

Supplementary data for article:

Ajaj, I. A.; Mijin, D.; Maslak, V.; Brkovic, D.; Milčić, M. K.; Todorović, N.; Marinković, A. A Simple and Convenient Synthesis of Tautomeric (6 or 2)-Hydroxy-4-Methyl-(2 or 6)-Oxo-1-(Substituted Phenyl)-(1,2 or 1,6)-Dihydropyridine-3-Carbonitriles. *Monatshefte Fur Chemie* **2013**, *144* (5), 665–675. <https://doi.org/10.1007/s00706-012-0911-5>

1 **Supplementary material**

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3 **A simple and convenient synthesis of tautomeric (6 or 2)-**
4 **hydroxy-4-methyl-(2 or 6)-oxo-1-(substituted phenyl)-(1,2 or**
5 **1,6)-dihydropyridine-3-carbonitriles**

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8 **Milčić • Nina Todorović • Aleksandar Marinković**

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2 *6-hydroxy-4-methyl-2-oxo-1-phenyl-1,2-dihydropyridine-3-carbonitriles (1a,*
3 *C₁₃H₁₀N₂O₂) and 2-hydroxy-4-methyl-6-oxo-1-phenyl-1,6-dihydropyridine-3-*
4 *carbonitriles (1b, C₁₃H₁₀N₂O₂)*
5 White-yellowish crystalline solid; yield 78%, m.p.: 281-283°C (Ref. [1] 280-283°C);
6 **1b**) ¹H NMR (500 MHz, DMSO-*d*₆): δ = 1.89 (s, 3H, 4-CH₃), 6.09 (s, 1H, 5-H),
7 7.26-7.28 (m, 2H, 5'-H, 3'-H), 7.45-7.49 (m, 1H, 4'-H), 7.50-7.54 (m, 2H, 2'-H,
8 6'-H), 12.72 (bs, 1H, OH) ppm; ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 21.7 (CH)₃,
9 83.4 (C3), 98.8 (C5), 115.2 (C≡N), 128.3 (C3', C5'), 128.8 (C4'), 129.4 (C2',
10 C6'), 137.5 (C1'), 152.8 (C4), 162.2 (C6), 171.6 (C2) ppm.

11 HRMS: *m/z* (MH⁺) calcd for C₁₃H₁₁N₂O₂ 227.0840, found 227.0815; IR (KBr): $\bar{\nu}$ =
12 571, 633, 698, 759, 824, 1037, 1131, 1230, 1312, 1412, 1539, 1659 (C=O), 2219
13 (C≡N), 2925, 3094, 3430 (O-H) cm⁻¹; UV-Vis (ethanol, *c* = 5.10⁻⁵ mol dm⁻³): λ_{max}
14 (ε) = 320 (46020) nm (mol⁻¹ dm³ cm⁻¹); Elemental Analysis:

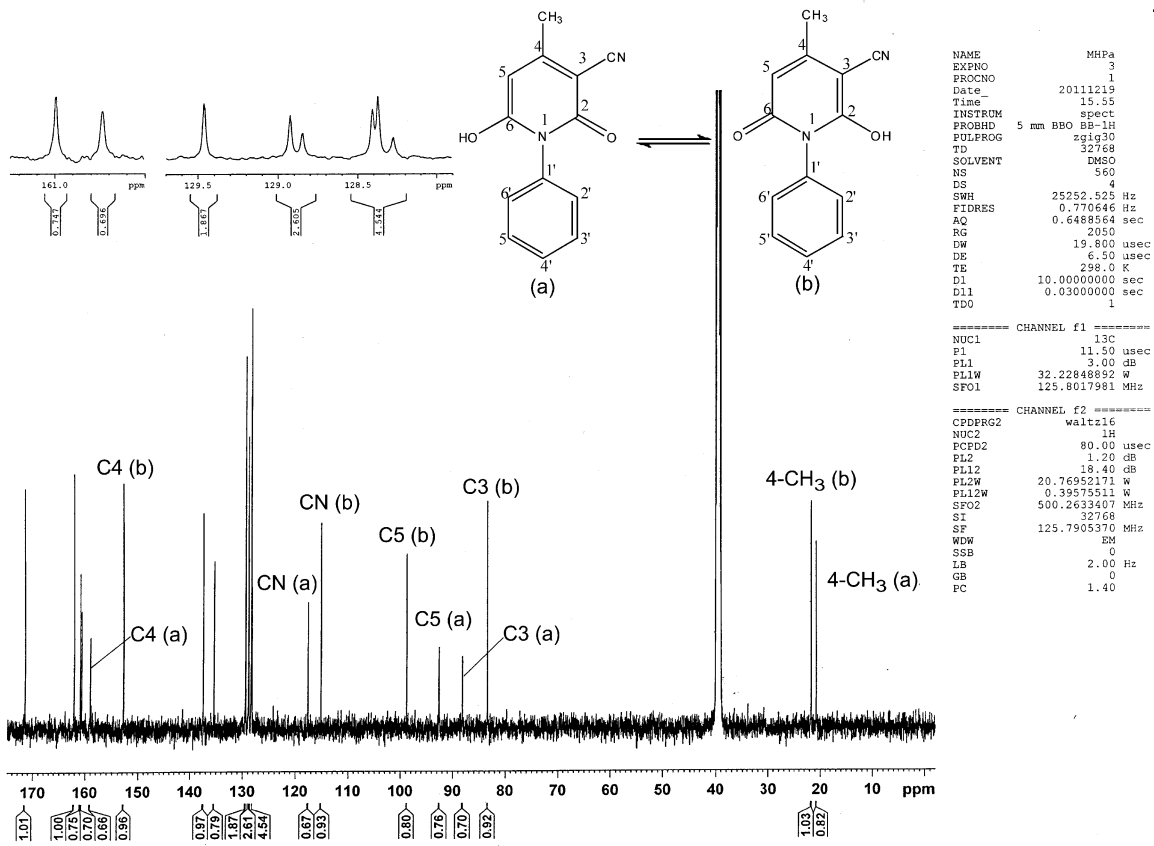
15 Calculated: %C 69.02, %H 4.46, %N 12.38, %O, 14.14

