SUBSTITUTED HYDRAZIDES OF HYDROXY CARBOXYLIC ACIDS

LXVI*. CONVERSION OF β-ALKYL-β-ARYLHYDRAZIDES OF DIARYLGLYCOLIC ACIDS INTO 1,2,3,4-TETRAHYDROCINNOLIN-3-ONE DERIVATIVES

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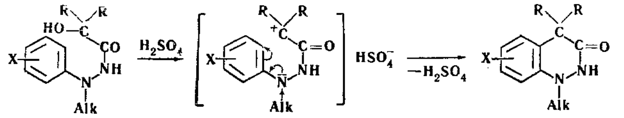
Under the action of concentrated sulfuric acid, a series of β-alkyl-β-arylhydrazides of diarylglycolic acids is converted into 1-alkyl-1,2,3,4-tetrahydrocinnolin-3-ones. The reaction takes place through the intermediate formation of a halochromic salt.

One of us [2] has previously shown that in the presence of concentrated sulfuric acid arylhydrazides of diarylglycolic acids are converted into 1,2,3,4-tetrahydrocinnoline derivatives. The present investigation was undertaken to determine the influence of an alkyl group attached to the nitrogen bearing the aryl radical in this group of hydrazides on their capacity for cyclization. As the starting materials we used the diarylglycolic acid β-alkyl-β-arylhydrazides synthesized previously [3-5]. Their conversion into cinnoline derivatives takes place through the intermediate formation of a halochromic salt [2] in the following way:



$X = H, CH_3$; $Alk = CH_3, C_2H_5$; $R = C_6H_5$, m-, p-$CH_3C_6H_4$, p-$(CH_3)_2CHC_6H_4$, p-ClC_6H_4

The rate of the cyclization reaction in the compounds studied is higher than in the nonalkylated compounds, which may be due to the exertion by the alkyl group of a +I effect promoting the creation of a nucleophilic center.

The cinnoline derivatives obtained are shown in Table 1. They are colorless crystalline substances soluble in alcohol, benzene, toluene, and other organic solvents.

It can be seen from Fig. 1 that the cinnoline derivatives lack a band of the stretching vibrations of the OH group in the IR region. The ν_{NH} band in the cyclic products and in the initial arylhydrazides has a frequency of 3435 cm^{-1}. The weak band at 3320 cm^{-1} in the cinnoline derivatives and in the initial hydrazides is connected with the inclusion of the NH group in a weak hydrogen bond. On passing to crystals, a fall in ν_{NH} to 3364 cm^{-1} takes place because of the increased participation of the NH group in hydrogen bonds. The amide-I band in the 1-alkyltetrahydrocinnolines synthesized has a somewhat higher frequency than in the unsubstituted compounds [2]. On cyclization, a strong band appears at 1190 cm^{-1} which, on the basis of results obtained previously [2], we assign to the new ring that has appeared. The cyclic derivatives show no band at 1060 cm^{-1} corresponding to the stretching vibrations of the C—OH bond in the initial arylhydrazides [5].

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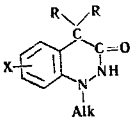
*For Communication LXV, see [1].

Gor'kii Perm University. Translated from Khimiya Geterotsiklicheskikh Soedinenii, Vol. 6, No. 6, pp. 844-846, June, 1970. Original article submitted May 27, 1968.

TABLE 1



Compound	X	Alk	R	Mp, °C	Empirical formula	N, %		Yield, %
						found	calc.	
I	H	CH_3	C_6H_5	138—139	$C_{21}H_{18}N_2O$	8,8	8,9	98
II	H	C_2H_5	,,	92—93	$C_{22}H_{20}N_2O$	8,4	8,5	98
III	H	CH_3	*m*-$CH_3C_6H_4$	97—98	$C_{23}H_{22}N_2O$	7,9	8,2	98
IV	H	C_2H_5	*p*-$CH_3C_6H_4$	112—113	$C_{24}H_{24}N_2O$	7,6	7,9	97
V	H	CH_3	*p*-ClC_6H_4	121—122	$C_{21}H_{16}Cl_2N_2O$	7,2	7,3	99
VI	6-CH_3	CH_3	C_6H_5	149—150	$C_{22}H_{20}N_2O$	8,4	8,5	98
VII	6-CH_3	,,	*p*-$CH_3C_6H_4$	162—163	$C_{24}H_{24}N_2O$	7,6	7,9	98
VIII	6-CH_3	,,	*p*-$(CH_3)_2CHC_6H_4$	179—180	$C_{28}H_{32}N_2O$	6,5	6,8	98
IX	7-CH_3	CH_3	C_6H_5	150—151	$C_{22}H_{20}N_2O$	8,3	8,5	98
X	8-CH_3	C_2H_5	,,	104—105	$C_{23}H_{22}N_2O$	7,9	8,2	97
XI	8-CH_3	CH_3	*p*-$CH_3C_6H_4$	118—119	$C_{24}H_{24}N_2O$	7,7	7,9	97
XII	8-CH_3	C_2H_5	C_6H_5	134—135	$C_{23}H_{22}N_2O$	8,0	8,2	97

