Supporting Information

Reactions of Grignard Reagents with Nitrous Oxide

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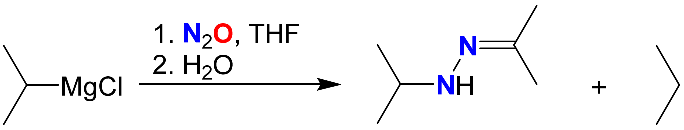
1. General remarks

Unless stated otherwise, the reactions were performed under an atmosphere of dry dinitrogen. Solvents were purified and dried according to standard procedures. MeMgI in Et_2O (0.3 M) was prepared by the dropwise addition of MeI to Mg powder in Et_2O. All other reagents were obtained from commercial sources. Grignard reagents were titrated with salicylaldehyde phenylhydrazone or by using No-D NMR spectroscopy prior to use according to a published procedures.[1] N_2O (99.999%) was purchased from Air-liquide. NMR spectra were measured on a Bruker Avance DPX-400 (^{1}H: 400 MHz, ^{13}C: 100 MHz). GC-MS analyses were carried out on a Varian CP-3800 gas chromatograph equipped with a Saturn 2200 mass spectrometer (detector: ion trap) with octane as the internal standard. An Agilent capillary column (30 m x 0.250 mm x 0.5 μm) with the stationary phase HP-5MS Ultra Inert and helium was used as carrier. Mass spectra were recorded with a Q-TOF Ultima (Waters) instrument. Combustion analysis was performed with a Thermo Scientific Flash 2000 Organic Elemental Analyzer.

2. Reaction between *i*PrMgCl and N_2O



GC-MS analysis of the reaction between iPrMgCl and N_2O.

A solution of *i*PrMgCl in THF (8 mL, 490 mM) was stirred under an atmosphere of N_2O. After 1 h, an aliquot (0.5 mL) of the reaction mixture was added to a wet THF solution (ca. 300 mM of H_2O) containing the internal standard octane (1.25 mL, 70 mM). A colorless precipitate was removed by filtration and the solution was analyzed by GC-MS.

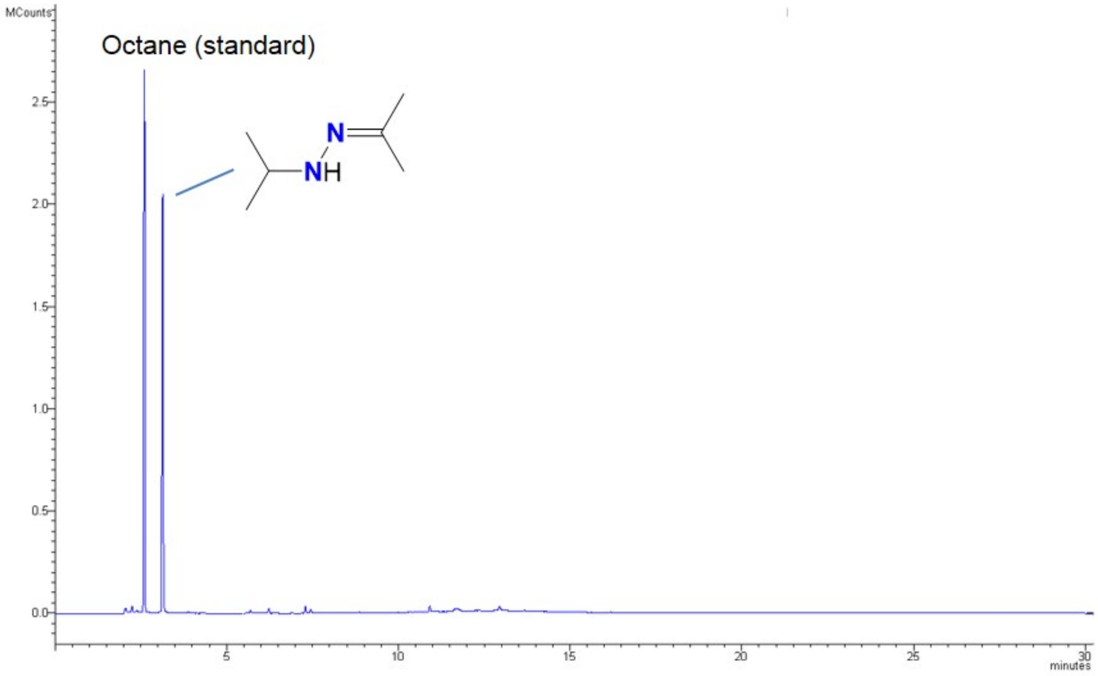


Figure S1. GC-MS spectrum of the reaction mixture obtained from *i*PrMgCl and N_2O.

^{1}H NMR analysis of the reaction between iPrMgCl and N_2O.

THF-*d*$_8$ (0.5 mL) was added to a solution of *i*PrMgCl (2.0 M) and naphthalene (used as an internal standard, 0.2 M) in THF (0.1 mL) in a J. Young NMR tube. The solution was saturated with N_2O at 0 ºC, warmed to room temperature, and analyzed by ^{1}H NMR spectroscopy after 1 h.

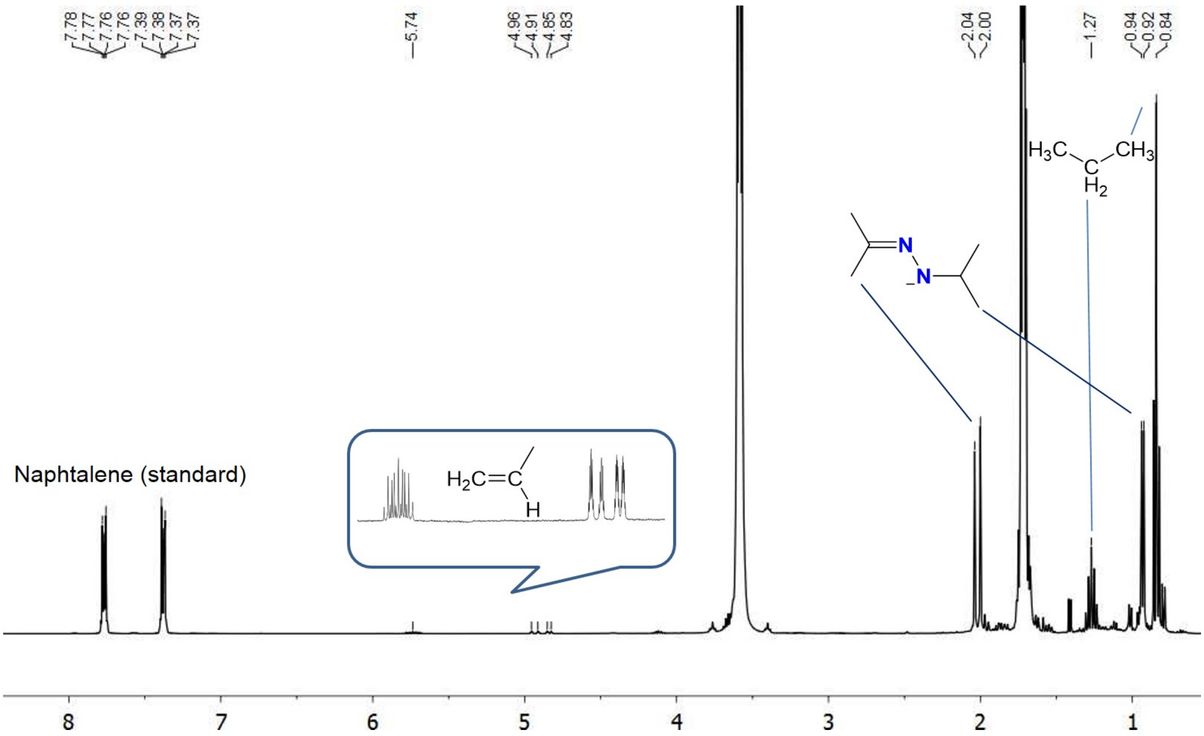


Figure S2. ^{1}H NMR spectrum of the reaction mixture obtained from *i*PrMgCl and N_2O.

