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SOME DERIVATIVES OF 4-(4-AMINOPHENYLAMINO)-2,2,6,6-TETRAMETHYLPIPERIDINE

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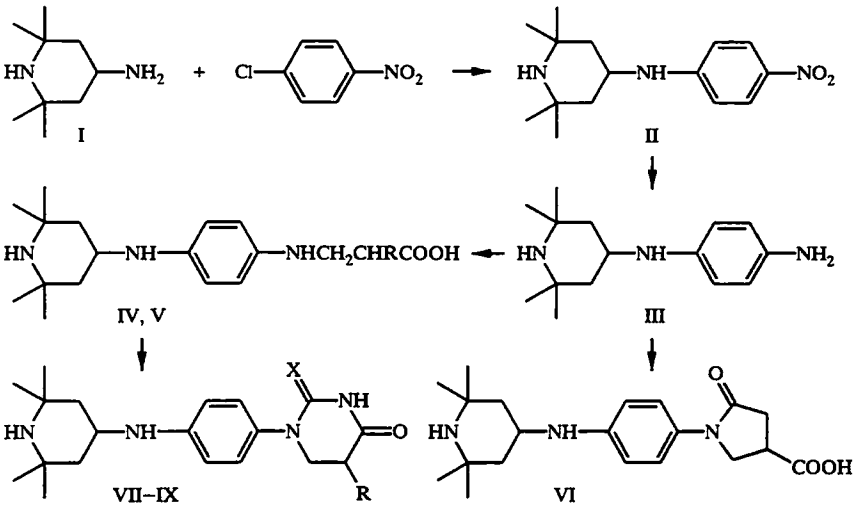
4-(4-Aminophenylamino)-2,2,6,6-tetramethylpiperidine was synthesized by alkylation of 4-aminotriacetoneamine with 4-chloronitrobenzene, followed by hydrogenation of the nitro derivative. Its reactions with acrylic, methacrylic, and itaconic acids were carried out. Transformations of the N-substituted amino acids to derivatives of 2-pyrrolidinone and dihydropyrimidinedione were studied.

Distinctive features of this class of light stabilizers are a high effectiveness, absence of color of the compositions, as well as a combination of light and heat stabilizing properties [1-3].

In the present study, we synthesized certain derivatives of 2,2,6,6-tetramethylpiperidine whose molecules contain aromatic and heterocyclic fragments. Alkylation of 4-amino-2,2,6,6-tetramethylpiperidine (I) with 4-chloronitrobenzene in dimethyl sulfoxide resulted in the synthesis of 4-(4-nitrophenylamino)-2,2,6,6-tetramethylpiperidine (II), which was catalytically reduced to the corresponding amine III with hydrazine in ethanol. The reaction of nucleophilic addition of 4-(4-aminophenylamino)-2,2,6,6-tetramethylpiperidine (III) to acrylic and methacrylic acids formed the corresponding *N*-substituted β-amino acids IV, V, and N-[4-(2,2,6,6-tetramethyl-4-piperidinyl)aminophenyl]-α-methyl-β-alanine (V) was separated as the dihydrochloride.



V, IX R = CH_3, for the rest R = H; VII X = S, for the rest X = O

In the reaction of amine III with itaconic acid, besides the addition reaction, cyclization of the intermediate 4-substituted 3-carboxybutanoic acid to 1-[4-(2,2,6,6-tetramethyl-4-piperidinyl)]-4-carboxy-2-pyrrolidinone (VI) takes place. In the ESR spectrum of this compound, in addition to the proton signals of tetramethylpiperidine and of the aromatic ring, the proton signals of the 4-carboxy-2-pyrrolidine ring at 2.86, 3.0-3.5, and 3.7-4.3 ppm are observed.

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TABLE 1. Data of Ultimate Analysis

Compound	Found, %			Empirical formula	Calculated, %		
	C	H	N		C	H	N
II	64,73	8,73	15,24	$C_{15}H_{23}N_3O_2$	64,91	8,35	15,21
III	72,48	10,41	17,16	$C_{15}H_{25}N_3$	72,78	10,17	17,05
IV	67,51	9,43	12,95	$C_{18}H_{29}N_3O_2$	67,64	9,14	13,20
V*	56,16	7,89	10,15	$C_{19}H_{31}N_3O_2 \cdot 2HCl$	56,41	8,22	10,43
VI	66,38	8,44	11,53	$C_{20}H_{29}N_3O_3$	66,79	8,13	11,74
VII	61,52	7,43	15,35	$C_{19}H_{28}N_4OS$	61,76	7,82	15,60
VIII	66,48	7,94	16,52	$C_{19}H_{28}N_4O_2$	66,20	8,19	16,33
IX	66,45	8,03	15,38	$C_{20}H_{30}N_4O_2$	66,97	8,43	15,69

*Calculated, %: Cl 17.53. Found, %: Cl 17.31.