16 Found: %C 69.08, %H 4.40, %N 12.34, %O, 14.18

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18 *6-hydroxy-4-methyl-2-oxo-1-(3-methylphenyl)-1,2-dihydropyridine-3-carbonitriles*
19 *(15a, C₁₄H₁₂N₂O₂) and 2-hydroxy-4-methyl-6-oxo-1-(3-methylphenyl)-1,6-dihydro-*
20 *pyridine-3-carbonitriles (15b, C₁₄H₁₂N₂O₂)*

1 Grayish crystalline solid; yield 54%, m.p.: 284-285°C (Ref. [2] 278-281°C);
2 **15a**) ¹H NMR (500 MHz, DMSO-*d*₆): δ = 2.28 (s, 3H, 4-CH₃), 2.33 (s, 3H, 3'-
3 CH₃), 5.69 (s, 1H, 5-H), 6.99-7.02 (m, 2H, 2'-H, 4'-H), 7.22 (d, *J* = 8 Hz, 1H, 6'-
4 H), 7.35 (t, *J* = 7.8 Hz, 1H, 5'-H), 12.70 (bs, 1H, OH) ppm; ¹³C NMR (125 MHz,
5 DMSO-*d*₆): δ = 20.7 (3'-CH₃), 20.8 (4-CH₃), 88.5 (C3), 92.5 (C5), 117 (C≡N),
6 125.4 (C4'), 128.8 (C2'), 129.0 (C5'), 129.2 (C6'), 135.3 (C1'), 138.4 (C3'),
7 159.2 (C4), 160.7 (C2), 162.2 (C6) ppm.
8 **15b**) ¹H NMR (500 MHz, DMSO-*d*₆): δ = 1.91 (s, 3H, 4-CH₃), 2.34 (s, 3H, 3'-
9 CH₃), 6.08 (s, 1H, 5-H), 7.04-7.08 (m, 2H, 2'-H, 4'-H), 7.28 (d, *J* = 8 Hz, 1H, 6'-
10 H), 7.39 (t, *J* = 7.8 Hz, 1H, 5'-H), 12.70 (bs, 1H, OH) ppm; ¹³C NMR (125 MHz,
11 DMSO-*d*₆): δ = 20.7 (3'-CH₃), 21.7 (4-CH₃), 83.4 (C3), 98.8 (C5), 115 (C≡N),
12 125.3 (C4'), 128.7 (C2'), 129.2 (C5'), 129.5 (C6'), 137.4 (C1'), 139.1(C3'), 152.8
13 (C4), 160.9 (C6), 171.6 (C2) ppm.
14 HRMS: *m/z* (MH⁻) calcd for C₁₄H₁₁N₂O₂ 239.0801, found 239.0826; IR (KBr): $\bar{\nu}$ =
15 581, 626, 703, 769, 832, 879, 1046, 1132, 1245, 1337, 1379, 1407, 1458, 1552, 1648
16 (C=O), 2223 (C≡N), 2608, 2861, 2928, 3084, 3433 (O-H) cm⁻¹; UV-Vis (ethanol, *c* =
17 5.10⁻⁵ mol dm⁻³): λ_{max} (ε) = 300 (2980) nm (mol⁻¹ dm³ cm⁻¹); Elemental Analysis:
18 Calculated: %C 69.99, %H 5.03, %N 11.66, %O 13.32
19 Found: %C 69.85, %H 5.12, %N 11.73, %O 13.30