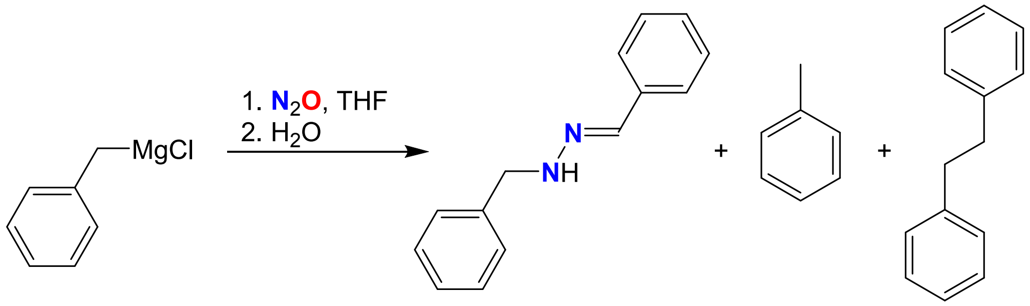
*Synthesis of **1** (iPrNHNCMe$_2$).*

A solution of *i*PrMgCl in THF (5 mL, 2.1 M) was stirred under an atmosphere of N_2O. After 3 h, water (0.5 mL) was added and the liquid phase was separated from the white precipitate and dried over $MgSO_4$. Removal of the solvent gave an oily residue, which was dried under vacuum. Isolated yield: 52 mg (14%). Crude yield according to GC-MS: 51 %. ^{1}H NMR (400 MHz, $CDCl_3$, δ): 1.07 (d, J = 6.4 Hz, 6 H, $CH(C\mathit{H}_3)_2$) 1.67 (s, 3 H, CMe_2), 1.86 (s, 3 H, CMe_2), 3.32 (sept, J = 6.4 Hz, 1 H, $C\mathit{H}(CH_3)_2$). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, δ): 15.60, 25.24 ($N{=}C(\mathit{C}H_3)_2$), 22.28 ($CH(\mathit{C}H_3)_2$), 50.64 ($\mathit{C}H(CH_3)_2$), 145.63 ($N{=}\mathit{C}(CH_3)_2$).

*Synthesis of **4** (iPrN$_2$H$_4$Cl).*

A solution of *i*PrMgCl in THF (5 mL, 2.1 M) was stirred under an atmosphere of N_2O. After 3 h, water (0.5 mL) was added and the liquid phase was separated from the white precipitate. Addition of HCl (4 N solution in dioxane, 1 mL) to the solution resulted in the formation of a precipitate, which was isolated by filtration, washed hexane (20 mL) and dried under vacuum. Yield: 256 mg (44 %). Elem. anal. calcd for $C_3H_{11}N_2Cl$: C 32.58; H 10.03; N 25.33. Found: C 32.81; H 9.78; N 25.47. ^{1}H NMR (400 MHz, CD_3OD, δ): 1.22 (d, 6.6 Hz, 6 H, CH(C*H$_3$*)$_2$), 3.26 (t, 6.6 Hz, 1 H, C*H*(CH$_3$)$_2$). ^{13}C{^{1}H} NMR (100 MHz, CD_3OD, δ): 17.88 (CH(*C*H$_3$)$_2$), 54.91 (*C*H(CH$_3$)$_2$). MS (ESI$^+$), found: 129.1411 $[M + H_3O]^+$; calcd for $C_3H_{14}N_2ClO$: 129.0867.

3. Reaction between BnMgCl and N_2O



GC-MS analysis of the reaction between BnMgCl and N_2O.

A solution of BnMgCl in THF (8 mL, 250 mM) was stirred under an atmosphere of N_2O. After 3 h, an aliquot (0.5 mL) of the reaction mixture was added to a wet THF solution (ca. 300 mM of H_2O) containing the internal standard octane (0.5 mL, 250 mM). A colorless precipitate was removed by filtration and the solution was analyzed by GC-MS.

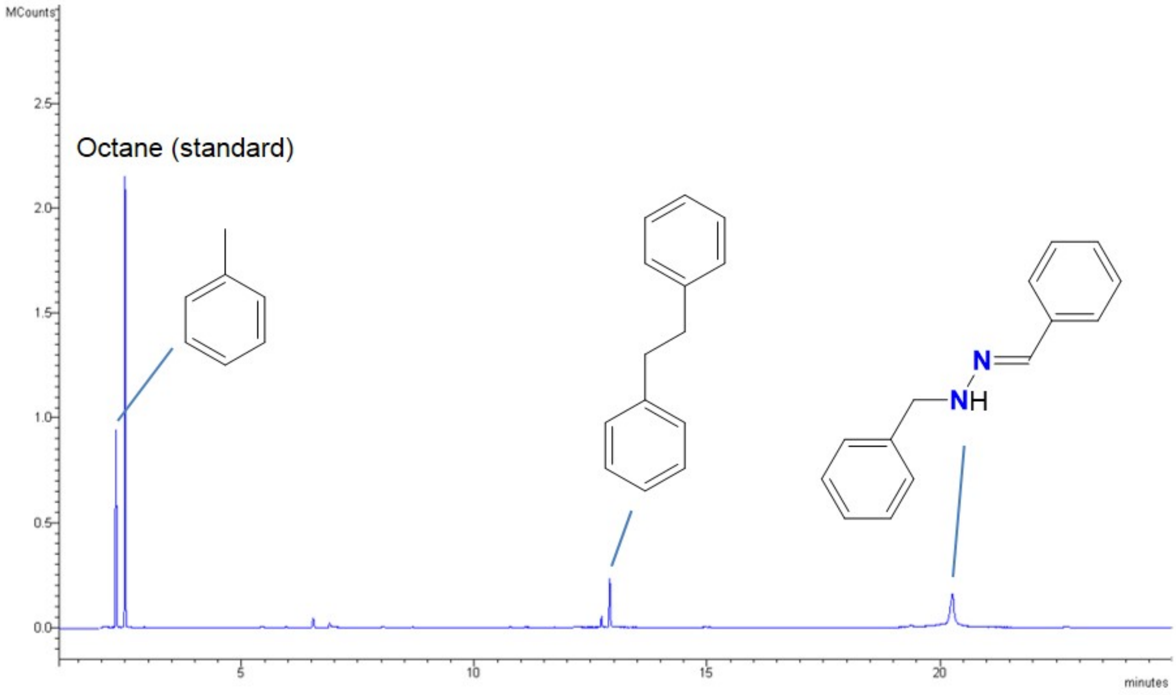


Figure S3. GC-MS spectrum of the reaction mixture obtained from BnMgCl and N_2O.

Synthesis of ***2*** *x HCl (BnNH$_2$NCHPhCl).*

A solution of BnMgCl in THF (5 mL, 2.0 M) was stirred under an atmosphere of N_2O. After 3 h, water (0.5 mL) was added and the liquid phase was separated from the white precipitate. Addition of HCl (4 N solution in dioxane, 1 mL) to the solution resulted in the formation of a precipitate, which was isolated by filtration, washed hexane (20 mL) and dried under vacuum. Yield: 456 mg (37 %). Elem. anal. calcd for $C_{14}H_{15}N_2Cl$: C 68.15; H 6.13; N 11.35. Found: C 68.33; H 6.55; N 11.44. ^{1}H NMR (400 MHz, CD_2Cl_2, δ): 4.47 (s, 2 H, CH_2), 7.33−7.72 (m, 10 H, Ph's), 8.83 (s, 1 H, C*H*Ph). $^{13}C\{^1H\}$ NMR (100 MHz, CD_2Cl_2, δ): 53.97 (CH_2), 125.65−132.96 (Ph's), 167.62 (*C*HPh). MS (ESI$^+$), found: 211.1235 $[M - Cl]^+$; calcd for $C_{14}H_{15}N_2$: 211.1229.

