SUBSTITUTED HYDRAZIDES OF HYDROXYCARBOXYLIC ACIDS

XLI. N-Methylpiperazino- and α,α'-Dimethylpyrrolidinoacetyl
Derivatives of the Phenylhydrazides of Diaryl- and Dialkylglycolic Acids*

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The action of N-methylpiperazine and α, α'-dimethylpyrrolidine on chloroacetyl derivatives of phenylhydrazides of diaryl- and dialkylglycolic acids has given the previously unknown N-methylpiperazinoacetyl and α, α'-dimethylpyrrolidnoacetyl derivatives of these phenylhydrazides.

The introduction of an acyl residue containing a group with a basic nature into the phenylhydrazides
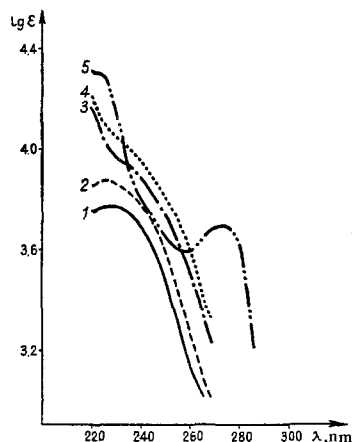

Fig. 1. UV spectra of methylpiperazinoacetyl and dimethylpyrrolidinoacetyl derivatives: 1) VIII, 2) XIX, 3) I, 4) XIII, 5) IV.

of disubstituted glycolic acids leads to an enhancement of their analgesic activity [2]. It appeared of interest to introduce methylpiperazino and dimethylpyrrolidino residues, which themselves may exhibit biological activity, into these phenylhydrazides.
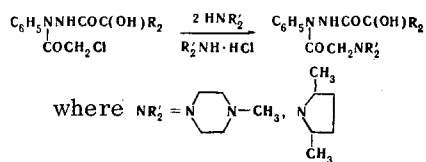
The introduction of the methylpiperazino and dimethylpyrrolidino residues was effected by heating the chloroacetyl derivatives of the phenylhydrazides of diaryl- and dialkylglycolic acids [3] with methylpiperazine and dimethylpyrrolidine in benzene.

The physical constants, yields, and analytical data of all the compounds synthesized are given in Tables 1 and 2. They are colorless crystalline substances

sparingly soluble in water and readily soluble in organic solvents. The UV spectra of ethanolic solutions of a number of the acyl derivatives synthesized were studied (Fig. 1). It can be seen from the absorption curves that the introduction of N-methylpiperazinoacetyl and α, α'-dimethylpyrrolidinoacetyl groups leads to a change in the nature of the absorption from that of the initial phenylhydrazides [4]. A levelling out of the maxima takes place in the derivatives of benzilic and dibutylglycolic acids. The nature of the acyl residue effects the value of the extinction, which is higher in the case of a dimethylpyrrolidino residue. The same influence of a dimethylpyrrolidino residue is observed in the case of the spectra of halochromic salts (Fig. 2). As compared with the spectra of the initial phenylhydrazides [5], the extinction was higher in the spectra of the halochromic salts of the acyl derivatives, but the position of the maxima remained the same. The halochromic solutions were prepared by adding 9 ml of concentrated sulfuric acid to 1 ml of a 0.002 M solution of an acyl derivative of a phenylhydrazide in glacial acetic acid. The measurements were carried out on an SF-10 recording spectrophotometer.
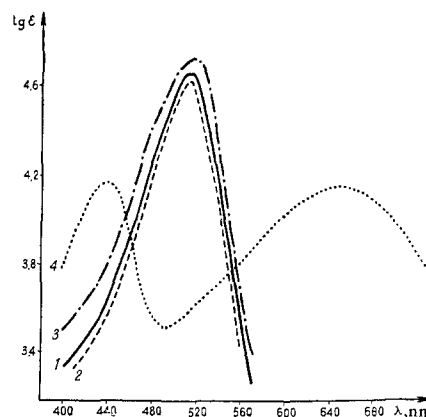
Fig. 2. Absorption spectra of solutions of halochromic salts: 1) morpholinoacetylphenylhydrazide of di(p-tolyl)glycolic acid [6]; 2) III; 3) XVI; 4) IV.

EXPERIMENTAL

Benzilic acid β-N-methylpiperazinoacetyl-β-phenylhydrazide (I). A mixture of 1 g of benzilic acid chloroacetylphenylhydrazide and 2 g of N-methylpiperazine in benzene was heated for 2 hr. The product separated after the evaporation of the solvent. The substance dissolves in benzene, toluene, and ethanol. Compounds II–XII were obtained similarly.

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*For part XL, see [1].

