Electronic supplementary materials *Mendeleev Commun.*, 2020, **30**, 372-373

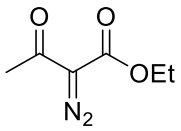
Taking diazo transfer to water: α-diazo carbonyl compounds from *in situ* generated mesyl azide

Robert M. Shevalev, Petr A. Zhmurov, Dmitry V. Dar'in and Mikhail Krasavin

General Information. Substrates for diazo transfer reactions were purchased from commercial sources and used as received or were synthesized according to known procedures. NMR spectra were recorded with a 400 MHz spectrometer (400.13 MHz for 1H) in $CDCl_3$ and were referenced to residual solvent proton signals (δ_H = 7.26). All chemical shifts are reported in parts per million (ppm). Abbreviations used in the description of resonances are: s (singlet), d (doublet), t (triplet), q (quartet), br (broad), m (multiplet). Coupling constants (J) are quoted to the nearest 0.1 Hz. Flash column chromatography was carried out on silica gel grade 60 (0.040−0.063 mm) 230−400 mesh. All α-diazo carbonyl compounds obtained in this work have been previously reported in the literature [S1-S3].

Preparation of diazo carbonyl compounds. ***Method A.*** A solution of sodium azide (2.4 mmol, 156 mg) in water (4 ml) was added to methanesulfonyl chloride (2.2 mmol, 0.177 ml), and the resulting heterogeneous mixture was intensively shaken in a 15 ml conical-bottom centrifuge tube for 10 min. The substrate for diazo transfer (2.0 mmol) and potassium carbonate (166 mg, 1.2 mmol) were subsequently added, acetonitrile (1 ml) was added additionally if indicated. The resulting mixture was intensively shaken for 30-60 minutes (as indicated). Upon completion of the reaction, another portion of potassium carbonate (276 mg, 2 mmol) was added, and the mixture was continued being shaken for additional 3 hours. The product was extracted with dichloromethane (2×8 ml), the combined organic extracts were washed with water (10 ml), dried over sodium sulfate, filtered and evaporated to dryness to afford the target α-diazo carbonyl compound. The purity of this material was judged to be above 95% by ^{1}H NMR.
Method B. A larger amount of MsCl (2.5 mmol, 0.194 ml) and sodium azide (3 mmol, 195 mg) were used for preparation of the compounds **2f-h.**

Ethyl 2-diazo-3-oxobutanoate (2a)

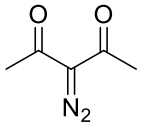


The title compound was synthesized from ethyl acetoacetate according to Method A. Reaction time – 0.5 hour. Yield 193 mg (77%). Transparent colorless liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.28 (q, J = 7.1 Hz, 2H), 2.46 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H) ppm.

^{1}H NMR spectrum is in accordance with literature data [S1].

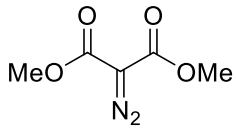
3-Diazopentane-2,4-dione (2b).



The title compound was synthesized from acetylacetone according to Method A. Reaction time – 0.5 hour. Yield 193 mg (77%). Transparent colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.39 (s, 6H, 2 CH_3).

^{1}H NMR spectrum is in accordance with literature data [S1].

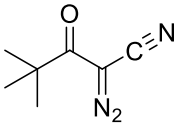
Dimethyl 2-diazomalonate (2c). The title compound was synthesized from dimethyl malonate according to Method A. Reaction time – 1 hour. Yield 170 mg (54%). Transparent colorless liquid.



^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.82 (s, 6H, 2 CH_3) ppm.

^{1}H NMR spectrum is in accordance with literature data [S1]

2-Diazo-4,4-dimethyl-3-oxopentanenitrile (2d).

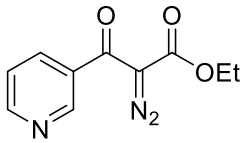


The title compound was synthesized from 4,4-dimethyl-3-oxopentanenitrile according to Method A. Reaction time – 0.75 hour. Yield 122 mg (41%). Orange viscous liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.31 (s, 9H, 3 CH_3) ppm.

^{1}H NMR spectrum is in accordance with literature data [S1].

Ethyl 2-diazo-3-oxo-3-(pyridin-3-yl)propanoate (2e).

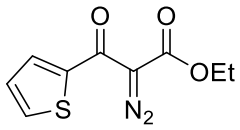


The title compound was synthesized from ethyl 3-oxo-3-(pyridin-3-yl)propanoate according to Method A with addition of MeCN (1 ml). Reaction time – 1 hour. Yield 306 mg (70%). Viscous yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.81 (d, J = 2.3 Hz, 1H), 8.71 (dd, J = 4.9, 1.7 Hz, 1H), 7.90 (dt, J = 7.9, 2.0 Hz, 1H), 7.34 (dd, J = 8.0, 4.9 Hz, 1H), 4.23 (q, J = 7.1 Hz, 2H), 1.24 (t, J = 7.1 Hz, 3H) ppm.

^{1}H NMR spectrum is in accordance with literature data [S1].

Ethyl 2-diazo-3-oxo-3-(thiophen-2-yl)propanoate (2f) .

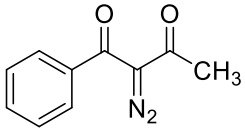


The title compound was synthesized from ethyl 3-oxo-3-(thiophen-2-yl)propanoate according to Method B with addition of MeCN (1 ml). Reaction time – 1 hour. Yield 318 mg (71%). Viscous yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.06 (d, J = 3.9, 1H), 7.66 (d, J = 5.0 Hz, 1H), 7.11 (dd, J = 5.0, 3.9 Hz, 1H), 4.32 (q, J = 7.2, 2H), 1.34 (t, J = 7.2 Hz, 3H) ppm.

^{1}H NMR spectrum is in accordance with literature data [S1].

2-Diazo-1-phenylbutane-1,3-dione (2g).

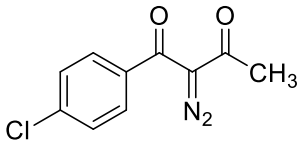


The title compound was synthesized from 1-phenylbutane-1,3-dione according to Method B with addition of MeCN (1 ml). Reaction time – 1 hour. Yield 313 mg (83%). Pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.69 – 7.64 (m, 2H), 7.63 – 7.58 (m, 1H), 7.52 (t, J = 7.5 Hz, 1H), 2.57 (s, 3H) ppm.

^{1}H NMR spectrum is in accordance with literature data [S1].

1-(4-Chlorophenyl)-2-diazobutane-1,3-dione (2h)



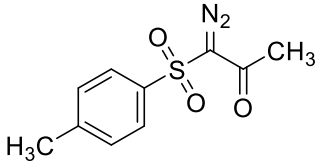
The title compound was synthesized from 1-(4-chlorophenyl)butane-1,3-dione according to Method B with addition of MeCN (1 ml). Reaction time – 1 hour.

Yield 355 mg (80%). Pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.59 (d, J = 8.5 Hz, 2H), 7.47 (d, J = 8.5 Hz, 2H), 2.53 (s, 3H) ppm.

^{1}H NMR spectrum is in accordance with literature data [S1].

1-Diazo-1-tosylpropan-2-one (2j).

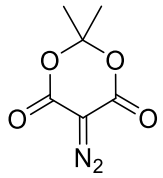


The title compound was synthesized from 1-tosylpropan-2-one according to Method A. Reaction time – 1 hour. Yield 351 mg (73%). Pale beige solid.

