Supplementary data for article:

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Supplementary material

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

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6-hydroxy-4-methyl-2-oxo-1-phenyl-1,2-dihydropyridine-3-carbonitriles (**1a**, $C_{13}H_{10}N_2O_2$) and *2-hydroxy-4-methyl-6-oxo-1-phenyl-1,6-dihydropyridine-3-carbonitriles* (**1b,** $C_{13}H_{10}N_2O_2$)

White-yellowish crystalline solid; yield 78%, m.p.: 281-283ºC (Ref. [1] 280-283ºC); **1b**) ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.89 (s, 3H, 4-CH_3), 6.09 (s, 1H, 5-H), 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, 6'-H), 12.72 (bs, 1H, OH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 21.7 $(CH)_3$, 83.4 (C3), 98.8 (C5), 115.2 (C≡N), 128.3 (C3', C5'), 128.8 (C4'), 129.4 (C2', C6'), 137.5 (C1'), 152.8 (C4), 162.2 (C6), 171.6 (C2) ppm.

HRMS: *m/z* (MH^+) calcd for $C_{13}H_{11}N_2O_2$ 227.0840, found 227.0815; IR (KBr): $\bar{\nu}$ = 571, 633, 698, 759, 824, 1037, 1131, 1230, 1312, 1412, 1539, 1659 (C=O), 2219 (C≡N), 2925, 3094, 3430 (O-H) cm^{-1}; UV-Vis (ethanol, $c = 5.10^{-5}$ mol dm^{-3}): λ_{max} (ε) = 320 (46020) nm (mol^{-1} dm^3 cm^{-1}); Elemental Analysis:

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

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

6-hydroxy-4-methyl-2-oxo-1-(3-methylphenyl)-1,2-dihydropyridine-3-carbonitriles (**15a**, $C_{14}H_{12}N_2O_2$) and *2-hydroxy-4-methyl-6-oxo-1-(3-methylphenyl)-1,6-dihydro-pyridine-3-carbonitriles* (**15b**, $C_{14}H_{12}N_2O_2$)

Grayish crystalline solid; yield 54%, m.p.: 284-285ºC (Ref. [2] 278-281ºC);

15a) ^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.28 (s, 3H, 4-CH_3), 2.33 (s, 3H, 3'-CH_3), 5.69 (s, 1H, 5-H), 6.99-7.02 (m, 2H, 2'-H, 4'-H), 7.22 (d, J = 8 Hz, 1H, 6'-H,), 7.35 (t, J = 7.8 Hz, 1H, 5'-H), 12.70 (bs, 1H, OH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 20.7 (3'-CH_3), 20.8 (4-CH_3), 88.5 (C3), 92.5 (C5), 117 (C≡N), 125.4 (C4'), 128.8 (C2'), 129.0 (C5'), 129.2 (C6'), 135.3 (C1'), 138.4 (C3'), 159.2 (C4), 160.7 (C2), 162.2 (C6) ppm.

15b) ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.91 (s, 3H, 4-CH_3), 2.34 (s, 3H, 3'-CH_3), 6.08 (s, 1H, 5-H), 7.04-7.08 (m, 2H, 2'-H, 4'-H), 7.28 (d, J = 8 Hz, 1H, 6'-H), 7.39 (t, J = 7.8 Hz, 1H, 5'-H), 12.70 (bs, 1H, OH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 20.7 (3'-CH_3), 21.7 (4-CH_3), 83.4 (C3), 98.8 (C5), 115 (C≡N), 125.3 (C4'), 128.7 (C2'), 129.2 (C5'), 129.5 (C6'), 137.4 (C1'), 139.1(C3'), 152.8 (C4), 160.9 (C6), 171.6 (C2) ppm.

