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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Palladium-Catalyzed Triazolopyridine Synthesis: Synthesis of 7-Chloro-3-(2-Chlorophenyl)-1,2,4-Triazolo[4,3-a]Pyridine
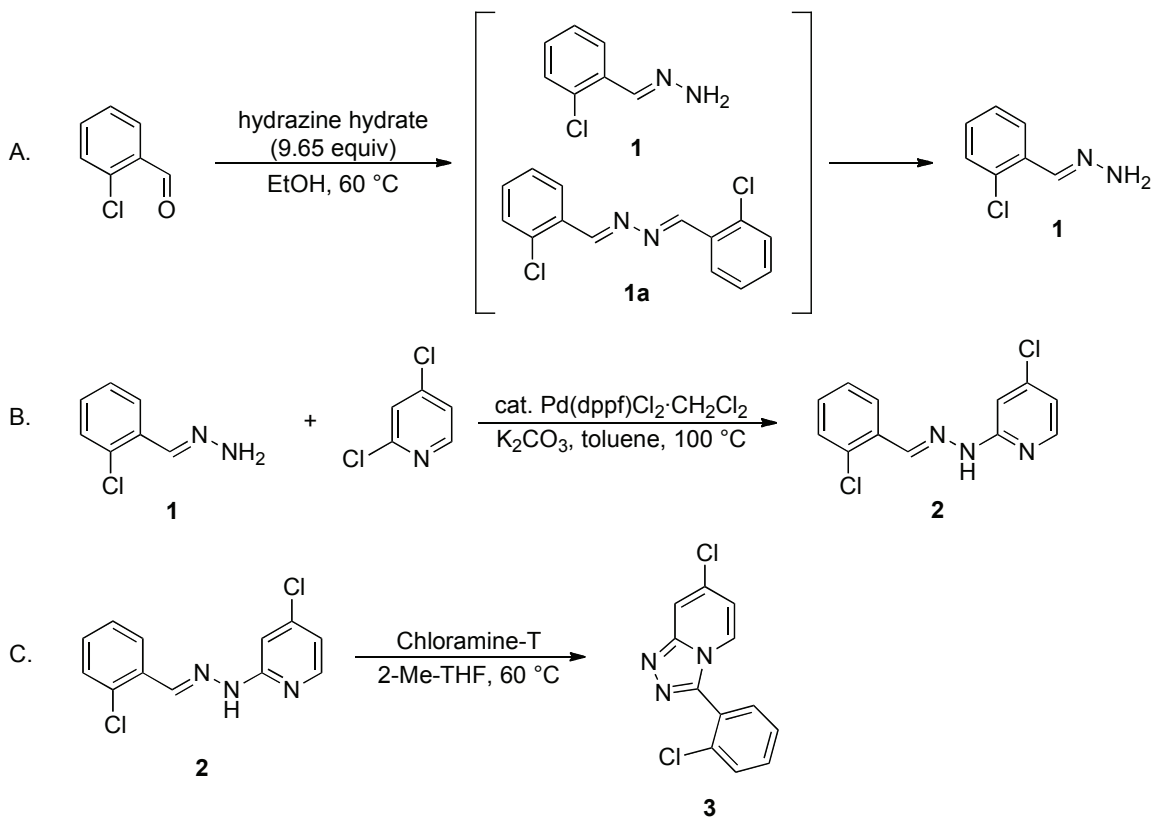
Submitted by Oliver R. Thiel and Michal M. Achmatowicz.[1]
Checked by Songchuan Tian and Dawei Ma.

Chloramine-T is thermally unstable and heating of chloramines-T beyond the temperature disclosed in this procedure should not be conducted without further safety evaluation. Hydrazine should be handled in a fume hood as it is an animal carcinogen and has been identified it as a potential human carcinogen. In addition, anhydrous hydrazine is potentially explosive, especially in contact with metals, and should only be handled as its hydrate.

1. Procedure

A. *(E)-(2-Chlorobenzylidene)hydrazine (1)*. A 1000-mL 3-necked, round-bottomed flask (24/40 joints) equipped with an overhead mechanical stirrer (Teflon paddle, 6 × 2 × 0.2 cm), water-cooled reflux condenser with

nitrogen inlet and a rubber septum with temperature probe is evacuated and refilled with nitrogen. Hydrazine hydrate ($H_2NNH_2·1.5H_2O$) (100 mL, 1.75 mol, 6.8 equiv) (Notes 1 and 2) and ethanol (105 mL) (Note 3) are charged and efficient stirring is established (Note 4). 2-Chlorobenzaldehyde (36.8 g, 0.259 mol, 1.00 equiv) (Note 5) is added using a 60 mL disposable syringe (Note 6) and the mixture (Note 7) is heated with a heating mantle to an internal temperature of 60 °C. The mixture is heated until a colorless solution is obtained (1 h) (Note 8) at which point complete transformation can be ascertained by ^{1}H NMR analysis (Note 9). The reaction mixture is cooled to room temperature, transferred into a 500-mL round-bottomed flask (24/40 joint) and concentrated by rotary evaporation (Note 10) until approx. 100 g of the distillate is removed (Note 11). The resulting biphasic mixture is transferred into a 500 mL separatory funnel. The product is extracted using two portions of methyl *tert*-butyl ether (0.10 L, 0.05 L) (Note 12). The aqueous residue is discarded (Note 13). The combined organic extracts (Note 14) are transferred into a 500-mL round-bottomed flask (24/40 joint) and concentrated using rotary evaporation (Note 15) to dryness. The resulting liquid is further vacuum-dried (Note 16) for 16 h to afford **1** as a colorless to white solid (Note 17) (41.3–42.1 g, > 99% (Note 18).

