C-H bond Cyanation: Electrochemical Synthesis of Phenylbenzimidoyl Cyanide Derivatives

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General

The electrolysis was carried out using a DC-Power Digital control supply 30V 30A Promax Model FA-672 as constant current supply (see Figure of Electrolysis setup at page 3). The temperature was maintained constant at 0 °C. Melting points were measured on a Reichert Thermovar microhot stage apparatus and are uncorrected. IR spectra were recorded on a Fourier spectrometer Infralum FT-801 in KBr pellets. ^{1}H and ^{13}C NMR spectra were acquired on a JEOL JNM-ECA 600 spectrometer (600 and 150 MHz, respectively) in $CDCl_3$ with solvent signal as internal standard (7.26 ppm for ^{1}H nuclei, 77.2 ppm for ^{13}C nuclei). The chemical shifts are given in ppm. Mass spectra of compounds were acquired on a Shimadzu LCMS-8040 system (electrospray ionization). Elemental analysis was performed on a Euro Vector EA-3000

Elemental Analyzer. Analysis of reaction products was carried out by means of Crystal 2000M chromatograph with Porapac column (2 m) with 3 mm diameter.

General procedure for the synthesis of starting imine compounds

Imine derivatives was prepared by the reported literature[1] . The reaction of the corresponding aldehyde (1.40 g, 10 mmol) with aniline (corresponding amine) (0.91 mL, 10 mmol) at 85 °C in ethanol for 2 min using a microwave reactor, the recrystallization was conducted with ethanol to yield colorless crystalline product.

General procedure for the synthesis of phenylbenzimidoyl cyanide derivatives compounds

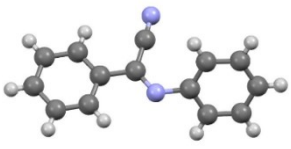
The electrochemical reaction was performed under constant current of 120mA conditions in a simple undivided cell equipped with a magnesium anode and a carbon cathode.
Electrolysis of acetonitrile at 0° C containing ^{n}-Bu_4NBF_4 as electrolyte during 30 min led to the radical anion acetonitrile. Once the desired quantity of the acetonitrile radical-anion is formed, the current supplier was turned off and immediately (*N*,1-diphenylmethanimine was added to the reaction medium. Then after 1 h the reaction was stopped. The acetonitrile was removed under reduced pressure and the residue was remained stirring in diethylether for 1 h, to extract the product from the supporting electrolyte sault. The final solution was filtered, the ether was removed by evaporation and the resulting compound was purified by flash column chromatography on silica gel using Hexane/ EtOAc 8/2 as eluent.

[1] *RSC Adv.*, 2023, **13**, 32063-32069

Electrolysis setup: undivided cell equipped with Magnesuim plate anode (9 mm × 5 cm × 0.1 mm), graphite rod cathode (Φ=5 mm), 1a (1 mmol), solvent (15 mL), constant current of 120mA.

2a: (*Z*)-N-phenylbenzimidoyl cyanide: M.p. = 79-80 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 7.2 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.44-7.58 (m, 5H), 8.13-8.16 (m, 2H). ^{13}C NMR (100 MHz, CDCl3) δ 110.8, 120.2, 127.2, 128.1, 128.9, 129.2, 132.8, 133.5, 139.7, 149. IR (neat): 3060, 2960, 2220, 1594, 1574, 1479, 1450, 1275, 1200, 1069, 1006, 835, 773, 721cm^{-1}. LCMS m/z: 207 $[M + H]^{+}$. Elemental analysis: calcd. for $C_{14}H_{10}N_2$ C, 81.53; H, 4.89; N, 13.58%, found C, 80.98; H, 4.6; N, 12.98.

Z-configuration of **(*Z*)-N-phenylbenzimidoyl cyanide** was also determined by X-ray single-crystal analysis.



2b: (*Z*)-4-fluoro-*N*-phenylbenzimidoyl cyanide: as a colorless crystal in 80% yield. M.p. = 105-108 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (q, *J* = 7.2 Hz, 2H), 7.47 (t, *J* = 7.6 Hz, 2H),

7.17-7.32 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 110.8, 116.3, 120.4, 130.6, 138.4, 164.8, 166.5. IR (neat): 2932, 2858, 1605, 1592, 1568, 1490, 1446, 1401, 1259, 1091, 1074, 1015, 721 cm-1 . LCMS m/z: 225 $[M + H]^+$. Elemental analysis: calcd. for $C_{14}H_9FN_2$ C, 74.99; H, 4.05; N, 12.49%, found C, 75.12; H, 3.9; N, 12.15.

2c: (*Z*)-4-nitro-*N*-phenylbenzimidoyl cyanide: as a colorless crystal in 60% yield. M.p. = 88-89 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (m, 4H), 7.50-7.52 (m, 2H), 7.39-7.40 (m, 1H), 7.25-7.29 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 110.8, 116.3, 120.4, 130.6, 138.4, 164.7, 166.5. IR (neat): 2960, 2850, 1605, 1592, 1568, 1490, 1446, 1401, 1259, 1091, 1074, 1015, 994, 835, 799, 721 cm^{-1} . LCMS m/z: 252 $[M + H]^+$. Elemental analysis: calcd. for $C_{14}H_9N_3O_2$ C, 66.93; H, 3.61; N, 16.73%, found C, 66.45; H, 3.95; N, 16.40.

2d: (*Z*)-2,3-dimethoxy-*N*-phenylbenzimidoyl cyanide: as a colorless crystal in 70% yield. M.p. = 85-90 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ7.09-7.48 (m, 7H), 4.1 (s, 3H), 3.90 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.17, 61.4, 111.9, 116.3, 120.2, 121.0, 124.1, 127.1, 129.3, 138.2, 148.9,149.2, 153.1. IR (neat): 2950, 2850, 1605, 1592, 1568, 1490, 1446, 1401, 1259, 1091, 1074, 1015, 994, 835, 799, 721 cm^{-1}. LCMS m/z: 267 $[M + H]^+$. Elemental analysis: calcd. for $C_{16}H_{14}N_2O_2$ C, 72.17; H, 5.30; N, 10.52%, found C, 71.10; H, 4.89; N, 10.40.

2e: (*Z*)-4-chloro-*N*-phenylbenzimidoyl cyanide: as a colorless crystal in 75% yield. M.p. = 59-61 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 – 8.05 (m, 1H), 7.51 (d, J = 8.5 Hz, 1H), 7.47 (t, J = 7.5 Hz, 1H), 7.33 (t, J = 6.9 Hz, 1H), 7.19 (d, J = 8.4 Hz, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ149.3, 139.4, 129.7, 129.5, 127.5, 121.1, 110.4. IR (neat): 2932, 2858, 1605, 1592, 1568, 1490, 1446, 1401, 1259, 1091, 1074, 1015, 994, 835, 799, 721 cm^{-1}. LCMS m/z: 241 $[M + H]^+$. Elemental analysis: calcd. for $C_{14}H_9ClN_2$ C, 69.86; H, 3.77; N, 11.64%, found C, 69.10; H, 3.3; N, 10.40.

2f: (*Z*)- 4-fluoro-N-(4-isopropylphenyl)benzimidoyl cyanide[2]: as a colorless crystal in 60% yield. M.p. = 60-65 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 – 8.00 (m, 1H), 7.32 (d, J = 12.2

Hz, 1H), 7.23 – 7.16 (m, 2H), 3.08 – 2.81 (m, 1H), 1.29 (dd, *J* = 6.9, 2.0 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 165, 148.8, 146.9, 137.1, 130.7, 127.6, 120.7, 116.5, 111.2, 33.8, 23.5. IR (neat): 29322, 2858, 1605, 1592, 1568, 1490, 1446, 1401, 1259, 1091, 1074, 1015, 994, 835, 799, 721 cm^{-1}. LCMS m/z: 267 [M + H] $^{+}$. Elemental analysis: calcd. for $C_{17}H_{15}FN_2$ C, 76.67; H, 5.68; N, 10.52%, found C, 75.90; H, 5.3; N, 10.40.

2g: (*Z*)-N-(3,5-dimethoxyphenyl)-3-fluorobenzimidoyl cyanide: as a colorless crystal in 40% yield. M.p. = 128-135 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 – 8.02 (m, 1H), 7.25 (s, 1H), 7.21 (t, *J* = 8.5 Hz, 1H), 7.11 – 7.01 (m, 1H), 6.88 (t, *J* = 8.7 Hz, 1H), 6.45 (s, 1H), 3.59 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 147.7, 130.5, 129, 120, 113.8, 110.8, 98.3, 56.1. IR (neat): 2930, 2858, 1605, 1592, 1568, 1490, 1 446, 1401, 1259, 1091, 1074, 1015, 994, 835, 799, 721 cm^{-1}. LCMS m/z: 285 [M + H]$^{+}$. Elemental analysis: calcd. for $C_{16}H_{13}FN_2O_2$ C, 67.60; H, 4.61; N, 9.85%, found C, 66.98; H, 4.41; N, 9.40.

2h: (*Z*)-3-nitro-*N*-phenylbenzimidoyl cyanide: as a colorless crystal in 70% yield. M.p. = 98-100 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (t, *J* = 2.0 Hz, 1H), 8.51 – 8.38 (m, 2H), 7.81 – 7.69 (m, 1H), 7.56 – 7.45 (m, 2H), 7.38 (t, *J* = 7.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148, 136, 135.2, 133.9, 130.3, 129.5, 128.4, 127., 122.8, 120.9, 110.5.IR (neat): 2960, 2840, 1605, 1592, 1568, 1490, 1446, 1401, 1259, 1091, 1074, 1015, 994, 835, 799, 721 cm^{-1} . LCMS m/z: 252 [M + H] $^{+}$. Elemental analysis: calcd. for $C_{14}H_9N_3O_2$ C, 66.93; H, 3.61; N, 16.73; %, found C, 66.50; H, 3.41; N, 12.03.

2i: (*Z*)-4-hydroxy-3-methoxy-N-phenylbenzimidoyl cyanide: as a colorless crystal in 55% yield. M.p. = 105-112 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.77 – 7.25 (m, 8H), 5.33 (d, *J*=8.1, 1H), 5.33 (d, *J*=8.1, 1H), 3.90 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ) 146.9, 146.6, 144.8, 129.8, 120.5, 120.2, 118.5, 115, 114.1, 109.7, 56.1. IR (neat): 3100, 2850, 1605, 1592, 1568, 1490, 1446, 1401, 1259, 1091, 1074, 1015, 994, 835, 799, 721 cm^{-1}. LCMS m/z: 253 [M + H]$^{+}$ Elemental analysis: calcd. for $C_{15}H_{12}N_2O_2$ C, 71.42; H, 4.79; N, 11.10 %, found C, 71.38; H, 4.73; N, 11.03.

