SUBSTITUTED HYDRAZIDES OF HYDROXYCARBOXYLIC ACIDS

XLVI. Conversion of Arylhydrazides of Diarylglycolic Acids into Derivatives of 3-Oxo-1, 2, 3, 4-tetrahydrocinnoline*

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Under the action of concentrated sulfuric acid, a number of arylhydrazides of diarylglycolic acids are converted into 4, 4-diaryl-3-oxo-1, 2, 3, 4-tetrahydrocinnolines. The cyclization reaction takes place through the intermediate formation of a halochromic salt. The UV and IR spectra of the cinnoline derivatives have been studied.

With concentrated sulfuric acid, arylhydrazides of diarylglycolic acids $ArNHNHCOC(OH)R_2$ give halochromic salts [2]. The coloration is stable when the carbinol carbon atom bears p- and o-anisyl residues, less stable in the case of a p-tolyl residue, and unstable with other aryl groups. When solutions of the halochromic salts are allowed to stand, the color disappears. As our investigations have shown, the disappearance of the color is connected with the conversion of the halochromic arylhydrazide salts into 4, 4-diaryl-3-oxo-1, 2, 3, 4-tetrahydrocinnolines. The cyclization reaction takes place in anisole in the presence of a small amount of concentrated sulfuric acid in the following way:

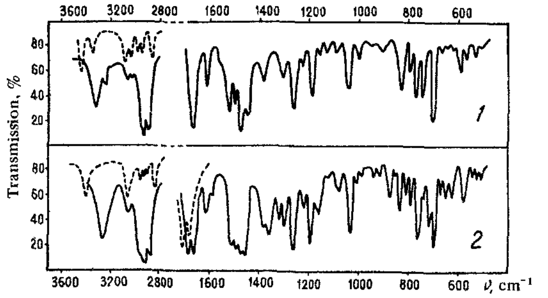
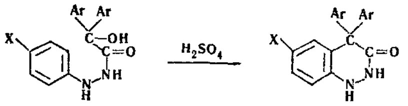


Fig. 1. IR spectra: 1) I; 2) XI (the dashed lines relate to 0.1% solutions in CCl_4 at a layer thickness of 20 mm).



X=H, CH_3, CH_3O; R=C_6H_5, p-, m-$CH_3C_6H_4$, p-ClC_6H_4

The cinnoline derivatives obtained are given in the table. They are colorless crystalline substances soluble in ethanol, benzene, toluene, and other organic solvents. Heating them with acetic anhydride gave their acetyl derivatives and heating with benzoyl chloride their benzoyl derivatives (see table).

Compound XV was obtained by independent synthesis through the cyclization of the β-acetyl-β-phenylhydrazide of di(p-chlorophenyl)glycolic acid [3], which showed the position of the acyl group.

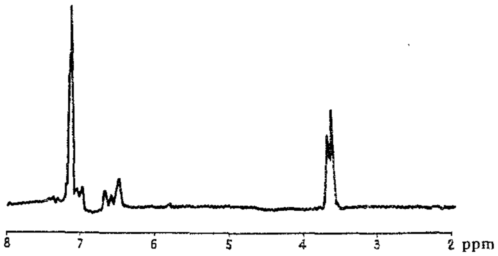


Fig. 2. NMR spectrum of compound VI.

It can be seen from Fig. 1 that in the IR region the cinnoline derivatives lack the band of the stretching vibrations of the OH group that is present in the initial arylhydrazides [4]. In the 3000 cm^{-1} region, solutions of the cinnoline derivatives show two well-defined bands at 3440 and 3316 cm^{-1} due to the two NH groups. On passage to the crystalline form, the frequencies of these bands fall, which indicates their participation in the formation of intermolecular hydrogen bonds. In this region the crystalline acyl derivatives (XI) have only one band, at 3270 cm^{-1}, due to the vibrations of one NH group. In solution its frequency rises to 3406 cm^{-1}.

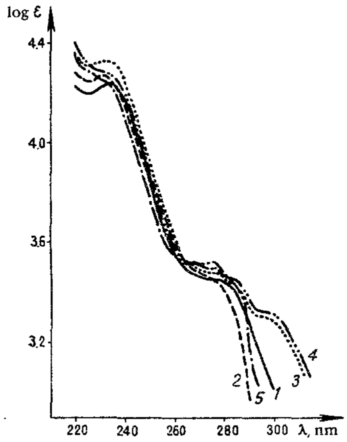


Fig. 3. UV spectra: 1) V; 2) XIX; 3) VII; 4) VIII; 5) III.