B. *(E)-4-Chloro-2-(2-(2-chlorobenzylidene)hydrazinyl)pyridine (2)*. A 1000-mL 3-necked, round-bottomed flask (2 × 24/40 side joints, 1 × 29/42 middle joint) equipped with an overhead mechanical stirrer (Teflon paddle, 8 × 2 × 0.2 cm), water-cooled reflux condenser with nitrogen inlet and a rubber septum with temperature probe is evacuated and refilled with nitrogen. (*E*)-(2-Chlorobenzylidene)hydrazine (**1**) (37.3 g, 0.241 mol, 1.00 equiv), toluene (300 mL) (Note 19), and potassium carbonate (50.3 g, 0.357 mol, 1.48 equiv) (Note 20) are charged and efficient stirring is established (Note 21). 2,4-Dichloropyridine (36.0 g, 0.243 mol, 1.01 equiv) (Note 22) is added (Note 23) and the resulting suspension is deoxygenated by performing vacuum-nitrogen refill (three cycles). $Pd(dppf)Cl_2·CH_2Cl_2$ (0.946 g, 1.16 mmol, 0.05 equiv) (Note 24) is pre-weighed in a 8 mL glass vial equipped with a septum-cap and flushed with nitrogen. The contents of the vial are rapidly transferred into the 1000-mL flask against a gentle positive nitrogen flow (Note 25) and the addition neck is sealed with a rubber septum (Note 26). The mixture (Note 27) is heated with a heating mantle to an internal temperature of 100 °C (Note 28) for 20-22 h, at which time the reaction mixture is sampled for analysis by ^{1}H NMR (Note 29). The reaction mixture is cooled to room temperature. Water (150 mL) is added

and the resulting mixture is stirred (Note 30) for at least 1 h at ambient temperature. The suspension is transferred onto an 800 mL sintered-glass funnel (medium porosity) connected to a 1000 mL suction flask. The filter cake is sequentially triturated on the filter with water (150 mL) and toluene (300 mL in two portions) (Note 31). The wet cake is air-dried overnight (Note 32) to afford crude **2** as fine off-white to yellow needles (61.4 g). The crude product is charged into a 500-mL 3-necked, round-bottomed flask (24/40 joints) equipped with an overhead mechanical stirrer (Teflon paddle, 6 × 2 × 0.2 cm), water-cooled reflux condenser with nitrogen inlet and a rubber septum with temperature probe. DMSO (0.16 L) (Note 33) is added, efficient stirring is established (Note 34), and the headspace is purged with nitrogen. The suspension is heated to an internal temperature of 80 °C for 1.5 h and then is allowed to cool to room temperature. The stirred mixture is aged for at least 1 h at ambient temperature. The suspension is transferred onto an 800 mL sintered-glass funnel (medium porosity) connected to a 1000 mL suction flask. The filter cake is triturated with DMSO (100 mL) (Note 35) and water (400 mL in two portions). The wet cake is air-dried (Note 32) to afford **2** as fine off-white to yellow needles (53.3–56.4 g, 83–88%) (Note 36).

C. *7-Chloro-3-(2-chlorophenyl)-[1,2,4]triazolo[4,3-a]pyridine (3).* A 1000-mL 3-necked, round-bottomed flask (24/40 joints) equipped with an overhead mechanical stirrer (Teflon paddle, 6 × 2 × 0.2 cm), water-cooled reflux condenser with nitrogen inlet and a rubber septum with temperature probe is evacuated and refilled with nitrogen (three cycles). (*E*)-4-Chloro-2-(2-(2-chlorobenzylidene)hydrazinyl)pyridine (**2**) (20.0 g, 0.075 mol, 1.00 equiv) and 2-methyltetrahydrofuran (200 mL) (Note 37) are charged, and efficient stirring is established (Note 38). Chloramine-T trihydrate (25.4 g, 0.090 mol, 1.20 equiv) (Note 39) is added and the mixture is heated with an oil bath to an internal temperature of 60 °C (Note 40). The mixture is heated for 2 h, at which time it is sampled for analysis by TLC (Note 41). Upon complete conversion of starting material the reaction mixture is cooled to room temperature. The reflux condenser is swapped for a 125 mL addition funnel. Sodium sulfite (10.0 g, 0.079 mol, 1.05 equiv) (Note 42) and water (90 mL) are added to a 250 mL Erlenmeyer flask and complete dissolution of the solids is achieved. The aqueous sodium sulfite solution is added via addition funnel to the reaction mixture over 10 min, while maintaining an internal temperature of 15–25 °C (Note 43). The mixture is stirred for at least 10 min and stirring rate is increased to aid in dissolution of solids from

