Supporting Information

Thermodynamic, Kinetic, and Mechanistic Studies of the Thermal Guanidine Metathesis Reaction

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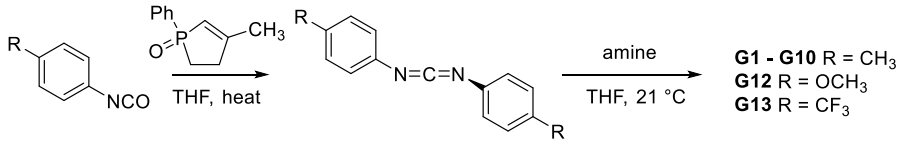
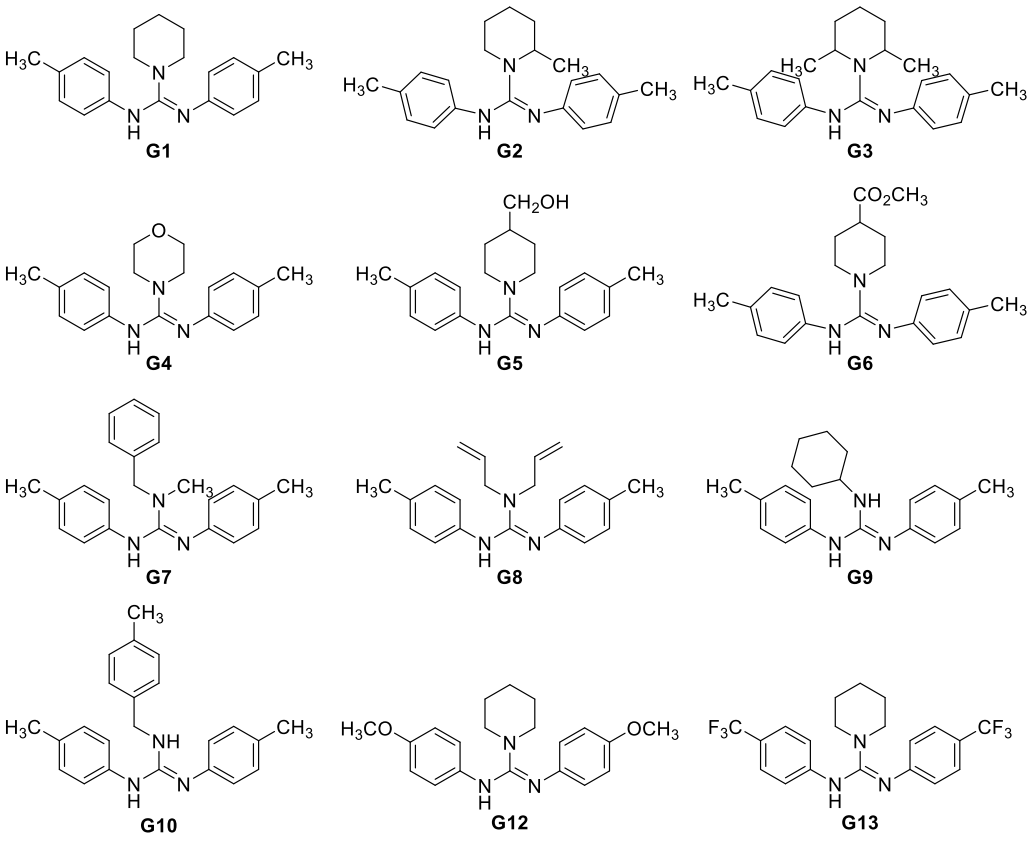
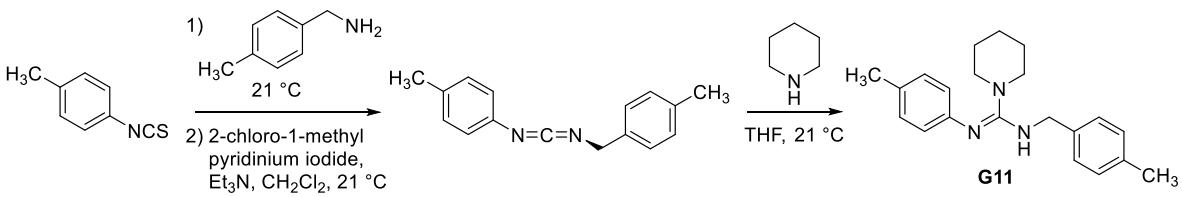
Scheme S1. Synthesis and structure of guanidines **G1 – G13** via aryl carbodiimides.

Symmetric aryl carbodiimides:





Asymmetric aryl-alkyl carbodiimides:



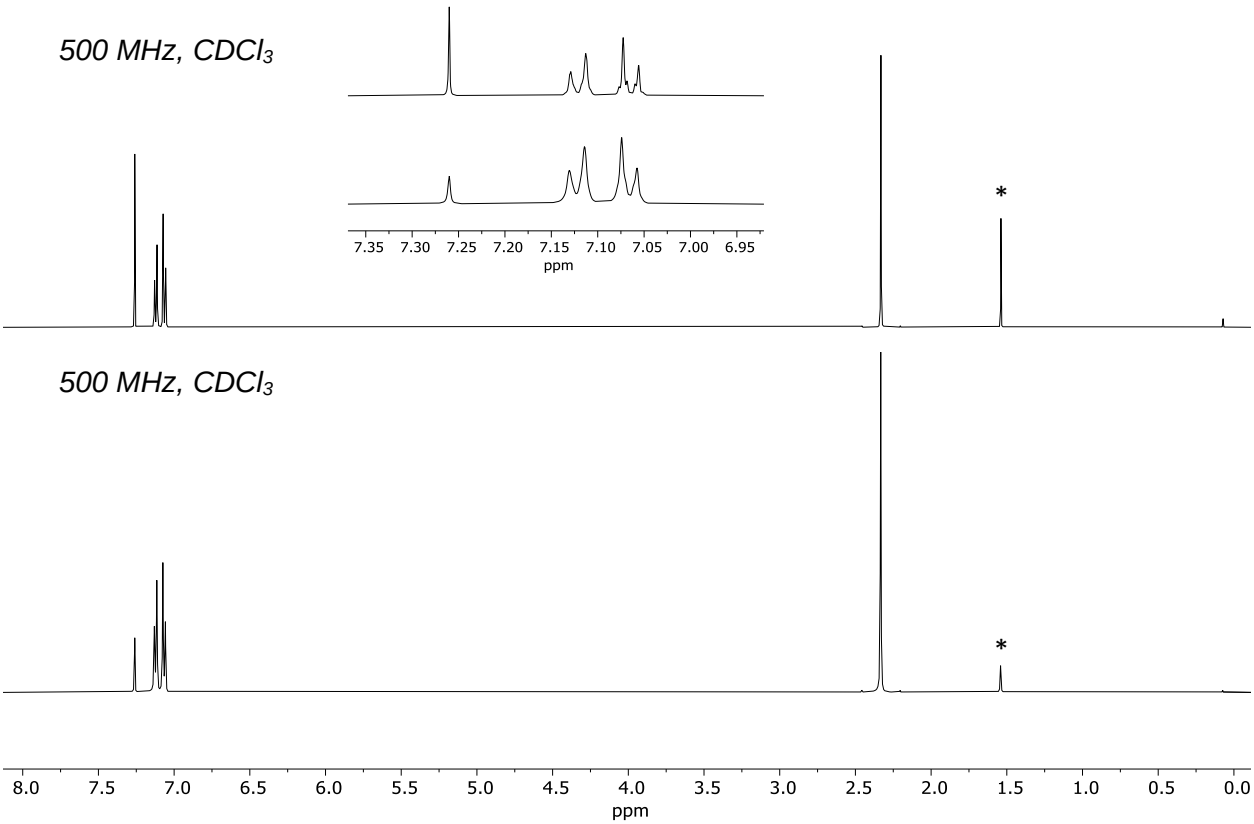


Figure S1. ^{1}H NMR spectra (500 MHz, $CDCl_3$) of as-synthesized *p*-tolyl carbodiimide (top) and the same sample approximately 2.5 years later (bottom) after being stored under ambient conditions. No precautions were taken to exclude air or moisture during storage. Inset: aromatic resonances; * = water (from $CDCl_3$).

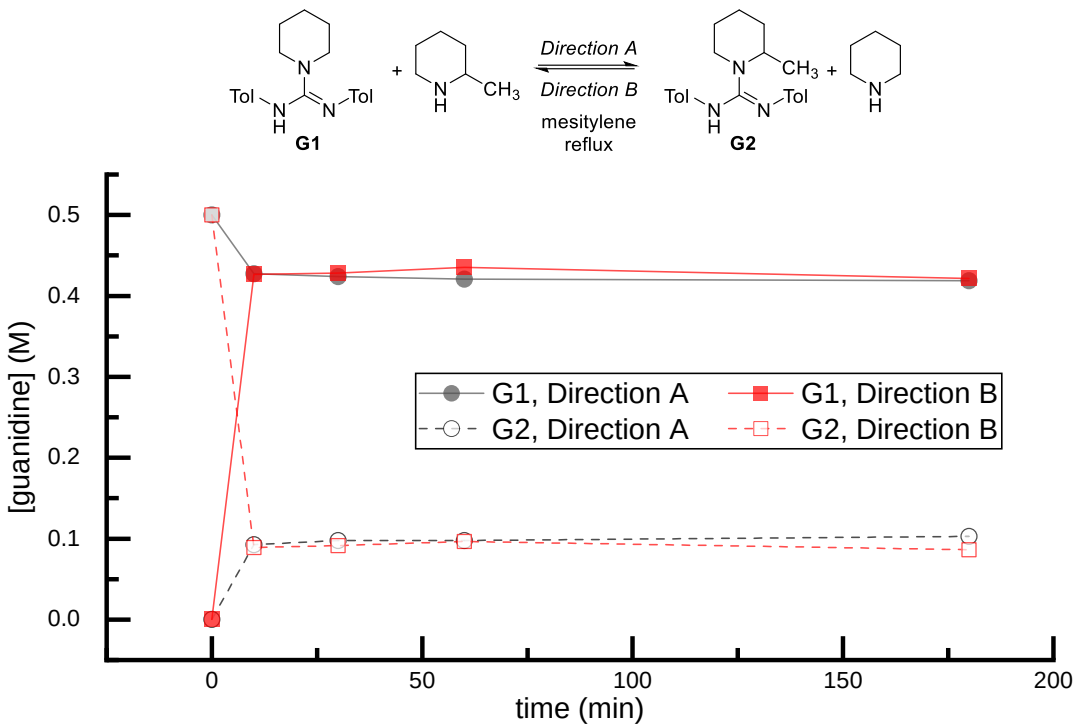


Figure S2. Concentration of **G1** and **G2** as a function of time, starting with **G1** and 2-methylpiperidine (Direction A) or **G2** and piperidine (Direction B).

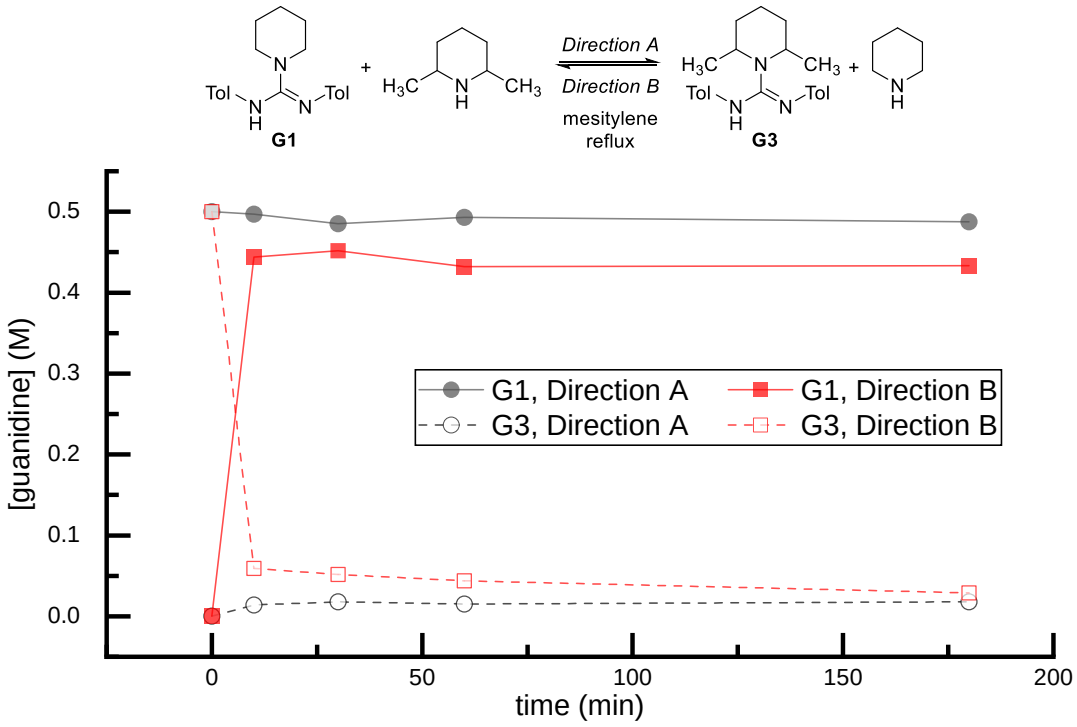


Figure S3. Concentration of **G1** and **G3** as a function of time, starting with **G1** and 2,6-dimethylpiperidine (Direction A) or **G3** and piperidine (Direction B).

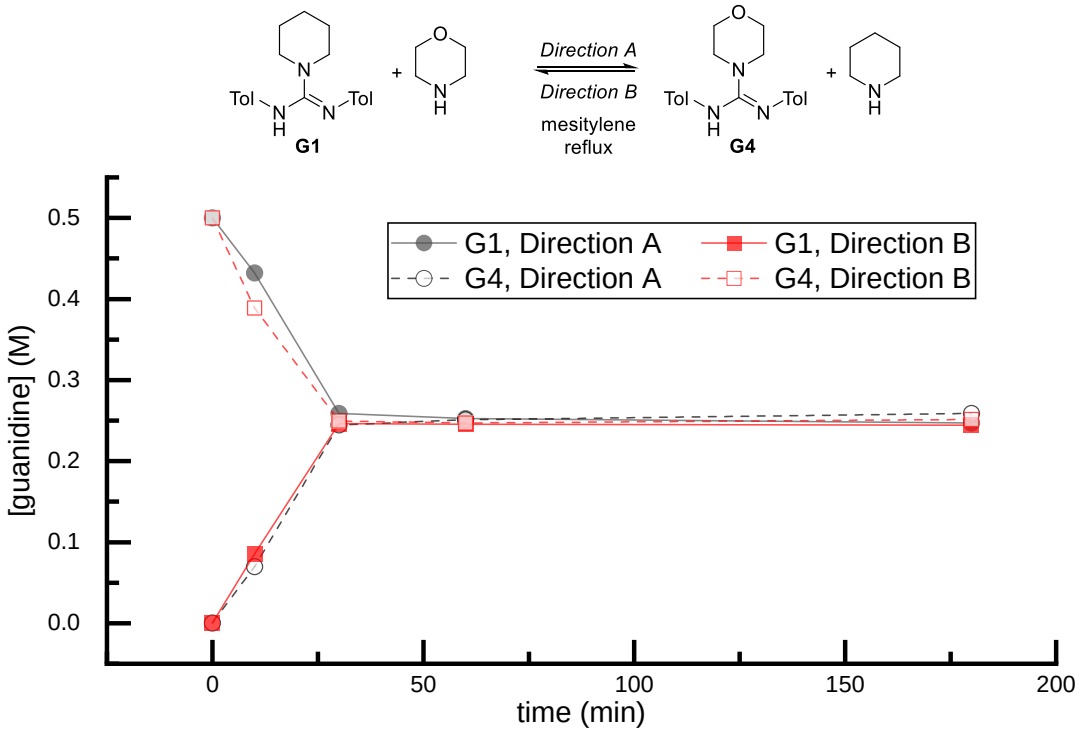


Figure S4. Concentration of **G1** and **G4** as a function of time, starting with **G1** and morpholine (Direction A) or **G4** and piperidine (Direction B).

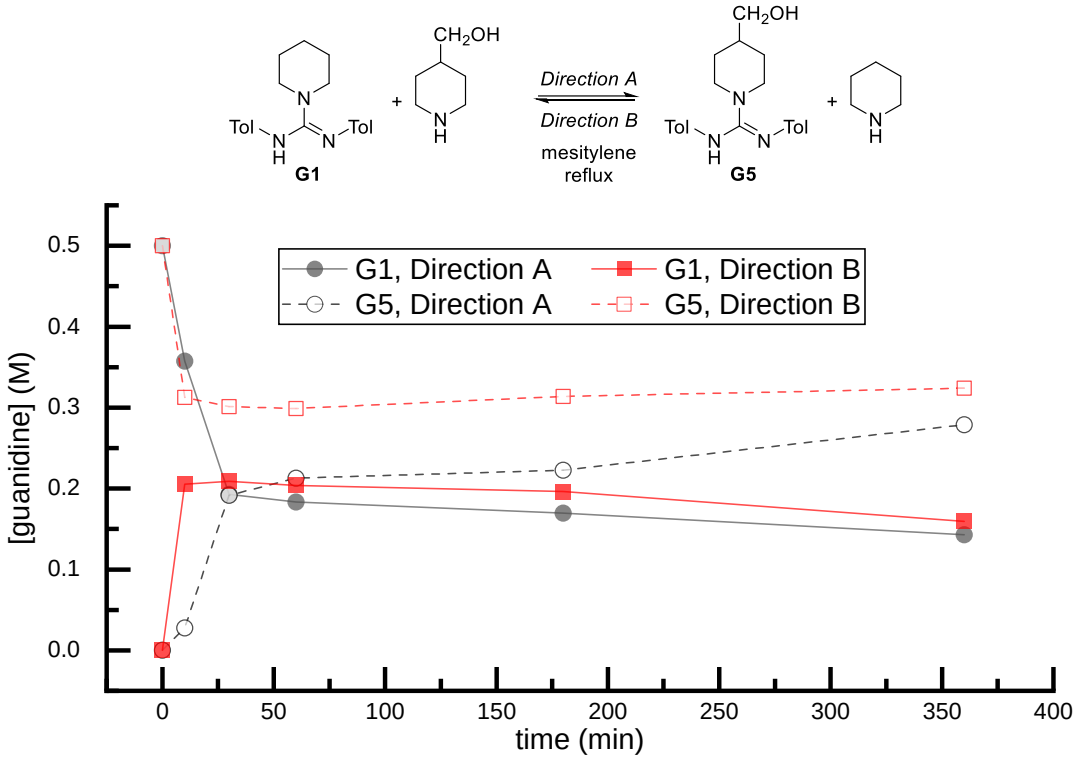


Figure S5. Concentration of **G1** and **G5** as a function of time, starting with **G1** and piperidine-4-methanol (Direction A) or **G5** and piperidine (Direction B).

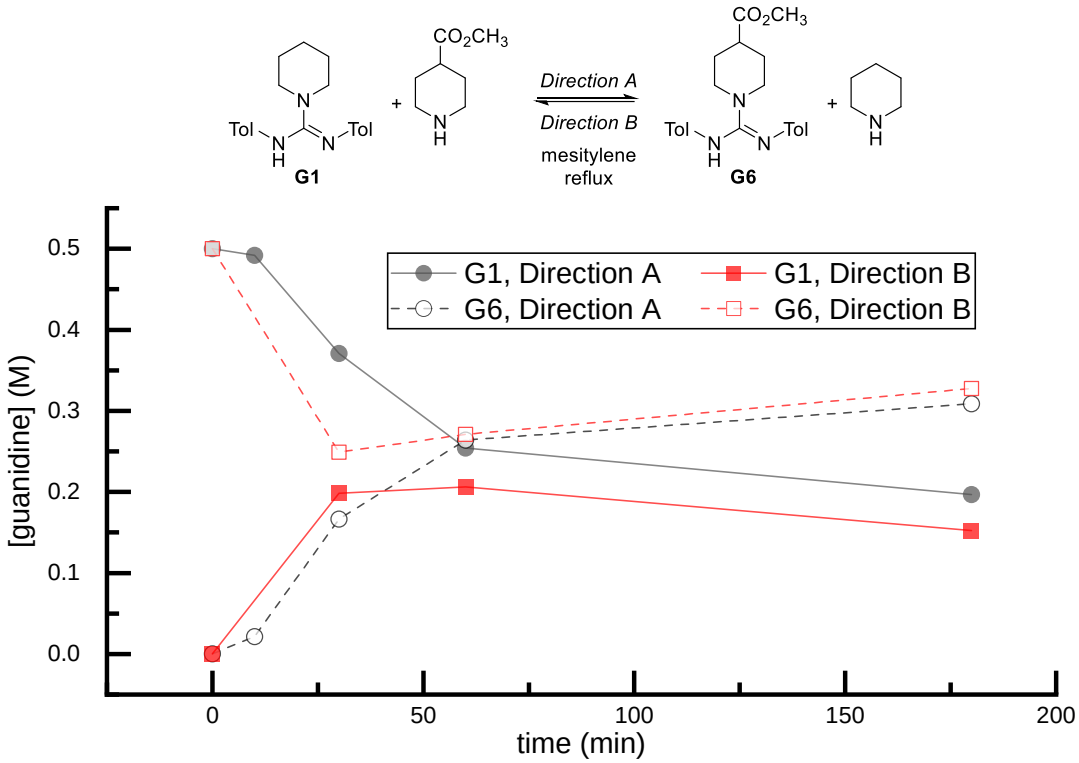


Figure S6. Concentration of **G1** and **G6** as a function of time, starting with **G1** and methyl piperidine-4-carboxylate (Direction A) or **G6** and piperidine (Direction B).

