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Hydrogen Isotope Effect on the Rate of an Intramolecular Tautomeric Rearrangement*

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1-Methylindene, deuterated in the 1-position has been synthesized. Its base-catalyzed rearrangement to 3-methylindene has been studied under conditions previously found to cause intramolecular and stereospecific proton transfer. Protium was found to migrate 5.5 times as fast as deuterium.

The authors have recently [1,2] investigated the base-catalyzed tautomeric rearrangement of 1-methylindene to 3-methylindene. Deuterated 1-methylindene (I) was now synthesized and the deuteron migration to the 3-position (II) studied by applying the same conditions as in the study of the proton transfer. Ethyl acetoacetate was reduced with amalgamated sodium in heavy water. Subsequent hydrolysis and dehydration gave the deuterated crotonic acid (III), which was recrystallized from D_2O. A Friedel-Crafts reaction with benzene yielded the indanone (IV). The latter (IV) was reduced with $LiAlH_4$ and the resulting alcohol (V) treated with 20 % sulphuric acid to give 1-methyl-1-D-indene (I). During the synthetic steps, several possibilities of exchange at the 2-position are plausible and the final product (I) therefore contained about 50 % of protium in the 2-position. In the crucial 1-position, however, the deuterium content was found to be 92 %.

The structure of (I) and its deuterium content were established by NMR analyses. The NMR-spectrum of (I) in approximately 40 % deuterochloroform solution showed the following characteristics. The methyl proton peak at 1.23 ppm (δ, relative to tetramethylsilane), was split into a triplet due to coupling with the deuteron in the 1-position. The peak separation in the triplet was 0.9 ± 0.1 cps, which is consistent with the coupling constant, 7.6 ± 0.2 cps, found in ordinary 1-methylindene.[1] The presence of a small amount of the latter compound was indicated by a weak doublet centred around the triplet. The spectrum also showed two signals with chemical shifts of 6.42 and 6.76 ppm

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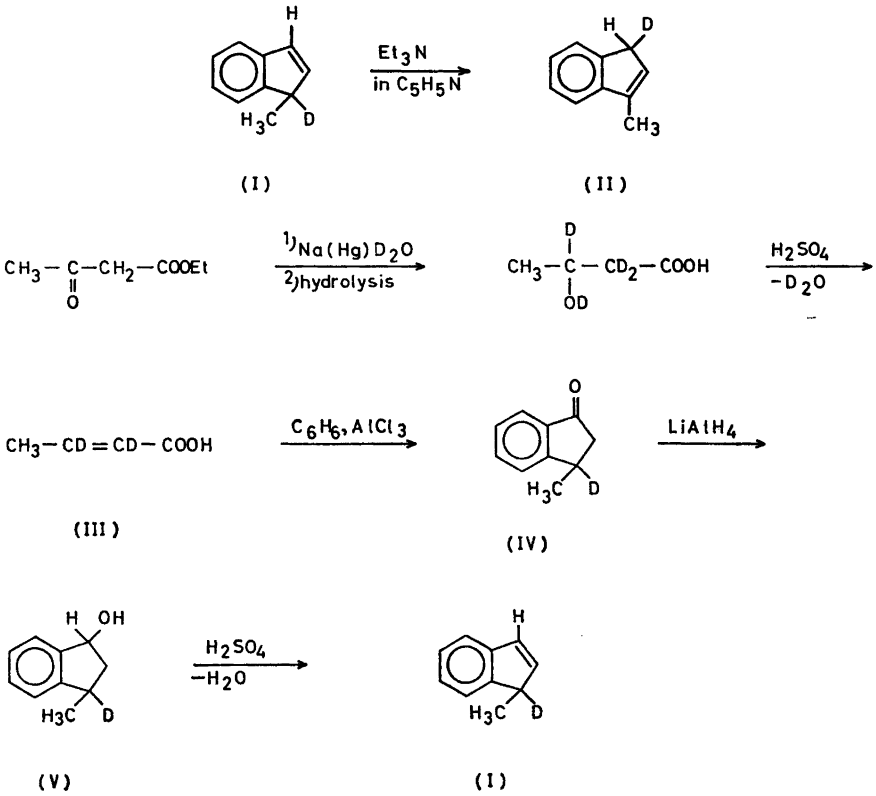

(δ), due to the protons in positions 2 and 3, respectively. The relative intensities were 1:2 indicating 50 % deuterium in the 2-position. The coupling constants were consistent with previous observations.[1] In addition a somewhat broadened peak was found in the 6.76 ppm region which originates from the proton in the 3-position of molecules, deuterated in the 2-position. The amount of protium (8 %) in position 1 was most conveniently determined from the intensity of its weak signal at 3.4 ppm (δ).

