Chemistry

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reaction scheme with compounds (I), (II), (III), and (IV)

Figure 1: reaction scheme with compounds (I), (II), (III), and (IV)

Abstract

Full Text

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INTRAMOLECULAR REVERSIBLE CYCLIZATION OF AMIDES OF 8-$(2^1, 3^1(\mathrm{CO}), 6^1, 5^1(\mathrm{CO})$-DIBENZOYLENEPYRIDYL-$4^1$)-NAPHTHOIC-1 ACID

The condensation product of indandione-1,3 with acenaphthenequinone—diindandionylacenaphthene-1—under the action of ammonia is converted into acenaphthenone-1-spiro-$(2 : 4^1) - 2^1, 3^1(\mathrm{CO}), 6^1, 5^1(\mathrm{CO})$-dibenzoylene-$1^1, 4^1$-dihydropyridine (I) (^{1}). In alcoholic alkali it dissolves with a green coloration, which is characteristic of many dibenzoylenedihydropyridines. Recently we developed a more convenient method for obtaining this compound and studied its oxidation: with cleavage of the acenaphthene ring, 8-$(2^1, 3^1(\mathrm{CO}), 6^1, 5^1(\mathrm{CO})$-dibenzoylenepyridyl-$4^1$)-naphthoic-1 acid (III) is formed. Some derivatives of this acid were also obtained: salts, esters, acid chloride*.
a) $R_1 = R_2 = \mathrm{H}$; b) $R_1 = \mathrm{C_2H_5}$, $R_2 = \mathrm{H}$; c) $R_1 = R_2 = \mathrm{C_2H_5}$; d) $R_1 = \mathrm{C_2H_5}$, $R_2 = \mathrm{CH_3CO}$; e) $R_1 = \mathrm{C_2H_5}$, $R_2 = n - \mathrm{O_2N{-}C_6H_4CO}$.

By the action of ammonia and of primary and secondary amines on the acid chloride of acid III, its amides (IV a, b, c) were prepared. In neutral and acidic media they are yellow in color, like all the other derivatives of acid III. However, those amides that have at the amide nitrogen at least one hydrogen atom (IV a, b) dissolve in alcoholic alkali with an intense violet coloration; upon acidification of the solution they are precipitated again in unchanged form. The sodium salt of amide IV a was isolated in pure form. Diethylamide (IV c) does not dissolve in alcoholic alkali and does not change its absorption spectrum in the ultraviolet and visible regions of light after the addition of alkali. *N*-ethyl-*N*-acetyl- and *N*-ethyl-*N*-*p*-nitrobenzoylamides (IV d, e), under the action of alcoholic alkali, dissolve slowly, gradually acquiring a violet color, which is evidently connected with cleavage of the acyl group and regeneration of ethylamide (IV b).

The phenomenon described cannot be attributed solely to the naphthamide amide group, since the latter does not give a similar coloration and, upon addition of alkali, does not change the character of its spectrum (Fig. 1), whereas amides IVa, b, on dissolving in alcoholic alkali, lose the absorption spectrum

Reaction scheme showing conversion of IV to VI and VII

Figure 2: Reaction scheme showing conversion of IV to VI and VII

Graph

Figure 3: Graph

characteristic of all aryldibenzoylenepyridines (Fig. 2). The violet coloration on dissolution of amides IV a, b in alkalis appears only in the case where the carbonyl groups have been retained; the coloration is absent in the dioxime ethylamide and in the reduction product of ethylamide (VII). It follows from this that, in the presence of alkali, both parts of the molecule—the naphthamide and the dibenzoylenepyridine parts—interact with formation of the violet anion VI, which on acidification is converted back into amide IV.

In the pyridine molecule the electron cloud is shifted toward nitrogen, and small positive charges appear on the α- and γ-carbons. They are the reason for the occurrence of nucleophilic substitution reactions in the pyridine ring. In our case, the carbonyl groups of benzoylene located in the β-position further intensify the electrophilic character of the α- and γ-carbons.

In the amide nitrogen the free electron pair is shifted toward the carbonyl group, and therefore the nucleophilic character of nitrogen is reduced. However, in an alkaline medium amides are capable of splitting off a proton, acquiring a strong nucleophilic character. This is supported by polarographic studies of amides ([2]). The same process apparently is the cause of the cyanoethylation reaction of amides in the presence of alkaline agents ([3], [4]). It is clear that, for this, the amide nitrogen must have at least one hydrogen atom.

It is no accident that, up to now, no reaction of pyridine with acid amides has been known either in a neutral or in an alkaline medium. In our case the amide nitrogen and the electrophilic γ-carbon of pyridine are in a very favorable position: together with the four carbon atoms connecting them they constitute a system of 6 atoms, which tends toward coplanarity and formation of a 6-membered ring. Such a possibility for a transannular-type reaction ([5]) appears in an alkaline medium. The reaction product (VI) essentially corresponds to an intermediate product of nucleophilic substitution in pyridine ([6]) or in aromatic nitro compounds ([7], [8]), but it can be stabilized in only one direction—toward the starting product (IV). These transitions proceed easily and rapidly at room temperature.

Fig. 1. UV absorption spectra of α-naphthamide:

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Fig. 2 and Fig. 3: UV absorption spectra

Figure 4: Fig. 2 and Fig. 3: UV absorption spectra

1—in methanol solution;
2—in alkaline methanol solution

The reaction product (VI), in its structure, very much resembles the anion of benzoylenedihydropyridine (II). This similarity of structures is reflected in the absorption spectra (Figs. 2 and 3). In a neutral medium the absorption spectra of amide (IVa) and ethylamide (IVb) differ substantially from the absorption spectrum of I. All this permits the conclusion that there is a nucleophilic, reversible, intramolecular addition of amides to dibenzoylenepyridine. It is interesting to note that recently a report appeared on the reversible addition of an active methylene group to the electrophilic C_9 atom of acridine (^{9}).