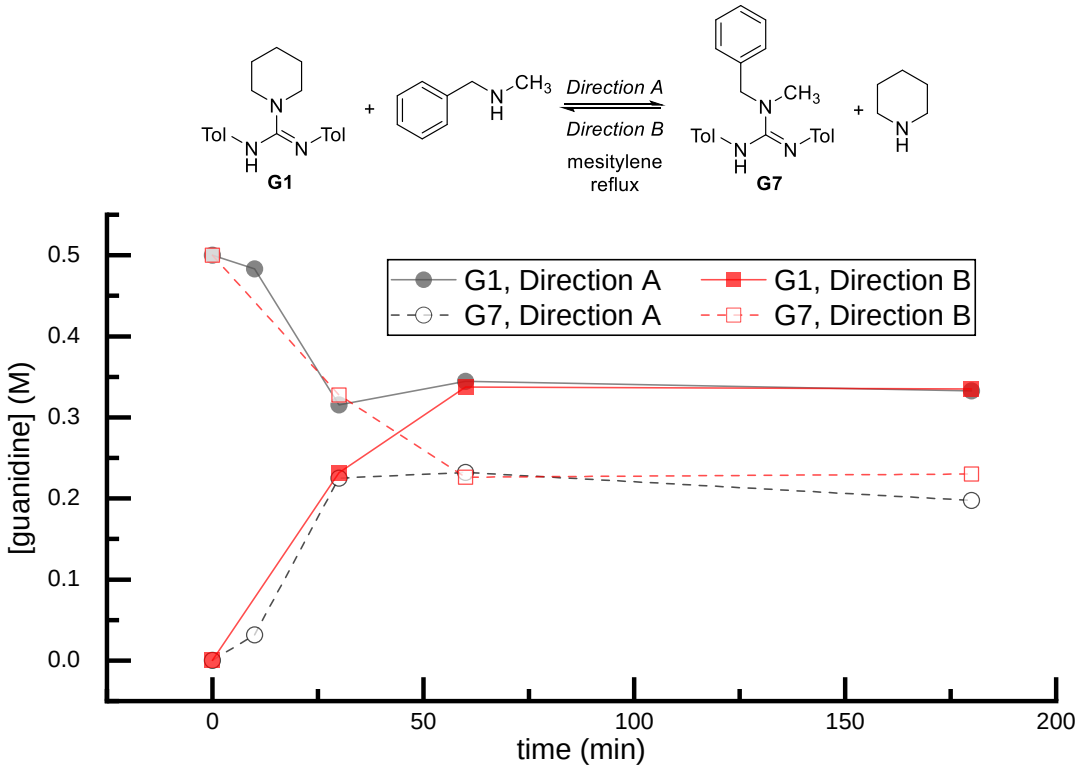


Figure S7. Concentration of **G1** and **G7** as a function of time, starting with **G1** and *N*-methylbenzylamine (Direction A) or **G7** and piperidine (Direction B).

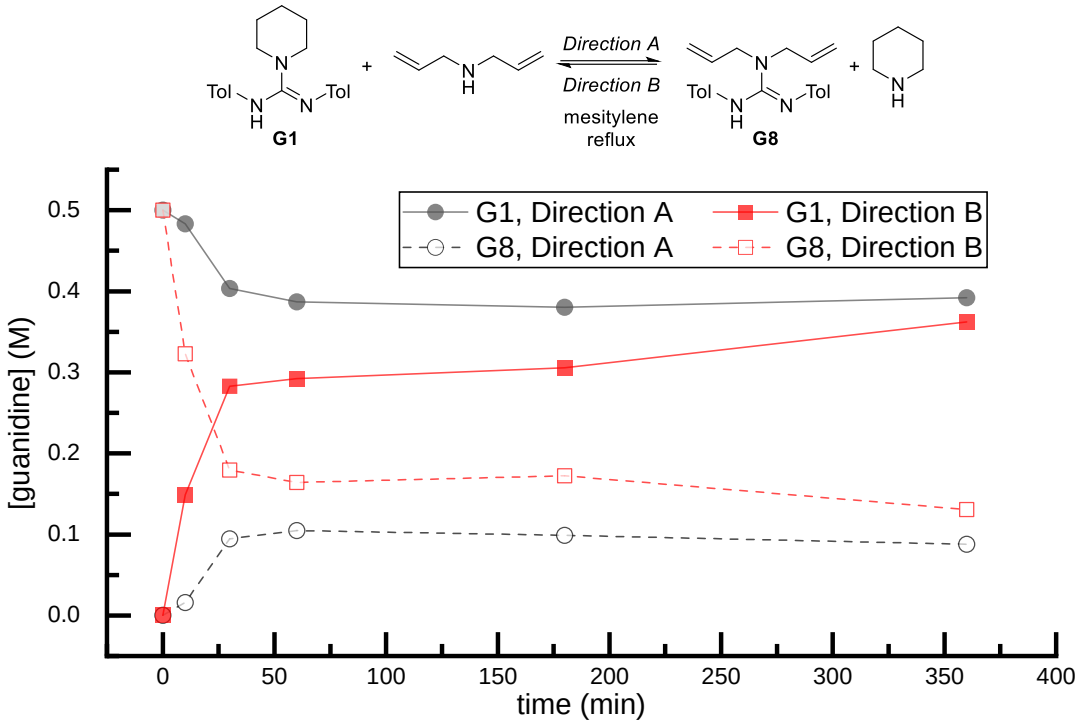


Figure S8. Mole fractions of **G1** and **G8** as a function of time, starting with **G1** and diallyl amine (Direction A) or **G8** and piperidine (Direction B).

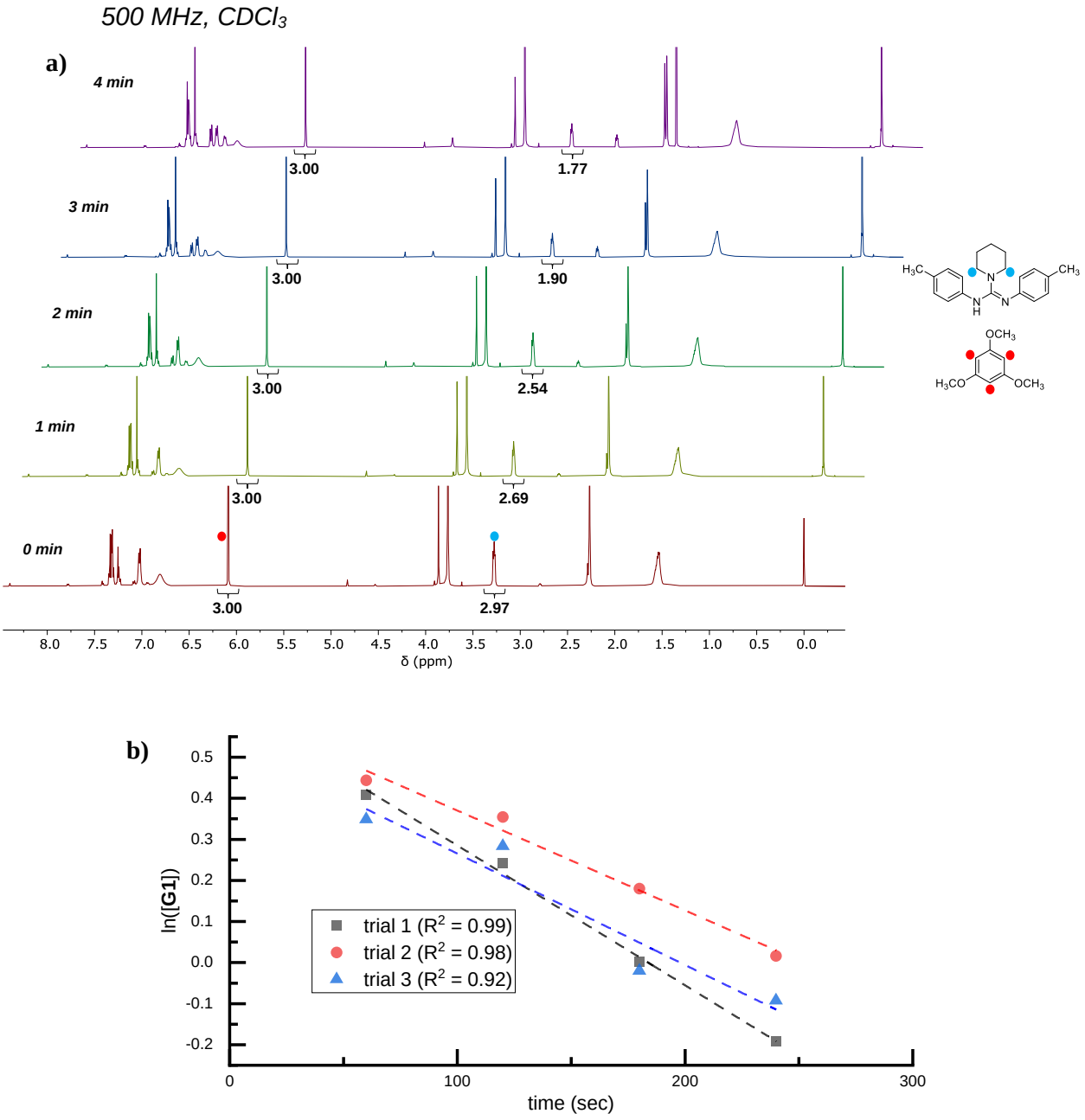


Figure S9. a) Representative ^{1}H NMR spectra (500 MHz, $CDCl_3$) with assigned resonances and peak integration values indicating changes in [**G1**] in the presence of equimolar benzyl amine at 160 °C. [**G1**] at each timepoint was calculated using the integration value of the **G1** resonance at δ = 3.28 ppm, with the aromatic resonance (δ = 6.09 ppm) of 1,3,5-trimethoxybenzene as an internal standard; specific data is that of Trial 3. Stacked spectra are clipped vertically for clarity. b) Plot of ln([**G1**]) versus time. The linear best fit of each trial was used to calculate *k*. The point at 0 sec was not used for fitting, as the time between 0 and 60 sec involved a temperature increase from 100 to 160 °C.

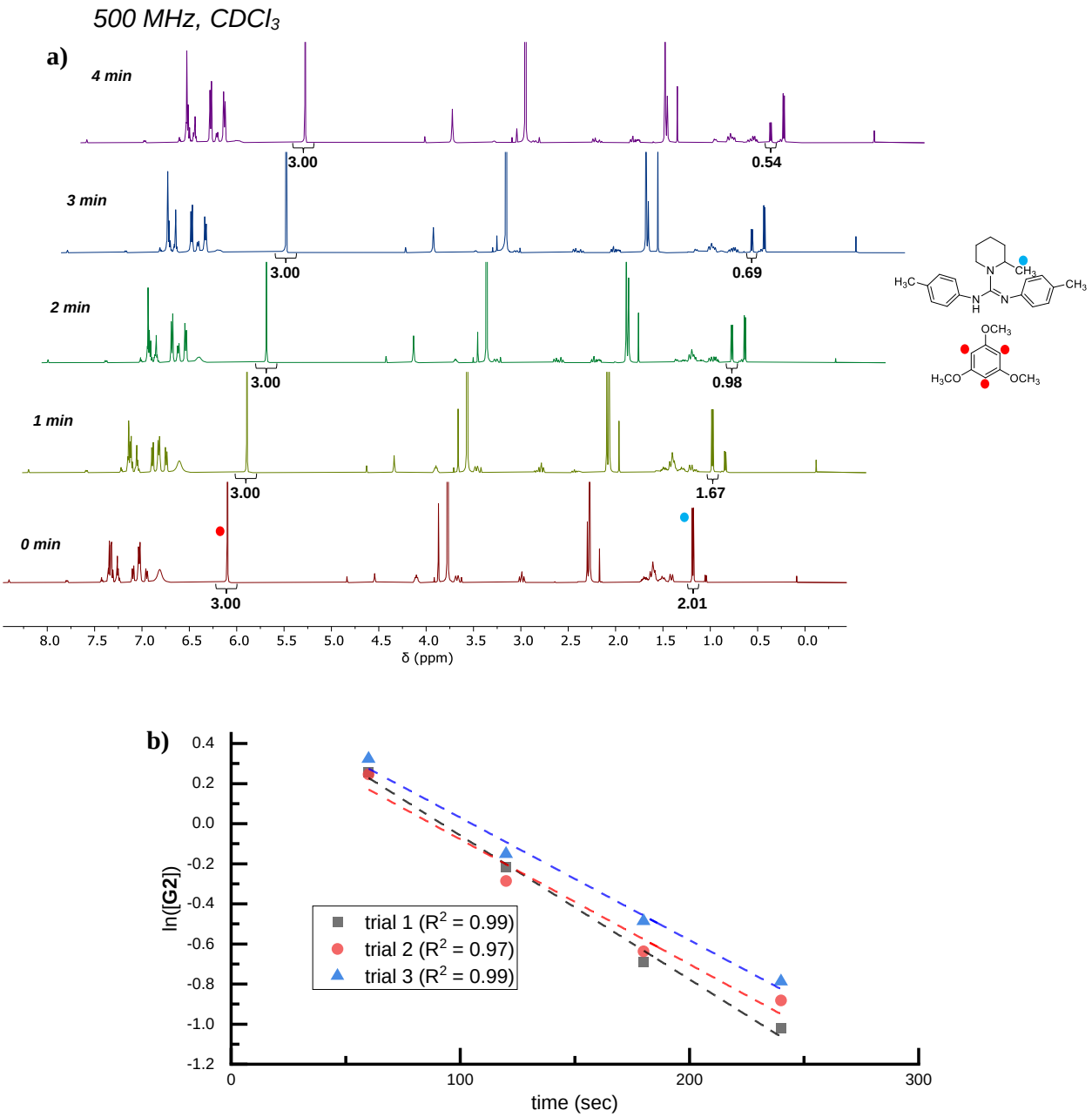


Figure S10. a) Representative ^{1}H NMR spectra (500 MHz, $CDCl_3$) with assigned resonances and peak integration values indicating changes in [**G2**] in the presence of equimolar benzyl amine at 160 °C. [**G2**] at each timepoint was calculated using the integration value of the **G2** resonance at δ = 1.18 ppm, with the aromatic resonance (δ = 6.09 ppm) of 1,3,5-trimethoxybenzene as an internal standard; specific data is that of Trial 2. Stacked spectra are clipped vertically for clarity. b) Plot of ln([**G2**]) versus time. The linear best fit of each trial was used to calculate *k*. The point at 0 sec was not used for fitting, as the time between 0 and 60 sec involved a temperature increase from 100 to 160 °C.

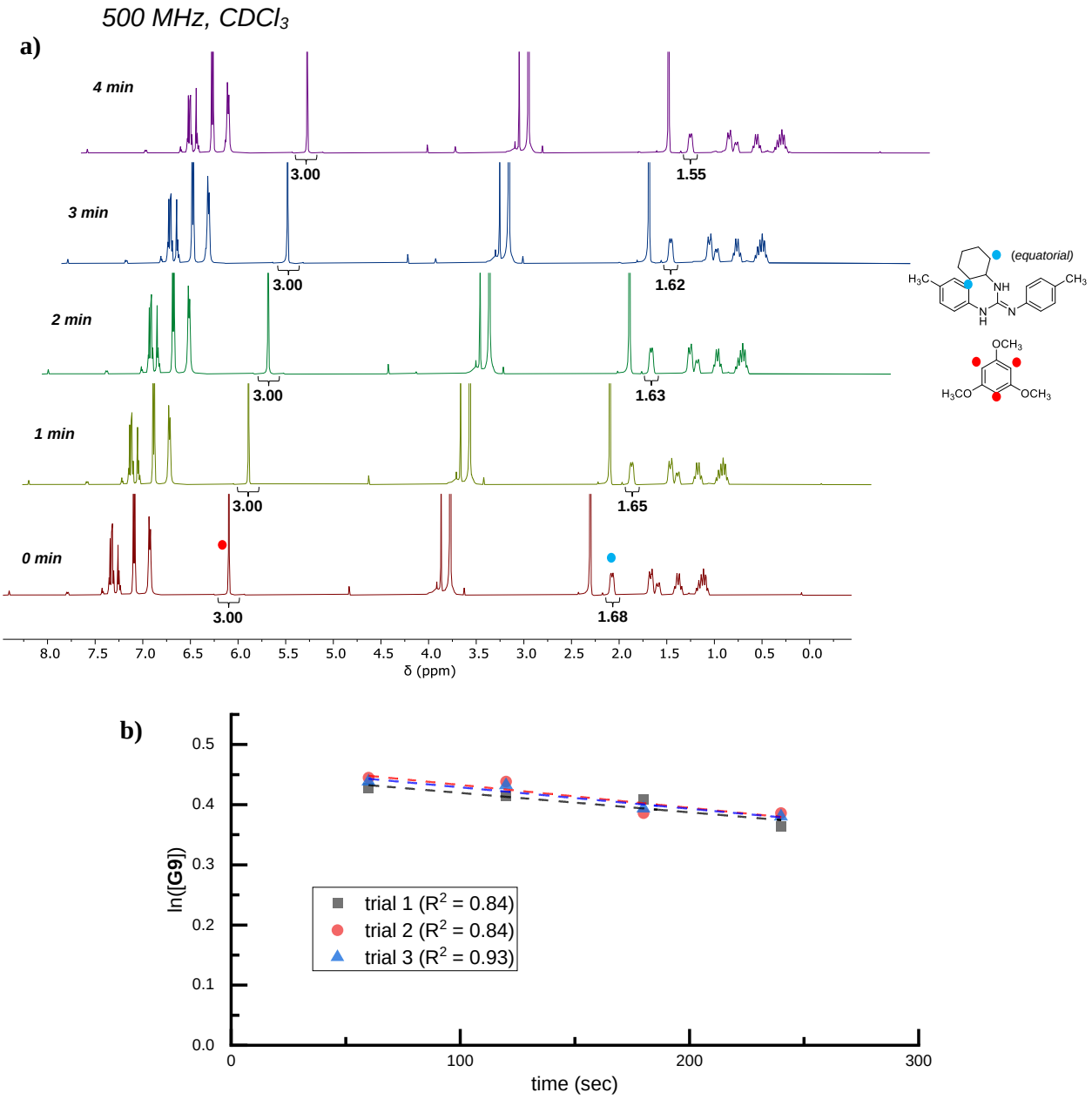


Figure S11. a) Representative ^{1}H NMR spectra (500 MHz, $CDCl_3$) with assigned resonances and peak integration values indicating changes in [**G9**] in the presence of equimolar benzyl amine at 160 °C. [**G9**] at each timepoint was calculated using the integration value of the **G9** resonance at δ = 2.07 ppm, with the aromatic resonance (δ = 6.09 ppm) of 1,3,5-trimethoxybenzene as an internal standard; specific data is that of Trial 1. Stacked spectra are clipped vertically for clarity. b) Plot of ln([**G9**]) versus time. The linear best fit of each trial was used to calculate *k*. The point at 0 sec was not used for fitting, as the time between 0 and 60 sec involved a temperature increase from 100 to 160 °C.

