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## Interaction of 2-substituted 7,7-dimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-4-carboxylic acids with pentafluorophenyl hydrazine. Synthesis of 5-substituted 8,8-dimethyl-2-pentafluorophenyl-3,7,8,9-tetrahydro-2H-pyrido[4,3,2-de]cinnolin-3-ones

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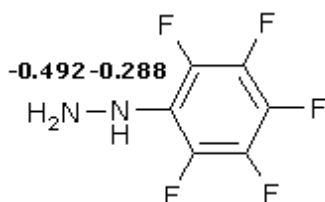
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**Abstract:** 2-Substituted 7,7-dimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-4-carboxylic acids react with pentafluorophenyl hydrazine to give 5-substituted 8,8-dimethyl-2-pentafluorophenyl-3,7,8,9-tetrahydro-2H-pyrido[4,3,2-de]cinnolin-3-ones. The structures of synthesized compounds were based on <sup>1</sup>H and <sup>19</sup>F NMR spectroscopic data.

**Keywords:** 2-substituted 7,7-dimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-4-carboxylic acids, pentafluorophenyl hydrazine, 5-substituted 8,8-dimethyl-2-pentafluorophenyl-3,7,8,9-tetrahydro-2H-pyrido[4,3,2-de]cinnolin-3-ones.

As known ethers of 2-substituted 5-oxo-5,6,7,8-tetrahydroquinoline-4-carboxylic acids react with hydrazine to afford 5-substituted 7,8,9-tetrahydro-2H-pyrido[4,3,2-de]cinnolin-3-ones [1]. Concordant results were obtained in the research on reaction between 2-substituted 7,7-dimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-4-carboxylic acids and hydrazine and its ethyl- and phenyl- derivatives [2]. Formation of pyridazine fragment is caused by participation in reaction of both hydrazine and its monoderivatives nitrogen atoms. The behavior of pentafluorophenyl hydrazine in such reaction hasn't been explored. The interest to this substance is conditioned by considerable difference in nucleophilicity of nitrogen atoms N<sup>1</sup> and N<sup>2</sup> in its molecule. It seems only one nitrogen atom N<sup>2</sup> able to take part in interaction. This assumption is based on nonobservational quantum-chemical calculations of Lowdin's total nitrogen atomic charges in pentafluorophenyl hydrazine molecule.



The reaction between equimolar quantities of 2-substituted 7,7-dimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-4-carboxylic acids **1a-i** and pentafluorophenyl hydrazine (**2**) leads to 5-substituted 8,8-dimethyl-2-pentafluorophenyl-3,7,8,9-tetrahydro-2H-pyrido[4,3,2-de]cinnolin-3-ones **5a-i** in good yields.



5i	C <sub>27</sub> H <sub>22</sub> F <sub>5</sub> N <sub>3</sub> O	65.03	4.28	8.34	19.03	192-193	85
		64.93	4.44	8.41	19.02	(BuOH)	

The scheme of formation compounds **5a-i** includes addition of pentafluorophenyl hydrazine molecule (**2**) to carbon atom C<sup>5</sup> of initial acid **1a-i** and intermediate **3a-i** cyclization by means of intramolecular nucleophilic attack of nitrogen atom connected with pentafluorophenyl radical at carboxylic carbon atom. Elimination of two water molecules leads to products **5a-i**. Probably intramolecular nucleophilic attack is more preferable in comparison with dehydration followed by formation of corresponding pentafluorophenyl hydrazones **6a-i**.

The structures of products were determined on IR, <sup>1</sup>H and <sup>19</sup>F NMR spectroscopic data. IR spectrum shows characteristic band of C<sup>3</sup>=O stretching vibrations in 1681-1695 cm<sup>-1</sup> region, C-F vibrations in 993-1005 cm<sup>-1</sup> and intensive band 1586-1596 cm<sup>-1</sup> attributed either to C=N or C=C bond stretching vibrations. <sup>1</sup>H NMR spectrum demonstrates signals of methyl protons at 1.14-1.21 ppm, methylen C<sup>7</sup>H<sub>2</sub> and C<sup>9</sup>H<sub>2</sub> protons at 3.03-3.17 and 2.82-2.91 ppm respectively, C<sup>4</sup>H proton in weak field at 7.64-8.44 ppm and also signals of substitute's protons.