HRMS: *m/z* (MH^-) calcd for $C_{14}H_{11}N_2O_2$ 239.0801, found 239.0826; IR (KBr): $\bar{\nu}$ = 581, 626, 703, 769, 832, 879, 1046, 1132, 1245, 1337, 1379, 1407, 1458, 1552, 1648 (C=O), 2223 (C≡N), 2608, 2861, 2928, 3084, 3433 (O-H) cm^{-1}; UV-Vis (ethanol, c = 5.10^{-5} mol dm^{-3}): λ_{max} (ε) = 300 (2980) nm (mol^{-1} dm^3 cm^{-1}); Elemental Analysis:

Calculated: %C 69.99, %H 5.03, %N 11.66, %O 13.32

Found: %C 69.85, %H 5.12, %N 11.73, %O 13.30

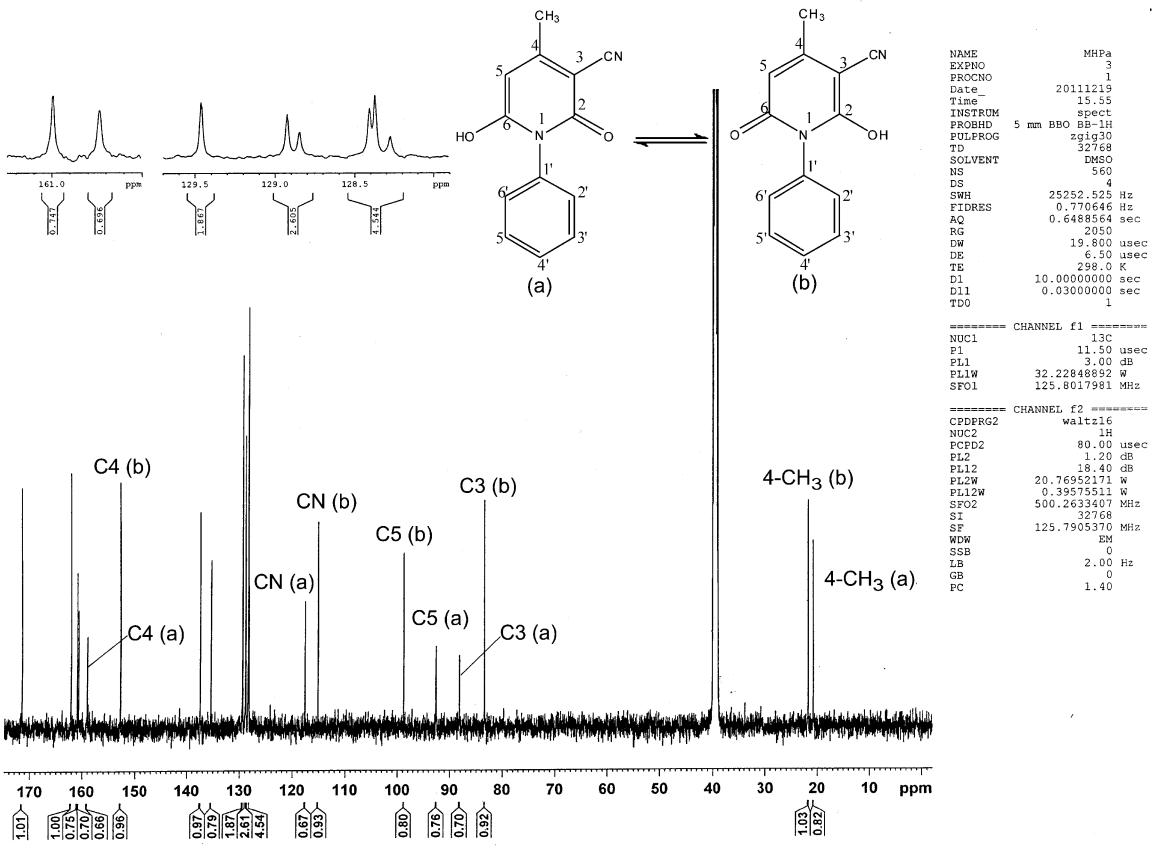


Fig. S1 Quantitative ^{13}C NMR spectrum of compound **1**

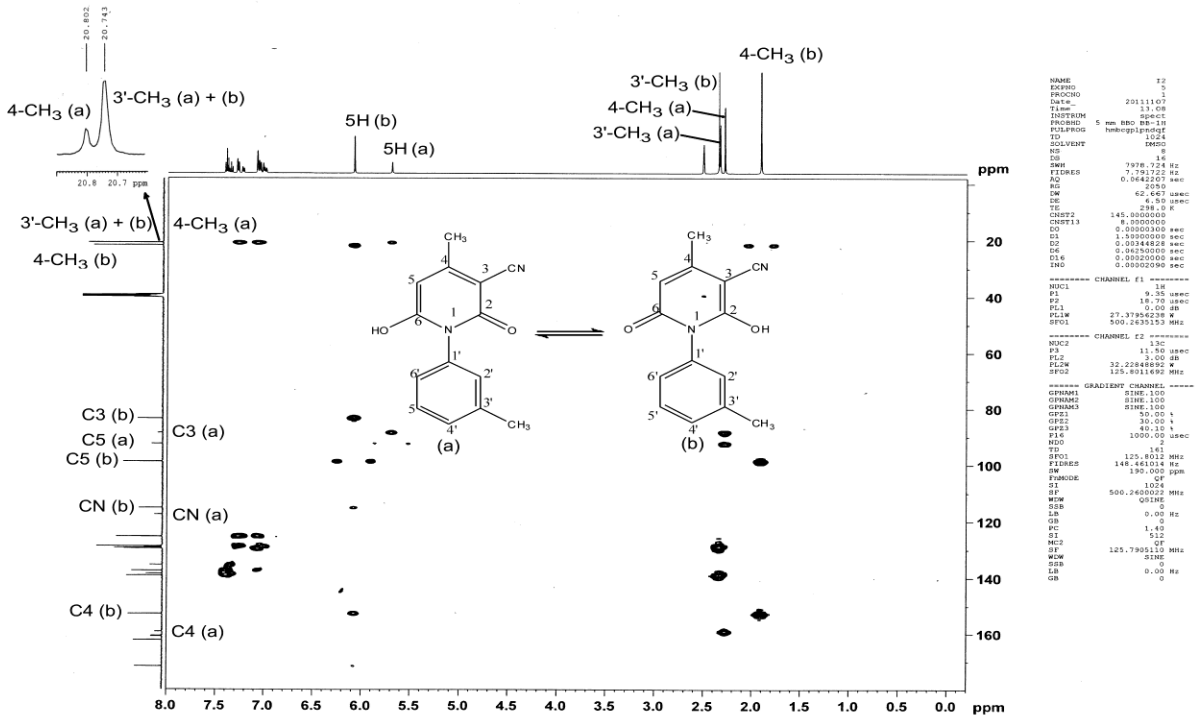
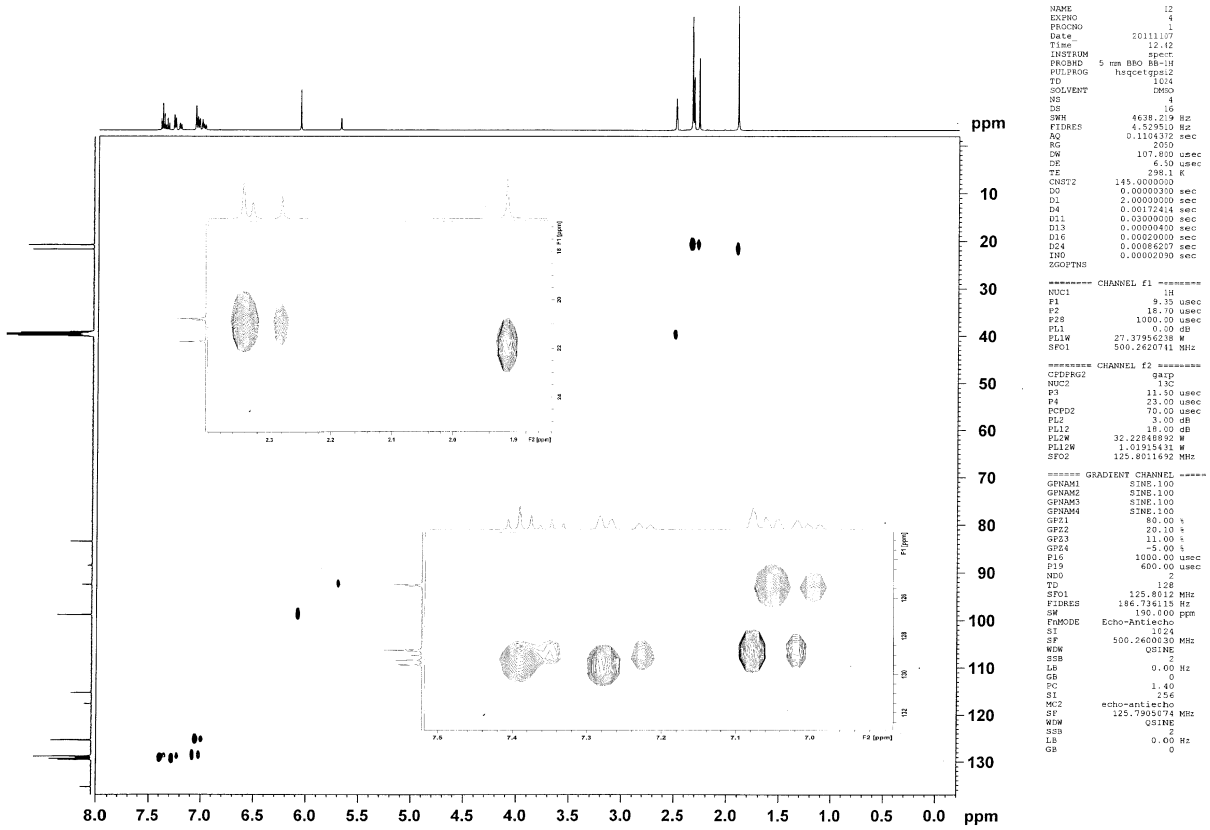