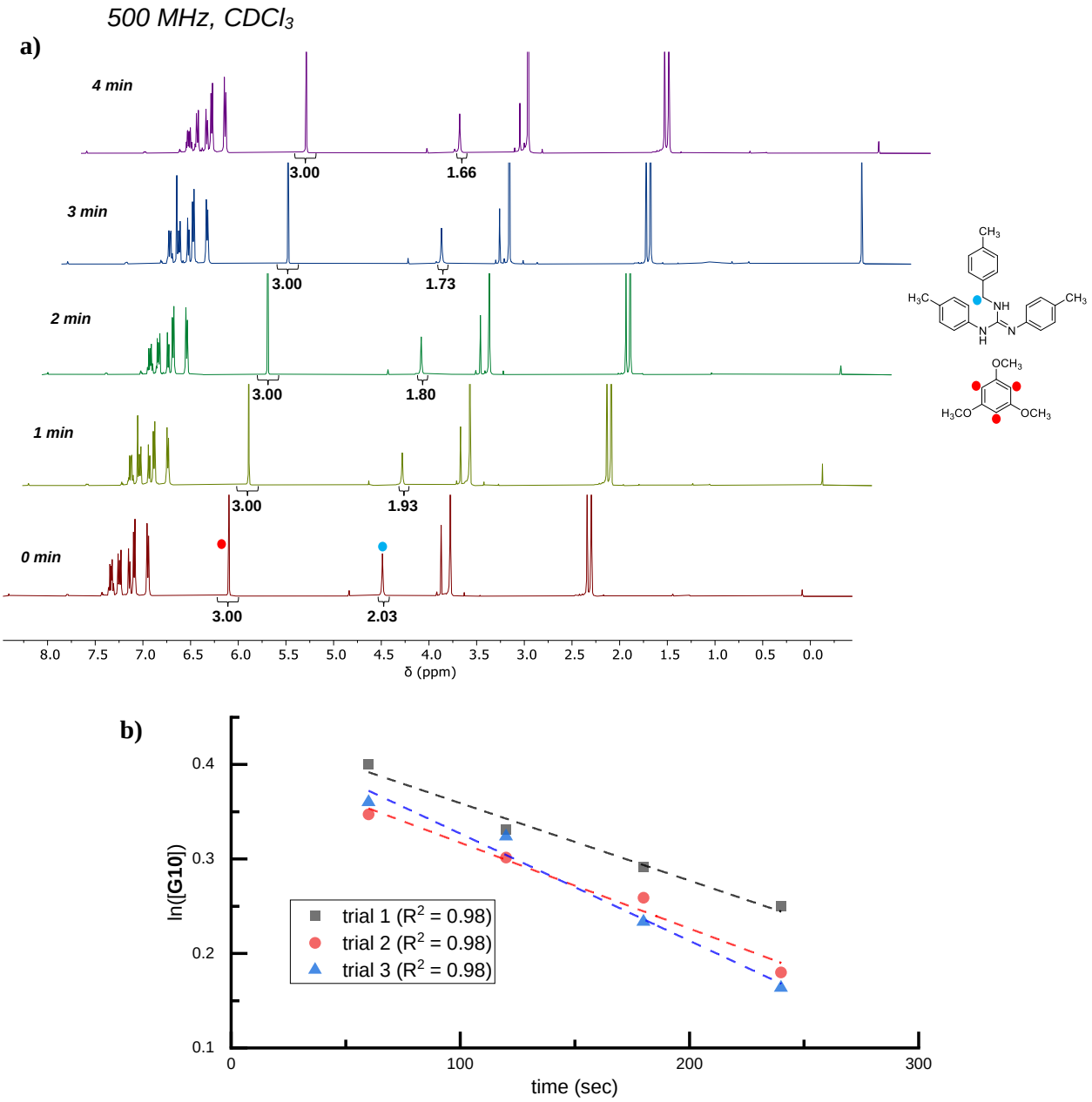


Figure S12. a) Representative ^{1}H NMR spectra (500 MHz, $CDCl_3$) with assigned resonances and peak integration values indicating changes in [**G10**] in the presence of equimolar benzyl amine at 160 °C. [**G10**] at each timepoint was calculated using the integration value of the **G10** resonance at δ = 4.50 ppm, with the aromatic resonance (δ = 6.09 ppm) of 1,3,5-trimethoxybenzene as an internal standard; specific data is that of Trial 1. Stacked spectra are clipped vertically for clarity. b) Plot of ln([**G10**]) versus time. The linear best fit of each trial was used to calculate *k*. The point at 0 sec was not used for fitting, as the time between 0 and 60 sec involved a temperature increase from 100 to 160 °C.

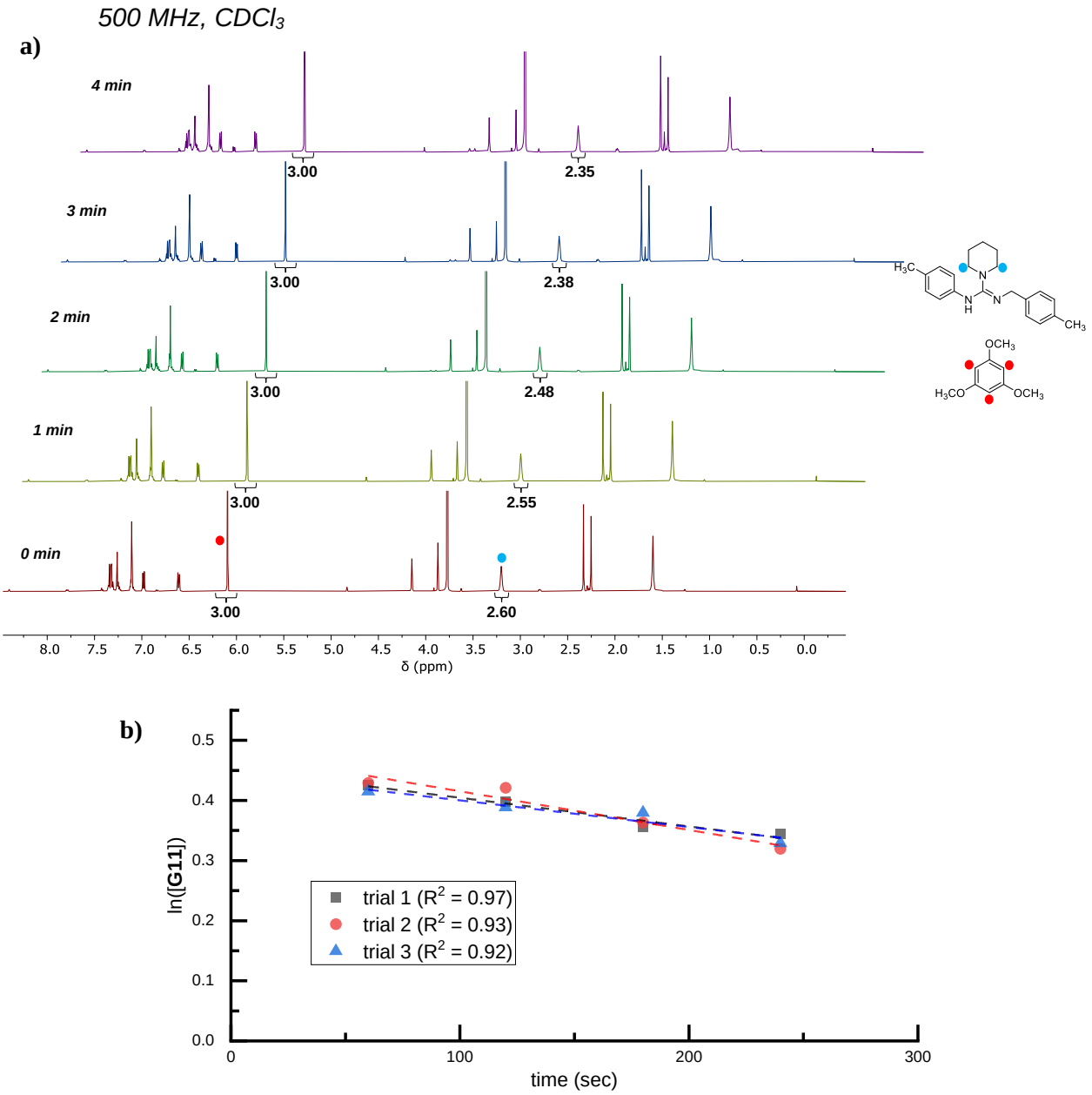


Figure S13. a) Representative ^{1}H NMR spectra (500 MHz, $CDCl_3$) with assigned resonances and peak integration values indicating changes in [**G11**] in the presence of equimolar benzyl amine at 160 °C. [**G11**] at each timepoint was calculated using the integration value of the **G11** resonance at δ = 3.20 ppm, with the aromatic resonance (δ = 6.09 ppm) of 1,3,5-trimethoxybenzene as an internal standard; specific data is that of Trial 1. Stacked spectra are clipped vertically for clarity. b) Plot of ln([**G11**]) versus time. The linear best fit of each trial was used to calculate *k*. The point at 0 sec was not used for fitting, as the time between 0 and 60 sec involved a temperature increase from 100 to 160 °C.

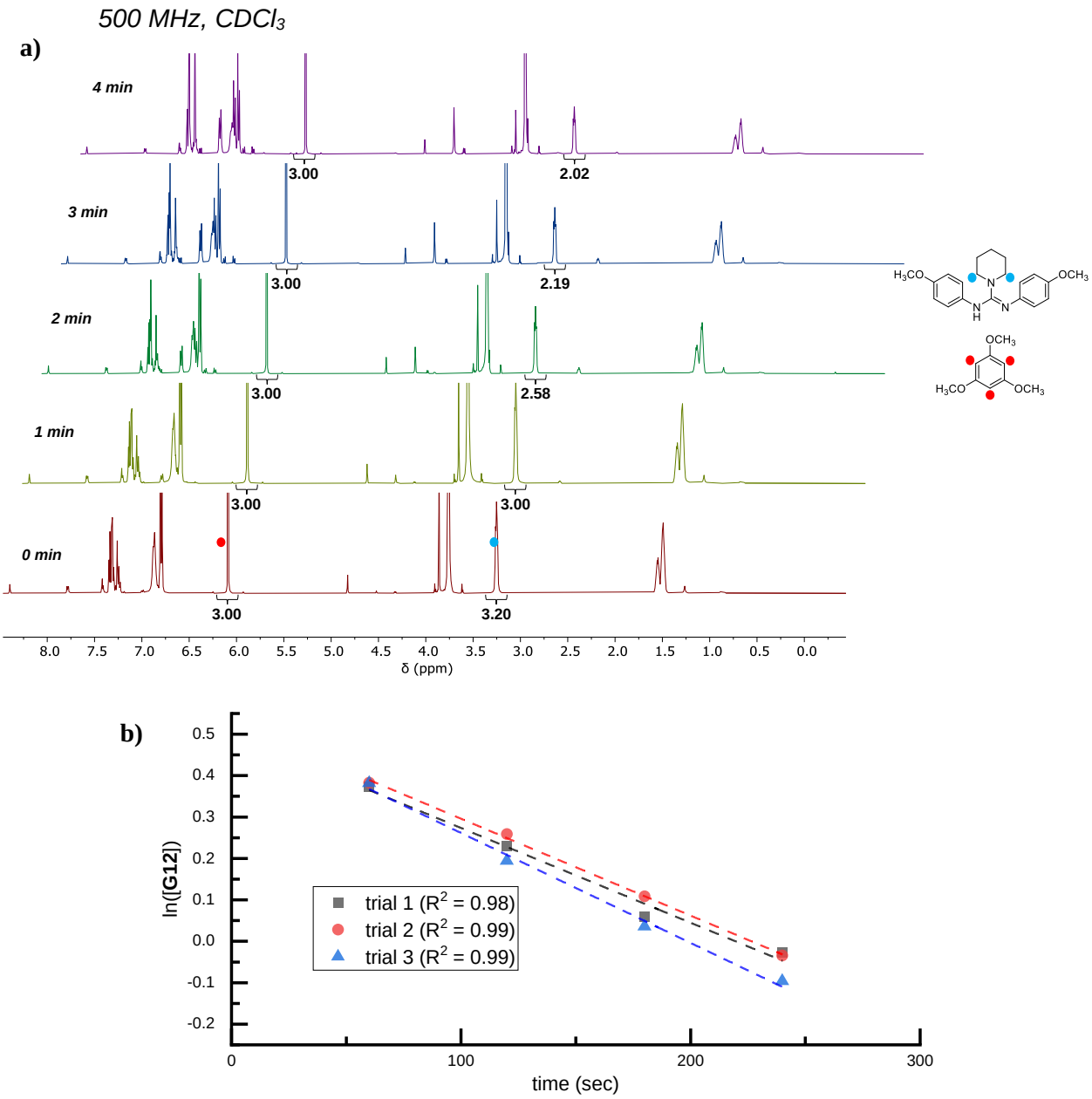


Figure S14. a) Representative ^{1}H NMR spectra (500 MHz, $CDCl_3$) with assigned resonances and peak integration values indicating changes in [**G12**] in the presence of equimolar benzyl amine at 160 °C. [**G12**] at each timepoint was calculated using the integration value of the **G12** resonance at δ = 3.25 ppm, with the aromatic resonance (δ = 6.09 ppm) of 1,3,5-trimethoxybenzene as an internal standard; specific data is that of Trial 1. Stacked spectra are clipped vertically for clarity. b) Plot of ln([**G12**]) versus time. The linear best fit of each trial was used to calculate *k*. The point at 0 sec was not used for fitting, as the time between 0 and 60 sec involved a temperature increase from 100 to 160 °C.

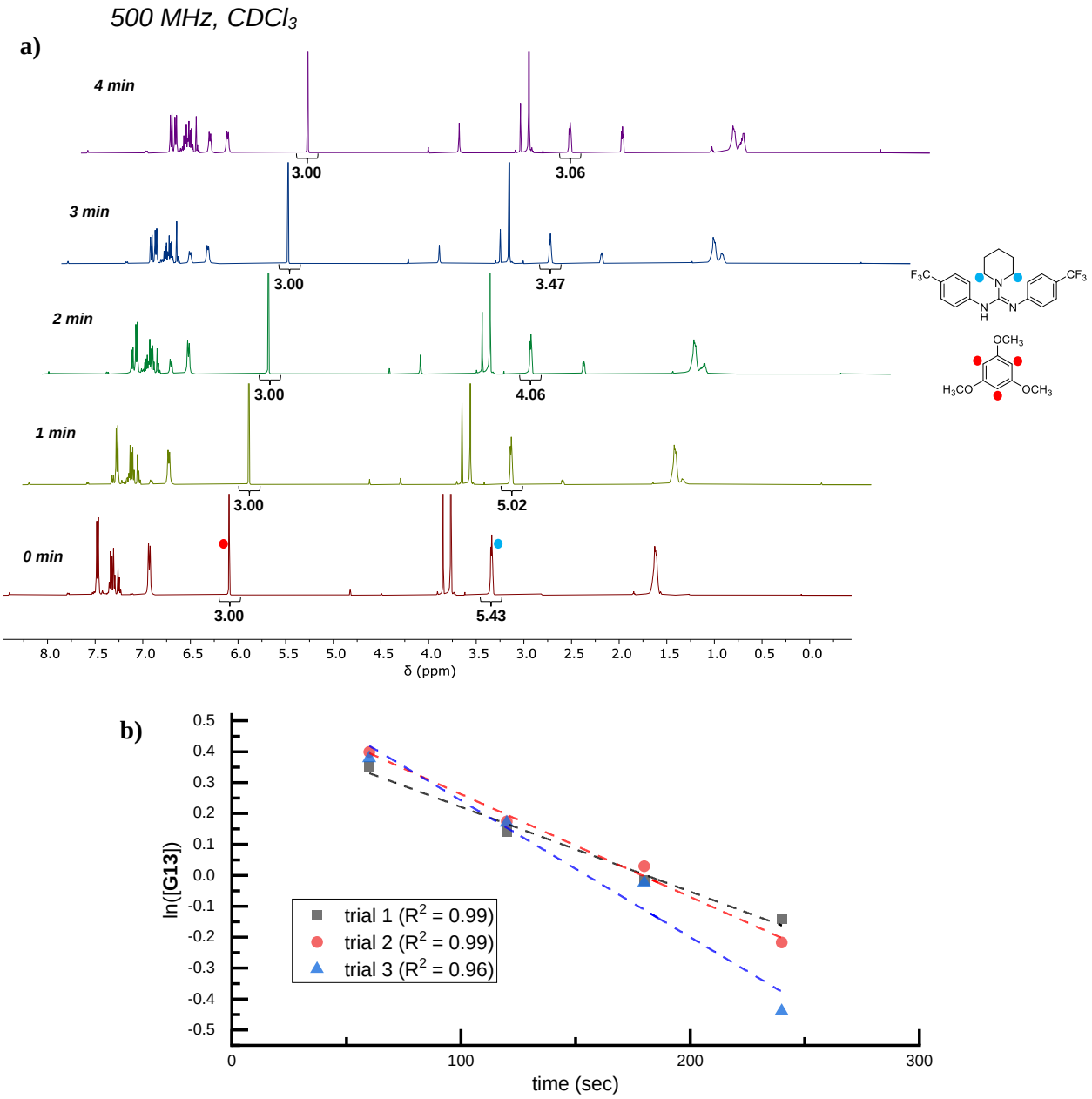


Figure S15. a) Representative ^{1}H NMR spectra (500 MHz, $CDCl_3$) with assigned resonances and peak integration values indicating changes in [**G13**] in the presence of equimolar benzyl amine at 160 °C. [**G13**] at each timepoint was calculated using the integration value of the **G13** resonance at δ = 3.35 ppm, with the aromatic resonance (δ = 6.09 ppm) of 1,3,5-trimethoxybenzene as an internal standard; specific data is that of Trial 1. Stacked spectra are clipped vertically for clarity. b) Plot of ln([**G13**]) versus time. The linear best fit of each trial was used to calculate *k*. The point at 0 sec was not used for fitting, as the time between 0 and 60 sec involved a temperature increase from 100 to 160 °C.

Table S1. Data for TGM kinetic experiments conducted at 160 °C (main text Table 2).

Guanidine	Trial	$[Guanidine]_{initial}$ (M)	$[benzyl\ amine]_{initial}$ (M)	k (s^{-1})
G1	1	1.6	1.6	3.4×10^{-3}
G1	2	1.6	1.6	2.4×10^{-3}
G1	3	1.6	1.6	2.7×10^{-3}
G2	1	1.6	1.6	7.2×10^{-3}
G2	2	1.5	1.5	6.2×10^{-3}
G2	3	1.5	1.5	6.1×10^{-3}
G9	1	1.6	1.6	3.2×10^{-4}
G9	2	1.6	1.6	3.8×10^{-4}
G9	3	1.6	1.6	3.6×10^{-4}
G10	1	1.5	1.5	8.2×10^{-4}
G10	2	1.5	1.5	9.1×10^{-4}
G10	3	1.5	1.5	1.1×10^{-3}
G11	1	1.6	1.6	4.8×10^{-4}
G11	2	1.6	1.6	6.4×10^{-4}
G11	3	1.6	1.6	4.4×10^{-4}
G12	1	1.6	1.6	2.3×10^{-3}
G12	2	1.6	1.6	2.3×10^{-3}
G12	3	1.6	1.6	2.7×10^{-3}
G13	1	1.5	1.5	2.7×10^{-3}
G13	2	1.5	1.5	3.3×10^{-3}
G13	3	1.5	1.5	4.4×10^{-3}

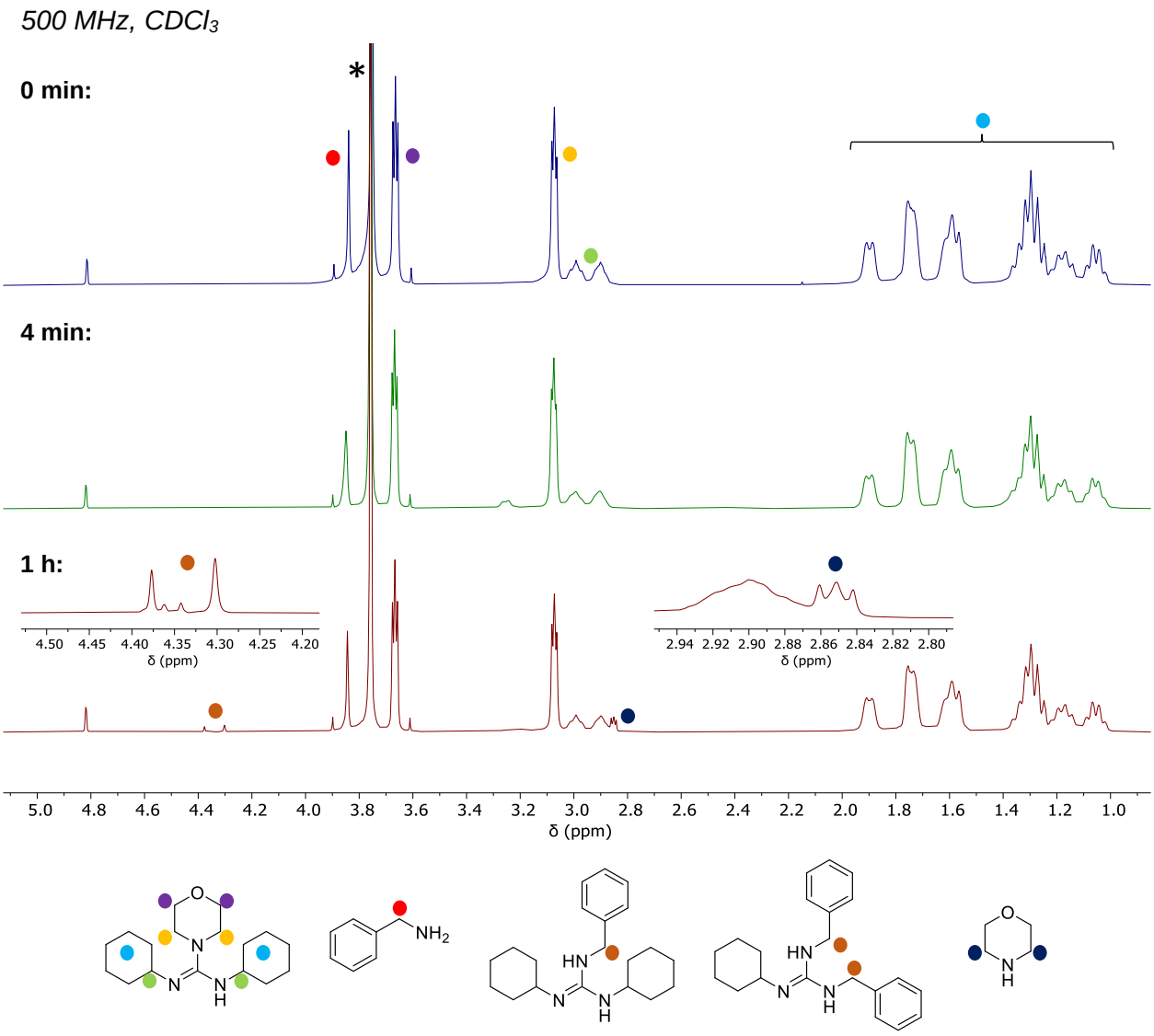


Figure S16. ^{1}H NMR spectra (500 MHz, $CDCl_3$) and assigned resonances of **G14**, equimolar benzyl amine, and potential new guanidines after different intervals of reaction time at 160 °C. No detectable amount of reaction has occurred under the standard conditions for kinetic experiments (4 min). A small amount of TGM product may potentially be present after 1h based on the appearance of new benzylic resonances at 4.37 ppm and 4.30 ppm and the appearance of a resonance assigned to free morpholine at 2.86 ppm. Inset: magnification of benzylic resonances (left) and morpholine resonances (right). * = 1,3,5-trimethoxybenzene (internal standard)