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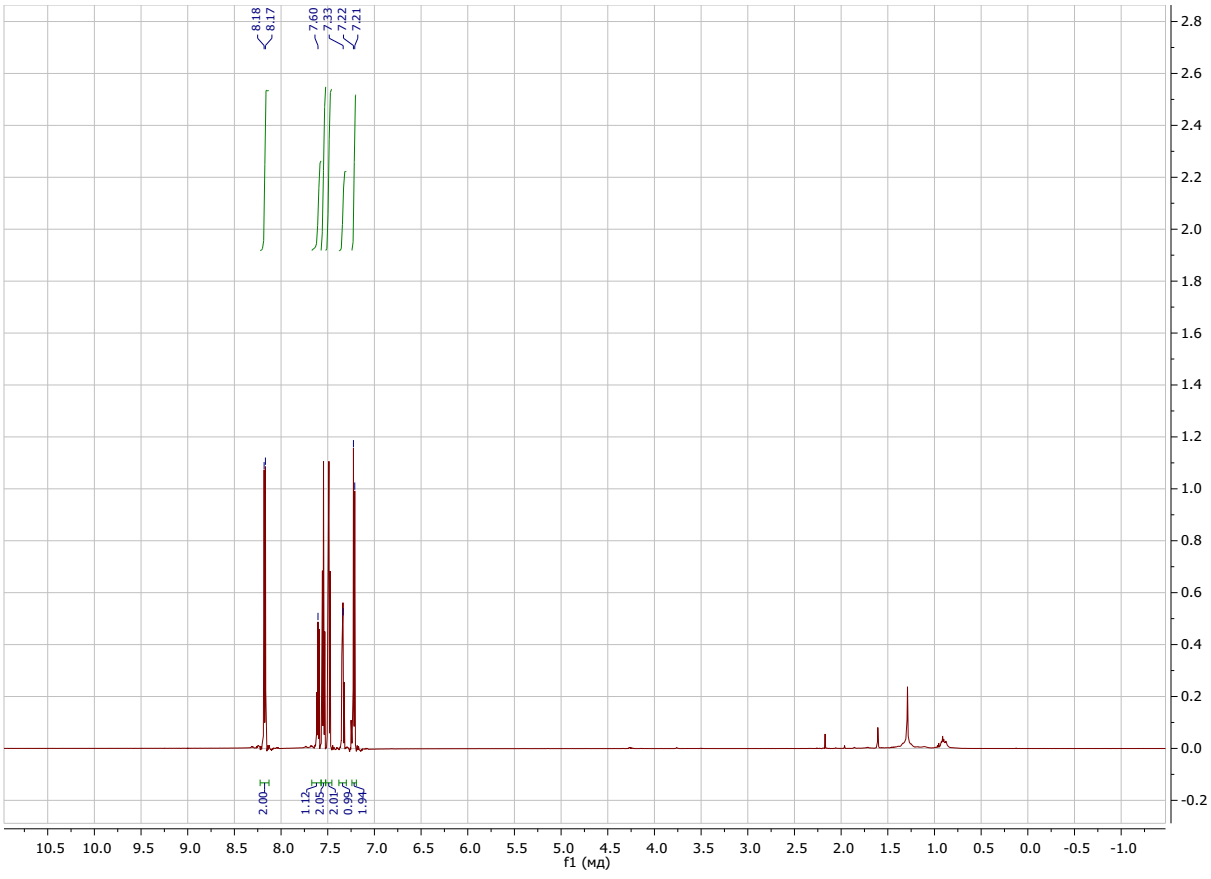
[2] Chen, T. T., Geng, H., Weng, Z. Y., & Huang, P. Q. (2022). Redox-Neutral Synthesis of α-Iminonitriles, α-Cyanoenamines, and N-Acyl Derivatives from Amides. *ACS Earth and Space Chemistry*, *7*(1), 243-251.

2j: (*Z*)-3,4-dichloro-N-phenylbenzimidoyl cyanide: as a colorless crystal in 55% yield. M.p. = 65-68 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ7.41 – 7.35 (m, 2H), 7.30 (dd, *J*=8.0, 1.6, 4H), 7.21 (t, *J*=6.9, 1H), 6.86 (dd, *J*=8.5, 1.2, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 135.4, 134.2, 132.3, 129.6, 129.2, 128.8, 128.3, 119.9, 110.5. IR (neat): 3100, 2850, 1605, 1592, 1568, 1490, 1446, 1401, 1259, 1091, 1074, 1015, 994, 835, 799, 721 cm^{-1}. LCMS m/z: 276 $[M + H]^{+}$. Elemental analysis: calcd. for $C_{14}H_8Cl_2N_2$ C, 61.12; H, 2.93; N, 10.18%, found C, 60.98; H, 2.83; N, 10.09

NMR spectrum:



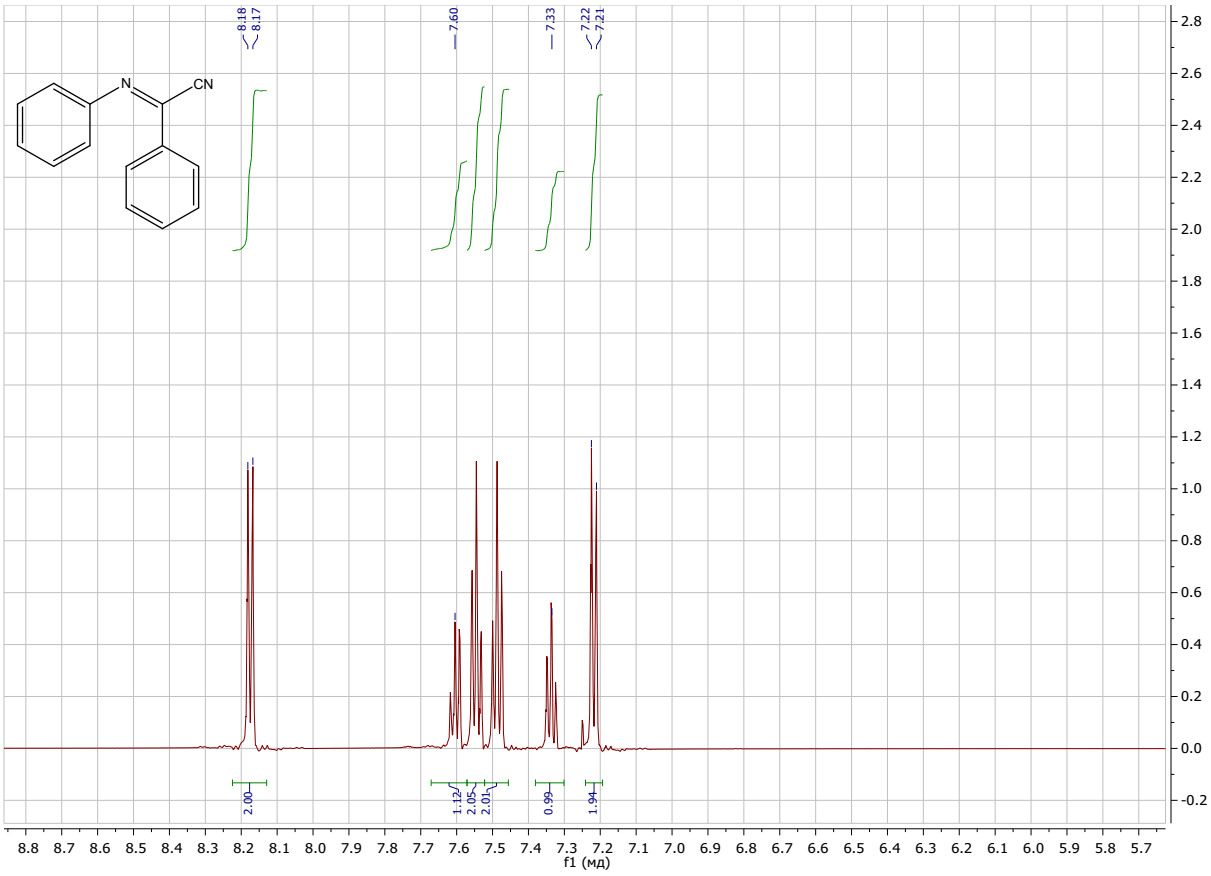


Figure S1: NMR ^{1}H of **(Z)-N-phenylbenzimidoyl cyanide 2a**

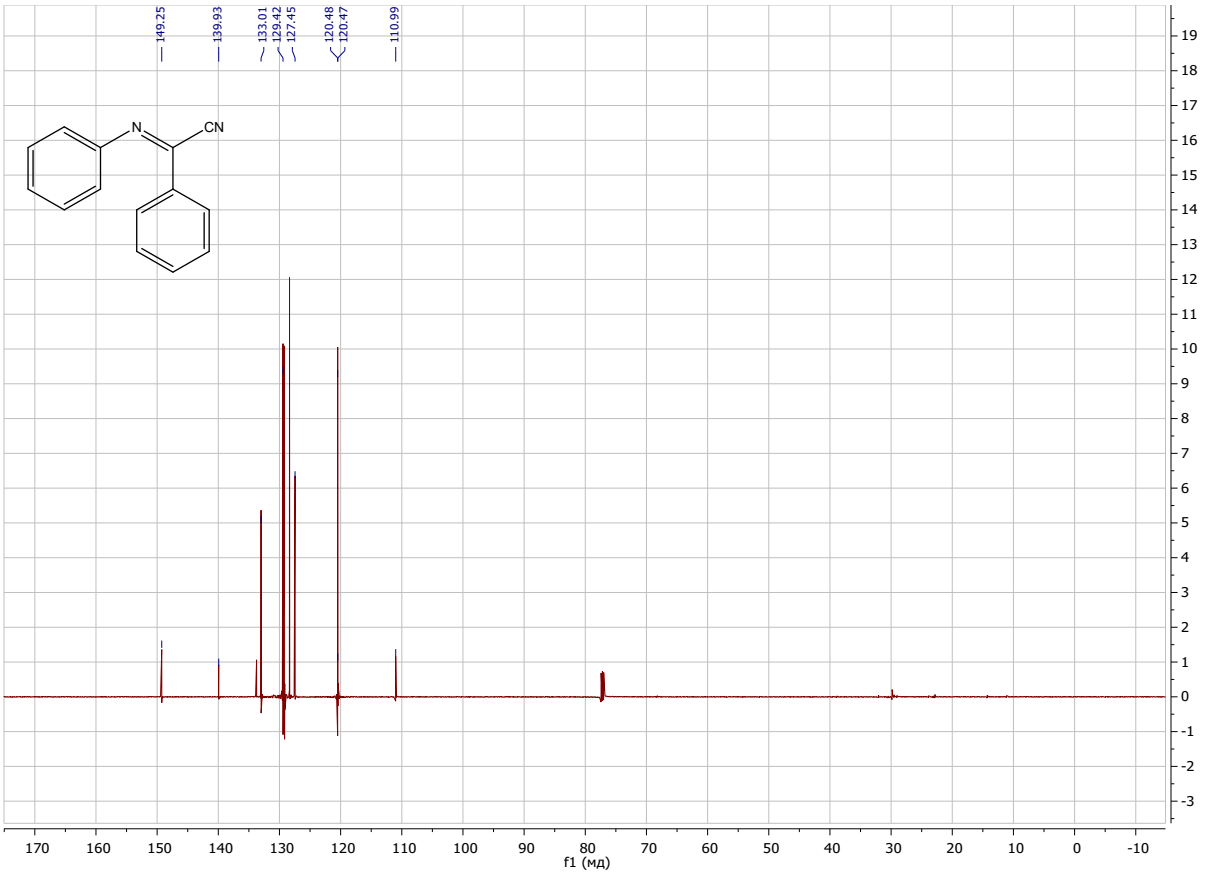


Figure S2: NMR ^{13}C of **(Z)-N-phenylbenzimidoyl cyanide 2a**

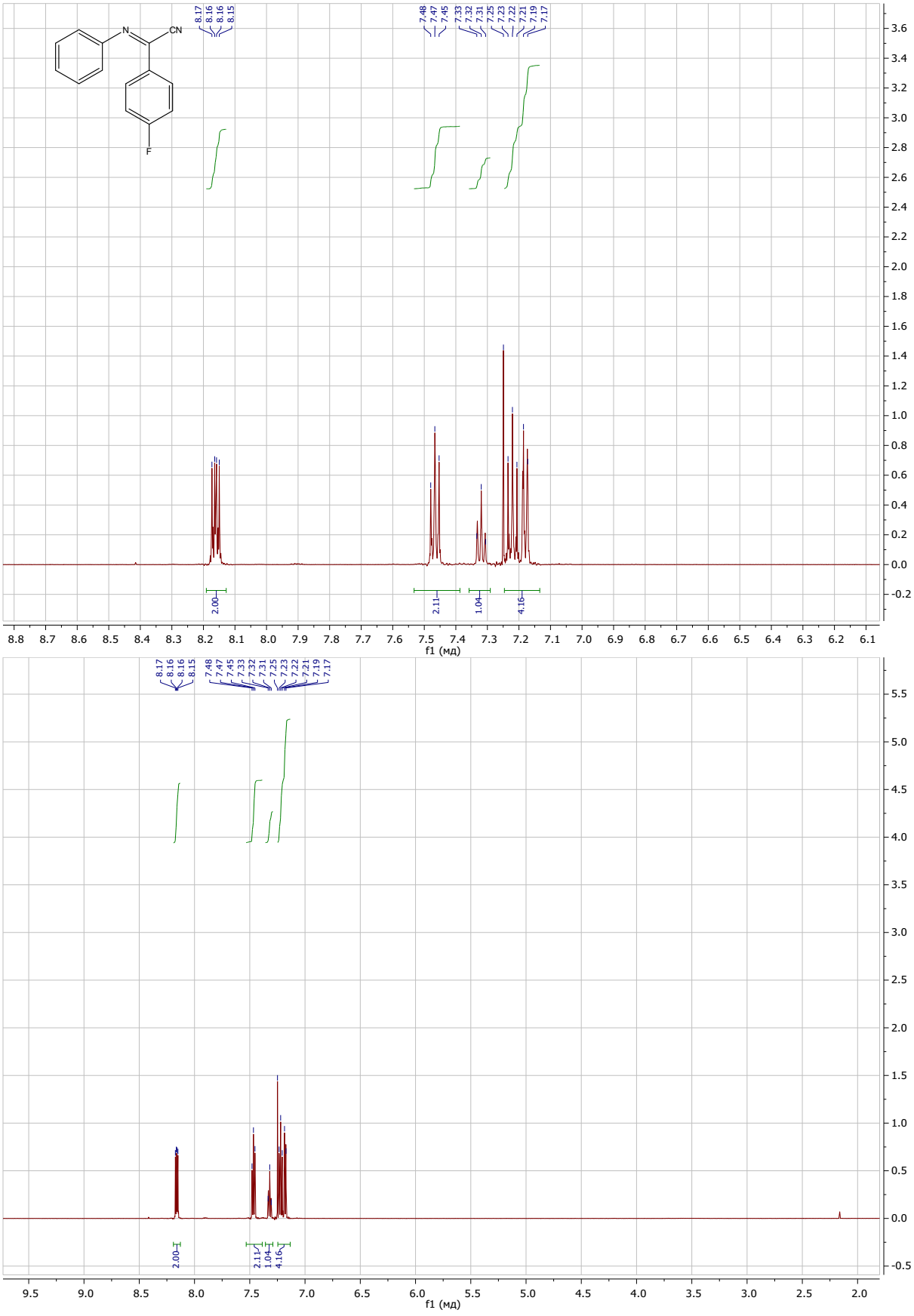


Figure S3: NMR ^{1}H of **(Z)-4-fluoro-*N*-phenylbenzimidoyl cyanide 2b**

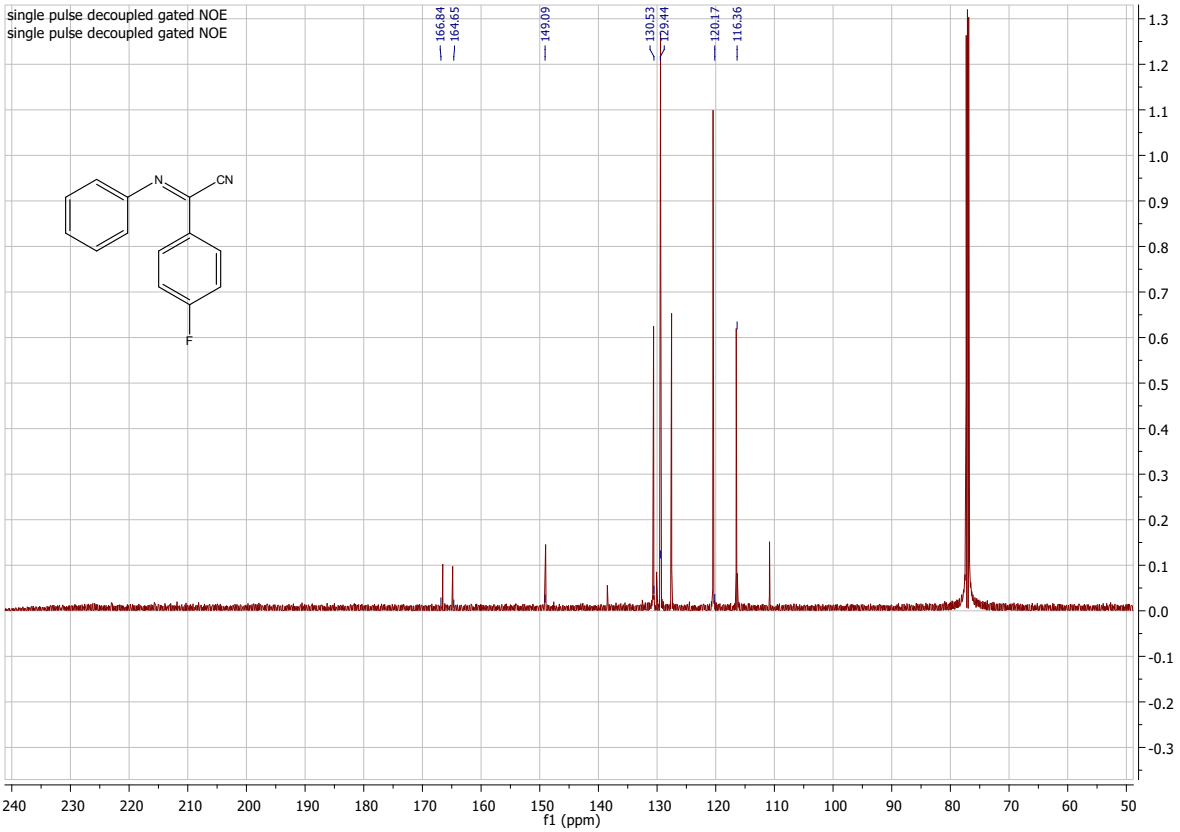


Figure S4: NMR ^{13}C of **(Z)-4-fluoro-*N*-phenylbenzimidoyl cyanide 2b**