the walls of the flask (Note 44). The reaction mixture is transferred to a 1000 mL separation funnel. The reaction flask is rinsed twice with 2-methyltetrahydrofuran (200 mL each) and the rinse is transferred to the separatory funnel (Note 45). The phases are split and the bottom aqueous layer is drained (Note 46). The organic phase is washed twice with aqueous 1 M NaOH (100 mL each) (Notes 46 and 47). The organic phase is washed with aqueous 5 M sodium chloride solution (100 mL) (Note 48). The solution is then transferred to a nitrogen-blanketed 1000 mL 3-necked, round-bottomed flask (24/40 joints) equipped with an overhead mechanical stirrer (Teflon paddle, $6 \times 2 \times 0.2$ cm), water-cooled reflux condenser with nitrogen inlet and a rubber septum with temperature probe. Darco G 60 (100 mesh powder) (4.0 g) (Note 49) is added and the mixture is heated with efficient stirring (Note 50) in an oil bath to an internal temperature of 60 °C for 12–14 h (Note 40). The mixture is cooled to room temperature and vacuum-filtered into a 1000-mL 3-necked, round-bottomed flask (24/40 joints) (Note 51) through a 150 mL sintered-glass funnel (medium porosity), packed with Celite 521 (15 g) (Note 52). The flask is equipped with an overhead mechanical stirrer (Teflon paddle, $6 \times 2 \times 0.2$ cm), water-cooled distillation head with 1000 mL receiving flask and a 250 mL addition funnel with nitrogen-inlet. Distillation is performed under efficient stirring in an oil bath heated to 100–105 °C (Note 53). Solvent is removed until the premarked 120 mL solvent line is reached (Note 51), upon which the reaction mixture is cooled to room temperature. Crystallization of the target compound is observed. The mixture is aged for at least 1 h at room temperature and then heptane (300 mL) (Note 54) is added via addition funnel over 90 min. The mixture is stirred for at least 1 h and then the product is collected by vacuum filtration. The filter cake is rinsed with a mixture of heptane/2-methyltetrahydrofuran (3:1 v/v, 2 portions of 50 mL). The solids are air-dried to afford analytically pure **3** as a yellow solid (17.4–18.0 g, 87–90%) (Note 55).

2. Notes

1.   Hydrazine hydrate ($H_2NNH_2 \cdot 1.5H_2O$, 85%) was purchased from Lingfeng Shanghai by the checkers and used as received. The submitters purchased hydrazine hydrate ($H_2NNH_2 \cdot 1.5H_2O$, 50-60%) from Aldrich and it was used as received.

2.   Use of excess hydrazine hydrate is required to ensure selective formation of mono-hydrazone **1**.

3.   Ethanol (≥99.5%) was purchased from Zhenxing Shanghai and used as received.

4.   The stirring was set to 400 rpm.

5.   2-Chlorobenzaldehyde (97%) was purchased from Alfa by the checkers and used as received. 2-Chlorobenzaldehyde (99%) was purchased by the submitters from Acros and used as received

6.   Addition is mildly exothermic. Adiabatic temperature increase from 20 °C to 32 °C was observed.

7. The reaction mixture was a colorless to pale yellow solution with a small amount of yellow precipitate (bis-hydrazone **1a**).

8.   During the warming up period the bis-hydrazone **1a** dissolved and the reaction mixture became a yellow solution. Complete decolorization was observed as the yellow colored bis-hydrazone gradually converted into the colorless mono-hydrazone **1** at 60 °C.

9.   Approx. 0.1 mL sample of the reaction mixture was diluted with 0.6 mL of d_6-DMSO. Typically nearly pure mono-hydrazone **1** is observed, no bis-hydrazone **1a** is detected.

10. Bath was set to 50 °C and distillation was carried out at 30-60 mmHg.

11. During the distillation product **1** separated as a liquid resulting in a milky emulsion.

12. Methyl *tert*-butyl ether (99.9%) was purchased from Aldrich and used as received.

13. The extracted aqueous layer consists predominantly of hydrazine hydrate and should be treated appropriately. *Combining with waste containing heavy metal impurities must be avoided.* Dilution with copious amount of water prior disposal is advised.

14. Combined MTBE extracts (150 g) were colorless and opalescent.

15. Bath was set to 50 °C and distillation was carried out at 40–300 mmHg.

16. Room temperature, 2 mmHg.

17. Neat product is typically a supercooled yellowish liquid. Brief cooling of the flask results in a rapid crystallization affording a waxy solid.

18. Yield is calculated on the basis of 97% purity of the starting aldehyde. Analytical data for compound **1**: mp 35.5–36.0 °C (neat); IR 3392, 3199, 1594, 1472, 1441, 1391, 1215, 1127, 1048, 1032, 914, 753, 707,

629 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.22–7.31 (m, 4 H), 7.40 (dd, J = 7.8, 1.6 Hz, 1 H), 7.83 (dd, J = 7.7, 1.9 Hz, 1 H), 8.06 (s, 1 H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 125.4, 127.1, 128.4, 129.5, 130.6, 133.1, 133.5; HRMS (m/z): [M+H$^+$] calcd for C$_7$H$_8$ClN$_2$$^+$: 155.03705; Found 155.03738. The crude product was utilized directly in the next step without further purification.

19. Toluene (99.8%) was purchased from Tianlian Shanghai and used as received.

20. Potassium carbonate (98%) was purchased from Sinopharm Chemical reagent and used as received.

21. The stirring was set to 400 rpm.

22. 2,4-Dichloropyridine (99%) was purchased from Energy Shanghai by the checkers and used as received. 2,4-Dichloropyridine (99%) was purchased by the submitters from Oakwood and used as received.

23. Minor bubbling was observed immediately following 2,4-dichloropyridine charge.

24. Pd(dppf)Cl$_2$·CH$_2$Cl$_2$ was purchased from Aldrich by the checkers and used as received. Pd(dppf)Cl$_2$·CH$_2$Cl$_2$ was purchased from Strem by the submitters and used as received.