The amide–I bands of the cinnoline derivatives have a frequency of 1688 cm^{-1} in solution, and this falls to 1667–1677 cm^{-1} in the crystals, which indicate the involvement of the carbonyl group in an intermolecular hydrogen bond in this state. In the acylated cinnoline

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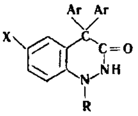
*For part XLV, see [1].



Compound	X	Ar	R	Mp*, °C	Empirical formula	N, (CH_3CO), %		Yield, %
						found	calculated	
I	H	C_6H_5	H	163—164	$C_{20}H_{16}N_2O$	9.16	9.33	96
II	H	p-$CH_3C_6H_4$	H	175—176	$C_{22}H_{20}N_2O$	8.42	8.59	94
III	H	m-$CH_3C_6H_4$	H	154—155	$C_{22}H_{20}N_2O$	8.48	8.59	93
IV	H	p-ClC_6H_4	H	189—190	$C_{20}H_{14}Cl_2N_2O$	7.38	7.59	92
V	CH_3	C_6H_5	H	142—143	$C_{21}H_{18}N_2O$	9.02	8.91	95
VI	CH_3O	C_6H_5	H	150—151	$C_{21}H_{18}N_2O_2$	8.22	8.43	95
VII	CH_3O	p-$CH_3C_6H_4$	H	188—190	$C_{23}H_{22}N_2O_2$	7.61	7.82	98
VIII	CH_3O	m-$CH_3C_6H_4$	H	144—146	$C_{23}H_{22}N_2O_2$	7.54	7.82	93
IX	CH_3O	p-FC_6H_4	H	158—159	$C_{21}H_{16}F_2N_2O_2$	7.81	8.08	86
X	H	C_6H_5	CH_3CO	162—163	$C_{22}H_{18}N_2O_2$	(12.86)	12.54	97
XI	H	C_6H_5	C_6H_5CO	199—200	$C_{27}H_{20}N_2O_2$	6.89	6.93	88
XII	H	p-$CH_3C_6H_4$	CH_3CO	219—220	$C_{24}H_{22}N_2O_2$	(11.81)	11.62	85
XIII	H	p-$CH_3C_6H_4$	C_6H_5CO	194—195	$C_{29}H_{24}N_2O_2$	6.38	6.48	90
XIV	H	m-$CH_3C_6H_4$	C_6H_5CO	140—141	$C_{29}H_{24}N_2O_2$	6.54	6.48	87
XV	H	p-ClC_6H_4	CH_3CO	246—247	$C_{22}H_{16}Cl_2N_2O_2$	(10.80)	10.46	91
XVI	H	p-ClC_6H_4	C_6H_5CO	236—238	$C_{27}H_{18}Cl_2N_2O_2$	6.06	5.92	92
XVII	CH_3	C_6H_5	CH_3CO	178—179	$C_{23}H_{20}N_2O_2$	(12.42)	12.08	96
XVIII	CH_3	C_6H_5	C_6H_5CO	181—182	$C_{28}H_{22}N_2O_2$	6.91	6.70	89
XIX	CH_3O	C_6H_5	CH_3CO	185—186	$C_{23}H_{20}N_2O_3$	(11.84)	11.56	95
XX	CH_3O	p-$CH_3C_6H_4$	C_6H_5CO	166—167	$C_{30}H_{26}N_2O_3$	5.96	6.06	91
XXI	CH_3O	m-$CH_3C_6H_4$	C_6H_5CO	148—149	$C_{30}H_{26}N_2O_3$	5.91	6.08	90

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*Solvents for crystallization: for XII, glacial acetic acid; for XVI, toluene; for V, XVII, and XIX, benzene; and for the others, ethanol.

derivatives, this band undergoes a broadening due to the interaction of the two carbonyls in the CONHNHCO grouping [5]. The frequencies of these bands in compound **XI**, 1661 and 1690 cm^{-1}, are lower than in the acyl derivative of the initial phenylhydrazide [6]. In solution, the frequencies of these bands rise. The amide-III bands have a frequency of 1250 cm^{-1}. In the cyclic products, a strong band appears at 1180 cm^{-1} which is not present in the initial arylhydrazide. This band may be connected with the appearance of a new ring. Because of the splitting out of the hydroxyl group, cyclization leads to the disappearance of the 1060 cm^{-1} band that was due to the stretching vibrations of the C—OH group in the initial arylhydrazides [4].

In the NMR spectrum of compound **VI** (Fig. 2), the protons of the methoxyl group give two singlet lines of different intensities at 3.63 and 3.67 ppm. This may be due to the presence of two conformations differing in the location of the CH_3O group with respect to the plane of the benzene ring. The presence of two conformations is possible because of steric hindrance between the phenyls attached to carbon atom 4. In the region of aromatic protons, the strong signal at 7.11 ppm belongs to the protons of two monosubstituted benzene rings. The quartet at 6.67 and 7.03 ppm is due to the ortho arrangement of the protons of the condensed benzene ring (positions 7 and 8). The splitting constant J is 8 Hz. The single signal at 6.47 ppm (unresolved multiplet with low constants) is due to the proton in the meta position (position 5).

