A Stereospecific Tautomeric Rearrangement

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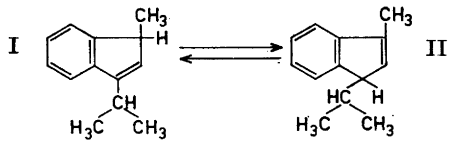
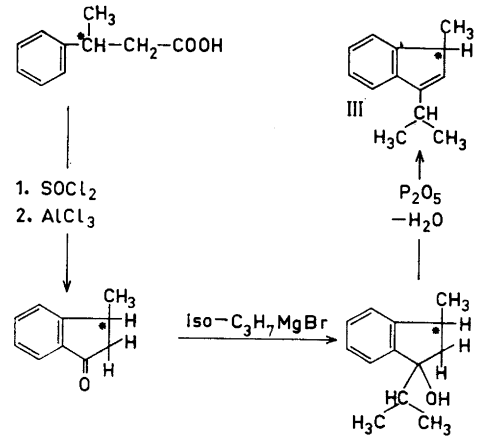
In a previous note [1] we reported that the rate of racemisation of optically active 1-methylindene in basic medium was almost equal to the rate of isomerisation to 3-methylindene. Furthermore, we found only a very small hydrogen-exchange on isomerisation in the presence of D_2O. For various reasons a concerted mechanism could be excluded. A step-wise mechanism is consistent with the above observations only if the intermediate anion is protonated exclusively at the position resulting in the formation of 3-methylindene. These considerations might suggest that the tautomeric rearrangement instead involved a pure intramolecular hydrogen migration.

In order to obtain further information about the peculiarities of tautomeric indenes, we synthesized and investigated 1-methyl-3-isopropylindene (I). In a medium consisting of pyridine and butylamine, (I) rearranged partially to 1-isopropyl-3-methylindene (II). The equilibrium mixture contained about 80 % of (II) and about 20 % of (I). The isomerisation rate was followed by NMR-measurement, the area of the 3-methyl-protons signal of (II) being the best criterium of the increase in concentration of (II). The



data thus obtained were in good agreement with reversible pseudo-first-order kinetics. With a butylamine concentration of 1.0 mole/litre, the sum of the forward and reverse rate constants was $(0.88 \pm 0.05) \times 10^{-2}$ min^{-1} at 30°C.

Since (II) has a centre of asymmetry it was of particular interest to follow the change in optical rotation when optically active (I) is subjected to the isomerizing conditions mentioned above. Therefore, we prepared 1-methyl-3-isopropylindene starting from optically active β-phenylbutyric acid according to the scheme below:



The product was chromatographically purified on silicic acid. Elementary analyses proved the correct composition, but the NMR-spectrum revealed a slight contamination (4–5 %) of 1-methyl-3-isopropylideneindane.

The change in optical activity of a pyridine solution containing 0.1 mole/litre of (III) and 1.0 mole/litre of butylamine was studied at 30°C. The rotation, initially negative, increased gradually to + 1.35° as shown in Fig. 1. This result indicates that the tautomeric rearrangement studied is stereospecific. (The small amount of 1-methyl-3-isopropylideneindane present can be responsible, at most for 5–10 %

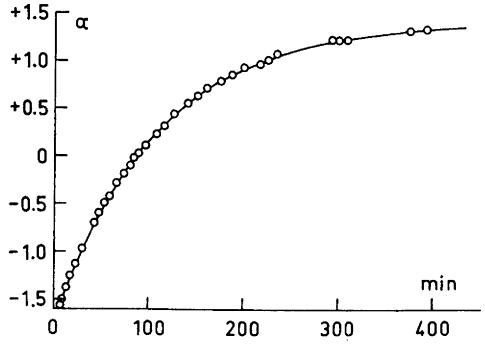


Fig. 1.

of the observed positive rotation.) Furthermore, the sum of the forward and reverse pseudo-first-order rate constants as evaluated from the rotation measurements was $(0.97 \pm 0.04) \times 10^{-2}$ min^{-1}, in fair agreement with the result obtained from the NMR-studies.

The stereospecificity is neither in accordance with a concerted mechanism nor with a step-wise mechanism involving free anions, but it is consistent with a pure intramolecular hydrogen migration.

A more detailed account of our findings will be reported later.

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1. Bergson, G. and Weidler, A.-M. *Acta Chem. Scand.* **17** (1963) 862.

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New γ-Glutamylpeptides Isolated from the Seeds of Chives (*Allium schoenoprasum*)

N,N′-bis-(γ-glutamyl)-cystine, N,N′-bis-(γ-glutamyl)-3,3′-(2-methylethylene-1,2-dithio)-dialanine, γ-glutamyl-S-propylcysteine

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The amino acids and acid peptides which had been separated on an Amberlite IR-120 column from a 70 % ethanol extract of the ground seeds of chives were fractionated on a Dowex 1 × 8 column in acetate form. 1 kg of seeds was used at a time and each fraction was 20.3 ml/25 min. 1025 fractions were taken, 170 fractions with 0.5 N acetic acid, then 346 fractions with 1 N acetic acid, 284 fractions with 2 N acetic acid, and finally 225 fractions with 1 N hydrochloric acid. On the basis of the paper chromatograms obtained from the fractions, using butanol-acetic acid-water (12:3:5) as solvent and ninhydrin reagent, the fractionation proceeded as shown in Fig. 1. The amino acids emerged from the column in the 240 first fractions. At least most of the ninhydrin-positive substances in later fractions are γ-glutamylpeptides. The compounds denoted R XII, R XIII, R X, R XVIII, R XVII, and R XIX have so far been isolated in crystalline form, and the chemical structure of the four first ones mentioned has been elucidated. In this preliminary communication the results are reported on briefly.

Peptide R XII, γ-L-glutamyl-S-(prop-1-enyl)-L-cysteine. The isolation and structure of this compound is described in our earlier communications [1].

Peptide R XVIII, N, N′-bis-(γ-L-glutamyl)-3,3′-(2-methyl-ethylene-1,2-dithio)-dialanine. The peptide was isolated from fractions 750—823 (Fig. 1) and separated from peptides R XIII and R XIX on a cellulose powder column with isopropanol-acetic acid-water and crystallized from an acetone-water mixture. The fractions containing peptide R XVIII alone were evaporated to dryness *in vacuo*. On addition of acetone to its aqueous solution the peptide precipitated as a sirup. When ground with acetone, a white, solid substance was obtained which by paper chromatography was shown to be the pure peptide R XVIII. The yield was 590 mg/kg of seeds. After hydrolysis both with a preparation from calf kidney and in 1 N HCl two amino acids were found: L-glutamic acid ($[\alpha]_D^{22}$ + 34.8 in 6 N HCl) and an unknown sulphur-containing amino acid. After fractionation with butanol-acetic acid-water the unknown amino acid was crystallized by addition of acetone to its aqueous solution. When hydrogenated with Raney nickel as a catalyst, hydrogen was not consumed, but alanine was formed and a gas, which was found to be propane by mass spectrometry. The unknown amino acid could be identified as

$$HOOC \cdot CH(NH_2) \cdot CH_2 \cdot S \cdot CH_2 \cdot CH(CH_3) \cdot S \cdot CH_2 \cdot CH(NH_2) \cdot COOH$$

3,3′-(2-methylethylene-1,2-dithio)-dialanine when this compound was synthesized. In three solvent systems the paper chromatograms of the natural and synthetic amino acids were identical. So were also the IR-spectra.