25. With the addition neck capped the nitrogen flow was set to high using bubbler as an indicator. The cap was removed and the nitrogen flow was adjusted as necessary to maintain minimal nitrogen flow through the bubbler.

26. Nitrogen pressure was adjusted to maintain a visible flow through the bubbler (approx. 1 bubble per sec.).

27. Orange-pink suspension of K$_2$CO$_3$ and pre-catalyst.

28. Upon reaching approximately 30 °C the suspension rapidly changed color from orange-pink to yellow. Gradual thickening of the suspension was observed as the reaction progresses. Gradual precipitation of palladium black was occasionally observed.

29. Approx. 0.1 mL sample of the supernatant was diluted with 0.6 mL of d$_6$-DMSO. The conversion was calculated by comparing the integration of diagnostic signals of 2,4-dichloropyridine (7.78 ppm, d, 1H) and/or **1** (8.02 ppm, s, 1H) with the integration of toluene signal at (2.30 ppm, s, 3H). Typical conversion is ≥90%.

30. Efficient stirring (400-600 rpm) facilitates dissolution of inorganic by-products in the aqueous layer. Fine uniform suspension was obtained.

31. Combined filtrates consisting of dark-orange organic layer and colorless aqueous layer were discarded.

32. Ambient air was passed through the wet cake overnight.

33. DMSO ($\geq$99%) was purchased from J&K and used as received.

34. The stirring was set to 250-450 rpm.

35. The dark supernatant was allowed to fully drain using suction before DMSO wash was introduced on the filter. The suction was cut-off and the filtercake was triturated with DMSO using spatula and again fully drained using suction.

36. Analytical data for compound **2**: mp 250–251 °C (DMSO); IR 1582, 1431, 849, 750, 704 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6, 80 °C) δ: 6.88–6.89 (m, 1 H), 7.28 (s, 1 H), 7.35–7.41 (m, 2 H), 7.48 (d, J = 7.3 Hz, 1 H), 8.08 (d, J = 7.7 Hz, 1 H), 8.11 (d, J = 5.1 Hz, 1 H), 8.43 (s, 1 H), 11.42 (s, 1 H); ^{13}C NMR (100 MHz, DMSO-d_6, 80 °C) δ: 105.1, 114.6, 125.8, 126.8, 129.1, 129.5, 131.3, 131.5, 135.4, 143.5, 148.8, 157.3; HRMS (*m/z*): [M+H$^+$] calcd for $C_{12}H_{10}Cl_2N_3^+$: 266.02463; Found 266.02474.

37. 2-Methyltetrahydrofuran (98%) was purchased from Aldrich and used as received.

38. The stirring was set to 300 rpm and an off-white to grey slurry formed.

39. Chloramine-T trihydrate (ACS reagent, 98%) was purchased from Alfa by the checkers and used as received. Chloramine-T trihydrate (ACS reagent, 98%) was purchased by the submitters from Aldrich or Acros and used as received.

40. The internal temperature was maintained in a range from 55 to 65 °C.

41. The reaction was monitored via TLC using the following method: The R_f values are 0.66 (EtOAc/petroleum ether=1/4) for product and 0.4 (EtOAc/petroleum ether=1/1) for starting material. The submitters monitored the reaction by HPLC by the following method: column: XBridge C18, 100x3 mm, 3.5 11m; flow rate: 0.8 mL/min; solvent A: 0.1% trifluoroacetic acid in water; Solvent B: 0.1% trifluoroacetic acid in acetonitrile; gradient: 5% B to 100% B over 12 min; wavelength: 235 nm; Retention times: **(2):** 6.28 min; **(3):** 6.12 min; Chloramine-**T:** 6.45 min; toluenesulfonamide: 4.34 min.

42. Sodium sulfite (ACS reagent, $\geq$98.0%) was purchased from Aldrich and used as received.

43. The addition is mildly exothermic; an ice-bath may be used to control the temperature.

44. The stirring was set to 600 rpm and a homogenous biphasic mixture was obtained.

45. The additional amount of solvent was required to avoid supersaturation and crystallization of the product during aqueous work-up and charcoal-treatment.

46. A small amount of rag layer was removed with the aqueous layer.

47. The 1M sodium hydroxide solution was prepared by dissolution of sodium hydroxide (Sinopharm Chemical reagent, 40 g) in water (1 L).

48. The 5M sodium chloride solution was prepared by dissolution of sodium chloride (Sinopharm Chemical reagent, 292 g) in water (1 L)

49. Darco G 60 (10 mesh) was purchased from Aldrich and used as received.

50. Stirring was set a 400 rpm.

51. 2-Methyltetrahydrofuran (120 mL) was added to the flask and the solvent line was marked with a pen. This line was used as reference mark during the distillation. Subsequently the flask is emptied.

52. Celite 521 was purchased from Sinopharm Chemical reagent and used as received.

53. Depending on solvent loss during vacuum filtration and efficiency of distillate condensation solvent amounts between 460 and 580 mL were collected.