In the UV region (Fig. 3), the cinnoline derivatives have a maximum at 232–234 nm, the extinction of which is higher than in the initial arylhydrazides [6, 8] and depends on the nature of the aryls attached to the quaternary atom. There is a second, weakly-expressed, maximum at 276 nm, and on acylation (compound **XIX**) this becomes smoothed out. In compounds VII and VIII, there is an inflection in the 300 nm region.

In conclusion, I express my thanks to Yu. N. Sheinker for advice on the interpretation of the NMR spectra.

EXPERIMENTAL

3-Oxo-4, 4-diphenyl-1, 2, 3, 4-tetrahydrocinnoline (I). A solution of 1 g of benzilic acid phenylhydraxide [9] in 20 ml of dry anisole was treated with 1 ml of conc H_2SO_4. The violet coloration that appeared rapidly disappeared after shaking. The reaction product was isolated after treating the reaction mixture with water. Compound I is soluble in ethanol, toluene, and glacial acetic acid. Found, %: C 79.63; H 5.42. Calculated, %: C 80.00; H 5.33.

Compounds **II–IX** were obtained similarly from the corresponding arylhydrazides [8–11] (see table).

1-Acetyl-3-oxo-4, 4-diphenyl-1, 2, 3, 4-tetrahydrocinnoline (X). A solution of 1 g of I in 10 ml of acetic anhydride was heated in the water bath. On cooling and dilution with water, the reaction product separated out. The acyl derivative **X** is soluble in ethanol, glacial acetic acid, and toluene.

Compounds **XII**, **XV**, **XVII**, and **XIX** were obtained similarly (see table).

1-Acetyl-4, 4-di(p-chlorophenyl)-3-oxo-1, 2, 3, 4-tetrahydrocinnoline (XV). A solution of 1 g of di(p-chlorophenyl)glycolic acid β-acetyl-β-phenylhydrazide [3] in anisole was treated with 1 ml of conc H_2SO_4. The violet coloration that appeared rapidly disappeared. The reaction product separated when the mixture was treated with water. Yield 0.4 g (44%). Mp 246–247° C. A mixture with the compound **XV** obtained by the acetylation of **IV** gave no depression of the melting point.

1-Benzoyl-3-oxo-4, 4-diphenyl-1, 2, 3, 4-tetrahydrocinnoline (XI). A solution of 1 g of I in dry benzene was heated with 1 g of benzoyl chloride for 1 hr. After cooling, the reaction product separated out. The benzoyl derivative **XI** is soluble in ethanol, glacial acetic acid, and toluene.

Compounds **XIII**, **XIV**, **XVI**, **XVIII**, **XX**, and **XXI** were obtained similarly.

The IR spectra were obtained on a UR-10 spectrophotometer using mulls in paraffin oil and solutions in CCl_4. The NMR spectra were obtained on a JNM-4H-100 spectrometer using 10% solutions in CCl_4. The UV spectra were obtained on an SF-4 spectrophotometer using ethanolic solutions.

REFERENCES

1. I. S. Berdinskii, L. V. Kazakova, N. A. Asanova, and L. A. Mikryukova, ZhOrKh, 4, 875, 1968.
2. I. S. Berdinskii and N. A. Kostareva, ZhOKh, 35, 876, 1965.
3. I. S. Berdinskii, ZhOrKh, 3, 1300, 1967.
4. I. S. Berdinskii and P. A. Petyunin, Uch. zap. Permsk. univ., 141, 313, 1966.
5. D. Birca-Galatenau and C. Demetresky, Rev. Roum. Chem., 9, 203, 1964.
6. I. S. Berdinskii, ZhOKh, 33, 1214, 1963.
7. I. S. Berdinskii, Z. D. Alekseeva, A. F. Perevozchikova, and N. A. Kostareva, ZhOrKh, 2, 318, 1966.
8. I. S. Berdinskii, N. N. Pugina, N. D. Bushina, and P. V. Korepanova, ZhOrKh, 1, 953, 1965.
9. I. S. Berdinskii and P. A. Petyunin, ZhOKh, 26, 2592, 1956.
10. I. S. Berdinskii, ZhOKh, 30, 2030, 1960.
11. I. S. Berdinskii and G. Ya. Anvarova, Uch. zap. Permsk. univ., 111, 192, 1964.
12. I. S. Berdinskii and I. D. Yatskova, ZhOKh, 33, 943, 1963.

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