^{1}H NMR (400 MHz, $CDCl_3$) = 7.84 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 8.1 Hz, 2H), 2.45 (s, 3H), 2.27 (s, 3H) ppm.

^{1}H NMR spectrum is in accordance with literature data [S1].

5-Diazo-2,2-dimethyl-1,3-dioxane-4,6-dione (4a).

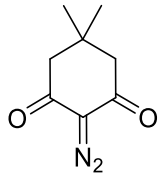


The title compound was synthesized from Meldrum's acid according to Method A. Reaction time – 0.5 hour. Yield 234 mg (69%). White solid.

^{1}H (400 MHz, $CDCl_3$) δ = 1.76 (s, 6H, 2 CH_3) ppm.

^{1}H NMR spectrum is in accordance with literature data [S1].

2-Diazo-5,5-dimethylcyclohexane-1,3-dione (4b).

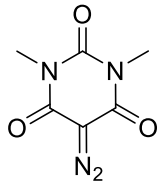


The title compound was synthesized from dimedone according to Method A. Reaction time – 0.75 hour. Yield 240 mg (72%). White solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.43 (s, 4H, 2 CH_2), 1.11 (s, 6H, 2 CH_3) ppm.

^{1}H NMR spectrum is in accordance with literature data [S1].

5-Diazo-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (4c).

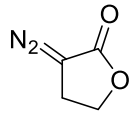


The title compound was synthesized from 1,3-dimethylbarbituric acid according to Method A. Reaction time – 0.75 hour. Yield 204 mg (56%). White solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.29 (s, 6H, 2 CH_3) ppm.

^{1}H NMR spectrum is in accordance with literature data [S1].

3-Diazodihydrofuran-2(3H)-one (6).



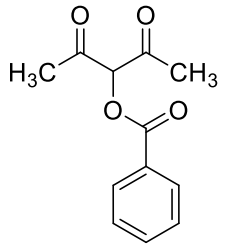
The title compound was synthesized from α-acetobutyrolactone according to Method A. Reaction time – 1 hour. Yield 354 mg (59%). Transparent colorless liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.36 (t, J = 7.8 Hz, 2H), 3.34 (t, J = 7.8 Hz, 2H) ppm.

^{1}H NMR spectrum is in accordance with literature data [S2].

Diazo transfer/ O-H insertion two-step procedure. Diazo compound was synthesized by general procedure and was used directly for the next step without further purification.

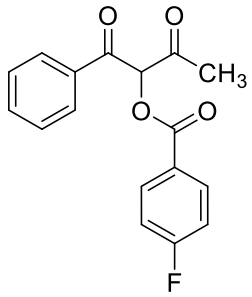
2,4-Dioxopentan-3-yl benzoate



To a stirred solution of $Rh_2(esp)_2$ (15 mg, 20 μmol, 1 mol %) and benzoic acid (244 mg, 2 mmol) in anhydrous dichloromethane (5 ml), a solution of crude 3-diazopentane-2,4-dione (**2b**) in anhydrous dichloromethane (5 ml) was added under argon, and the mixture was stirred at ambient temperature for 18 hours. The solvent was removed *in vacuo*, the residue was dissolved in diethyl ether (5 ml) and washed with $NaHCO_3$ (aq., 10 ml).

The aqueous layer was separated and washed with diethyl ether (4×5 ml). The combined organic extracts were dried over sodium sulfate, filtered, and concentrated to dryness.The residue was subjected to flash column chromatography on silica gel (eluent: EtOAc –hexane = 1:5→1:3→1:1). Yield 167 mg (38% from acetylacetone), diketone/keto enol mixture ~1.7:1. Dark amber colored oil. R_f = 0.61 (EtOAc –hexane =1 : 3) ^{1}H NMR (400 MHz, $CDCl_3$), of the diketone tautomer, δ: 8.12 (d, J = 8.2 Hz, 2H), 7.63 (q, J = 7.4 Hz, 1H), 7.50 (t, J = 7.9 Hz, 2H), 5.73 (s, 1H), 2.40 (s, 6H); keto enol tautomer, δ 14.50 (s, 1H), 8.19 – 8.16 (m, 2H), 7.70 – 7.61 (m, 1H), 7.56 – 7.47 (m, 2H), 2.07 (s, 6H). ^{1}H NMR spectrum is close to literature [S3].

1,3-Dioxo-1-phenylbutan-2-yl 4-fluorobenzoate



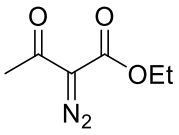
To a stirred solution of $Rh_2(esp)_2$ (15 mg, 20 μmol, 1 mol %) and 4-fluorobenzoic acid (280 mg, 2 mmol) in anhydrous dichloromethane (5 ml) was added 2-diazo-1-phenylbutane-1,3-dione **2g** (solution in 5ml of anhydrous dichloromethane) under argon, and the mixture was stirred at ambient temperature for 18 hours, evaporated and subjected to flash column chromatography on silica gel (eluent: EtOAc –hexane =1 : 5 → 1 : 3 → 1 : 1). Yield 132 mg (22% from 1-phenylbutane-1,3-dione).

Viscous yellow liquid, diketone/keto enol mixture ~ 9:1. R_f = 0.57 (EtOAc –hexane = 1 : 3) ^{1}H NMR (400 MHz, $CDCl_3$), diketone tautomer), δ: 8.12 (dd, J = 8.8, 5.4 Hz, 2H), 8.07 (d, J = 7.3 Hz, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.7 Hz, 2H), 7.15 (t, J = 8.6 Hz, 2H), 6.47 (s, 1H), 2.39 (s, 3H); characteristic signals of minor isomer, δ 15.18 (s, 1H), 7.78 – 7.74 (m, 2H), 7.42 – 7.37 (m, 2H), 7.35 – 7.30 (m, 2H), 2.19 (s, 3H). ^{1}H NMR spectra are close to literature [S1].

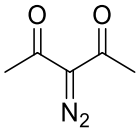
References

[S1] D. Dar'in, G. Kantin and M. Krasavin, *Chem. Commun.*, 2019, **55**, 5239.
[S2] D. P. Hari and J. Waser, *J. Am. Chem. Soc.*, 2016, **138**, 2190.
[S3] M. Uyanik, D. Suzuki, T. Yasui and K. Ishihara, *Angew. Chem., Int. Ed.*, 2011, **50**, 5331.