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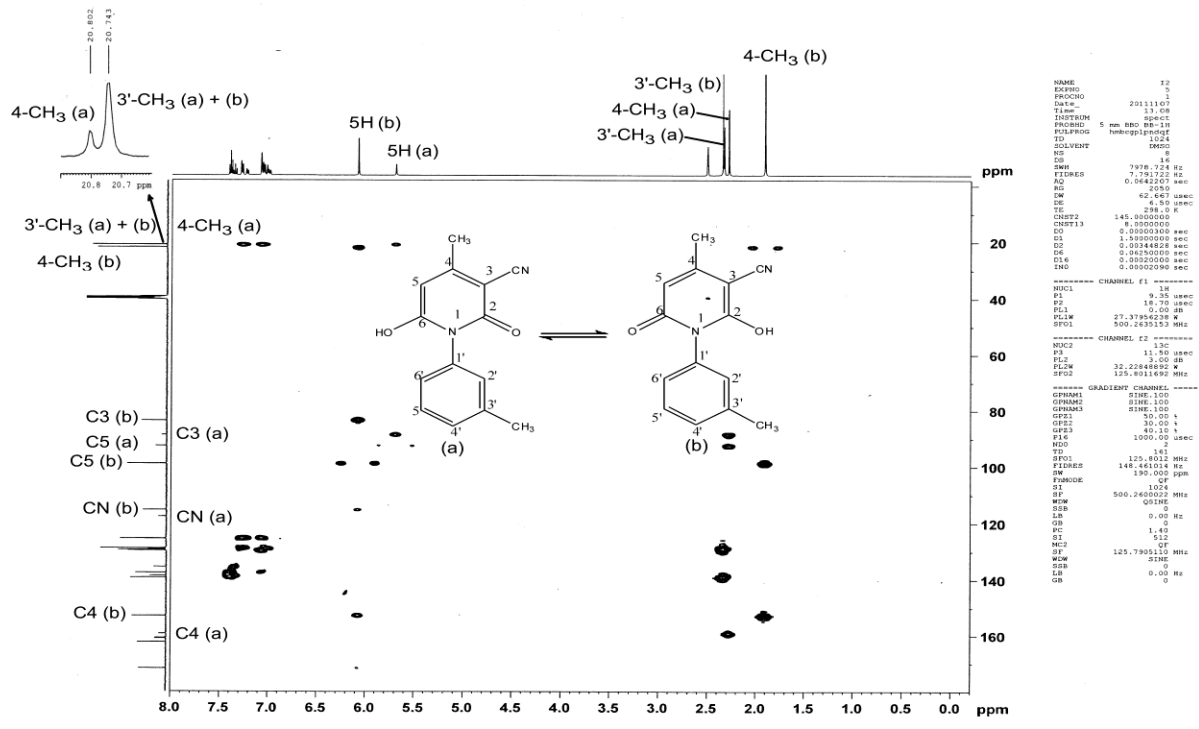
3 **Fig. S1** Quantitative ¹³C NMR spectrum of compound 1