Fig. S2 HMBC spectrum of compound **15**

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EXPNO                 4
PROCNO                1
Date_          20111107
Time              12.42
INSTRUM            spect
PROBHD   5 mm BBO BB-1H
PULPROG      hsqcetgpsi2
TD                 1024
SOLVENT            DMSO
NS                    4
DS                   16
SWH           4638.219 Hz
FIDRES        4.529510 Hz
AQ            0.1104372 sec
RG                 2050
DW              107.800 usec
DE                6.50 usec
TE              298.1 K
CNST2       145.0000000
D0            0.00000300 sec
D1            2.00000000 sec
D4            0.00172414 sec
D11           0.03000000 sec
D13           0.00000400 sec
D16           0.00020000 sec
D24           0.00086207 sec
IN0           0.00002090 sec
2GOPTNS

======== CHANNEL f1 ========
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P1                 9.35 usec
P2                18.70 usec
P28             1000.00 usec
PL1                0.00 dB
PL1W        27.37956238 W
SFO1        500.2620741 MHz

======== CHANNEL f2 ========
CPDPRG2           garp
NUC2                13C
P3                11.50 usec
P4                23.00 usec
PCPD2             70.00 usec
PL2                3.00 dB
PL12              18.00 dB
PL2W        32.22848892 W
PL12W        1.01915431 W
SFO2        125.8011692 MHz

====== GRADIENT CHANNEL =====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPNAM3          SINE.100
GPNAM4          SINE.100
GPZ1               80.00 %
GPZ2               20.10 %
GPZ3               11.00 %
GPZ4               -5.00 %
P16              1000.00 usec
P19               600.00 usec
ND0                   2
TD                  128
SFO1          125.8012 MHz
FIDRES        186.736115 Hz
SW            190.000 ppm
FnMODE     Echo-Antiecho
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SSB                   2
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GB                    0
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LB                 0.00 Hz
GB                    0
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Fig. S3 HSQC spectrum of compound **15**