54. Heptane (Chromasolv, $\geqslant$99.0%) was purchased from Tianlian Shanghai and used as received.

55. mp 140–142 °C (MeTHF/heptane); IR 1630, 1522, 1435, 1371, 1257, 1051, 982, 936, 864, 747, 714 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 6.85 (d, J = 7.2 Hz, 1 H), 7.49–7.51 (m, 1 H), 7.56–7.61 (m, 2 H), 7.68 (d, J = 7.6, 1 H), 7.75 (d, J = 7.4, 1 H), 7.85 (s, 1 H). ^{13}C NMR (101 MHz, CDCl$_3$) δ: 115.1, 115.9, 124.0, 125.4, 127.6, 130.3, 132.3, 133.3, 134.0, 134.3, 145.2, 150.2; HRMS (m/z): [M+H$^+$] calcd for (C$_{12}$H$_8$Cl$_2$N$_3$): 264.0090; Found 264.0100. Anal. Calcd. for C$_{12}$H$_7$Cl$_2$N$_3$: C, 54.57; H, 2.67; N, 15.91. Found: C, 54.57; H, 2.71; N, 15.87.

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3. Discussion

Triazolopyridines constitute an important class of heteroaromatic compounds. The [1,2,4]triazolo[4,3-*a*]pyridine moiety[2] can be found in a variety of biologically active compounds, including antibacterial, antithrombotic, antiinflammatory, antiproliferative, and herbicidal agents.[3] Traditional approaches to this class of compounds rely on oxidative or dehydrative cyclizations of a linear precursor.[2] These intermediates are usually obtained through reaction of 2-hydrazinopyridines with aldehydes or acid chlorides. Depending on the underlying heterocyclic core the access to the required 2-hydrazinopyridines can be challenging.

To overcome this issue we recently described a palladium-catalyzed coupling reaction of 2-chloropyridines with aldehyde derived hydrazones (Scheme 1).[4] Aldehyde-derived mono-hydrazones can be obtained in a straightforward fashion by the reaction with an excess of hydrazine.[5] The initial mixture of kinetically favored bis-hydrazone and mono-hydrazone can be readily equilibrated in the presence of an excess of hydrazine to afford the desired mono-hydrazone in nearly quantitative yields. The reaction system for the coupling is very simple and the catalyst Pd(dppf)Cl$_2$ is stable and readily available. Procedurally the reaction is simple and the products can be isolated by direct filtration at the end of the reaction. The oxidative cyclization step makes use of Chloramine-T as a clean oxidant.[6] The isolation involves a simple basic aqueous work-up to remove the toluene-sulfonamide byproduct and a charcoal treatment to remove colored trace-impurities. Crystallization is achieved from 2-methyltetrahydrofuran and heptane.
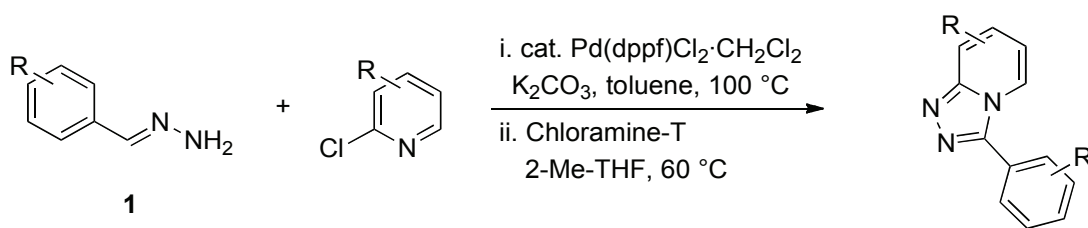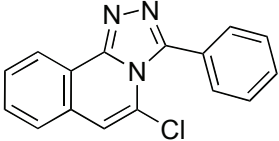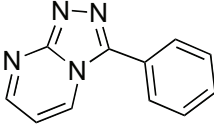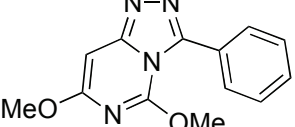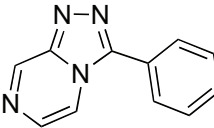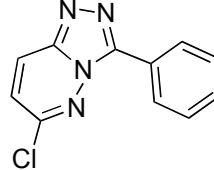
Scheme 1. Synthesis of triazolopyridines.

The reaction has a broad scope with regards to the pyridine and aldehyde component (Table 1). Additional examples have been disclosed in the original communication.[4] Satisfyingly the reaction is also suitable for other chloroazines, with a partial scope shown in Table 2, with additional examples in the original manuscript.[4]

Table 1. Synthesis of triazolopyridines.

Entry	Product	Yield % - Step 2	Yield % - Step 3
1		89	91
2		85	83
3		84	75
4		42	95
5		58	93

Table 2. Synthesis of related heterocycles.

Entry	Product	Yield % - Step 2	Yield % - Step 3
1		81	69
2		63	99
3		90	79
4		87	75
5		79	82