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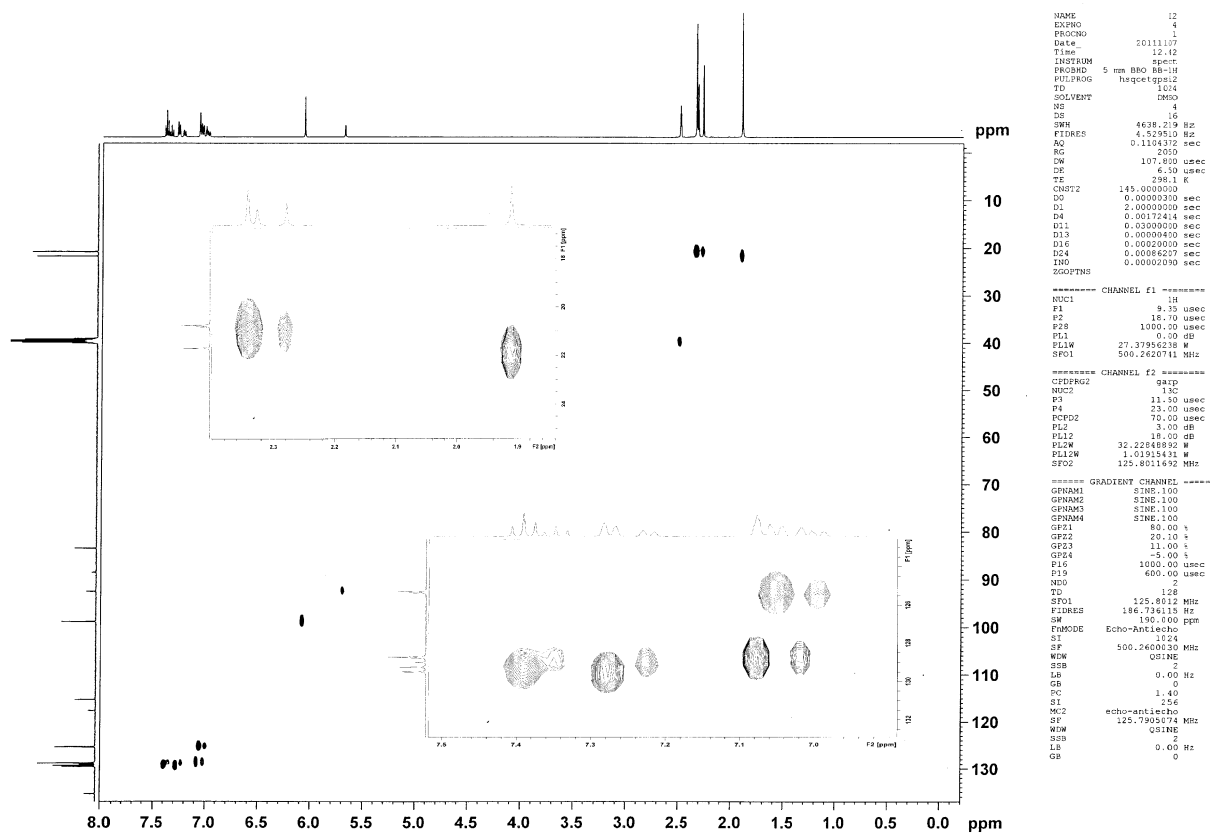
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Fig. S2 HMBC spectrum of compound **15**



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2 **Fig. S3** HSQC spectrum of compound **15**