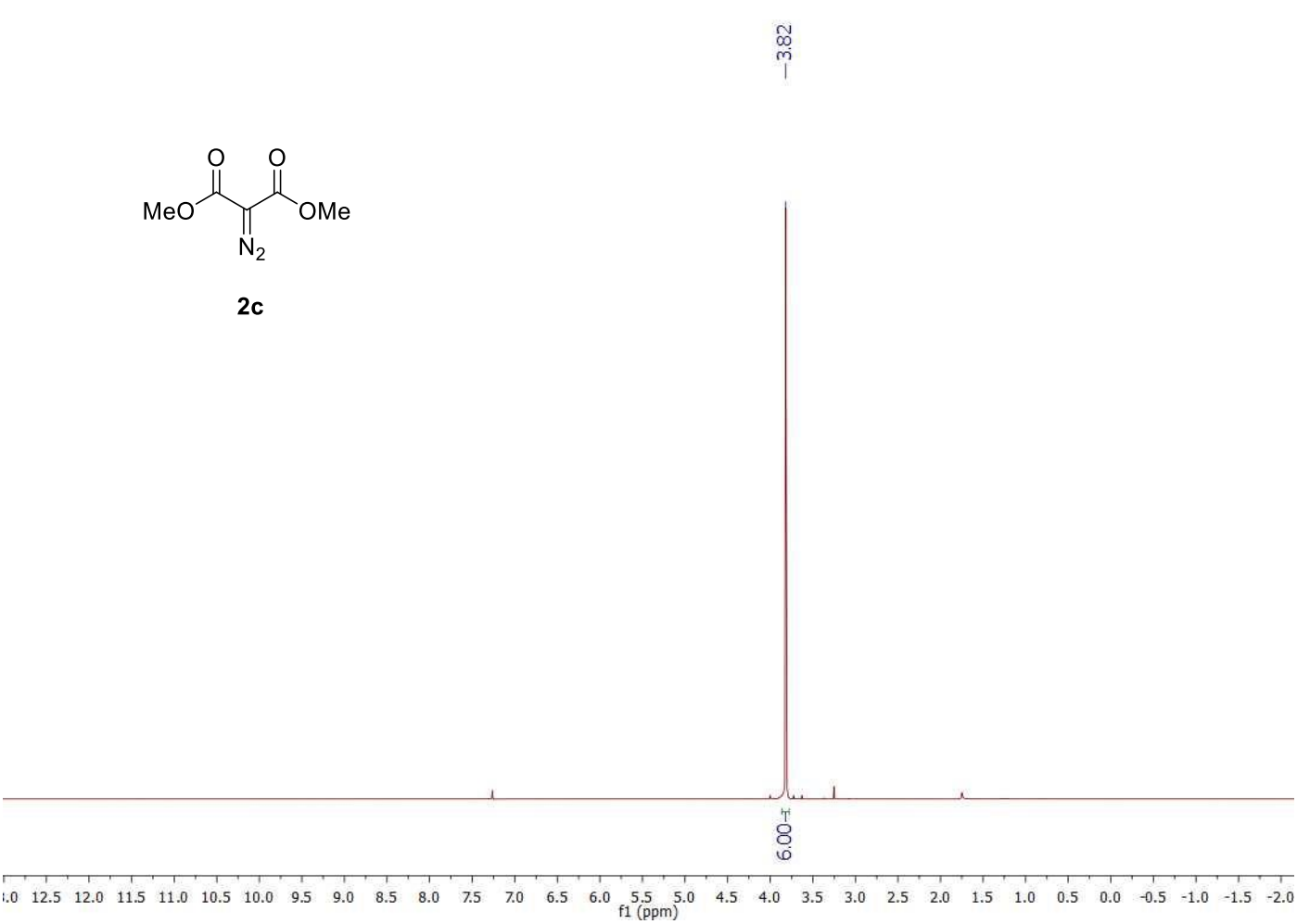
NMR Spectra



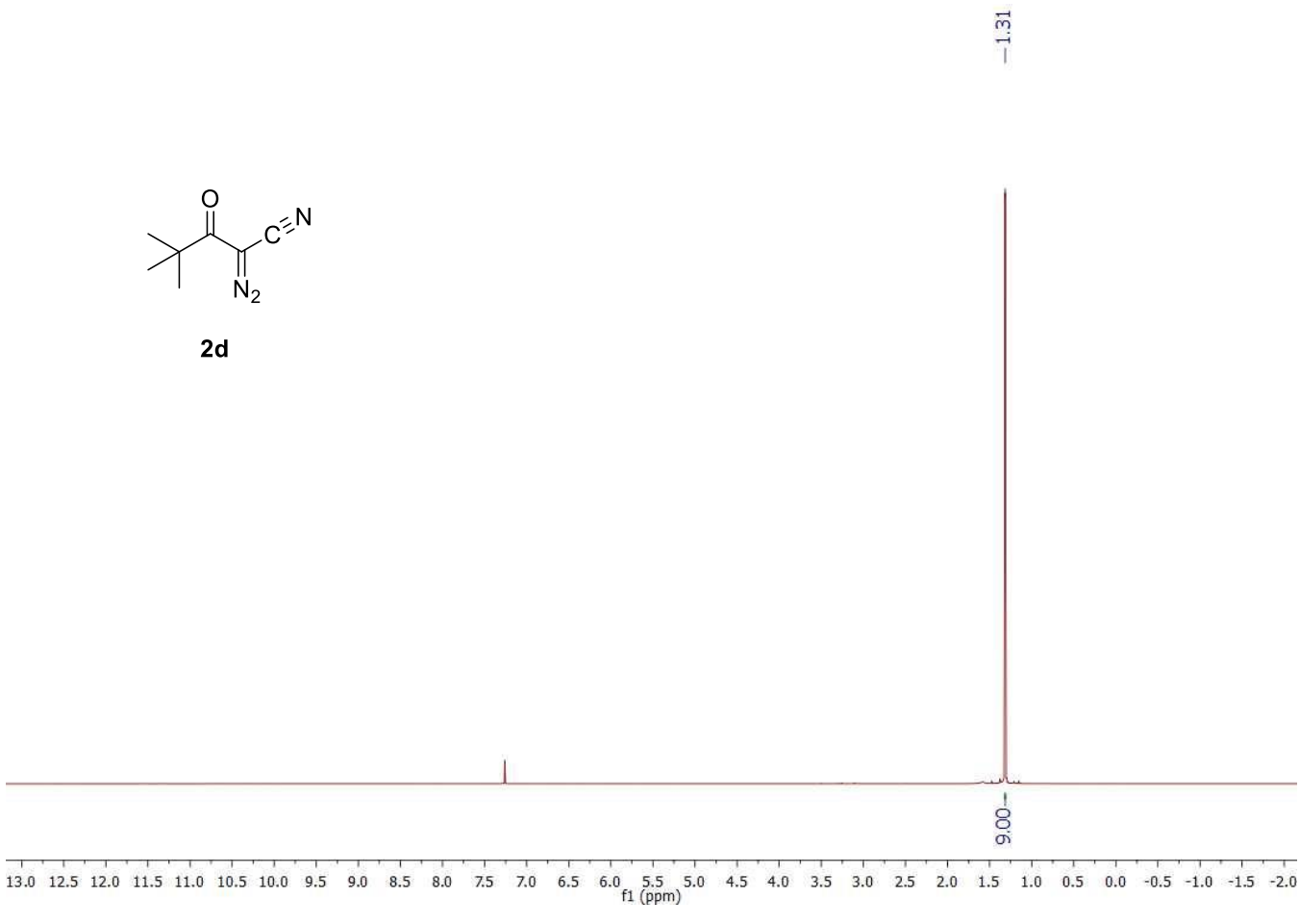
2a



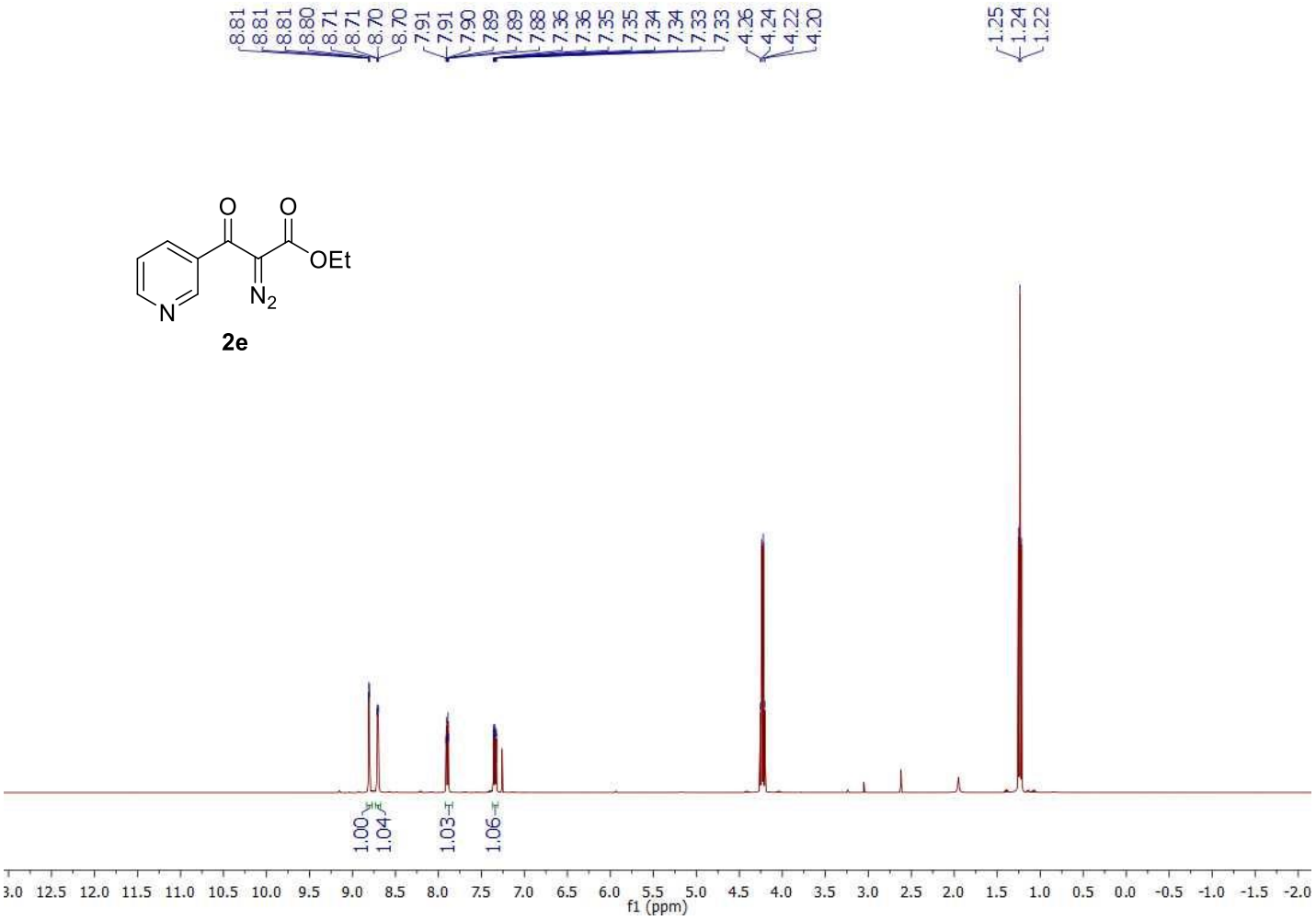
2b