The compound prepared in this procedure can be a useful building block for further functionalization. This was demonstrated by conducting a second metal-catalyzed coupling reaction on the more activated chloride substituent. Both palladium-catalyzed Suzuki-coupling[7] and iron-catalyzed coupling with a Grignard-reagent[8] afforded the desired products in good yields (Scheme 2).
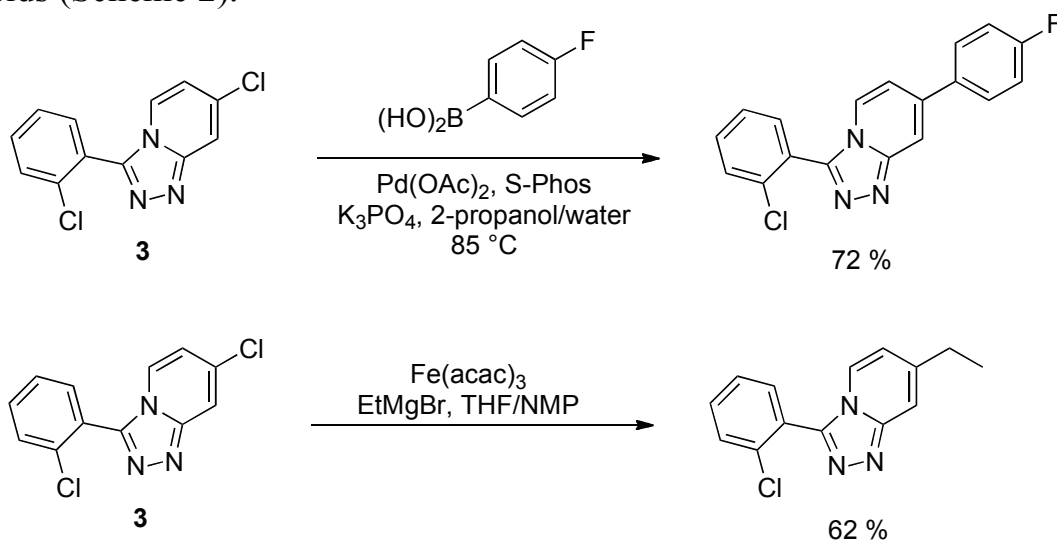
Scheme 2. Further functionalization by metal-mediated coupling reactions.

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Appendix
Chemical Abstracts Nomenclature; (Registry Number)

Hydrazine hydrate; (10217-52-4)
Benzaldehyde, 2-chloro-; (35913-09-8)
Benzaldehyde, 2-chloro-, hydrazone; (52372-78-8)
Potassium carbonate; (584-08-7)

Pyridine, 2,4-dichloro; (26452-80-2)

Dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium (II) dichloromethane adduct; (72287-26-4)

Benzaldehyde, 2-chloro-: 2-(4-chloro-2-pyridinyl)hydrazone; (1258542-95-8)

2-Methyltetrahydrofuran: Furan, tetrahydro-2-methyl-; (96-47-9)

Chloramine-T trihydrate: Benzenesulfonamide, N-chloro-4-methyl-, sodium salt, hydrate (1:1:3); (7080-50-4)

Sodium sulfite; (7757-83-7)

1,2,4-Triazolo[4,3-a]pyridine, 7-chloro-3-(2-chlorophenyl)-; (1019918-88-7)

Oliver R. Thiel studied chemistry at the Technical University Munich, Germany, and completed a Diploma thesis on rhodium-catalyzed hydroaminations under supervision of Professor Matthias Beller. He then pursued a Ph.D. (1998-2001) at the Max-Planck-Institut für Kohlenforschung Mülheim, Germany, under guidance of Professor Alois Fürstner, exploring RCM-reactions in natural product synthesis. After a postdoctoral appointment (2001-2003) at Stanford University with Professor Barry M. Trost, Oliver joined the Chemical Process Research & Development department at Amgen in Thousand Oaks, where he has been involved in the development of synthetic processes of numerous clinical candidates.

Michal Achmatowicz received his undergraduate education at the University of Warsaw, Poland where he completed his undergraduate thesis in chemistry in 1997. He then joined Prof. Janusz Jurczak's research group at the Institute of Organic Chemistry of Polish Academy of Sciences in Warsaw to pursue his Ph.D. in organic chemistry. From 2001 to 2003 he was a postdoctoral research fellow with Prof. Louis S. Hegedus at the Colorado State University. Subsequently he joined the Chemical Process Research and Development group at Amgen in Thousand Oaks, California, where he has been developing robust processes toward active pharmaceutical ingredients, co-authoring several publications, and enjoying rock-climbing in the spare time.
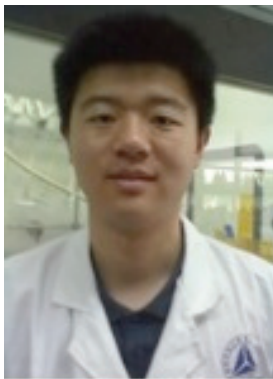
Songchuan Tian received his undergraduate education in China Pharmaceutical University, China where he completed his undergraduate thesis in traditional medicine in 2007. He then pursued a Ph. D. in organic chemistry (2007-2012) in Prof. Dawei Ma's research group at Shanghai Institute of Organic Chemistry of Chinese Academy of Sciences in Shanghai. Now he is an assistant researcher in Prof. Ma's group.
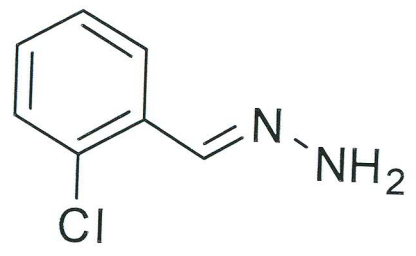
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2.530

4.07

1.00 1.01 1.03

8 7 6 5 4 3 2 1 PPM

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					Nuts - $2007163_-1.1

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129.486
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127.079
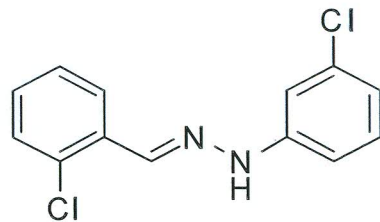125.431