4. Synthesis of 5−7

*Synthesis of **5** (CyN$_2$H$_4$Cl).*

A solution of CyMgCl in THF (5 mL, 2.0 M) was stirred under an atmosphere of N_2O. After 3 h, water (0.5 mL) was added and the liquid phase was separated from the white precipitate. Addition of HCl (4 N solution in dioxane, 1 mL) to the solution resulted in the formation of a precipitate, which was isolated by filtration, washed hexane (20 mL) and dried under vacuum. Yield: 316 mg (42 %). Elem. anal. calcd for $C_6H_{15}N_2Cl$: C 47.84; H 10.04; N 18.60. Found: C 47.60; H 10.50; N 4.77. ^{1}H NMR (400 MHz, CD_3OD, δ): 1.19−2.14 (m, 10 H, CH_2), 3.02−3.10 (m, 1 H, CH). $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD, δ): 25.26, 26.27, 29.06 (CH_2), 61.50 (CH). MS (ESI$^+$), found: 115.1235 $[M - Cl]^+$; calcd for $C_6H_{15}N_2$: 115.1229.

*Synthesis of **6** (EtN$_2$H$_4$Cl).*

A solution of EtMgCl in THF (5 mL, 2.0 M) was stirred under an atmosphere of N_2O. After 3 h, water (0.5 mL) was added, liquid phase was separated from the white precipitate. Addition of HCl (4 N solution in dioxane, 1 mL) to the solution resulted in the formation of a precipitate, which was isolated by filtration, washed hexane (20 mL) and dried under vacuum. Yield: 302 mg (63%). Elem. anal. calcd for $C_2H_9N_2Cl$: C 24.88; H 9.39; N 29.01. Found: C 24.80; H 8.98; N 28.70. ^{1}H NMR (400 MHz, CD_3OD, δ): 1.18 (t, 7.3 Hz, 3 H, $C\mathit{H_3}CH_2$), 3.02 (q, 7.3 Hz, 2 H, $CH_3C\mathit{H_2}$). $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD, δ): 10.16 ($\mathit{C}H_3CH_2$), 47.71 ($CH_3\mathit{C}H_2$). MS (ESI$^+$), found: 113.1126 $[M + HO]^+$; calcd for $C_2H_{10}N_2ClO$: 113.0554.

Synthesis of 7 (Ph(CH$_2$)$_2$N$_2$H$_4$Cl).

A solution of $Ph(CH_2)_2MgCl$ in THF (10 mL, 1.0 M) was stirred under an atmosphere of N_2O. After 3 h, water (0.5 mL) was added, liquid phase was separated from the white precipitate. Addition of HCl (4 N solution in dioxane, 1 mL) to the solution resulted in the formation of a precipitate, which was isolated by filtration, washed hexane (20 mL) and dried under vacuum. Yield: 409 mg (47%). Elem. anal. calcd for $C_8H_{13}N_2Cl$: C 55.65; H 7.59; N 16.23. Found: C 55.56; H 7.69; N 16.59. ^{1}H NMR (400 MHz, CD_3OD, δ): 2.87 (m, 4 H, $PhCH_2$), 3.19 (m, 4 H, $BnCH_2$), 7.19 (m, 5 H, Ph). $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD, δ): 31.23 ($PhCH_2$), 52.18 ($BnCH_2$), 126.65, 128.33, 128.48, 136.93 (Ph). MS (ESI$^+$), found: 137.1079 $[M - Cl]^+$; calcd for $C_8H_{13}N_2$: 137.1073.

5. Kinetic analyses

General procedure for monitoring of the reactions of N_2O with Grignard reagents in THF.

THF-d_8 (0.5 mL) was added to a THF solution (0.1 mL) of the corresponding Grignard reagent (2.0 M) and naphthalene (used as an internal standard, 0.2 M) in a J. Young NMR tube. The solution was saturated with N_2O at 0 ºC. The time course of the conversion of the starting material was determined by ^1H NMR spectroscopy at RT.

General procedure for monitoring of the reactions of N_2O with Grignard reagents in Et_2O.

Et_2O (0.4 mL) was added to an Et_2O solution (0.2 mL) of *i*PrMgCl or MeMgI (1.0 M) and naphthalene (used as an internal standard, 0.2 M) in a J. Young NMR tube. The solution was saturated with N_2O at 0 ºC. One drop of C_6D_6 was added in order to shim the sample. The time course of the conversion of the starting material was determined by ^1H NMR spectroscopy at RT.

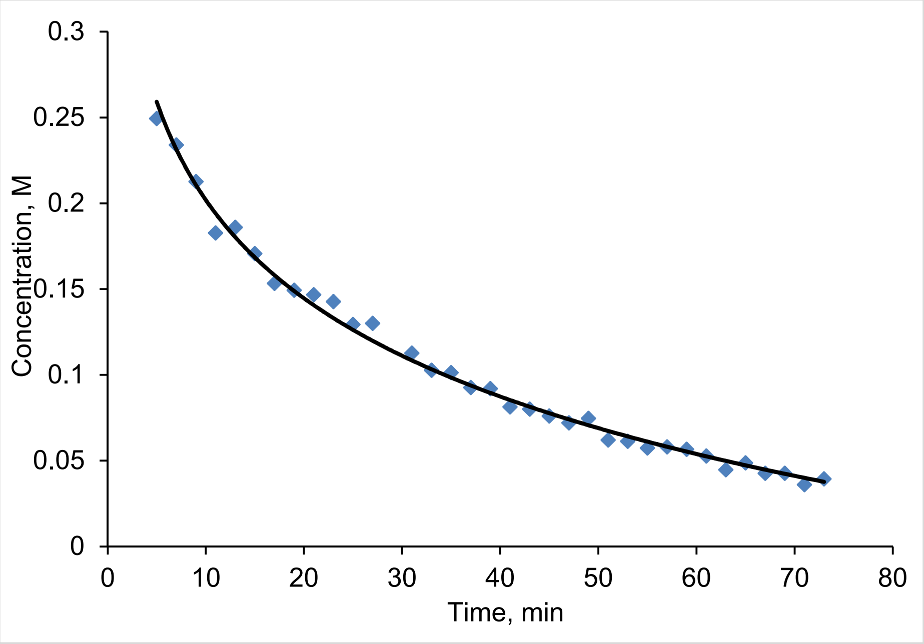


Figure S4. Concentration vs. time for the reaction between BnMgCl and N_2O in THF-d_8 (0.3 M, 25 ºC).