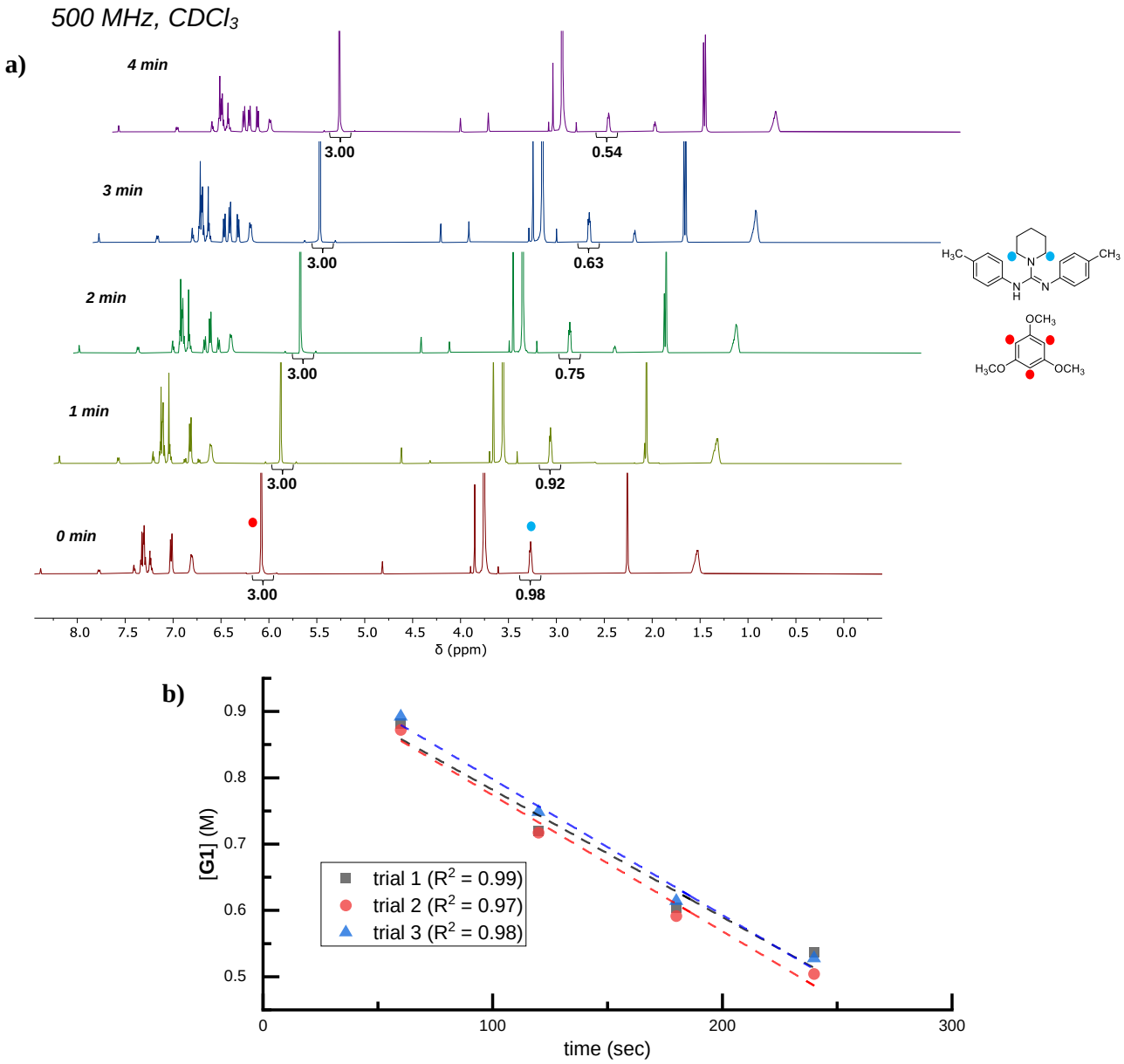


Figure S17. a) Representative ^{1}H NMR spectra (500 MHz, $CDCl_3$) with assigned resonances and peak integration values indicating changes in [**G1**] at 0.94 M in the presence of 1.6 M benzyl amine at 160 °C (initial concentrations). [**G1**] at each timepoint was calculated using the integration value of the **G1** resonance at δ = 3.28 ppm, with the aromatic resonance (δ = 6.09 ppm) of 1,3,5-trimethoxybenzene as an internal standard; specific data is that of Trial 1. Stacked spectra are clipped vertically for clarity. b) Plot of [**G1**] versus time. The linear best fit of each trial was used to calculate reaction rate. The point at 0 sec was not used for fitting, as the time between 0 and 60 sec involved a temperature increase from 100 to 160 °C.

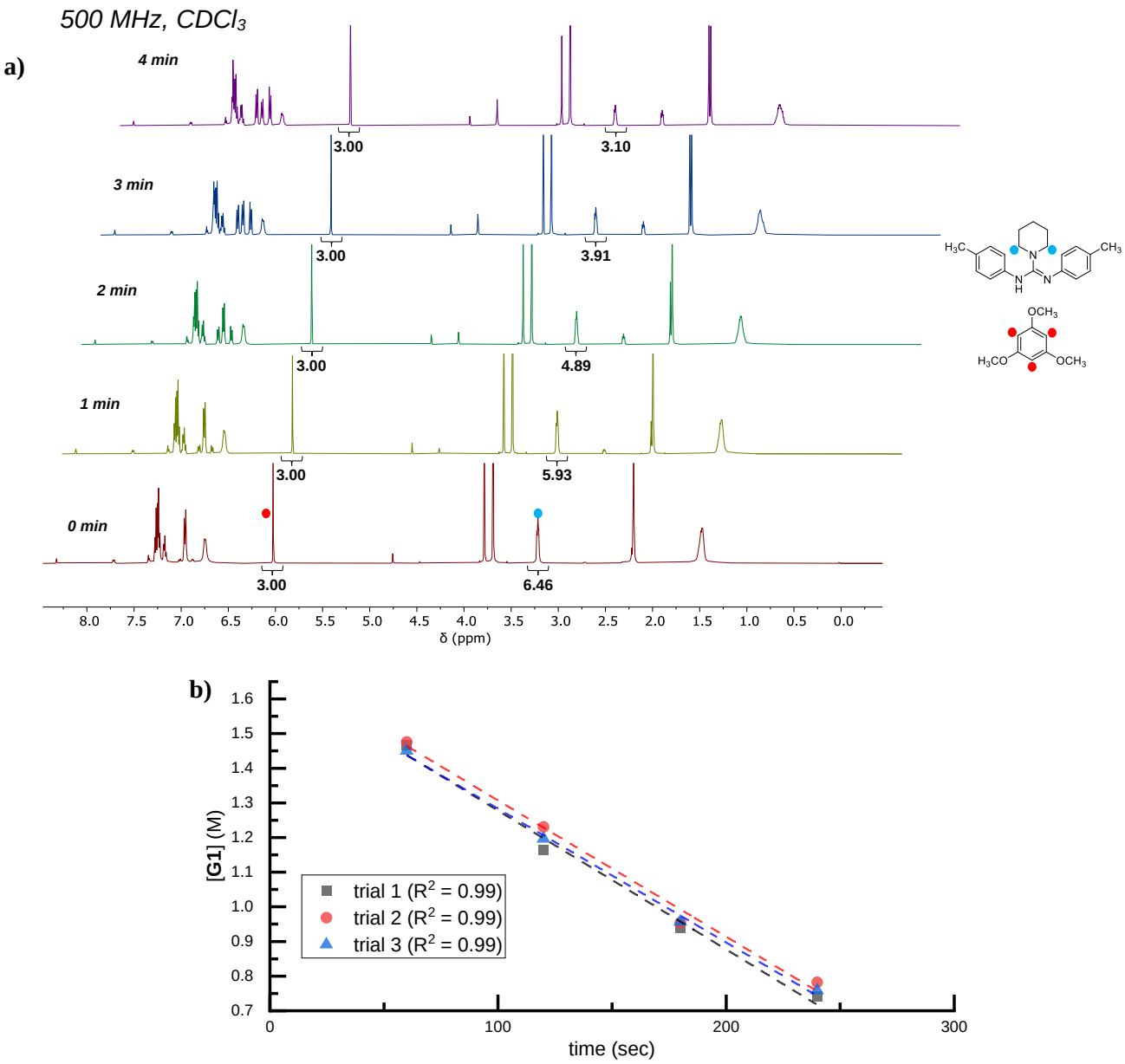


Figure S18. a) Representative ^{1}H NMR spectra (500 MHz, $CDCl_3$) with assigned resonances and peak integration values indicating changes in [**G1**] at 1.6 M in the presence of 3.2 M benzyl amine at 160 °C (initial concentrations). [**G1**] at each timepoint was calculated using the integration value of the **G1** resonance at δ = 3.28 ppm, with the aromatic resonance (δ = 6.09 ppm) of 1,3,5-trimethoxybenzene as an internal standard; specific data is that of Trial 3. Stacked spectra are clipped vertically for clarity b) Plot of [**G1**] versus time. The linear best fit of each trial was used to calculate reaction rate. The point at 0 sec was not used for fitting, as the time between 0 and 60 sec involved a temperature increase from 100 to 160 °C.

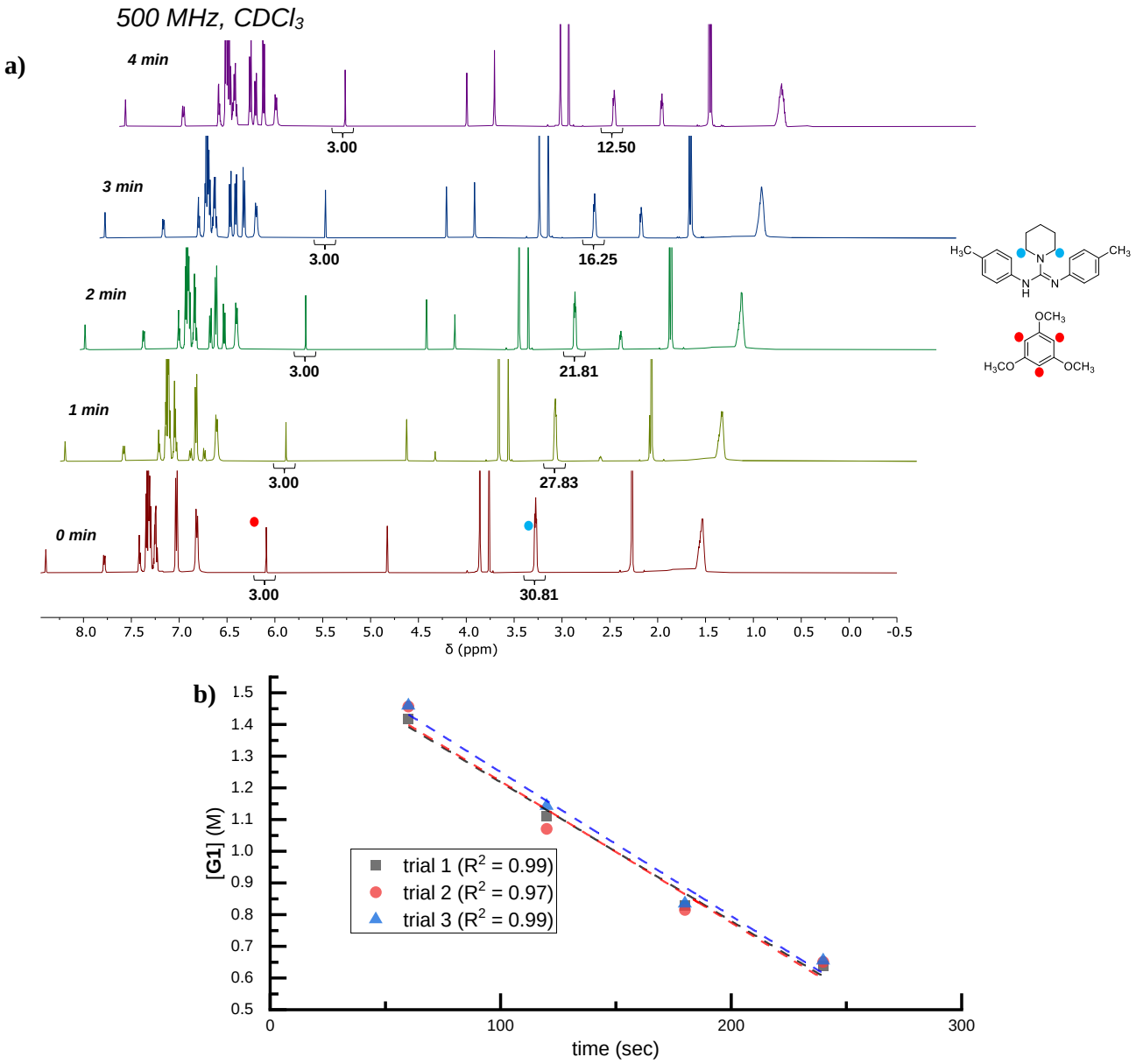


Figure S19. a) Representative ^{1}H NMR spectra (500 MHz, $CDCl_3$) with assigned resonances and peak integration values indicating changes in [**G1**] at 1.5 M in the presence of 4.6 M benzyl amine at 160 °C (initial concentrations). [**G1**] at each timepoint was calculated using the integration value of the **G1** resonance at δ = 3.28 ppm, with the aromatic resonance (δ = 6.09 ppm) of 1,3,5-trimethoxybenzene as an internal standard; specific data is that of Trial 1. Stacked spectra are clipped vertically for clarity. b) Plot of [**G1**] versus time. The linear best fit of each trial was used to calculate reaction rate. The point at 0 sec was not used for fitting, as the time between 0 and 60 sec involved a temperature increase from 100 to 160 °C.

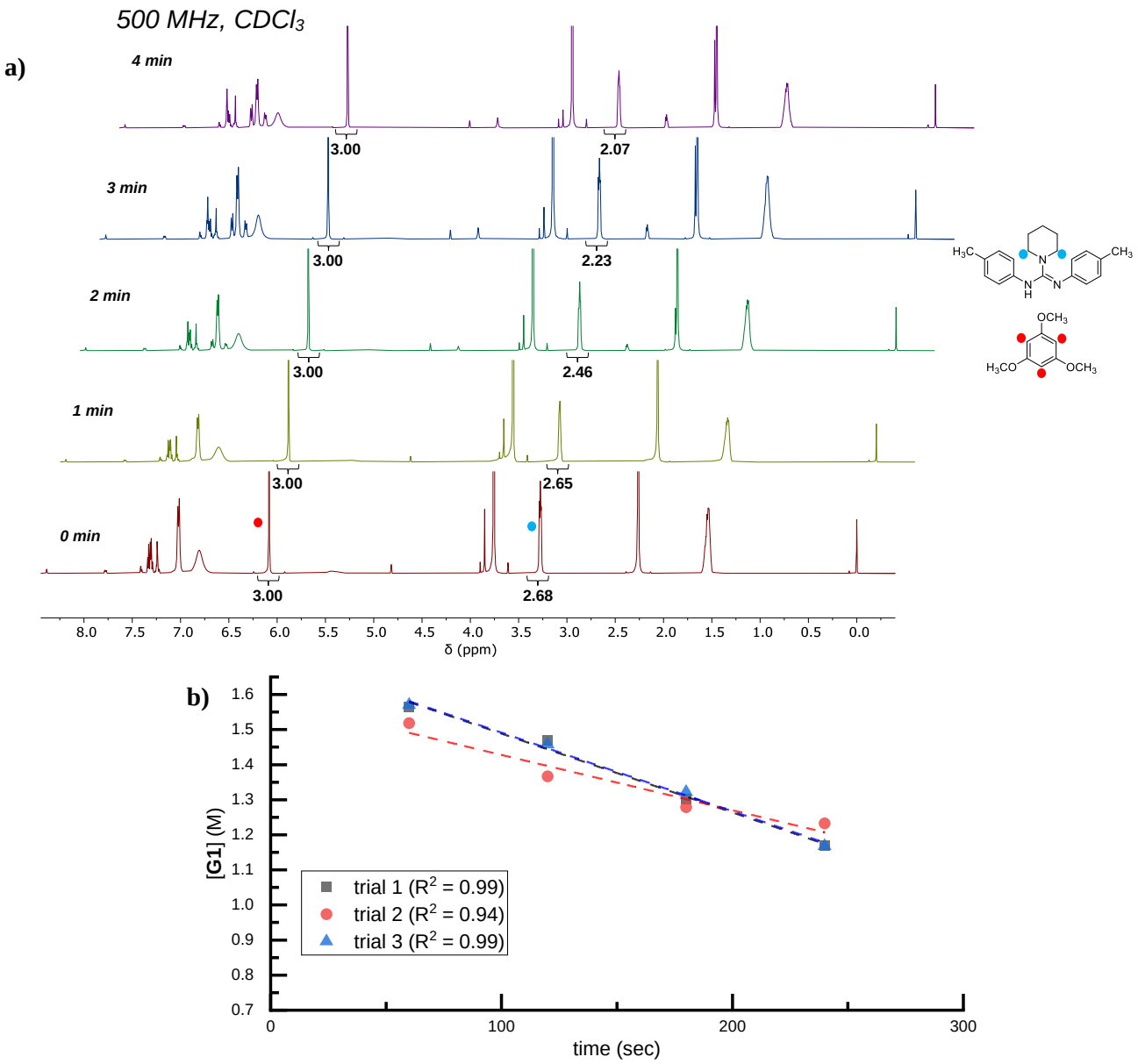


Figure S20. a) Representative ^{1}H NMR spectra (500 MHz, $CDCl_3$) with assigned resonances and peak integration values indicating changes in [**G1**] at 1.6 M in the presence of 0.8 M benzyl amine at 160 °C (initial concentrations). [**G1**] at each timepoint was calculated using the integration value of the **G1** resonance at δ = 3.28 ppm, with the aromatic resonance (δ = 6.09 ppm) of 1,3,5-trimethoxybenzene as an internal standard; specific data is that of Trial 3. Stacked spectra are clipped vertically for clarity. b) Plot of [**G1**] versus time. The linear best fit of each trial was used to calculate reaction rate. The point at 0 sec was not used for fitting, as the time between 0 and 60 sec involved a temperature increase from 100 to 160 °C.

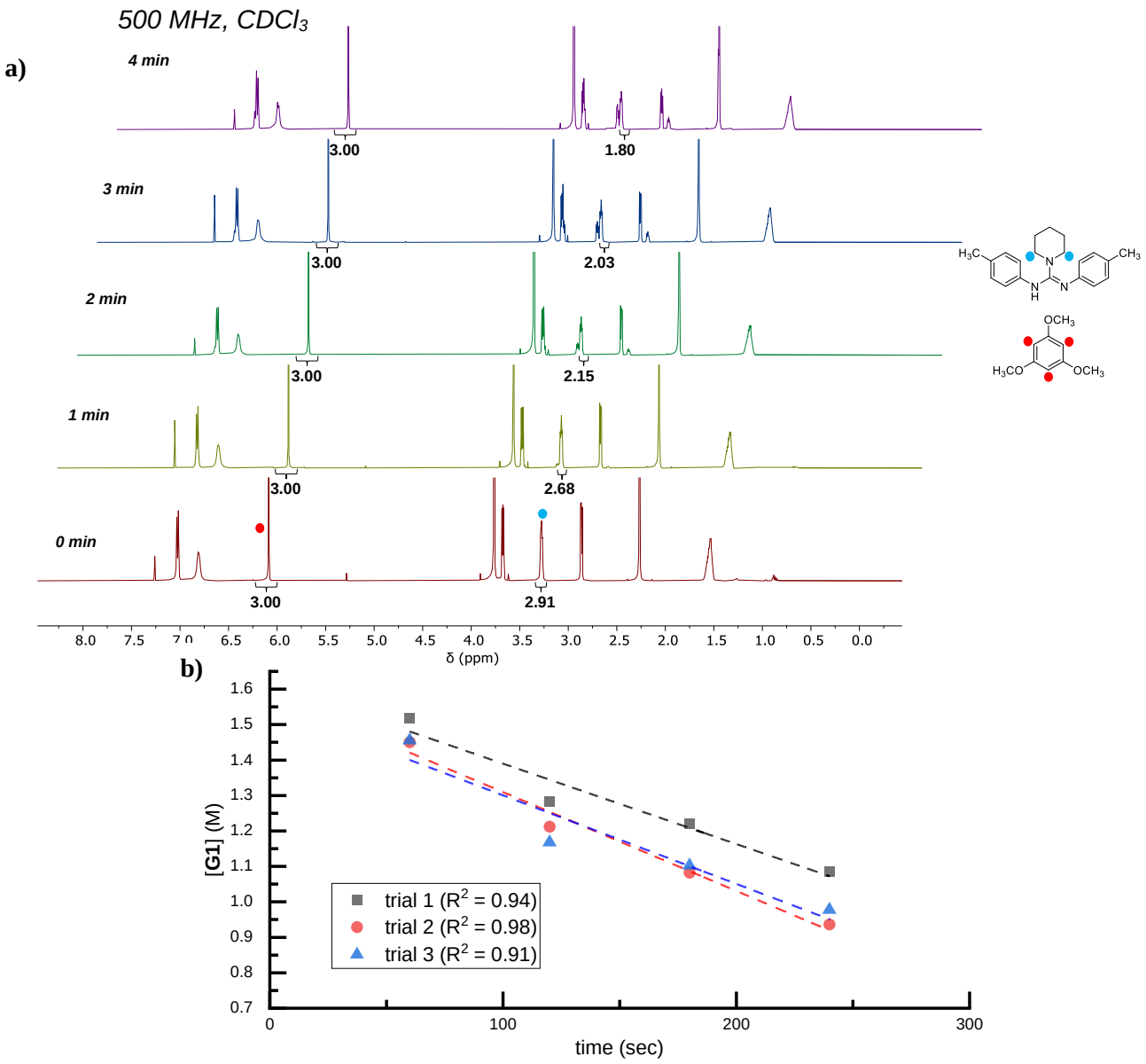


Figure S21. a) Representative ^{1}H NMR spectra (500 MHz, $CDCl_3$) with assigned resonances and peak integration values indicating changes in [**G1**] at 1.6 M in the presence of 1.6 M morpholine at 160 °C (initial concentrations). [**G1**] at each timepoint was calculated using the integration value of the **G1** resonance at δ = 3.28 ppm, with the aromatic resonance (δ = 6.09 ppm) of 1,3,5-trimethoxybenzene as an internal standard; specific data is that of Trial 1. Stacked spectra are clipped vertically for clarity. b) Plot of [**G1**] versus time. The linear best fit of each trial was used to calculate reaction rate. The point at 0 sec was not used for fitting, as the time between 0 and 60 sec involved a temperature increase from 100 to 160 °C.