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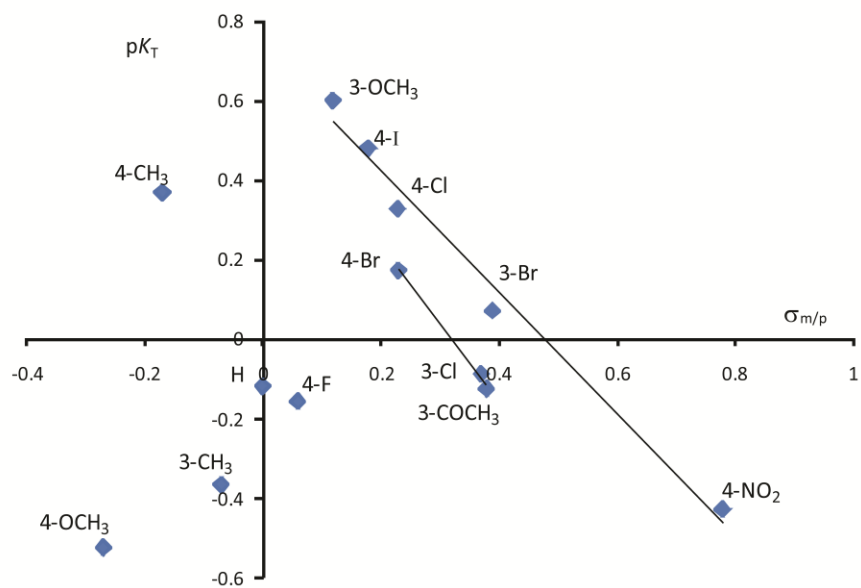
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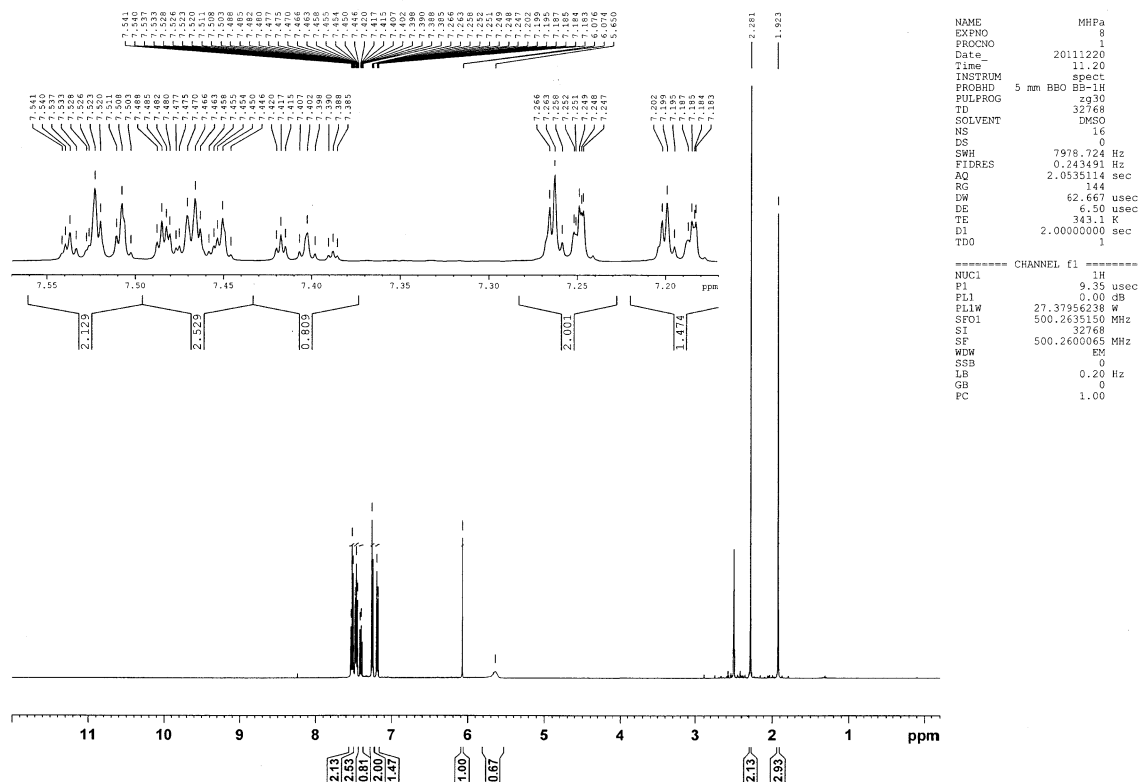


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5 **Fig. S4** Graphical presentation of relation pK_T vs $\sigma_{m/p}$

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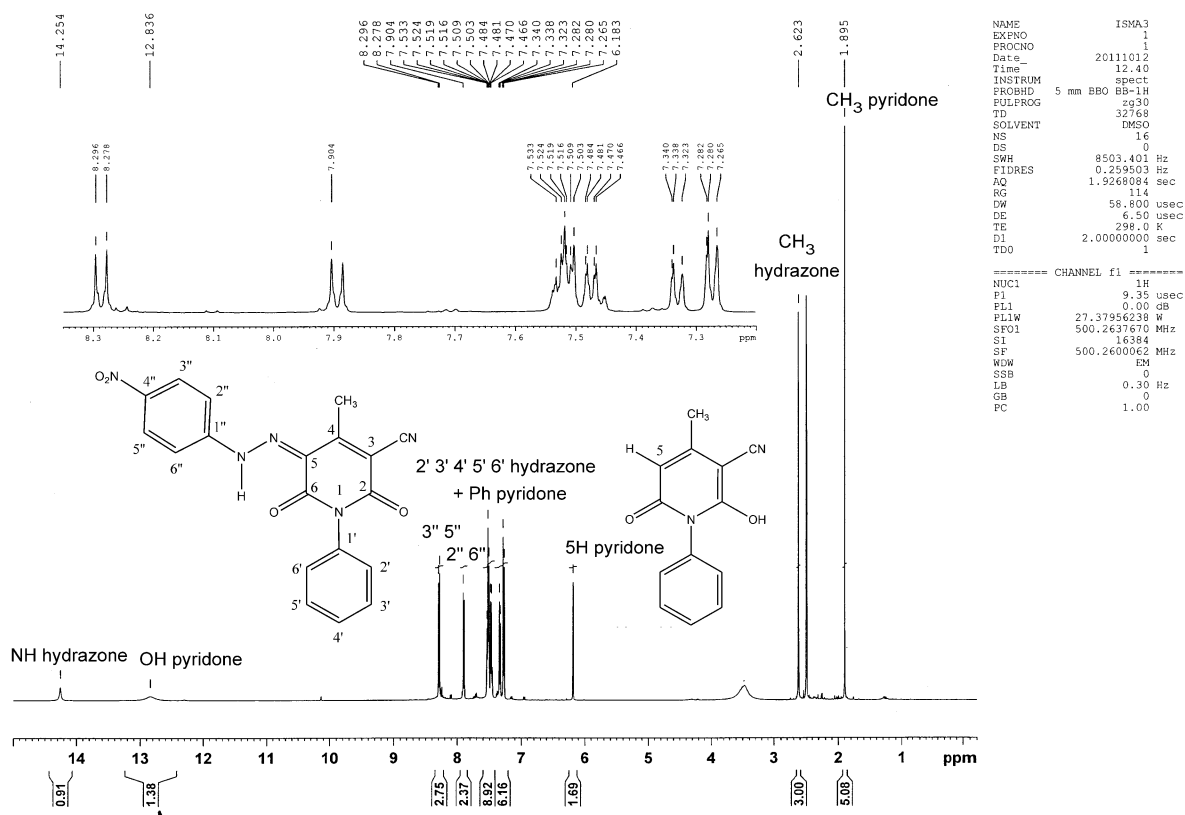
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Fig. S5 ¹H NMR spectra of compound **1** recorded at 343 K