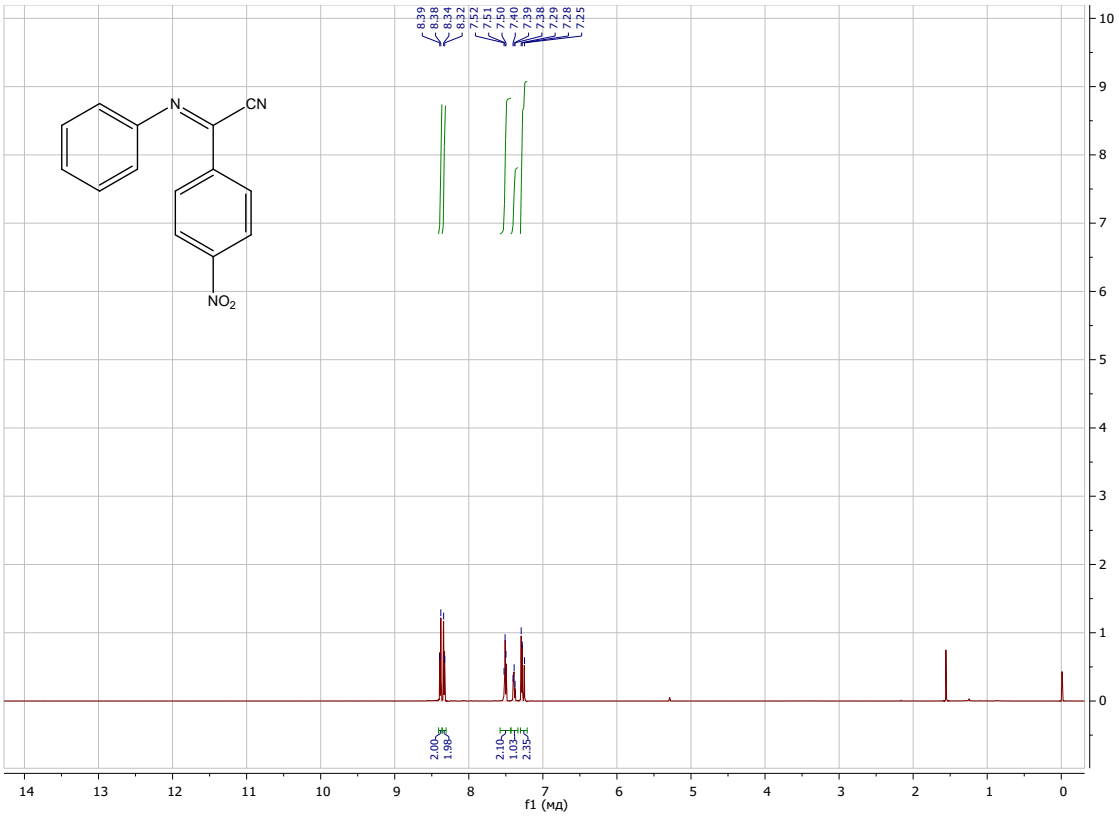


Figure S5: NMR ^{1}H of **(Z)-4-nitro-N-phenylbenzimidoyl cyanide 2c**

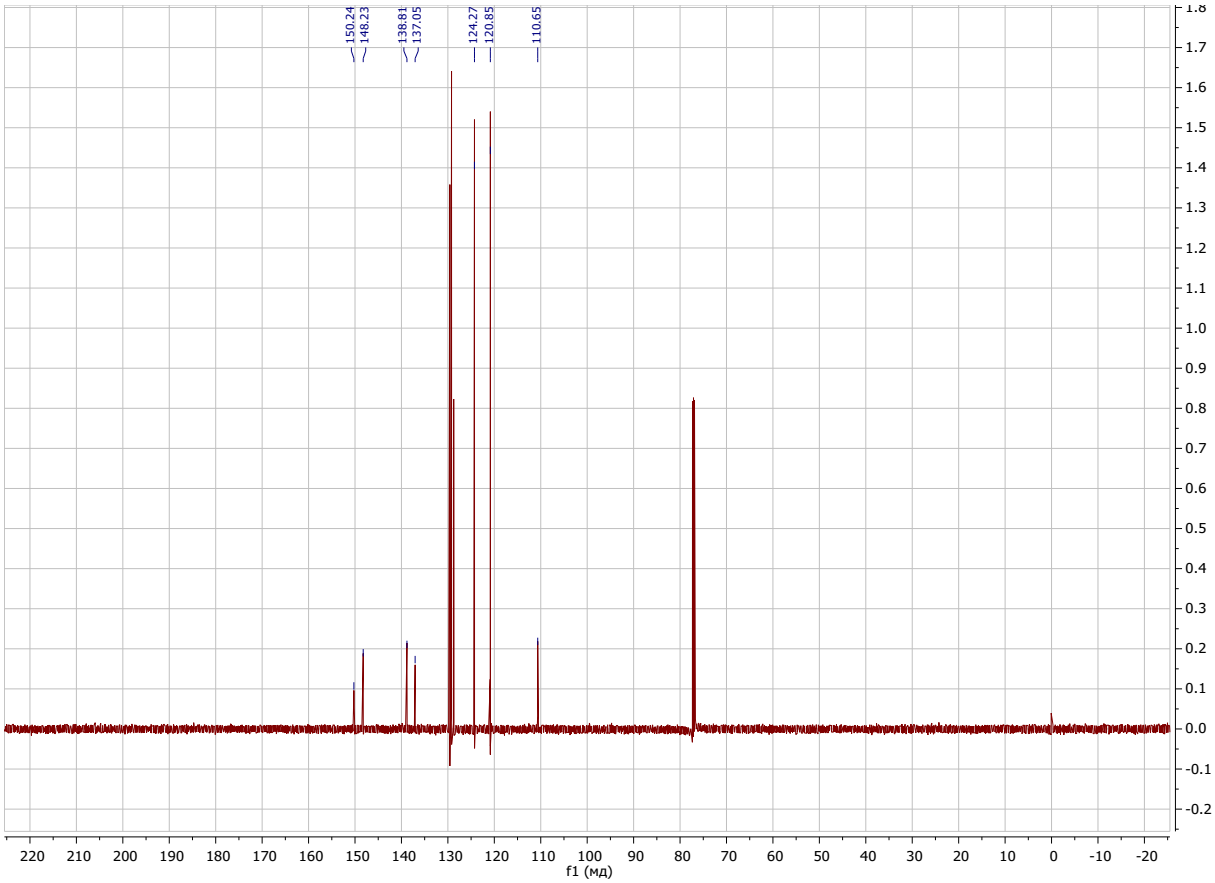


Figure S6: NMR ^{13}C of **(Z)-4-nitro-N-phenylbenzimidoyl cyanide 2c**

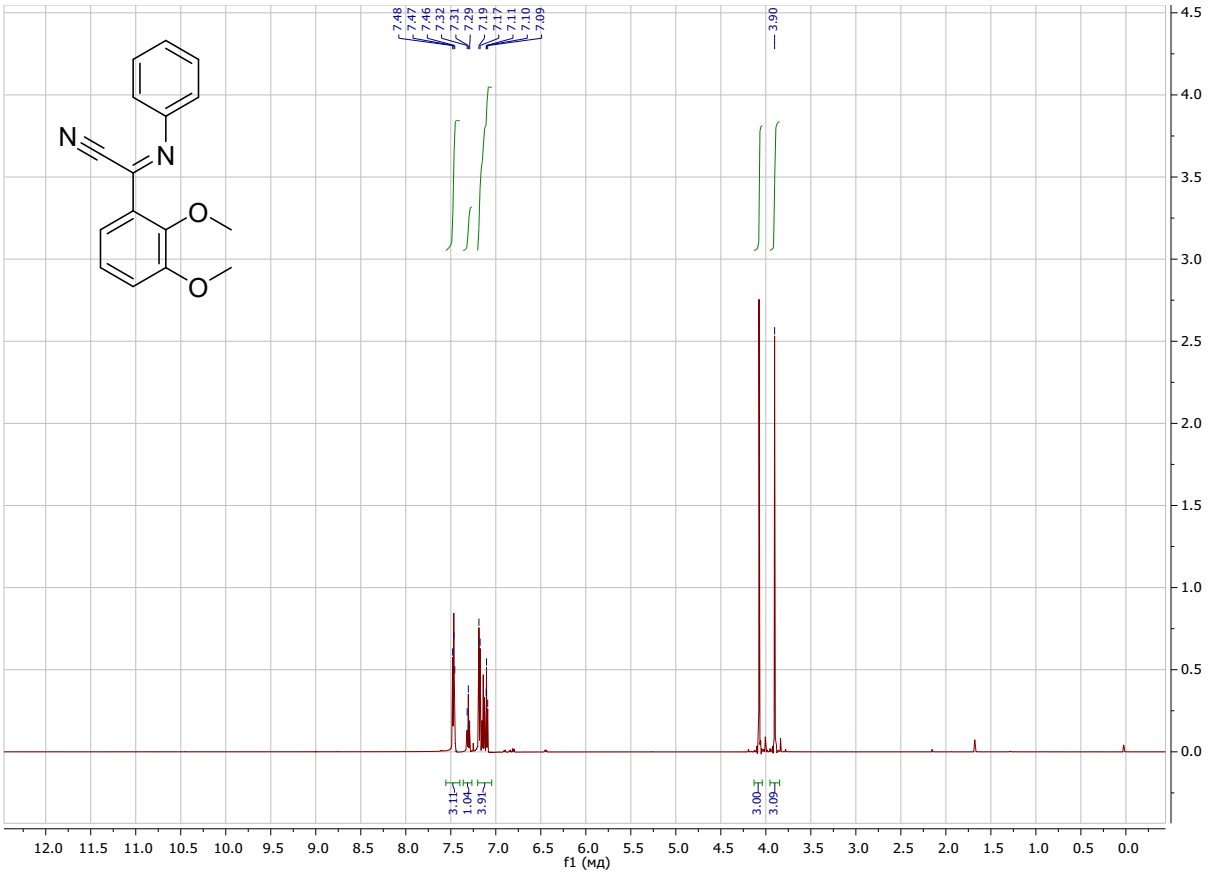


Figure S7: NMR ^{1}H of **(*Z*)-2,3-dimethoxy-*N*-phenylbenzimidoyl cyanide 2d**

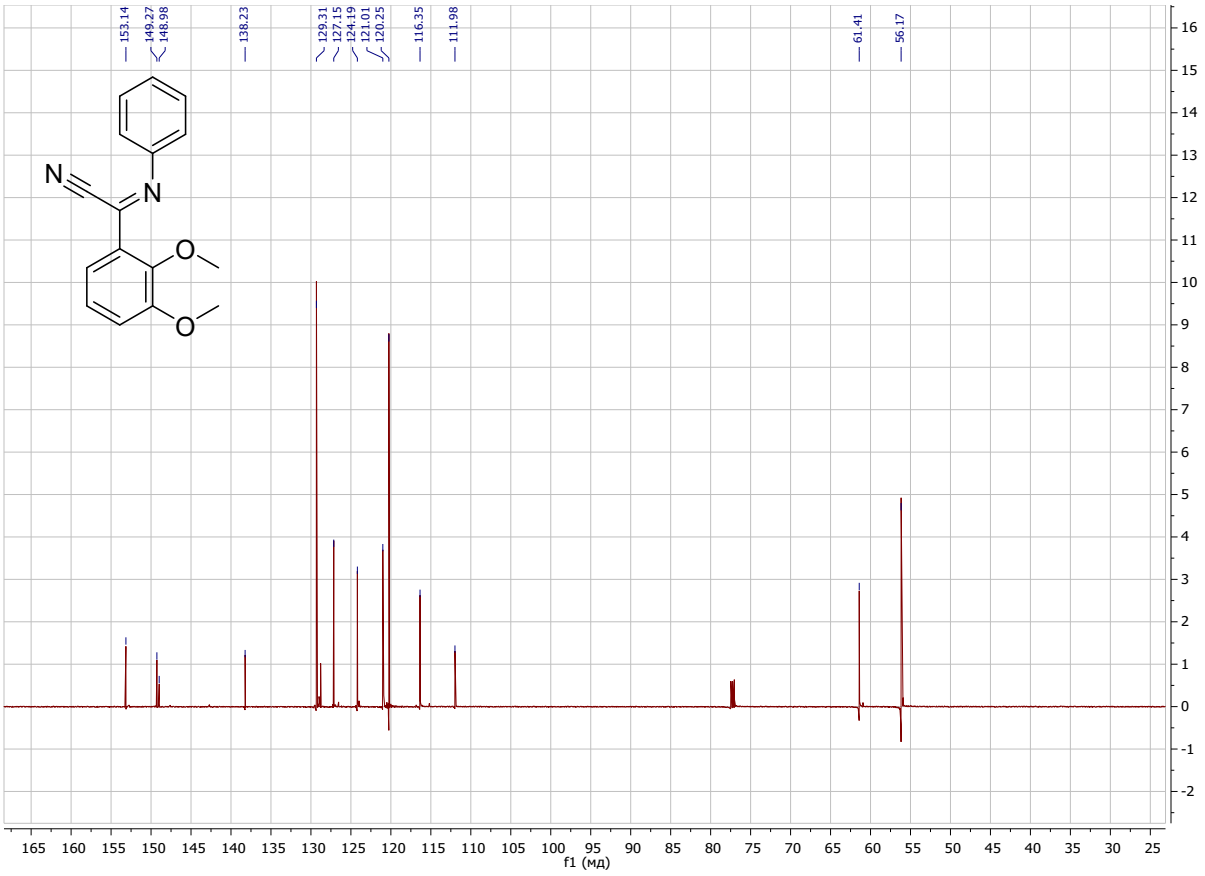
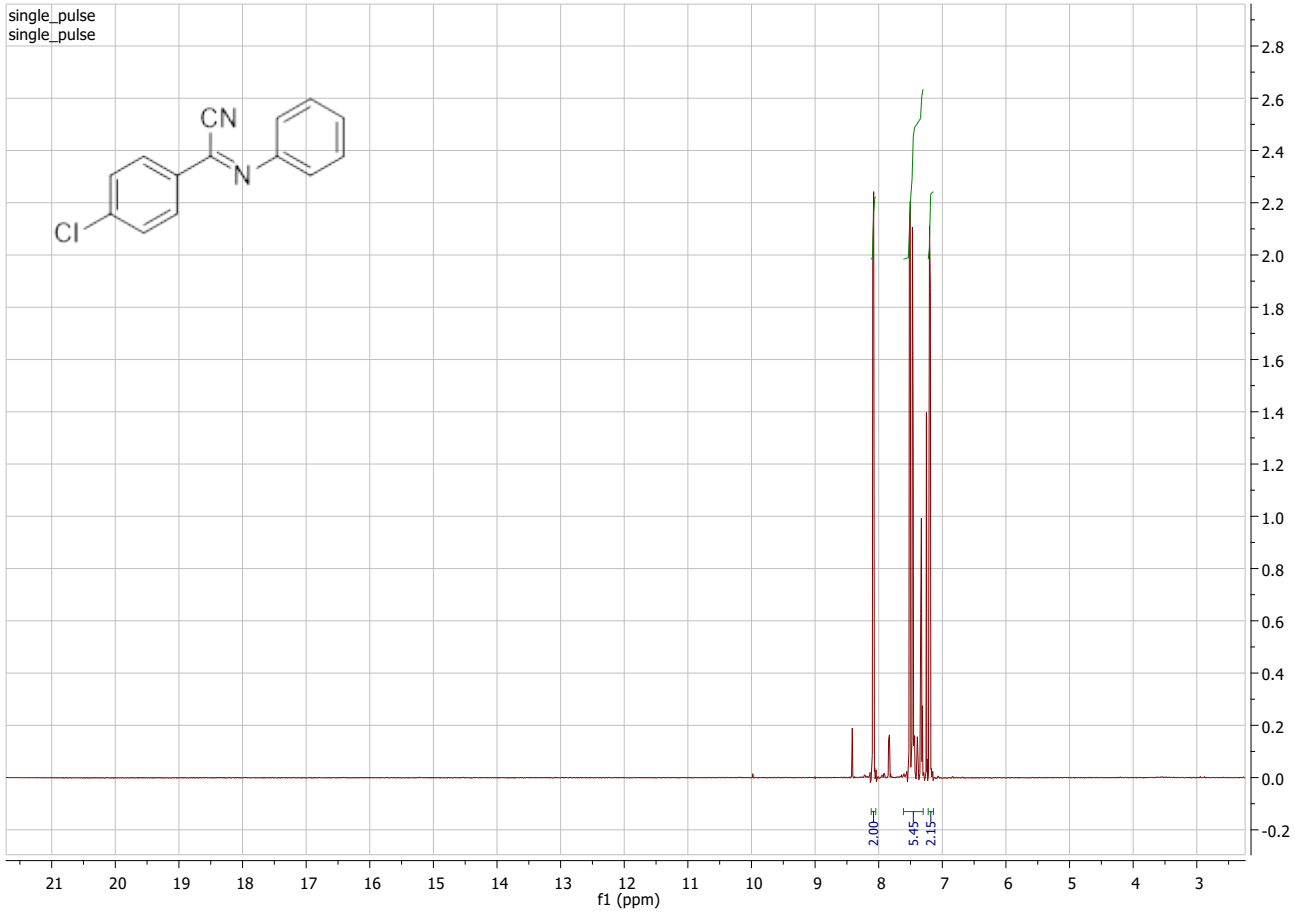