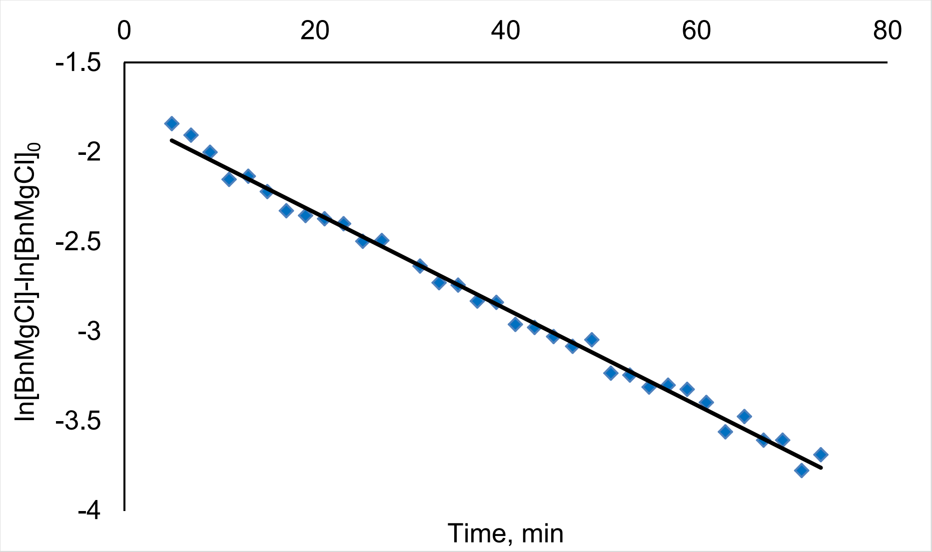


Figure S5. Plot of rate ln[BnMgCl]-ln[BnMgCl]$_0$ vs. time for the reaction between BnMgCl and N_2O in THF-d_8 (0.3 M, 25 ºC). $k = 0.027$ min^{-1}, $t_{1/2} = 26$ min.

6. NMR spectra

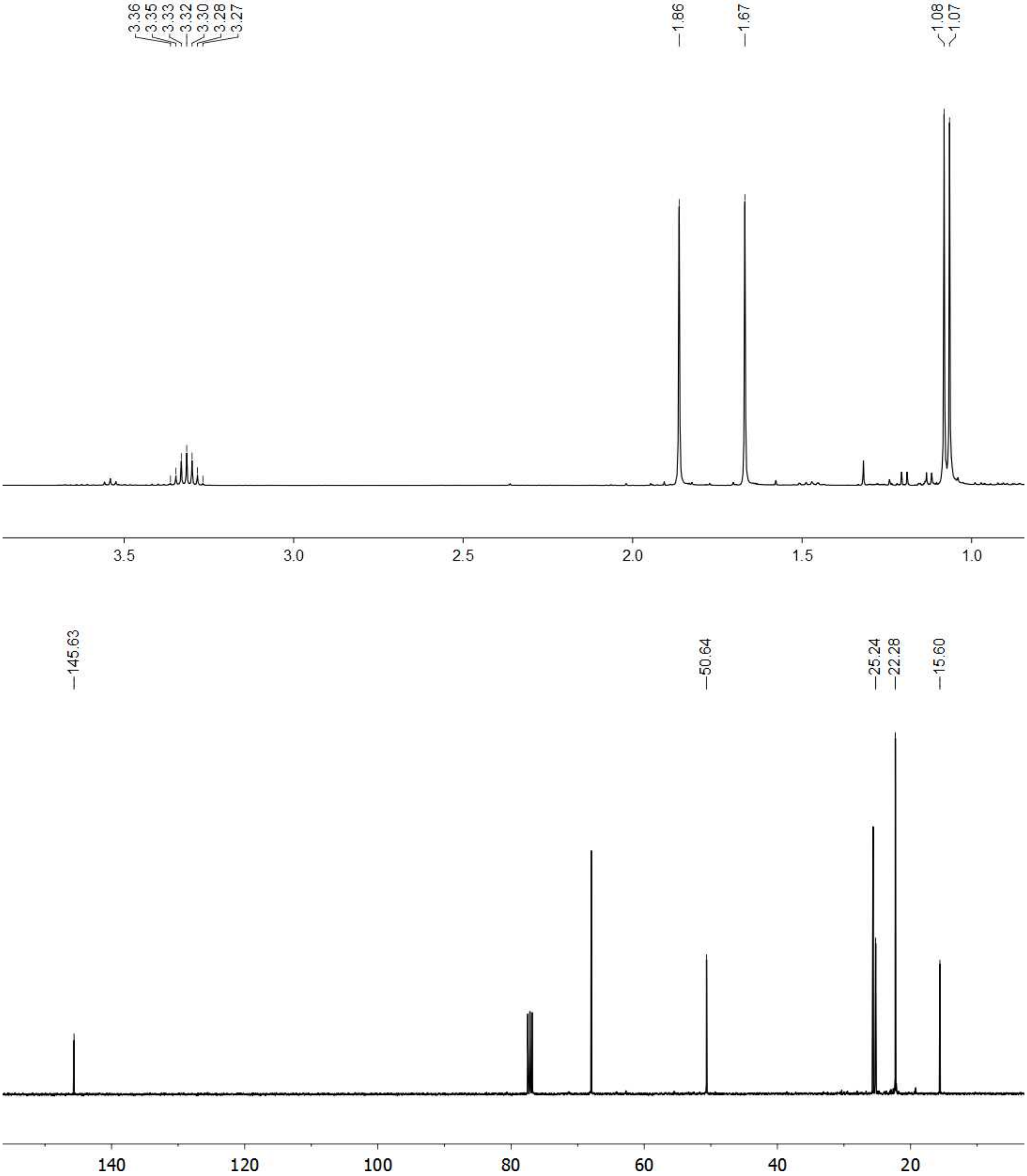


Figure S6. ${}^{1}H$ (top) and ${}^{13}C$ (bottom) NMR spectrum of *i*PrNHNCMe$_2$ (**1**) at RT (CDCl$_3$).

