ALKYLATION OF 3-SUBSTITUTED CYCLOHEXANONE ENAMINES

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The behavior of 4-substituted cyclohexanone enamines when condensed with acryloyl chloride was described in a previous communication [1]. The behavior of cyclohexanones that have a substituent in the 3 position was studied in the present paper. In contrast to 4-benzoylcyclohexanone, 3-benzoylcyclohexanone (III) does not form the enamine when reacted with morpholine. Instead the morpholine salt of benzoic acid (IV) is formed under a wide range of conditions.

In contrast to 1,4-cyclohexadione, 1,3-cyclohexadione (V) reacts with morpholine to give only the monoamine (VI).

In contrast to monoketone enamines, 1-morpholinocyclohexen-3-one (VI) is stable, which can be explained by the conjugation of the carbonyl group with the intracyclic double bond. This apparently explains the fact that the alkylation of enamine (VI) with acryloyl chloride leads to the monoalkylation product (VIII) and not the bicyclic product (VII). Probably, due to conjugation with the carbonyl group, in (VI) the isomerization of the double bond in the 6 position is made difficult and alkylation at this center fails to occur. Since in the literature only the melting point is given for (VIII), additional data was needed in order to identify the compound obtained by us. The $H_A$ and $H_B$ protons have acid properties, and acid (VIII) when titrated with 0.1 N alkali solution behaves like a dibasic acid ($g$-eq $= 92$, which is half of the molecular weight). The NMR spectrum of (VIII) was taken in pyridine and is easily interpreted as being the spectrum of the pyridinium salt: $12.97 = 2H_A$ (region of acid protons that form an H bond), $2.95 = 2H_B$, $2.86 = 2H_C$, $2.44 = 2H_E$, $1.84 = 2H_D$.

A number of transformations was run in order to confirm the structure of (VIII) chemically.

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\begin{align*}
\text{COOH} & \quad \text{COOCH}_3 \\
\text{CH}_3 & \quad \text{OCH}_3
\end{align*}
\]

Structures (IX)-(XI) are in agreement with the physicochemical and elemental analysis data.

**EXPERIMENTAL**

The IR spectra were taken on a UR-20 instrument, while the NMR spectra were taken on a Varian A-60DA spectrometer (60 MHz). The mass spectra were obtained on a Varian CH-6 MAT GmbH instrument using the following conditions: direct insertion of the sample into the ion source, energy of ionizing electrons 70 eV, emission current 100 μA, accelerating voltage 1.75 kV, and temperature of ion source 180°C.

3-Benzoylcyclohexanone (III) was synthesized as described in [2, 3]. Morpholine salt of benzoic acid (IV) [4], mp 121-122° (from water). The IR spectrum resembles the spectrum of benzoic acid. Based on the mixed melting point and IR spectrum, the salt obtained by counter synthesis is identical with the salt isolated from the reaction.

1-Morpholinocyclohexen-3-one (VI) was obtained as described in [4] and has mp 92-94°, cf. [5]. Infra-red spectrum (ν, cm⁻¹): 1640 (C=O), 1580 (C=C). PMR spectrum (δ, ppm): 1.97-2.5 m (6Hδ), 3.21-3.27 q (4 Hβ), 3.65-3.81 q (4 Hδ), 5.25 s (1 Hβ). Mass spectrum (m/e): 181(M⁺), 153(M⁺ - CO), 125(M⁺ - 2CO), 95(M⁺ - C₄H₆ON).

1-(Cyclohexa-1',3'-dion-2'-yl)-3-propanoic Acid (VIII). The alkylation with acryloyl chloride was run as described in [6]. The immonium salt was decomposed by refluxing with water for 1 h to give (VIII) in 32% yield, mp 179-180°, cf. [7]. Infrared spectrum (ν, cm⁻¹): 1700 (COO), 1580, 1610 (C=O), 1645 (C=O), 3250-3280 (OH).

Lactone of 1-(Cyclohexa-1',3'-dion-2'-yl)-3-propanoic Acid (IX). Acid (VIII) was sublimed twice at 180° (10 mm) to give the lactone (IX) in 90% yield, mp 48-50°. Infrared spectrum (ν, cm⁻¹): 1600 (C=O-C=O), 1660 (C=O), 1285 (=C=O), 1040, 1090 (=C=O). Mass spectrum (m/e): 166 (M⁺), 138 (M⁺ - CO), 110 (M⁺ - 2CO), 82 (M⁺ - 3CO). Found: C 65.42; H 6.01%. C₄H₁₀O₄. Calculated: C 65.65; H 6.07%.

Dimethyl Ester of 1-(Cyclohexa-1',3'-dion-2'-yl)-3-propanoic Acid. The esterification was run as described in [8]. Removal of the solvent gave a viscous oil, which was purified on Al₂O₃ (I activity). Infrared spectrum (ν, cm⁻¹): 1200, 1170 (=C-OC₂H₅), 1250 (=C=O), 1030 (O-CH₃), 1615 (C=C), 1740 (C=O).

Perhydrocoumarin (XI). Amalgamated Zn dust was obtained by stirring a mixture of 15 g of Zn dust, 1 g of HgCl₂, 0.8 ml of conc. HCl, and 5 ml of water for 5 min. Then the aqueous layer was decanted, 25 ml of conc. HCl, 25 ml of water, and 1.9 g of acid (VIII) were added, the mixture was refluxed for 10 h, and then 25 ml of the solution was distilled off, another 25 ml of conc. HCl was added, and 25 ml of the solution was again distilled off. This operation was repeated once more and the residue was steam-distilled. The distillate was extracted with ether, dried over Na₂SO₄, the ether was removed, and the residue was distilled at 96-101° (2 mm). Yield 81%, nD²⁰ 1.4778. Found: C 70.40; H 9.56%. C₄H₁₄O₂. Calculated: C 70.20; H 9.19%.

**CONCLUSIONS**

The behavior of 3-substituted cyclohexanones in enamination and alkylation reactions was studied; the reaction of morpholinocyclohexen-3-one with acryloyl chloride gives 1-(cyclohexa-1',3'-dion-2'-yl)-3-propanoic acid.