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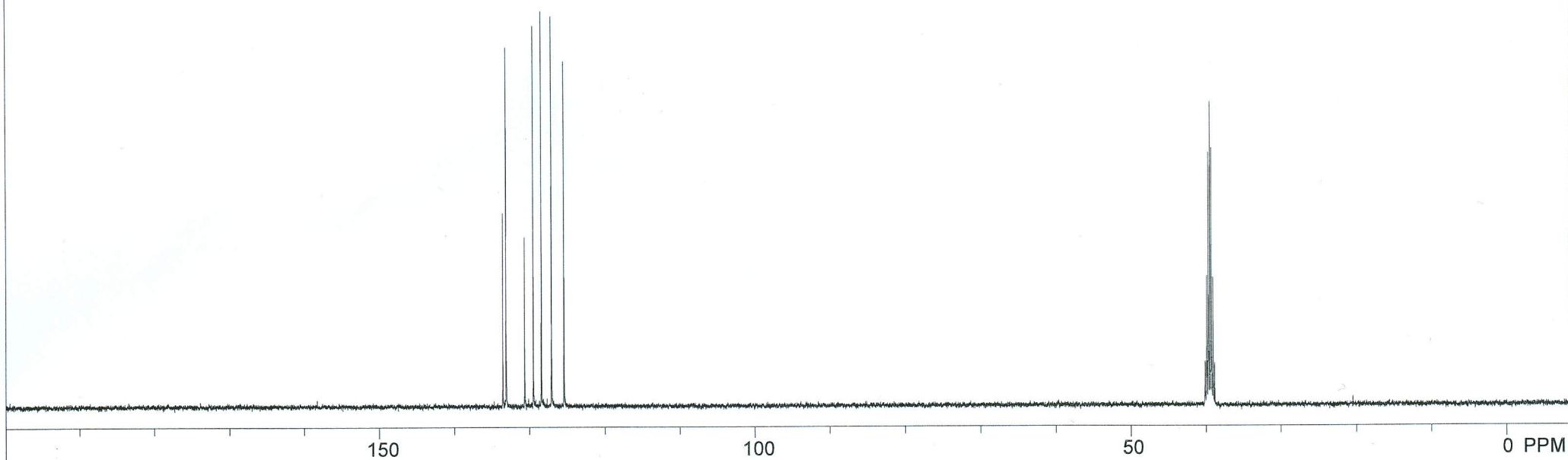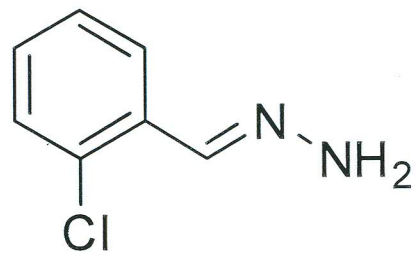
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8.119 8.105 8.100 8.087 8.082 7.495 8.435 7.491 7.478 7.473 7.412 7.397 7.393 7.384 7.378 7.365 7.360 7.347 7.342 7.294 7.289 6.895 6.890 6.882 6.877

11.420

3.330

2.507 2.503 2.498

1.505

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0.87

1.00 2.01 1.03 .08 2.11 0.99

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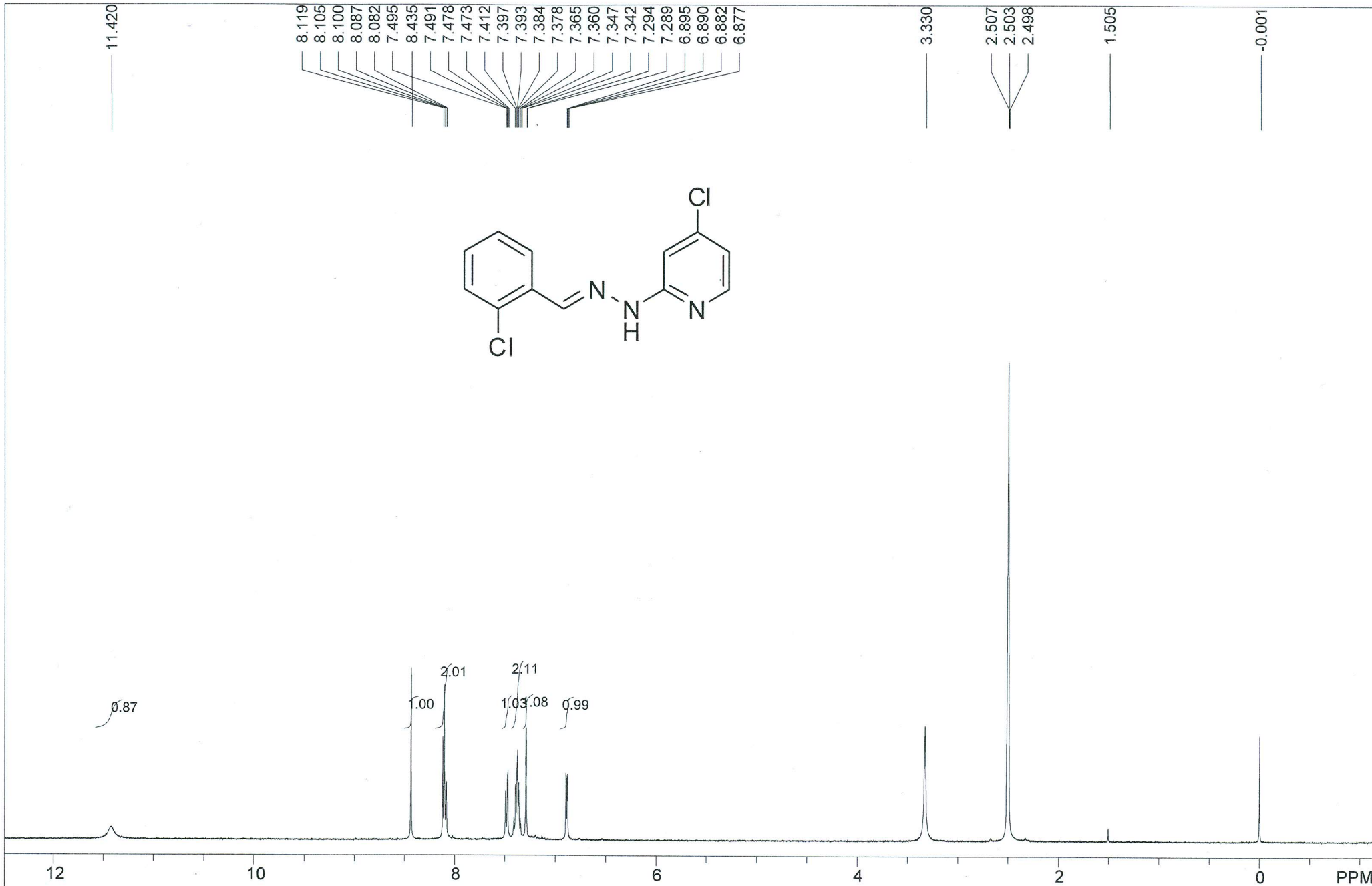
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131.479
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129.066
126.813
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114.573
105.053