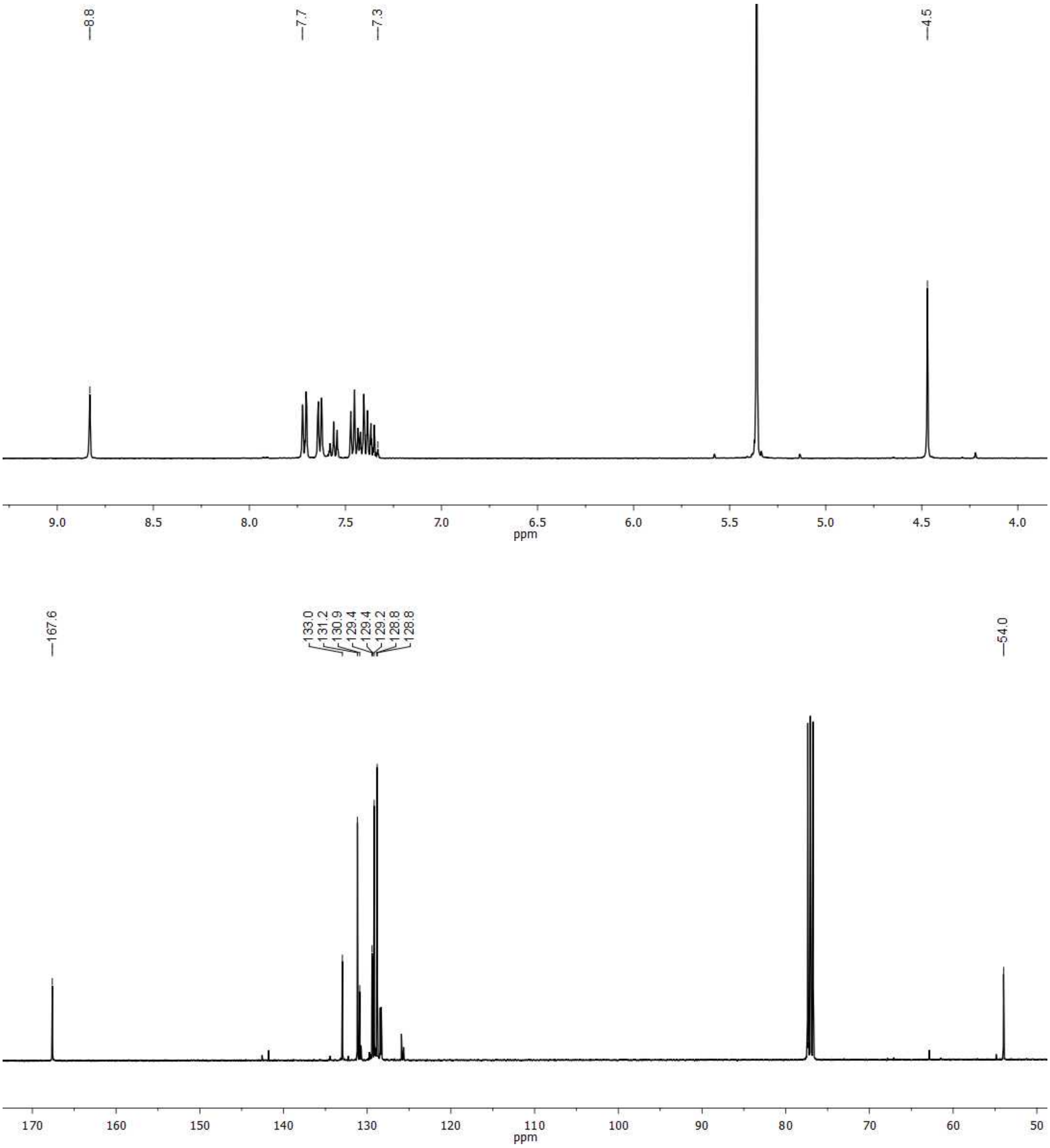


Figure S7. ^{1}H (top, CD_2Cl_2) and ^{13}C (bottom, $CDCl_3$) NMR spectrum of $BnNH_2NCHPhCl$ (**2**) at RT.

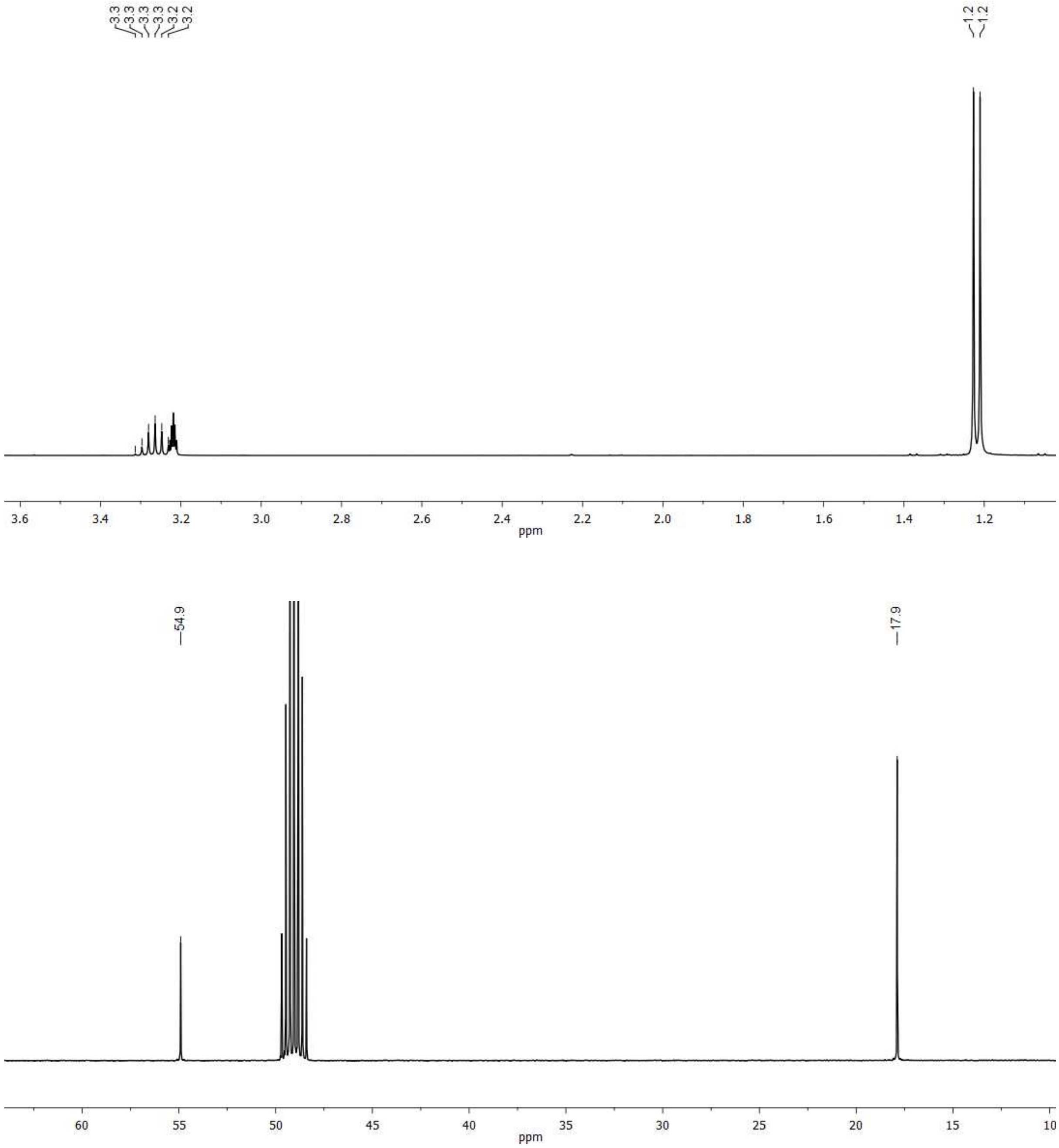


Figure S8. ^{1}H (top) and ^{13}C (bottom) NMR spectrum of *i*PrN$_2$H$_4$Cl (**4**) at RT (CD$_3$OD).