**Table 2.** IR and <sup>1</sup>H NMR spectra data.

Compound	IR spectra, ν, cm <sup>-1</sup>			<sup>1</sup> H NMR spectra, δ, ppm (J, Hz)				
	C=C + C=N	C <sup>3</sup> =O	C-F	6H, 2CH <sub>3</sub> (c)	2H, C <sup>7</sup> H <sub>2</sub> (c)	2H, C <sup>9</sup> H <sub>2</sub> (c)	1H, C <sup>4</sup> H (c)	R-signal
<b>5a</b>	1596	1687	998	1.14	3.09	2.82	7.97	1.44 (9H, s, C(CH <sub>3</sub> ) <sub>3</sub> )
<b>5b</b>	1591	1681	993	1.17	3.17	2.85	8.43	7.49-7.59 (3H, m, C <sub>6</sub> H <sub>5</sub> ) 8.27-8.30 (2H, m, C <sub>6</sub> H <sub>5</sub> )
<b>5c</b>	1587	1688	1002	1.17	3.16	2.84	8.41	2.41 (3H, s, CH <sub>3</sub> ) 7.37 (2H, d, J = 8.0, H Ar) 8.20 (2H, d, J = 8.0, H Ar)
<b>5d</b>	1591	1684	1003	1.17	3.13	2.83	8.35	3.89 (3H, s, OCH <sub>3</sub> ) 7.10 (2H, s, J = 9.0, H Ar) 8.27 (2H, s, J = 9.0, H Ar)
<b>5e</b>	1586	1689	1003	1.17	3.13	2.82	8.35	1.40 (3H, t, J = 7.0, OCH <sub>2</sub> CH <sub>3</sub> ) 4.15 (2H, q, J = 7.0, OCH <sub>2</sub> CH <sub>3</sub> ) 7.08 (2H, d, J = 9.0, H Ar) 8.26 (2H, d, J = 9.0, H Ar)
<b>5f</b>	1596	1688	1004	1.17	3.17	2.85	8.44	7.72 (2H, d, J = 9.0, H Ar) 8.25 (2H, d, J = 9.0, H Ar)
<b>5g</b>	1598	1687	1005	1.17	3.16	2.85	8.43	7.57 (2H, d, J = 9.0, H Ar) 8.31 (2H, d, J = 9.0, H Ar)

<b>5h</b>	1592	1689	999	1.21	3.03	2.91	7.64	7.82-7.50 (4H, m, C <sub>10</sub> H <sub>7</sub> ) 8.23-8.02 (3H, m, C <sub>10</sub> H <sub>7</sub> )
<b>5i</b>	1596	1695	998	1.17	3.14	2.86	8.05	2.29 (6H, s, 2CH <sub>3</sub> ) 2.39 (3H, s, CH <sub>3</sub> ) 7.11 (1H, s, C <sub>6</sub> H <sub>2</sub> (CH <sub>3</sub> ) <sub>3</sub> ) 7.37 (1H, s, C <sub>6</sub> H <sub>2</sub> (CH <sub>3</sub> ) <sub>3</sub> )

<sup>19</sup>F NMR spectrum contains characteristic signals of pentafluorophenyl group (table 3).

**Table 3.** <sup>19</sup>F NMR spectra data.

Product	<sup>1</sup> NMR spectra, δ, ppm (J, Hz)		
	F <sub>p</sub> (t)	F <sub>o</sub> (d)	F <sub>m</sub> (set of signals)
<b>5a</b>	-78.36 J = 14	-70.08 J = 14	-87.35
<b>5b</b>	-78.28 J = 20	-69.86 J = 20	-87.25
<b>5c</b>	-78.32 J = 17	-69.91 J = 17	-87.28
<b>5d</b>	-78.39 J = 17	-69.90 J = 17	-87.32
<b>5e</b>	-78.39 J = 20	-69.88 J = 20	-87.31
<b>5f</b>	-78.20 J = 14	-69.81 J = 14	-87.22
<b>5g</b>	-78.21 J = 17	-69.80 J = 17	-87.22
<b>5h</b>	-78.63 J = 14	-70.34 J = 14	-87.67
<b>5i</b>	-74.54 J = 17	-67.80 J = 17	-83.91

In conclusion, an efficient procedure for the synthesis of 5-substituted 8,8-dimethyl-2-pentafluorophenyl-3,7,8,9-tetrahydro-2H-pyrido[4,3,2-de]cinnolin-3-ones from 2-substituted 7,7-dimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-4-carboxylic acids and pentafluorophenyl hydrazine is developed. It is found that nature of substituent at second position in initial acids doesn't effect at yield.

## Experimental

IR spectra were recorded on IFS 66ps "Bruker" FT-spectrometer in mineral oil suspension.  $^1\text{H}$  and  $^{19}\text{F}$  NMR spectra were obtained for solution in acetone- $d_6$  with HMDSO ( $\delta = 0.059$  ppm) and trifluoroacetic acid ( $\delta = 0.000$  ppm) as internal standards using Varian MERCURY+300 spectrometer at 300 MHz and 282 MHz correspondingly. Element analyses were carried out using certified methodolodes: MVI 88-16358-124-2011 "Determination of carbon, hydrogen and nitrogen mass fraction in organic compounds" at automatic "CHN" EA-2400, II analyzer (Perkin Elmer Instruments, USA). F-analysis was done using MVI # 88-16358-95-2009 "Determination of fluor mass fraction in organic compounds using spectrophotometric method" at spectrophotometer "Specord 200" PC ("Analytic Jena AG" Germany).

Quantum-chemical calculations were carried out with program package Firefly [3] on personal computer Toshiba 400 PORTEGE.

**5-Substituted 8,8-dimethyl-2-pentafluorophenyl-3,7,8,9-tetrahydro-2H-pyrido[4,3,2-de]cinnolin-3-ones 5a-i** (general procedure). A mixture of corresponding 2-substituted 7,7-dimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-4-carboxylic acid **1a-i** (3 mmol) and pentafluorophenyl hydrazine (**2**) (0.6 g, 3 mmol) is heated at reflux in ethyl or butyl alcohol (30 ml) for 2 h. After cooling the reaction mixture crude product is filtered and recrystallised from ethyl or butyl alcohol.

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