Table S2. Data for TGM kinetic experiments of **G1** conducted at 160 °C (main text Table 3).

Trial	$[G1]_{initial}$ (M)	$[benzyl\ amine]_{initial}$ (M)	Rate ($M\ s^{-1}$)
1	1.6	1.6	3.9×10^{-3}
2	1.6	1.6	3.1×10^{-3}
3	1.6	1.6	3.1×10^{-3}
1	0.94	1.6	1.9×10^{-3}
2	0.94	1.6	2.1×10^{-3}
3	0.94	1.6	2.1×10^{-3}
1	1.6	3.2	3.8×10^{-3}
2	1.6	3.2	4.0×10^{-3}
3	1.6	3.2	3.9×10^{-3}
1	1.5	4.6	4.4×10^{-3}
2	1.5	4.6	4.5×10^{-3}
3	1.5	4.6	4.5×10^{-3}
1	1.6	0.8	2.3×10^{-3}
2	1.6	0.8	1.6×10^{-3}
3	1.6	0.8	2.2×10^{-3}
1	1.6	[a]1.6	2.3×10^{-3}
2	1.6	[a]1.6	2.8×10^{-3}
3	1.6	[a]1.6	2.5×10^{-3}

[a]Morpholine used in place of benzyl amine.

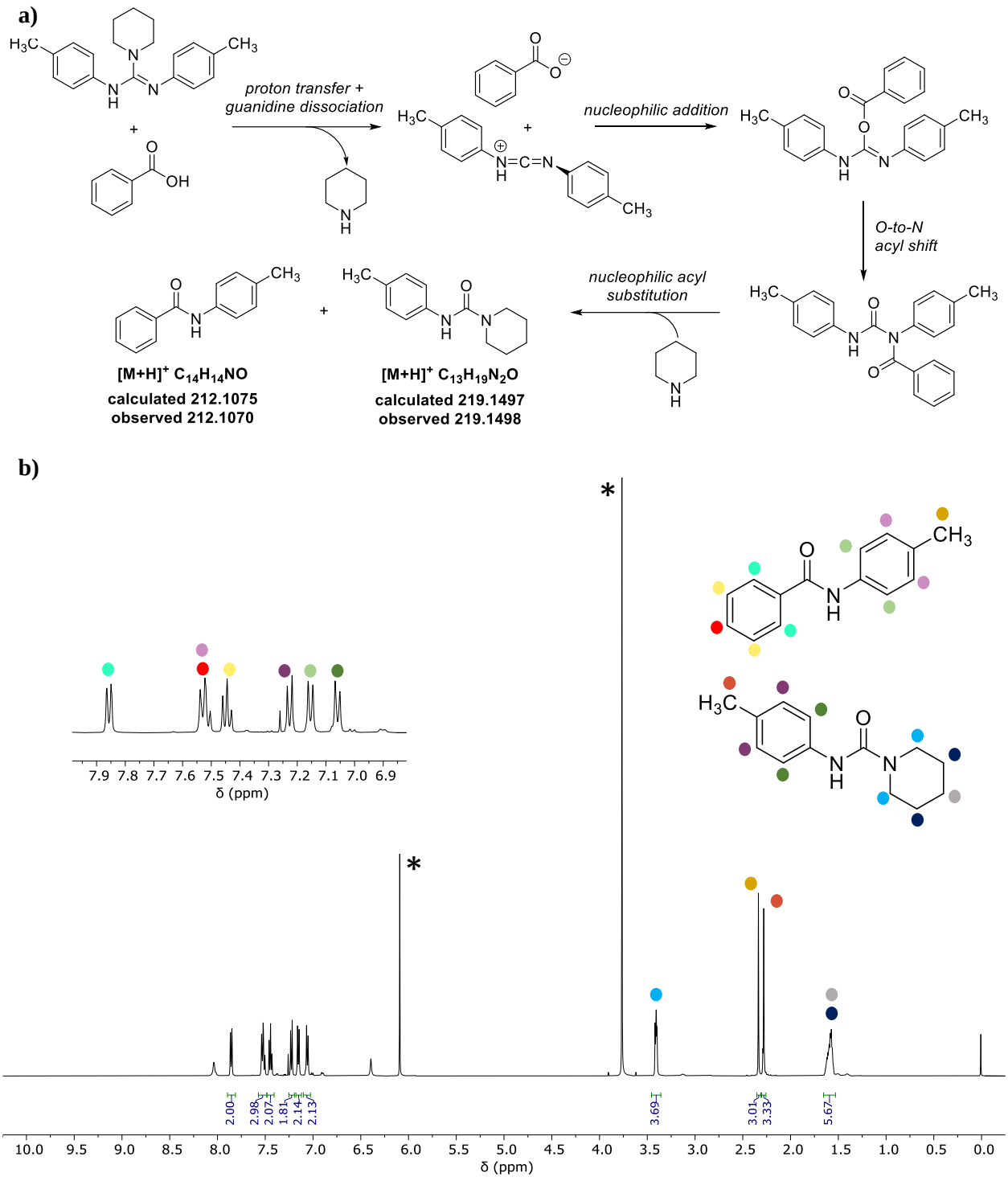
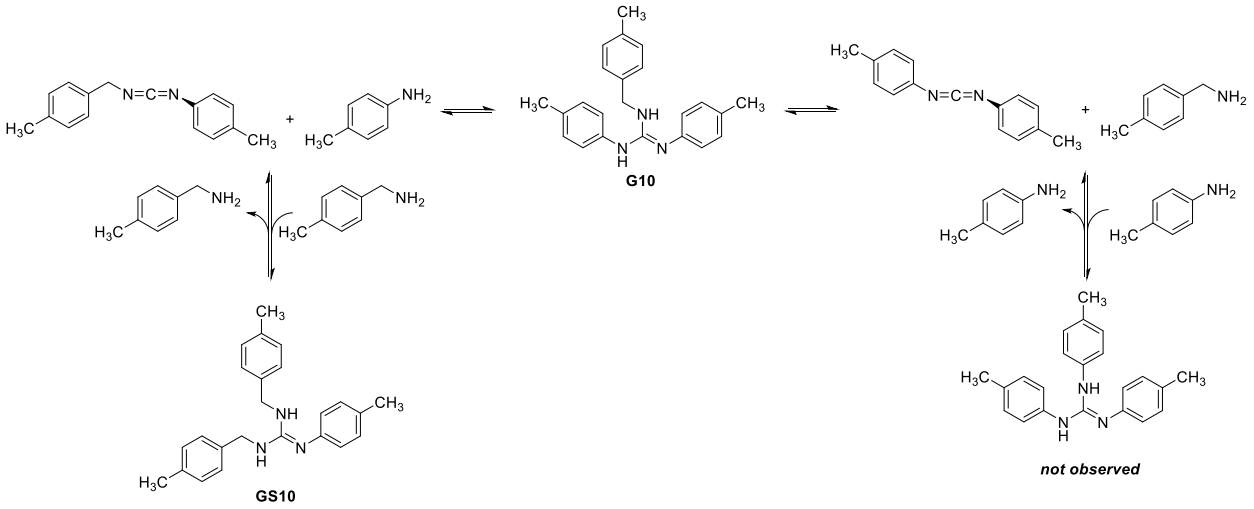


Figure S22. a) Proposed reaction pathway that occurs upon heating equimolar **G1** and benzoic acid to 150 °C. MS results were obtained from a sample of the crude reaction mixture. b) ^{1}H NMR spectrum (500 MHz, $CDCl_3$) and assignments of the products obtained upon heating equimolar **G1** and benzoic acid at 150 °C for 2 h; * = internal standard (1,3,5-trimethoxybenzene).

Scheme S2. Fragmentation pathways of guanidines derived from primary amines and aryl carbodiimides. The equilibrium between **G10** and **GS10** is provided as a representative example.



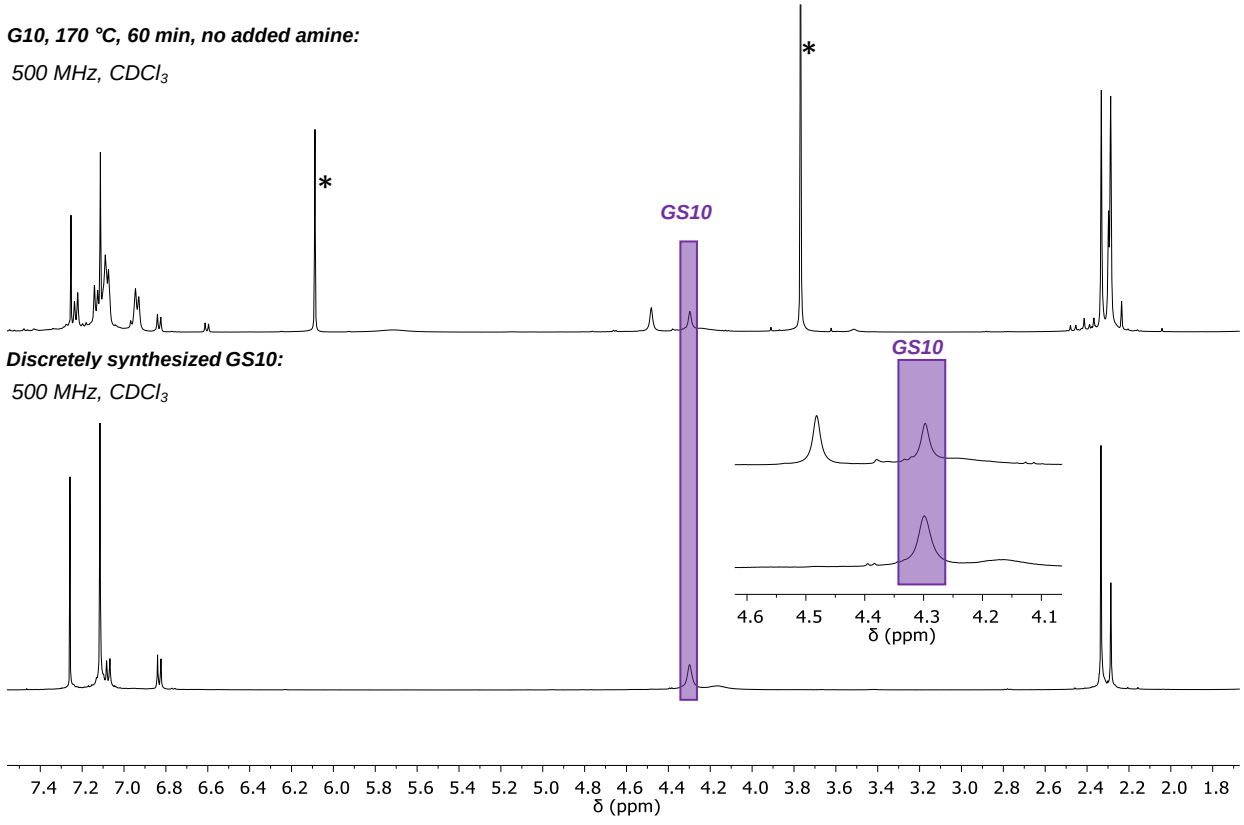


Figure S23. Spectroscopic identification (500 MHz, $CDCl_3$) of guanidine **GS10** derived from TGM reaction of **G10** without added amine. Inset: magnification of benzylic resonances; * = internal standard (1,3,5-trimethoxybenzene). Reproduced with permission from main text reference 29, ©2020 American Chemical Society.

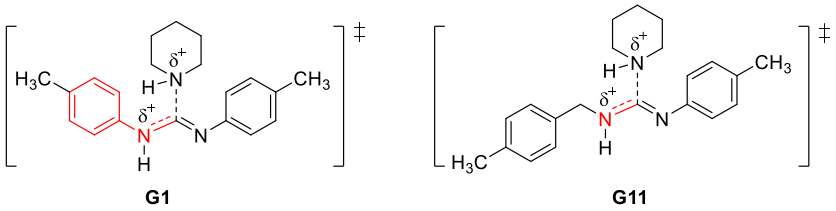
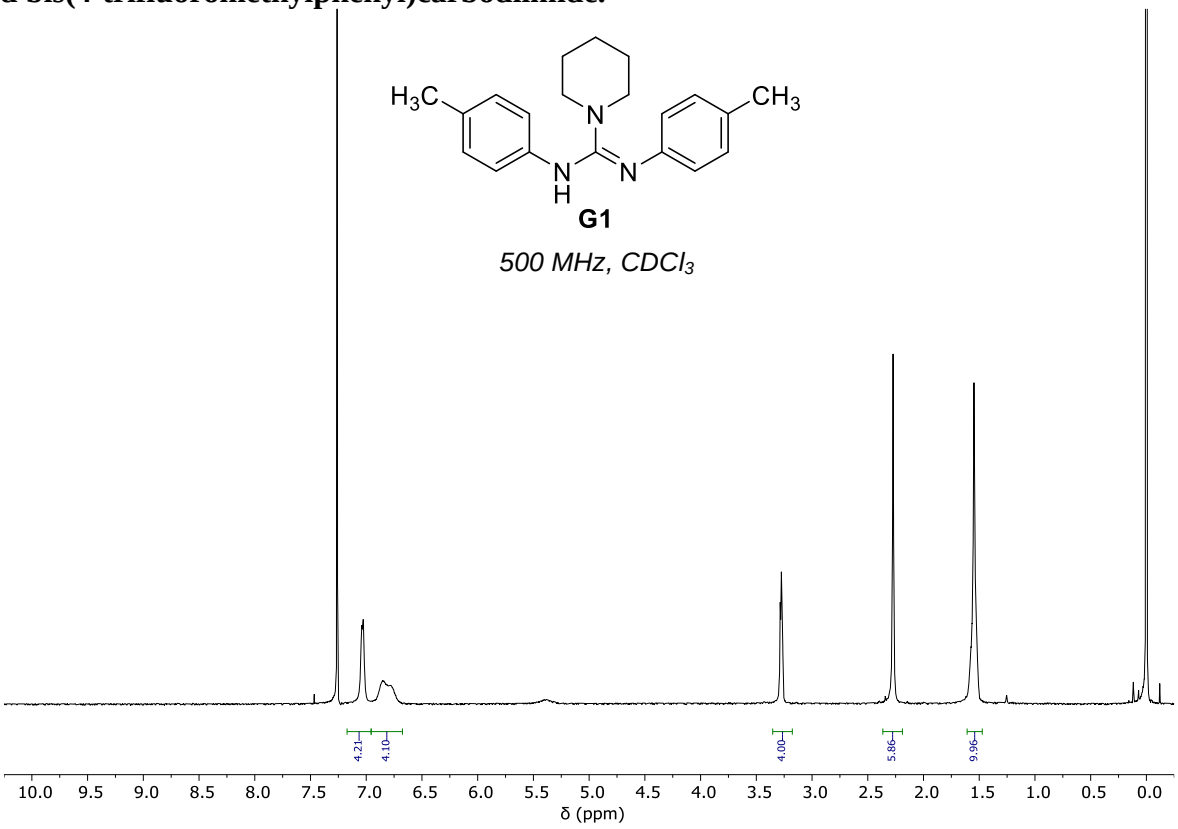
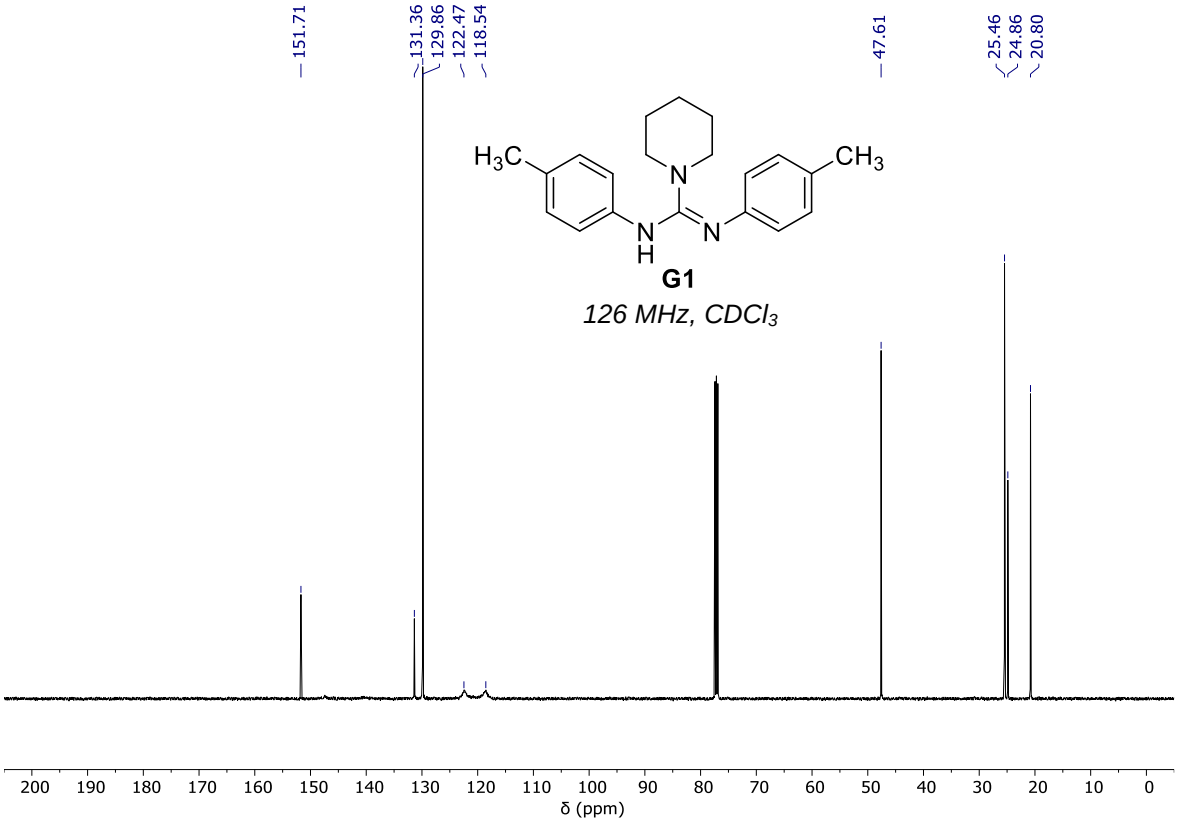
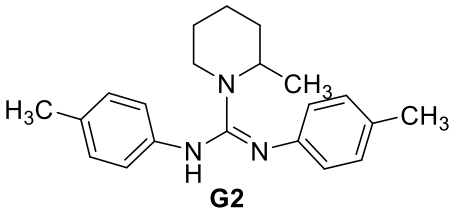


Figure S24. Comparison of the proposed transition states of **G1** and **G11** upon rate-determining fragmentation. The incipient π-system is highlighted in red in both cases; additional resonance stabilization in **G1** results in a faster reaction rate.

^{1}H and ^{13}C{^{1}H} NMR spectra of G1 – G9, G11 – G13, bis(4-methoxyphenyl)carbodiimide, and bis(4-trifluoromethylphenyl)carbodiimide.