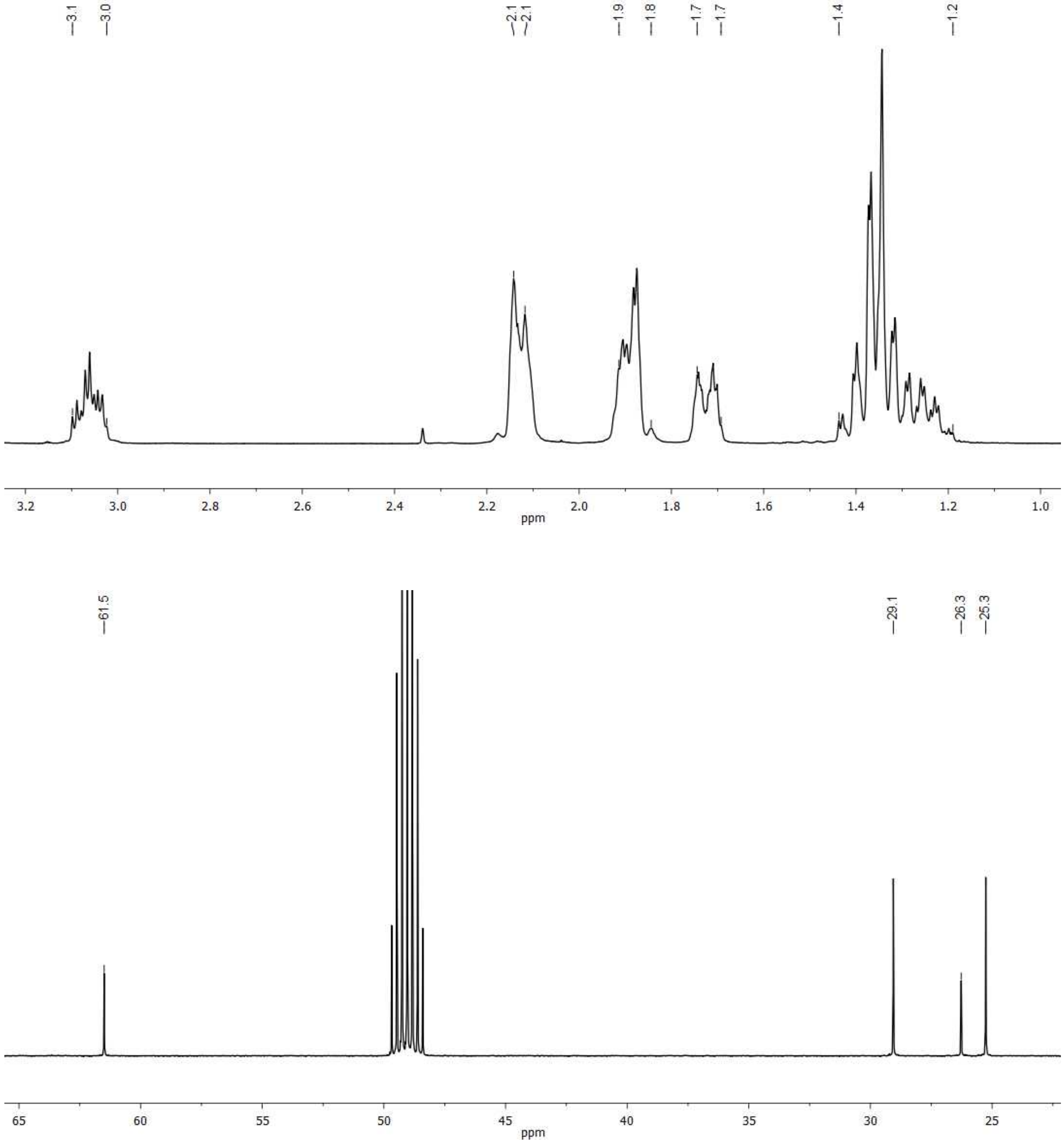


Figure S9. ^{1}H (top) and ^{13}C (bottom) NMR spectrum of CyN_2H_4Cl (**5**) at RT (CD_3OD).

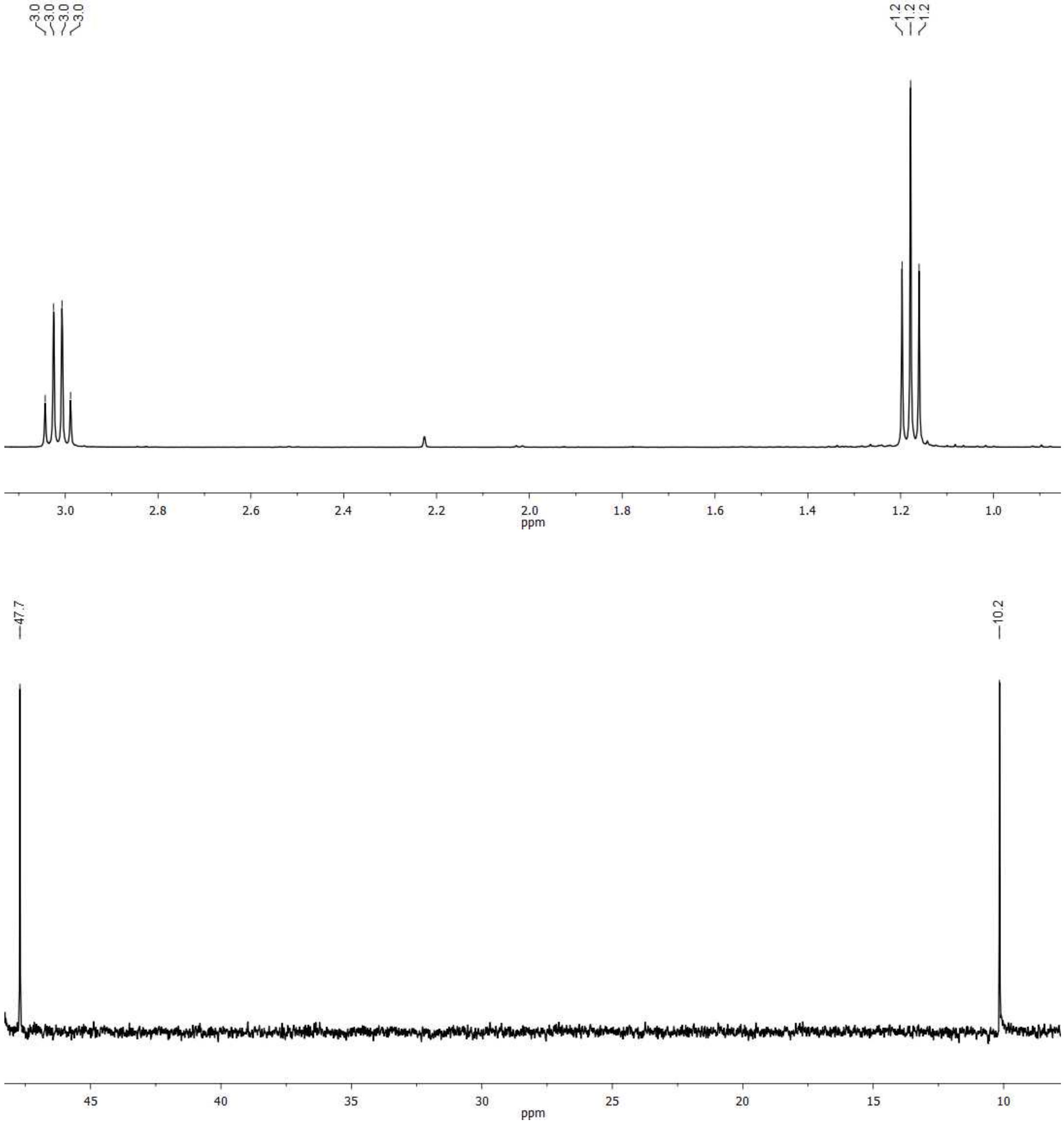


Figure S10. ^{1}H (top) and ^{13}C (bottom) NMR spectrum of EtN_2H_4Cl (**6**) at RT (CD_3OD).