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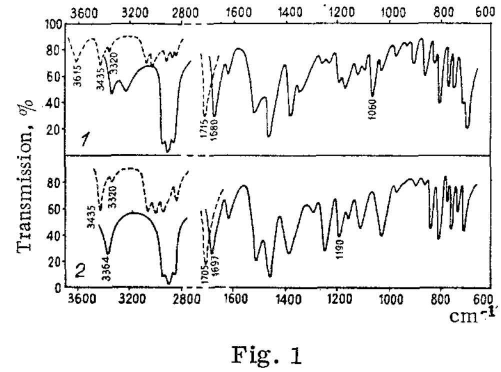
* Solvent for crystallization: ethanol.



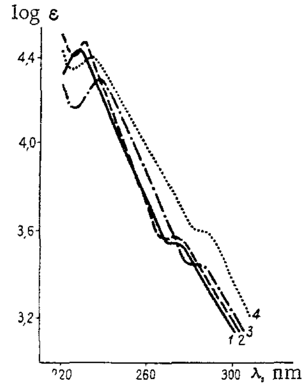


Fig. 1

Fig. 2

Fig. 1. IR spectra (the dashed line denotes 0.2% solutions in CCl_4 with a layer thickness of 5 mm): 1) β-methyl-β-p-tolylhydrazide of benzilic acid; 2) compound VI.

Fig. 2. UV spectra: 1) β-methyl-β-phenylhydrazide of di(p-chlorophenyl)glycolic acid; 2) compound V; 3) compound I; 4) compound VII.

In the UV region (Fig. 2), the cinnoline derivatives exhibit a maximum at 230-238 nm, depending on the nature of the aryl groups in position 4. A second, feebly expressed, maximum is found at 272 nm in compound V and at 284 nm in the others. As compared with the initial arylhydrazides, there is an increase in the extinction and a change in the nature of the absorption in the 230-nm region.

EXPERIMENTAL

p-Tolylhydrazide of Di(p-cumenyl)glycolic Acid. To a solution of the Grignard reagent prepared from 30.0 g of p-bromocumene and 3.7 g of magnesium was added 6.7 g of the ethyl ester of the p-tolylhydrazide of oxalic acid [6]. The reaction mixture was heated in the water bath for 40 min and was then decomposed with dilute hydrochloric acid. The reaction product was extracted with ether. Yield 10 g (80%). The substance is soluble in ethanol, toluene, chloroform, xylene, and anisole. Needles (from toluene) with mp 183-184°C. Found, %: N 6.7. $C_{27}H_{32}N_2O_2$. Calculated, %: N 6.7.

β-Methyl-β-(p-tolyl)hydrazide of Di(p-cumenyl)glycolic Acid. To a solution of 0.13 g of sodium in 10 ml of anhydrous ethanol was added 1.2 g of the p-tolylhydrazide of di(p-cumenyl)glycolic acid and another 10 ml of ethanol to dissolve it. The resulting solution was treated with 1.65 g of methyl iodide and was heated until the reaction was neutral, after which the product was extracted with chloroform. Yield 1.0 g (81%). The substance is soluble in toluene, benzene, and ethanol. Needles (from toluene) with mp 171-172°C. Found, %: N 6.5. $C_{28}H_{34}N_2O_2$. Calculated, %: N 6.5.

β-Methyl-β-phenylhydrazide of Di(p-chlorophenyl)glycolic Acid. This was obtained in a similar manner to the compound described above from the phenylhydrazide of di(p-chlorophenyl)glycolic acid [7]. Yield 96%. Colorless plates (from toluene) with mp 182-183°C. Found, %: N 6.8. $C_{21}H_{18}Cl_2N_2O_2$. Calculated, %: N 7.0.

1-Methyl-4,4-diphenyl-1,2,3,4-tetrahydrocinnolin-3-one (I). A solution of 1 g of benzilic acid β-methyl-β-phenylhydrazide [3] in 20 ml of anhydrous anisole was treated with 1.5 ml of concentrated sulfuric acid. The coloration that appeared rapidly disappeared. The product separated out after the reaction mixture had been treated with water. The substance is soluble in ethanol, toluene, benzene, and glacial acetic acid. Found, %: C 79.7; H 6.0. $C_{21}H_{18}N_2O$. Calculated, %: C 80.3; H 5.7.

Compounds II-XII were obtained similarly from the corresponding arylhydrazides.

The IR spectra were measured on an IKS-14 spectrophotometer using mulls of the substances in paraffin oil and solutions in CCl_4. The UV spectra were obtained on an SF-4 spectrophotometer using ethanolic solutions.

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