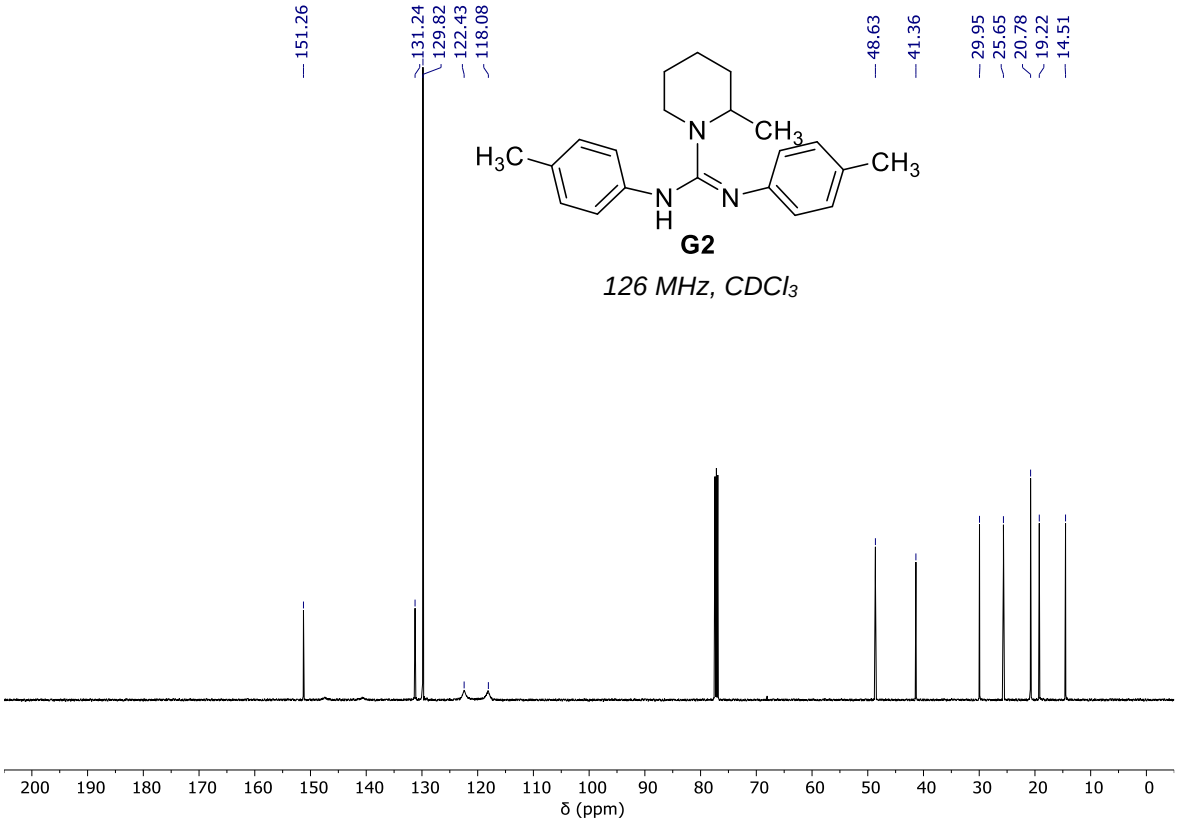






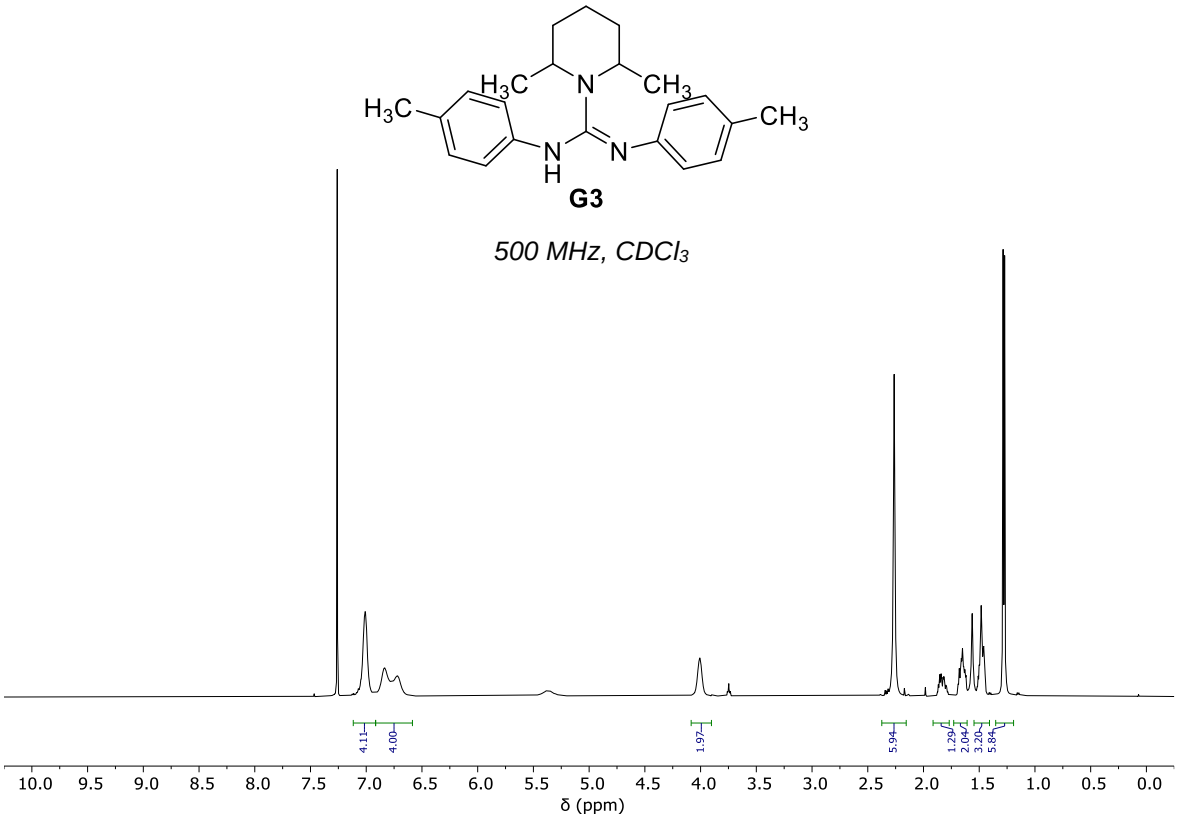
G2

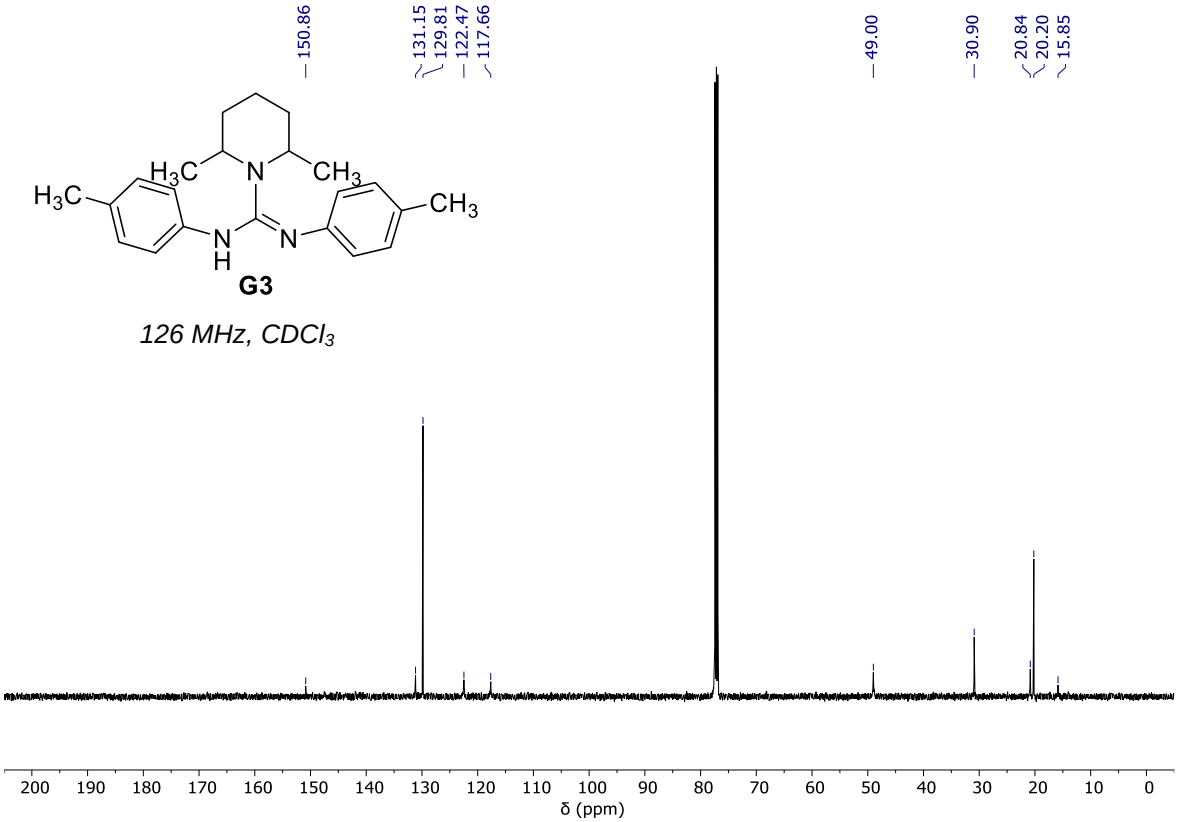
500 MHz, $CDCl_3$

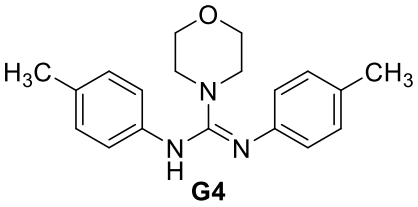


G2

126 MHz, $CDCl_3$

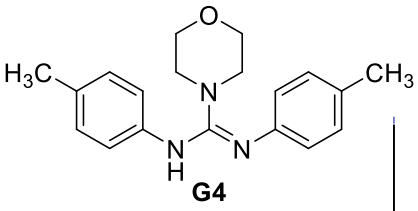

H3C
N
CH3
H3C
CH3
N
H
N
G3
500 MHz, CDCl3
4.11
4.00
1.97
5.94
1.29
2.04
3.20
5.84
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
δ (ppm)


150.86
131.15
129.81
122.47
117.66
49.00
30.90
20.84
20.20
15.85
H3C
N
CH3
H3C
CH3
N
H
N
G3
126 MHz, CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
δ (ppm)



