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Some New Experiments on the Proton-Mobility in the Indene Ring-System*

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Optically active 1-deutero-1-methylindene, (+)-1,3-dimethylindene and racemic 1-methyl-3-trideuteromethylindene have been synthetized. 1,3-Prototropic shifts have been investigated in these molecules. With quinine as catalyzing base, (+)- and (−)-1-methylindene rearrange at different rates to 3-methylindene.

As a part of our investigations of the mechanism of intramolecular and stereospecific proton-transfer reactions, we have now synthetized optically active 1-deutero-1-methylindene (I) and racemic 1-methyl-3-trideuteromethylindene (II). Optically active 1,3-dimethylindene (III) has also been prepared.

Using the substances II and III, we have been able to study the proton-mobility in 1,3-dimethylindene. This investigation is of importance in connection with problems concerning mechanism and substituent effects as explained below. With optically active and isotopically labelled 1-methylindene it is possible to make a polarimetric determination of the kinetic isotope effect in the base-catalyzed isomerization to 3-methylindene. This method gives a higher accuracy than the NMR-technique used earlier.[1] In this communication we can also report the first successful demonstration of stereoselective catalysis in the 1,3-tautomeric shift of indene derivatives. Unsuccessful experiments along this line were described earlier.[2]

The synthesis of I followed the same schemes as previously described for the preparation of the racemic compound [1] and optically active 1-methylindene.[3] Thus, deuterated β-phenylbutyric acid was resolved by means of α-

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phenylethylamine, and the active acid cyclized to the corresponding indanone. Reduction followed by dehydration finally gave I. Addition of deuterated methyl magnesium iodide to 3-methyl-1-indanone and subsequent dehydration gave the inactive II in good yield. Similarly, we obtained III when starting from active 3-methyl-1-indanone and methyl magnesium iodide.

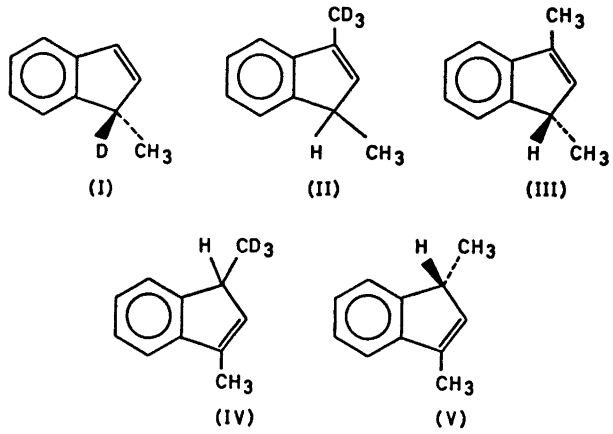

Fig. 1.

The absolute configurations of the optically active products can be deduced from our previous stereochemical studies.[3] The (+)-forms of both I and III have the S-configuration shown in Fig. 1.

The isomerization II ⇌ IV was studied by the NMR-technique at 30°C in pyridine solution using 1,4-diaza-bicyclo[2.2.2]octane (DABCO) or butylamine (BUA) as catalysts. The second order rate constants were found to be 0.023 and 0.006 l mole^{-1} min^{-1} with DABCO and BUA, respectively. Using the data obtained previously,[2,4] we get the following relative rates of isomerization in the series 1-methyl-3-*tert*-butyl-, 1-methyl-3-isopropyl-, 1,3-dimethyl-, 1,2-dimethyl-, and 1-methylindene using DABCO as the catalyzing base: 1: 1.25:1.11:9.5:70. Thus, the nature of the 3-alkyl substituent has practically no influence on the isomerization rate. Furthermore, the comparison between 1,3-dimethyl- and 1,2-dimethylindene is quite interesting. One factor of importance in this latter context must be the difference in π-electron energy between the activated complexes. Since the indenyl anion has a greater electron density in the 3-(or 1-)position than in position 2, this must be qualitatively true also for the activated complex. Therefore, an alkyl substituent will create a larger perturbation in position 3 than in position 2.

The 1,3-prototropic shift was previously found to be completely stereospecific in the rearrangement of 1-methyl-3-isopropylindene and 1-methyl-3-*tert*-butylindene.[2] The configurational relationship between the rearranged products and the starting materials has not been established, however, but it seems probable that the tautomeric rearrangements involve inversion of

the configuration.[2] A comparison of the behaviour of II and III under rearrangement conditions is of interest in this context. Since II rearranges under exactly the same conditions as the other 1,3-dialkylindenes, and with comparable rate, it seems safe to assume that the reaction II $\rightleftharpoons$ IV is stereospecific. Therefore, no change in optical activity should be observed when we use optically active 1,3-dimethylindene if the tautomeric shift results in the creation of an asymmetric carbon atom with the *same* configuration as in the starting material. When III was subjected to rearrangement conditions we found, however, that mutarotation occurred with the rate constants 0.047 l mole^{-1} min^{-1} (DABCO) and 0.012 l mole^{-1} min^{-1} (BUA). These constants are just twice as large as those found for the rearrangement of II into IV. Therefore we conclude, that the 1,3-tautomeric shift brings about the conversion of III into its optical antipode, V, as required by the reaction mechanism proposed.[2] Equilibrium is reached, of course, when III and V are present in equal amounts.

