RING – CHAIN TAUTOMERISM AND REACTIONS OF 4-ARYL-4-HYDROXY-2,3-DIMETHYL-3,4-DIHYDROPHTHALAZINONES

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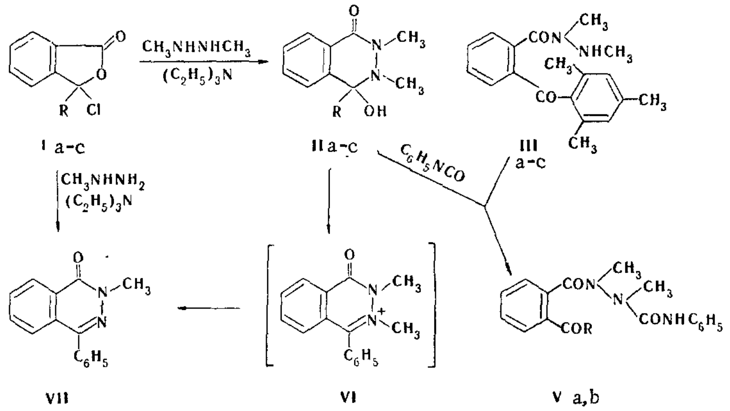
It has been established by IR spectroscopy that the N,N'-dimethylhydrazides of 2-aroylbenzoic and benzil-o-carboxylic acids, with the exception of 2-mesitoylbenzoic acid, have the ring structure of 4-aryl- or 4-benzoyl-4-hydroxy-2,3-dimethyl-3,4-dihydrophthalazinones. The action of electrophilic agents on 4-hydroxy-2,3-dimethyl-4-phenyl-3,4-dihydrophthalazinone under mild conditions leads to $N_{(3)}$-demethylation with the formation of 2-methyl-4-phenylphthalazinone.

It has been shown previously [1] that N',N'-dialkylhydrazides of 2-aroylbenzoic acids have the ring structure of 2-dialkylamino-3-aryl-3-hydroxyisoindolinones. It appeared of interest to study the structure of N,N'-dialkylhydrazides of 2-aroylbenzoic acids. For these the formation of a ring structure is possible by the intramolecular addition to the keto group of the more nucleophilic β-hydrazine nitrogen atom. A hypothesis has recently been put forward of a ring–chain tautomeric equilibrium, displaced in the direction of the open form, in the case of the hexahydropyridazide of 3-(p-methoxybenzoyl)propionic acid [2].

In the present work we have effected the synthesis of the N,N'-dimethylhydrazides of 2-aroylbenzoic acid and benzil-o-carboxylic acids from 3-aryl- or 3-benzoyl-3-chlorophthalides (Ia-c). The IR spectra of these substances in the crystalline state show broad OH bands at 3300 cm^{-1} (IIa in chloroform 3580 and 3317 cm^{-1}) and a C=O band at 1630 cm^{-1} (in dioxane 1660 cm^{-1}). The considerable decrease in $\nu_{C=O}$ in the crystalline state as compared with the dissolved state can be explained by the existence of C=O ···H–O intermolecular hydrogen bonds.

Because of the steric shielding of the C=O group by a voluminous substituent [3-5] in the case of the N,N'-dimethylhydrazide of 2-mesitoylbenzoic acid (II), intramolecular nucleophilic addition cannot take place. In the IR spectrum of the hydrazide (III) there are a comparatively narrow N–H band (Table 1) and two closely adjacent (in dioxane) C=O bands of a diaryl ketone and of a hydrazide the total integral in-



I, II a R=C6H5; b R=2,4-(CH3)2C6H4, c R=C6H5CO

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TABLE 1. Characteristics of the Compounds Synthesized

Comp.	R	mp, °C	Empirical formula	Found, %			Calc., %			IR spectra, ν, cm^{-1}*				Yield, %
										solid substances		solutions in dioxane		
				C	H	N	C	H	N	$\nu_{C=O}$	ν_{O-H}, ν_{N-H}	$\nu_{C=O}$	A (ε)	
IIa	C_6H_5	163—164	$C_{16}H_{16}N_2O_2$	71,6	6,0	10,5	71,6	6,0	10,4	1632	3285 br	1662	3,9	80
IIb	2,4-$(CH_3)_2C_6H_3$	149—150	$C_{18}H_{20}N_2O_2$	72,9	6,8	9,6	73,0	6,8	9,5	1630	3268 br	1663	3,6	73
IIc	C_6H_5CO	184 разл	$C_{17}H_{16}N_2O_3$	69,3	5,3	9,6	68,9	5,4	9,5	1687 † 1632	3139 br	1693*† 1671	1,6 3,3	61
III		124—125	$C_{19}H_{22}N_2O_2$	73,7	7,1	9,1	73,5	7,1	9,0	1635	3286	1668sh 1659	5,5	17
IV		266—268	$C_{36}H_{36}N_2O_4$	77,0	6,5	5,1	77,1	6,5	5,0	1684 1670	—			20
Va	C_6H_5	171—172	$C_{23}H_{21}N_3O_3$	71,2	5,5	10,8	71,3	5,5	10,9	1682 br 1643	3439	1703 1667	(485) (650)	80
Vb	2,4,6-$(CH_3)_3C_6H_2$	184—185	$C_{26}H_{27}N_3O_3$	72,8	6,4	9,8	72,7	6,3	9,8	1683 1661	3433	1703 1677	(495) (750)	75
VII		165—166	$C_{15}H_{12}N_2O$	76,3	5,1	12,0	76,3	5,1	11,9	1654	—	1661	5,1	

* br, broad band; sh, shoulder; A, integral intensity in practical units of measurement equal to 10^4 liter · mole^{-1} · cm^{-2} (ln).

