REACTION OF ESTERS OF β,γ-ACETYLENIC α-KETO ACIDS WITH o-PHENYLENEDIAMINE*

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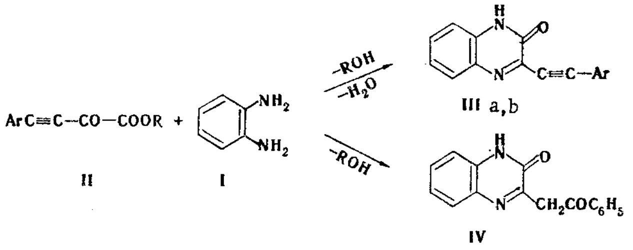
The reaction of esters of β,γ-acetyleneic α-keto acids with o-phenylenediamine (I) leads, in the case of esters of arylethynylglyoxylic acids (II) in an anhydrous solvent solvent, to 2-arylethynyl-3-quinoxalones (III). 2-Phenacyl-3-quinoxalones (IV) are formed when III are treated with alcoholic alkali. The reaction of esters of alkylethynylglyoxylic acids (V) with I leads to 2-(β-oxoalkyl)-3-quinoxalones (VI). The structures of III and VI were confirmed by the IR spectra.

Compounds I and II react in isopropyl alcohol to give 2-aryl-4-carbalkoxybenzo[b]-1,5-diazepines (VII), a small amount of resinous substances, and IV. To ascertain the mechanism of the formation of IV, we studied this reaction in various solvents.

When the reaction is carried out in absolute ether, the acetylene bond does not become involved, and the major products are III.



III a $Ar=C_6H_5$; b $Ar=p\text{-}CH_3C_6H_4$

The IR spectra of III contain a band at 2197 and 2220 cm^{-1}, which corresponds to the stretching vibrations of the acetylene bond, but absorption bands due to a ketone carbonyl group and a primary amine group are absent.

When III is heated with a 10% solution of aqueous alcoholic alkali, one obtains IV, which is identical to the compound synthesized from methyl benzoylpyruvate and I.

The acetylenic bond in III is capable of adding to nucleophilic reagents under relatively severe conditions. Thus the reaction with excess phenylhydrazine gives phenylhydrazone IV.

The addition of amines is accompanied by intramolecular condensation to give 2-arylpyrrolo[2,3-b]-quinoxaline.

The formation of a quinoxaline ring in the reaction of I and II in an aqueous organic solvent is always accompanied by hydration of the acetylenic bond to give IV.

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The best results were obtained in the case of 70-75% aqueous ethanol. The use of a solvent with a higher percentage of water lowers the yields of IV because of a decrease in the solubility of the substances.

2-Alkylethynyl-3-quinoxalones cannot be obtained by reaction of V with I even in nonaqueous solvents. The only reaction products are VI, which are formed as a result of addition of the water generated during the cyclization.

The IR spectra of these compounds contain lines due to the stretching vibrations of the amide carbonyl group (1680 cm^{-1}) and the deformation vibrations of the N−H group (1580 cm^{-1}), but absorption characteristic for the stretching vibrations of the acetylene bond is absent. Compounds VI and IV have similar IR spectra.

EXPERIMENTAL

The IR spectra in mineral oil were recorded with a UR-10 spectrophotometer with NaCl and LiF prisms.

2-Phenylethynyl-3-quinoxalone (VIII). A. A solution of 2.02 g (0.01 mole) of ethyl phenylethynylglyoxylate in 25 ml of absolute ether was added dropwise with stirring to a solution of 1.08 g (0.01 mole) of I in 50 ml of absolute ether. After 2 h at 20°, the reaction mixture was filtered to give 1.68 g (68%) of yellow prisms of VII with mp 207-208° (from nitromethane). Found: N 11.1%. $C_{16}H_{10}N_2O$. Calculated: N 11.4%.

B. Similarly, 1.6 g (65%) of VII was obtained from 2.16 g (0.01 mole) of isopropyl phenylethynylglyoxylate (VIII).

2-(p-Tosylethynyl)-3-quinoxalone (IX). Similarly, 0.98 g (38%) of yellow needles of IX with mp 209-210° (from nitromethane) was obtained from 2.3 g (0.01 mole) of isopropyl p-tolylethynylglyoxylate. Found: N 11.1%. $C_{17}H_{12}N_2O$. Calculated: N 10.8%.

2-Phenacyl-3-quinoxalone (IV). A mixture of 0.25 g (1 mmole) of VII and a tenfold excess of 10% aqueous alcoholic alkali was heated for 2 h, after which the cooled mixture was poured into 50 ml of water. The aqueous mixture was acidified with H_2SO_4 (1:4) and filtered to give 0.22 g (83%) of IV. No melting-point depression was observed for a mixture of this product with IV obtained from methyl benzoylpyruvate (X) and I [2].

2-Phenacyl-3-quinoxalone Phenylhydrazone. A mixture of 0.3 g (1.4 mmole) of VII and 12.5 ml of phenylhydrazine was heated at 140-150° for 3 h, after which the cooled mixture was poured into 200 ml of 20% acetic acid. The acid mixture was filtered to give 0.47 g (95%) of a crystalline substance, which was identical to the 2-phenacyl-3-quinoxalone phenylhydrazone obtained from IV.

Reaction of Isopropyl Phenylethynylglyoxylate (VIII) with o-Phenylenediamine in 70% Ethanol. A solution of 1.08 g (0.01 mole) of I in 20 ml of 70% ethanol was added dropwise with stirring to 2.16 g (0.01 mole) of VIII in 20 ml of 70% ethanol. The mixture was allowed to stand for 24 h at room temperature, after which it was filtered to give 2.0 g (75%) of yellow needles of IV with mp 269-270° (from glacial acetic acid). No melting-point depression was observed for a mixture of this product with IV obtained from X and I.

1-(2'-Quinoxalon-3-yl)-2-hexanone (XI). A solution of 5.4 g (0.05 mole) of I in 200 ml of absolute diethyl ether was added with stirring to a solution of 9.8 g (0.05 mole) of isopropyl butylethynylglyoxylate in 25 ml of the same solvent. The mixture was then allowed to stand at room temperature for 96 h, after which it was filtered to give 7.93 g (65%) of yellow needles of XI with mp 217.5-218°. (from nitromethane). Found: N 11.4%. $C_{14}H_{16}N_2O$. Calculated: N 11.3%.

1-(2'-Quinoxalon-3-yl)-2-octanone (XII). Similarly, 2.11 g (38%) of yellow needles of XII with mp 197-198° (from nitromethane) was obtained from 4.48 g (0.02 mole) of isopropyl hexylethynylglyoxylate and 2.16 g (0.02 mole) of I. Found: N 10.2%. $C_{16}H_{20}N_2O_2$. Calculated: N 10.1%.

1-(2'-Quinoxalon-3-yl)-2-nonanone (XIII). Similarly, 0.39 g (27%) of yellow needles of XIII with mp 191.5-192.5° (from nitromethane) was obtained from 1.19 g (5 mmole) of isopropyl heptylethynylglyoxylate and 0.56 g (5 mmole) of I. Found: N 9.7%. $C_{17}H_{22}N_2O_2$. Calculated: N 9.8%.

LITERATURE CITED

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2. S. Fatutta and A. Stener, Gazz. Chim. Ital., 88, 89 (1958).