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3 **Fig. S6** ^1H NMR spectrum of unpurified product from (Z)-4-methyl-5-[2-(4-

4 nitrophenyl)hydrazono]-2,6-dioxo-1-phenyl-1,2,5,6-tetrahydro-3-carbonitriles

5 synthesis

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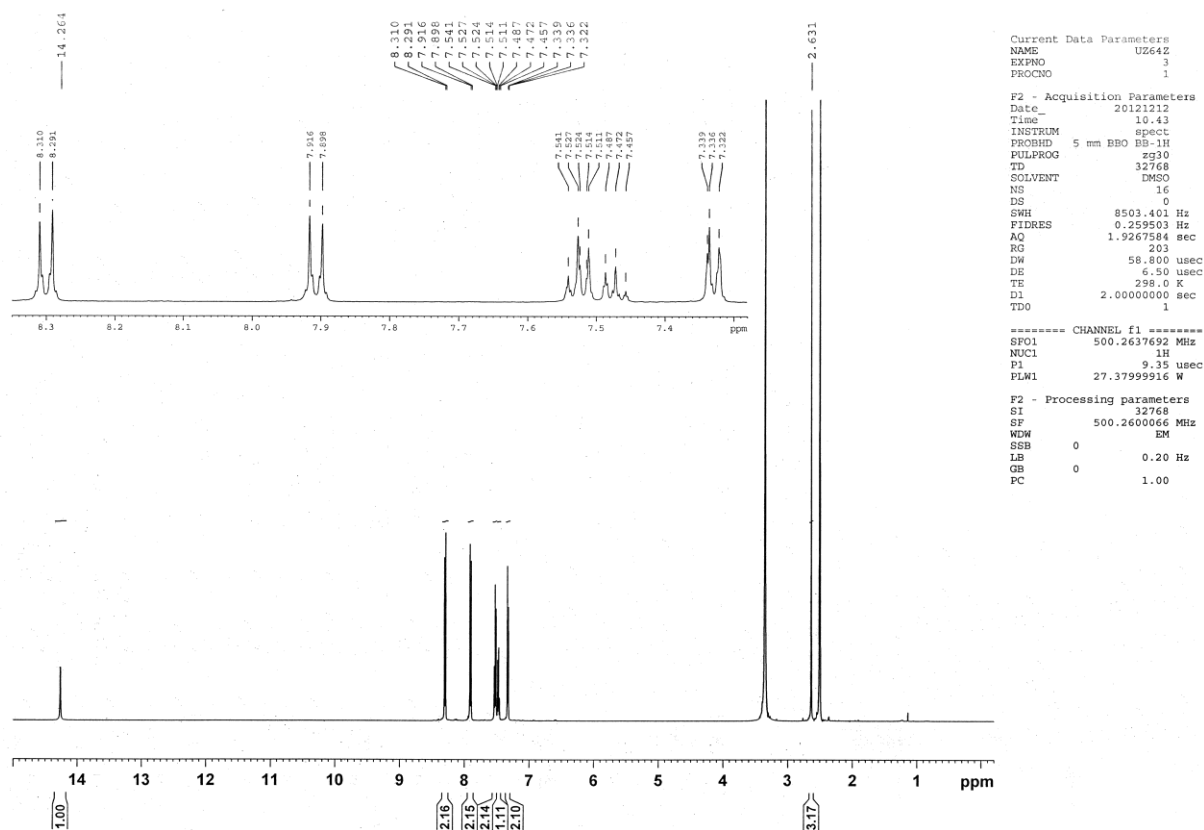