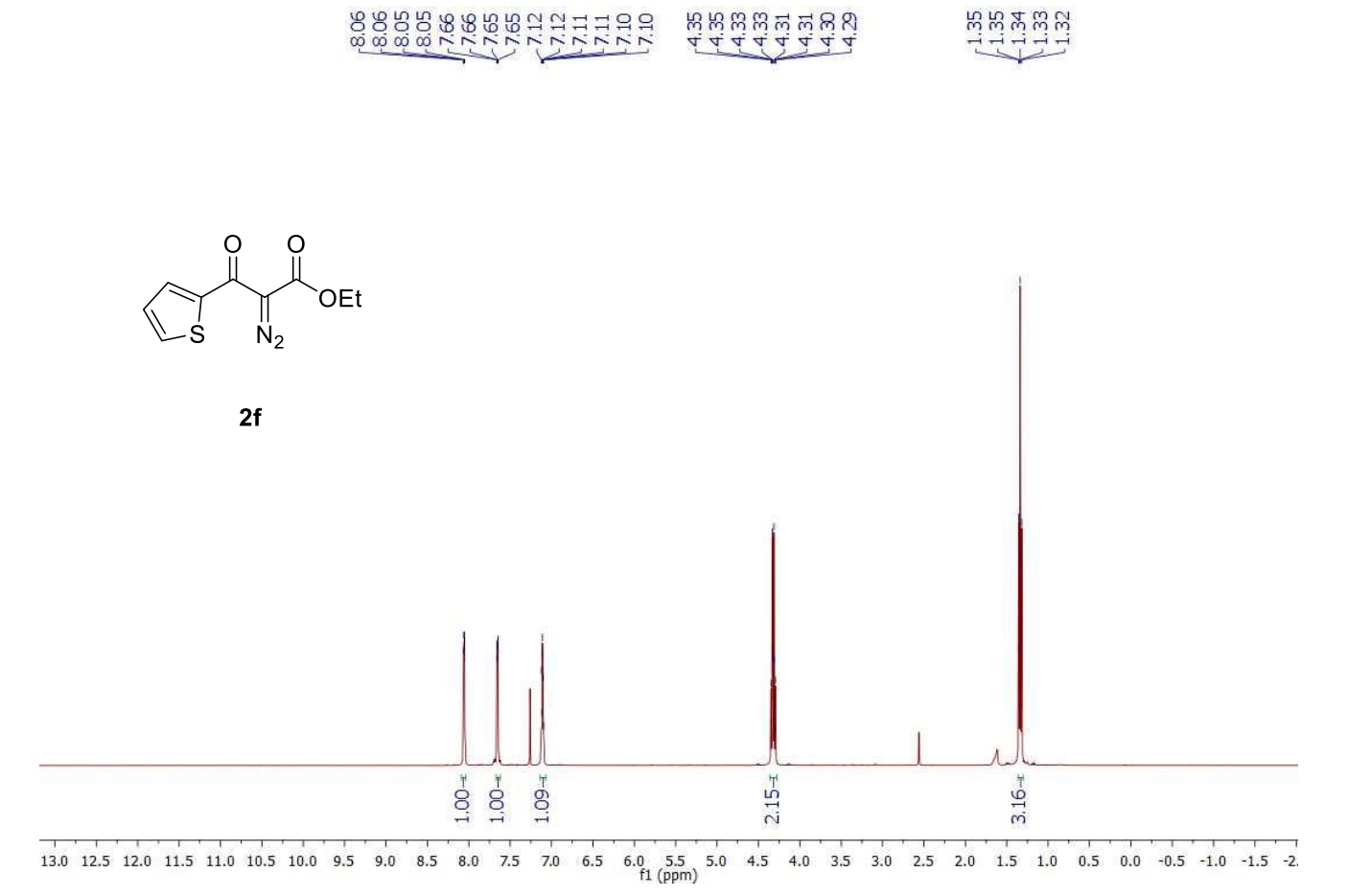


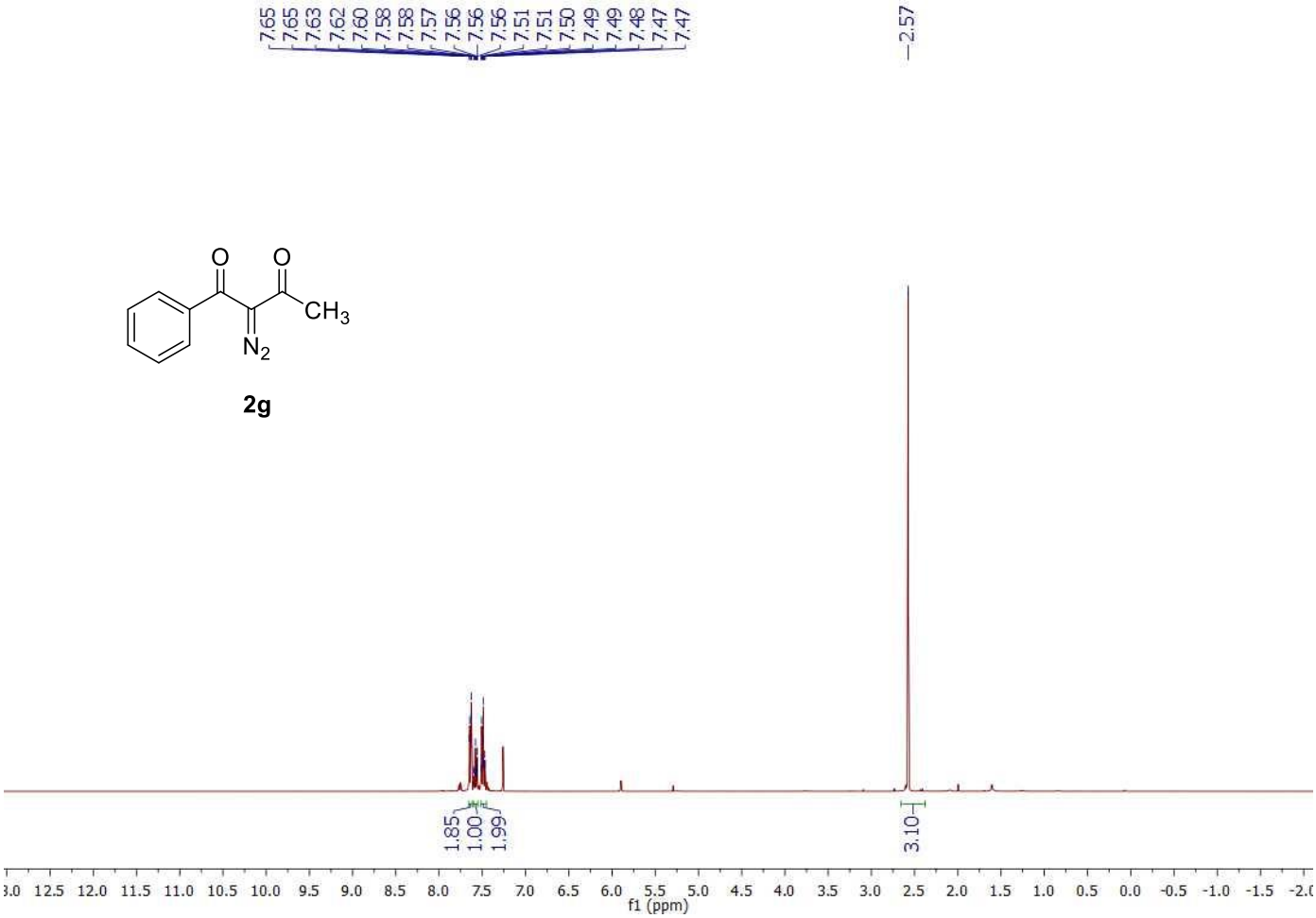
2c



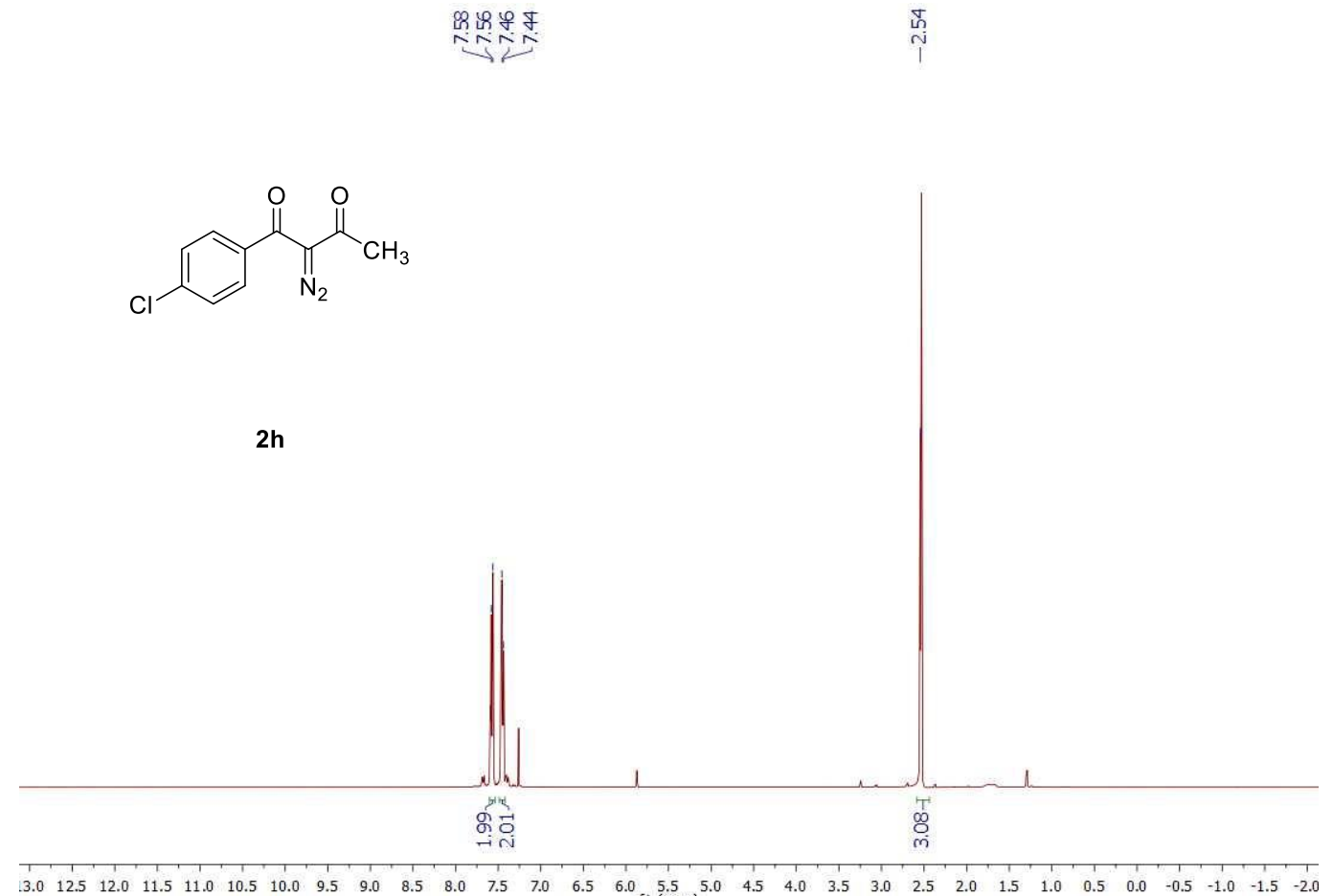
2d


8.81
8.81
8.81
8.80
8.71
8.71
8.70
8.70
7.91
7.91
7.90
7.89
7.89
7.88
7.36
7.36
7.35
7.35
7.34
7.34
7.33
7.33
4.26
4.24
4.22
4.20
1.25
1.24
1.22
O
O
OEt
N2
N
2e
1.00
1.04
1.03
1.06
f1 (ppm)