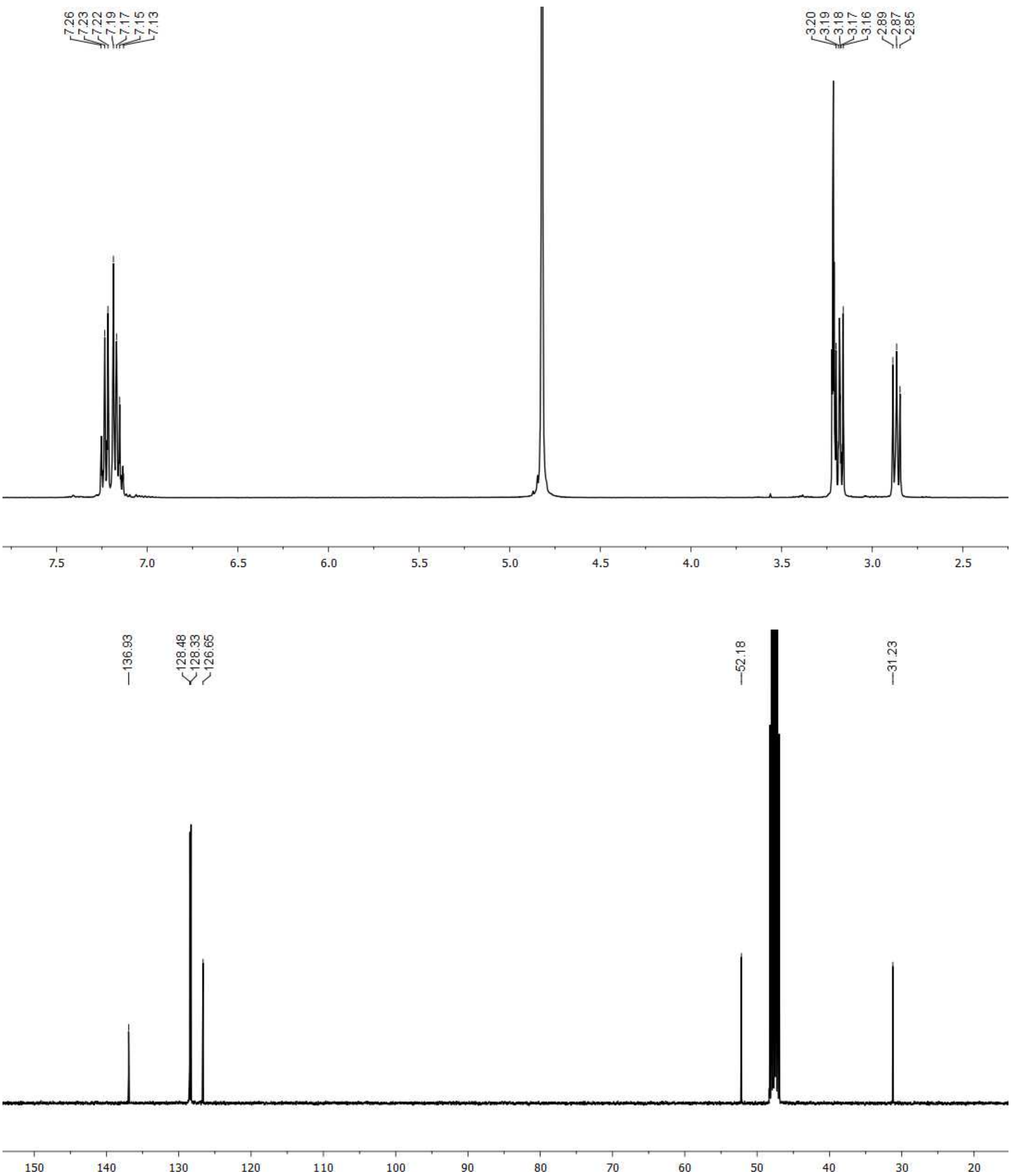
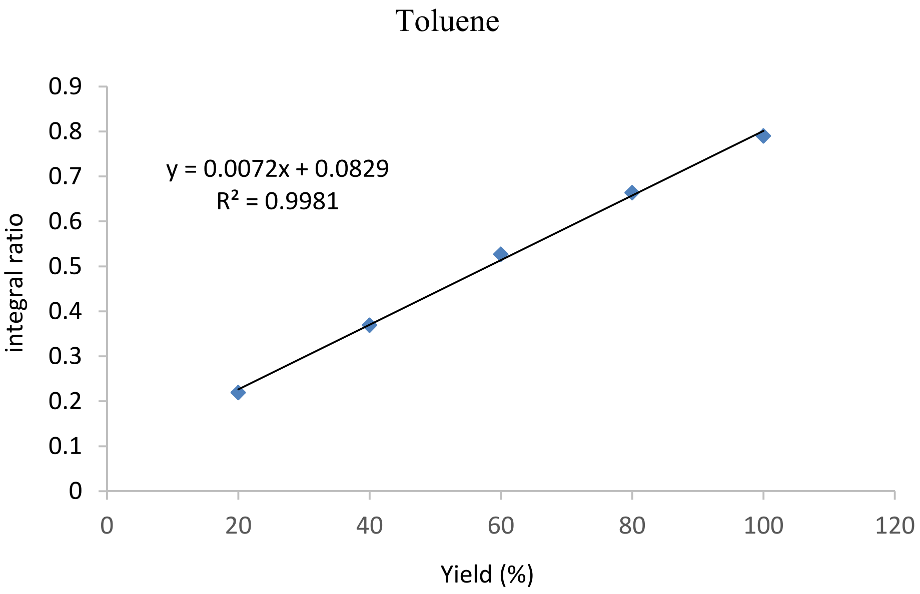


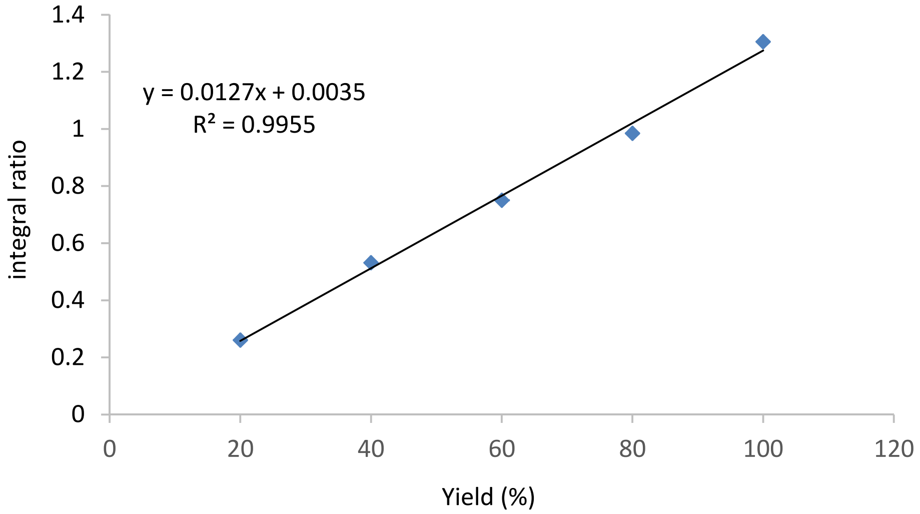
Figure S11. ^{1}H (top) and ^{13}C (bottom) NMR spectrum of $Ph(CH_2)_2N_2H_4Cl$ (**7**) at RT (CD_3OD).

7. Calibration curves for the GC-MS analyses

For the calibration curves for toluene and bibenzyl, a stock solution of the internal standard octane (0.250 M in THF) and stock solutions of toluene (0.250 M) or 1,2-diphenylethane (0.125 M) in THF were prepared. Aliquots of the stock solutions were mixed and diluted with THF to give a total volume of 1.0 mL. The final concentration of the internal standard was 0.125 M and the concentrations of the product 0.025 M (20% yield), 0.075 M (60% yield), 0.100 M (80% yield), 0.125 M (100% yield) for toluene; 0.013 M (20% yield), 0.038 M (60% yield), 0.05 M (80% yield), 0.063 M (100% yield) for 1,2-diphenylethane. The calibration curve gives the ratio of the chromatogram peak integrals in relation to the corresponding yield.