Fig. S7 ^1H NMR spectrum of (Z)-4-methyl-5-[2-(4-nitrophenyl)hydrazono]-2,6-dioxo-1-phenyl-1,2,5,6-tetrahydro-3-carbonitriles

Table S1 Yields and melting points of the obtained product in conventional synthesis

Comp.	X	Yield / %	M.p. / °C	Comp.	X	Yield / %	M.p. / °C
1	H	40	280-2	9	4-Br	36	275-7
2	4-CH ₃	38	283-5	10	4-F	41	282-4
3	4-OCH ₃	41	270-2	11	3-CF ₃	37	314-5
4	4-NO ₂	32	236-40	12	3-Cl	34	273-6
5	4-COCH ₃	25	226-9	13	3-Br	36	277-80
6	4-OH	24	284-6	14	3-OCH ₃	28	250-2
7	4-I	38	286-7	15	3-CH ₃	29	281-3
8	4-Cl	40	285-7	16	3-COCH ₃	27	242-4

Table S2 Results of calculations of ^1H and ^{13}C NMR chemical shifts for tautomer **a**

No.	Substituent	q_{C5}	C4	C3	C2	C6	C5	H5	C4'	4-CH ₃
1	H	-0.602	158.9	93.3	154.6	154.4	89.4	5.89	124.5	19.2
2	4-CH ₃	-0.601	158.9	93.1	154.8	154.6	89.5	5.88	137.3	19.3
3	4-OCH ₃	-0.588	158.8	93.2	154.9	154.7	89.6	5.89	155.1	19.2
4	4-NO ₂	-0.581	160.0	93.9	154.0	153.4	90.1	5.97	147.4	19.3
5	4-COCH ₃	-0.579	159.4	93.7	154.2	153.7	89.9	5.94	132.9	19.3
6	4-OH	-0.602	158.7	93.2	154.9	154.7	89.5	5.87	152.5	19.1
7	4-I*	-	-	-	-	-	-	-	-	-
8	4-Cl	-0.598	159.4	93.5	154.5	154.0	89.7	5.91	131.7	19.2
9	4-Br	-0.600	159.3	93.4	154.4	154.0	89.7	5.92	124.9	19.3
10	4-F	-0.615	159.2	93.4	154.7	154.3	89.6	5.90	159.0	19.2
11	3-CF ₃	-0.600	159.4	93.4	154.3	153.8	89.8	5.94	132.9	19.3
12	3-Cl	-0.602	159.3	93.4	154.4	153.9	89.6	5.91	124.8	19.3
13	3-Br	-0.601	159.3	93.4	154.4	153.9	89.6	5.90	127.4	19.2
14	3-OCH ₃	-0.613	158.9	93.3	154.6	154.4	89.6	5.89	115.8	19.1
15	3-CH ₃	-0.621	158.9	93.1	154.6	154.4	89.6	5.89	124.9	19.2
16	3-COCH ₃	-0.586	159.2	93.3	154.4	153.9	89.9	5.95	126.3	19.2

*basis set for I substituent is not available

Table S3 Results of calculations of ^1H and ^{13}C NMR chemical shifts for tautomer **b**