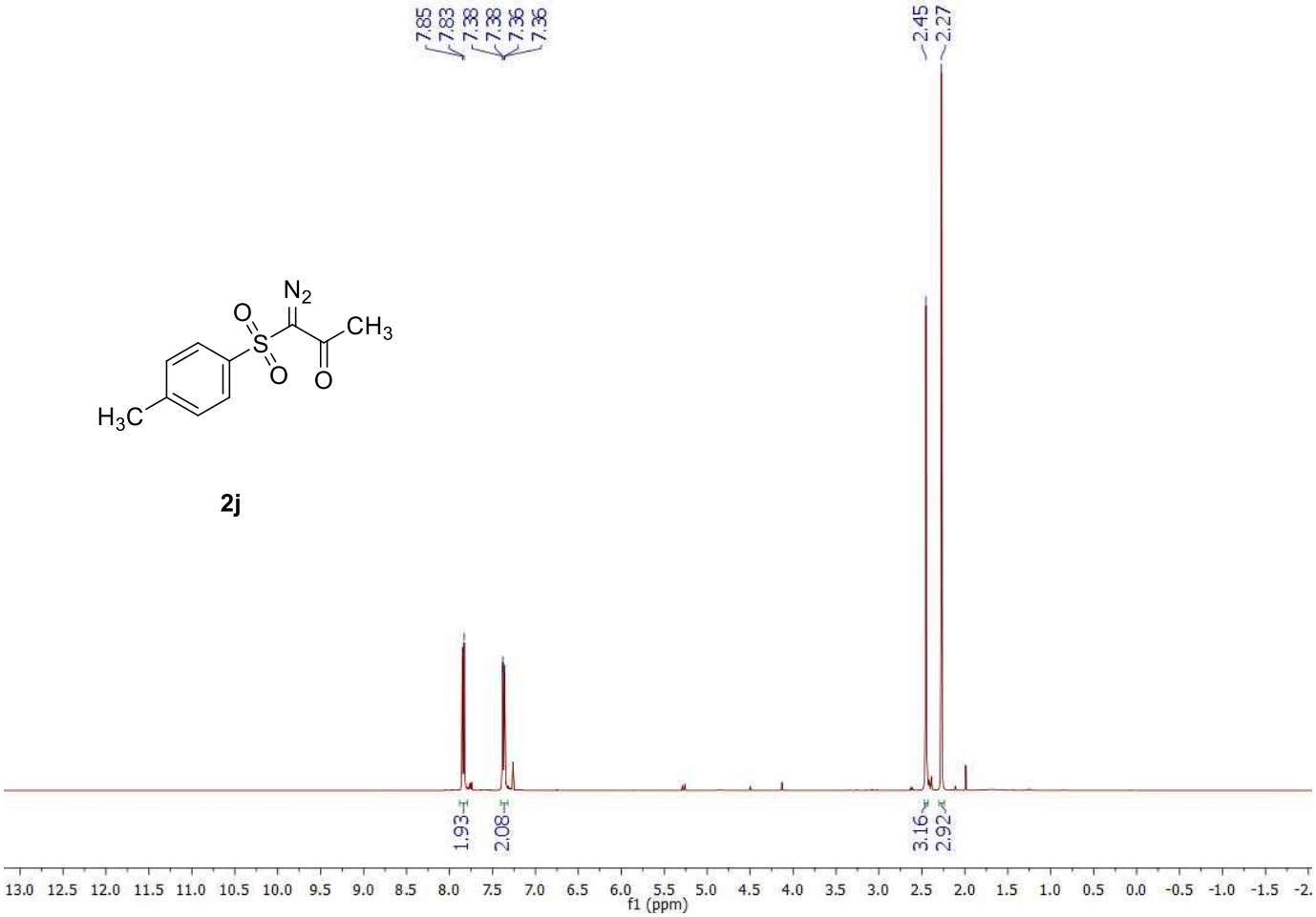

8.06
8.06
8.05
8.05
7.66
7.66
7.65
7.65
7.12
7.12
7.11
7.11
7.10
7.10
4.35
4.35
4.33
4.33
4.31
4.31
4.30
4.29
1.35
1.35
1.34
1.33
1.32
O
O
OEt
S
N2
2f
1.00
1.00
1.09
2.15
3.16
f1 (ppm)


7.65
7.65
7.63
7.62
7.60
7.58
7.58
7.57
7.56
7.56
7.56
7.51
7.51
7.50
7.49
7.49
7.48
7.47
7.47
2.57
O
O
CH3
N2
1.85
1.00
1.99
3.10
f1 (ppm)