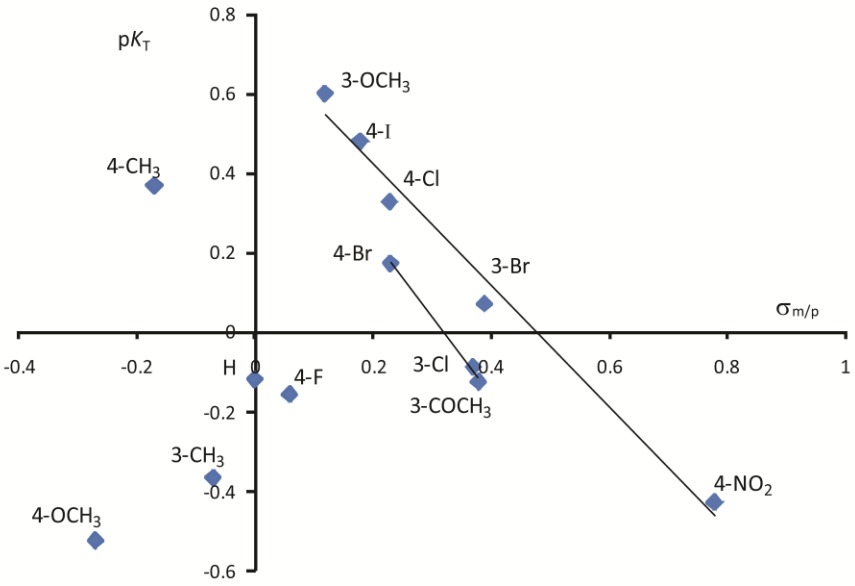

Fig. S4 Graphical presentation of relation pK_T *vs* $\sigma_{m/p}$

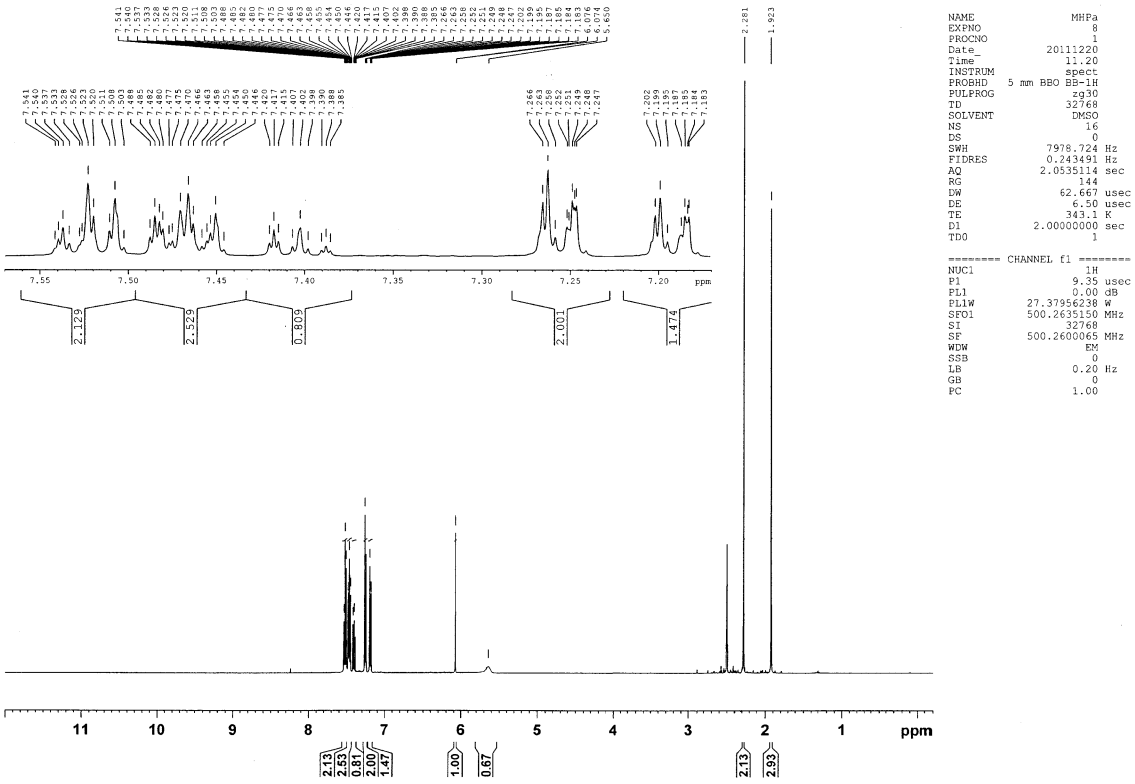

Fig. S5 ^{1}H NMR spectra of compound **1** recorded at 343 K