Figure S8: NMR ^{13}C of **(*Z*)-2,3-dimethoxy-*N*-phenylbenzimidoyl cyanide 2d**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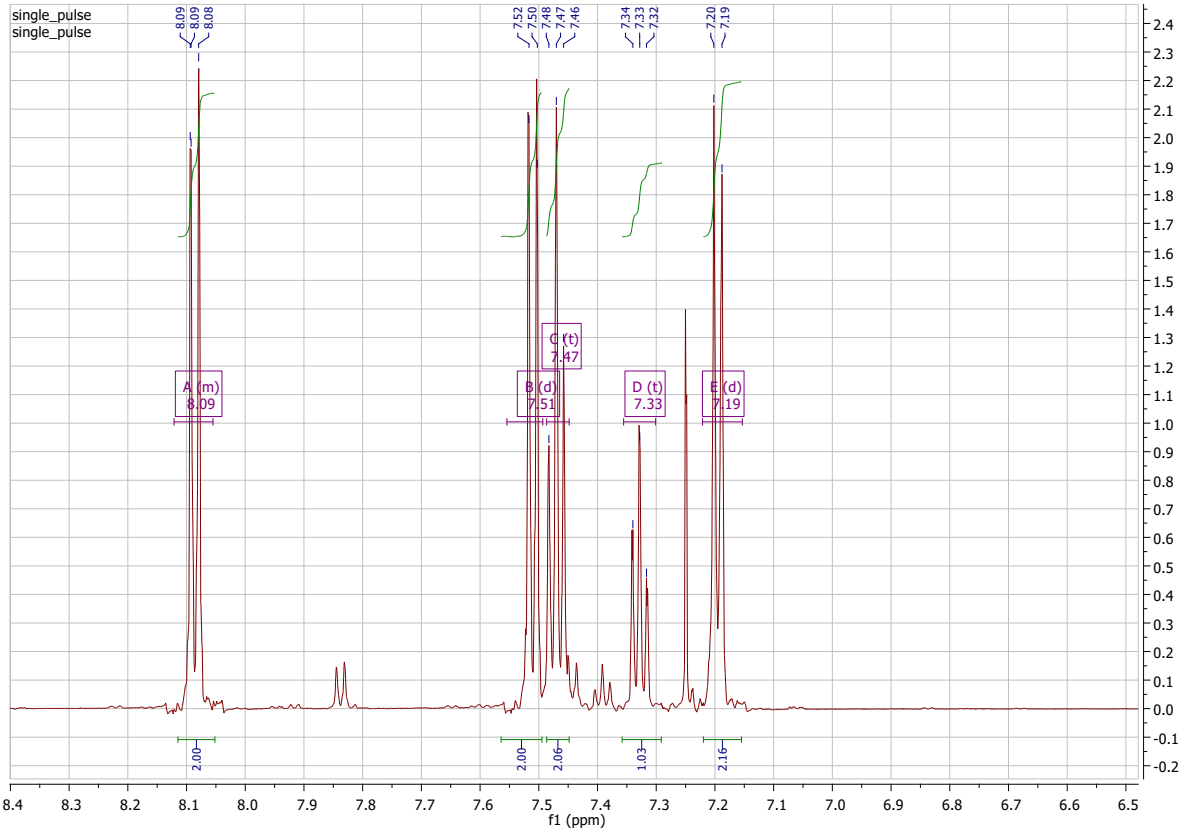
single_pulse
CN
N
Cl
2.00
5.45
2.15
f1 (ppm)


single_pulse
single_pulse
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8.09
8.08
7.52
7.50
7.48
7.47
7.46
7.34
7.33
7.32
7.20
7.19
A (m)
8.09
B (d)
7.51
C (t)
7.47
D (t)
7.33
E (d)
7.19
2.00
2.00
2.06
1.03
2.16
f1 (ppm)

Figure S9: NMR ^{1}H of **(Z)-4-chloro-N-phenylbenzimidoyl cyanide 2e**

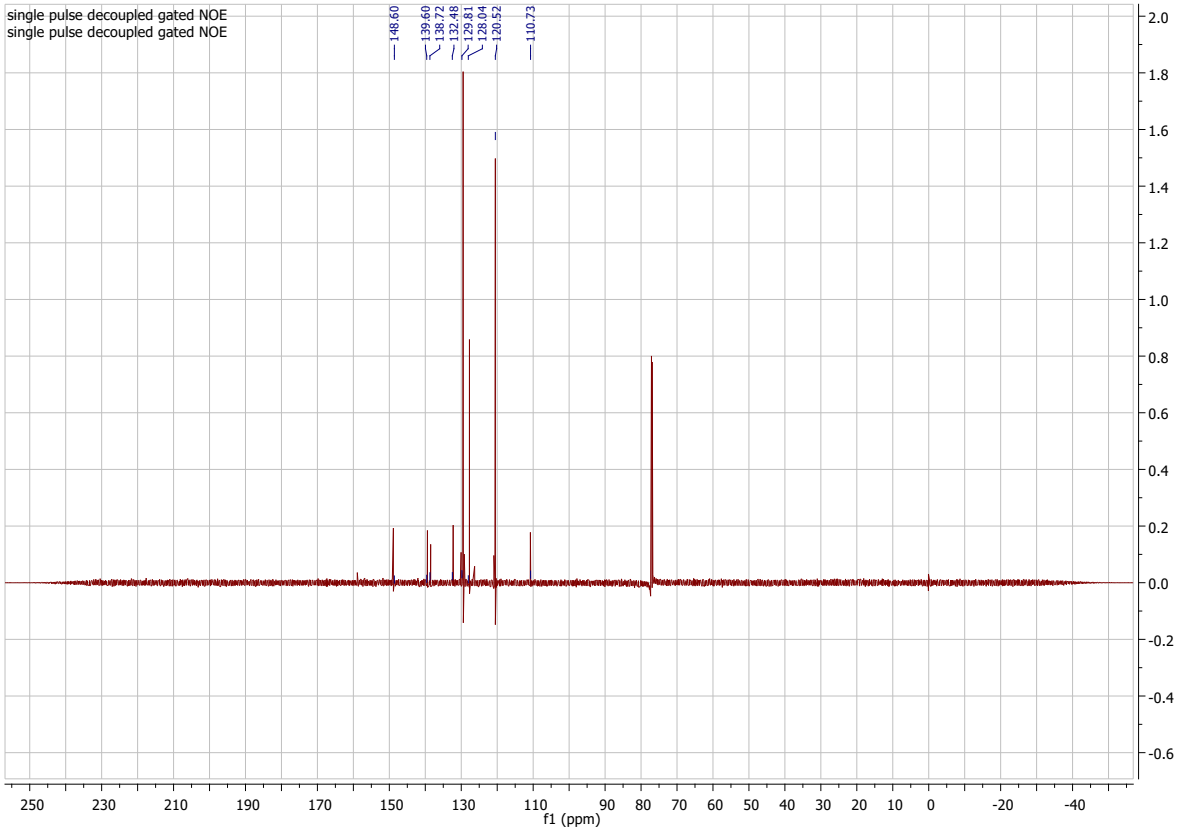

Figure S10: NMR ^{13}C of **(Z)-4-chloro-N-phenylbenzimidoyl cyanide 2e**

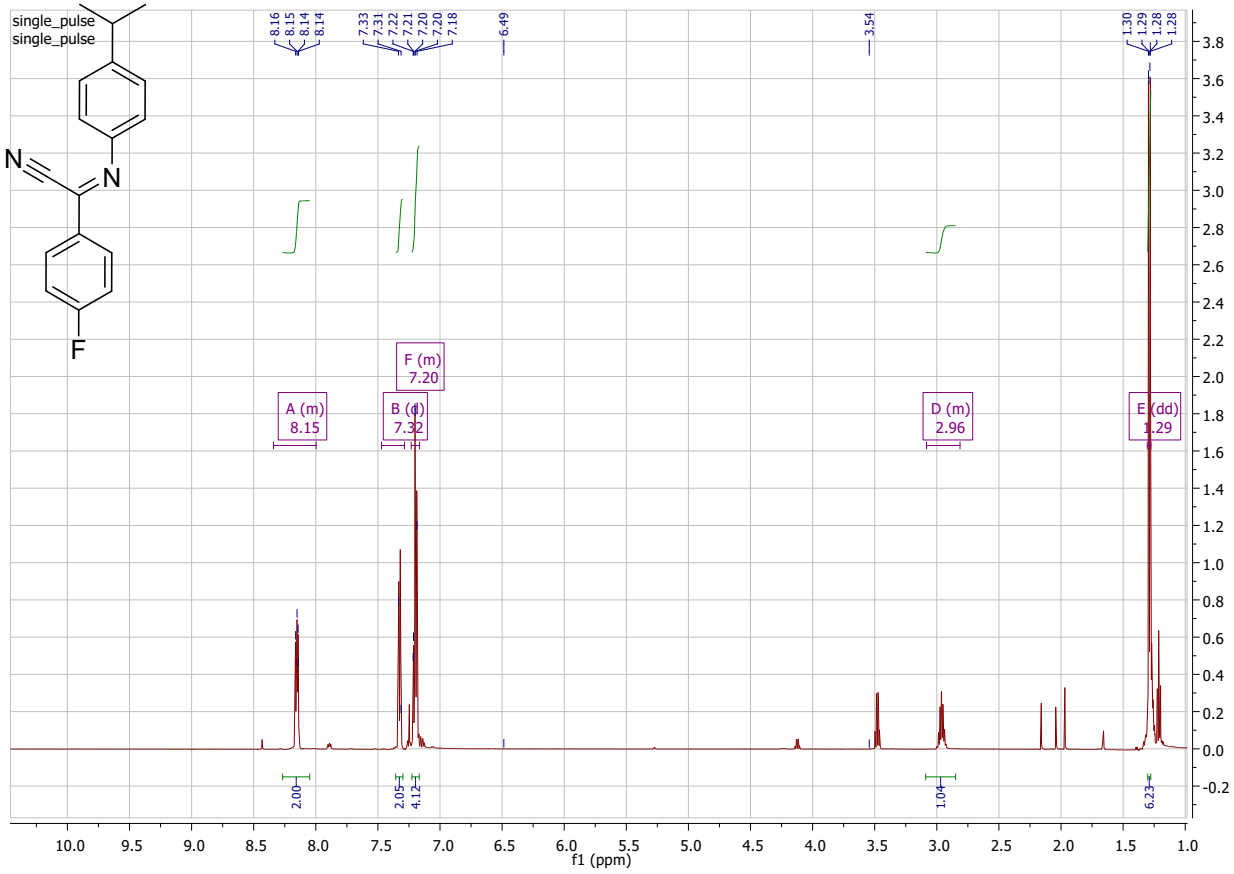

Figure S11: NMR ^{1}H of **(*Z*)-1-(4-fluorophenyl)-N-(4-isopropylphenylbenzimidoyl cyanide 2f**

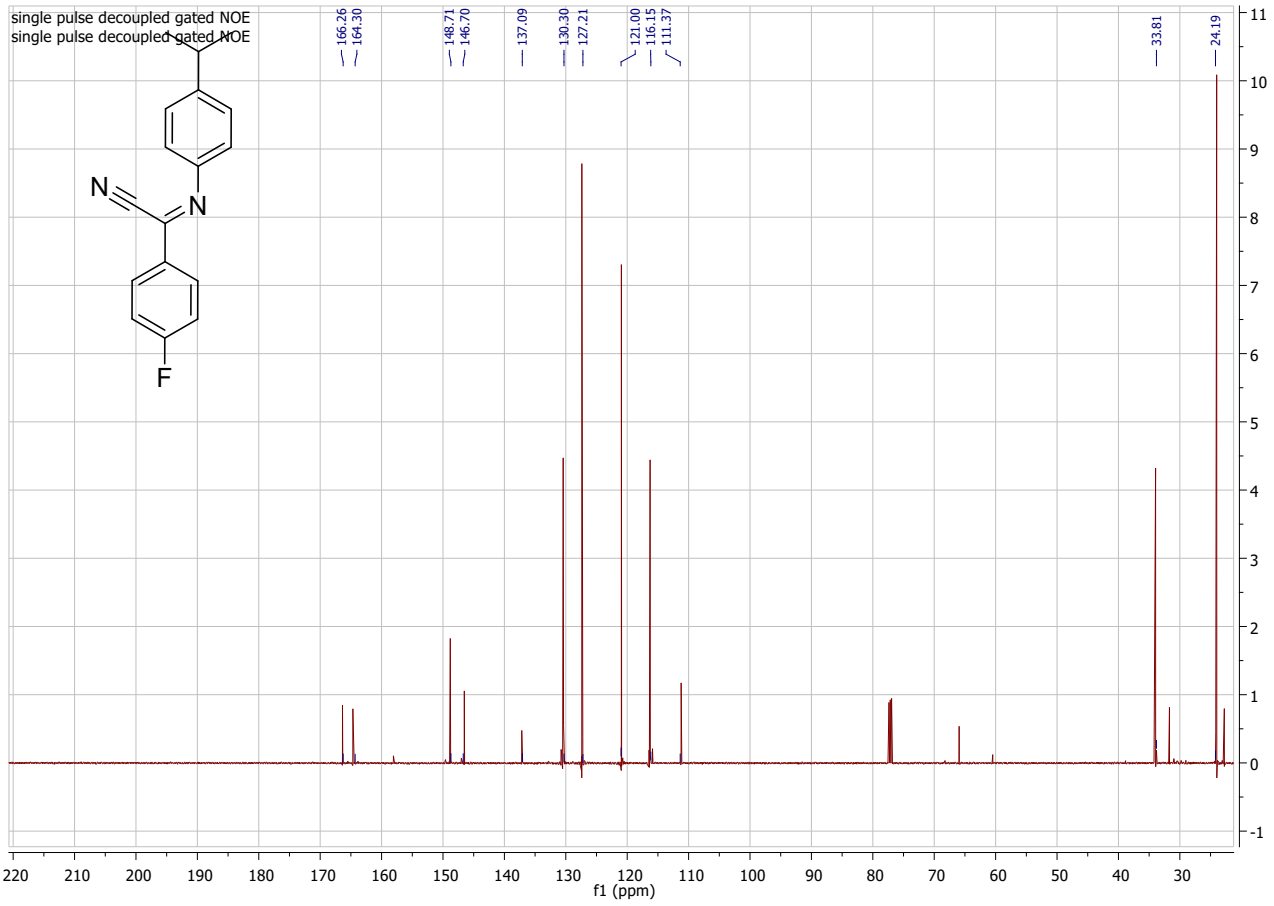

Figure S12: NMR ^{13}C of **(*Z*)-1-(4-fluorophenyl)-N-(4-isopropylphenylbenzimidoyl cyanide 2f**

