# SYNTHESIS AND PROPERTIES OF 1,3,3-TRIMETHYLCYCLOHEXANONE-2-CARBOXYLIC AND CAMPHENONIC ACIDS

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While studying the effect of steric factors on the properties of  $\sigma_{,\pi}$ -conjugated systems [1, 2], we turned our attention to the decarboxylation of the structurally similar  $\beta$ -ketocarboxylic acids: 1,3,3-trimethylcyclohexanone-2-carboxylic (I) and camphenonic (II) acids. This study was made simultaneously with [2] more than 12 years ago.

 $\begin{array}{c|c} & & & \\ & & \\ & & \\ CH_3 & COH \\ (I) & (II) \\ \end{array} \begin{array}{c} CH_3 \\ COH \\ COH \\ COH \\ (II) \\ (III) \\ (III) \\ \end{array} \begin{array}{c} CH_3 \\ COH \\ COH \\ (III) \\ (III)$ 

It was reported in [3] that (II) and its analogs withstand a temperature of the order of  $300^{\circ}$  without being decarboxylated. This stability, completely unexpected for  $\beta$ -keto acids, is characteristic for bicyclic keto acids with small rings [4-6]. The rigidity of the system decreases with increase in the size of the rings and, along with this, the stability toward decarboxylation [7-9]. We were able to decarboxylate (II) via radical processes, by reacting its silver salt with bromine under comparatively mild conditions [2]. The mixture of the mercury salt of (II) and CH<sub>3</sub>COOH when fused with camphenonoyl peroxide at 70-80° was also decomposed vigorously (G. A. Razuvaev reaction) with the evolution of CO<sub>2</sub> and the formation of 1chloromercuricamphenilone [1, 10]. The mercury salt of (II) is completely stable in the absence of initiators. As a result, under the conditions of free-radical reaction the carboxyl, found in the "bridgehead" position of even a very rigid system, is cleaved with comparative ease. Apparently, the free radical formed here is quite active, since when the decomposition is run in benzene, for example,  $\alpha$  -phenylcamphenilone is isolated [1].

In contrast to (II), monocyclic acid (I) is so unstable that it could not be isolated by us in the free state. Some of its derivatives were obtained: salts, ethyl ester, 3,4-(1,1-dimethyltetramethylene)-4-methyl-5pyrazolone (IV), and 1,2,3,3-tetramethylcyclohexanol-2-carboxylic acid (V). The instability of (I) was also mentioned by Bell and co-workers [11].

Two reaction mechanisms have been proposed for the decarboxylation of  $\beta$ -keto acids. Since the rate of CO<sub>2</sub> evolution and the rate of halogen addition, if the reaction is run in the presence of halogen, coincide, it was postulated that the enol form takes part in one of the steps of the reaction [12, 13]. Later it was concluded that the reaction goes in harmony with an intramolecular mechanism involving (III), and that the formation of the enol form of the ketone is the concluding step of the reaction [14]. But since according to the Bredt rule the formation of a "bridgehead" enol does not occur, the bicyclic  $\beta$ -keto acids should be stable. An alternate mechanism [7] postulates involvement of the carbanion with the charge on the bridge carbon, which cannot be stabilized by resonance with the CO group for the same reason — because of the impossibility of closing the double bond.

We believe that an explanation of this fact can also be related to the absence of conjugation of the bonds in (III) because of their mutually perpendicular orientation in space. It seemed interesting to us to check the influence of the studied factors on the ionization constants of compounds having a functional group attached to the bridge carbon. For this purpose we measured the basicity constant of 1-aminocamphene and the dissociation constant of (II). The basicity constant ( $K_b$ ) of 1-aminocamphene, calculated from the pH

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values of aqueous solutions partially neutralized with HCl, measured with a glass electrode at  $25\pm0.1^{\circ}$  [15], is equal to  $0.87 \cdot 10^{-5}$ . The dissociation constant of (II) (K<sub> $\alpha$ </sub>), determined by the same method, is equal to  $1.0 \cdot 10^{-4}$  ( $25\pm0.1^{\circ}$ , water). As a result, both compounds have ionization constants of the same order of magnitude as their analogs with an open chain (allylamine K<sub>b</sub> 5.7  $\cdot 10^{-5}$ , dimethylacetoacetic acid K<sub>a</sub>  $3.08 \cdot 10^{-4}$ ), i.e., the factors, affecting the lability of the group as a whole, are without effect on the ionization constants of this group.