It is necessary to note also certain other features of the amides described: for example, they are extremely resistant to hydrolysis reactions; they could not be obtained from esters of acid III by an ammonolysis reaction; they burn with great difficulty; correct results of microanalysis for nitrogen were obtained only when nickel oxide was used.

Experimental Part

Amide of 8-[2^1, 3^1 (CO), 6^1, 5^1 (CO)-dibenzoylenepyridyl-4^1]naphthoic-1 acid (IVa). To a hot solution of 3.4 g of the acid chloride of acid III in 170 ml of dry dioxane, 40 ml of 25% ammonia is added in small portions. On the following day the solution is diluted with 350 ml of water and acidified. The precipitate that separates is suspended in 100 ml of a saturated $NaHCO_3$ solution and separated the next day. Yield: 2.8 g of a yellow substance, m.p. 314-316° (from chlorobenzene or glacial acetic acid). It dissolves in aqueous alcoholic alkali with a blue-violet coloration.

Fig. 2. UV absorption spectra of derivatives of acid III: 1 —ethylamide (IVb) in $CHCl_3$ solution; 2 —ethyl ester of III in $CHCl_3$ solution; 3 —ethylamide in alkaline methanol solution (VI)

Fig. 3. UV absorption spectra of acenaphthenedibenzoylenedihydropyridine (I): 1 —in $CHCl_3$ solution, 2 —in alkaline methanol solution (II)

Found, %: N 6.14
$C_{30}O_{16}O_3N_2$. Calculated, %: N 6.19

Sodium salt of the amide (VI). The amide is boiled in 0.5% NaOH solution, filtered, and 20% NaOH solution is slowly added to the filtrate until a 1% NaOH solution is obtained. Small dark-blue plate-like crystals separate, decomposing at 275-280°.

Found, %: N 5.87; Na 4.90
$C_{30}H_{15}O_3N_2Na$. Calculated, %: N 5.90; Na 4.85

Ethylamide of 8-[2^1, 3^1 (CO), 6^1, 5^1 (CO)-dibenzoylenepyridyl-4^1]naphthoic-1 acid (IVb). To 10 g of the acid chloride of acid III in 350 ml of anhydrous dioxane are added 10.38 g of $C_2H_5NH_2 \cdot HCl$ and 5.1 g of NaOH; the mixture is heated on a water bath for 2 hours, diluted with water, and acidified. The precipitate is treated twice with 500 ml of 2% Na_2CO_3, and the residue is crystallized from glacial acetic acid. Yield: 8 g of a yellow substance, m.p. 320°. It dissolves in aqueous alcoholic alkali with a blue-violet coloration.

Found, %: N 5.81
$C_{32}H_{20}O_3N_2$. Calculated, %: N 5.83

Oximation. 0.75 g of ethylamide (IVb), 10 ml of anhydrous pyridine, and 2 g of $NH_2OH \cdot HCl$ are heated for 2 hours on a water bath and poured

in 100 ml of hydrochloric acid (1 : 1). The precipitate is dissolved in 100 ml of 2.5% NaOH, and the filtrate is acidified. Light-yellow needles are formed (from alcohol), m.p. 290°, soluble in aqueous alkali with a yellow coloration.

Found, %: N 10.74
$C_{32}H_{22}O_3N_4$. Calculated, %: N 10.97

Acetylation. Ethylamide (IV) is boiled for 6 h in acetic anhydride and crystallized from benzene; yellow plates (IV), m.p. 263° (from benzene).

Found, %: N 5.12
$C_{34}H_{22}O_4N_2$. Calculated, %: N 5.36

p-Nitrobenzoylation. 0.5 g of ethylamide (IV), 2 g of *p*-nitrobenzoyl chloride, and 5 ml of anhydrous pyridine are boiled for 2 h, poured into 50 ml of water, and the precipitate is purified by treatment with 100 ml of 5% Na_2CO_3. Small yellow plates (IV) are formed (from glacial acetic acid), m.p. 274°.

Found, %: N 6.72
$C_{39}H_{23}O_6N_3$. Calculated, %: N 6.67

Reduction. 2 g of ethylamide (IV) in 60 ml of glacial acetic acid are boiled with zinc dust until the solution is decolorized, diluted with water, and treated with an excess of concentrated ammonia. Yield: 1.85 g of colorless ethylamide of 8-[di-*o*-benzylenopyridyl-4^1]-naphthoic-1-acid (VII), m.p. 316–318° (from glacial acetic acid or xylene).

Found, %: N 5.91
$C_{32}H_{24}O_3N_2$. Calculated, %: N 5.78

Diethylamide of 8-[2^1, 3^1 (CO), 6^1, 5^1 (CO)-dibenzoylenepyridyl-4^1]-naphthoic-1-acid (IV). 1.8 g of acid chloride III, 150 ml of dry chloroform, and 10 ml of diethylamine are boiled on a water bath for 2 h; most of the chloroform is removed, and alcohol and water are added. The precipitate is purified by treatment with 0.5% NaOH. A yellow substance is formed, m.p.

332° (from glacial acetic acid). It does not dissolve in alcoholic alkali and does not change color.

Found, %: N 5.55
$C_{34}H_{24}O_3N_2$. Calculated, %: N 5.51

The spectra were recorded on an SF-4 spectrophotometer. The authors express their gratitude to A. Grinvalde for recording the spectra.

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