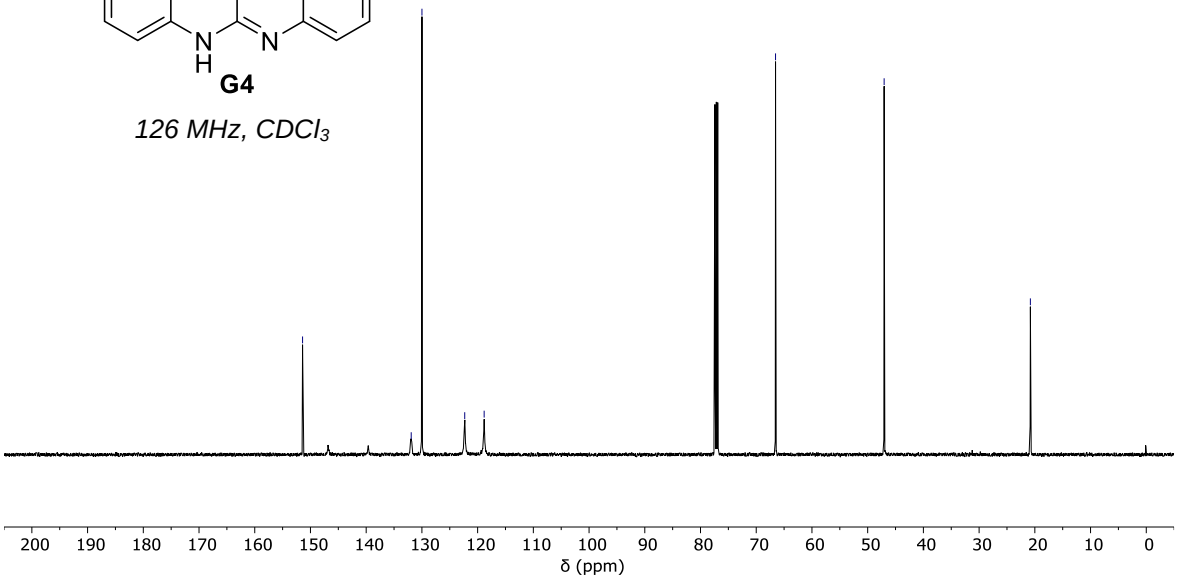
G4

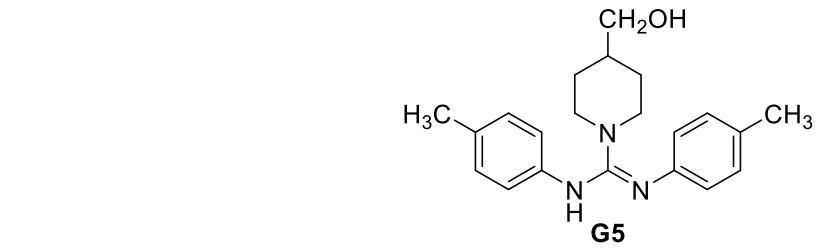
500 MHz, $CDCl_3$



G4

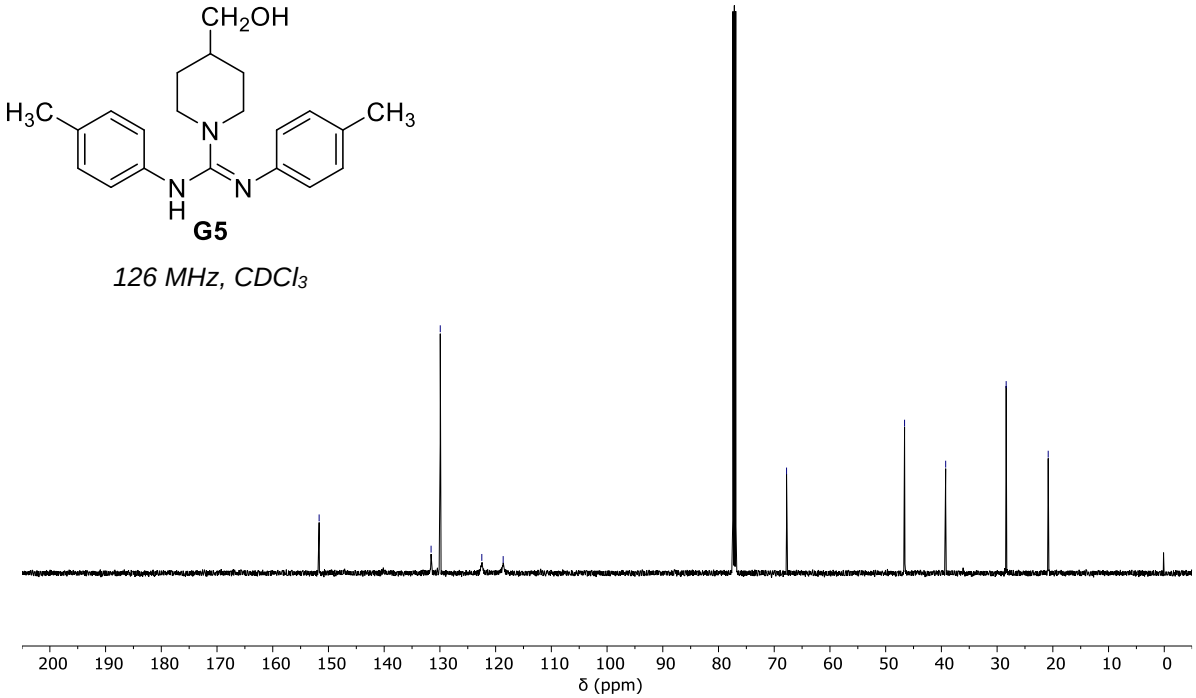
126 MHz, $CDCl_3$





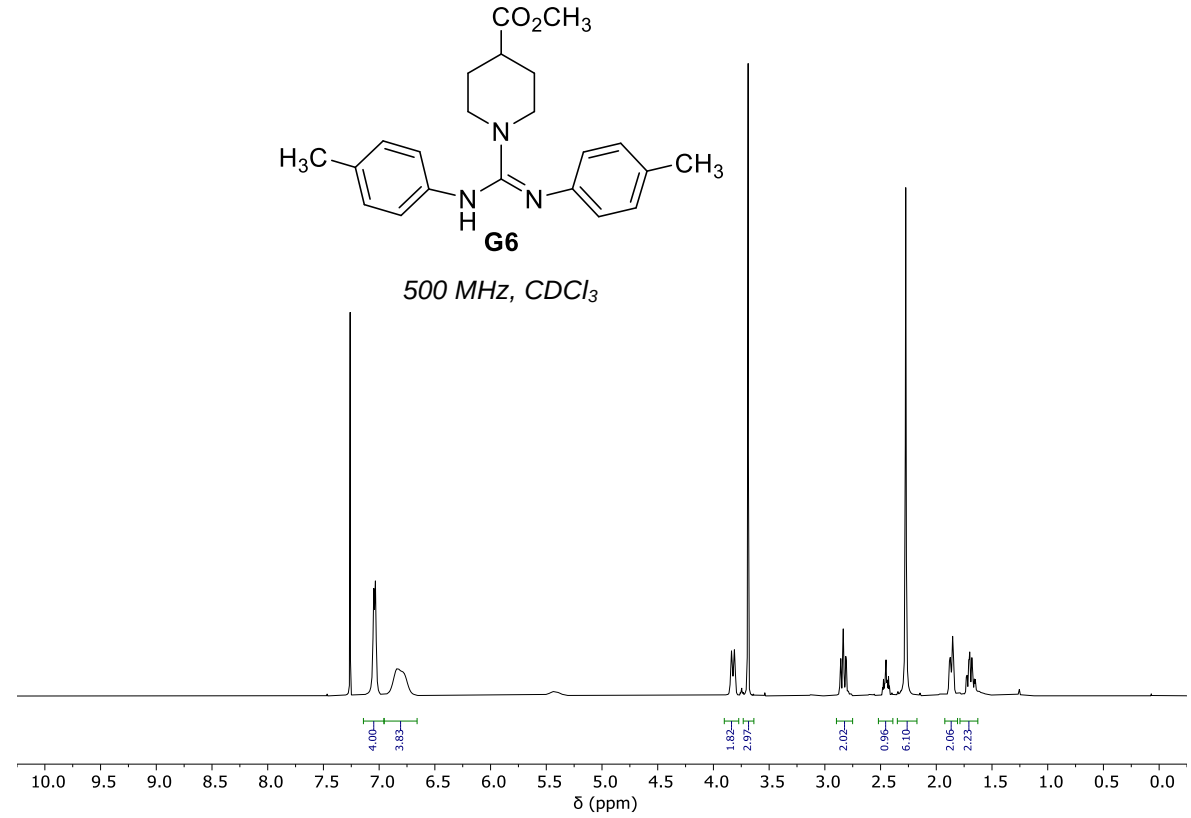
G5

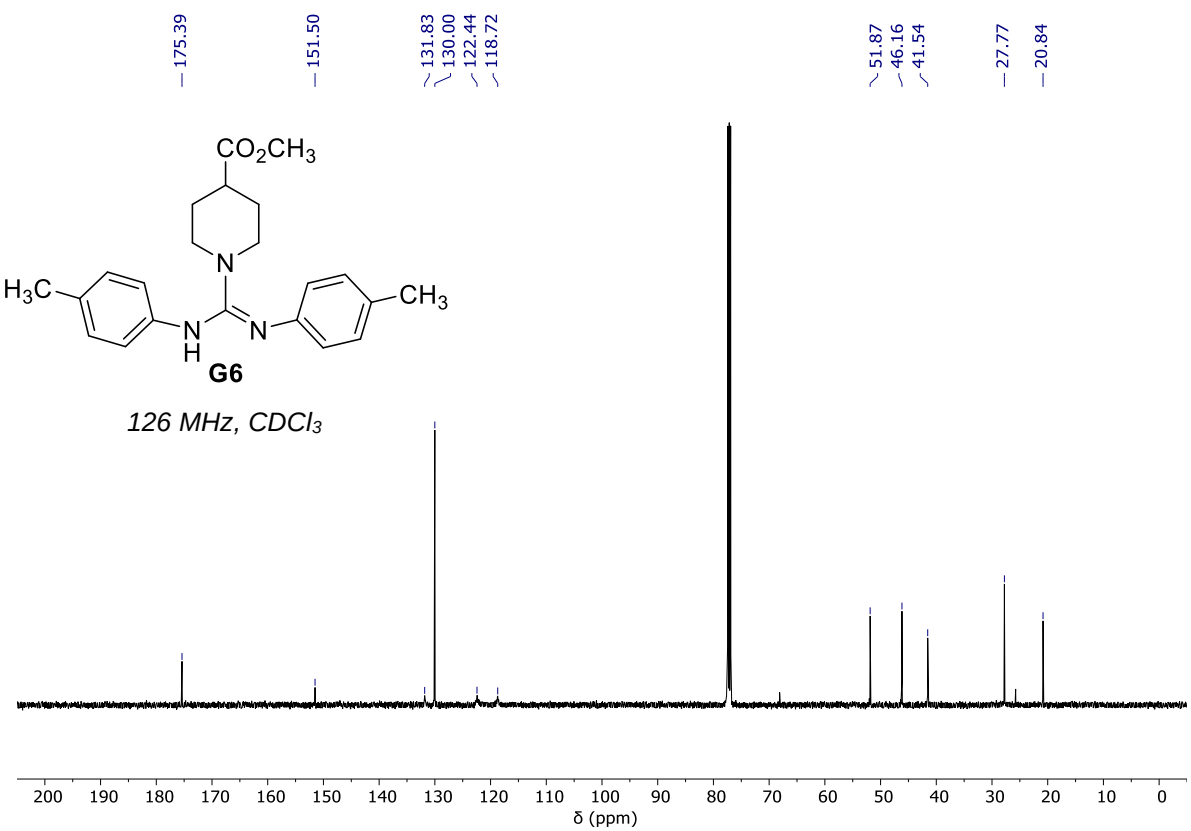
500 MHz, $CDCl_3$

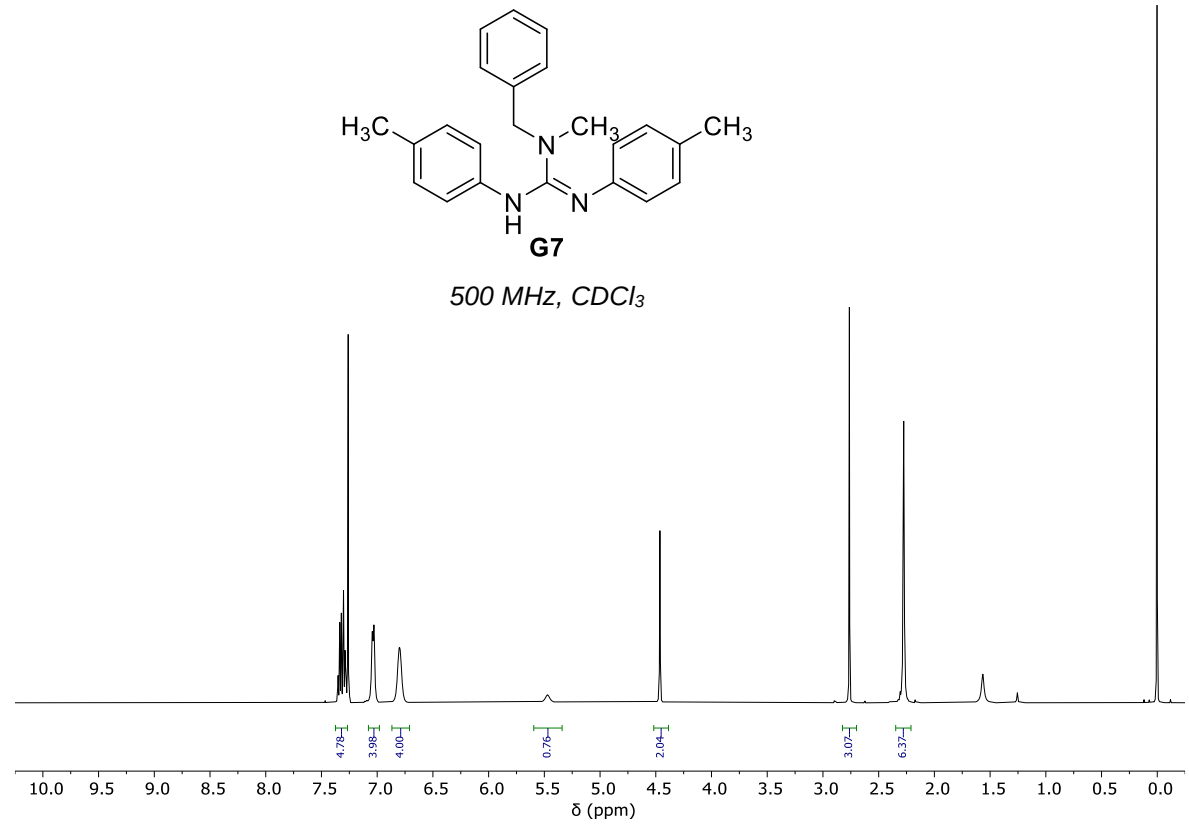


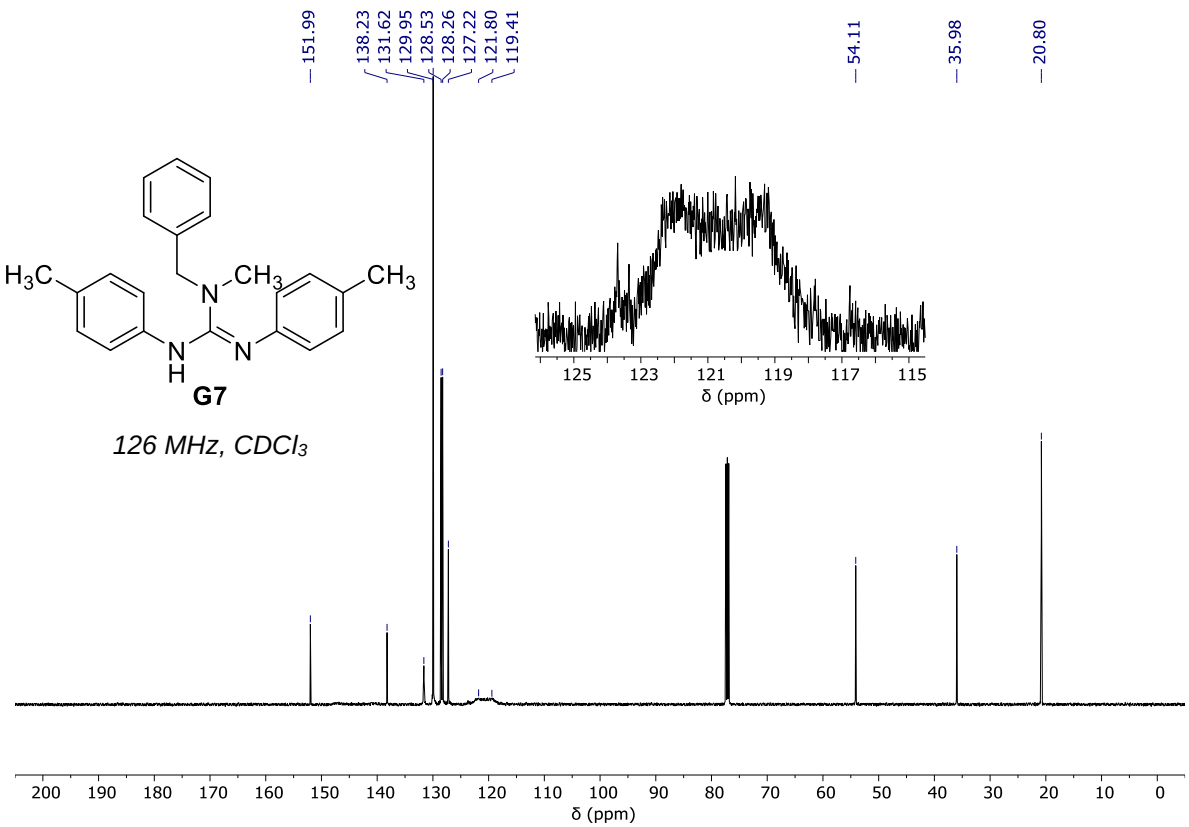
G5

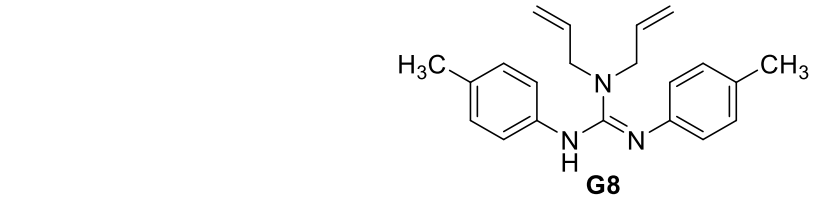
126 MHz, $CDCl_3$


CO2CH3
N
H3C
CH3
N
H
N
G6
500 MHz, CDCl3
4.00
3.83
1.82
2.97
2.02
0.96
6.10
2.06
2.23
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
δ (ppm)

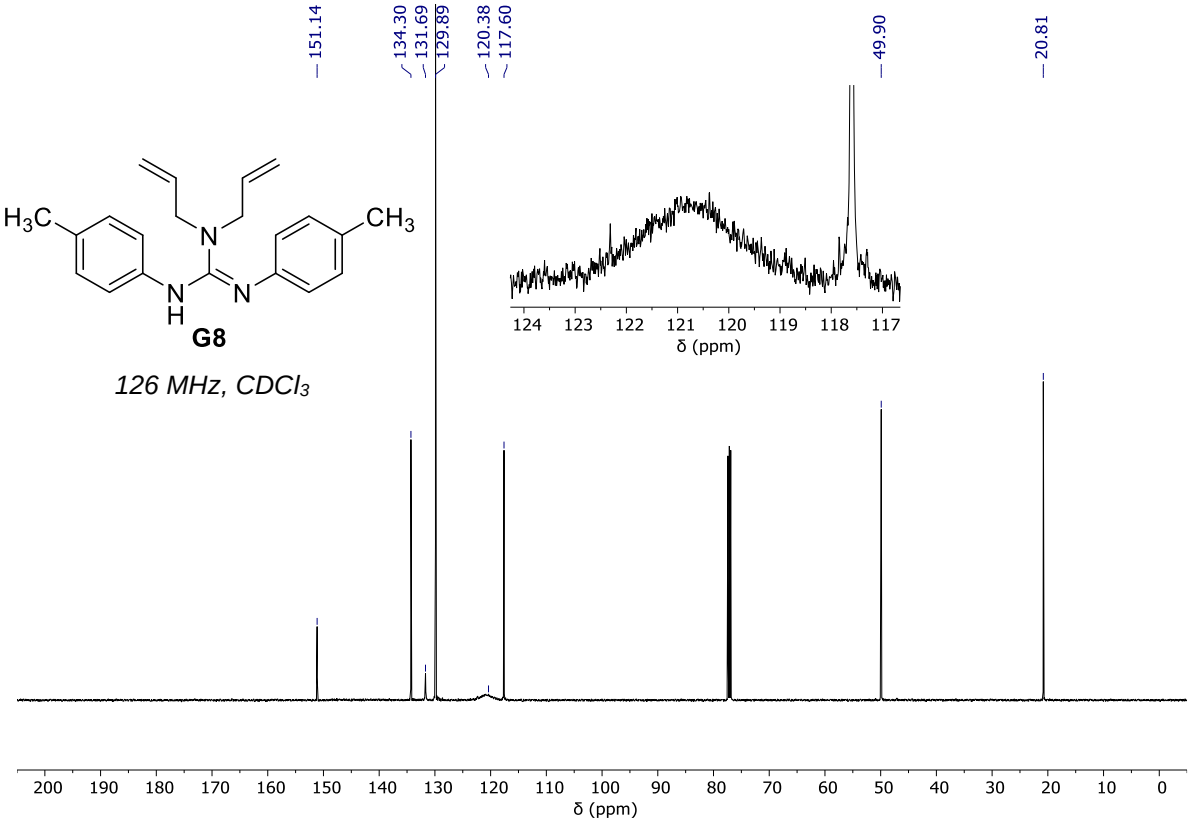

175.39
151.50
131.83
130.00
122.44
118.72
51.87
46.16
41.54
27.77
20.84
CO2CH3
N
H3C
CH3
N
H
N
G6
126 MHz, CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
δ (ppm)


G7
500 MHz, CDCl3
4.78
3.98
4.00
0.76
2.04
3.07
6.37
δ (ppm)

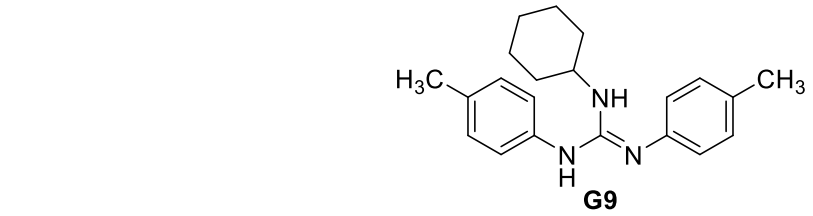

151.99
138.23
131.62
129.95
128.53
128.26
127.22
121.80
119.41
54.11
35.98
20.80
G7
126 MHz, CDCl3
δ (ppm)
δ (ppm)



