REACTIONS OF 1,5-DIKETONES

VIII.* AMINOMETHYLATION OF 1,3-DIPHENYL-1-(α,α-DIMETHYLTETRAHYDRO-γ-PYRON-β-YL)-3-PROPANONE

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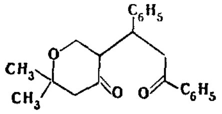
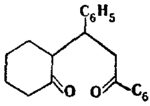
UDC 547.811'812.5:542.953

1,3-Diphenyl-1-(α,α-dimethyltetrahydro-γ-pyron-β'-yl)-2-dimethylaminomethyl-3-propanone was obtained by Mannich condensation of 1,3-diphenyl-1-(α,α-dimethyltetrahydro-γ-pyron-β'-yl)-3-propanone with formaldehyde and dimethylamine hydrochloride. Its deaminomethylation, deamination, and conversion to the corresponding oxatetrahydroquinoline on reaction with hydroxylamine hydrochloride were studied.

Up until now, heterocyclic 1,5-diketones have not been implicated in the Mannich reaction.



I



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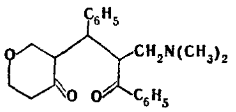
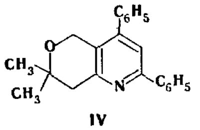


III

The aminomethylation of diketone I in alcohol under conditions analogous to those in the aminomethylation of diketone II [2] leads only to aminodiketone III in low yield (~4%). When the reaction is carried out in acetic acid, the yield of diketone III reaches 74%. Here the ring CH_2 group in the α position does not participate in the reaction, apparently because of steric hindrance. The hindered character of this group was previously noted in the aminomethylation of α,α-dimethyltetrahydro-γ-pyrone [3]. The structure of aminodiketone III is confirmed by the results of elementary analysis, the IR spectrum, and the chemical properties. The IR spectrum of aminodiketone III differs from the IR spectrum of the starting diketone I only with respect to the presence of two additional absorption bands at 2830 and 2780 cm^{-1}, which belong to the $CH_2N(CH_3)_2$ group [4]. When the hydrochloric acid salt of aminodiketone III is heated in water and in alcohol, it undergoes deaminomethylation to give starting diketone I. In this case, the reaction proceeds considerably more rapidly in alcohol than in water; this was apparently the reason for the low yield of diketone III when the aminomethylation was carried out in alcohol. Oxahydroquinoline IV, which is also obtained from diketone I [5], is obtained in quantitative yield when III is heated for 8 h in water in the presence of hydroxylamine hydrochloride. The rate of deaminomethylation falls on heating in 4% hydrochloric acid in the presence of $H_2NOH \cdot HCl$, and, as a result, oxahydroquinoline V (in 50% yield), i.e., the product of pyridinization of aminodiketone III itself, is obtained along with IV (in 45% yield). The capacity of diketone (III) for effective retro-Mannich reaction attests to the fact that the aminomethyl group in it is actually in the 2 position (between C_6H_5CO and C_6H_5) [2].



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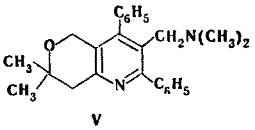
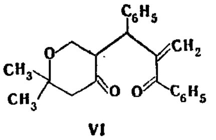


V



VI

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* See [1] for communication VII.

Far-Eastern State University, Vladivostok. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 738-740, June, 1973. Original article submitted January 19, 1972.

A stable methylidene diketone (VI) is obtained in the deamination of the methiodide of diketone (III). Its structure is confirmed by its IR spectrum: the absorption band of a heterocyclic carbonyl group is retained at 1710 cm^{-1}, as in starting diketone III, while the absorption band of an aryl-aliphatic carbonyl group, owing to additional conjugation with the double bond [6], was shifted from 1690 cm^{-1} to 1660 cm^{-1}, and a weak band characteristic for the stretching vibrations of the double bond of a methylidene group appeared at 1635 cm^{-1}.

EXPERIMENTAL

The IR spectra were recorded with a UR-20 spectrophotometer.

1,3-Diphenyl-1-(α,α-dimethyltetrahydro-γ-pyron-β'-yl)-3-propanone (I). This compound was obtained by addition of α,α-dimethyltetrahydro-γ-pyrone to chalcone [5].