39.428
39.212
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150

100

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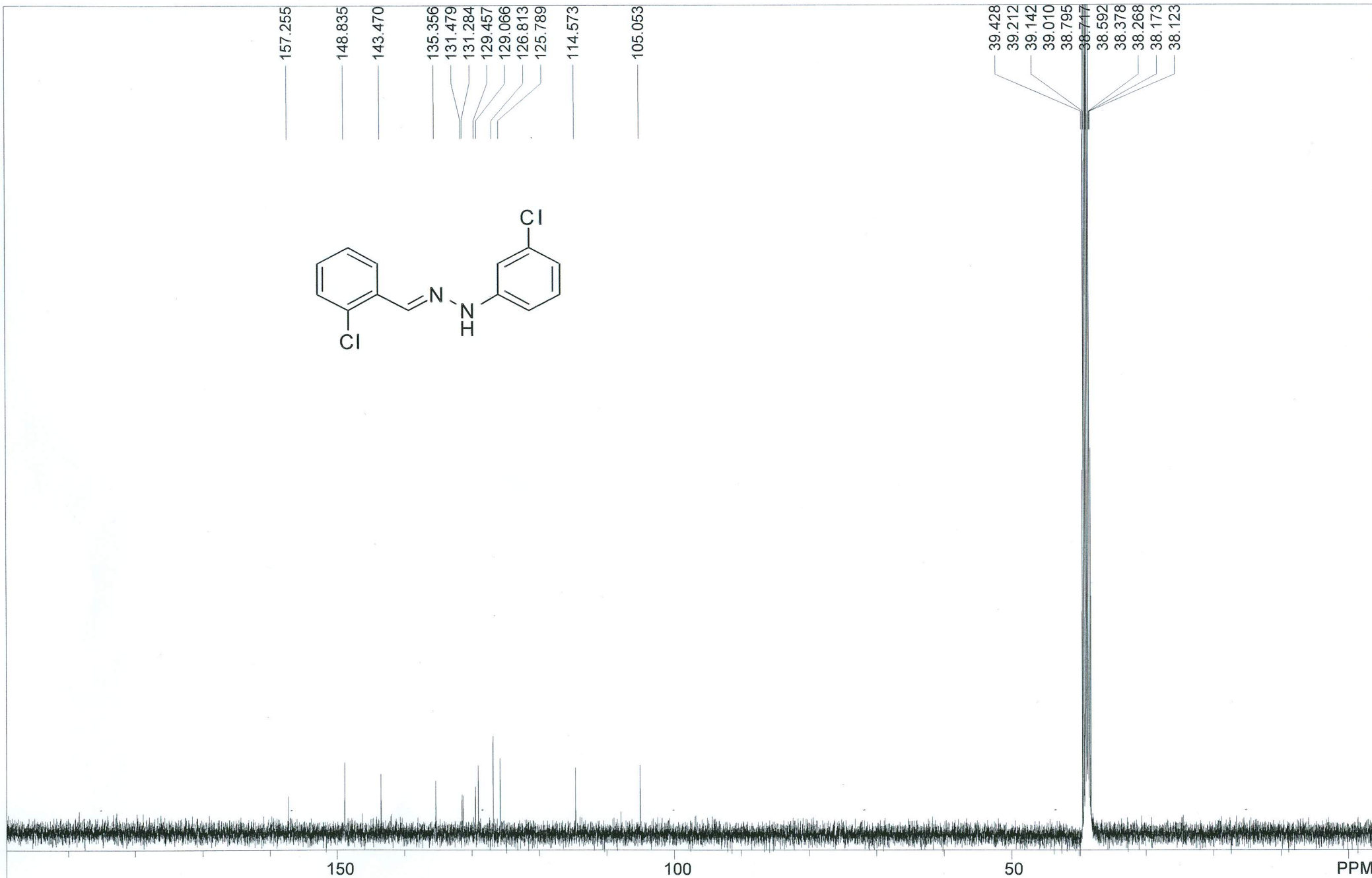
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130.256
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115.116

77.407
77.094
76.773

150   100   50   0   PPM