500 MHz, $CDCl_3$

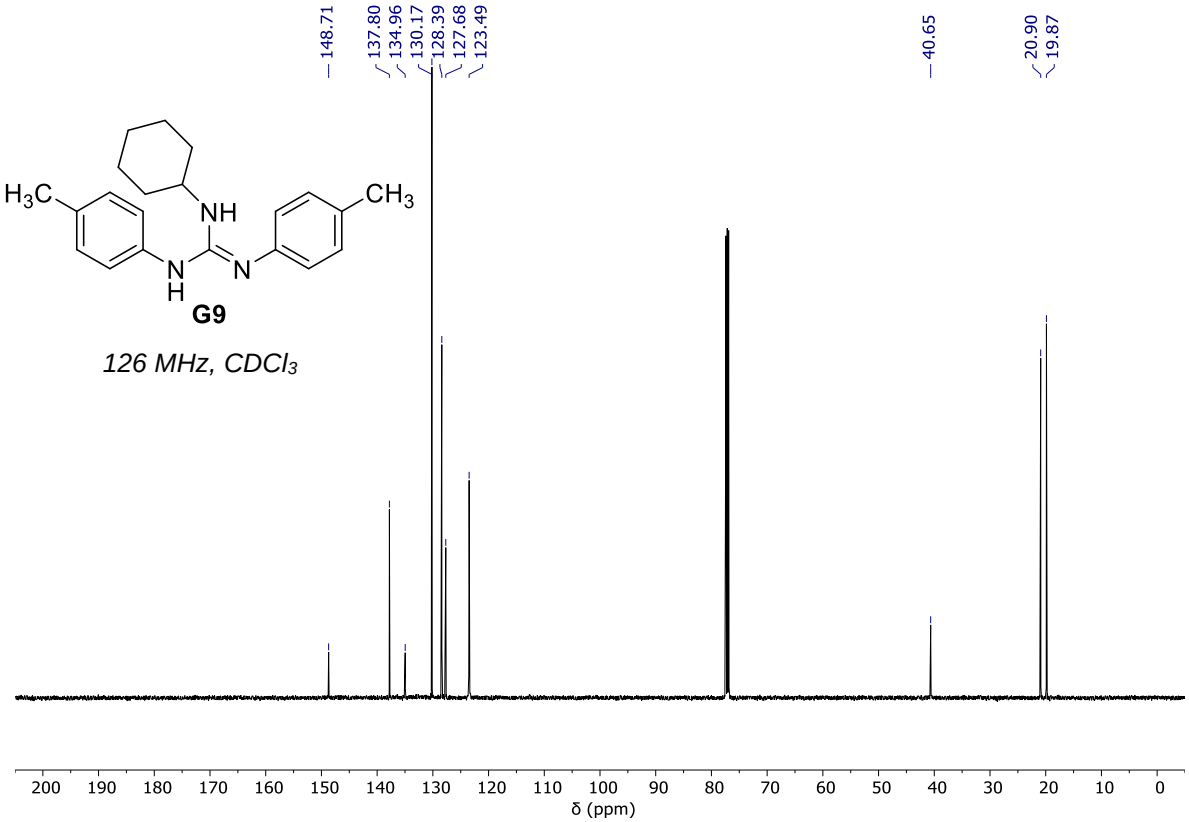


126 MHz, $CDCl_3$



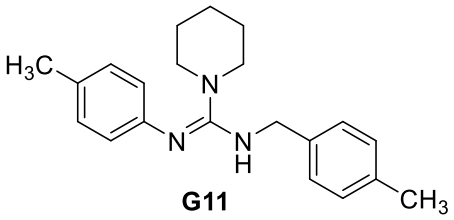
G9

500 MHz, $CDCl_3$



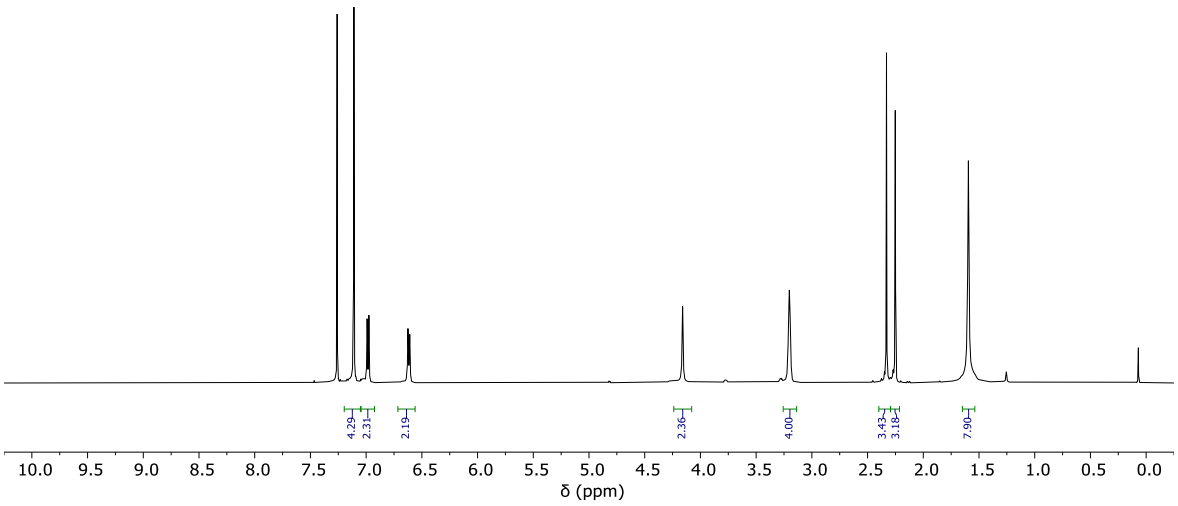
G9

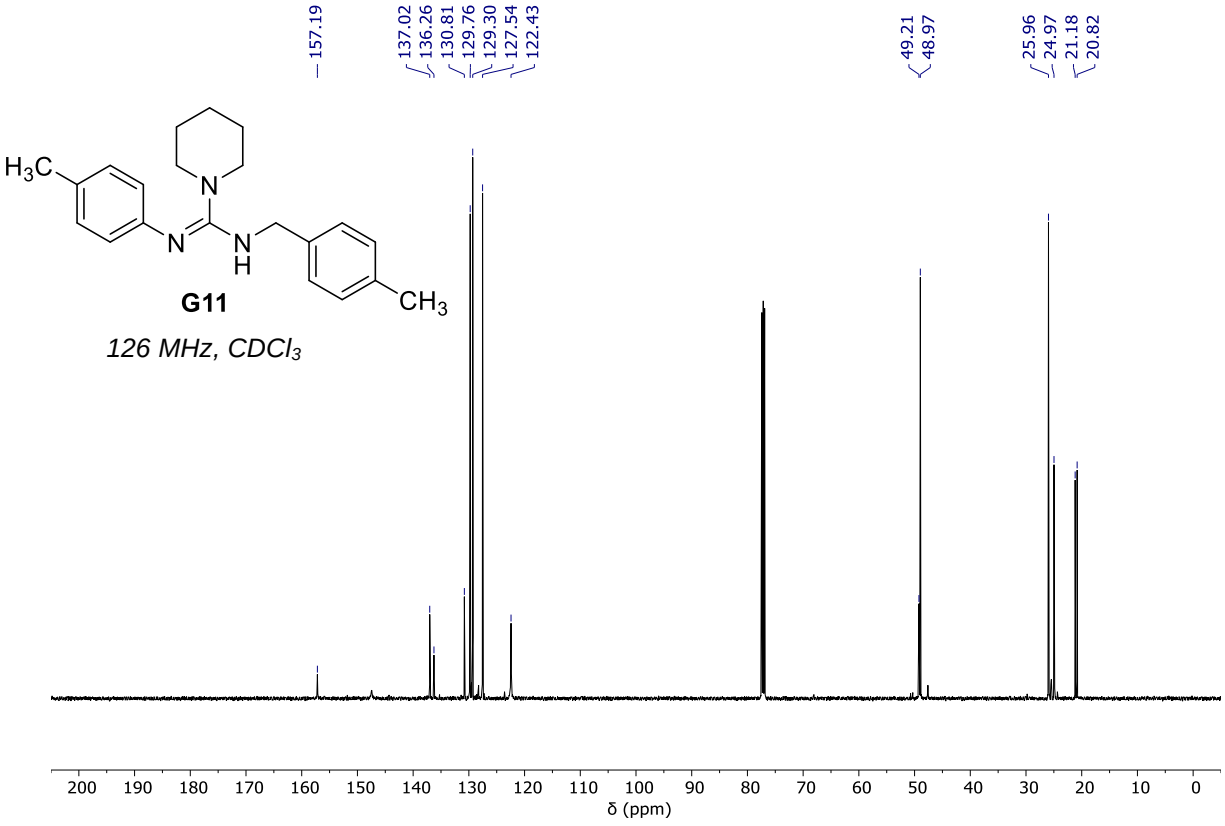
126 MHz, $CDCl_3$



G11

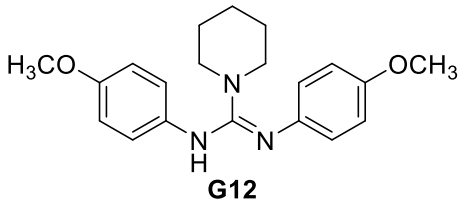
500 MHz, $CDCl_3$





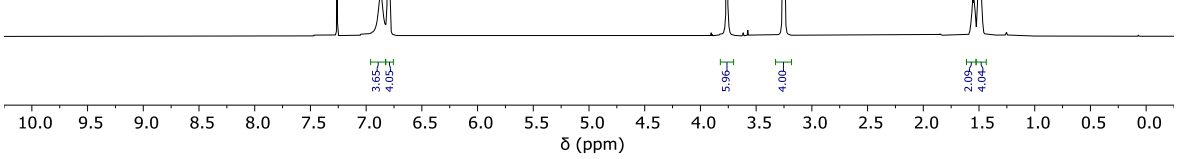
G11

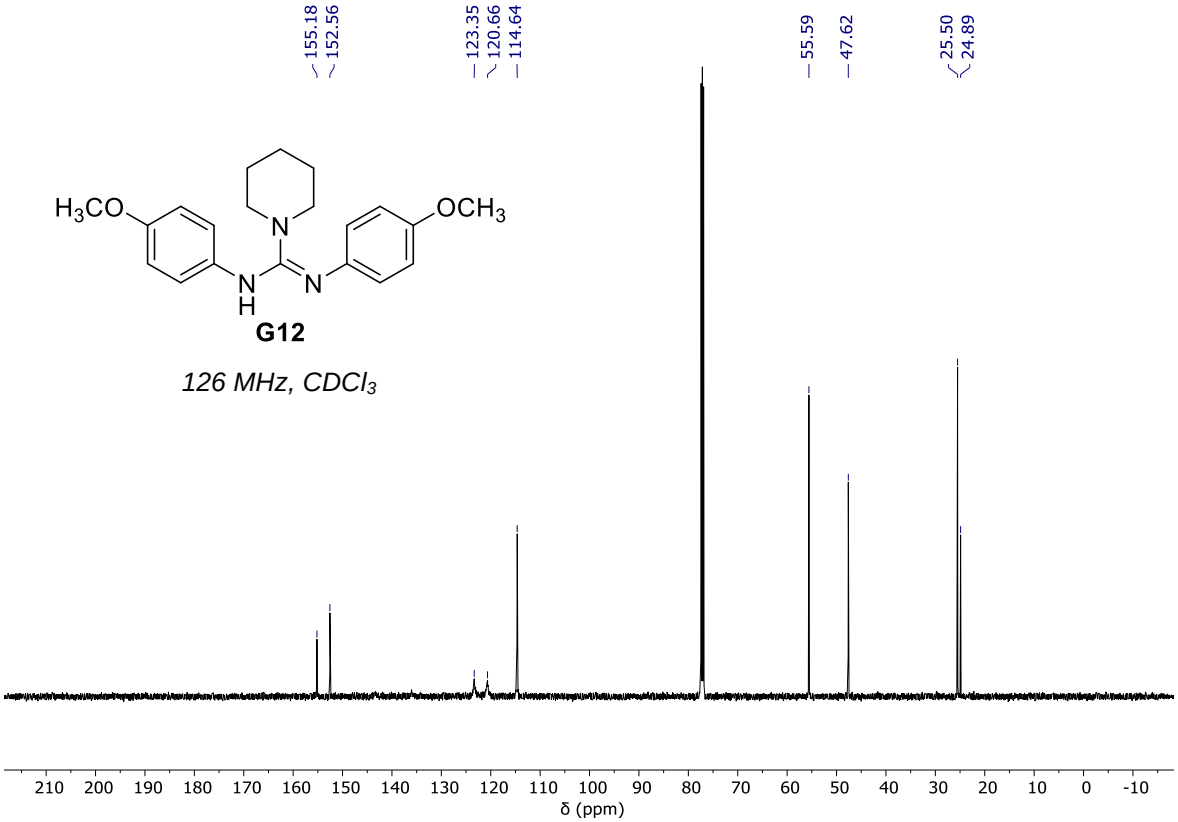
126 MHz, $CDCl_3$



G12

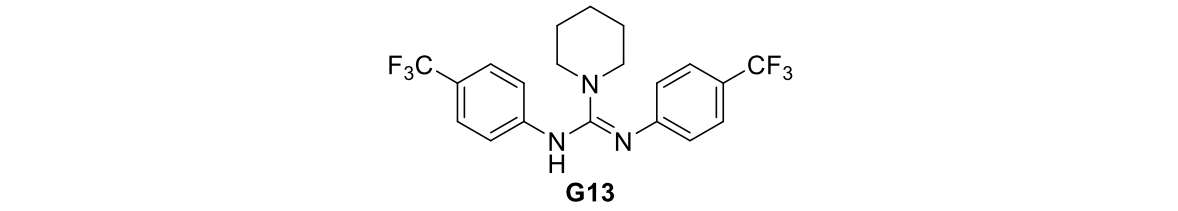
500 MHz, $CDCl_3$





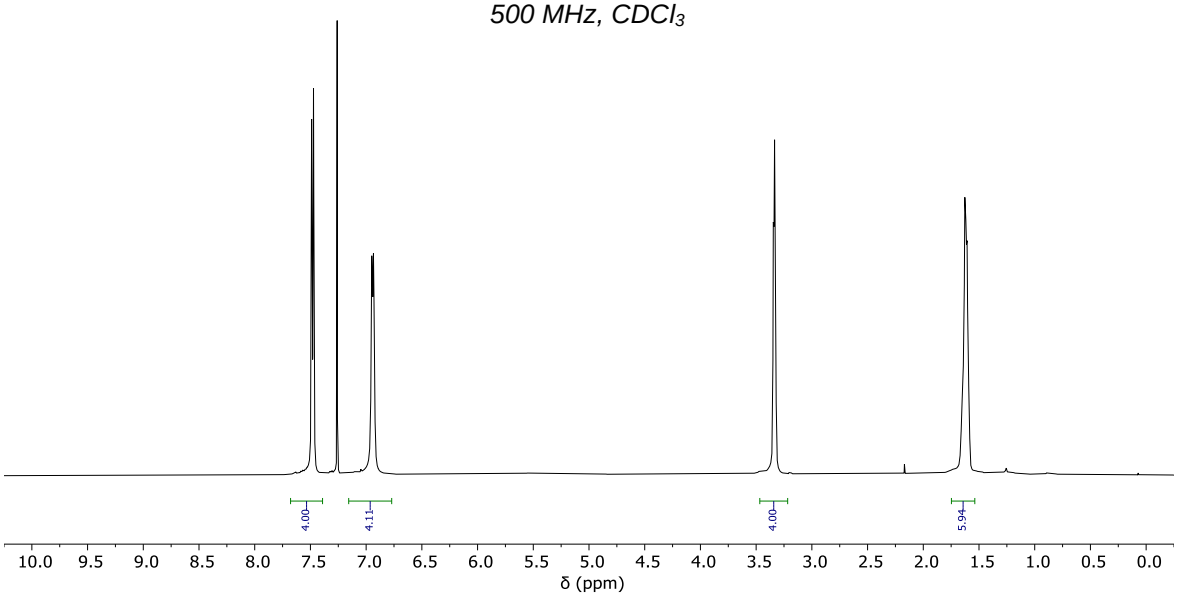
G12

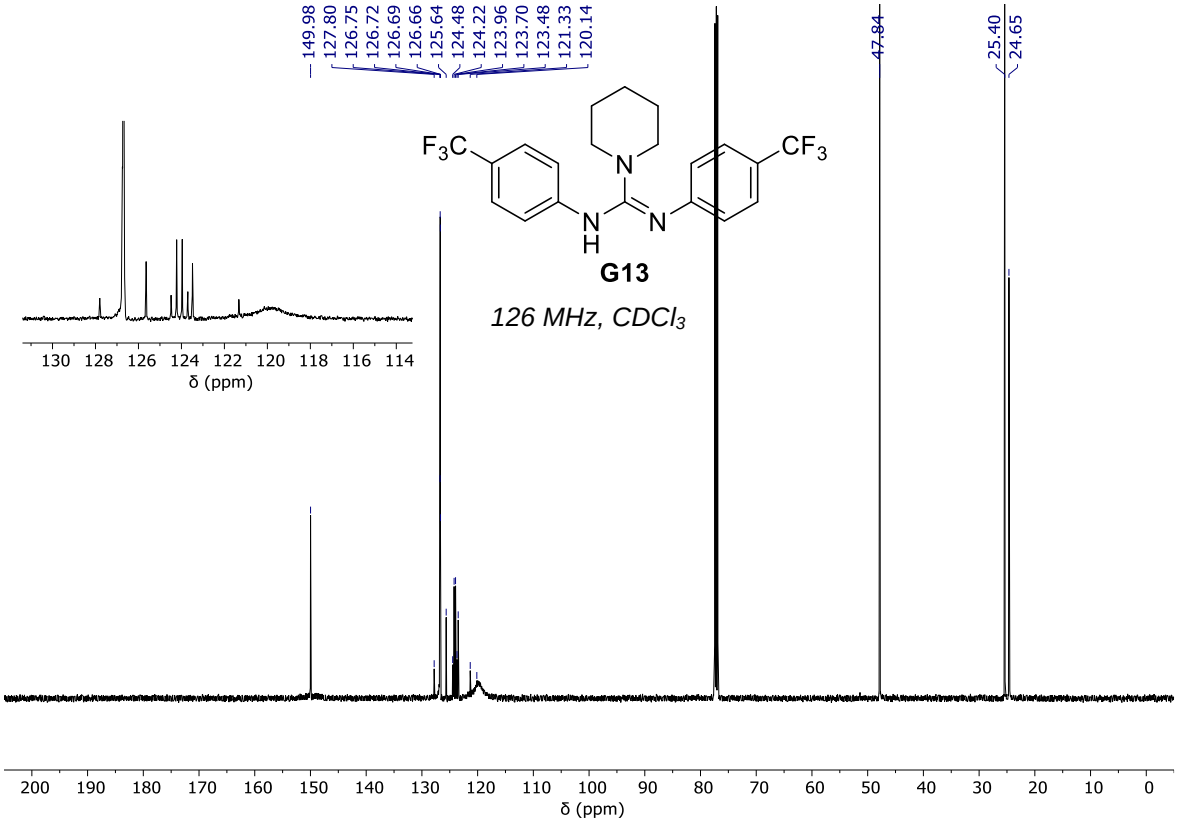
126 MHz, $CDCl_3$



G13

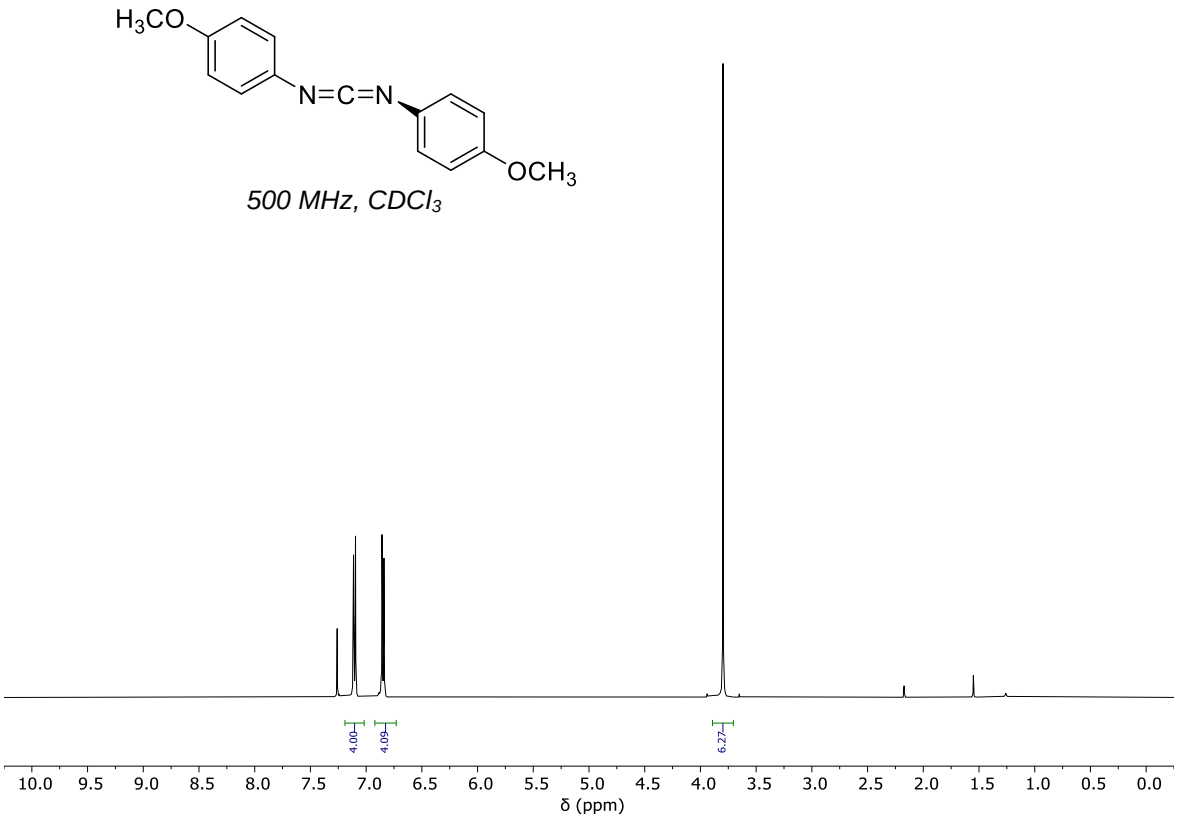
500 MHz, $CDCl_3$

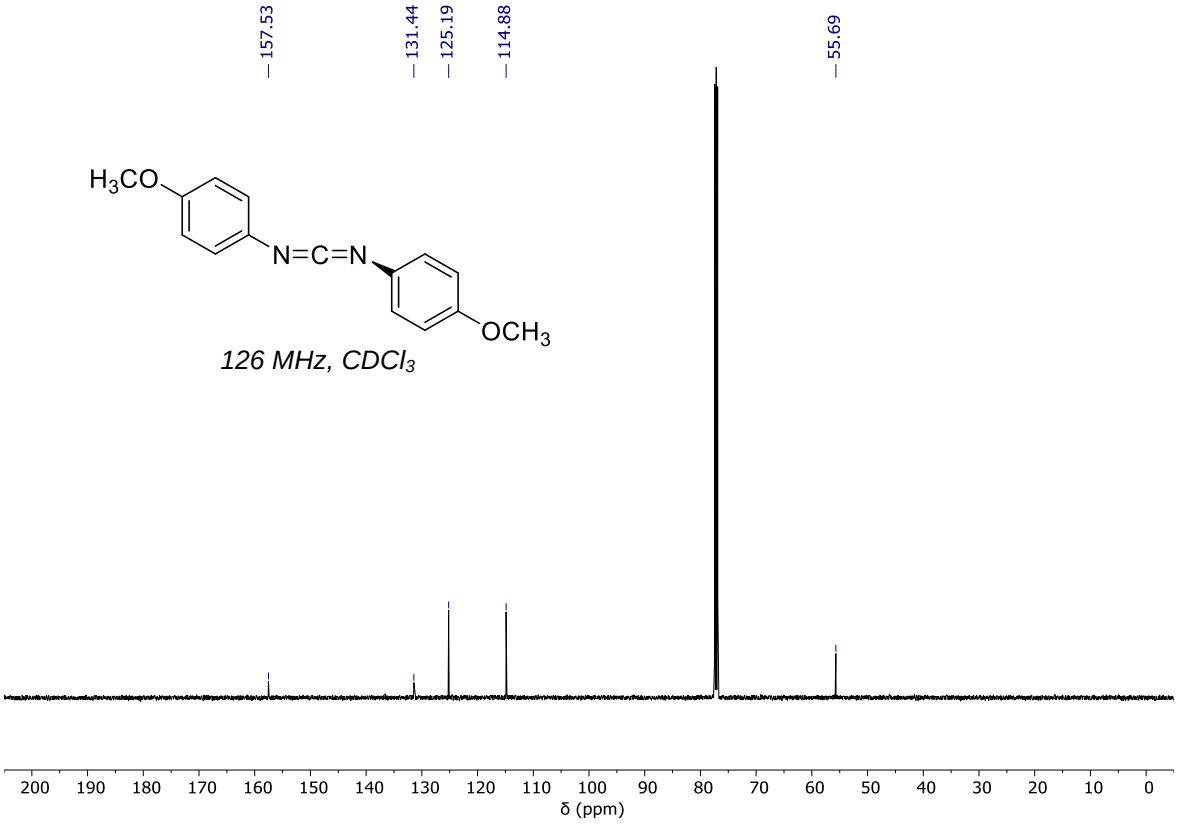


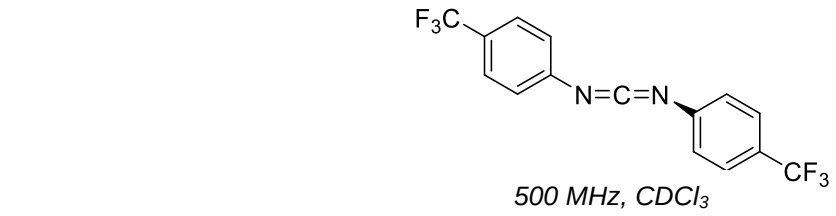


G13

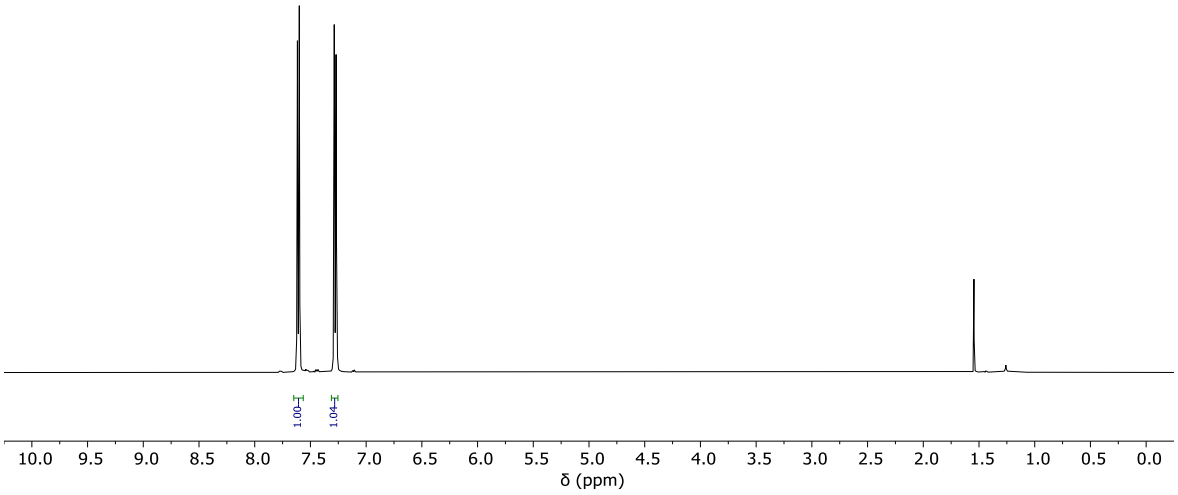
126 MHz, $CDCl_3$

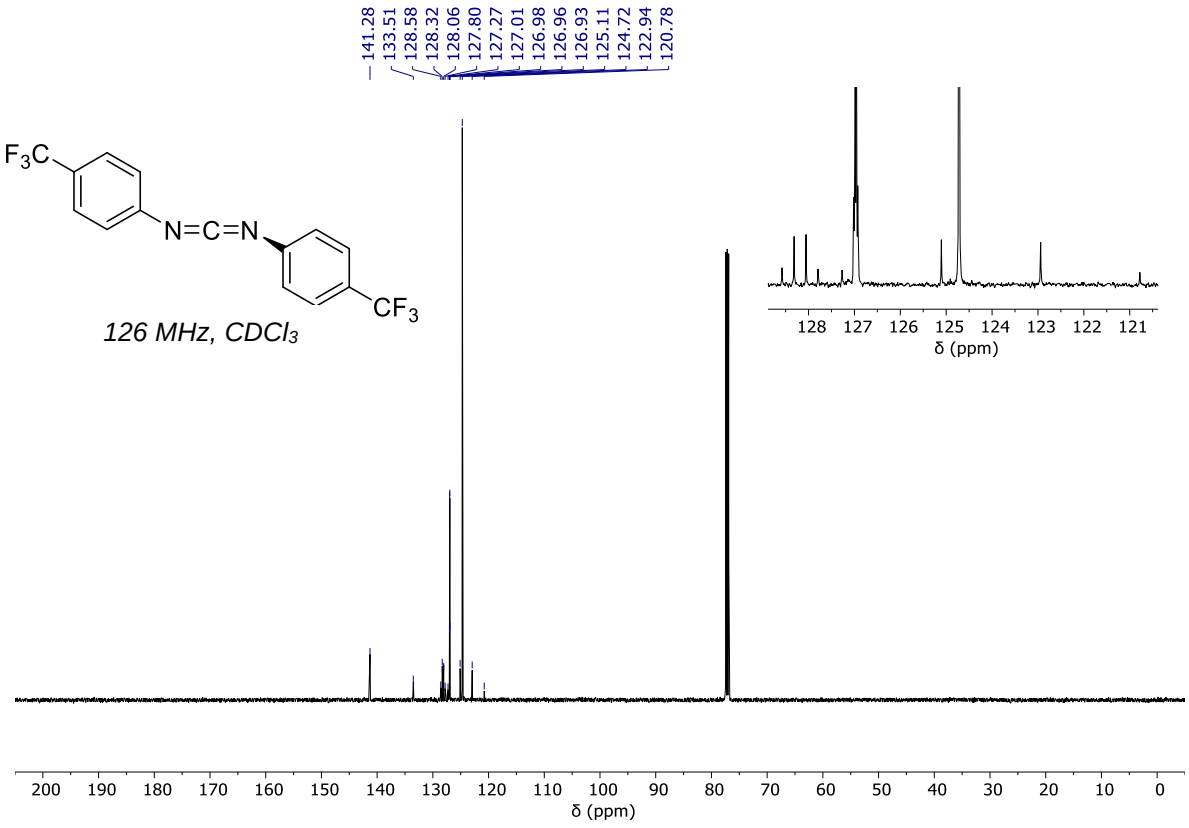

H3CO
N=C=N
OCH3
500 MHz, CDCl3
4.00
4.09
6.27
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
δ (ppm)


157.53
131.44
125.19
114.88
55.69
H3CO
N=C=N
OCH3
126 MHz, CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
δ (ppm)



500 MHz, $CDCl_3$





126 MHz, $CDCl_3$