Table 1

$$C_6H_5\text{NNHCOCOHR}_2$$
$$\text{COCH}_2\text{N}\!\!\!\diagdown\!\!\!\!\diagup\text{N}-CH_3$$
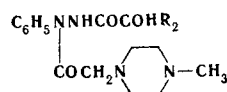
Com-pound	R	Mp, °C (solvent for crystallization)	Empirical formula	N, %		Yield, %
				Found	Calcu-lated	
I	C_6H_5	119—120 (Toluene)	$C_{27}H_{30}N_4O_3$	11.91; 12.40	12.23	85.5
II	m-$CH_3C_6H_4$	95—96 (Ether)	$C_{29}H_{34}N_4O_3$	11.20; 11.31	11.52	95.5
III	p-$CH_3C_6H_4$	166—167 (Benzene)	$C_{29}H_{34}N_4O_3$	11.76; 11.26	11.52	94.4
IV	o-$CH_3OC_6H_4$	134—135 (Toluene)	$C_{29}H_{34}N_4O_5$	10.53; 10.61	10.81	87.5
V	C_6H_{11}	198—199 (Ethanol)	$C_{27}H_{42}N_4O_3$	11.84; 11.62	11.91	86.3
VI	C_2H_5	162—163 (Toluene)	$C_{19}H_{30}N_4O_3$	15.36; 15.68	15.47	94.6
VII	C_3H_7	124—126 (Benzene)	$C_{21}H_{34}N_4O_3$	14.11; 14.09	14.36	95.6
VIII	C_4H_9	136—137 (Benzene)	$C_{23}H_{38}N_4O_3$	13.23; 13.11	13.39	96.7
IX	C_5H_{11}	115—117 (Toluene)	$C_{25}H_{42}N_4O_3$	12.75; 12.29	12.56	95.5
X	i-C_5H_{11}	151—152 (Ethanol)	$C_{25}H_{42}N_4O_3$	12.83; 12.42	12.56	96.3
XI	C_6H_{13}	118—119 (Ethanol)	$C_{27}H_{46}N_4O_3$	12.02; 11.51	11.81	86.0
XII	C_7H_{15}	117—118 (Ethanol)	$C_{29}H_{50}N_4O_3$	11.22; 10.87	11.15	94.6

Table 2

$$C_6H_5\text{NNHCOC(OH)R}_2'$$
$$\text{COCH}_2\text{N}\quad CH_3$$
$$CH_3$$
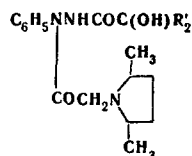
Com-pound	R	Mp, °C (from toluene)	Empirical formula	N, %		Yield, %
				Found	Calcu-lated	
XIII	C_6H_5	171—171.5	$C_{28}H_{31}N_3O_3$	9.27; 9.14	9.19	69.7
XIV	o-$CH_3C_6H_4$	76—77*	$C_{30}H_{35}N_3O_3$	8.44; 8.86	8.66	70.0
XV	m-$CH_3C_6H_4$	166—167	$C_{30}H_{35}N_3O_3$	8.35; 8.53	8.66	84.1
XVI	p-$CH_3C_6H_4$	181—181.5**	$C_{30}H_{35}N_3O_3$	8.75; 8.95	8.66	93.4
XVII	C_6H_{11}	159—160	$C_{28}H_{43}N_3O_3$	8.48; 8.86	8.95	96.6
XVIII	C_3H_7	112—113	$C_{22}H_{35}N_3O_3$	10.44; 10.89	10.79	84.0
XIX	C_4H_9	127—128	$C_{24}H_{39}N_3O_3$	10.37; 10.00	10.07	99.9
XX	C_5H_{11}	110—111	$C_{26}H_{43}N_3O_3$	9.64; 9.92	9.44	86.2
XXI	i-C_5H_{11}	120—121	$C_{26}H_{43}N_3O_3$	9.48; 9.64	9.44	95.7
XXII	C_6H_{13}	105—106	$C_{28}H_{47}N_3O_3$	9.17; 8.77	8.88	96.6
XXIII	C_7H_{15}	92—93	$C_{30}H_{51}N_3O_3$	8.63; 8.08	8.38	70.1

*From benzene.
**From ethanol.

Benzilic acid β-(α,α'-dimethylpyrrolidino)acetyl-β-phenylhydra-zide (XIII). A solution of 1 g of benzilic acid chloroacetylphenylhy-drazide in benzene was heated with 1.5 g of α,α'-dimethylpyrrolidine for 2 hr. The product was isolated after the evaporation of the solvent. The substance dissolves in benzene, toluene, ethanol, and glacial acetic acid. Compounds XIV–XXIII were obtained similarly.

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