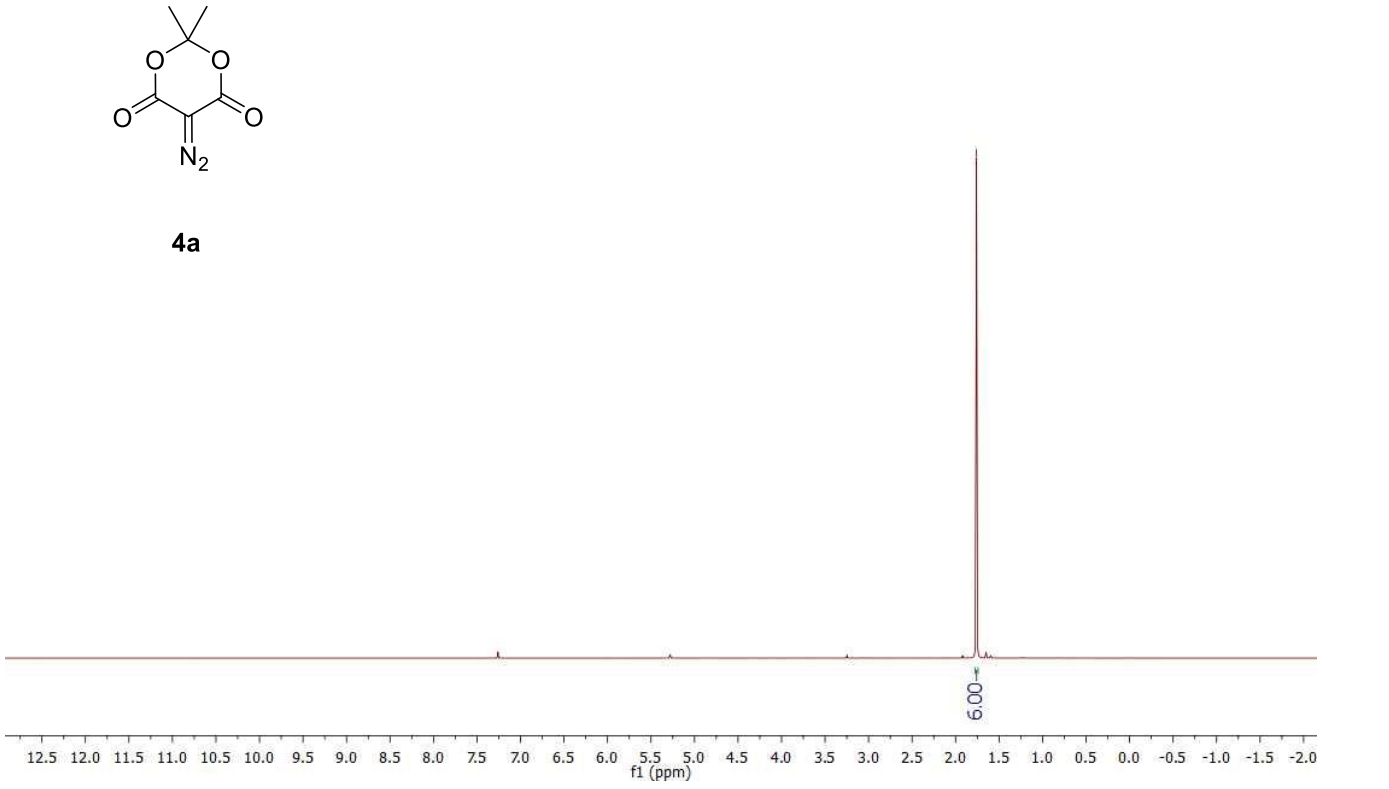
2g


7.58
7.56
7.46
7.44
2.54
O
O
CH3
N2
Cl
1.99
2.01
3.08
f1 (ppm)

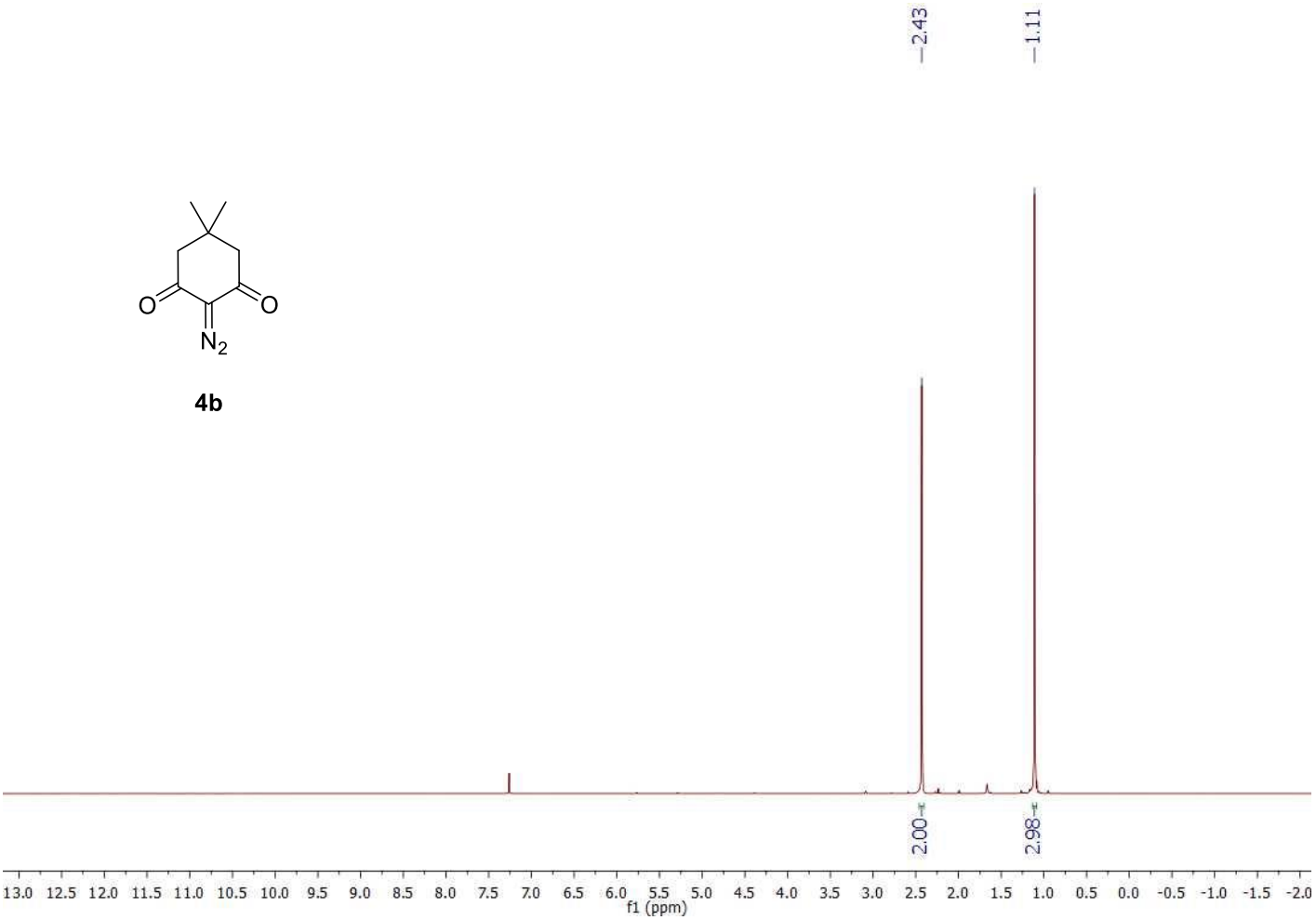
2h


7.85
7.83
7.38
7.38
7.36
7.36
2.45
2.27
1.93
2.08
3.16
2.92
f1 (ppm)

