CHEMISTRY OF ESTERS OF KETO ACIDS OF THE ACETYLENE SERIES

VIII.* 2-ARYL-4-CARBALKOXYBENZO[b]-1,5-DIAZEPINES

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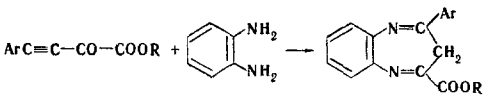
UDC 547.892.863:543.422.25.4

The reaction of esters of arylethynylglyoxylic acids with o-phenylenediamine gave 2-aryl-4-carbalkoxybenzo[b]-1,5-diazepines, the structures of which were proved by IR and PMR spectroscopy.

It has been shown that esters of arylethynylglyoxylic acids add amines, arylhydrazines, and carboxylic acid hydrazides under extremely mild conditions to give adducts involving the γ-carbon atom [2,3]. In this connection, it seemed of interest to investigate the reaction of esters of ethynylglyoxylic acids with o-phenylenediamine. The introduction of a second amino group into the arylamine molecule provides the possibility of the formation of not only addition products but also cyclic compounds. It is known that α-keto acids and their esters form quinoxalones on reaction with o-phenylenediamine [4,5].

We obtained 2-aryl-4-carbalkoxybenzo[b]-1,5-diazepines (I) when we carried out the indicated reaction in alcohol at room temperature.

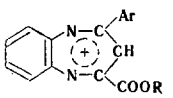


I

The structures of I were confirmed by a study of their IR and PMR spectra. The IR spectra (Fig. 1) contain a band at 1708 cm^{-1}, corresponding to the valence vibrations of an ester carbonyl group, while absorption bands caused by an acetylene bond, a ketone carbonyl group, and the N–H group are absent.

The PMR spectrum of 2-phenyl-4-carbisopropoxybenzo[b]-1,5-diazepine demonstrated the presence of six protons of the two equivalent methyl groups of the isopropyl radical (1.30 ppm, doublet), two equivalent protons of the methylene group of the benzodiazepine ring (3.46 ppm, singlet), and one proton of the methylidyne group of the isopropyl radical (5.05 ppm, multiplet). The multiplet at 7.33 ppm corresponds to the four protons of the condensed benzene ring and to the meta and para protons of the phenyl group. The multiplet at 8.20 ppm corresponds to the signals of the two ortho protons of the phenyl group (Fig. 2).

There is one absorption maximum at 270 nm in the electronic spectra of the synthesized compounds (Fig. 3), while the spectra of ω-(2-quinoxalon-3-yl)acetophenones (III), the formation of which as a result of the investigated reaction is possible, have a second absorption maximum at 440 nm.



II

*See [1] for communication VII.

Perm Pharmaceutical Institute. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1702-1704, December, 1972. Original article submitted December 7, 1971.

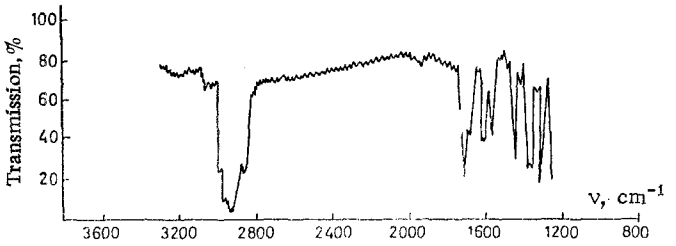


Fig. 1. IR spectrum of 2-phenyl-4-carbisopropoxybenzo[b]-1,5-diazepine.

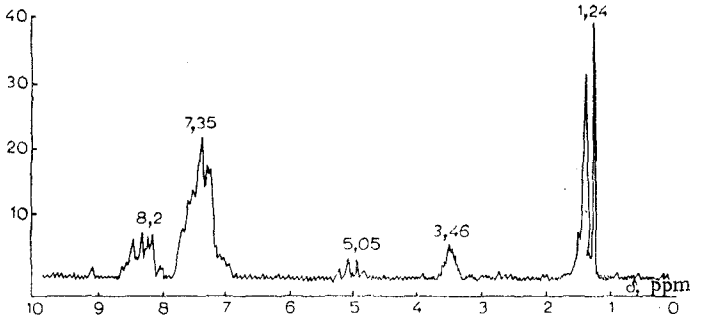


Fig. 2. PMR spectrum of 2-phenyl-4-carbisopropoxybenzo[b]-1,5-diazepine.

