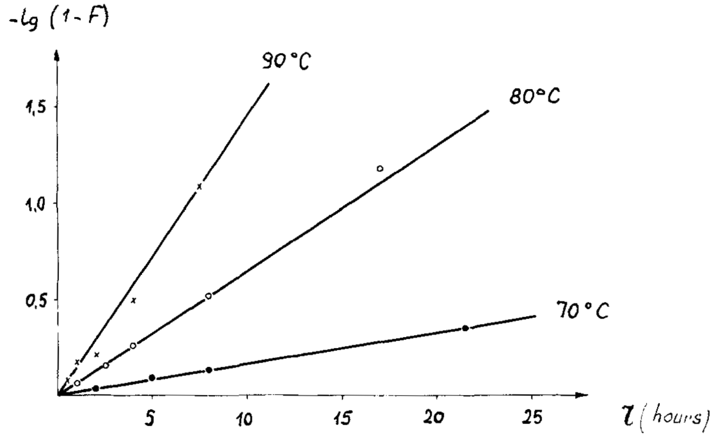


FIG. 1.

In order to verify these conclusions, the IR spectra of both labelled and unlabelled compounds were taken. We found in the spectrum of the deuterated compound a clear doublet at 2223 and 2210 cm^{-1}, due undoubtedly to the stretching vibration mode of the C-D bond. The appearance of these bands is accompanied by the complete disappearance of the C-CH_3 bending band, occuring in the spectrum of the undeuterated compound at 1370 cm^{-1}. The N-CH_3 bending vibration at 1418 cm^{-1} was found unaltered in the spectra of both compounds.

The kinetics of the isotopic exchange was investigated at 70° C, 80° C and 90° C respectively; by plotting $-\ln(1\text{-}F)$ against the time the straight lines represented in Figure 1 were obtained, from whose slopes the corresponding reaction rates could be calculated. An activation energy of 26.0 kcal/mole and a frequency factor (lg A) of 11.6 (Fig. 2) were calculated.

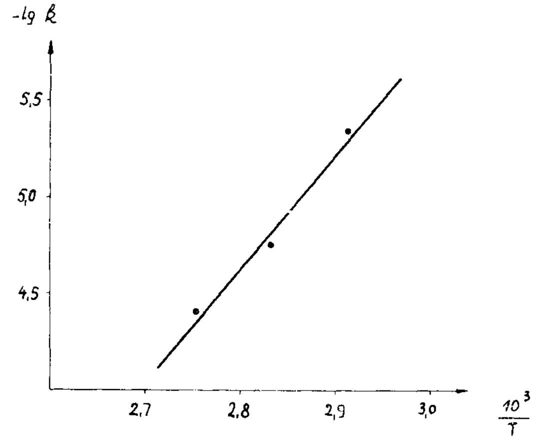


FIG. 2.

EXPERIMENTAL

The non-catalyzed isotopic exchange of 2,3-dimethylbenzothiazolium iodide was studied under the following conditions :

Solutions of the same concentration (0.032 g/mole) were prepared by disolving the iodide in D_2O at room temperature and then they were kept in sealed vials in a constant temperature bath at 70,80 and 90° C respectively. At appropiate times the vials were removed, their content evaporated, dried and the residues analyzed.

The deuterium content was determined by combustion in a stream of oxygen, and the water resulted decomposed to hydrogen; the isotopic concentration of the latter was then measured by gas-chromatography. The catalytic packing used in the combustion tube was made by succesive layers of decom-

TABLE 1. Kinetics of isotopic exchange between 2,3-dimethylbenzothiazolium iodide and D_2O.

Temperature	70° C	80° C	90° C
$10^5.k$, sec^{-1}	0.46	1.79	3.93
— *lg k*	5.34	4.75	4.41

E = 26.0 kcal/mol; lg A = 11.6.

position products of $KMnO_4$ and $AgMnO_4$, respectively. A quantitative absorption, at 500° C, of halogen, sulfur and nitrogen compounds was thus assured (6, 7). A special trap cooled with dry ice and acetone was used for the separation of water. Its dilution with a certain amount of water of standard isotopic concentration (147 ppm deuterium) was carried out in the same trap and the precise dilution ratio determined by weighing.

The diluted samples were introduced using a syringe in an apparatus conected with a vacuum line in which the decomposition of the water under the action of calcium hydride was carried out (8). The resulting hydrogen was collected in a manometric tube and then introduced in the by-pass of the gas chromatograph (9). The catharometric detector of the gas chromatograph was equipped with platinum filaments of 20 $\mu\varnothing$ and 17 Ω resistance disposed in a Wheatstone bridge. At a current supply of 400 mA, the detector give a signal of 1.2 mV for an isotopic concentration of 1 % deuterium in a hydrogen sample. The chromatograph was equipped with a column of 2 m lenght and 0.4 cm diameter, filled with active charcoal (in order to separate the peak of the deuterium from that of the air), and with another column of the same dimensions filled with a molecular sieve type 5A (in order to separate the O_2 and N_2 peaks). The chromatograph was thermostated to 45 ± 0.1° C. Microvalves for the introduction of samples were used.

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