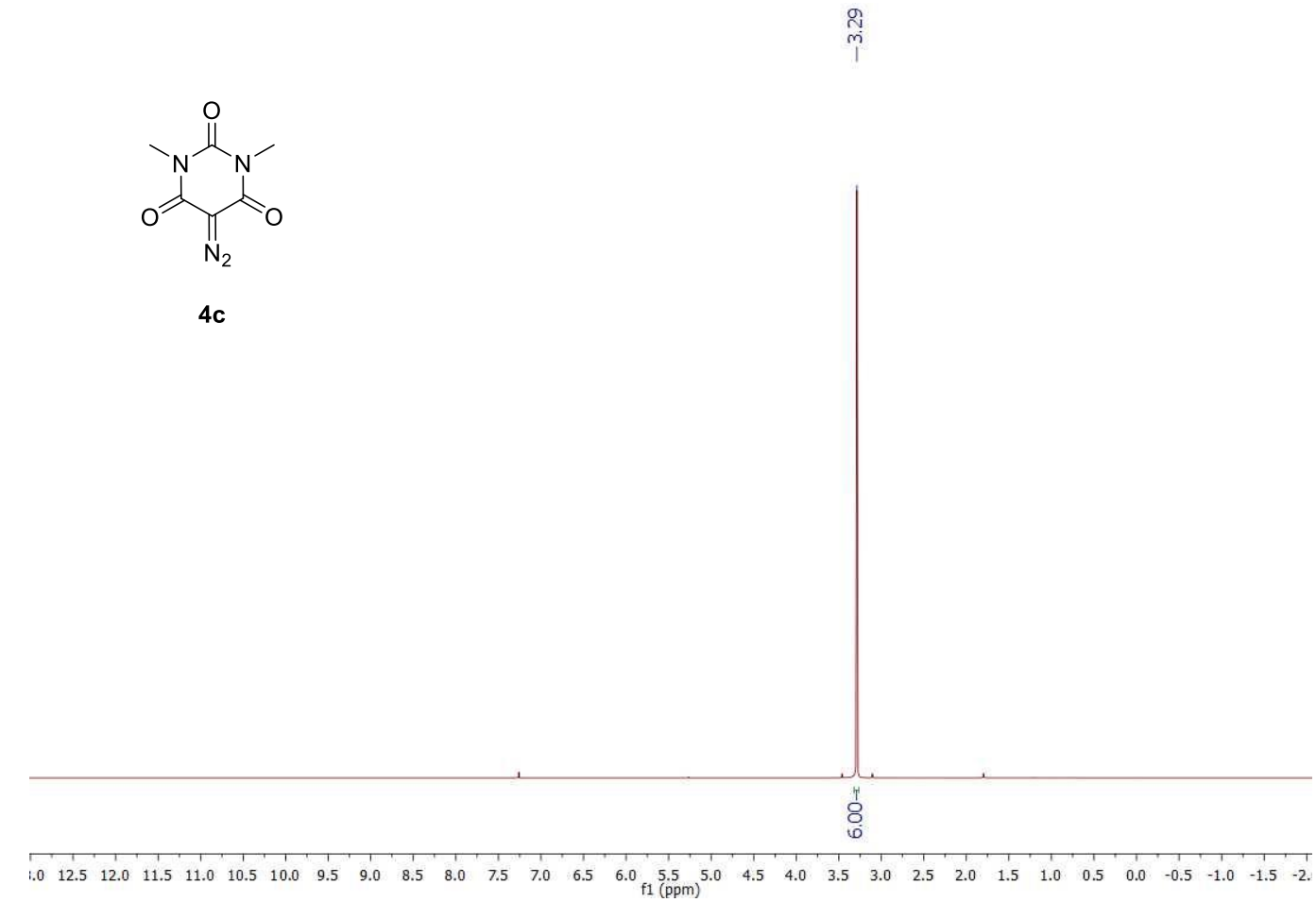
2j


1.76
6.00
f1 (ppm)

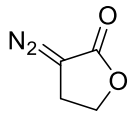
4a


2.43
1.11
2.00
2.98
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2.0
f1 (ppm)

4b

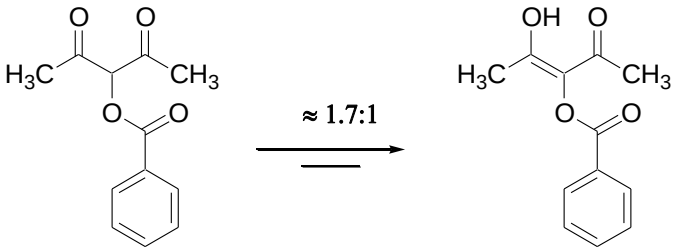

3.29
6.00
f1 (ppm)

4c



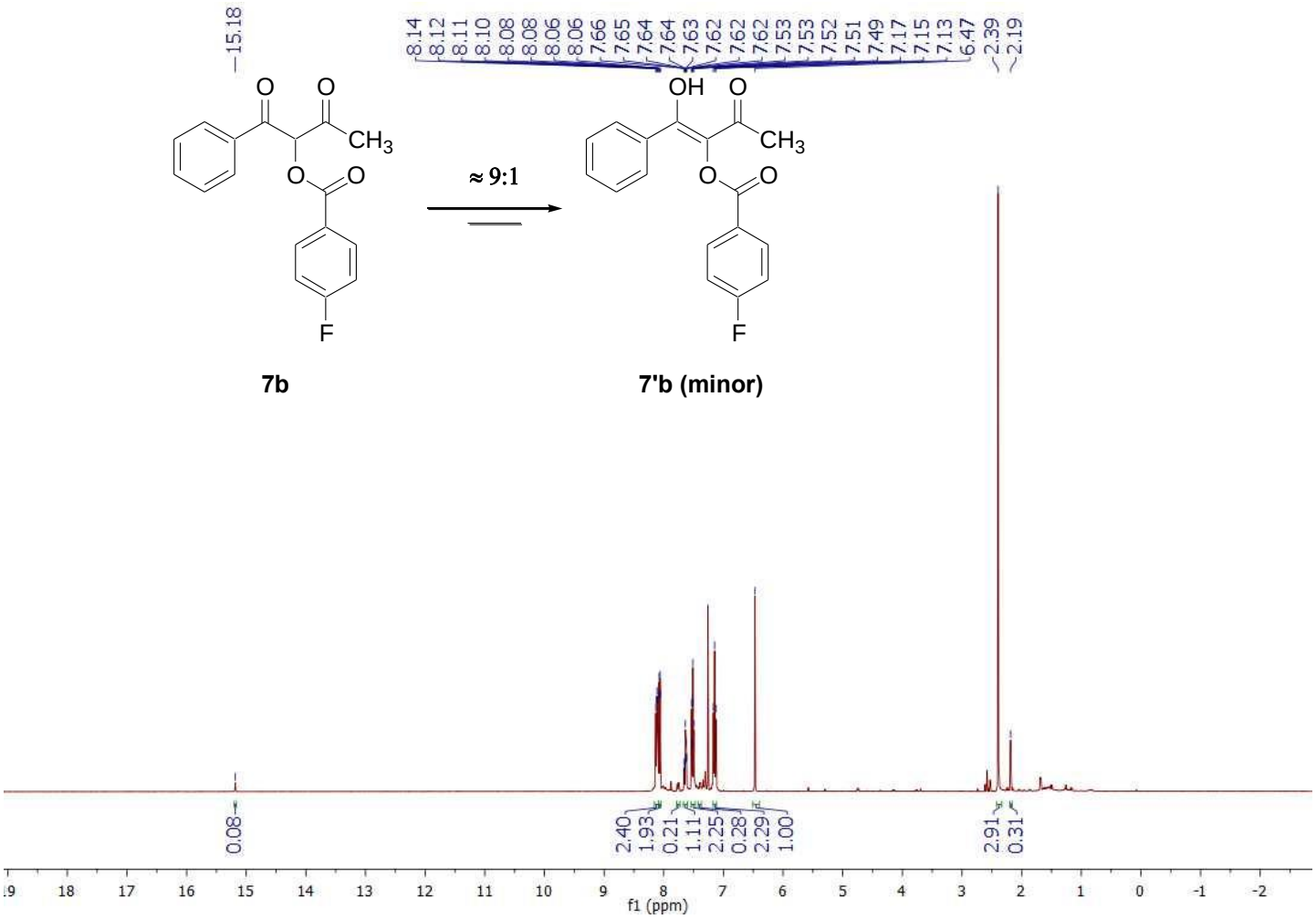
6

4.38
4.36
4.34
3.36
3.34
3.32
2.00
2.00
f1 (ppm)



7a **7'a (minor)**

14.50
8.19
8.17
8.16
8.13
8.12
8.11
7.67
7.66
7.64
7.62
7.55
7.53
7.52
7.50
7.48
5.73
2.40
2.07
1.19
2.08
1.77
3.60
f1 (ppm)
0.59
1.19
2.08
1.77
3.60
1.00
6.40
3.56
f1 (ppm)


15.18
8.14
8.12
8.11
8.10
8.08
8.08
8.06
8.06
7.66
7.65
7.64
7.64
7.63
7.62
7.62
7.62
7.53
7.53
7.52
7.51
7.49
7.17
7.15
7.13
6.47
2.39
2.19
O
O
CH3
O
O
F
≈ 9:1
OH
O
CH3
O
O
F
0.08
2.40
1.93
0.21
1.11
2.25
0.28
2.29
1.00
2.91
0.31
f1 (ppm)

7b **7'b (minor)**