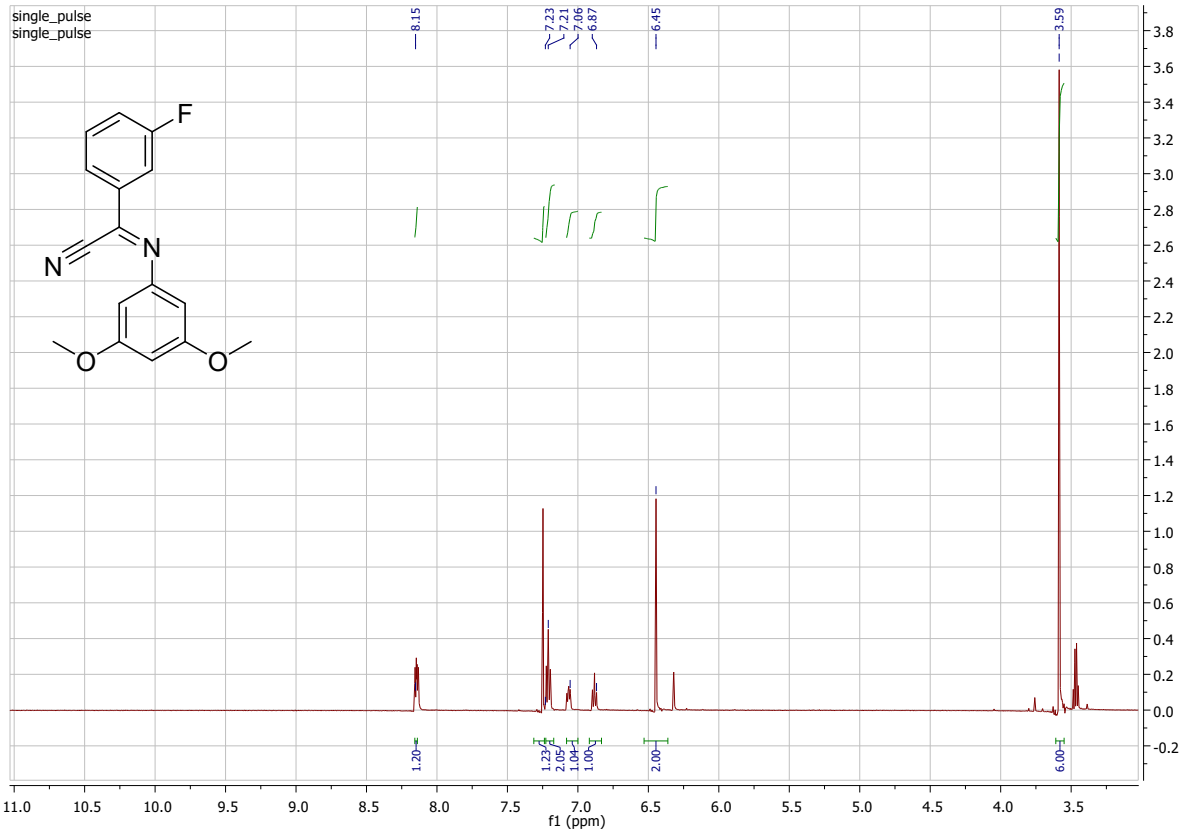

Figure S13: NMR ^{1}H of **(Z)-N-(3,5-dimethoxyphenyl)-3-fluorobenzimidoyl cyanide 2g**

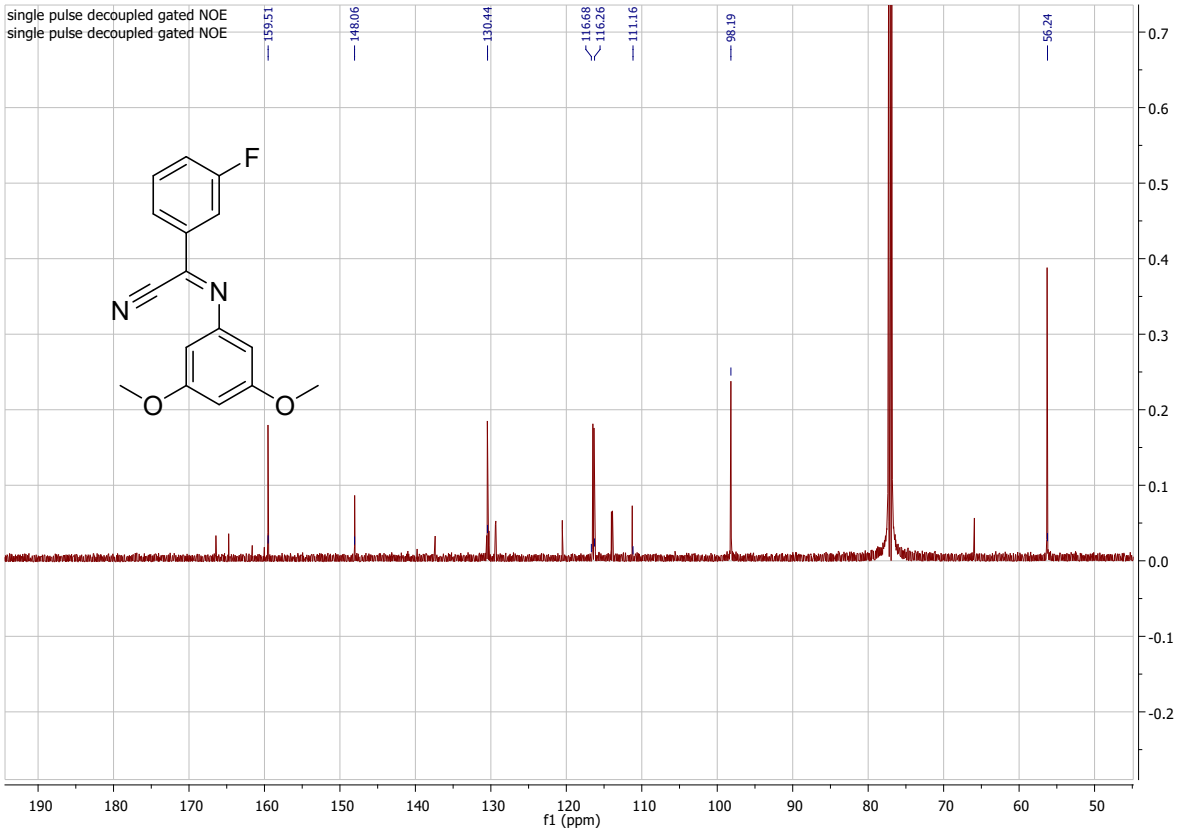

Figure S14: NMR ^{13}C of **(Z)-N-(3,5-dimethoxyphenyl)-3-fluorobenzimidoyl cyanide 2g**