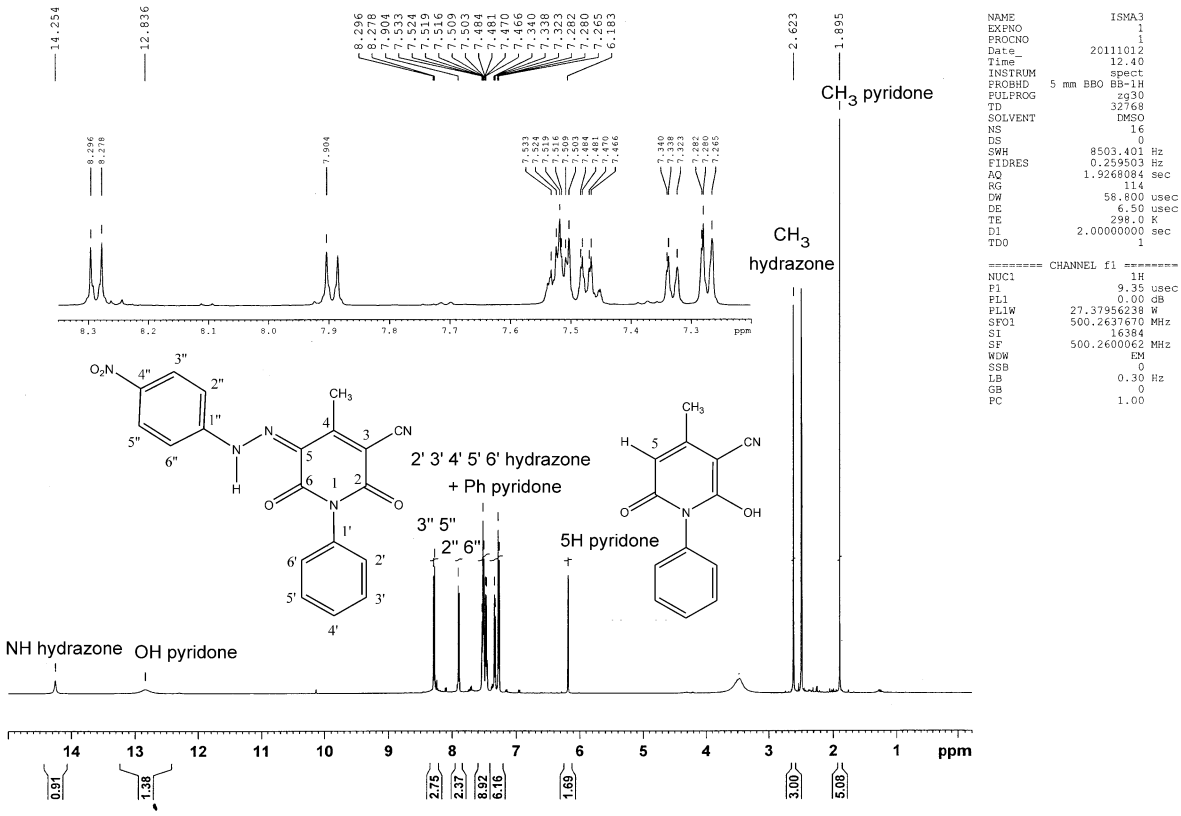

Fig. S6 ^{1}H NMR spectrum of unpurified product from (*Z*)-4-methyl-5-[2-(4-nitrophenyl)hydrazono]-2,6-dioxo-1-phenyl-1,2,5,6-tetrahydro-3-carbonitriles synthesis