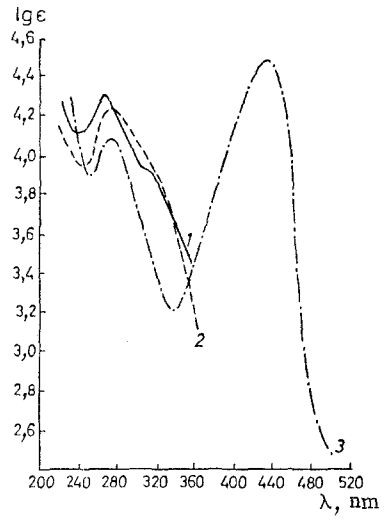
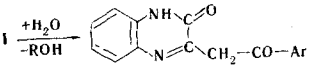


Fig. 3. UV spectra of 2-phenyl-4-carbalkoxybenzo[b]-1,5-diazepinones: 1) 2-phenyl-4-carbisopropoxybenzo-[b]-1,5-diazepine; 2) 2-(p-tolyl)-4-carbisopropoxybenzo[b]-1,5-diazepine; 3) ω-(2-quinoxalon-3-yl)acetophenone.

Dark blue colored salts containing 2-aryl-4-carbalkoxybenzo[b]diazepinium ions (II) [6,7] precipitate when benzene solutions of the synthesized compounds are saturated with hydrogen chloride. These chloride salts can be reconverted to benzodiazepines by the action of bases.

An attempt to hydrolyze the synthesized compounds to 2-aryl-4-carboxybenzo[b]-1,5-diazepines by means of alcoholic alkali was unsuccessful, since the hydrolysis of I is accompanied by rearrangement to ω-(2-quinoxalon-3-yl)acetophenones (III) under these conditions:



III

EXPERIMENTAL

The UV spectra of 10^{-3}-10^{-4} M ethanol solutions of the compounds were recorded with an SF-4 spectrometer at 220-400 nm. The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-10 spectrophotometer (NaCl and LiF prisms). The PMR spectra of 10% solutions in $CDCl_3$ were recorded with a JNM-C-60 HL spectrometer at 20° with hexamethyldisiloxane as the standard.

2-Phenyl-4-carbisopropoxybenzo[b]-1,5-diazepines. A solution of 3.24 g (15 mmole) of isopropyl phenylethynylglyoxylate in 25 ml of isopropyl alcohol was added dropwise with stirring to a solution of 1.62 g (15 mmole) of o-phenylenediamine in 25 ml of isopropyl alcohol, and the reaction mixture was allowed to stand at room temperature for 12 h. Filtration gave 1.6 g (35%) of light yellow needles with mp 115-116° (from isopropyl alcohol). Found,%: N 9.0. $C_{19}H_{18}N_2O_2$. Calculated,%: N 9.1.

Bubbling of hydrogen chloride into a 10% solution of the substance in benzene resulted in quantitative precipitation of dark blue prisms of 2-phenyl-4-carbisopropoxybenzo[b]-1,5-diazepinium chloride with mp 191-192°.

2-Phenyl-4-carbethoxybenzo[b]-1,5-diazepine. A solution of 2.02 g (0.01 mole) of ethyl phenylethynylglyoxylate in 25 ml of absolute diethyl ether was added dropwise with stirring to a solution of 1.08 g (0.01 mole) of o-phenylenediamine in 25 ml of absolute methanol, and the mixture was allowed to stand at room temperature for 24 h. The solution was then cooled to −5°, and the resulting crystals were removed by filtration. The filtrate was allowed to stand at −25° for 48 h, and the resulting precipitate was removed by filtration to give 0.75 g (26%) of light yellow needles with mp 87-88° (from ethanol). Found,%: N 9.6. $C_{18}H_{16}N_2O_2$. Calculated,%: N 9.5.

2-(p-Tolyl)-4-carbisopropoxybenzo[b]-1,5-diazepine. A solution of 1.08 g (0.01 mole) of o-phenylenediamine in 20 ml of isopropyl alcohol was added dropwise with stirring to a solution of 2.24 g (0.01 mole) of isopropyl p-tolylethynylglyoxylate in 30 ml of isopropyl alcohol. After 36 h, the mixture was cooled to −5°, and the resulting precipitate was removed by filtration to give 0.6 g (19%) of a product with mp 97-98° (from ethanol). Found,%: N 8.8. $C_{20}H_{20}N_2O_2$. Calculated,%: N 8.9.

Rearrangement of 2-Phenyl-4-carbisopropoxybenzo[b]-1,5-diazepine to ω-(2-Quinoxalon-3-yl)acetophenone. A 0.25-g sample of the benzodiazepine derivative was refluxed with a solution of 0.16 g of potassium hydroxide in 3.2 ml of alcohol for 20 min. The alcohol solution was then poured into 25 ml of water, and the mixture was acidified to pH 1 with 10% hydrochloric acid, during which the solution turned green and a yellow precipitate formed. Two hours after the green solution also became yellow, the precipitate was removed by filtration to give 0.18 g (76%) of a product with mp 264-265° (from glacial CH_3COOH). No melting-point depression was observed for a mixture of this product with a sample of ω-(2-quinoxalon-3-yl)acetophenone obtained from methyl benzoylpyruvate and o-phenylenediamine [5].

LITERATURE CITED

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