1,3-Diphenyl-1-(α,α-dimethyltetrahydro-γ-pyron-β-yl)-2-dimethylaminomethyl-3-propanone (III). A mixture of 32.7 g (0.097 mole) of diketone I, 20 g (0.24 mole) of dimethylamine hydrochloride, 9 g (0.3 mole) of paraformaldehyde, and 100 ml of glacial acetic acid was heated on a boiling-water bath for 6 h, after which the acetic acid (~ 85 ml) was removed by vacuum distillation (20 mm), and the residue was treated with a mixture of 300 ml of water and 200 ml of ether. The ether layer was separated and dried with $MgSO_4$, and the ether was removed to give 6.5 g (~ 20%) of unchanged starting diketone I. The aqueous layer was made alkaline and extracted with ether to give 29 g (74%) of colorless crystals of aminodiketone III with mp 124-126° (from heptane). IR spectrum in CCl_4, cm^{-1}: 2830, 2780, 1710, and 1690. Found: C 76.45; H 8.04; N 3.68%. $C_{25}H_{31}NO_3$. Calculated: C 76.34; H 7.89; N 3.56%. The hydrochloride of III was obtained as colorless crystals with mp 205-206° (from propanol). Found: Cl 8.81%. $C_{25}H_{31}NO_3 \cdot HCl$. Calculated: Cl 8.72%. The picrate of III was obtained as lemon-yellow plates with mp 163-164° (from alcohol). Found: N 9.20%. $C_{25}H_{31}NO_3 \cdot C_6H_3N_3O_7$. Calculated: N 9.00%. The methiodide of III was prepared as follows. A 2-ml (32 mmole) sample of methyl iodide was added to a solution of 5.1 g (13 mmole) of aminodiketone III in 250 ml of ether, and the resulting precipitate was removed by filtration to give 6 g (73.5%) of colorless crystals with mp 249.5-250° (from methanol). Found: I 23.81%. $C_{25}H_{31}NO_3 \cdot CH_3I$. Calculated: I 23.74%.

1,3-Diphenyl-1-(α,α-dimethyltetrahydro-γ-pyron-β-yl)-2-methylidene-3-propanone (VI). A suspension of 4.7 g (9 mmole) of the methiodide of aminodiketone III in 30 ml of water, 80 ml of benzene, and 20 ml of 8% aqueous potassium hydroxide was heated on a water bath at 50-60° for 4 h with vigorous stirring. The mixture was cooled, the benzene layer was separated and washed with water, and the benzene was removed by distillation. The yield of colorless crystals of diketone VI, with mp 115° (from methanol), was 3.2 g (99.5%). IR spectrum in CCl_4, cm^{-1}: 1710, 1660 (C=O, two bands), 1635 ($C{=}CH_2$). Found: C 79.50; H 7.33%. The hydrogen number was 100. $C_{23}H_{24}NO_3$. Calculated: C 79.31; H 6.89%. Hydrogen No. 101.36.

Deaminomethylation of Aminodiketone III. A. A solution of 2 g of the hydrochloride of aminodiketone III in 1000 ml of water was refluxed for 4 h. It was then cooled and extracted with ether to give 0.58 g (34%) of diketone I with mp 149-150° (from alcohol); its identity with diketone I was confirmed by a mixed melting-point determination and the IR spectrum.

B. Similar treatment of 0.7 g of the salt in alcohol gave 0.4 g (70%) of diketone I.

C A 2-g sample of the salt was refluxed in 100 ml of 4% hydrochloric acid to give 0.1 g (6%) of diketone I.

D. The reaction was carried out by method A but in the presence of 2 g of hydroxylamine hydrochloride with refluxing for 8 h. Cooling and alkalization gave 1.4 g (96%) of 7,7-dimethyl-2,4-diphenyl-6-oxa-5,6,7,8-tetrahydroquinoline IV as colorless crystals with mp 87-87.5° (from alcohol). Found: C 84.14; H 6.72; N 4.65%. $C_{22}H_{21}NO$. Calculated: C 83.81; H 6.67; N 4.44%.

7,7-Dimethyl-2,4-diphenyl-3-dimethylaminomethyl-6-oxa-5,6,7,8-tetrahydroquinoline (V). A mixture of 30 g (0.07 mole) of the hydrochloride of aminodiketone III, 30 g (0.23 mole) of hydroxylamine hydrochloride, 250 ml of water, and 500 ml of concentrated HCl was refluxed for 8 h, after which it was cooled and made alkaline to pH 6. The precipitated hydroquinoline (IV) was removed by filtration to give 10.2 g (45%) of a product with mp 87-87.5° (from alcohol). The identity of this preparation with hydroquinoline IV was confirmed by a mixed melting-point determination and the IR spectrum. The filtrate was made alkaline to pH 10 to give 14.6 g (50%) of hydroquinoline V with mp 124-126° (from acetone). IR spectrum in CCl_4, cm^{-1}: 2780, 2830 [$CH_2N(CH_3)_2$]. Found: C 80.62; H 7.68; N 7.74%. $C_{25}H_{28}N_2O$. Calculated: C 80.65; H 7.53; N 7.53%.

The picrate of V was obtained as yellow prisms with mp 189-190° (dec., from alcohol). Found: N 13.84%. $C_{25}H_{28}N_2O \cdot 2C_6H_3N_3O_7$. Calculated: N 13.49%. The hydrochloride of V was obtained as colorless crystals with mp 222-223° [alcohol–acetone (1 : 10)]. Found: Cl 15.90%. $C_{25}H_{28}N_2O \cdot 2HCl$. Calculated: Cl 15.96%.

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