REACTION OF ACETALDEHYDE WITH IMINODIMEDONE

A. A. Akhrem, A. M. Moiseenkov,
and V. V. Veselovskii

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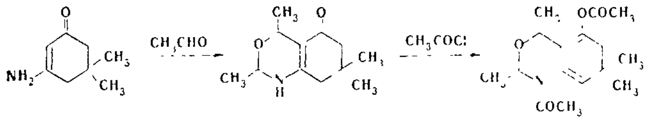
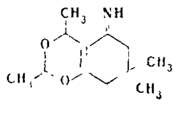
The condensation of acetaldehyde with iminodimedone leads to 2,4,7,7-tetramethyl-5-oxo-1,2,5,6,7,8-hexahydro-4H-3,1-benzoxazine.

The reaction of primary and secondary keto vinylamines with various aldehydes is a well-known modification of the Hantzsch synthesis of dihydropyridines [1]. This reaction, which is extremely sensitive to the conditions of its performance, usually takes place with the participation of two moles of enamino ketones and one mole of aldehyde. Cases with the inverse ratio of the reactants, leading to the formation of pyrimidine derivatives have been described considerably more rarely [2, 3]. The present paper discusses a previously unknown synthesis of oxazine derivatives by the condensation of two moles of an aldehyde and one mole of an enamino ketone.

When iminodimedone (I) was allowed to stand in acetaldehyde solution, a compound was formed which, according to elementary and mass-spectrometric analysis, had the empirical formula $C_{12}H_{19}NO_2$ and, according to its absorption spectra, retained the transoid enamino ketone function present in the initial compound (I). The reaction product was ascribed the structure (II) mainly on the basis of its PMR spectrum (in $CDCl_3$) showing the presence in the molecule under consideration of the protons of a dimedone fragment together with an NH proton, δ 6.40 ppm. In addition to this, the PMR spectrum contained the signals of two secondary methyl groups in the form of doublets with δ 1.30 ppm (J 6.5 Hz) and 1.32 ppm (J 5.5 Hz). The resonance signals of the methine protons in positions 2 and 4 have the form of two overlapping quartets with centers at 4.70 and 4.80 ppm with the same constants J. In addition, the spectrum shows the singlet of a gem-dimethyl group (0.98 ppm) and the broadened singlet of methylene protons (2.01 and 2.15 ppm).



I II III



IIa

In agreement with the proposed enamino ketone structure (II), and not its possible isomer (IIa), the compound proved to be stable under ordinary conditions of catalytic hydrogenation and to the action of $NaBH_4$, but gave a complex mixture of substances on treatment with $LiAlH_4$ (see [4]). The enamino ketone (II) is stable to the action of acylating agents under mild conditions, but under severe conditions [5] it is converted into the N,O-diacetate (III), the structure of which was assigned on the basis of its spectra. Thus, its PMR spectrum (in CCl_4) contains singlet signals of an olefinic proton, δ 5.08 ppm, and of gem-dimethyl protons, δ 1.14 and 1.17 ppm. The resonance signal of the methylene protons in position 6 has the form of an AB spectrum with its center at 2.90 ppm and the 2-H and 4-H protons form two overlapping quartets with centers at 5.45 ppm (J 8.5 Hz) and 5.48 ppm (J 7.8 Hz). The corresponding doublet signals of the 2-CH_3 and 4-CH_3 methyl protons are located at 1.27 and 1.39 ppm, and the singlets of the $COCH_3$ groups at 2.12 and 2.14 ppm.

The reactions considered apparently have a fairly general nature, which permits the possibility of obtaining new heterocycles of the 3,1-benzoxazine series to be envisaged.

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EXPERIMENTAL

The melting points were determined on a Kofler block. The IR spectra were obtained on a UR-10 instrument in KBr tablets and the PMR spectra on an RS-60 spectrometer (with HMDS as internal standard).

2,4,7,7-Tetramethyl-5-oxo-1,2,5,6,7,8-hexahydro-4H-3,1-benzoxazine (II). A solution of 3 g of (I) [6] in 90 ml of acetaldehyde was left to stand at 5°C for three days and was then evaporated; the residue was treated with cold ether, and the reaction product, after isolation from the ether, was crystallized from acetone. This gave 2.5 g (55%) of (II) in the form of colorless needles with mp 170-171°C (decomposition, subl.). IR spectrum: ν 1525, 1550, 1580, 3255 cm^{-1}. UV spectrum: λ_{max} 295 nm (ε 25,000) (in ethanol). Found,%: C 69.1; H 9.2; N 6.6. $C_{12}H_{19}NO_2$. Calculated,%: C 68.9; H 9.2; N 6.7.

5-Acetoxy-1-acetyl-2,4,7,7-tetramethyl-1,2,6,7-tetrahydro-4H-3,1-benzoxazine (III). A solution of 3 g of acetyl chloride in 10 ml of THF was added dropwise with stirring at room temperature to a solution of 1.22 g of (II) and 3 ml of pyridine in 40 ml of THF, and the mixture was allowed to stand for 1 h 30 min and was then boiled for 15 min. After the elimination of the solvent in vacuum, the residue was treated with ice water and was extracted with ether. The usual working up of the extract yielded 1.0 g (60%) of (III) with mp 49-50°C (from hexane). IR spectrum: ν 1618, 1676, 1755 cm^{-1}. Found, %: C 65.6; H 7.8; N 4.8. $C_{16}H_{23}NO_4$. Calculated,%: C 65.5; H 7.9; N 4.8.

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