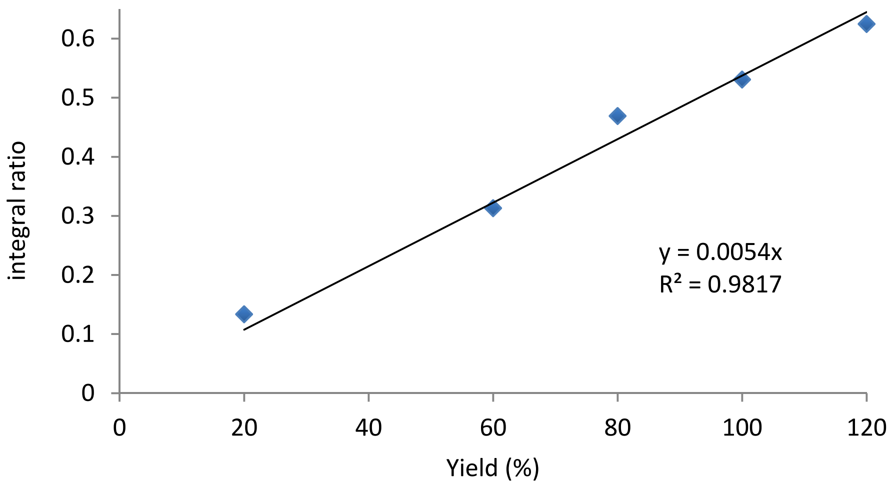


1,2-Diphenylethane



For the calibration curve for hydrazone **1**, 5 THF solutions (1.75 mL) were prepared, which contained octane (70 mM) and hydrazone **1** 20% yield (14 mM), 60% yield (42 mM), 80% yield (56 mM), 100% yield (70 mM), 120% yield (84 mM). The calibration curve gives the ratio of the chromatogram peak integrals (hydrazone vs. octane) in relation to the corresponding yield.

Hydrazone **1**



8. X-ray crystallography

Upon storage of **1** under air at −35 °C, the formation of single crystals was observed. A structural analysis revealed that hydrazone **1** had co-crystallized with its corresponding hydroperoxide (denoted **1·O$_2$**). The diffraction data (except compound **2**) were measured at low temperature [100(2) K] using Mo K_α radiation on a Bruker APEX II CCD diffractometer equipped with a kappa geometry goniometer. The datasets were reduced by EvalCCD[2] and then corrected for absorption.[3] The data collection of compound **2** was performed at room temperature using Cu K_α radiation on an Agilent Technologies SuperNova dual system in combination with an Atlas CCD detector. The data reduction was carried out by Crysalis PRO.[4] The solutions and refinements were performed by SHELX.[5] The crystal structures were refined using full-matrix least-squares based on F^2 with all non hydrogen atoms anisotropically defined. Hydrogen atoms were placed in calculated positions by means of the "riding" model. Some refinement problems (dealing with disordered THF) were encountered in the last stages of refinement of compound **3** and solved by the split model and by applying some geometrical constraints (SADI card). Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited at the Cambridge Crystallographic Data Center (CCDC) as Supplementary Publication No. CCDC 989041 (**2**), 989042 (**1**+**1·O$_2$**) and 989043 (**3**). Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge, CB2 1EZ, U.K. (fax, (internat.) +44-1223-336033; E-mail, deposit@ccdc.cam.ac.uk).

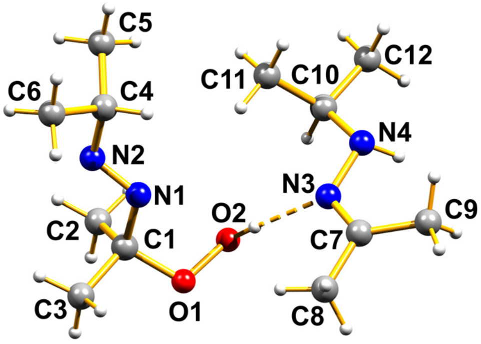


Figure S12. Molecular structures of co-crystallized **1** + **1**·$\mathbf{O_2}$.

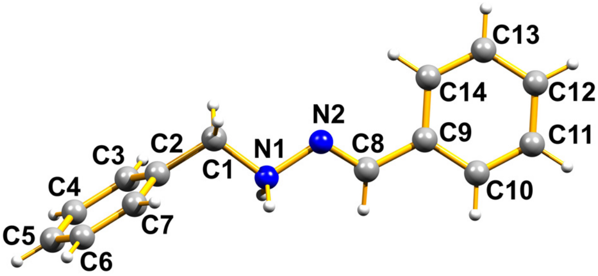


Figure S13. Molecular structure of **2**. Cl anion is omitted.

Table S1. Crystallographic data for compounds **1** + **1·O$_2$**, **2**, and **3**.

Complex	**1 + 1·O$_2$**	**2**	**3**
Empirical formula	$C_{12}H_{28}N_4O_2$	$C_{14}H_{15}ClN_{25}$	$C_{32}H_{64}Cl_4Mg_5N_4O_6$
Mol. Weight / g mol^{-1}	260.38	246.73	864.22
Temperature / *K*	100(2)	293(2) K	100(2)
Wavelength / Å	0.71073	1.54178	0.71073 Å
Crystal system	Triclinic	Orthorhombic	Monoclinic
Space group	*P*-1	$P2_12_12_1$	$P2_1/n$
a / Å	8.3803(6)	a = 7.5186(3)	a = 11.483(2)
b / Å	10.3708(6)	b = 13.2135(4)	b = 18.8942(15)
c / Å	11.0004(3)	c = 27.5125(13)	c = 21.2253(17)
α / °	115.652(4)	90	90
β / °	99.615(4)	90	100.705(9)
γ / °	101.009(6)	90	90
Volume / Å^3	811.58(8)	2733.26(19)	4525.1(10)
Z	2	8	4
Density / g cm^{-3}	1.066	1.199	1.269
Absorption Coeff. / mm^{-1}	0.074	2.299	0.373
Crystal size / mm^3	0.44 x 0.32 x 0.27	0.53 x 0.44 x 0.12	0.46 x 0.33 x 0.20
Θ range / °	3.38 to 31.70	3.21 to 73.18	3.09 to 30.02°.
Index ranges	$-12 \leq h \leq 12$ $-15 \leq k \leq 15$ $-16 \leq l \leq 15$	$-8 \leq h \leq 8$ $-16 \leq k \leq 15$ $-33 \leq l \leq 29$	$-16 \leq h \leq 16$ $-26 \leq k \leq 26$ $-29 \leq l \leq 29$
Reflections collected	18097	7203	61326
Independent reflections	5425 (R_{int} = 0.0203)	4633 (R_{int} = 0.0381)	12819 (R_{int} = 0.0340)
Completeness	98.6 % (to θ=31.70°)	99.9 % (θ= 67.00°)	99.3 % (θ=25.00°)
Absorption correction	Semi-empirical from equivalents	Gaussian	Semi-empirical from equivalents
Transmission max/min	0.7463 and 0.6809	0.686 and 0.115	0.7460 and 0.6558
Data/restraints/param.	5425 / 0 / 179	4633 / 0 / 308	12819 / 21 / 499
Goodness-of-fit on F^2	1.086	1.039	1.108
Final *R* indices [I > 2 s (I)]	*R*1 = 0.0341 w*R*2 = 0.0892	*R*1 = 0.0688 w*R*2 = 0.1710	*R*1 = 0.0401 w*R*2 = 0.0820
R indices (all data)	*R*1 = 0.0409 w*R*2 = 0.0952	*R*1 = 0.0756 w*R*2 = 0.1841	*R*1 = 0.0612 w*R*2 = 0.0928
Larg. diff. peak/hole / eÅ^{-3}	0.388 and -0.181	1.187 and -0.260	0.934 and -0.527

9. References

[1] (a) Hoye, T. R.; Eklov, B. M.; Voloshin, M. *Org. Lett.* **2004,** *6*, 2567-2570. (b) Love, B. E.; Jones, E. G. *J. Org. Chem.* **1999**, *64*, 3755-3756.

[2] Duisenberg, A. J. M.; Kroon-Batenburg, L. M. J.; Schreurs, A. M. M. *J. Appl. Crystallogr.* **2003**, *36*, 220-229.

[3] Blessing, R. H. *Acta Crystallogr.*, *Sect. A* **1995**, *51*, 33-38.

[4] *Crysalis PRO*, Agilent Technologies, release 1.171.37.31, **2014**.

[5] *SHELX*, Sheldrick, G. M. *Acta Crystallogr.*, *Sect. A* **2008**, *64*, 112-122.