No.	Substituent	q_{C5}	C3	C2	C4	C5	C6	H5	C4'	4-CH ₃
1	H	-0.562	76.3	159.0	148.4	107.3	153.4	6.10	132.5	19.5
2	4-CH ₃	-0.534	76.2	159.1	148.3	108.3	153.6	6.09	137.6	19.4
3	4-OCH ₃	-0.559	76.3	159.3	148.2	108.4	153.6	6.09	155.2	19.4
4	4-NO ₂	-0.564	76.3	158.3	149.3	107.5	152.5	6.18	147.5	19.5
5	4-COCH ₃	-0.525	76.9	158.6	148.8	107.4	152.9	6.15	133.1	19.4
6	4-OH	-0.529	76.3	159.3	148.1	107.2	153.6	6.08	152.6	19.4
7	4-I*	-	-	-	-	-	-	-	-	-
8	4-Cl	-0.561	76.7	158.8	148.7	107.3	153.1	6.12	131.4	19.4
9	4-Br	-0.552	76.7	158.8	148.7	107.3	153.1	6.12	124.7	19.4
10	4-F	-0.553	76.6	159.0	148.6	107.3	153.3	6.11	159.2	19.4
11	3-CF ₃	-0.546	76.9	158.7	148.8	107.3	152.9	6.16	123.4	19.5
12	3-Cl	-0.555	76.7	158.7	148.8	107.4	153.0	6.12	125.0	19.5
13	3-Br	-0.552	76.6	158.7	148.7	107.3	153.0	6.13	127.8	19.5
14	3-OCH ₃	-0.549	76.2	159.1	148.4	107.4	153.3	6.10	113.8	19.4
15	3-CH ₃	-0.574	76.2	159.1	148.2	107.5	153.5	6.09	125.4	19.5
16	3-COCH ₃	-0.545	76.9	158.7	148.7	107.3	153.0	6.16	126.6	19.5

*basis set for I substituent is not available

Table S4 Results of Hammett^a correlations pK_T vs $\sigma_{m/p}$ for electron-acceptor substituted compounds **4**, **7-9**, **12-14** and **16**

scale	h^b	ρ^c	r^d	sd^e	F^f	n^g
$\sigma_{m/p}$	0.638 (± 0.102)	-1.528 (± 0.264)	0.92	0.143	33	8
$\sigma_{m/p}$	0.475 (± 0.021)	-0.642 (± 0.048)	0.99	0.039	175	5 ^h
$\sigma_{m/p}$	0.618 (± 0.036)	-1.931 (± 0.109)	0.99	0.013	311	3 ⁱ

^a $pK_T = \rho\sigma + h$; ^bintercept; ^cproportionality constant; ^dCorrelation coefficient; ^e Standard deviation; ^fFisher test of significance; ^g

number of data included in correlation; ^h compounds **4**, **7**, **8**, **13** and **14**; ⁱ compounds **9**, **12** and **16**

Table S5 Elements of geometry of the tautomers **a** and **b** obtained by the use of B3LYP/6-311++G(d,p) method

No.	substituent	a				b			
		Torsion angle	Bond length			Torsion angle	Bond length		
		θ_a^a	N1-C2	N1-C6	N1-C1'	θ_b^b	N1-C2	N1-C6	N1-C1'
1	H	79.65	1.4406	1.3632	1.4487	78.19	1.3562	1.4525	1.4485
2	4-CH ₃	80.18	1.4408	1.3629	1.4482	77.85	1.3560	1.4524	1.4480
3	4-OCH ₃	76.25	1.4418	1.3633	1.4467	74.04	1.3564	1.4534	1.4465
4	4-NO ₂	66.55	1.4445	1.3672	1.4435	66.07	1.3596	1.4571	1.4433
5	4-COCH ₃	68.93	1.4433	1.3655	1.4459	68.58	1.3579	1.4553	1.4459
6	4-OH	73.35	1.4420	1.3638	1.4463	73.44	1.3566	1.4534	1.4462
7	4-I*	-	-	-	-	-	-	-	-
8	4-Cl	73.05	1.4423	1.3650	1.4457	71.82	1.3576	1.4544	1.4456
9	4-Br	73.05	1.4424	1.3649	1.4458	71.46	1.3577	1.4546	1.4456
10	4-F	75.69	1.4417	1.3643	1.4462	67.22	1.3571	1.4536	1.4461
11	3-CF ₃	68.54	1.4426	1.3630	1.4454	69.63	1.3582	1.4549	1.4454
12	3-Cl	73.57	1.4424	1.3652	1.4462	73.16	1.3578	1.4544	1.4461
13	3-Br	72.50	1.4424	1.3653	1.4460	73.86	1.3576	1.4542	1.4461
14	3-OCH ₃	74.09	1.4414	1.3635	1.4495	82.77	1.3561	1.4519	1.4498
15	3-CH ₃	77.42	1.4410	1.3630	1.4492	80.91	1.3556	1.4521	1.4492
16	3-COCH ₃	66.19	1.4429	1.3656	1.4464	67.22	1.3579	1.4541	1.4465

*basis set for I substituent is not available; ^a torsional angle C2-N1-C1'-C2'; ^b torsional angle C6-N1-C1'-C6'

References

- [1] A. Habashi, (1986) Ann 9:1632
- [2] H. Mustroph, R. Bartel, Reinhard; T. Seele, (1990) DD Patent 276171