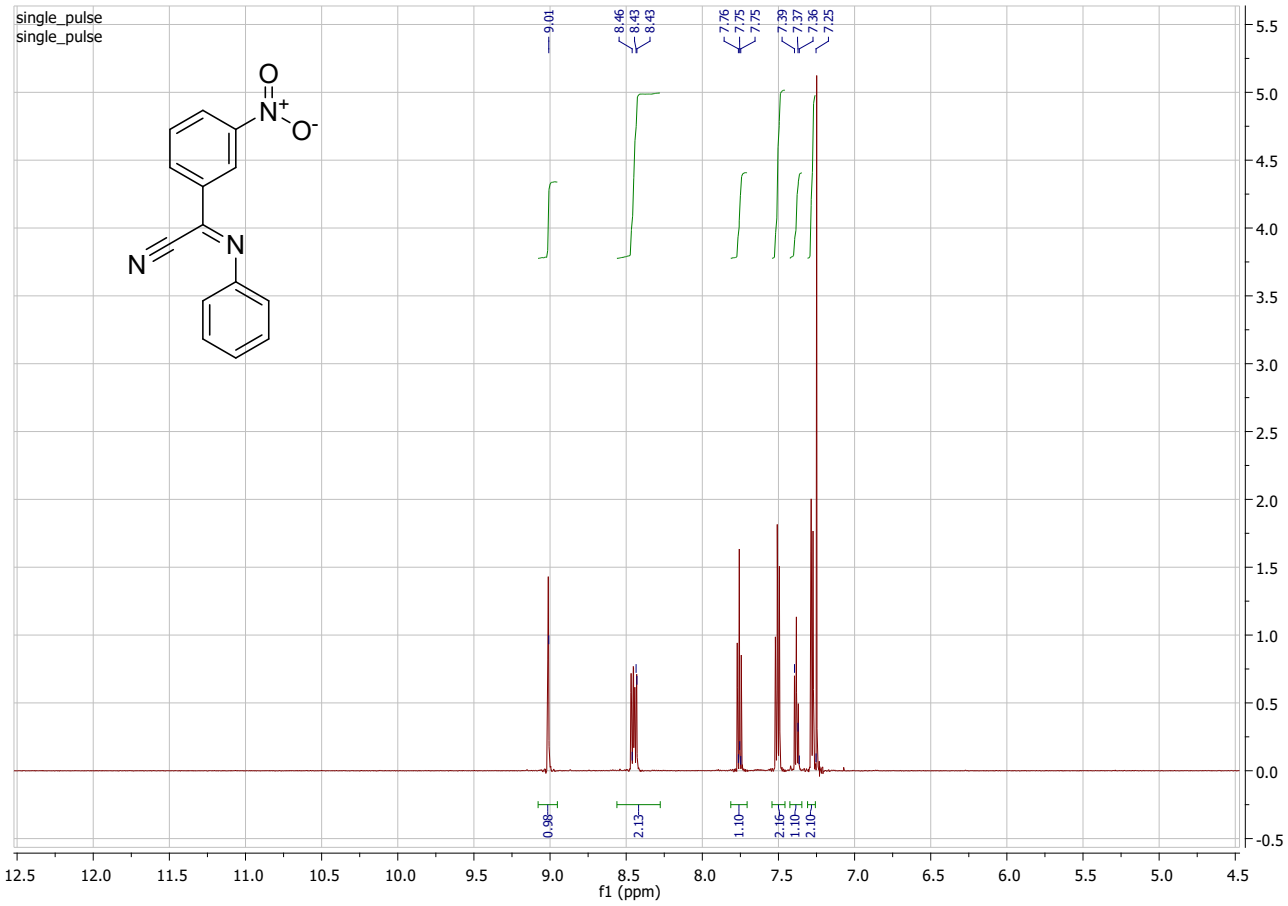

Figure S15: NMR ^{1}H of **(Z)-3-nitro-N-phenylbenzimidoyl cyanide 2h**

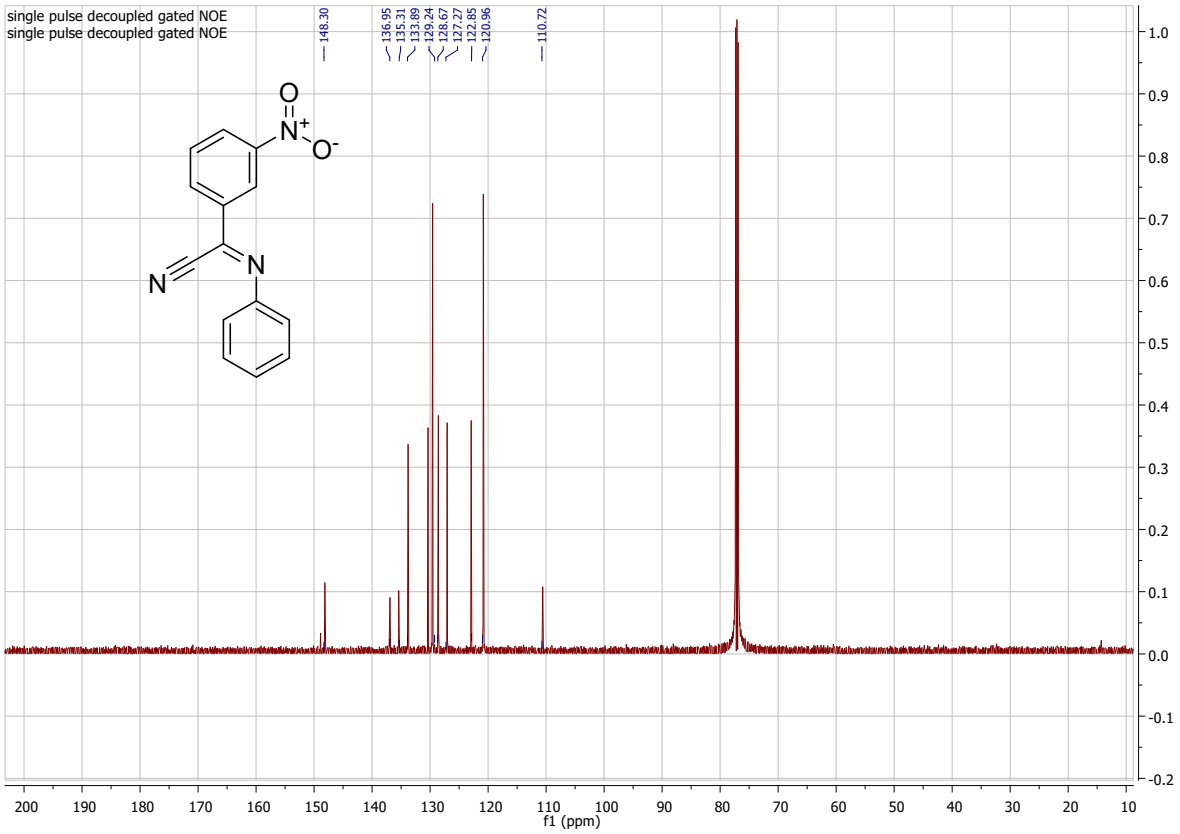

Figure S16: NMR ^{13}C of **(Z)-3-nitro-N-phenylbenzimidoyl cyanide 2h**

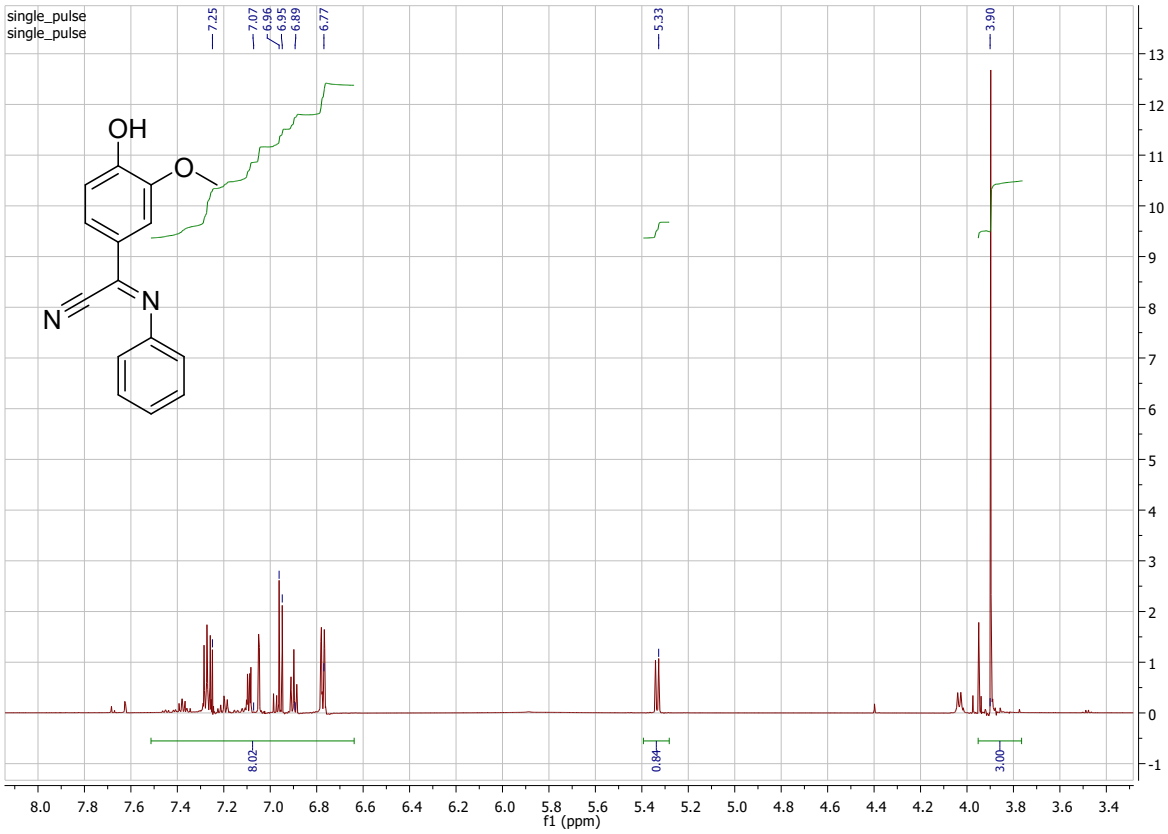

Figure S17: NMR [1]H of **(Z)-4-hydroxy-3-methoxy-N-phenylbenzimidoyl cyanide 2i**

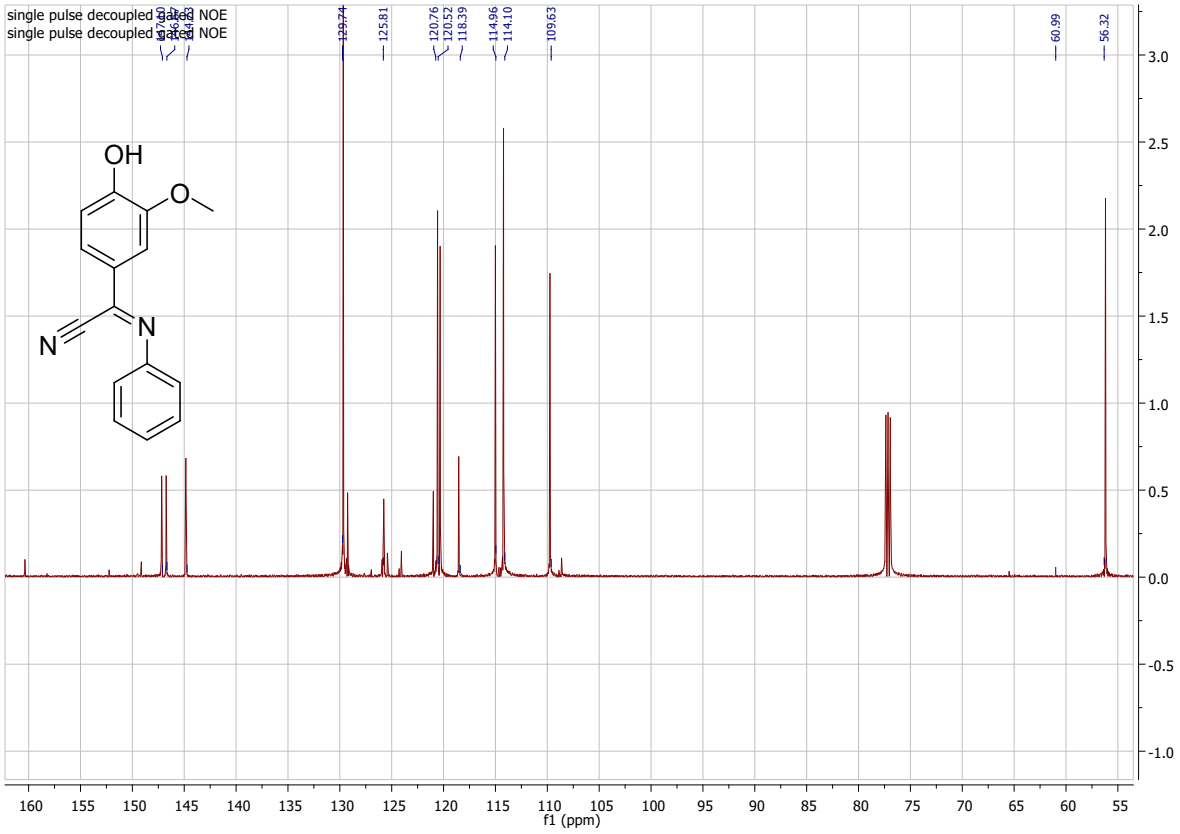

Figure S18: NMR ^{13}C of **(Z)-4-hydroxy-3-methoxy-N-phenylbenzimidoyl cyanide 2i**