The action of potassium thiocyanate in acetic acid on N-[4-(2,2,6,6-tetramethyl-4-piperidinyl)]-β-alanine (IV) and subsequent addition of dilute (1:1) HCl formed 1-[4-(2,2,6,6-tetramethyl-4-piperidinyl)aminophenyl)]dihydro-4(1H,3H)-pyrimidinone-2-thione hydrochloride, which was converted with sodium acetate to the base VII. In the same way, from β-alanines IV, V, using urea instead of the thiocyanate, we obtained the corresponding 1-substituted dihydro-2,4(1H,3H)-pyrimidinediones VIII-IX. Derivatives of 1-substituted dihydropyrimidinedione are formed during condensation of N-substituted β-alanines with alkali metal thiocyanates or urea in acid medium via the intermediate N-aryl-N-carbamoyl(thiocarbamoyl)-β-alanines, which in strongly acidic medium, and also under the influence of temperature, cyclize to derivatives of dihydropyrimidinedione [4]. The structures of the synthesized compounds confirm the data of the ultimate analysis, ESR, and mass spectra.

EXPERIMENTAL

The ESR spectra were recorded on a Hitachi R-22 (90 MHz) spectrometer, with HMDS as the internal standard, and the mass spectra were recorded on an MCLKB 2091 (70 eV) spectrometer. The course of the reaction and the purity of the compounds obtained were monitored by TLC on Silufol UV-254 plates, with development in UV light or iodine.

The data of the ultimate analysis were consistent with the calculated data.

4-(4-Nitrophenylamino)-2,2,6,6-tetramethylpiperidine (II). For that 180°C, 125 g (0.8 mole) of 4-amino-2,2,6,6-tetramethylpiperidine (I), 49 g (0.5 mole) of potassium carbonate, 78.8 g (0.5 mole) of 4-nitrochlorobenzene, 3 g of CuO and 125 ml of dimethyl sulfoxide are heated for 4 h. The contents of the flask are carefully diluted with 250 ml of water, and the oily mass is washed three times with water, dissolved in 200 ml of hot ethanol, and filtered. On cooling, the precipitated crystals are filtered off and washed with 100 ml of cold ethanol. Yield, 91 g (65%), 108-109°C (from ethanol). ESR spectrum (CF_3COOH): 1.25 (12H, s, $(CH_3)_4$), 1.5-2.5 (5H, m, $(CH_2)_2$ + CH), 3.8-4.6 (1H, m, CH), 6.3-7.2 (1H, br. s, NH), 7.45 and 8.08 (4H, 2d, H_{arom}).

4-(4-Aminophenylamino)-2,2,6,6-tetramethylpiperidine (III). In a three-neck flask with a reflux condenser, 55.5 g (0.2 mole) of 4-(4-nitrophenylamino)-2,2,6,6-tetramethylpiperidine (II) and 300 ml of ethanol are heated to boiling, and a catalytic amount of Raney nickel and 50% hydrazine dropwise are added at such a rate as not to interrupt the boiling of the solution. The reduction is continued until the yellow color of the solution disappears. The hot solution is filtered, the solvent is driven off in vacuum, and the product is crystallized from ethanol. Yield, 38 g (76.8%), 140-141°C (from ethanol). ESR spectrum (CF_3COOH): 1.20 (12H, s, $(CH_3)_4$), 1.8-2.3 (4H, m, $(CH_2)_2$), 3.7-4.3 (1H, m, CH), 6.4-7.0 (1H, br.s, NH), 7.47 (4H, s, H_{arom}).

N-[4-(2,2,6,6-Tetramethyl-4-piperidinyl)aminophenyl]-β-alanine (IV). One heats 24.7 g (0.1 mole) of 4-(4-aminophenylamino)-2,2,6,6-tetramethylpiperidine (III), 7.2 g (1 mole) of acrylic acid and 70 ml of water for 2 h; the mixture is cooled, and the precipitated crystals are filtered and washed with water, yielding 27.1 g (84.8%) of product. MP 287°C (dec.). Mass spectrum (m/z, %): 320 (M^+ + 1, 12), 319 (M^+, 100).

N-[4-(2,2,6,6-Tetramethyl-4-piperidinyl)aminophenyl]-α-methyl-β-alanine Dihydrochloride (V). One boils 24.7 g (0.1 mole) of 4-(4-aminophenylamino)-2,2,6,6-tetramethylpiperidine (III), 25.8 g (0.3 mole) of methacrylic acid, and 1 g

of hydroquinone in 50 ml of toluene for 14 h, 150 ml of 10% sodium hydroxide solution is added, the solution is cooled, and the unreacted amine is extracted with chloroform (4 × 100 ml). The aqueous layer is acidified with acetic acid to pH 7 and extracted with $CHCl_3$ (4 × 50 ml), the extract is dried, and gaseous HCl is passed through it to saturation. The precipitated crystals are washed with chloroform, acetone, and ether. Yield, 8 g (21%), mp 200°C (dec.). ESR spectrum (CF_3COOH): 1.02 (3H, d, CH_3), 1.22 (12H, s, $(CH_3)_4$), 1.7-2.4 (4H, m, $(CH_2)_2$), 2.7-3.1 (1H, m, CHCO), 3.3-3.6 (2H, m, $NHCH_2$), 3.8-4.4 (1H, m, CH-piperidine ring), 6.5-7.2 (1H, br. s, NH), 7.2-7.9 (4H, m, H_{arom}).