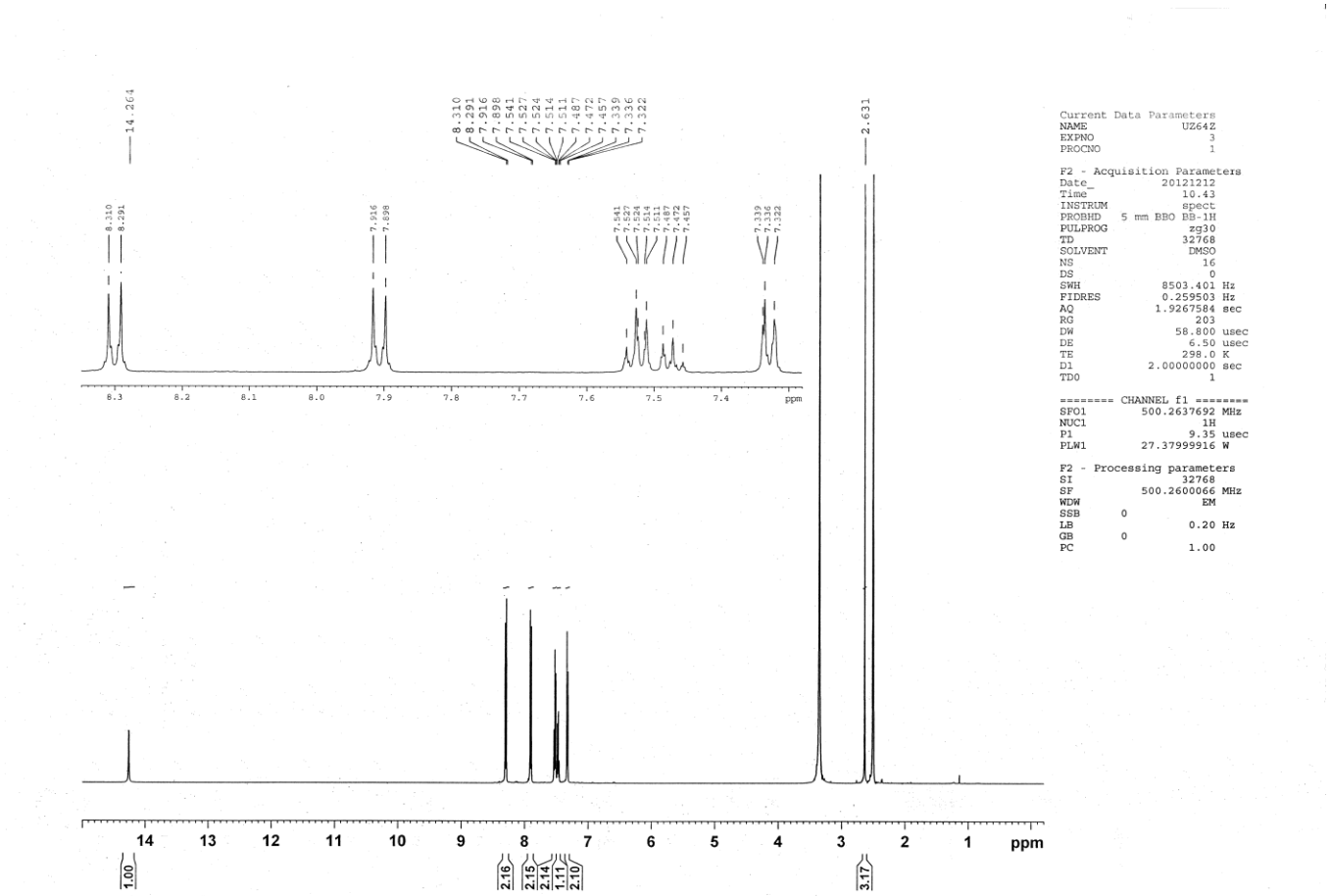

Fig. S7 ^{1}H NMR spectrum of (*Z*)-4-methyl-5-[2-(4-nitrophenyl)hydrazono]-2,6-dioxo-1-phenyl-1,2,5,6-tetrahydro-3-carbonitriles

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

Comp.	X	Yield / %	M.p. / ^{o}C	Comp.	X	Yield / %	M.p. / ^{o}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 ^{1}H 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 ^{1}H 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] p$K_T = \rho\sigma + h$; [b]intercept; [c]proportionality constant; [d] Correlation coefficient; [e] Standard deviation; [f] Fisher 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