Stereoselective catalysis was observed when quinine was used as a base in the rearrangement of 1-methylindene. The rate constants 0.0350 and 0.0210 l mole^{-1} min^{-1} were found at 25°C for the mutarotation when using (+)- and (−)-1-methylindene, respectively. This rate difference thus corresponds to the difference in free energy between the diastereomeric activated complexes. In Fig. 2 the optical rotation is shown as a function of time when *racemic* 1-methylindene is rearranged with quinine. Since the (+)-form reacts faster than the (−)-form, the rotation shows a minimum at $t = (\ln k_+ - \ln k_-)/[B](k_+ - k_-)$, where k_+ and k_- are the rate constants for the antipodes and [B] is the concentration of quinine. No stereoselective catalysis was observed, as expected, for 1,3-dimethylindene. In this case the activated complex will be symmetric if the mobile proton is placed midway between the methyl groups and no diastereomers will occur. If the proton is placed in an unsymmetrical way in the activated complex, the two diastereomeric complexes will both show up in each reaction, and no rate difference will thus appear.

With regard to the kinetic isotope effect we found, for example, the rate constants 1.33 and 0.248 l mole^{-1} min^{-1} for ordinary and deuterated 1-methylindene, respectively, with DABCO as catalyst at 25°C. This isotope effect is thus approximately the same as that found with triethylamine as catalyst using the NMR-technique.[1]

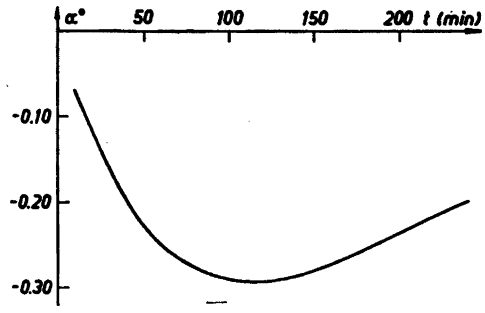

Fig. 2. Optical rotation (corrected for the rotation of quinine) as a function of time for a pyridine solution with an initial concentration of 0.0256 g/ml racemic 1-methylindene and 0.336 mole/litre in quinine at 25°C. A Perkin-Elmer 141 photoelectric polarimeter was used.

A more detailed report, including, for example activation energy measurements, further studies of the stereoselective catalysis, and the isotope effect, will be published later.

EXPERIMENTAL

(+)-1-Deutero-1-methylindene (I). Deuterated racemic β-phenyl-β-deuterobutyric acid was prepared from deuterated crotonic acid [1] and benzene according to the procedure used for the non-labelled compound.[3,5] The NMR-spectrum showed 95 % deuteration in the β-position, m.p. 36–38° (from petroleum ether). 22.0 g of the racemic acid was resolved using α-phenylethylamine.[3] In this way we obtained 8.2 g of (+)-β-phenyl-β-deutero-butyric acid, $[\alpha]_D^{25} = +53.0°$, and 6.0 g of the (−)-form, $[\alpha]_D^{25} = -52.8°$ (benzene).

8.1 g (0.050 mole) of the (+)-acid was converted into 5.0 g (70 %) of crude 3-deutero-3-methyl-1-indanone in the usual way.[3] Reduction of 4.9 g (0.034 mole) of the indanone using $LiAlH_4$ gave 3.0 g (60 % yield) of 3-deutero-3-methyl-1-hydroxyindane, m.p. 85–86°, $[\alpha]_D^{25} = -38.0°$ (benzene). Dehydration of 3.0 g of this product using sulphuric acid as described for the racemic compound,[1] gave 1.4 g of (+)-1-deutero-1-methylindene, $[\alpha]_D^{25} = +172°$ (pyridine). The NMR-spectrum showed 86 % deuteration in the 1-position.

Racemic 1-methyl-3-trideuteromethylindene (II). Trideuteromethyl magnesium iodide was prepared from 8.6 g (0.059 mole) of trideuteromethyl iodide [6] and 1.41 g (0.059 mole) of magnesium in 50 ml of dry ether. To this Grignard reagent was added dropwise a solution of 6.2 g (0.042 mole) of 3-methyl-1-indanone in 30 ml of ether. The reaction mixture was refluxed for 4 h and then poured into 100 ml of an ice-cooled saturated aqueous ammonium chloride solution. The aqueous phase was extracted with 100 ml of ether. The combined ether phases were washed with water and dried over magnesium sulphate. Evaporation of the ether gave the crude dimethylindanol. Dehydration was accomplished by heating the indanol in vacuum. The fraction boiling at 81–82°/10 mm was collected and consisted of 1-methyl-3-trideuteromethylindene (4.5 g, 73 %). The NMR-spectrum showed 95 % deuteration in the 3-methyl group.

(+)-1,3-Dimethylindene (III) was prepared in analogy with the synthesis of (II), starting from 5.7 g (0.039 mole) of (+)-3-methyl-1-indanone.[3] The yield of (+)-1,3-dimethylindene was 4.0 g (72 %), $[\alpha]_D^{25} = +162°$ (benzene), b.p. 78–80°/9 mm, $n_D^{20} = 1.5508$. (Literature [7] value for racemic compound, $n_D^{18} = 1.5509$).

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