**Tetrahedron Letters No.2, pp. 223-226, 1966. Pergamon Press Ltd.
Printed in Great Britain.**

AN ANOMALOUS CYCLIZATION OF 2,2,5,5-TETRAMETHYLADIPIC ACID*

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(Received 22 November 1965)

According to Farmer and Kracovski, no 2,2,5,5-tetramethylcyclopentanone (I) was formed from 2,2,5,5-tetramethyladipic anhydride under conditions which normally effect this type of cyclization (1). This has been taken as evidence for a cyclization mechanism demanding the presence of at least one α-hydrogen in the diacid (2). However, Rand et al. (3) recently described the preparation of I in good yield by slow distillation of 2,2,5,5-tetramethyladipic acid (II) in the presence of a small amount of potassium fluoride or barium oxide. A mechanism involving formation of a carbanion by loss of carbon dioxide from the acid anion was proposed in order to account for this result.

Following the directions given by Rand et al. it was, however, impossible to obtain I even in trace amounts. Slow distillation of II (4)

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* This work was supported by a grant from the Swedish Natural Science Research Council.

in the presence of barium oxide gave a mixture containing II (and its anhydride) and a liquid material. After removal of the starting material the residue distilled at 205-210°/760 mm with no fore-run. Gas chromatographic analysis (5) of this liquid showed that it contained one major component contaminated with two compounds with slightly longer retention times. The major component (III) was isolated and purified by preparative gas chromatography (6) and identified as 3,6,6-trimethylcyclohexen-2-one on the basis of the data given below. The yield of III was 31 %. The reaction was also run with potassium fluoride as a base, but the same mixture was obtained, as could be shown by gas chromatographic analysis on several different columns.

Compound III was obtained in a purity of about 97 %, n_D^{20} 1.4750. It gave a 2,4-dinitrophenylhydrazone, m.p. 204-205° and a semicarbazone, m.p. 193-196° (7). Its infra-red spectrum had a strong carbonyl stretching frequency band at 1660 cm^{-1} and a C=C stretching frequency band at 1632 cm^{-1}, indicative of an α,β-unsaturated ketone. The NMR-spectrum had a singlet at 1.01, a triplet at 1.77, a somewhat broadened singlet at 1,92, a triplet at 2.29, and a multiplet at 5.67 p.p.m. from TMS with integrated band areas in the proportions 6:2:3:2:1, respectively, in good agreement with the assigned structure. $J_{CH_2-CH_2}$ was 6 cps. The ultra-violet spectrum (in ethanol) had maxima at 234 and 317 mμ, compared with the spectrum of 3,5,5-trimethylcyclohexen-2-one (isophorone) which has maxima at 231.5 and 311 mμ.

For 3,6,6-trimethylcyclohexen-2-one the following data have been reported (8): b.p.$_{13}$ 86°, n_D^{20} 1.4798, m.p. of semicarbazone 201.0-201.1°.

It may be noted that the sample prepared by Rand et al. gave a 2,4-dinitrophenylhydrazone with the same melting point as that from III, indicating that this compound was actually present in their sample.

An authentic sample of I, prepared by methylation of 2,5-dimethylcyclopentanone by means of methyl iodide-potassium t-butoxide in ether (9), did not give a 2,4-dinitrophenylhydrazone under normal reaction conditions.

In view of the above results, it would seem a necessary requirement that the diacid possess at least one α-hydrogen to be able to take part in the normal cyclization reaction. In the absence of α-protons the cyclization occurs at a β-carbon atom, possibly *via* a homoconjugated carbanion (10). An analogous case in the acyclic series, formation of t-butyl isobutyl ketone instead of di-t-butyl ketone by passing pivalic acid over a thorium oxide catalyst at 490°, has been reported (11).

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4. D.D. Coffmann, E.L. Jenner, and R.D. Lipscomb, *J. Am. Chem. Soc.*, **80**, 2864 (1958). The acid prepared by this method was identical with a sample prepared by an independent method (1).
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6. On a 6 m silicon gum rubber SE-30 on Chromosorb P column at 170°.
7. This m.p. was determined with aid of a Kofler melting point microscope. In a capillary, it was 200-202°.
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9. 2,5-Dimethylcyclopentanone was prepared by barium oxide cyclization (3) of 2,5-dimethyladipic acid. Methylation was effected by treatment of a mixture of the ketone and a 2.5 molar excess of potassium t-butoxide in absolute ether with a 2.5 molar excess of methyl iodide. After work-up and distillation of the product (b.p._{760} 145-155°) it was treated with a 3 molar excess of acrylonitrile in t-butanol with

a few drops of 30 % KOH in ethanol added in order to cyanoethylate any remaining starting material and any trimethyl derivative formed. The tetramethyl compound was simply isolated by extraction with pentane and purified by distillation, b.p.$_{760}$ 152-156°, n_D^{20} 1.4260. The NMR-spectrum had singlets at δ 1.75 and 1.00 p.p.m. with integrated band areas in the proportion 1:3, demonstrating that the cyanoethylation procedure removed starting material and trimethyl derivative effectively.

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