The NMR-spectrum of (II) showed three signals besides those due to the aromatic protons. The methyl proton peak at 2.05 ppm (δ) was split into six peaks due to the superposition of a quartet and a doublet. The quartet originates from the molecules with one proton in the 1-position and one in the 2-position, and the doublet comes form molecules with deuterium in the 2-position and one proton in the 1-position. No D-H coupling (<0.4 cps) could be found in this case. The proton in the 1-position gives a signal at 3.14 ppm (δ). The couplings with the methyl protons, the vinylic proton and deuterium at the same carbon atom, are all of the same magnitude, which makes it practically impossible to estimate the individual coupling constants. The vinylic proton peak appeared, as earlier observed at 6.07 ppm (δ).[1]

The deuterium migration was studied in 2.0 M pyridine solution using triethylamine (TEA) as a catalyst. The progress of the reaction was followed by measuring the increase of the area of the 3-methyl proton signal of (II). Further, the decrease of (I) was determined from the area of the 2-proton peak, thus providing a check on the rate measurements. With a fixed base concentration, the reaction obeyed first-order kinetics as shown in Fig. 1. In the original

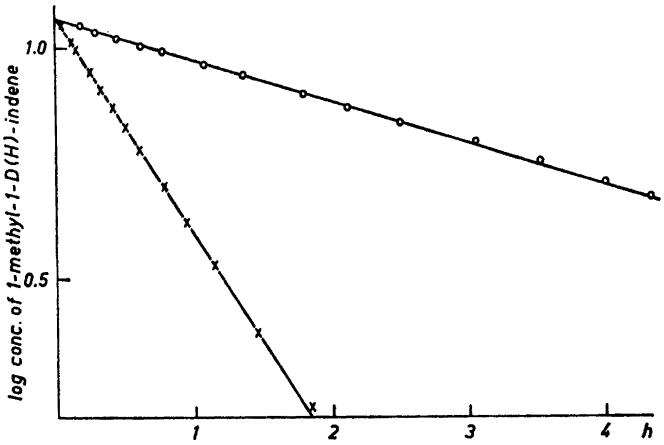

Fig. 1. Rate of isomerization of O, 1-methyl-1-D-indene to 1-D-3-methylindene, and ×, 1-methylindene to 3-methylindene: (30° C).

plot the first part of the curve showed a somewhat steeper slope due to the faster reaction of the 8 % of "light compound" present. Correction for this reaction gave the straight line shown in Fig. 1. With 0.257 moles/litre of TEA the pseudo-first-order rate constant was found to be $(0.35 \pm 0.03) \times 10^{-2}$ min^{-1} and the second-order constant consequently 1.36×10^{-2} l mole^{-1} min^{-1}, at 30°C. For proton migration under the same conditions, we found the rate constants $(1.89 \pm 0.05) \times 10^{-2}$ min^{-1} and 7.34×10^{-2} l mole^{-1} min^{-1}. The ratio k_H/k_D is thus about 5.5. We have previously found that the tautomeric rearrangements of alkyl-indenes are purely intramolecular under the above mentioned conditions.[3]

Further investigations of isotope effects in intramolecular tautomeric shifts are in progress.

EXPERIMENTAL

The NMR-spectra were obtained with a Varian A-60 high resolution spectrometer, and the IR-spectra with a Perkin Elmer Model 237 infrared spectrometer.

Deuterated crotonic acid[4] *(III).* 35 g of anhydrous aluminium sulphate, dried at 150° for three days were dissolved in 125 ml of heavy water (99.8 % from Norsk Hydro) and cooled to 0°C. To this solution, 26 g (0.20 moles) of freshly distilled ethyl acetoacetate were added. 2.5 % amalgamated sodium,[5] prepared from 13.8 g (0.6 g atom) of sodium and 540 g of mercury, was added in small pieces over a peroid of about 3 h. The mercury was separated and the precipitated inorganic salts were removed by filtration, and washed

with absolute ethanol. The ethanol solution was separately evaporated at room temperature and the residue combined with the original filtrate.

The hydrolysis to the deuterated β-hydroxy-butyric acid was performed by addition under nitrogen of a small excess of sodium to the obtained filtrate at 0°C. The alkaline solution was kept under reflux for 40 min and the heavy water then recovered by evaporation. To the solid residue, 30 ml of 50 % sulphuric acid were carefully added. Distillation gave water, and crotonic acid which was extracted with ether. The ether solution was dried over magnesium sulphate and evaporated yielding 6.0 g (0.069 moles, 35 %) of deuterated crotonic acid. The latter was recrystallized from D_2O giving 4.0 g of the pure acid, m.p. 71–72°.

Deuterated 3-methyl-1-indanone (*IV*), was prepared from 4.0 g of deuterated crotonic acid, analogous to the method described by Koelsch *et al.*[6] The crude ketone was obtained in 95 % yield.

Deuterated 1-hydroxy-3-methylindane[2] (*V*): Without further purification, the ketone (IV) (6.4 g, 0.044 moles) was reduced with $LiAlH_4$ to give the corresponding alcohol (6.8 g). Recrystallization from petroleum ether gave the pure alcohol (3.0 g, 44 %), m.p. 69.5–71.0°

Deuterated 1-methylindene (*I*). 3.0 g of the alcohol (V) were treated with 15 ml of 20 % sulphuric acid at 100° for 40 min. The mixture was extracted with ether, washed with water and dried over magnesium sulphate. Evaporation of the solvent gave the crude product (2.75 g), which was chromatographically purified on 50 g of silicic acid (Mallinckrodt). Elution with petroluem ether (b.p. 35–50°) gave the pure 1-methyl-1-D-indene (0.9 g 35 %.) In IR, the C–D absorption band appeared at 4.71 μ.

3-Methyl-1-D-indene (*II*), was isolated from the pyridine solution of various kinetic runs. The solution was evaporated and the residue chromatographed on 20 g of silicic acid. Elution with petroleum ether gave the pure compound, which was identified by its NMR-spectrum.

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