1-[4-(2,2,6,6-Tetramethyl-4-piperidinyl)]-4-carboxy-2-pyrrolidinone (VI). One boils 2.47 g (0.01 mole) of amine II, 1.43 g (0.11 mole) of itaconic acid, and 10 ml of water for 2 h, the water is driven off in vacuum, and the residue is flooded with acetone. On standing, the mass crystallizes out. There was obtained 3.1 g (86%). MP 320°C (dec.) (from 80% ethanol). ESR spectrum (CF_3COOH): 1.27 (12H, s, $(CH_3)_4$), 1.6-2.2 (4H, m, $(CH_2)_2$-piperidine ring), 3.7-4.3 (3H, m, CH-piperidine ring + CH_2-pyrrolidine ring), 6.3-6.8 (1H, br. s, NH), 7.31 and 7.53 (4H, 2d, H_{arom}).

1-[4-(2,2,6,6-Tetramethyl-4-piperidinyl)aminophenyl]dihydro-4-(1H,3H)-pyrimidinone-2-thione (VII). One boils 9.6 g (0.03 mole) of N-[4-(2,2,6,6-tetramethyl-4-piperidinyl)aminophenyl]-β-alanine (IV), 10 g of potassium thiocyanate, and 20 ml of acetic acid for 8 h, adds 17% HCl to pH 1 and boils for another 10 min. The contents of the flask are diluted with 50 ml of water and neutralized with sodium acetate to pH 7, and the precipitated crystals are filtered off, washed with 15 ml of cold water, and dried. Yield, 2.3 g (21.3%), mp 322°C (dec. from CH_3COOH-H_2O) mixture). ESR spectrum (CF_3COOH): 1.20 (12H, s, $(CH_3)_4$), 1.7-2.1 (4H, m, $(CH_2)_2$ piperidine ring), 2.73 (2H, t, $5CH_2$), 3.2-4.2 (3H, m, $6CH_2$-dihydropyrimidine ring and CH-piperidine ring), 6.2-6.8 (1H, br. s, NH), 6.8-7.8 (4H, m, H_{arom}).

1-[4-(2,2,6,6-Tetramethyl-4-piperidinyl)aminophenyl]dihydro-2,4-pyrimidinedione (VIII) is obtained from 9.6 g of β-alanine IV similarly to compound VII, with 9 g (0.03 mole) of urea used instead of potassium thiocyanate. Yield, 2.1 g (20.3%), mp > 350°C (from acetic acid).

5-Methyl-1-[4-(2,2,6,6-tetramethyl-4-piperidinyl)aminophenyl]dihydro-2,4-(1H,3H)-pyrimidinedione (IX). One boils 3.7 g (0.01 mole) of N-[4(2,2,6,6-tetramethyl-4-piperidinyl)aminophenyl]-α-methyl-β-alanine dihydrochloride (V), 1.8 g (0.03 mole) of urea, and 20 ml of acetic acid for 10 h, adds a 17% solution of HCl to pH 1 and boils the mixture for another 10 min. The solvents are driven off on a vacuum rotary evaporator, the residue is dissolved in a minimum amount of water, and the solution is neutralized to pH 7. The precipitated product is filtered off and washed with cold water (10 ml) and ethanol. Yield, 2.5 g (69.8%), mp > 350°C (from acetic acid). ESR spectrum (CF_3COOH): 1.07 (3H, d, CH_3), 1.7-2.3 (4H, m, $(CH_2)_2$), 2.7-3.0 (1H, m, 5-CH), 3.5-3.8 (2H, m, 6-CH_2), 3.8-4.1 (1H, m, CH-piperidine ring), 6.4-6.8 (1H, br. s, NH), 7.3-7.6 (4H, m, H_{arom}). Mass spectrum (m/z, %): 359 (M^+, 20.5), 358 (M^+, −1.84).

REFERENCES

1. H. Oertel and P. Uhrhan, German Pat. 2,642,446; Chem. Abstr., **89**, 431252 (1978).
2. L. Avar, German Pat. 3,408,948; Chem. Abstr., **102**, 113303 (1985).
3. Sumitomo Chemical Co., Ltd., Jpn. Pat. 58,120,646; Chem. Abstr., **100**, 52565 (1984).
4. V. Yu. Mitskyavichyus and R. S. Baltrushis, Khim. Geterotsikl. Soedin., No. 10, 1391 (1992).