† C = O

intensity ($A_{C=O}$) of which considerably exceeds $A_{C=O}$ in the spectra of (IIa-c). In the synthesis of the hydrazide (III) N,N'-di(2-mesitoylbenzoyl)-N,N'-dimethylhydrazine (IV) is formed as a by-product.

On reacting with phenyl isocyanate, compounds of both types (IIa) and (III) form products with the structure of N-(2-aroylbenzoyl)-N,N'-dimethyl-N'-phenylcarbamoylhydrazines (Va,b). In the region of double-bond stretching vibrations the IR spectra of (Va) and (Vb) are complex: in dioxane the C = O band of the N-phenylcarbamoyl group is found at 1703 cm^{-1}, and the C = O band of a diaryl ketone and the band of a hydrazine overlap (about 1670 cm^{-1}). There are also amide II (at about 1540 cm^{-1}) and ν_{N-H} bands (Table 1). The formation of (Va) (and not the corresponding N-phenylurethane) from (IIa) can be explained either by the existence of a tautomeric equilibrium between the ring and open forms of compound (IIa) and rapid reaction of phenyl isocyanate with the open form or by the opening of the hydroxyphthalazinone ring during the reaction, which takes place with the primary attack of the phenyl isocyanate at the $N_{(3)}$ atom in the molecule of (IIa).

In reactions with a number of electrophilic agents (acetyl chloride in pyridine, acetic anhydride, thionyl chloride, methanolic hydrogen chloride) the hydroxyphthalazinone (IIa) forms one and the same product: 2-methyl-4-phenylphthalazinone (VII). This unexpectedly easy $N_{(3)}$-demethylation apparently takes place through an intermediate immonium ion (VI). The structure of (VII) was shown by independent synthesis from (Ia) and methylhydrazine. The IR spectrum of (VII) taken in dioxane has a strong combination band ($\nu_{C=O} + \nu_{C=N}$) at 1661 cm^{-1} (see [6]). The frequency of this band is lowered only very slightly in the crystalline substance since the molecule of (VII), unlike that of (IIa), lacks a proton-donating group.

EXPERIMENTAL

The IR spectra of the compounds were taken in the form of mulls in paraffin oil and hexachlorobutadiene and in the form of solutions in dioxane (c $5 \cdot 10^{-2}$ M, l = 0.011 cm). The integral intensities of the C = O bands ($A_{C=O}$) were calculated by the Wilson–Wells method with Ramsay's wing correction [7].

4-Aryl- and 4-Benzoyl-4-hydroxy-2,3-dimethyl-3,4-dihydrophthalazinones (IIa-c). A solution of 0.01 mole of (Ia-c) in 10-20 ml of anhydrous benzene was poured into a solution of equimolar amounts (0.01 mole) of N,N'-dimethylhydrazine and triethylamine in 10 ml of benzene. After 24 h, the precipitate was separated off and washed free from triethylamine hydrochloride with water to give (IIa) (from benzene) and (IIc) (from ethanol, Table 1). To isolate the (IIb), the filtrate after the separation of the precipitate was evaporated in vacuum. The residue was recrystallized from benzene and dried in vacuum (20 mm) at 100°C for 4 h, since the substance crystallizes from benzene in the form of the solvate (IIb · C_6H_6).

N,N'-Dimethylhydrazide of 2-mesitoylbenzoic acid (III) and N,N'-di(2-mesitoylbenzoyl)-N,N'-dimethylhydrazine (IV) were obtained from 0.01 mole of 2-mesitoylbenzoyl chloride in a similar manner to that described above. After the separation of the triethylamine hydrochloride the filtrate was evaporated in vacuum. The residue was recrystallized from 30 ml of a mixture of benzene and n-hexane (1 : 1) to give (IV). The filtrate was evaporated in vacuum and the residue was twice recrystallized from a mixture of benzene and n-hexane to give (III) (Table 1).

N-(2-Aroylbenzoyl)-N,N'-dimethyl-N'-phenylcarbamoylhydrazines (Va, b). A solution of 0.5 g of (IIa) or (III) and 0.3 ml of phenyl isocyanate in 10 ml of benzene was boiled for 2 h. Then it was evaporated in vacuum and the residue was twice recrystallized from a mixture of benzene and n-hexane (Table 1).

2-Methyl-4-phenylphthalazinone (VII). A. With shaking, 0.4 ml of acetyl chloride was added to a solution of 0.5 g of (IIa) in 5 ml of pyridine. After 24 h, the mixture was diluted with water and the precipitate was separated off. The yield of (VII) was 0.27 g (61%), mp 165-166°C (from ethanol).

B. In a similar manner to the synthesis of (IIa), 0.01 mole of (Ia), 0.015 mole of methylhydrazine, and 0.01 mole of triethylamine yielded 1.1 g (47%) of (VII) with mp 164-165°C (from ethanol, Table 1). The identity of the two samples was shown by a mixed melting point.

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