### EXPERIMENTAL

Ethyl Ester (I). The compound was obtained by the methylation of the ethyl ester of 3,3-dimethylcyclohexanone-2-carboxylic acid [16] using CH<sub>3</sub>I in the presence of C<sub>2</sub>H<sub>5</sub>ONa, in alcohol, with heating for 4 h. Yield 39%, b.p. 92° (2 mm);  $n_D^{20}$  1.4555,  $d_4^{20}$  1.0052. Found: C 68.25; 68.32; H 9.22; 9.18%. C<sub>12</sub>H<sub>20</sub>O<sub>3</sub>. Calculated: C 67.89; H 9.50%.

The heating of ester (I) with 50% hydrazine hydrate in pyridine for 4 h gave (IV), m.p. 162.162.5° (from water). Found: N 15.82; 15.88%.  $C_{10}H_{16}N_2O$ . Calculated: N 15.55%. The mixing of ethyl ester (I) with alcoholic NaOH solution at 25° gave Na<sub>2</sub>CO<sub>3</sub> and 2,2,6-trimethylcyclohexanone, yield approximately 35%, b.p. 66° (11 mm); nD<sup>20</sup> 1.4485; d<sub>4</sub><sup>20</sup> 0.9032. The latter is also formed, instead of the desired acid, when the preparation of the latter is attempted from 6-bromo-2,2,6-trimethylcyclohexanone through the organomagnesium derivative. If the MgBr salt of (I) is not isolated, but instead is treated with 1 mole of CH<sub>3</sub>MgI under conventional conditions, then the completely stable (V) is obtained, m.p. 142-143° (from CCl<sub>4</sub>). Found: C 66.05; 65.91; H 9.89; 9.96%.  $C_{11}H_{20}O_3$ . Calculated: C 65.97; H 10.07%.

<u>1-Aminocamphene</u>. Obtained by the Forster method [17]. The oxidation of camphor oxime with excess KOBr in aqueous medium gave 2-bromo-2-nitrocamphane in 82% yield, m.p. 220° (decomp.) (from alcohol). Found: C 45.91; 45.95; H 6.10; 6.12; Br 30.65; 30.37; N 5.69; 5.74%.  $C_{10}H_{16}BrNO_2$ . Calculated: C 45.83; H 6.11; Br 30.49; N 5.34%. The cleavage of HBr using AgNO<sub>3</sub> in absolute CH<sub>3</sub>OH medium is accompanied by rearrangement and i-nitrocamphene is obtained, yield 54%, m.p. 55° (from alcohol.. Found: N 7.64; 7.68%.  $C_{10}H_{15}NO_2$ . Calculated: N 7.73%. To confirm the position of the NO<sub>2</sub> group and exclude a possible tricyclic structure the 1-nitrocamphene was oxidized with ozone in glacial CH<sub>3</sub>COOH to 1-nitrocamphenilone, yield 81%, m.p. 98-99° (from alcohol). Found: C 59.12; 59.31; H 7.33; 7.36; N 7.66; 7.53%.  $C_9H_{13}NO_3$ . Calculated: C 58.99; H 7.15; N 7.64%.

The 1-nitrocamphene was then reduced with Zn and  $CH_3COOH$  in conventional manner and gave 1aminocamphene, which was isolated by steam distillation from acid solution; yield 64%, m.p. 46°. It was obtained as a glassy solid, with a very disagreeable odor, highly volatile, and resistant to oxidation. Found: C 79.35; 79.19; H 11.41; 11.32%.  $C_{10}H_{17}N$ . Calculated: C 79.41; H 11.25%.

#### CONCLUSIONS

1. A comparison was made of the ease of decarboxylation of the 1,3,3-trimethylcyclohexanone-2carboxylic and camphenonic acids, and a possible explanation was offered for the stability of the latter.

2. The ionization constants of camphenonic acid and 1-aminocamphene were measured.

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