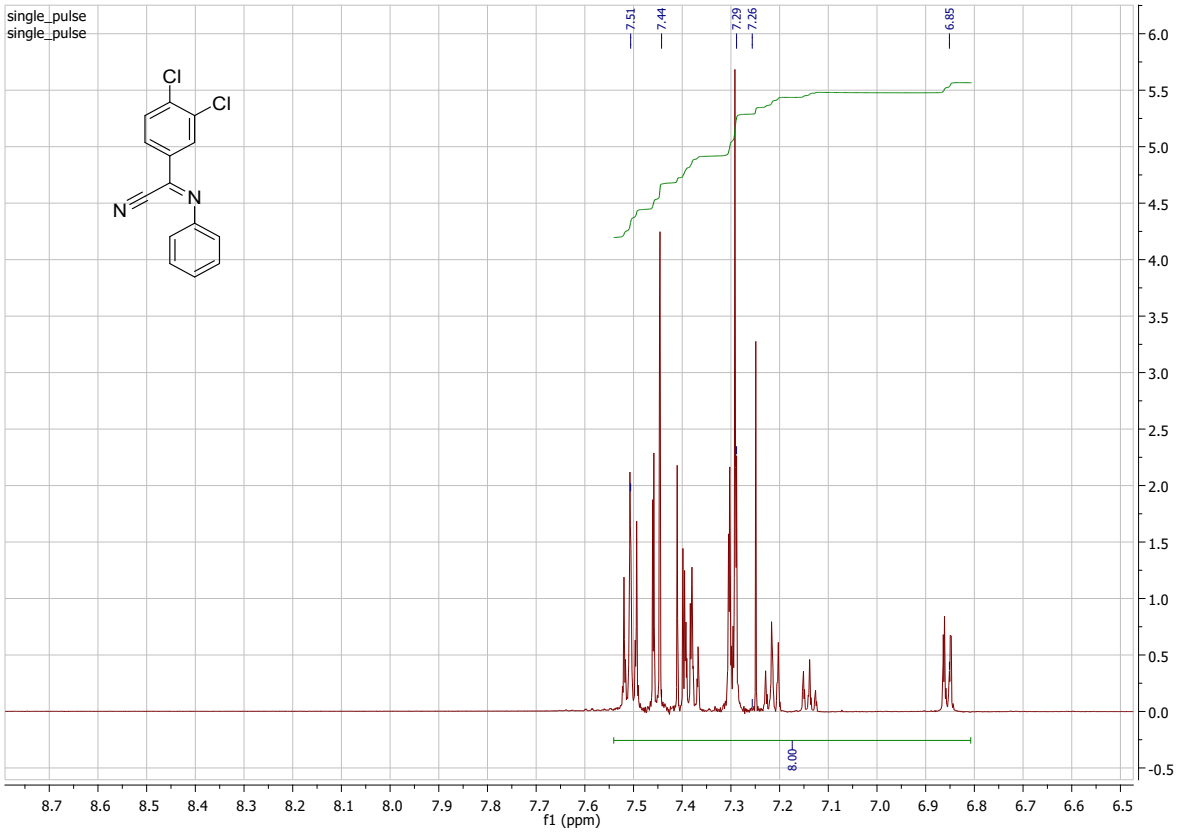

Figure S19: NMR ^{1}H of **(Z)-3,4-dichloro-N-phenylbenzimidoyl cyanide**

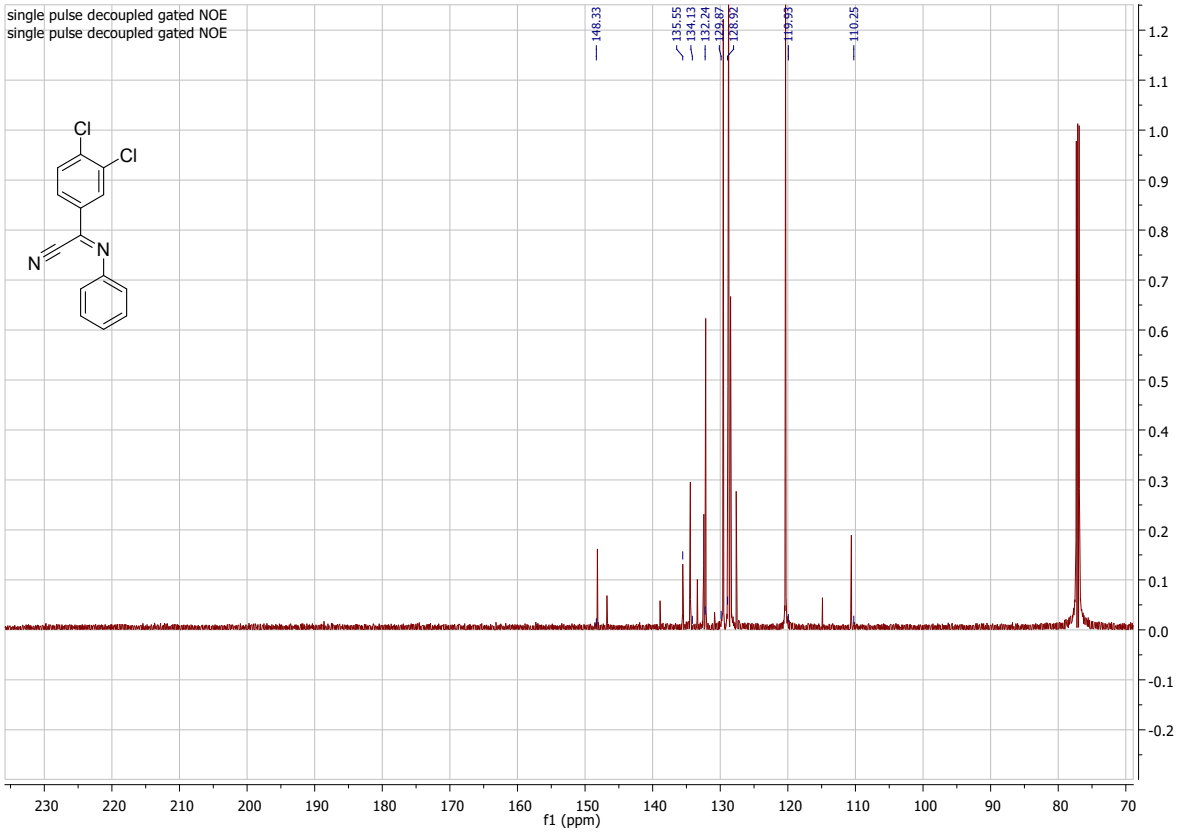

Figure S20: NMR ^{13}C of **(Z)-3,4-dichloro-N-phenylbenzimidoyl cyanide**

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) ne-1

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: ne-1

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Hall group	-P 2ac 2ab	-P 2ac 2ab
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h,k,lmax	15,9,31	15,9,31
Nref	2384	2379
Tmin,Tmax	0.981,0.985	0.919,1.000
Tmin'	0.981	

Correction method= # Reported T Limits: Tmin=0.919 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.998 Theta(max)= 27.099

R(reflections)= 0.0442(2028) wR2(reflections)= 0.1242(2379)

S = 1.078 Npar= 145

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

PLAT906_ALERT_3_C	Large K Value in the Analysis of Variance	2.367	Check
PLAT911_ALERT_3_C	Missing FCF Refl Between Thmin & STh/L= 0.600	4	Report

Alert level G

PLAT230_ALERT_2_G	Hirshfeld Test Diff for C7 --C8 .	5.0	s.u.
PLAT910_ALERT_3_G	Missing # of FCF Reflection(s) Below Theta(Min).	1	Note
PLAT913_ALERT_3_G	Missing # of Very Strong Reflections in FCF	3	Note
PLAT978_ALERT_2_G	Number C-C Bonds with Positive Residual Density.	7	Info

0 ALERT level A = Most likely a serious problem - resolve or explain
0 ALERT level B = A potentially serious problem, consider carefully
2 ALERT level C = Check. Ensure it is not caused by an omission or oversight
4 ALERT level G = General information/check it is not something unexpected

0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
2 ALERT type 2 Indicator that the structure model may be wrong or deficient
4 ALERT type 3 Indicator that the structure quality may be low
0 ALERT type 4 Improvement, methodology, query or suggestion
0 ALERT type 5 Informative message, check

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

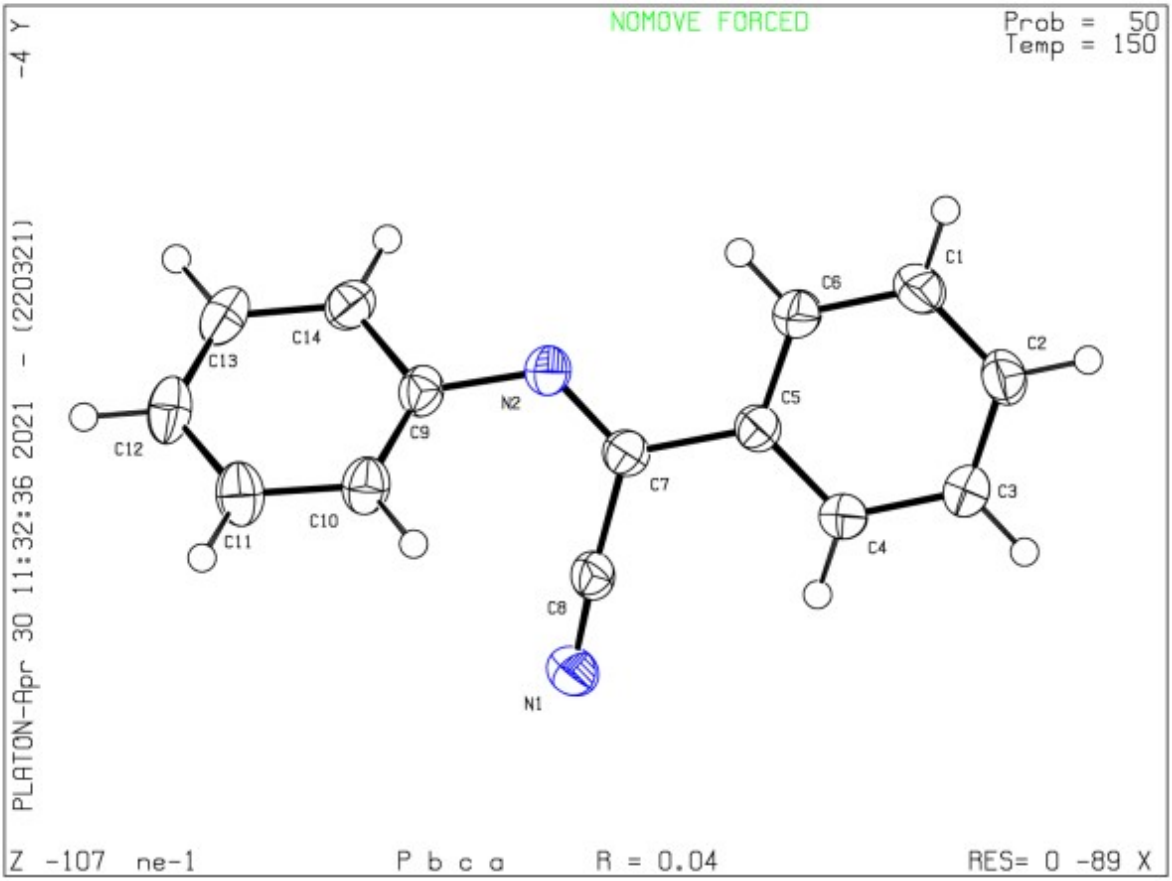
A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 22/03/2021; check.def file version of 19/03/2021

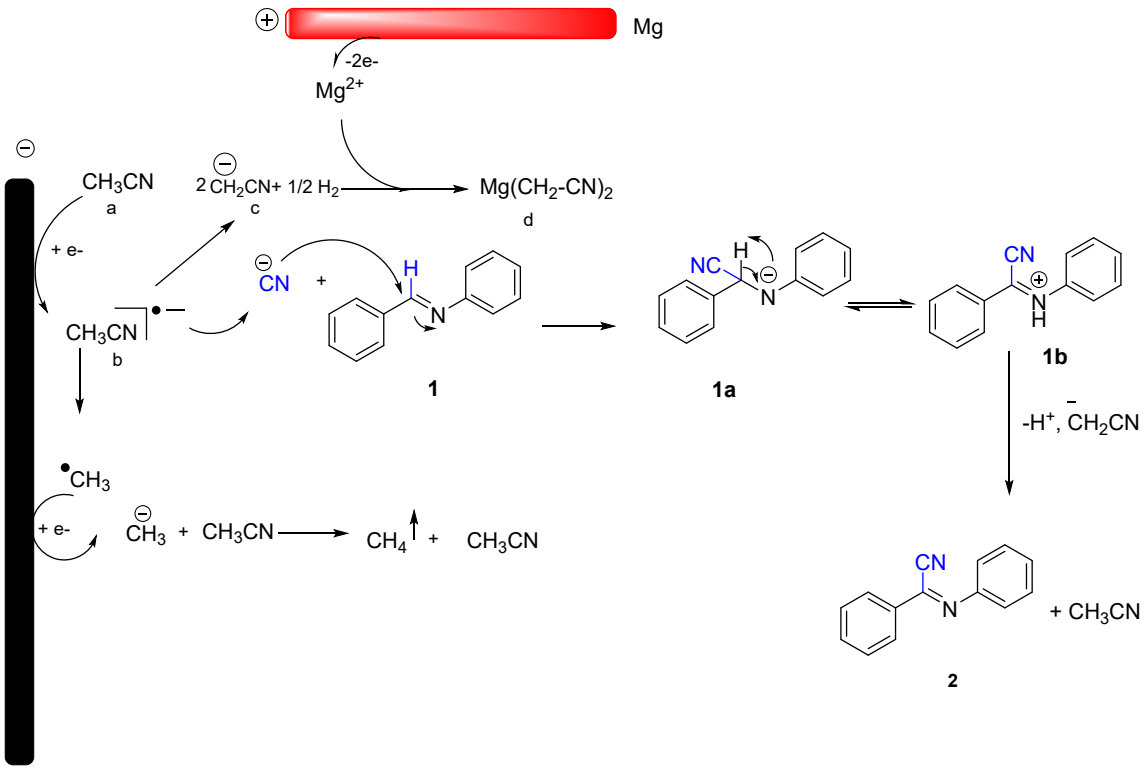
Datablock ne-1 - ellipsoid plot



Reaction Mechanism:

A possible mechanism for the electrochemical synthesis of **2** is described in the Scheme **S1**. The reaction begins at the cathode with the reduction of acetonitrile which produced a radical-anion **b** (Scheme **S1**). This anion releases cyanide, that reacts with the imine derivatives **1** to form the intermediate **1a** and a methyl radical, which is transformed into a methane molecule (detected by GC chromatography) through further hydrogen abstraction. The intermediate **1a** is than tautomerized to give the intermediate **1b**, which after deprotonation by the cyanomethyl anion yields the final product **2**.

For further clarification of the mechanism, acetonitrile was first reduced in the cell. The starting substrate was then introduced when the current was switched off, meaning that the second part of the synthesis involves a simple chemical reaction rather than an electrochemical process,



Scheme S1. A plausible mechanism for the electrosynthesis of phenylbenzimidoyl cyanide derivatives.